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Magnitude and Associated Factors of Chewing Khat During Pregnancy and its Impact on Maternal, Pregnancy and Neonatal Outcomes in Eastern Ethiopia, 2022: Cross Sectional, Prospective Cohort and Histopathologic Study.

PhD Dissertation

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Declaration

I hereby declare that this dissertation "**Magnitude and Associated Factors of Chewing Khat During Pregnancy and its Impact on Maternal, Pregnancy and Neonatal Outcomes in Eastern Ethiopia, 2022: Cross Sectional, Prospective Cohort and Histopathologic Study.**" is my original work and that all sources of materials used for this dissertation have been duly acknowledged. This work has not been submitted and presented to any other university for achieving any academic degree or diploma awards.

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Abstract

Introduction: Less is established about the maternal and fetal effects of chewing khat during gestation and hence, it is problematic to elaborate a robust evidence base on its effects. So far, a few reports exist which demonstrate the relationship between khat chewing and a few birth outcomes. In addition, these limited studies did not perform mediation analysis to explain how khat chewing affected the reported birth outcomes. Therefore, the present study is the first to demonstrate a model that clarifies how selected variables mediate the relationship between khat chewing during gestation and pregnancy outcomes, providing an explanation for how khat chewing during gestation can affect pregnancy outcomes. Additionally, to date there exists no attempt to demonstrate the effects of chewing khat during gestation on maternal, pregnancy and neonatal outcomes in a prospective cohort study design. More importantly, there exists no pervious attempt to demonstrate the effects of chewing khat during gestation on placenta and umbilical cord in histopathologic study approach.

Objectives: The aim of the present study was to assess the magnitude and associated factors of chewing khat during pregnancy and its impact on maternal, pregnancy and neonatal outcomes in eastern Ethiopia, 2022: A Sequential Mixed Method Study.

Methods: To measure the magnitude of chewing khat**,** a cross-sectional study was conducted on hospital settings in eastern Ethiopia, using 242 randomly selected pregnant mothers, through both quantitative and qualitative methods. Univariable and multivariable binary logistic regression analysis was performed to identify significantly associated factors for khat chewing during pregnancy. To measure the effect of khat chewing on maternal, pregnancy and neonatal outcomes, a prospective cohort study was conducted in hospitals setting. Both the exposures and outcomes data were collected prospectively using ultrasound, anthropometric, blood and clinical measurements and interviewers administered questionnaires. Data analysis was done using SPSS version 27 and Stata version 16 software. The generalized linear model for the binomial family analysis and survival analysis (cox proportional hazards model) were performed to estimate the relative risk and attributable risk with corresponding 95% CI of chewing khat during pregnancy on selected maternal, pregnancy and neonatal outcomes. The Generalized Structural Equation Modeling analysis was performed using Stata to examine the mediation effect of the possible mediators on selected pregnancy outcomes. In all of the cases statistical significance was declared at *p*-value less than 0.05. Furthermore, to see the effect of khat chewing on placental

and umbilical cord histopathologic changes; 40 randomly selected tissue samples were taken at time of delivery. Then, tissue processing and staining procedures were undertaken for microscopic investigations.

Results: The overall magnitude of chewing khat during pregnancy in the present study was 27.4% (95% CI: 22.2-33.0). Variables which significantly associated with chewing khat during pregnancy were being >=26 years [adjusted odds ratio (AOR)=2.81 95% CI 1.19-6.59], being a rural resident (AOR=2.82 95% CI 1.19-6.69), being illiterate (AOR=4.31 95% CI 1.02-18.20), participants having chewer husbands (AOR=3.51 95% CI 1.33-9.24) and respondents having other chewer family members (AOR=3.05 95% CI 1.19-7.77).

The magnitude of anemia among khat chewer cohorts was 76 (48.7%) (p<0.001). Additionally, the relative risk of developing anemia among khat chewer cohorts was significantly higher (aRR=1.85; 95%CI 1.47-2.33). Moreover, the attributable risk of maternal anemia due to khat chewing was 19.5% (95%CI 8.96-29.93) (p<0.001). The magnitude of gestational hypertension among khat chewers cohorts was 45 (28.8%) (p=0.001. The relative risk of developing gestational hypertension among chewer cohorts was significantly higher (aRR=2.44; 95%CI 1.43-4.18). Moreover, the attributable risk of gestational hypertension due to khat chewing was 14.8% (95%CI 5.95-23.69) (p=0.001). The magnitude of fetal growth restriction (FGR) among khat chewer cohorts was 81 (51.9%). The relative risk of fetal growth restriction among khat chewer cohort mothers was significantly higher (aRR=4.32; 95%CI 2.62-7.12). In the present study the proportion of abruption placenta among khat chewer cohorts was 26 (16.7%). The relative risk of developing abruptio placenta among khat chewer cohorts was higher (aRR=3.18; 95%CI 1.11-9.08). Among the present study cohorts, the magnitude of pre-labor rupture of the membranes among khat chewers was 70 (44.9%). The risk of developing pre-labor rupture of membranes was significantly higher (aRR=7.97; 95%CI 4.49-14.44) among khat chewer cohorts. The magnitude of still birth and observed congenital anomalies in the present study was 4.1% and 5%, respectively. The magnitude of preterm births in the present study among births of khat chewer cohorts was 76 (48.7%). The risk of occurrence of preterm birth was significantly higher among khat chewer study cohorts (aRR=2.19; 95%CI 1.21-3.96). More importantly, in further analysis after adjusting for gestational hypertension and cesarean delivery, the regression coefficient of khat chewing during pregnancy on preterm birth has been decreased in size from path n, β=0.37, p<0.001 to path n', β=0.15, p<0.005. The low birth weight magnitude among

births of khat chewer cohorts was 94 (60.3%). The risk of occurrence of low birth weight among khat chewer cohorts was significantly higher (aRR=4.17; 95%CI 2.11-8.25). The very low birth weight magnitude among births of the present study cohorts was 23 (7.2%). Additionally, in further analysis after adjusting for gestational hypertension, cesarean delivery, preterm birth and maternal anemia, the regression coefficient of khat chewing during pregnancy on low birth weight has been decreased in size from path q, β=0.4, $p<0.001$ to path q', β=0.2, $p<0.001$. Moreover, the magnitude of small for gestational age at birth among the present study cohorts was 100 (31.3%); 84 (53.8%) were among khat chewer cohorts' deliveries. The magnitude of low 1 minute Apgar score (<7scores) was 49 (16%), while the magnitude of low 5-minute Apgar score (<7score) was 23 (7.5%). The proportion of neonatal death in the current analysis was found to be 7.5%. The umbilical cord insertion in the present study cohorts was, central in 230 (71.9%) births, eccentric in 57 (17.8%) births and marginal in 33 (10.3%) births. The mean (SD) placental weight of births of the study cohorts was 490.73±75.00grams, while the mean (SD) placental-to-birth-weight ratio was 19.71±7.35 (range 8.63-49.17).

In the present histopathologic study, the placenta among khat chewers revealed a significantly increased occurrence of placental hypoplasia (85%), syncytial knots (60%), villous hemorrhage/thrombosis (70%), villous hyalinization (50%) and villous calcification (40%) compared to the occurrence among non-chewers placentas. Moreover, in the present histopathologic study of umbilical cord of the two comparison study groups, there were no abnormal findings observed.

Conclusion: In the present study, a relatively higher proportion of mothers chewed khat during their current pregnancy. Being older age, living in rural area, being illiterate, having khat chewer husbands and other family members were statistically significant variables associated with khat chewing during pregnancy.

In the current follow-up study, the level of anemia, gestational hypertension, fetal growth restriction, abruption placenta and pre-labor rupture of the membranes were higher in proportion among khat chewer cohorts as compared to its counterparts. Similarly, the magnitude of preterm birth and low birth weight were higher in proportion among births of khat chewer cohorts. Moreover, the magnitude of small for gestational age at birth was also higher in percentage from births of khat chewer cohorts. More importantly, further analysis of the present study found that the effect of khat chewing during pregnancy on preterm birth was partially mediated by

gestational hypertension and emergency cesarean delivery. In the same way, the effect of khat chewing during gestation on low birth weight was partially mediated by gestational hypertension, emergency cesarean delivery, preterm birth and maternal anemia. The present histopathologic study of the placenta revealed a significant connection between khat chewing during pregnancy and placental hypoplasia, increased syncytial knots, villous hemorrhage/thrombosis, villous hyalinization and villous calcification which in turn is correlated with poor fetal outcomes like fetal growth restriction and low birth weight. Overall, the present study revealed that khat chewing is not only a worry of the current population but also a public health concern of the generation affecting unborn fetuses.

Keywords: Chat/khat chewing, substance use/misuse/abuse, magnitude, prevalence, associated factors, perceived reasons, maternal outcomes, fetal development, pregnancy outcomes, birth outcomes, neonatal outcomes, Ethiopia.

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List of abbreviations

ANC: Ante Natal Care

AOR: Adjusted Odds Ratio

ARR: Adjusted Relative Risk

AR: Attributable Risk

BMI: Body Mass Index

CI: Confidence Interval

COR: Crude Odds Ratio

EDHS: Ethiopia Demographic and Health Survey

FGR: Fetal Growth Restriction

GLM: Generalized Linear Model

GSEM: Generalized Structural Equation Modeling

HH: Household

LMP: Last Menstrual Period

LBW: Low Birth Weight

MVP: Maximum Vertical Pocket

MUAC: Mid-Upper Arm Circumference

NICU: Neonatal Intensive Care Unit

PROM: Pre-labor Rupture of Membranes

PTD: Preterm Delivery

SGA: Small for Gestational Age

SD: Standard deviation

VLBW: Very Low Birth Weight

WHO: World Health Organization

List of publications and manuscripts arising from this dissertation

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Wondemagegn AT, Bekana M, Bekuretsion Y, Afework M. **The effect of possible mediators on the association between chewing khat during pregnancy and fetal growth and newborn size at birth in Eastern Ethiopia. BMC Pregnancy Childbirth. 2024 Jan 13; 24(1):63.** doi: 10.1186/s12884-024-06243-2. PMID: 38218789; PMCID: PMC10787403.

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Amsalu Taye Wondemagegn, Miressa Bekana, Yonas Bekuretsion and Mekbeb Afework. **The histopathologic changes in placenta associated with chewing khat during pregnancy and its correlation with fetal outcomes in eastern Ethiopia: A Comparative Study**. Manuscript.

1. Introduction

1.1 Background

Beginning in the 1960s, the topic of drug or substance usage during pregnancy attracted international attention. The rubella (German measles) outbreak during this time period, as well as the catastrophes brought about by the medications thalidomide and diethylstilbestrol (DES), increased public awareness of the need to safeguard unborn children from the risks connected with drug usage. Preclinical animal research results indicated that thalidomide was safe and mostly utilized as a sedative and an antidote for early pregnancy sickness. However, a 1962 investigation revealed that 10,000 human children had been impacted by an uncommon collection of deformities on human fetuses produced by the medicine thalidomide, most of which were limb malformations (meromelia or amelia)[1].

In addition, in 1970's, several studies had been conducted in the United States[2-4] and revealed the effects of alcohol consumption during pregnancy which includes, growth retardation, central nervous system problems, long term retardation and developmental delays which collectively called the syndrome of fetal alcohol (FAS).

Currently substance use during pregnancy is a public phenomenon. The most consistently studied substance in pregnancy includes tobacco smoking, alcohol drinking, and use of cocaine, opioid, cannabis and other illicit drugs. However, there are less research reports about the substance, khat worldwide in general population and littler is known about khat use during pregnancy worldwide.

Khat (*Catha edulis* Forsk) is an evergreen flowering tree or shrub which grows mainly in East Africa and the Arabian Peninsula. It belongs to the suborder Rosidae and family Celastraceae. *Catha edulis* Forsk, is commonly known as “Chat” in Ethiopia but largely mentioned in the literature as khat. It is perceived economically, spiritually, and socially as the most important plant in many countries of Eastern Africa especially in Ethiopia, Somalia, Kenya and Yemen.
In Ethiopia, khat is cultivated in almost all corner of the country on a commercial bases and exported to other countries, specially to neighboring countries. It is also freely marketed and consumed within the country more significantly in eastern Ethiopia, Harar and Dire Dawa. Based

on existing evidences, chewing of khat in Ethiopia is being usual and increasing at alarming rate with an estimated prevalence ranged from almost 30% to 53%[5-8]. The highest report is in the Harari region[8]. According to 2016 Ethiopia Demographic and Health Survey (EDHS), about 27% of men and 12% of women had khat chewing practice[9]. In almost all of the cases fresh leaves of khat are chewed in Ethiopia. It is widely consumed with sugar and coffee. Now a days khat chewing is practiced worldwide but consumption of khat is more in countries of east Africa and middle east.

Khat encompasses many chemical constituents that could have various effect on the body structures. The main active component of khat accountable for its stimulant effect is a psychoactive alkaloid biochemical known as cathinone [10, 11], which is structurally, functionally, and chemically similar to amphetamine.

Cathinone is an extremely forceful stimulant, which resulted in sympathomimetic and centralized nervous system stimulation and causes release of symptoms like euphoria and hyperactivity following consumption of leaves, which is equivalent to the effect of amphetamine[11]. The results of numerous *in-vivo* and *in-vitro* experiments[12-15] showed that the substance, khat might be considered as a natural amphetamine.

1.2 Problem statement

Antenatal substance use is the most common public health problem[16]. Pregnancy period especially period of organogenesis is sensitive to outside stimuli like tobacco smoking, alcohol drinking, and different drugs and chemicals. According to previous findings, the most commonly utilized substances in pregnancy includes, alcohol drinking, smoking, cocaine use and cannabis use[17, 18]. According to nationwide prevalence surveys carried out in the United States, about 6% of pregnant mothers use illegal drugs, about 9% consume alcohol, and about 16% smoke cigarettes [18]. As a result, more than 380,000 children are exposed to illegal drugs, more than 550,000 to alcohol, and more than a million are exposed to tobacco smoke while their mothers are pregnant. Similar usage patterns have been noted in Europe[19, 20] and Australia[21].

The level of substance use, outside from tobacco smoking, among pregnant mothers in middle- and low-income countries are not well documented. These countries have an overall tobacco use prevalence of about 3%, with some having substantially higher rates of maternal usage—up to 15%[16]. Although most middle- and low-income countries lack statistics on drug use during gestation, the World Health Organization reports that cannabis is the most often used illicit drug globally, with amphetamine-kind stimulants and opiates following closely behind[22]. As a result, women who are of reproductive age are probably going to use them. The scant data available on substance utilization during pregnancy in Africa, most of which comes from South Africa, shows that 3.6% to 8.8% of pregnant mothers use illegal drugs and 19.6% drink alcohol [23]. Methamphetamine and cannabis are the two illegal narcotics that are most frequently used in South Africa[24]. There is limited research evidence of drug use in Ethiopia, especially, during pregnancy. Evidence from both few scientific studies and undocumented sources indicates that khat, one of the stimulant substances, is commonly used in Ethiopia. In addition to adults, youths and pregnant women are widely chewing khat in Ethiopia. According to recent reports, 16.7%[25] of adolescents and 20%[26] of pregnant women in Ethiopia are practicing chewing khat. In addition, a recent study done in eastern Ethiopia showed that 19.6% [27] of pregnant women chew khat. Despite the habit, the perceived reasons for consuming khat during pregnancy have not yet been qualitatively explored.

Antenatal substance use is related with numerous damaging maternal and fetal effects. Alcohol use, smoking, cocaine use, cannabis use and other drug use in pregnancy has been associated

with a range of negative maternal and birth outcomes[2-4, 28, 29]. In same way according to few available animal experimental studies khat use during pregnancy is associated with adverse maternal and fetal outcomes. Studies conducted using experimental animals mainly albino mice and rats to evaluate teratogenic effects of khat extract have been revealed genotoxic potential of the extract[30-33], but no such evidences have been observed in human[34, 35].

Unlike with that of khat, there are ample clinical/human evidence documented which reveal effects of alcohol drinking, tobacco smoke, cocaine and other substances on maternal, embryonic/fetal, birth and neonatal outcomes. There are experimental or preclinical animal studies mainly done in Saudi Arabia that revealed the effects of khat administration during pregnancy on embryonic, fetal, and birth outcomes; however, all of these experimental studies did not try to see neonatal outcomes. Although animal or preclinical studies give useful insights to explain the action of khat, there are main differences in the brain, behavior and physiology of animals and humans that put a limitation in the interpretation of findings from these experimental animals[36, 37]. Thus, clinical evidence is largely needed. Furthermore, there exists few human studies reported regarding the association between khat chewing during pregnancy and low birthweight[38]. But the existing human studies on khat did not report whether chewing khat during pregnancy has association with maternal, fetal, other birth outcomes, neonatal, placental, and umbilical cord outcomes or not. The existing limited human studies available worldwide in general and in Ethiopia in particular, which reported the association between khat chewing during pregnancy and few birth outcomes (mainly low birth weight) is of cross sectional and case control studies in nature which is not suitable to establish temporal relationship unlike that of cohort study. Thus, evidence of existing effects of chewing khat during pregnancy on low birth weight may be highly confounded due to weak design and weak approaches of previous studies to establish temporal relationship. Hence, good-powered, superior controlled studies are lacking. Without such study findings it is difficult to develop a strong evidence base on its effects. Moreover, despite reporting of the relationship between chewing khat and low birth weight using cross sectional and case control data, these studies were not conducted mediation analysis to explain how khat chewing affects low birth weight. Hence, the present study is the first to demonstrate a model by which selected variables (gestational hypertension, maternal anemia, emergency cesarean section delivery and preterm birth) mediate the association between

khat chewing during pregnancy and selected pregnancy outcomes, thereby explaining the mechanism by which khat chewing during pregnancy can influence selected pregnancy outcomes.

Furthermore, there exists no previous study which investigated the relationship between khat consumption during gestation and adverse maternal, fetal, birth, neonatal, placental, and umbilical cord outcomes with a rigorous prospective cohort study design in Ethiopia.

Lastly, there is no previous histopathologic microscopic study on human placenta and umbilical cord of khat chewers and thus, this study is the first in its nature. Thus, the current study could fill many knowledge gaps. Even though khat is consumed in all corners of the country, it is freely chewed by almost every segment of the population including pregnant mothers in eastern parts of Ethiopia. Hence, conducting the current study in this area is more appropriate.

1.3 Significance of the study

Since the present study is the first in its nature the finding will serve as a baseline data on which further human studies will be carried out. In addition, the finding of the present study will enable the policy makers and healthcare planners to have evidence regarding the impacts of chewing khat during pregnancy and thereby to find out solutions for problematic outcomes related to khat chewing during pregnancy. It will also enable for the healthcare providers and the respective maternal and child health unit leaders to have scientific evidence about the impacts of chewing khat during pregnancy on maternal and newborn health which in turn will enable them to provide health education about khat chewing impacts for mothers coming for antenatal care services, delivery services and postnatal care services. The findings of the current study will also enable the respective hospitals leaders, woreda health offices, zonal health departments, regional health offices and the federal ministry of health to have scientific evidence about impacts of chewing during pregnancy on birth outcomes and as well on the generation. Knowing the impact, especially negative impacts will enable them to have an input to design, cascade and implement guidelines and actions on how to minimize or stop the practice of chewing khat during pregnancy.

2. Literature review

As reviewed below, various scientific findings have revealed khat chewing practice during pregnancy and its predictors, as well as the effects of prenatal khat administration on pregnancy and fetal/neonatal outcomes on both human and experimental animals.

2.1 Magnitude and associated factors of chewing khat during pregnancy

According to the Yemen Demographic and Maternal Health Survey (YDMHS), data on 7343 ever-married women shows that about 41% of the women surveyed reported chewing khat while pregnant[39]. This study found that being old, having no education, living in a rural area, living in mountainous areas, and having a low level of wealth were significant risk factors for chewing khat during pregnancy.

A systematic study and meta-analysis found that 20% of Ethiopian pregnant women reported eating khat on average [26]. The following characteristics were associated with khat chewing during gestation in this earlier study: being a Muslim, having less education, having a family history of mental illness, and having previously engaged in khat chewing with a partner. In southern Ethiopia, chewing khat during gestation was also frequent, according to cross-sectional research, with rates of 35.8% [40] and 9.9% [41].

An investigation into the extent of substance use among 510 pregnant women was carried out in eastern Ethiopia using a facility-based cross-sectional research [27]. Researchers discovered that 19.6% of pregnant women chewed khat. According to the study, there is a positive correlation between substance usage before pregnancy, substance use by partners, monthly household income, and substance use by family members and substance use during pregnancy.

2.2 Pregnancy and fetal/neonatal outcomes following administration of khat during pregnancy

An experimental study in Saudi Arabia was conducted using male mice by administering a maximum tolerable dose (500 mg/kg) of an aqueous solution of khat extract orally once daily for five successive days as compared to controls. This study found that khat decreased the

proportion of pregnancy rates and increased the mean post-implantation losses in the treated group[30].

Using the dominant lethal test on albino mice, another experimental investigation conducted in Saudi Arabia likewise demonstrated the mutagenic effect of khat extract on male germ cells. In this study, khat extract also resulted in increased post- implantation loss among treated group compared with control group[31].

An experimental study [32] was done in Saudi Arabia through oral administration of rats with methanolic khat extract between days 6 and 15 of gestation. By day 20, the toxicities to the mother and fetus were assessed using multiple daily doses. This study exposed that khat intake reduced food intake and maternal mass gain as compared to control groups (0-dose groups). Administration of khat produced a significant dose-related increase in fetal loss. This increase in fetal loss following the khat-intake at doses of 125, 250, and 500 mg/kg body weight resulted in 32.7%, 40.7%, and 44.6% loss, respectively, as compared to 5.4% in the control mothers. Khat consumption in utero significantly decreased fetal weight and length (CRL and TL). Intake of the highest dose of khat (500 mg/kg) resulted in anomalies such as cleft lip, club foot, and appendage flexure. In this study, administration of khat resulted in cleft palate, microcephaly, and hydrocephaly; distended renal pelvis and bladder; absence of sternbrae and ribs; malformed premaxilla, maxilla, and clavicle; and unilateral fused and missing ribs.

Another experimental study[33] was also conducted in Saudi Arabia in 2018 and aimed to look into the khat extract's teratogenic and embryotoxic effects. The exposed group received an oral dose of 100 mg/kg of khat extract four days prior to mating and up until day 16 of pregnancy. Overall, the study's findings demonstrated that a sizable portion of the moms who received khat had embryos that were deformed and had different sizes and shapes compared from the mothers in the control group. In this investigation, giving pregnant rats khat caused a extremely significant raise in the average number of resorbed embryos in comparison to the control groups. This, in turn, led to a significant decline in the number of live embryos in the mothers who received khat in comparison to the control group who did not receive khat. The results of this investigation showed that some of the decidua of the resorbed embryos had no discernible

embryonic tissues, and that the embryos themselves looked like a cellular collection in their placenta. In this experiment, the primitive layers of the given embryos were underdeveloped by day eight of pregnancy, but the control embryos demonstrated that all three germ layers had formed, and the differentiation process had begun normally. The control embryos were almost the same size, exhibited a similar normal morphology, and had fully formed somites and neural tubes by day ten of pregnancy. Embryos given khat varied in sizes and shapes, and their somites and neural tubes did not develop. On days 12 and 14 of pregnancy, the control embryo showed signs of normalcy, including closed cervical sinuses and visceral arches, developed tongue and limb buds, particularly noticeable head folds, and typical neural closure. Normal embryonic development also including the heart, liver, gut, mesonephros, brain, lung, and tail buds. Conversely, the embryos of the moms who were given khat showed signs of morphological abnormalities, including varying sizes and forms as well as opening visceral pouches. Based on this study, many of the khat-administered embryos hurt from interrupted neural tubes, undifferentiated brain vesicles and unfinished closure of the brain flexures and loss of recognizable internal organ structures with some of the deciduae had no visible embryonic tissues.

The liver, kidney, brain, spinal cord, spleen, gut, heart, and lung were among the visceral organs that showed adverse effects in the experimental prenatal exposure study of khat in rabbits conducted in New Zealand[42]. Four equal groups of female rabbits were used for the investigation. From day 8 to day 18 of gestation, three groups (low, medium, and high dose groups) received daily doses of 3 mL, 6 mL, and 12 mL of khat extract/kg body weight, respectively. All that was given to the control group was distilled water. Visceral organ histopathological analyses were carried out on all females killed on the 28th day of pregnancy. In addition to mild vacuolar degeneration of some renal tubular epithelium and the presence of atrophied glomeruli, the study reported that the fetus kidney of the administered group showed subcapsular hemorrhages, moderate degenerative changes in renal tubular epithelium, and hemorrhages between renal tubules. The investigation also found that the liver of the administered mother's fetus had hemorrhages, pyknotic clumped nuclei, vacuolar degeneration, necrotic hepatitis, congestion of the hepatic sinusoids and central veins, and hyperplasia of megakaryocytic cells. The study also revealed that khat treatment caused bleeding, edema,

degenerative alterations, swelling, and necrotic changes in certain nerve cells and supporting cells in the brain. Damage to the spinal cord also revealed degeneration of some neurons in the grey matter and nerve fibers in the white matter. The given fetus's heart displayed diffuse cardiac muscle deterioration and epicardial blood vessel congestion. According to the results, the group that received khat exhibited evidence of blood vessel congestion in the alimentary canal and lungs.

Even though, the effects of khat that are teratogenic have been discussed above; existed, human studies of cross-sectional and case-control in nature did not support the finding. For example, a cross sectional facility-based study[35] of 1141 consecutive deliveries at delivery centers in the Yemen found that no difference in rates of stillbirth or congenital anomalies among user and non-user mothers.

One experimental study[43] done in Ethiopia on albino Wistar rats found reduced fetal weight and crown rump length. The study also reported significant decrement in maternal weight gain among khat administered group compared to control group. However, in contrast to the above experimental study's findings, this study did not reveal congenital malformations among khat administered pregnant rats.

On the other hand, besides of animal studies there are also a limited human studies done on prenatal khat exposure impacts which revealed negative outcomes. A cross sectional institution based study [35] conducted using sample size of 1141 in Yemen reported that khat chewing mothers were shown to give birth to more low birth-weight babies than non-khat-chewers (total n=1141).

Another institution based study[44] was conducted in Yemen to see the influences of khat chewing on birthweight on full term newborn using 1181 consecutive deliveries. The results of this study revealed significantly lowered birth weight among khat chewer mothers during pregnancy.

Similarly, a facility based case control study[38] in Ethiopia found that maternal khat chewing during pregnancy have been statistically associated with lower birth weight (birth weight <2500 gm).

Although not controlled for potential confounders in analysis, a case control study[45] done using sample size of 180 (2:1) in Yemen reported various maternal and fetal negative outcomes. In this study, pregnant women who chewed khat showed a statistically significant odds of going into premature labor 6 times more compared to non-chewer, 3.83 times more risk of developing labor induction among chewers. Even though not statistically significant this study found the risk of preeclampsia among chewer were 4.10 times higher than non-chewer, 2.78 times greater for fetal embarrassment and blood transfusion, 2.05 times more for pre-labor rupture of the membrane (PROM), 2.03 times higher for postpartum hemorrhage (PPH), perineal tears, and intrauterine fetal death (IUFD), which is 2.02 times more common. The research found, significant lower mean hemoglobin concentration at delivery when compared with the control. This study also reported chewing khat during pregnancy had resulted in statistically significant risk of 6.56 times higher for breech presentation; 8.94 times higher for low birth weight (<2500 gm); 6.0 times higher for neonatal admission to intensive care unit (ICU) and statistically insignificant risk of 3.54 times higher for perinatal mortality and 2.02 times higher for congenital malformations.

A cross sectional study conducted in Ethiopia reported, 23.5% proportion of PROM and 1.5 times increased risk of khat chewers for PROM as compared to non-khat chewers[46].

3. Objectives of the studies

3.1 General objective

- To assess the magnitude and associated factors of chewing khat during pregnancy and its impact on maternal, pregnancy and neonatal outcomes in eastern Ethiopia, 2022: A Sequential Mixed Method Study.

3.2 Specific objectives

- To calculate the magnitude of khat chewing during pregnancy in the study area.
- To identify factors associated with chewing khat during pregnancy in the study area.
- To explore perceived reasons of chewing khat during pregnancy in the study area.
- To measure the effect of chewing khat during pregnancy on maternal outcomes in the study area.
- To determine the effect of chewing khat during pregnancy on fetal growth status in the study area.
- To examine the effect of chewing khat during pregnancy on the occurrence of stillbirths and live births in the study area.
- To examine the effect of chewing khat during pregnancy on the occurrence of low birth weight, preterm birth, and premature rapture of membrane in the study area.
- To assess the effect of chewing khat during pregnancy on neonatal outcomes in the study area.
- To identify the potential mediators of the association between khat chewing during pregnancy and selected pregnancy outcomes in the study area.
- To examine the effect of chewing khat during pregnancy on the morphological changes in placentas and umbilical cords in the study area.
- To examine the effect of khat chewing during pregnancy on placental and umbilical cord histopathologic changes.

4. Methods and Materials

4.1 Methods and Materials for magnitude and associated factors of chewing khat during pregnancy

4.1.1 Study Design and Study Period

Institution based cross-sectional study was conducted from August 1 to 14, 2022 using both qualitative and quantitative methods of data collection.

4.1.2 Study area

This mixed method study was conducted in selected hospitals of Dire Dawa administration, Harari regional state and Jigjiga city, capital of Somali regional state.

4.1.2.1 Background information of Dire Dawa

Dire Dawa, which is one of the main cities of Ethiopia, is the capital for the Dire Dawa Administration. It is located at 515 kilometers away from the capital, Addis Ababa. Only 2% of the estimated 133,043 hectares that make up the Dire Dawa Administration's total land area are designated as urban areas. Rural Dire Dawa is the term for the remaining 98% of the land. The entirety of Dire Dawa is situated in the Awash River Basin, specifically between latitudes 9027' and 9049'N and longitudes 41038' and 42019'E. Dire Dawa Administration is generally, in the kola climate zone of the country Ethiopia. Therefore, the administration climatic condition is hot throughout the year with minor seasonal variation. It is one of the hottest regions in Ethiopia, with an average annual temperature of about 26^0c. As per 2007 population and housing census conducted by the Central Statistical Agency of Ethiopia (CSA)[47], the total population of the Dire Dawa administration is 342,827 of which 171,930 (50.2%) were men and 170,897 (49.9%) women. Unlike other regions of the country of which the majority is living in rural areas, the majority 67.5% (232,854) lives in urban Dire Dawa while the remaining 109,973 (32.5%) lives in rural Dire Dawa. The bulk of the Dire Dawa resident’s livelihood depends on trade activities including trade of khat. In Dire Dawa administration there are four regional hospital, 10 public health centers, 10 private clinics, and several government and private company clinics, and three NGO clinics.

4.1.2.2 Background information of Harari Region

In terms of both population and land area, Ethiopia's Harari region is the smallest regional state. Harari had a total population of 183,415 as per the 2007 Central Statistical Agency of Ethiopia

(CSA) Census [47], with 92,316 males and 91,099 females. Unlike people in most other regions of Ethiopia, the majority of people in Harari region live in urban areas, 145,000 people (56%), while the remaining 113,000 inhabitants live in rural areas[47]. The region has its capital Harar city, which is 518 kilometers away from Addis Ababa, predominantly inhabited by Muslim religion followers where majority of the people livelihood are depends on trading. Like in another place in Ethiopia, the rural population in Harari mostly depends on rain-fed and small-scale farming. There are four regional hospitals in Harari regional state. The region has an estimated area coverage of 311.25 square kilometers.

4.1.2.3 Background information of Jigjiga city

Jigjiga is one of the woreda in Somali region, Ethiopia which is located 621 kilometers away from Addis Ababa. The elevation of Jigjiga on average is 1935 meters above sea level. As per the 2007 Central Statistical Agency of Ethiopia (CSA) population and housing census[47], Jigjiga has a total residents of 277,560, with 149,292 males and 128,268 females. According to the report, 125,876 or about 45% were urban inhabitants, and 6,956 or about 2.5% were pastoralists. About 99% of the population in the area were Muslim in religion, and about 0.6% were Orthodox Christian. Jigjiga experiences subtropical highland climates. Similar to the remaining highlands of Ethiopia, incredibly lush and wet during the rainy season. Since mornings are often chilly to moderate and afternoons are consistently extremely warm but not hot, the only seasonal variations are related to rainfall. There are two distinct rainy seasons: the primary meher rains, which occur from July to September, and the brief belg rains, which occur between April and June. Due to less cloud cover, the arid period, called bega, is cooler in the morning than the rainy seasons but just as hot in the afternoon due to decreased humidity. There are 6 hospitals, 290 health centers, and 851 health posts in the Somali region.

4.1.3 Population

4.1.3.1 Source Population

Pregnant mothers in Dire Dawa administration, Harari regional state, and Jigjiga city who had antenatal care follow up was the sources population.

4.1.3.2 Study Population

Pregnant mothers in Dire Dawa administration, Harari regional state, and Jigjiga city who had antenatal care follow up in the selected hospitals was our study population.

4.1.4 Sample Size

Sample size was calculated using single population proportion determination formula:

$$\mathbf{N} = \frac{(\mathbf{Z}_{\frac{\alpha}{2}})^2 \times \mathbf{p}(\mathbf{1}-\mathbf{p})}{(\mathbf{d})^2}$$

by considering proportion of khat chewing (p) 19.6% from previous study [27], 95% confidence interval (α = 0.05), and a margin of error (d) 5%; the final sample size is calculated to be 242.

For qualitative data, 20 planned and 18 actual pregnant mothers on antenatal care follow up in the selected hospitals who had chewing experiences were in-depth interviewed.

4.1.5 Sampling procedure

To get study participants, firstly, a total of 4 hospitals (jugula, hiwot fana, dil chora and kara mara); two from Harari regional state (jugula and hiwot fana), one from Dire Dawa administration (dil chora) and the other one from Jigjiga city, capital of Somalia regional state (kara mara) was selected by lottery. Next, the sampling procedures followed to include and interview the study participants were systematic random sampling techniques. First, the number of pregnant mothers visiting the selected hospitals for antenatal care were observed from the recording offices of the respective selected hospitals. It has been found that on average 25-30 pregnant mothers visited the hospitals ANC units per day. From this, the total number of pregnant mothers who would visit the respective selected hospitals ANC units within 2 weeks of data collection period were determined. The number of study participants to be included and interviewed per day per hospital within 2 weeks of data collection period were determined to be 4. Hence, the sampling interval, which was 6, is obtained by dividing the total number of pregnant mothers who visited the selected hospitals per day with the number of pregnant mothers interviewed per day. Lastly, every 6^{th} pregnant mothers who had visited the selected hospitals ANC units were included and interviewed during 2 weeks of data collection.

For qualitative data, purposive sampling was used to select pregnant mothers on ante natal care follow up.

4.1.6 Study variables

4.1.6.1 Independent Variables

Age, residence, ethnicity, religion, educational status, occupational status, marital status, household income status, current pregnancy related healthy practices and khat chewing and other substances use history are the independent variables.

4.1.6.2 Dependent Variable

Magnitude of khat chewing is the dependent variable.

4.1.7 Data collection

4.1.7.1 Data collection instrument

The data collection tool for the interview was developed by reviewing different literature. The questionnaires were prepared in English, translated into the respective local languages, and back translated in to English to maintain consistency.

4.1.7.2 Data collection procedure

Data was collected by an interviewer-administered questionnaire. The questionnaire consists of sociodemographic, pregnancy related, and behavioral characteristics. Health professionals with BSc qualifications were used for data collection and supervision after training by the principal investigators. The training was given by focusing on the objectives of the study, the confidentiality of information, and the contents of the questionnaire in detail. For qualitative data an in-depth interview of selected pregnant mothers on ANC was conducted using an interview guide.

4.1.8 Data processing and analysis

Each questionnaire data was given a code and entered into Epi-Data version 3.1 statistical package and exported to SPSS version 27.0 statistical package for statistical analysis. Data cleaning and editing was made before analysis. The result of study is presented in both descriptive statistics (percent, table, mean, median values, dispersion measurements like standard deviation, interquartile range) and inferential statistics (odds ratio). Binary logistic regression was performed to calculate the univariable and multivariable crude and adjusted odds ratio respectively and to determine independent predictors of dependent variable. In multi-variable binary logistic regressions model, only those variables associated with dependent variable with p-value $\leq$ 0.2 in univariable analysis, and not collinear was entered. Statistical significance was declared at p-value <0.05. Distributions of sociodemographic and behavioral characteristics between khat chewers and non-khat chewer study participants were compared using chi-square tests (Pearson, *P*-values tested two-sided). The multicollinearity check among independent variables were performed through variance inflation factor and tolerance. Moreover, the model goodness of fit was checked by Hosmer and Lemeshow goodness of fit test.

Analysis of qualitative data was through thematic framework analysis: 1st the interview was typed up or transcribed and was translated into English, then the text was read, and key themes were identified. In addition, the responses given was sorted into meaningful categories (groups) by keeping the variations of respondents' answers in order to aid comparison among respondents. Finally, the qualitative result was presented through narrative form with support of evidence from raw data as direct quotes (paraphrases).

4.1.9 Data quality management

To maintain data quality, training was given for data collectors and supervisors. Properly designed data collection material was developed by reviewing different literature. Supervision was carried out on daily base to check completeness and consistency by the principal investigator. The principal investigator collected correctly completed questionnaires from data collectors and entered the data to confirm correct data entry. In addition, at the end of data entry data cleaning was done using frequencies, cross tabulations, sorting and listing to check missed values and outliers. Errors identified was corrected by revising the original questionnaire. More importantly, pretest was done using five percent of the sample size on those pregnant women who was not included in the final data collection and errors identified during pre-test was corrected accordingly.

4.1.10 Ethical considerations

Ethical approval was obtained from Institutional Review Board of College of Health Sciences, Addis Ababa University. Permission was also obtained from the concerned bodies of Dire Dawa administration, Harari region and Somalia region. The study subjects were given all the information they need to participate in the study through an informed consent form, which was read to those not able to read their local language by the interviewer, and informed written consent was obtained from the study participants as witnessed by data collectors name and signature before they are involved in the study. To keep confidentiality all collected data was coded and locked in a separate room before entering to the computer. After entered to the computer all data was locked by password. Moreover, the name and other personal identifiers of the participants was not included in the data collection form, and the data was not disclosed to any person other than investigators.

4.1.11 Dissemination of result

The findings of this study have been published in a reputable peer reviewed journal (PAMJ). Additionally, the report of the study will be presented and discussed in the department of Anatomy, College of Health Sciences, Addis Ababa University. Finally, the results of the study will be disseminated to college of health science, Addis Ababa University; school of medicine, Debre Markos University, Ethiopian Public Health Institute, Federal Ministry of Health, ministry of education, Harari, Somalia and Dire Dawa administration regional health bureau, Harari regional state, Somalia regional state, Dire Dawa administration and for other interested governmental and non-governmental organizations.

4.2 Methods and Materials for maternal, pregnancy and neonatal outcomes following consumption of khat during pregnancy

4.2.1 Study design and period

Multi-site prospective cohort study of pregnant women who chewed khat (exposed) and not chewed khat (unexposed) was conducted from August to December 2022. The recruitment time was from August 15 to September 15, 2022. The current study compared maternal, pregnancy, birth and neonatal outcomes for women with confirmed khat chewing practice during pregnancy **(**exposed**)** with pregnant women not practiced khat chewing during pregnancy period **(**unexposed). Assignment of participants into exposed and unexposed groups were based on self-reporting of the study participants.

4.2.2 Study setting

The study was conducted in selected hospitals of Dire Dawa administration, Harari region and Jigjiga city administration, eastern Ethiopia (for the details, see methods for the first study).

4.2.3 Population

4.2.3.1 Source population

All pregnant women in Dire Dawa administration, Harari regional state, and Jigjiga city who had antenatal care follow up during the study period.

4.2.3.2 Study population

All pregnant women who had antenatal care follow up in selected hospitals in Dire Dawa administration, Harari regional state, and Jigjiga city and who fulfilled inclusion criteria during the study period.

4.2.3.3 Eligibility criteria

Inclusion criteria

Study participants living in the area for at least 6 months (permanent resident) and have initiated antenatal care in the selected hospitals of the study area during the study period was included in the study.

Exclusion criteria

Those participants at high risk of adverse birth outcomes like having known major chronic illness such as diabetes mellitus and cardiovascular diseases; and having previous history of congenital anomalies were excluded. Moreover, those pregnant mothers with multiple pregnancy were also excluded.

4.2.4 Sample size

The sample size was determined by using double population proportion determination formula:

$$n1 = \frac{[Za/2\ (\sqrt{1+1/r})\ p\ (1-p) + \boldsymbol{Z\beta}\sqrt{p1\ (1-p1) + p2\ (1-p2)/r}]^2}{(p1-p2)^2}$$

Where P1: is percent of exposed with the outcome, P2: is percent of non-exposed with the outcome, and r is the ratio of non-exposed to exposed.

Thus by, using 28.6% proportion of low birth weight in khat chewer groups (exposed) and 9.8% in non-khat chewers (non-exposed) from previous local study [38] and based on the assumptions of **Zα/2:** 95% CI, **Zβ:** 80% power and r 1:1, the sample size was calculated using open Epi version 3 statistical package. The final sample size after using design effect 2 and adding 10% for loss to follow up is calculated to be 344.

4.2.5 Recruitment /sampling procedures

Dire Dawa administration, Harari regional state and Jigjiga city were purposively selected due to exposure of interest. Then, 4 hospitals (jugula, hiwot fana, dil chora and karamara); 2 from Harari regional state (jugula and hiwot fana), one from Dire Dawa administration (dil chora) and one from Jigjiga city (kara mara) were selected by lottery. As shown in the flow diagram below (Figure 1), study participants (exposed and non-exposed) were enrolled in selected hospitals in

the study area utilizing a consecutive prospective recruitment approach with a sampling interval of 4 (details of the interval calculation procedures are stated in the first study). All pregnant women being in the late second trimester and early third trimester of pregnancy visiting the selected hospitals for the 1st or 2nd time during the study period was included based on sampling interval until the required sample size of exposed and unexposed groups are fulfilled. The appropriate recruitment timing of participants was at 1st or 2nd antenatal care visit with gestational age in the late second and early third trimester specifically from 24 to 28 weeks of gestation and the pregnancy follow up contact period/time was at antenatal care appointments.

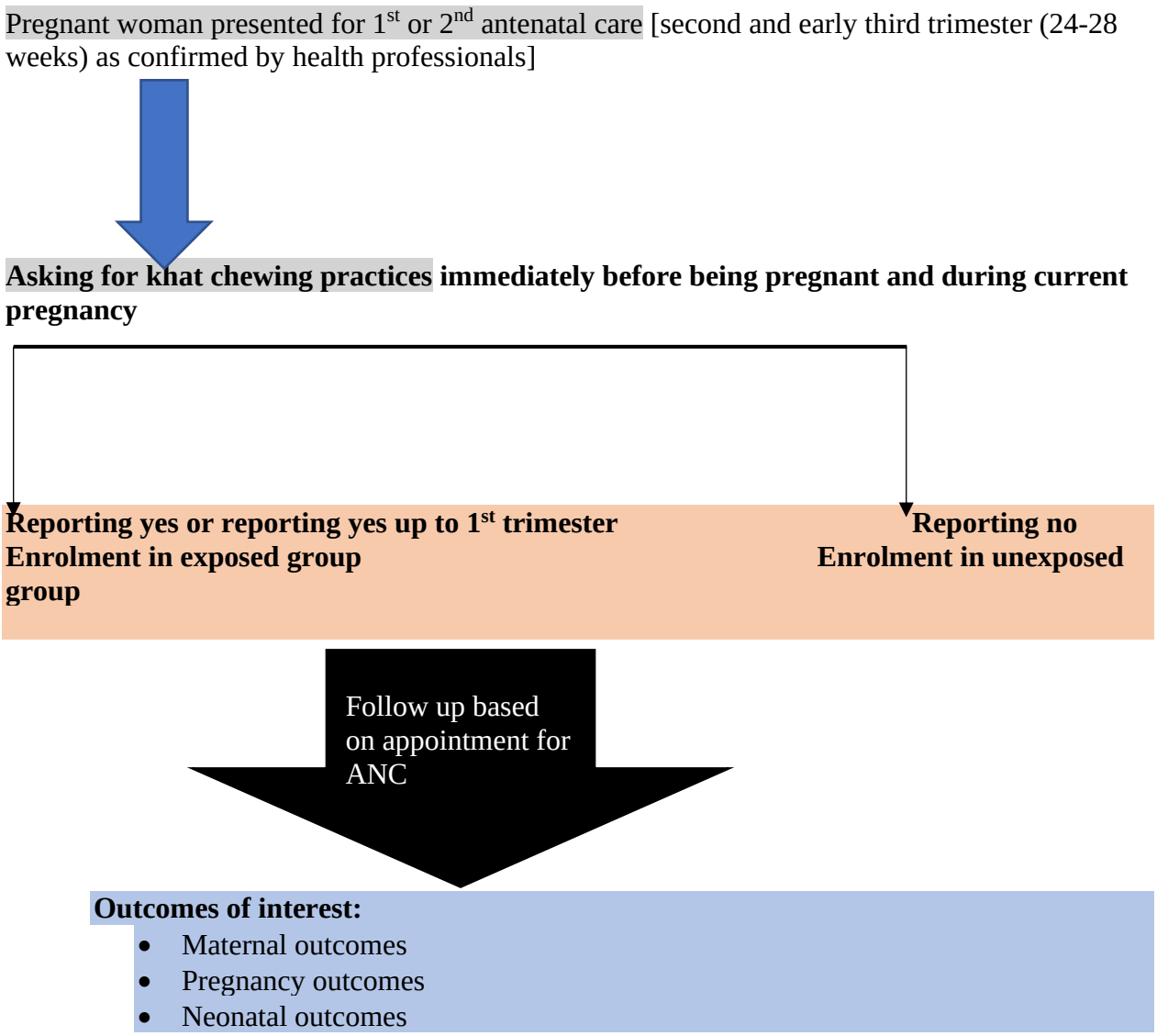


Figure 1: Study overview, recruitment procedures of study participants in Dire Dawa, Harar and Jigjiga selected hospitals, eastern Ethiopia, August to September 2022.

4.2.6 Study variables

4.2.6.1 Dependent Variables and measurements

1. Maternal outcomes: (**maternal anemia, gestational hypertension, gestational diabetes mellites**).

The diagnosis of anemia during pregnancy was trimester specific and elaborated as follows: Hgb<10.5 g/dl for study cohorts in the second trimester and Hgb<11 g/dl for study cohorts in the third trimester of pregnancy[48, 49]. In addition, 10-10.9g/dl, 7-9.9g/dl and <7g/dl Hgb concentration levels were considered as mild, moderate and severe maternal anemia, respectively[50]. To adjust the measured hemoglobin values at sea level, the correction factors were used at every 500-meter increase in altitude for altitudes more than 1000 meters above sea level[51]. In similar way, the measured hemoglobin value has been corrected for smoking practice[51]. Blood samples from pregnant cohorts were drawn from cubital fossa puncture after the site was disinfected with disinfectants and collected in the test tubes. Then, hemoglobin concentration levels were measured using complete blood count (CBC) machine.

Gestational hypertension was diagnosed when as systolic BP>=140 mm Hg or diastolic BP>=90 mm Hg[52]. The measurement was performed on at least 2 separate days (at enrollment and at follow up period). The first measurement was undertaken after at least 5-minute rest of the study cohorts being seated and arm at the heart level and the 2^{nd} measurement of same day after at least 2 minutes of the 1^{st} measurement. The average of the two measurements separated by at least 2 minutes for each day was taken. Overall, the average of the 2 days two times measurement was taken to declare gestational hypertension.

Diagnosis of gestational diabetes was made using fasting plasma glucose level between 92-125mg/dl[53] and associated clinical manifestations. At first measurement of random blood sugar was performed for each study cohorts using a glucometer; portable and battery-powered devices. A drop of blood from the fingertip of each study cohorts was placed on paper test strip and then the test strip was inserted into blood glucose meter and glucose level in the blood was determined. Then for those cohorts with random blood sugar level of >=200 mg/dl; fasting plasma glucose level was determined to declare gestational diabetes. Participants who had

random blood sugar level of >=200 mg/dl were told to come early in the morning before eating breakfast and their fingertip bloods were collected. A drop of the collected blood was placed on the strip and inserted on blood glucose meter; hence fasting blood glucose level was determined.

2. Pregnancy outcomes: (live birth, stillbirth, fetal growth restriction, PROM, preterm labor, oligohydramnios, abruptio placenta, preterm birth, birth weight).

In the present study, the diagnosis of stillbirth was declared when a newborn had been delivered with no signs of life at the time of birth confirmed by physical examination and ultrasound examination verifying lack of cardiac activity of the fetus[54].

In the present study, fetal growth restriction (FGR) was identified using 1) ultrasound when the estimated fetal weight is below 10^{th} percentile for gestational age[55]. The ultrasound measurements performed to estimate fetal weight for identification of FGR in the present study were measurements of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL). The recent WHO fetal growth charts[56] conducted through ultrasound biometric measurements was used to declare FGR using the estimated fetal weight[57]. Moreover, body proportion methods such as abdominal circumference for gestational age, head circumference to abdominal circumference ratio (HC/AC), and femur length to abdominal circumference ratio (FL/AC) has been performed for identification of fetal growth restriction. In addition, 2) birth weight, sex of the newborns and gestational age at birth were used to determine small for gestational age (SGA)[58] among all births; since FGR and SGA are highly related[58]. Small for gestational age was declared at birth when birth weight is below 10^{th} percentile of the sex specific birth weight for gestational age growth chart[58-62].

Pre-labor rupture of membranes (PROM) is well-defined as a spontaneous discharge of amniotic fluid, happening after 28 weeks of gestational age (after fetal viability, in Ethiopia) and at least one hour before the onset of true labor[63, 64]. Pre-labor rupture of membranes is further divided into preterm PROM and term PROM. Preterm PROM occurs after twenty-eight weeks of gestational age and before 37 weeks and term PROM occurs at and above 37 completed weeks of gestational age. In the present study, the diagnosis of PROM was performed by experienced health professionals using woman's complaint of a painless sudden leakage of fluid from her vagina, followed by a sterile speculum examination. Ultrasound examination was performed for some cases to confirm the diagnosis.

Preterm labor was declared when spontaneous onset of labor had existed before 37 completed weeks of gestational age and after twenty-eight completed weeks of gestation. Labor onset was determined by experienced health professionals using either 1) recognized regular uterine contractions (at least one every 10 minute), with recognized cervical changes: cervical dilation of >2 cm at external os and cervix length ≤ 1 cm, or 2) using recognized rupture of membranes.

Amniotic fluid volume has been assessed mainly through ultrasound examination. On ultrasound examinations, the volume of amniotic fluid was measured by experienced obstetrician using maximum vertical pocket (MVP) or single deepest pocket (SDP) in the late second trimester and early third trimester of pregnancy of the study cohorts. Cutoffs of 2 and 8 cm MVP/SDP values were used to declare the amniotic fluid volume levels. An MVP value ranged between 2 and 8 cm was declared normal; below 2cm value was declared oligohydramnios and above 8 cm value declared polyhydramnios[65, 66].

Preterm birth was declared when gestational age at birth of neonates becomes less than 37 completed weeks and after 28 completed weeks of pregnancy[67] and full-term birth when the neonates' gestational age at birth becomes 37 and above completed weeks. Gestational age was estimated in terms of weeks using maternal recall of last normal menstrual period (LMP). In addition, symphysis-fundal height (SFH) measurement in centimeters was performed to confirm LMP-based evaluation of gestational age.

Low birth weight (LBW) was defined when birth weight becomes below 2.5kg and very low birth weight (VLBW) was declared when birth weight becomes below 1.5kg[58]. Weight at birth of the neonates were measured through weighing scale to the nearest 0.1kg.

3. Neonatal outcomes: (neonatal mortality, neonatal morbidity, low Apgar score).

Apgar score is a rapid and an easy method to evaluate a newborn's status following birth. The newborn of present study has been evaluated by experienced health professionals at one and five minutes of birth using five criteria; pulse rate, breathing effort, appearance, muscle tone, and response when stimulated[68] and each criterion has been valued from zero to two. Then values of the five criteria were summed to get the total score ranged from zero to 10 for each neonate.

4.2.6.2 Exposure variable and measurements

Khat chewing during gestation was the exposure variable for this study. Khat use during current pregnancy is defined as ever chewing of khat during current pregnancy for at least 4 days per week which lasts for at least 4 hours per chewing day or chewing for at least 4 days per week of

at least 50-75 grams of khat leaves (1/4th pack) per chewing day. This is based on a previous local study [69] which found chewer's of khat spend on average 3.75 hours while chewing khat and chewed more than 75 grams of khat leaves on single session. Here, in the present study, those pregnant cohorts who were consumed without measuring in grams, were asked the amount they consumed in terms of local measurements like how many bundles, how many sticks they have consumed, and their responses were converted into gram equivalents. One bundle of khat is about 100-300grams and contains about 5-16 sticks. Study cohorts who had chewing practices in terms of stick were considered khat chewer cohort if they have consumed at least 5 sticks of khat per day. Non khat chewers in the present study were those who did not reported any chewing practices before and during current pregnancy.

Measurement of the exposure status to the exposure variable was performed through maternal self-report. All pregnant women to be included in the study were first assessed for khat use at the first or second prenatal visit with the use of validated questionnaire. The world health organization (WHO) also recommended for identification of substance use during gestation through interview about substance use at antenatal care visits[70]. For this study, the 4Ps plus screening questions[71] was modified for use. The list of modified questions include:

(1) Parents: Did either of your parents have a practice with khat chewing or any other drug use?
(2) Peers: Do you any of your friends have a practice with khat chewing or another drug use?
(3) Partner: Does your partner have a practice with khat or drugs use?
(4) Past: Have you ever chewed khat?
(5) Pregnancy: In the month before you knew you were pregnant: how many grams or packs of khat you chewed per day or how many times per day you chewed? After you knew your pregnancy have you continued to practice chewing? how much alcohol did you drink? how much cigarette did you smoke?

4.2.6.3 Mediators

Gestational hypertension, maternal anemia, emergency cesarean section delivery and preterm birth were the potential mediators in the present investigation.

4.2.6.4 Explanatory variables (covariates) and measurements

Socio-demographic variables, obstetrics related variables, past pregnancy history, diagnoses, or symptoms in relation to the current pregnancy, past medical history, other substance use related

variables (other substance use status during current pregnancy), personal factors, and other previously identified confounding variables.

Alcohol use information including frequency and number of consumptions were obtained using questionnaire. Alcohol content standards for each beverage (beer, wine) was estimated and added to fix the total exposure volume of absolute alcohol (in grams per week). It is estimated that a bottle of beer (330 ml) in Ethiopia is expected to contain around 16.5 grams of alcohol and 250 ml (1 glass) of wine in Ethiopia is expected to contain around 27.5 grams of alcohol. It is defined in previous literature that one standard drink is nearly equal to 0.5 ounces (14 grams) absolute alcohol [72, 73]. Hence, alcohol exposure status of participants can be categorized as <1.5 drinks/week, 1.5-3.5 drinks/week, >3.5-7 drinks/week, and >7 drinks/week [72]. Furthermore, participants can be categorized as low (<1.5 drinks/week), moderate (1.5-3.5 drinks/week) and high (>3.5 drinks/week) ethanol/alcohol drinkers. Those who did not reported use of any alcohol types during current pregnancy were considered as non-users of alcohol.

The mid-upper arm circumference (MUAC) of each pregnant cohorts were measured at the midway between the tips of the shoulder (acromion) and the tips of elbow (olecranon) of the left or right arm using soft tape meter. The measured values were documented to the nearest one millimeter. Accordingly, the present study declared, poor nutritional status of the mother when MUAC<23cm or >=33cm[74].

In addition, weight and height of pregnant cohorts were measured by experienced health professionals using a weighing scale and a stadiometer placed at each ANC service delivery units of the study hospitals. Next, body mass index (BMI) of each study cohorts were calculated as weight in kg divided by height in meter squared [weight in kg/ (height in meter)^2]. A BMI value of <18.5kg/m^2 were used to declare under nutritional status of the study cohorts[58].

In addition of these measurements, all the other details such as sociodemographic characteristics, medical and obstetric history, physical and clinical measurements were also performed by experienced health professionals at ANC, delivery, and postnatal care service delivery units.

4.2.7 Data collection instruments, methods and procedures

Outcome variables data were collected with the use of ultrasound measurement, clinical measurements such as weight, height, vital sign, urinary glucose, urinary protein, pulse oximetry, fetal heartbeat measurements, and others, selected laboratory measurements, measurement of

birth weight, performing physical exams for observation of external and internal anomalies, and other neonatal and maternal outcomes at birth and at 5 minutes postpartum.

Explanatory variables data such as: socio-demographic characteristics, obstetrics related characteristics, past pregnancy history, diagnoses or symptoms in relation to the current pregnancy, substance use related characteristics (substance use during current pregnancy), personal factors were collected through the use of interviewer-administered structured and semi-structured questionnaire at entry to the study. To maintain uniformity and ease of comprehension during administration, the questionnaire was initially created in English and then translated into Afan Oromo, Afan Somali, and Amharic languages. In addition, anthropometric and clinical measurements were performed at entry, follow up time and delivery (end of pregnancy) to collect the necessary data for the explanatory variables.

4.2.8 Operational definition

The term "neonatal period" refers to a newborn's first four weeks of life.

The term "postpartum period" refers to the 42 days after birth or the end of the pregnancy.

4.2.9 Data quality control

To maintain data quality, three days of intensive training were given to data collectors and supervisors aimed at the objectives, how to get the consent of study participants to participate in the study, and measurement issues of the study. Interviewer-administered data were collected on the respective service delivery units by experienced health professionals of selected hospitals. Ultrasound measurements, physical and clinical examinations and selected laboratory measurements were done by qualified specialist doctors, qualified midwiferies, qualified nurses and laboratory specialists working in the selected hospitals in the study area. Properly designed data collection material was developed by reviewing different literatures. Strict supervision was carried out by both supervisors and principal investigator to check completeness and consistency. Correctly completed data was collected from data collectors by the principal investigator. Moreover, pre-test of questionnaires was done before the definite data collection work, by using 5 percent of the sample size in health institutions not selected for actual data collection and identified errors were corrected accordingly.

The data was entered by the principal investigator to confirm the right data entry. Furthermore, at the end of data record data cleaning was done using frequencies, cross tabulations, sorting and

listing to check missed values and outliers. Errors identified was corrected by revising the original questionnaire.

4.2.10 Data processing and analysis

Each questionnaire and outcome data were given a code and entered on Epi-Data version 3.1 statistical package and exported to SPSS version 27 and Stata version 16 software for analysis. Before analysis, data cleaning using frequency, listing and sorting was performed to identify any outliers and missed values and then corrections was made by revising the original questionnaire. Descriptive statistics such as median, interquartile range (IQR), and mean and standard deviation (SD) for continuous data and frequency distribution for categorical data is used to summarize the characteristics of the cohorts. Differences of characteristics between khat chewers and non-khat chewer participants were determined using chi-square test (Pearson, *p*-values tested two-sided). In addition, survival analysis was conducted to calculate the incidence rate of selected pregnancy outcomes (fetal growth restriction, preterm birth, and low birth weight) categorized by khat chewing practice. Survival analysis was also performed to calculate the rate of neonatal mortality among chewers and non-chewers. The Kaplan-Meier curve was examined in order to detect variations in the risk of neonatal mortality, and the log-rank test was used to find statistical differences in this curve.

The generalized linear model for the binomial family analysis was performed to estimate the crude and adjusted relative risk and attributable risk (AR) with corresponding 95% CI of chewing khat during pregnancy on selected maternal, pregnancy, and birth outcomes. Survival analysis (cox proportional hazards model) was performed to estimate the relative risk with corresponding 95% CI of chewing khat during pregnancy on neonatal mortality. Variables as potential confounders (covariates) with a univariable *p*-value less than or equal to 0.25 was used in the multivariable model to estimate the aRRs of chewing khat during pregnancy on selected maternal, pregnancy, birth and neonatal outcomes. The relative risk with 95% confidence interval and *p*-values was used to measure the strength of association and to declare statistically significant association. In multivariable analysis model chewing of khat during pregnancy have been considered as statistically significant predictor of adverse outcomes of interest at *p*-value < 0.05. Since chewing khat during pregnancy revealed a significant association with selected pregnancy outcomes at a *p*-value of less than 5% in the multivariable GLM for the binomial family analysis, the mediation analysis was taken into consideration to test whether the presumed

mediators (i.e., gestational hypertension, cesarean delivery, preterm birth and maternal anemia) mediated the analyzed associations.

This is because, initially, there should be a significant relationship between the exposure variable (khat chewing during pregnancy) and the selected outcome variables (fetal growth restriction, preterm birth, and low birth weight) in order to perform additional mediation analysis for observing the mediation effects of the possible mediators (gestational hypertension, cesarean delivery, preterm birth, and maternal anemia)[75]. Next, the Generalized Structural Equation Modeling (GSEM) analysis was performed to examine the mediation effect of the possible consecutive mediators (i.e., gestational hypertension and cesarean delivery) on preterm birth. In same way, a Generalized Structural Equation Modeling (GSEM) analysis was also performed to examine the mediation effect of the possible consecutive mediators (i.e., gestational hypertension, cesarean delivery and preterm birth) and a possible mediator (i.e., maternal anemia) on low birth weight. Additionally, a possible mediators (maternal anemia and gestational hypertension) effect on fetal growth restriction has also been examined through the model. The analysis was performed using Stata 'gsem' command on drop-down menu bar. The steps of analysis were performed as follows. At first, the relationships between khat chewing during pregnancy and preterm birth as well as khat chewing during pregnancy and low birth weight were observed on the initial path models adjusted for potential covariates. Then, keeping in controlling of the potential covariates, the mediation analysis models were fitted to reveal the adjusted relationships between khat chewing during pregnancy, the possible consecutive mediators (i.e., gestational hypertension and cesarean delivery) and preterm birth as well as khat chewing during pregnancy, the possible mediators (i.e., gestational hypertension, cesarean delivery, preterm birth and maternal anemia) and low birth weight. In same way the model was fitted to reveal adjusted relationship between khat chewing, the possible mediators (maternal anemia and gestational hypertension) and fetal growth restriction. All of the outcome variables in the present study were a binary outcome variable which has been calculated with the assumption of a Bernoulli response distribution and logit link function. Mediation has different forms. One, mediation may be complete or partial [76, 77]. Complete mediation means the total effect of an exposure variable (i.e., khat chewing during pregnancy) on the outcome variables (i.e., fetal growth restriction, preterm birth and low birth weight) is transmitted through one or more mediators (i.e., gestational hypertension, cesarean delivery, preterm birth and maternal anemia).

In this case, the exposure variable has no direct effect on the outcome variables, which means, its total effect is indirect. Whereas partial mediation means, an exposure variable has both direct and indirect effects on the outcome variables. Second, mediators may be single or multiple (may be consecutive) [76, 77]. A single mediator means there is only one variable in the causal pathway between exposure (i.e., khat chewing during pregnancy) and outcome variable (i.e., fetal growth restriction, preterm birth or low birth weight). Whereas multiple mediators mean more than one mediator variables which function jointly at the identical period in a causal model. When the indirect effect of exposure variable (i.e., khat chewing during gestation) on the outcome variables (i.e., fetal growth restriction, preterm birth or low birth weight) is transmitted via a series of mediator variables, the multiple mediators are called consecutive mediators. In the present study, gestational hypertension and cesarean delivery can be seen as the consecutive mediators of the effect of khat chewing on preterm birth. Additionally, gestational hypertension, cesarean delivery and preterm birth can be seen as the consecutive mediators of the effect of khat chewing on low birth weight.

In the present study, the indirect effects of khat chewing on fetal growth restriction, preterm birth and low birth weight were calculated through the multiplications of regression coefficients [78]. In addition, direct, indirect, and total effects of khat chewing on fetal growth restriction, preterm birth and low birth weight has been calculated using Stata 'nlcom' command. The GSEM model fitness was checked using Akaike's information criterion (AIC) and Bayesian information criteria (BIC). First hypothetical models were formulated as shown (annex 1) and the final fitted models were also revealed in figures 5, 6 and 7. Then fitted GSEM model was tested for model adequacy based on AIC and BIC values. Accordingly, the AIC and BIC values for fetal growth restriction; AIC= 1034.892 and BIC= 1121.564 for hypothesized model and in the fitted model AIC= 1046.082 and BIC= 1125.216. The AIC and BIC values for preterm birth; AIC= 1024.78 and BIC= 1100.147 for hypothesized model and in the fitted model AIC= 1042.177 and BIC= 1106.239 as well as AIC and BIC values for low birth weight; AIC= 1952.351 and BIC= 2061.633 for hypothesized model and in the fitted model AIC= 1948.844 and BIC= 2039.284. In all of the cases, there is a reduction in score of the value of AIC and BIC from hypothesized models to the fitted models which indicates that the fitted final models are adequate/good for analysis.

4.2.11 Ethical considerations

Same as the first study. Hence, see the first study ethical considerations.

4.2.12 Dissemination plan

Part of this study findings have been published in a peer reviewed journal (BMC Pregnancy and Childbirth) for wider dissemination of information. Moreover, the findings of this study will be presented in the Department of Anatomy, College of Health Science, Addis Ababa University. In addition, after the presentation, the finding will be disseminated to Dire Dawa administration, Somalia region and Harari region where the study was conducted through hard and soft copy.

4.3 Materials and Methods of macroscopic and histopathologic examination of umbilical cord and placenta

4.3.1 Variables studied

- Placental and umbilical cord macroscopic and histopathologic statuses

4.3.2 Procedures and materials for macroscopic examination of umbilical cord and placenta

In same way with examination of any other specimen, examination of placenta and umbilical cord in this study was based on routine protocol [79-81]. This provides a systematic approach so that nothing was omitted. Materials that was important for gross examination includes tape measure, a long sharp knife, forceps with teeth and scissors.

4.3.2.1 Gross examination and measurement procedures for umbilical cord

It is most recommended to start examining the umbilical cord, then the membranes and finally the placenta. On gross observation, cord length was measured first. In the present study each umbilical cord at delivery was clamped and cut using scissors at about 5cm from its attachment to the abdomen of the newborn. Next, the length of the cord attached to the placenta was measured from the cut end of the cord to the level of placental insertion sites using tape meter and then 5cm of the length of cord attached to newborn abdomen was added to get the total length of the umbilical cords. Related approaches were followed by another author elsewhere[82]. Length of umbilical cord at term has a considerable discrepancy, with outliers ranging from no cord (achordia) to umbilical cord lengths up to 300 cm. As visualized during delivery, a term umbilical cord normally measures about 50-60cm in length. An umbilical cord

length of >100 cm is declared as long umbilical cord and cord length<30cm is declared as short umbilical cord.

The study also identified hypo coiled/ and hyper coiled/ umbilical cords, and compares it among the study groups. The normal umbilical cord coiling is around 1 coil/5 cm of umbilical cord length or in terms of umbilical coiling index the normal umbilical cord is around 0.20 to 0.24 coils per cm[83-85]. Umbilical coiling index can be obtained by dividing the entire number of umbilical cord coils/twists by the whole length of the umbilical cord in centimeters[86] immediately after birth. True knots in the umbilical cord were also diagnosed through observations at time of birth.

The umbilical cord insertion site on placenta can be diagnosed as central, eccentric/paracentral, marginal/battledore, and velamentous/membranous insertions. The central and eccentric cord insertions are considered as normal phenomenon and accounted for more than 90% of term placental insertions[87]. On the other hand, marginal cord insertion and membranous cord insertion phenomena are considered as abnormal placental cord insertions[87]. In the case of marginal cord insertions, the cord inserts at the margin of the placenta, and still arises directly from the placental mass. But in case of membranous cord insertions, the umbilical vessels crisscross between the amnion and the chorion before reaching the placenta. Singleton pregnancies are subject to an estimated occurrence of 7% marginal and 1% velamentous cord insertions[87].

In the present study, following delivery of placentas, measurements of the distances from margins of placenta to umbilical cord insertion sites on placenta were performed by using tape meter. Next, central cord insertion was declared when cord insertion becomes near the center of the placenta or cord insertion less than 3 cm from the center of the placentas. Eccentric cord insertion was declared when insertion of the cord become more than 3 cm from the center and when the distance from the cord insertion site to the nearest margin of the placenta is >2 cm and marginal cord insertion was declared when the distance of cord insertion site to the nearest placental margin is <=2 cm. In addition, the number of vessels in the cord were checked and which normally are three in number. More importantly any umbilical cord abnormalities such as discoloration, hemorrhage, cysts, thrombosis, surface nodules, or masses were checked. The cords were then removed from the placenta at the insertion site.

4.3.2.2 **Measurements procedures of placental parameters**

A thorough examination of placenta was performed using freshly delivered placenta. Immediately following delivery and observation and measurements of umbilical cord parameters, each placenta was examined on both fetal and maternal surfaces. Fetal surfaces were examined with the aim of observation of membrane status and for any amniotic or chorionic hematoma. Evaluation of maternal surface was performed to check for the appearance of retroplacental hematoma, calcification of villous tissue, infarction of villous tissue, compression of villous tissue and any villous lesions.

After these thorough examination of placenta, fetal membranes were trimmed from the placenta and adherent blood clots were removed from the maternal surfaces of the placenta. Then, the placenta of all study cohorts was weighted at delivery ward by using a calibrated weighing scale and values were recorded to the nearest grams. In addition, the shapes of the placenta were determined through appropriate observations of experienced health professionals as round, oval and irregular. Next of weighing, the placenta was put on flat surface and its diameter was measured using tape meter and values were recorded to the nearest cm. One measurement value was considered due to the fact that most of the placenta on observation were round and only few irregular placentae were noticed in the present study. The thickness of the placenta was measured using a needle. The procedures were first piercing of the placenta from chorionic plate to the level of basal plate at 2 places (center and edge) of placenta were performed. Next, pierced values were measured on cm calibrated tape meter and the average of the two measurements were calculated to get the thickness of the placenta. A related procedures have been utilized elsewhere[88].

Finally, placenta to birth weight ratio was determined by dividing placental weight (in grams) to birth weight (in grams) and it was multiplied by 100 to get the proportion of placental weight relative to birth weight.

4.3.3 **Microscopic examination procedures for umbilical cord and placenta**

4.3.3.1 Sample size calculation for histopathologic study

The sample size was calculated using double population proportion determination formula; using a 25% proportion of vascular dilatation in non-anemic placenta and a 75% proportion of vascular dilatation in anemic placenta in a previous local study[89], and by considering a 95% CI, 80% power and a 1:1 ratio. Accordingly, the calculated sample size was 40.

4.3.3.2 Sampling for histopathologic analysis

Based on existed literatures histological sampling is recommended while conducting histopathologic examinations/study and the required samples were taken as follows:

- Two transverse sections of umbilical cord, one near the placental insertion and one near the fetal end
- Two full thickness blocks of the placental parenchyma (away from the placental edge) to include the fetal and maternal surfaces
- Additional blocks depending on the macroscopic findings [81].

4.3.3.3 Eligibility criteria for tissue samples

Based on existed literatures there are indications for placental histopathologic examination. Accordingly, all placentas from stillbirths [90], fetal growth restriction (FGR –fetal weight below 10^{th} percentile for gestational age in fetal growth curve during pregnancy)[91, 92], immaturity (less than 32 completed weeks gestation)[91, 92], and cases of severe fetal distress requiring admission to a neonatal intensive care unit (NICU)[93], maternal pyrexia (>38°C) and late miscarriages (20 to 23+6 completed weeks gestation) would be referred for histopathologic examination. Moreover, submission of placentas succeeding other pregnancy problems might depend on local resources and the value placed on placental inspection in these circumstances by the local obstetricians[94].

But, for the current histopathological study, placental and umbilical cord tissue samples were taken from study cohorts 1) with ultrasound confirmed singleton pregnancy, 2) who had delivered full term live births through vaginal mode of delivery, 3) having no current diagnosis of gestational hypertension and maternal anemia, and 4) having no history of previous chronic illnesses such as DM, HTN, and others.

4.3.3.4 Specimen collection, processing and staining procedures

After macroscopic examination representative specimens from each fresh placental tissue and umbilical cord for microscopic examination was taken and labeled and was kept in formalin for fixation.

Processing human placenta and umbilical cord

Examination of human placenta and cord at the tissue levels demands precise processing of the specimens to optimally stabilize structural and molecular elements. Standard histopathological

protocols use a systematic sequence of steps (Annex 2) and the steps are outlined below in the order in which they are performed when preparing specimens.

Fixation

Main practices for tissue fixation have been explained elsewhere[95, 96]. The most common fixatives for human placenta similar with another specimen are 10% neutral buffered formalin and 4% paraformaldehyde. In the present study, 10% neutral buffered formalin preparation was used to preserve the umbilical cord and placental specimen.

Post fixation activities

There are also post fixation steps performed which includes: dehydration, clearing and infiltration (see the details in Annex 2).

Paraffin sectioning

Paraffin blocks was sectioned after the paraffin wax solidify completely. Paraffin sections for this histopathologic study was generally cut at almost 5μm in thickness.

Staining and mounting paraffin sections

Paraffin sections need to be rehydrated before they can be stained. This step is accomplished by progressive reverse transfer through organic solvents and graded alcohols (see details in Annex 3).

After the procedures of staining and mounting with DPX were finalized, the prepared slide was examined by routine light microscopy using different magnification powers. All-out probable fields were inspected for each slide to assess abnormalities of blood vessels within the villi (greater in the number of terminal villi vessels, dilated villi vessels), villous hypoplasia, villous/intervillous hemorrhage/thrombosis, width of intervillous space, villous calcification, villous hyalinization, villous edema, villous infarction/necrosis, villous fibrosis, fibrinoid necrosis, cytotrophoblast proliferation and presence of syncytial knots in excess amount. Then, images of the representative sections were captured using microscope camera. The width of intervillous spaces were measured by ocular and stage micrometer.

4.3.4 Data processing and analysis

The study data was coded and entered using Epi-Data version 3.1 and was exported to SPSS version 27 for analysis. Descriptive statistics like frequency, mean, and standard deviation were computed to describe the study variable and the results are presented in texts, tables and

microscopic pictures. The relationships among the studied variables were confirmed by chi-squared test. Placental histopathologic findings were compared by the khat chewing characteristics of the study participants using Pearson chi-squared test. In the same way, the placental histopathologic findings were compared with selected fetal outcomes using Pearson chi-squared statistics. Comparison of intervillous space width in the two study groups placenta was performed using comparison of means analysis. Differences at p value <0.05 was considered statistically significant.

4.3.5 Data quality assurance

For data quality assurance, training was given for data collectors and supervisors concerning on how to measure the placental and umbilical cord parameters, how to take placental and umbilical cord tissue samples, about fixation, and appropriate disposal of the placenta and umbilical cord after measurements and after taking tissue samples. Data was collected by experienced Bachelor of science graduates in midwifery. Experienced BSc health professionals (midwives) working in the selected health institution was considered for this study. Finally, the pathologist assessed the histopathologic changes of the placenta and the cord using prepared slides blindly**.**

4.3.6 Ethical Considerations

Ethical approval was obtained from institutional review board of College of Health Sciences, Addis Ababa University. Permission was also obtained from the concerned bodies of Harari regional state, Somalia regional state and Dire Dawa Administration. To protect confidentiality no personal identifier was recorded in the questionnaire and the recorded data was not accessed by a third person. Lastly, written informed consent was obtained from study participants to use their placenta and umbilical cord for the research purpose.

5. Results

5.1 Magnitude and associated factors of chewing khat during pregnancy

5.1.1 Sociodemographic characteristics of study participants

Out of 242 expected study participants, 230 were involved in the study, making a response rate of the study, 95%. In this study, the mean age of the respondents was 26.7 years with standard deviation (SD) of 4.69 years. Slightly higher study participants (51.3%) were living in rural area. Ethnically, most study participants, 96 (41.7%) were Oromo followed by Harari, 43 (18.7%) and Amhara, 40 (17.4%). The majority (65.7%) of the study participants were Muslim in religion followed by orthodox Christians (25.7%). A relatively greater number of study participants, 96 (41.7%) and, 60 (26.1%) were illiterate and farmer respectively. More than half (74.8%) of involved study participants were married. The median monthly household income of the study participants was 4500 Ethiopian birr with inter quartile range of 2700 Ethiopian birr (Table 1).

Table 1: Distribution of sociodemographic characteristics by their khat chewing status of study participants in eastern parts of Ethiopia, 2022 (N=230).

Variables	**Khat chewing practices of study participants**		**Total**	***p*-value**
	Non-chewers, No (%)	**Chewers, No (%)**		
Age group of study participants				
<26 years	82 (49.1%)	16 (25.4%)	98	0.001
>=26 years	85 (50.9%)	47 (74.6%)	132	
Total	167(100%)	63 (100%)	230	
Participants area of residence				
Urban	99 (59.3%)	13 (20.6%)	112	<0.001
Rural	68 (40.7%)	50 (79.4%)	118	
Total	167(100%)	63 (100%)	230	
Participants ethnicity				
Oromo	63 (37.7%)	33 (52.4%)	96	0.139
Harari	32 (19.2%)	11 (17.5%)	43	
Amhara	35 (20.9%)	5 (7.9%)	40	
Somali	25 (15%)	9 (14.3%)	34	
Others (Tigre and Gurage)	12 (7.2%)	5 (7.9%)	17	
Total	167(100%)	63 (100%)	230	
Participants				

religion				
Muslim	105 (62.9%)	46 (73%)	151	0.347
Orthodox	46 (27.5%)	13 (20.6%)	59	
Protestant	16 (9.6%)	4 (6.4%)	20	
Total	167(100%)	63 (100%)	230	
Participants educational status				
No formal education	61 (36.5%)	35 (55.6%)	96	0.004
Primary education	41 (24.6%)	19 (30.1%)	60	
Secondary education	34 (20.4%)	5 (7.9%)	39	
Tertiary education	31 (18.5%)	4 (6.4%)	35	
Total	167(100%)	63 (100%)	230	
Participants Occupation				
Housewife/ Homemaker	32 (19.2%)	22 (34.9%)	54	0.012
Farmer	42 (25.1%)	18 (28.6%)	60	
Government employee	39 (23.3%)	3 (4.8%)	42	
Non-government employee	9 (5.4%)	2 (3.2%)	11	
Merchant	36 (21.6%)	13 (20.6%)	49	
Daily laborer	9 (5.4%)	5 (7.9%)	14	
Total	167(100%)	63 (100%)	230	
Participants marital status				
Currently married	122 (73.1%)	50 (79.4%)	172	0.326
Divorced and widowed	45 (26.9%)	13 (20.6%)	58	
Total	167(100%)	63 (100%)	230	
Participants monthly HH income (ETB)				
<4500	72 (43.1%)	31 (49.2%)	103	0.407
>=4500	95 (56.9%)	32 (50.8%)	127	
Total	167(100%)	63 (100%)	230	

HH: household; ETB: Ethiopian birr.

5.1.2 Khat chewing patterns of respondents and their perceived reasons of chewing khat

Out of 230 respondents, 63 [27.4% (95% CI: 22.2-33.0)] had practiced chewing khat during current pregnancy. Of these, 24 (38.1%) of them chewed daily, 21 (33.3%) chewed more than

one day per week and the remaining 18 (28.6%) chewed khat once per week. Multiple reasons were given for chewing khat among chewers in the current study. Among the reported reasons, the most frequent were chewing for socialization, 40(63.5%), to obey tradition, 38 (60.5%), for excited way of life, 31 (49.2%), and unawareness of its harm, 24 (38.1%) (Table 2). These results are also supported by qualitative findings obtained through in-depth interview of pregnant mothers. The major perceived reasons of khat chewing reported by study participants at time of in-depth interview were for socio-cultural issues, to be happy with friends, to be free from tensioned situations, to be effective in performing daily activities, and lack of knowledge of its harm (Table 3). An in-depth interview of a 28 years old 9 months pregnant study participant said, *"I have begun to chew khat with my lovely friends. One day I was in a space with my friends which I usually pass my time for recreation. During that time a friend of my friend who had a previous khat chewing experience joined us holding khat and told and encouraged us to start chewing to feel free and to be joyful and gave us a few sticks and then we repeated on the other days. That is how I experienced chewing khat."*

An in-depth interview of another 25 years old 7 months pregnant respondents also explained, "*I really remembered how I enforced to be a khat chewer. When my friends chew khat in a group, I became triggered to join them. I decided to taste it in the first time I started and gradually repeated it for several days in a small amount. Now I become a daily user of khat with large amount. That is how I became a regular khat chewer."*

An in-depth interview of a 30 years old 6 months pregnant respondent added, *"My family is not using khat. I started chewing with my friends while being a high school student. When I was in high school most of my friends were practiced chewing khat and even encourage and enforce others to practice chewing and then I tasted it with one stick the first time and repeated it on consecutive days. Now my eyes did not open in the afternoon without chewing."*

A 27 years old 6 months pregnant respondent added, *"At the first time, I have begun chewing khat with my friends, aiming to try its taste and to know the type of effects it would have on our body, and we continued consuming repeatedly being in groups. Now I become a daily consumer of khat. Enjoy chewing of khat."*

A 32 years old 8 months pregnant respondent reported, *"Life is difficult without khat chewing. Without chewing of khat an individual cannot be able to perform the activities given to him and hence, cannot become competent. In order for me to perform my daily activities effectively*

chewing of khat is a must. Otherwise, I will lose everything, because I will be enforced to leave my occupation when I cannot perform the activities given to me effectively. So, enjoy chewing of khat."

A 32 years old 7 months pregnant respondent explained, *"I did not believe khat chewing bring any health problems to me and my unborn child. My family and the community hear at large also feel like I said. I had 3 children born before without any health problems in spite of my khat chewing practices and hence, I continued chewing khat by decreasing its amount from my pre pregnancy amount. This is even due to fear of the healthcare providers' advice of chewing khat during my current pregnancy will bring problems on my unborn child."*

A 22 years old 6 months pregnant respondent also added, *"In the early period of my pregnancy, I was a daily consumer of khat. But when I visited health institutions for antenatal care the health care providers told me that my khat chewing practices are dangerous for my unborn child. Then after I stopped chewing due to fear of the problems that will occur on my unborn child."*

Table 2: Khat chewing patterns and perceived reasons of pregnant mothers in eastern parts of Ethiopia, 2022 (N=230).

Variables	Response choices	Frequency	Percent
Khat chewing during current pregnancy (n=230)	Yes	63	27.4%
	No	167	72.6%
Frequency of khat chewing (n=63)	Daily	24	38.1%
	More than one day per week	21	33.3%
	Once per week	18	28.6%
Reasons of chewing khat of the respondents (n=63)	For socialization	40	63.5%
	For obeying tradition	38	60.5%
	For excited way of life	31	49.2%
	Unaware of its harm	24	38.1%
	For coping up partner pressure	19	30.2%
	For coping up peer pressure	18	28.6%
	For coping up family pressure	16	25.4%
	For managing life pressure	7	11.1%

Table 3: Revealed the identified themes, sub-themes/categories, and sample quotations from qualitative data of study participants in eastern Ethiopia, 2022 (N=18).

Themes	Sub-themes	Sample quotations
Socio-cultural factors	Social interaction Cultural norms Community norm Cultural habit of the area Influences from peer, close family, and relatives	*As part of this community, I consumed khat daily because I received it from the population, and I feel proud of my chewing.* *Everybody is buying his/her own khat and comes together to chew and to discuss different issues related to the community.* *My friends chewed khat being in a group.* *My chewer friend encouraged me to start chewing to feel free and to be joyful.* *My husband encouraged and enforced me to start chewing khat to be part of the community.* *Our elders encouraged us to begin chewing khat by providing a small amount and also told us on how to use it the first time.*
Dependency	Excitement/as a means of satisfaction Perform activities	*I chewed for feeling of freedom and joy.* *Without khat an individual cannot be able to perform the activities effectively.*
Poor literacy on effect of khat	Lack of awareness on its harm Lack of regular antenatal care visits	*Stopped chewing following antenatal care visits.*

5.1.3 Khat chewing related behaviors and current pregnancy related healthy practices of respondents

Among the total study participants, only 23 (10%) had reported alcohol use during the current pregnancy with a relatively higher proportion (17.5%) among chewers as compared to proportion among non-chewers, 7.2%. Similarly, only 15 (6.5%) of study participants reported tobacco

smoking during current pregnancy with a comparable proportion among chewers and non-chewer study participants. Almost half, 110 (47.8%) and, 111 (48.3%) of study participants respectively had husbands and other family members who practiced khat chewing. All chewer study participants' gestational ages at the time of conducting the study were 8 and 9 months with a higher proportion of 9 months. On the other hand, non-chewer study participant's gestational ages at the time of the interview were between 5 and 9 months. A higher proportion (74.6%) among chewers in the present study had one ANC visit at the time of the interview (Table 4).

Table 4: Comparison of khat chewing related behaviors and current pregnancy related healthy practices of respondents in eastern parts of Ethiopia, 2022 (N=230).

Variables	**Khat chewing practices of study participants**		**Total**	***p*-value**
	Non-chewers, No (%)	**Chewers, No (%)**		
Alcohol use during current pregnancy				
Yes	12 (7.2%)	11 (17.5%)	23	0.021
No	155 (92.8%)	52 (82.5%)	207	
Total	167(100%)	63 (100%)	230	
Cigarette smoke during current pregnancy				
Yes	10 (6%)	5 (7.9%)	15	0.59
No	157 (94%)	58 (92.1%)	215	
Total	167(100%)	63 (100%)	230	
Husbands' khat use				
Yes	60 (35.9%)	50 (79.4%)	110	<0.001
No	107 (64.1%)	13 (20.6%)	120	
Total	167(100%)	63 (100%)	230	
Other family members khat use				
Yes	61 (36.5%)	50 (79.4%%)	111	<0.001
No	106 (63.5%)	13 (20.6%)	119	
Total	167(100%)	63 (100%)	230	
Gestational age at time of interview				
5months	6 (3.6%)	0	6	<0.001

7months	37 (22.2%)	0	37	
8months	46 (27.5%)	23 (36.5%)	69	
9months	78 (46.7%)	40 (63.5%)	118	
Total	167(100%)	63 (100%)	230	
ANC visits number at time of interview				
1	27 (16.2%)	47 (74.6%)	74	<0.001
2	14 (8.4%)	8 (12.7%)	22	
3	43 (25.7%)	3 (4.8%)	46	
4	83 (49.7%)	5 (7.9%)	88	
Total	167(100%)	63 (100%)	230	
Is current pregnancy planned?				
Yes	153 (91.6%)	53 (84.1%)	206	0.098
No	14 (8.4%)	10 (15.9%)	24	
Total	167(100%)	63 (100%)	230	

ANC: ante natal care.

5.1.4 Factors associated with chewing khat during current pregnancy

In the present study, binary logistic regression analysis showed: age, area of residence, educational level, occupation, alcohol use, partners khat chewing and other family members khat chewing were among the factors which significantly associated with current khat chewing of study participants. Of these factors, occupation and alcohol use did not show significant association with current khat chewing on multivariable logistic regression analysis.

In this study, participants aged 26 and above years had a 2.81 times higher (AOR=2.81 95% CI 1.19-6.59) risk of khat chewing practices during their current pregnancy as compared to those participants aged less than 26 years. Participants living in rural area had 2.82 times increased (AOR=2.82 95% CI 1.19-6.69) risk of khat chewing as compared to those study participants living in urban area. Illiterate study participants were 4.31 times at higher risk of khat chewing compared to those participants with tertiary education level (AOR=4.31 95% CI 1.02-18.20). Participants having chewer husbands were 3.51 times at higher (AOR=3.51 95% CI 1.33-9.24) risk of chewing khat as compared to those respondents having no chewer husbands. In the current study, respondents with other family members who practiced khat chewing were 3.1 times (AOR=3.05 95% CI 1.19-7.77) at increased risk of khat chewing during current pregnancy as compared to those study participants having no other chewer family members (Table 5). There was no identified multicollinearity among independent variables [variance inflation factor

(VIF)<5) and tolerance >0.1]. Moreover, the Hosmer and Lemeshow goodness of fit test result value was insignificant (p>0.05).

Table 5: Bivariable and multivariable logistic regression of chewing khat during current pregnancy in eastern Ethiopia, 2022 (N=230).

Variables	Khat chewing practices of study participants		COR (95%CI)	AOR (95%CI)
	Non-chewers, No (%)	Chewers, No (%)		
Age group of study participants				
<26 years	82 (49.1%)	16 (25.4%)	1	1
>=26 years	85 (50.9%)	47 (74.6%)	2.83 (1.49-5.39)**	2.81 (1.19-6.59)*
Participants area of residence				
Urban	99 (59.3%)	13 (20.6%)	1	1
Rural	68 (40.7%)	50 (79.4%)	5.6 (2.83-11.09)***	2.82 (1.19-6.69)*
Participants ethnicity				
Oromo	63 (37.7%)	33 (52.4%)	1.26 (0.41-3.87)	1.60 (0.33-7.69)
Harari	32 (19.2%)	11 (17.5%)	0.83 (0.24-2.87)	1.71 (0.31-9.32)
Amhara	35 (20.9%)	5 (7.9%)	0.34 (0.08-1.39)	0.98 (0.15-6.37)
Somali	25 (15%)	9 (14.3%)	0.86 (0.24-3.15)	1.02 (0.17-6.04)
Others (Tigre and Gurage)	12 (7.2%)	5 (7.9%)	1	1
Participants religion				
Muslim	105 (62.9%)	46 (73%)	1.75 (0.56-5.53)	0.85 (0.19-3.71)
Orthodox	46 (27.5%)	13 (20.6%)	1.13 (0.32-3.97)	0.95 (0.18-5.07)
Protestant	16 (9.6%)	4 (6.4%)	1	1
Participants educational status				
No formal education	61 (36.5%)	35 (55.6%)	4.45 (1.45-13.64)**	4.31 (1.02-18.20)*
Primary education	41 (24.6%)	19 (30.1%)	3.59 (1.11-11.63)*	2.43 (0.53-11.13)
Secondary education	34 (20.4%)	5 (7.9%)	1.14 (0.28-4.63)	0.75 (0.13-4.38)

Tertiary education	31 (18.5%)	4 (6.4%)	1	1
Participants Occupation				
House wife/ Homemaker	32 (19.2%)	22 (34.9%)	1	1
Farmer	42 (25.1%)	18 (28.6%)	0.62 (0.29-1.35)	0.52 (0.19-1.39)
Government employee	39 (23.3%)	3 (4.8%)	0.11 (0.03-0.41)**	0.37 (0.07-2.04)
Non-government employee	9 (5.4%)	2 (3.2%)	0.32 (0.06-1.64)	1.06 (0.12-9.47)
Merchant	36 (21.6%)	13 (20.6%)	0.53 (0.23-1.21)	0.83 (0.27-2.52)
Daily laborer	9 (5.4%)	5 (7.9%)	0.81 (0.24-2.74)	1.38 (0.26-7.34)
Participants marital status				
Currently married	122 (73.1%)	50 (79.4%)	1.42 (0.71-2.86)	2.11 (0.82-5.39)
Divorced and widowed	45 (26.9%)	13 (20.6%)	1	1
Participants monthly HH income (ETB)				
<4500	72 (43.1%)	31 (49.2%)	1	1
>=4500	95 (56.9%)	32 (50.8%)	0.78 (0.44-1.39)	1.58 (0.68-3.68)
Alcohol use during current pregnancy				
Yes	12 (7.2%)	11 (17.5%)	2.73 (1.14-6.56)*	2.28 (0.64-8.18)
No	155 (92.8%)	52 (82.5%)	1	1
Cigarette smoking during current pregnancy				
Yes	10 (6%)	5 (7.9%)	1.35 (0.44-4.13)	2.06 (0.44-9.65)
No	157 (94%)	58 (92.1%)	1	1
Husbands' khat use				
Yes	60 (35.9%)	50 (79.4%)	6.86 (3.45-13.64)***	3.51 (1.33-9.24)*
No	107 (64.1%)	13 (20.6%)	1	1
Other family members khat use				
Yes	61 (36.5%)	50 (79.4%)	6.68 (3.36-	3.05 (1.19-7.77)*

			13.28)***	
No	106 (63.5%)	13 (20.6%)	1	1

*=p<0.05, **=p<0.005, ***=p<0.001, COR= crude odds ratio, AOR= adjusted odds ratio, CI= confidence interval.

5.2 Maternal, pregnancy, neonatal, umbilical cord, and placental outcomes following chewing of khat during pregnancy

5.2.1 Participants classification

A total of 344 study participants were enrolled (172 non-khat chewers and 172 khat chewers) at the beginning of the study. Of them, 320 (164 non-khat chewers and 156 khat chewers) completed the follow up resulting in a loss to follow up rate of 7%. The reasons of loss to follow up in the present study were refusal to continue (7 enrolled respondents), moved to other places (3 enrolled respondents), death (3 enrolled respondents) and home delivery (11 enrolled respondents) (Figure 2).

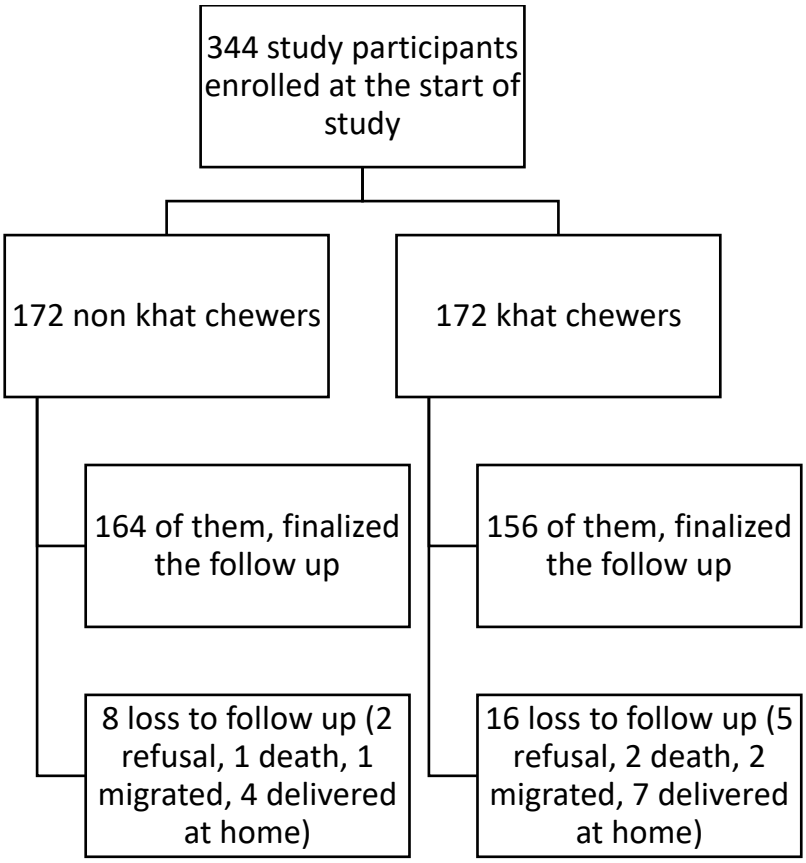


Figure 2: Flow diagram of the study participants' involvement status in the follow up of current study conducted in Dire Dawa, Harar and Jigjiga selected hospitals, eastern Ethiopia, August to December 2022.

5.2.2 Sociodemographic characteristics of the study cohorts

The overall mean (SD) age of cohort mothers in the present study was 26.29 ±5.49 years (range 17-45 years), with the majority (38.1%) aged between 25 and 29 years old. The majority of the study cohorts were ethnic Oromo, 147 (45.9%); Muslim religion followers, 216 (67.5%); and residing in urban areas, 176 (55%). Of the study cohorts, 99 (30.9%) had no formal education and 80 (25%) had a primary education level while 93 (29.1%) and 90(28.1%) were merchants and farmers in occupation, respectively. The great majority, 269 (84.1%) of the study cohorts were married. The median [inter quartile range (IQR)] monthly household income of the study cohorts was 4800.0±3500.0 Ethiopian birr (range 1,000.0-15,000.0 Ethiopian birr) (Table 6).

Table 6: Distribution of sociodemographic characteristics of study participants followed from midterm of pregnancy to delivery by their khat chewing status in eastern parts of Ethiopia, 2022 (N=320).

Characteristics	Study cohorts khat chewing status		*p*-value
	Chewers, Frequency (%)	Non-chewers, Frequency (%)	
Age of study participants (in years)			
<=19	0	17 (10.4%)	<0.001
20-24	48 (30.8%)	57 (34.8%)	
25-29	63 (40.4%)	59 (35.9%)	
30-34	20 (12.8%)	24 (14.6%)	
>=35	25 (16%)	7 (4.3%)	
Mean (SD) age (in years)	27.48±5.96	25.17±4.77	
Residence of participants			
Urban	50 (32.1%)	126 (76.8%)	<0.001
Rural	106 (67.9%)	38 (23.2%)	
Ethnicity of participants			
Oromo	74 (47.4%)	73 (44.5%)	0.004
Amhara	33 (21.2%)	29 (17.7%)	
Harari	26 (16.7%)	28 (17.1%)	
Somali	23 (14.7%)	19 (11.6%)	
Others	0	15 (9.1%)	
Religion of participants			
Muslim	110 (70.5%)	106 (64.6%)	0.529
Orthodox	40 (25.6%)	50 (30.5%)	
Protestant	6 (3.9%)	8 (4.9%)	
Education status of			

participants			
No formal education	54 (34.6%)	45 (27.5%)	0.017
Primary education	47 (30.1%)	33 (20.1%)	
Secondary education	30 (19.2%)	43 (26.2%)	
Tertiary education	25 (16.1%)	43 (26.2%)	
Participants Occupation			
Merchant	51 (32.7%)	42 (25.6%)	0.605
Farmer	43 (27.6%)	47 (28.7%)	
Homemaker	32 (20.5%)	36 (21.9%)	
Employee	23 (14.7%)	27 (16.5%)	
Daily laborer	7 (4.5%)	12 (7.3%)	
Participants marital status			
Currently married	129 (82.7%)	140 (85.4%)	0.479
Divorced	25 (16%)	20 (12.2%)	
Widowed	2 (1.3%)	4 (2.4%)	
Monthly HH income (ETB)			
<=4950.0	86 (55.1%)	78 (47.6%)	0.176
>4950.0	70 (44.9%)	86 (52.4%)	

HH=household; ETB=Ethiopian birr.

5.2.3 Description of khat chewing characteristics of chewer cohorts

The mean (SD) duration of khat chewing for chewer cohorts in this study was 34.77±15.37 months (range 12-60 months), with the higher duration of chewing, 76 (48.7%) for 12-24

months. More than half, 82 (52.6%) of chewer cohorts had a khat chewing frequency of greater or equal to 4 days per a week. The median [inter quartile range (IQR)] amount of khat consumed at a single khat chewing session was 90±50grams. Fifty-eight (37.2%), 56 (35.9%), and 42 (26.9%) of chewer cohorts consumed 50-75, 76-100 and >100 grams of khat per single khat chewing session, respectively. The mean (SD) duration of khat chewing in a single chewing session was 3.95±0.69 hours, with the duration for majority of chewer cohorts, 122 (78.2%) 3-4 hours (Table 7).

Table 7: Description of khat chewing characteristics of chewer cohorts in eastern parts of Ethiopia, 2022 (n=156).

Chewing characteristics	**Frequency**	**Percent**
Duration of khat chewing practices of chewer cohorts (in months)		
12-24months	76	48.7%
25-48months	62	39.7%
>=49months	18	11.5%
Frequency of khat chewing practices of chewer cohorts		
Daily	74	47.4%
>=4 days per a week	82	52.6%
Amount of khat consumed per single chewing session (in grams)		
50-75grams	58	37.2%
76-100grams	56	35.9%
>100grams	42	26.9%
Duration of khat chewing per a single chewing session (in hours)		
3 hours	42	26.9%
4 hours	80	51.3%

5 hours	34	21.8%

5.2.4 Distribution of behavioral characteristics of study cohorts

In total, 43 study participants; 31 (19.9%) among chewers and 12 (7.3%) among non-khat chewers consumed alcohol of any type when they were pregnant. Out of all study participants, 27(8.4%), 13 (4.1%) and 9 (2.8%) consumed beer, wine and locally prepared alcohol (Tela) respectively. Among consumers of alcohol, 6 (15%) of the consumer cohorts consumed 16.5grams of alcohol in a week; 14 (35%) consumed 27.5-33grams of alcohol in a week, and the remaining consumer cohorts, which is 20 (50%) consumed 49.5-55 grams of alcohol in a week. Out of the total, 18 (5.63%) of the cohorts were practiced smoking of tobacco products, and almost all (95%) of the study cohorts were consumed coffee (Table 8).

Table 8: Distribution of behavioral characteristics of khat chewer and non-chewer cohorts in eastern Ethiopia, 2022 (N=320).

Characteristics	**Khat chewing practices of the study cohorts**		**p-value**
	Chewers, Frequency (%)	**Non-chewers, Frequency (%)**	
Alcohol intake in last 1 months of pregnancy			
Yes	31 (19.9%)	12 (7.3%)	<0.001
No	125 (80.1%)	152 (92.7%)	
Beer intake in last 1 months of pregnancy			
Yes	21 (13.5%)	6 (3.7%)	0.002
No	135 (86.5%)	158 (96.3%)	
Amount of beer consumed (in bottle and gram equivalents) in a week			
1 bottle (16.5grams of alcohol)	5 (23.8%)	1 (16.7%)	0.755

2 bottles (33 grams of alcohol)	7 (33.3%)	3 (50%)	
3 bottles (49.5 grams of alcohol)	9 (42.9%)	2 (33.3%)	
Wine intake in last 1 months			
Yes	8 (5.1%)	5 (3%)	0.346
No	148 (94.9%)	159 (97%)	
Amount of wine consumed (in glass and gram equivalents) in a week			
1 glass (27.5 grams of alcohol)	2 (25%)	2 (40%)	0.569
2 glasses (55 grams of alcohol)	6 (75%)	3 (60%)	
Homemade alcohol drinks (Tela)			
Yes	6 (3.8%)	3 (1.8%)	0.275
No	150 (96.2%)	161 (98.2%)	
Overall levels of alcohol consumed in a week (converted to standard measures)			
<1.5drinks (16.5grams of alcohol) (low)	5 (17.2%)	1 (9%)	0.641
1.5-3.5drinks (27.5-33 grams of alcohol) (moderate)	9 (31.1%)	5 (45.5%)	
>3.5drinks (49.5-55 grams of alcohol) (high)	15 (51.7%)	5 (45.5%)	

Smoking of any tobacco products			
Yes	14 (9%)	4 (2.4%)	0.011
No	142 (91%)	160 (97.6%)	
Frequency of tobacco smoking			
Daily	4 (28.6%)	3 (75%)	0.093
More than one day per a week	10 (71.4%)	1 (25%)	
Coffee use of study cohorts			
Yes	151 (96.8%)	153 (93.3%)	0.151
No	5 (3.2%)	11 (6.7%)	

5.2.5 Obstetric distribution patterns of study cohorts

The majority, 174 (54.4%) of the study cohorts, were multigravida (having >=three pregnancies); of them, 106 (67.9%) were among chewer cohorts, and the rest, 68 (41.5%), were among non-chewer cohorts. Of the total, 148 (46.3%) of the study cohorts were multipara (having >=two children); of them, 87 (55.8%) were among chewer cohorts, and the remaining 61 (37.2%) were among non-chewer cohorts. Fifty-three (16.6%) of the study cohorts had a previous history of cesarean section delivery. One hundred four (32.5%) of the study cohorts had a previous history of spontaneous abortion; of them, 84 (53.8%) were among khat chewer cohorts. Fifty (15.6%) of the study cohorts had a previous history of stillbirth, with 26 (16.7%) were among chewer cohorts and 24 (14.6%) among non-chewer cohorts. The majority, 264 (82.5%) of the study cohorts' gestational age at the time of enrollment to the study was 24-26 weeks, and the majority, 240 (75%) of the study cohorts, had the first time visit of the hospitals at the time of enrollment to the study. Only 37 (11.6%) of the study cohorts had at least 4 ANC visits at the end of pregnancy; of this, the majority (19.5%) were among non-khat chewer cohorts (Table 9).

Table 9: Distribution of obstetric characteristics of study cohorts by their khat chewing practices in eastern Ethiopia, 2022 (N=320).

Obstetric characteristics	Khat chewing status of study cohorts		
	Chewers, Frequency (%)	Non-chewers, Frequency (%)	*p*-value
Gravida			
1 (primigravida)	24 (15.4%)	60 (36.6%)	<0.001
2 (secundigravida)	26 (16.7%)	36 (21.9%)	
>=3 (multigravida)	106 (67.9%)	68 (41.5%)	
Para			
0 (nullipara)	42 (26.9%)	68 (41.5%)	0.003
1 (primipara)	27 (17.3%)	35 (21.3%)	
>=2(multipara)	87 (55.8%)	61 (37.2%)	
Mode of delivery of previous pregnancies			
Vaginal deliveries	123 (78.8%)	144 (87.8%)	0.031
Cesarean section deliveries	33 (21.2%)	20 (12.2%)	
Spontaneous abortion history			
Yes	84 (53.8%)	20 (12.2%)	<0.001
No	72 (46.2%)	144 (87.8%)	
Previous still birth history			
Yes	26 (16.7%)	24 (14.6%)	0.617
No	130 (83.3%)	140 (85.4%)	
Gestational age at time of enrollments			
24-26 weeks	125 (80.1%)	139 (84.8%)	0.276
27-28 weeks	31 (19.9%)	25 (15.2%)	
ANC visits at time of enrollments			
1st	126 (80.8%)	114 (69.5%)	0.02

2nd	30 (19.2%)	50 (30.5%)	
Number of ANC visits attended at the end of delivery			
<4 ANC visits	151 (96.8%)	132 (80.5%)	<0.001
>=4 ANC visits	5 (3.2%)	32 (19.5%)	
History of malaria			
Yes	5 (3.2%)	6 (3.7%)	0.824
No	151 (96.8%)	158 (96.3%)	

5.2.6 Physical measurements of the study cohorts

The overall mean (SD) weight of study cohorts was 63.28±9.19kg. Out of the total study participants, 150 (46.9%) of them weighed between 61 to 70kg. The mean (SD) height of the study cohorts was 157.46±13.34cm, with the highest cohorts, 205 (64.1%), measured above 157cm high. The overall mean (SD) BMI of the cohorts was 25.7±3.9 kg/m^2 (range 17.6-37.8 kg/m^2). Out of the total study participants, 8 (2.5%) of them had BMI <18.5kg/m^2, and 50 (15.6%) had BMI >=30kg/m^2. The mean (SD) MUAC of the cohorts was 26.92±3.49cm. Out of the total study participants, 46 (14.4%) of them had less than 23 cm MUAC value, and 19 (5.9%) had >=33cm. The mean (SD) heart rate and respiratory rate of the study cohorts were 92.68±8.97 beats per minute and 22.49±1.56 breaths per minute, respectively. The overall mean (SD), systolic and diastolic blood pressure of the study cohorts, respectively, was 121.19±14.26 and 77.01±14.53mmHg (Table 10).

Table 10: Comparison of bodily measurements of khat chewer and non-khat chewer study cohorts in eastern Ethiopia, 2022 (N=320).

Measurements	**Khat chewing characteristics of the study cohorts**		***p*-value**
	Chewers, Frequency (%)	**Non-chewers, Frequency (%)**	
Weight (in kg)			
<50kg	8 (5.1%)	9 (5.5%)	<0.001

50-60kg	63 (40.4%)	47 (28.7%)	
61-70kg	54 (34.6%)	96 (58.5%)	
>70kg	31 (19.9%)	12 (7.3%)	
Mean (SD) weight (in kg)	63.48±10.67	63.08±7.55	0.697
Height (in cm)			
<145cm	18 (11.5%)	19 (11.6%)	0.967
145-157cm	39 (25%)	39 (23.8%)	
>157cm	99 (63.5%)	106 (64.6%)	
Mean (SD) height (in cm)	157.31±13.92	157.59±12.81	0.85
BMI (in kg/m^2)			
<18.5	4 (2.6%)	4 (2.4%)	<0.001
18.5-24.9	82 (52.6%)	70 (42.7%)	
25-29.9	35 (22.4%)	75 (45.7%)	
>=30	35 (22.4%)	15 (9.2%)	
Mean (SD) BMI (in kg/m^2)	25.86±4.29	25.61±3.39	0.559
MUAC (in cm)			
<23cm	22 (14.1%)	24 (14.6%)	0.013
23-27.9cm	77 (49.4%)	62 (37.8%)	
28-32.9cm	44 (28.2%)	72 (43.9%)	
>=33cm	13 (8.3%)	6 (3.7%)	
Mean (SD) MUAC (in cm)	26.96±3.77	26.81±3.24	0.701
Mean (SD) body temperature (in degree Celsius)	36.68±0.50	36.65±0.60	0.627
Mean (SD) respiratory rate (in breaths per minute)	22.58±1.96	22.41±1.06	0.336

Mean (SD) heart rate (in beats per minute)	93.09±9.54	92.29±8.39	0.424
Mean (SD) fetal heart rate (in beats per minute)	141.11±11.86	141.91±10.42	0.531
Mean (SD) pulse oximetry (in %)	96.22±4.00	96.81±5.43	0.274
Mean (SD) SBP (in mmHg)	124.33±16.48	118.21±10.67	<0.001
Mean (SD) DBP (in mmHg)	78.53±16.25	75.55±12.56	0.067
Urinary glucose (in dipstick)			
Negative	140 (89.7%)	146 (89%)	0.878
(+)	11 (7.1%)	11 (6.7%)	
(+++)	5 (3.2%)	7 (4.3%)	
Urinary protein (in dipstick)			
Negative	121 (77.6%)	141 (86%)	0.015
(+)	10 (6.4%)	12 (7.3%)	
(++)	18 (11.5%)	4 (2.4%)	
(+++)	7 (4.5%)	7 (4.3%)	

SBP=systolic blood pressure; DBP=diastolic blood pressure.

5.2.7 Blood sample analysis results of the study cohorts

The study cohorts' overall mean (SD) haemoglobin concentration was 11.25±2.12g/dl, and their mean (SD) hematocrit was 32.84±5.97%. The overall mean (SD) random blood sugar level of the study cohorts was 98.78±27.32mg/dl (range;78-250mg/dl). In the present study, a significantly low mean (SD) random blood glucose level was observed among khat chewer cohorts (95.19±22.48mg/dl) compared to non-khat chewer cohorts (102.19±30.92mg/dl) (p<0.05) (Table 11).

Table 11: Comparison of the mean blood sample analysis results of khat chewer and non-khat chewer study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing status of the study cohorts		
Blood sample analysis	**Chewers, Frequency (%)**	**Non-chewers, Frequency (%)**	***p*-value**
Mean (SD) haemoglobin (Hgb) (in g/dl)	11.11±2.38	11.38±1.83	0.259
Mean (SD) hematocrit (Hct) (in %)	32.54±6.74	33.13±5.14	0.376
Mean (SD) White Blood Cells count (per µL)	9164.85±2341.86	8799.21±2713.25	0.199
Mean (SD) platelets (per µL)	229,589.7±107,095.79	213,945.1±80,837.43	0.14
Mean (SD) random blood glucose (in mg/dl)	95.19±22.48	102.19±30.92	0.022

5.2.8 **Identified maternal outcomes of the study cohorts**

The overall magnitude of anemia among pregnant cohorts was 124 [38.8% (95% CI:33.1-44.1)]; of them, 76 (48.7%) were among khat chewer cohorts, and 48 (29.3%) were among non-khat chewer cohorts (p<0.001). The overall magnitude of gestational hypertension among pregnant cohorts was 68 [21.3% (95% CI: 17.2-25.9); of them, 45 (28.8%) were among khat chewers cohorts, and 23 (14%) were among non-khat chewer cohorts (p=0.001) (Table 12). Among the study cohorts, there were 3 (0.9%) maternal deaths and the cause of maternal deaths claimed by the cases handling physician were abruptio placenta and hemorrhage.

Table 12: Comparison of identified maternal outcomes among khat chewer and non-khat chewer study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing characteristics of the study cohorts	
Maternal findings	**Chewers, Frequency**	**Non-chewers,**

	(%)	Frequency (%)	*p*-value
Maternal anemia (Hgb<10.5g/dl for 2nd TM; Hgb<11 for 3rd TM)			
Yes	76 (48.7%)	48 (29.3%)	<0.001
No	80 (51.3%)	116 (70.7%)	
Gestational hypertension (systolic BP>140mmHg or diastolic BP>40mm Hg)			
Yes	45 (28.8%)	23 (14%)	0.001
No	111 (71.2%)	141 (86%)	
Gestational diabetes (FBS: 92-125mg/dl)			
Yes	1 (0.6%)	3 (1.8%)	0.339
No	155 (99.4%)	161 (98.2%)	
Vaginal bleeding			
Yes	22 (14.1%)	7 (4.3%)	0.002
No	134 (85.9%)	157 (95.7%)	
Vaginal watery discharge			
Yes	7 (4.5%)	3 (1.8%)	0.172
No	149 (95.5%)	161 (98.2%)	
Vision changes			
Yes	14 (9%)	11 (6.7%)	0.45
No	142 (91%)	153 (93.3%)	

TM=trimester; FBS=fasting blood sugar.

5.2.9 Identified pregnancy outcomes of the study cohorts

The overall mean (SD) estimated fetal weight of the study cohorts was 2519.72±796.54grams. Moreover, a significantly low mean (SD) estimated fetal weight was observed among khat chewer cohorts (2110.14±788.84grams) compared to non-khat chewer cohorts (2909.32±580.25grams) (p<0.001).

The overall magnitude of fetal growth restriction among the study cohorts was 95 (29.7%); of this, 81 (51.9%) were among khat chewer cohorts, and the remaining 14 (8.5%) were among non-khat chewer cohorts. More importantly, in the present study, 98.95% of the ultrasound-identified fetuses with FGR were found to be SGA at birth. Hence, in the current study, FGR was highly associated with SGA at birth. The overall magnitude of oligohydramnios in the present study was 66 (20.6%), and there were 3 (0.9%) identified cases of polyhydramnios and 2 (0.6%) identified cases of hydrops fetalis. In the present study, the overall magnitude of abruption placenta among the study cohorts was 31(9.7%); of this, 26 (16.7%) were among khat chewer cohorts. Among the present study cohorts, the magnitude of preterm labor was 21 (6.6%), with the highest magnitude, 18 (11.5%) among chewers; and the magnitude of pre-labor rupture of the membranes was 83 (25.9%) with the greatest magnitude, 70 (44.9%) being among khat chewer cohorts (Table 13).

Furthermore, the incidence rate of fetal growth restriction among khat chewer cohorts was 45.5 per 1000 fetuses week (95%CI 36.6-56.5), whereas the incidence of fetal growth restriction among births of non-chewer cohorts was 6.5 per 1000 fetuses week (95%CI 3.8-10.9).

Table 13: Comparison of identified pregnancy outcomes among khat chewer and non-khat chewer study cohorts in eastern Ethiopia, 2022 (N=320).

Pregnancy outcomes identified	**Khat chewing characteristics of the study cohorts**		
	Chewers, Frequency (%)	**Non-khat chewers, Frequency (%)**	***p*-value**
Fetal growth restriction (estimated fetal weight below 10th percentile for			

GA)			
Yes	81 (51.9%)	14 (8.5%)	<0.001
No	75 (48.1%)	150 (91.5%)	
Oligohydramnios			
Yes	47 (30.1%)	19 (11.6%)	<0.001
No	109 (69.9%)	145 (88.4%)	
Abruption placenta			
Yes	26 (16.7%)	5 (3%)	<0.001
No	130 (83.3%)	159 (97%)	
Preterm labor			
Yes	18 (11.5%)	3 (1.8%)	<0.001
No	138 (88.5%)	161 (98.2%)	
Pre-labor rupture of membranes			
Yes	70 (44.9%)	13 (7.9%)	<0.001
No	86 (55.1%)	151 (92.1%)	
Decreased or no fetal movement			
Yes	7 (4.5%)	6 (3.7%)	0.707
No	149 (95.5%)	158 (96.3%)	
Fetal distress			
Yes	16 (10.3%)	10 (6.1%)	0.173
No	140 (89.7%)	154 (93.9%)	

GA=gestational age.

5.2.10 Delivery characteristics of the study cohorts

The majority (52.8%) of the study cohorts gave birth due to spontaneous labor. One hundred eighty-one (56.6%) of the study participants gave birth through normal vaginal delivery. For the great majority (90%) of the study cohorts, fetal presentation at delivery was cephalic, and 262 (81.9%) of this study cohorts had a clear amniotic fluid seen at delivery. Following delivery, 188 (58.8%) of the study cohorts were discharged, and the remaining lived maternal cohorts were getting admission to the ward (Table 14).

Table 14: Comparison of the delivery related features of khat chewer and non-khat chewer study cohorts in eastern Ethiopia, 2022 (N=320).

Delivery related features	Khat chewing practices of the cohorts		
	Chewers, Frequency (%)	**Non-chewers, Frequency (%)**	***p*-value**
Indication for delivery/childbirth			
Spontaneous labor	55 (35.3%)	114 (69.5%)	<0.001
Pre-labor rupture of membranes	42 (26.9%)	10 (6.1%)	
Fetal growth restriction	23 (14.7%)	4 (2.4%)	
Gestational hypertension	15 (9.6%)	11 (6.7%)	
Abruptio placenta and vaginal bleeding	11 (7.1%)	7 (4.3%)	
Fetal distress	5 (3.2%)	6 (3.7%)	
Others	5 (3.2%)	12 (7.3%)	
Fetal presentation at delivery			
Cephalic	135 (86.5%)	153 (93.3%)	0.044
Breech	21 (13.5%)	11 (6.7%)	
Mode of delivery			
Normal vaginal	69 (44.2%)	112 (68.3%)	<0.001
Instrumental	13 (8.3%)	11 (6.7%)	
Planned C/S	14 (9%)	13 (7.9%)	
Emergency C/S	60 (38.5%)	28 (17.1%)	
Amniotic fluid at delivery			
Clear	118 (75.6%)	144 (87.8%)	0.005
Meconium stained	38 (24.4%)	20 (12.2%)	

Maternal status following delivery			
Discharge	72 (46.2%)	116 (70.7%)	<0.001
Admission	84 (53.8%)	45 (27.5%)	
Death	0	3 (1.8%)	

Others=previous C/S scare, still birth and fetal presentation; C/S=cesarean section.

5.2.11 Birth outcomes of the study cohorts

Out of the total pregnancies, 307 (95.9%) of them ended in live births and the rest, 13 (4.1%), ended in stillbirths. The overall magnitude of congenital anomalies observed on all births, i.e., live births and stillbirths of the study cohorts, was 16 (5%), and the major birth defects identified were neural tube defects, clubfoot, orofacial clefts, malformation of the external ear and defects of upper and lower limbs.

The overall magnitude of preterm births in the present study cohorts was 96 (30%); of this, 76 (48.7%) of them was among births of khat chewer cohorts. The overall low birth weight magnitude among births of the study cohorts was 127 (39.7%); of this, 94 (60.3%) of the low birth weight was among births of khat chewer cohorts. The overall very low birth weight magnitude in the births of the present study cohorts was 23 (7.2%). Moreover, the overall magnitude of small for gestational age at birth among the present study cohorts was 100 (31.3%); 84 (53.8%) were among khat chewer cohorts' deliveries (Table 15).

Moreover, the preterm incidence rate among births of khat chewer cohorts was 42.7 per 1000 live births week (95%CI 34.1-53.4), and the incidence among births of non-khat chewers was 9.2 per 1000 live births week (95%CI 5.9-14.3). Furthermore, the incidence of low birth weight was 52.8 per 1000 live births week (95%CI 43.1-64.6) among newborns born from cohorts who had khat chewing practice. Whereas the incidence of low birth weight among newborns born from mothers who had no khat chewing practice was 15.2 per 1000 live births week (95%CI 10.8-21.4).

Table 15: Comparison of birth outcomes among khat chewer and non-khat chewer maternal study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing behaviors of study cohorts		
	Chewers, Frequency	**Non-chewers,**	***p*-value**

Birth outcomes	(%)	Frequency (%)	
Newborn status at birth			
Live birth	149 (95.5%)	158 (96.3%)	0.707
Still birth	7 (4.5%)	6 (3.7%)	
Noticed congenital anomalies on both births			
Yes	10 (6.4%)	6 (3.7%)	0.259
No	146 (93.6%)	158 (96.3%)	
Gestational age at birth (in weeks)			
>=37 weeks (full term birth)	80 (51.3%)	144 (87.8%)	<0.001
<37 weeks (preterm birth)	76 (48.7%)	20 (12.2%)	
Birth weight (in kg)			
>=2.5kg (normal birth weight)	62 (39.7%)	131 (79.9%)	<0.001
<2.5kg (low birth weight)	94 (60.3%)	33 (20.1%)	
>=1.5kg (LBW and NBW)	134 (85.9%)	163 (99.4%)	<0.001
<1.5kg (very low birth weight)	22 (14.1%)	1 (0.6%)	
SGA (birth weight <10th percentile for sex specific GA)			
Yes	84 (53.8%)	16 (9.8%)	<0.001
No	72 (46.2%)	148 (90.2%)	

LBW=low birth weight; NBW=normal birth weight; SGA=small for gestational age

5.2.12 Neonatal findings of the study cohorts

Out of the total births, 165 (51.6%) were male in sex and 155 (48.4%) females. The overall mean (SD) gestational age at births of neonates of the study cohorts was 37.3±2.18 weeks. The mean (SD) gestational age at births of neonates of khat chewer cohorts was 36.46±2.34 weeks while the mean (SD) gestational age at births of neonates of non-chewer cohorts was 38.10±1.66 weeks ($p<0.001$). The overall mean (SD) birth weight of neonates born from the study cohort mothers was 2717.81±739.29 grams. The mean (SD) birth weight of neonates among khat chewer cohorts was 2379.49±685.59grams; while the mean (SD) birth weight of neonates among non-khat chewer cohorts was 3039.63±639.49grams ($p<0.001$). The mean (SD) Apgar score of newborns at 1-minute of births of khat chewer and non-khat chewer study cohorts was, 6.99±1.5 and 7.82±0.96 respectively; and also, the mean (SD) Apgar score of newborns at 5-minute of births of khat chewer and non-khat chewer cohort mothers was, 7.74±1.85 and 8.62±0.96 respectively. Moreover, the overall magnitude of low 1-minute Apgar score (<7scores) was 49 (16%) while the magnitude of low 5-minute Apgar score (<7score) was 23 (7.5%). The mean (SD) body temperature of the newborn at birth among khat chewer and non-khat chewer cohort mothers was, 35.74±5.23°C and 36.51±0.83°C respectively. The mean (SD) respiratory rate of the newborn at birth of khat chewer and non-khat chewer study cohorts was, 54.33±18.44 and 51.41±17.68 breaths per minute respectively; and the mean (SD) heart rate of the neonate at birth among khat chewer and non-khat chewer cohort mothers was, 123.38±24.88 and 118.22±28.12 beats per minute respectively (Table 16).

The major neonatal complications identified at the birth of the study cohorts were respiratory distress (19.2%), poor breastfeeding (7.8%), body temperature below 36.5°C (7.5%), body temperature above 37.5°C (3.9%), severe chest indrawing (3.6%), convulsions (2%) and unable to move spontaneously (0.7%). Out of total live births followed from birth to the end of 4th weeks postpartum (end of being neonates), 242 (78.8%) were healthy, 42 (13.7%) of them were admitted to hospital NICU and wards due to being diseased, and 23 (7.5%) died. The mean (SD) age at death of neonates was 2.35±3.43 days. Professionals suggested causes of neonates' death were low birth weight, 11 (47.8%); preterm birth, 10 (43.5%) and congenital anomalies, 2 (8.7%).

Furthermore, the neonatal death rate among khat exposed neonates was 5.4 per 1000 live birth day (95%CI 3.4-8.4), and the death rate among non-khat exposed neonates was 0.9 per 1000 live birth day (95%CI 0.4-2.5).

As shown in figure 3 variations in the survival chance of newborns over the neonatal period had been observed; khat exposed neonates had significantly lower calculated survival probability than non-khat exposed neonates (survival chance during neonatal period in non-khat exposed neonates: 97.9%; 95%CI 95.9%-99.9%; in khat exposed neonates: 88.0%; 95%CI 82.9%-93.1%; log-rank p<0.001).

Table 16: Comparison of neonatal findings of the khat chewer and non-khat chewer maternal study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing characteristics of the cohorts		
Measurements	**Chewers, Frequency (%)**	**Non-khat chewers, Frequency (%)**	***p*-value**
Sex of neonates			
Male	80 (51.3%)	85 (51.8%)	0.922
Female	76 (48.3%)	79 (48.2%)	
Mean (SD) gestational age at birth of neonates (in weeks)	36.46±2.34	38.10±1.66	<0.001
Mean (SD) birth weights of neonates (in grams)	2379.49±685.59	3039.63±639.46	<0.001
Mean (SD) 1-minute Apgar score	6.99±1.5	7.82±0.96	<0.001
Mean (SD) 5-minute Apgar score	7.74±1.85	8.62±0.96	<0.001
Level of 1-minute Apgar scores			
<7 scores	40 (26.8%)	9 (5.7%)	<0.001
>=7scores	109 (73.2%)	149 (94.3%)	

Level of 5-minutes Apgar scores			
<7 scores	18 (12.1%)	5 (3.2%)	0.003
>=7 scores	131 (87.9%)	153 (96.8%)	
Body temperature at birth (in degree Celsius)	35.74±5.23	36.51±0.83	0.072
Mean (SD) respiratory rate at birth (in breaths per minute)	54.33±18.44	51.41±17.68	0.158
Mean (SD) heart rate at birth (in beats per minute)	123.38±24.88	118.22±28.12	0.091
Pulse oximetry (in %)	93.26±15.43	96.20±4.14	0.022
Identified neonatal problems at birth (physical examination)			
Respiratory distress at birth			
Yes	46 (30.9%)	13 (8.2%)	<0.001
No	103 (69.1%)	145 (91.8%)	
Other neonatal complications at birth			
No	100 (67.1%)	129 (81.6%)	0.002
Poor feeding	17 (11.5%)	7 (4.4%)	
Temperature<36.5°C	11 (7.4%)	12 (7.6%)	
Temperature>37.5°C	4 (2.7%)	8 (5.1%)	
Severe chest indrawing	9 (6%)	2 (1.3%)	
Convulsions	6 (4%)	0	

Not able to move spontaneously	2 (1.3%)	0	
Neonates' status at the end of 4th weeks postpartum			
Healthy	105 (70.4%)	137 (86.7%)	<0.001
Admitted to NICU and wards	25 (16.8%)	17 (10.8%)	
Died	19 (12.8%)	4 (2.5%)	

NICU=neonatal intensive care unit.

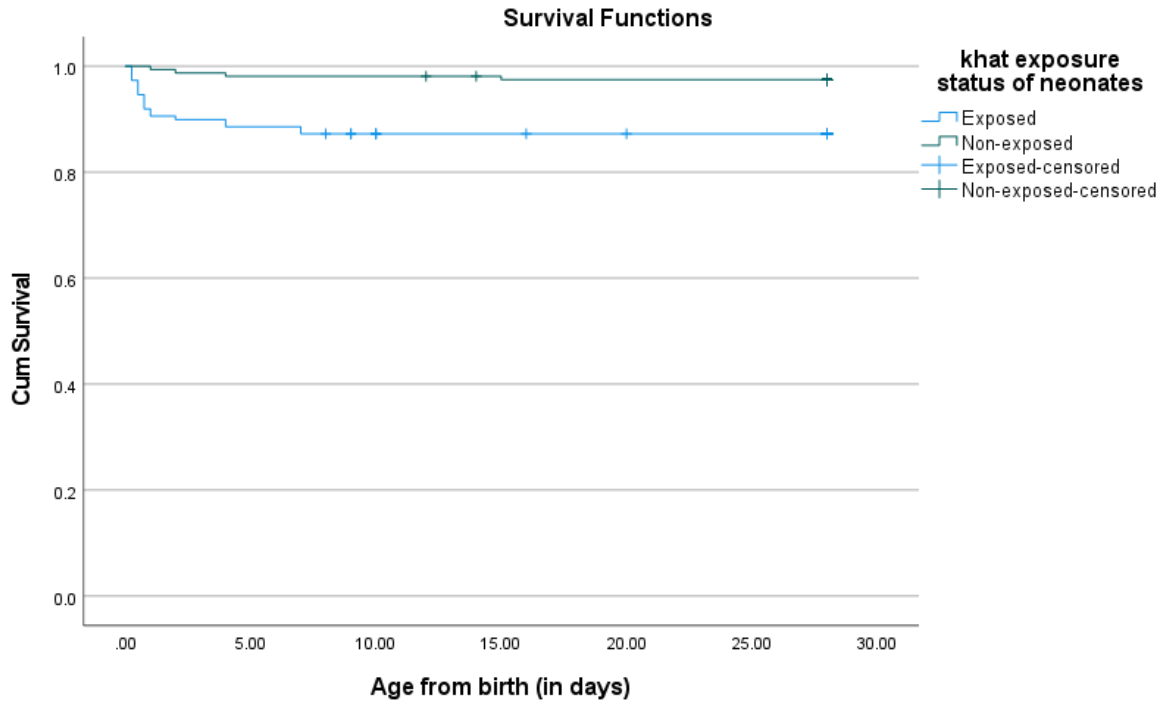


Figure 3: Revealed the probability of survival of the newborn during the neonatal period among live births of the study cohorts in eastern Ethiopia, 2022 (N=307).

5.2.13 Umbilical cord and placental outcomes

The overall mean (SD) umbilical cord length of births of the cohort mothers was 53.59±14.59 cm (range 25-90cm), with 9 (2.8%) births, umbilical cord length <30cm.

The umbilical cord insertion in the present study cohorts was, central in 230 (71.9%) births, eccentric in 57 (17.8%) births and marginal in 33 (10.3%) births. The umbilical cord of 253 (79.1%) study cohorts was normally twisted; and the magnitude of under and hyper coiled umbilical cords among the study cohorts was 41 (12.8%), and 26 (8.1%) respectively. In addition, true knot was identified in 43 (13.4%) umbilical cords of the study cohorts.

The overall mean (SD) placental weight of births of cohort mothers was 490.73±75.00grams (range 300-610grams) while the overall mean (SD) placental-to-birth-weight ratio was 19.71±7.35 (range 8.63-49.17). Two hundred thirteen (66.6%) of the placental shape of the study cohorts was rounded whereas 101 (31.6%) and 6 (1.9%) of the study cohorts placental shape was oval and irregular respectively (Table 17).

Table 17: Comparison of umbilical cord and placental findings of the khat chewer and non-khat chewer maternal study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing characteristics of the study cohorts		
Parameters	**Chewers, Frequency (%)**	**Non-khat chewers, Frequency (%)**	***p*-value**
Mean (SD) umbilical cord length (in cm)	56.62±16.56	50.71±11.78	<0.001
Umbilical cord insertions			
Central	101 (64.7%)	129 (78.7%)	0.02
Eccentric	34 (21.8%)	23 (14%)	
Marginal	21 (13.5%)	12 (7.3%)	
Twists of umbilical cord			
Under coiled	29 (18.6%)	12 (7.3%)	0.002
Normal	111 (71.1%)	142 (86.6%)	
Hyper twisted	16 (10.3%)	10 (6.1%)	
True knots identified in umbilical cords			
Yes	27 (17.3%)	16 (9.8%)	0.048

No	129 (82.7%)	148 (90.2%)	
Mean (SD) placental weight (in grams)	497.87±74.61	483.94±74.97	0.097
Mean (SD) placental diameter (in cm)	22.61±3.23	21.84±2.77	0.022
Mean (SD) placental thickness (in cm)	3.05±0.55	2.86±0.59	0.004
Shape of placenta at delivery			
Round	104 (66.7%)	109 (66.5%)	0.035
Oval	46 (29.5%)	55 (33.5%)	
Irregular	6 (3.8%)	0	

5.2.14 **The relationship between khat chewing practices during pregnancy and maternal anemia and gestational hypertension**

As detailed in table 18, the generalized linear model (GLM) for the binomial family analysis results revealed that the adjusted relative risk of developing anemia among khat chewer cohorts was 1.85 times higher (aRR=1.85; 95%CI 1.47-2.33) compared to non-chewer cohorts. Moreover, the attributable risk of maternal anemia due to khat chewing was 19.5% (95%CI 8.96-29.93) (p<0.001). In the same way, the adjusted relative risk of developing gestational hypertension among chewer cohorts was 2.44 times higher (aRR=2.44; 95%CI 1.43-4.18) compared to non-chewer cohorts. Moreover, the attributable risk of gestational hypertension due to khat chewing was 14.8% (95%CI 5.95-23.69) (p=0.001).

Table 18: The association between khat chewing practices during pregnancy and selected maternal outcomes of the study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing characteristics			
Maternal outcome	**Chewers, Frequency (%)**	**Non-chewers, Frequency (%)**	**(aRR)*(95% CI)**	***p*-value**
Maternal anemia				

Anemic	76 (48.7%)	48 (29.3%)	1.85 (1.47-2.33)	<0.001
Non-anemic	80 (51.3%)	116 (70.7%)	1	
Maternal outcome			**(aRR)**(95% CI)**	
Gestational hypertension				
Yes	45 (28.8%)	23 (14%)	2.44 (1.43-4.18)	<0.001
No	111 (71.2%)	141 (86%)	1	

*=adjusted for altitude, residence, religion, occupation, monthly HH income, smoking, number of ANC visits, MUAC, BMI. **=adjusted for residence, educational status, occupational status, alcohol use, tobacco smoking, number of ANC visits, MUAC, BMI.

Furthermore, a slight difference has been observed between khat chewing duration and maternal anemia and gestational hypertension as shown in figure 4.

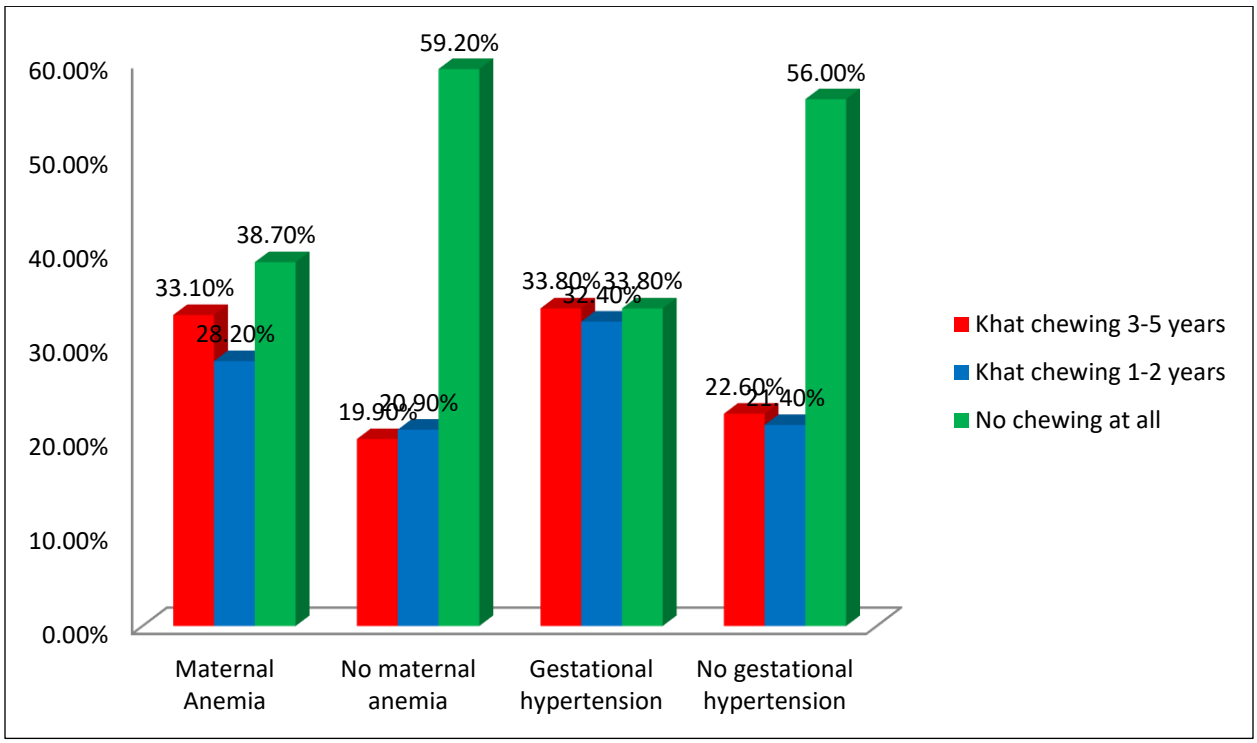


Figure 4: Revealed khat chewing duration association with maternal anemia and gestational hypertension among the study cohorts in eastern Ethiopia, 2022 (N=320).

5.2.15 The association between khat chewing practices during pregnancy and selected pregnancy outcomes

As explained in table 19, the GLM for the binomial family analysis revealed that, the adjusted relative risk of fetal growth restriction among khat chewer cohort mothers was 4.32 times higher (aRR=4.32; 95%CI 2.62-7.12) (p<0.001) compared to non-khat chewer cohorts. In addition, the attributable risk of fetal growth restriction due to khat chewing was 43.4% (95%CI 34.46-52.32). In the same manner, the adjusted relative risk of developing abruptio placenta among khat chewer cohorts was 3.18 times higher (aRR=3.18; 95%CI 1.11-9.08) (p<0.05) compared to non-khat chewer cohorts. In addition, the attributable risk of developing abruptio placenta due to khat chewing was 13.6% (95%CI 7.21-20.03) (p<0.001). In the present cohort study, the adjusted relative risk of developing pre-labor rupture of membranes was 7.97 times higher (aRR=7.97; 95%CI 4.49-14.44) (p<0.001) among khat chewers compared to non-khat chewers. More importantly, the attributable risk of pre-labor rupture of membranes due to khat chewing in the current study was 36.9% (95%CI 28.11-45.78).

Table 19: The association between khat chewing practices during pregnancy and selected pregnancy outcomes of the study cohorts in eastern Ethiopia, 2022 (N=320).

	Khat chewing practices of cohorts			
Pregnancy outcome	**Chewers, Frequency (%)**	**Non-chewers, Frequency (%)**	**(aRR)*(95%CI)**	***p*-value**
Fetal growth restrictions				
Yes	81 (51.9%)	14 (8.5%)	4.32 (2.62-7.12)	<0.001
No	75 (48.1%)	150 (91.5%)	1	
Pregnancy outcome			**(aRR)**(95%CI)**	
Abruption placenta				
Yes	26 (16.7%)	5 (3%)	3.18 (1.11-9.08)	<0.05
No	130 (83.3%)	159 (97%)	1	
Pregnancy outcome			**(aRR)***(95%CI)**	

Pre-labor rupture of membranes				
Yes	70 (44.9%)	13 (7.9%)	7.97 (4.49-14.44)	<0.001
No	86 (55.1%)	151 (92.1%)	1	

*=adjusted for maternal age, residence, education status, occupation status, alcohol use, tobacco smoke, ANC visits, MUAC, BMI, oligohydramnios, placental abruptio, true knots in umbilical cord.

**=adjusted for education status, occupational status, multiparity, tobacco smokes, maternal anemia, previous C/S scare, PROM, spontaneous abortion history.

***= adjusted for residence, educational status, occupational status, alcohol use, tobacco use, maternal anemia, gestational hypertension, BMI, previous C/S scare, spontaneous abortion history.

5.2.16 **Mediation analysis results**

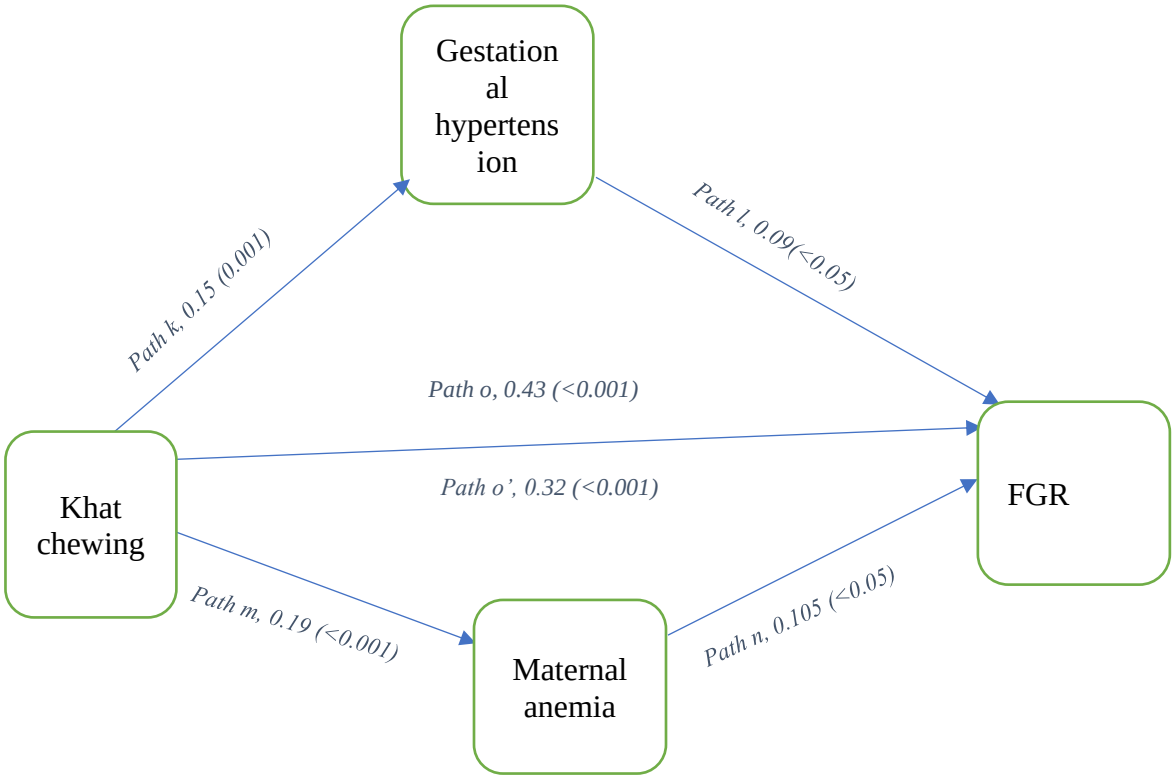
The mediation analysis results of the effect of khat chewing during pregnancy on fetal growth restriction is detailed in table 20 and figure 5. Khat chewing during pregnancy was significantly associated with FGR (path o, β=0.43, p<0.001). More importantly significant associations were also observed between khat chewing during gestation and gestational hypertension (path k, β=0.15, p=0.001), gestational hypertension and FGR (path l, β=0.09, p<0.05), khat chewing during gestation and maternal anemia (path m, β=0.19, p<0.001), maternal anemia and FGR (path n, β=0.105, p<0.05). After adjusting for gestational hypertension and maternal anemia, the regression coefficient of khat chewing during pregnancy has been decreased in size from path o, β=0.43, p<0.001 to path o', β=0.32, p<0.001 (Figure 5). Therefore, the present study revealed that the effect of khat chewing during pregnancy on fetal growth restriction was partially mediated by gestational hypertension and maternal anemia.

Table 20: The relationship between khat chewing during pregnancy, potential mediators and fetal growth restriction of the study cohorts in eastern Ethiopia, 2022 (N=320): A generalized structural equation modeling analysis.

Model	**β*(95% CI)**	***p*-value**

Fetal growth restriction	Khat use effect on gestational hypertension	0.15 (0.06-0.24)	0.001
	Gestational hypertension effect on FGR	0.09 (0.011-0.11)	<0.05
	Khat use effect on maternal anemia	0.19 (0.089-0.29)	<0.001
	Maternal anemia effect on FGR	0.105 (0.016-0.19)	<0.05
	Khat use effect on FGR before adjustment for gestational hypertension and maternal anemia	0.43 (0.35-0.52)	<0.001
	Khat use effect on FGR after adjustment for gestational hypertension and maternal anemia	0.32 (0.24-0.43)	<0.001

*=adjusted for maternal age, residence, education status, occupation status, alcohol use, tobacco smoke, ANC visits, MUAC, BMI, oligohydramnios, placental abruptio, true knots in umbilical cord.



β(p-value) of path k, l, m and n is the indirect effects of khat chewing during pregnancy on FGR through gestational hypertension and maternal anemia.

β(p-value) of path o and o' is the direct effects of khat chewing during pregnancy on FGR before and after adjusting for gestational hypertension and maternal anemia respectively.

Figure 5: Revealed the adjusted effect sizes of khat chewing during pregnancy on fetal growth restriction via the potential mediators.

5.2.17 The relationship between khat chewing practices during pregnancy and selected birth and neonatal outcomes

As displayed in table 21, analysis results of the generalized linear model for the binomial family revealed the adjusted relative risk of occurrence of preterm births was 2.19 times higher among khat chewer study cohorts (aRR=2.19; 95%CI 1.21-3.96) (p<0.005) compared to non-khat chewer study cohorts. Moreover, the occurrence of preterm births among the current study cohorts attributed to khat chewing was 36.5% (95%CI 27.22-45.83) (p<0.001). In a similar analysis, the adjusted relative risk of occurrence of low birth weight among khat chewer cohorts was 4.17 times higher (aRR=4.17; 95%CI 2.11-8.25) (p<0.001) compared to non-chewer cohorts. In addition, the occurrence of low birth weight in the current study cohorts attributed to khat chewing was 40.1% (95%CI 30.30-49.96) (p<0.001).

The GLM for the binomial family analysis result revealed that, the adjusted relative risk of small for gestational age among khat chewer cohorts was almost 4 times higher (aRR=3.89; 95%CI 2.38-6.38) (p<0.001) compared to non-khat chewer cohorts. Moreover, the attributable risk of small for gestational age due to khat chewing was 44.1% (95%CI 35-53.1) (p<0.001).

In the crude analysis, the relative risk of still birth (RR=1.89; 95%CI 0.62-5.77) and neonatal mortality (RR=2.48; 95%CI 0.73-8.47) were not significantly different among chewers as compared to non-chewers (p>0.05). Therefore, there were no statistically significant difference in the occurrence of still birth and neonatal death among khat chewer and non-chewer study cohorts in the present study (p>0.05).

Table 21: The association between khat chewing practices during pregnancy and selected birth and neonatal outcomes of the study cohorts in eastern Ethiopia, 2022 (N=320).

Birth outcome	Khat chewing characteristics of cohorts			
	Chewers, Frequency (%)	**Non-chewers, Frequency (%)**		***p*-value**
Gestational age at birth (in weeks)			**aRR* (95%CI)**	
Preterm birth	76 (48.7%)	20 (12.2%)	2.19 (1.21-3.96)	<0.005
Full term birth	80 (51.3%)	144 (87.8%)	1	
Birth outcome				
Birth weight (in kg)			**aRR** (95%CI)**	
Low birth weight	94 (60.3%)	33 (20.1%)	4.17 (2.11-8.25)	<0.001
Normal birth weight	62 (39.7%)	131 (79.9%)	1	
Birth outcome				
SGA (birth weight <10th percentile for sex specific GA)			**aRR*** (95%CI)**	
Yes	84 (53.8%)	16 (9.8%)	3.89 (2.38-6.38)	<0.001
No	72 (46.2%)	148 (90.2%)	1	
Birth outcomes				
Neonates' status at birth			**RR (95%CI)**	
Live birth	149 (95.5%)	158 (96.3%)	1	0.26
Still birth	7 (4.5%)	6 (3.7%)	1.89 (0.62-5.77)	
Neonates' status at the end of 4th weeks postpartum			**RR (95%CI)**	

(N=307)				
Died	19 (12.8%)	4 (2.5%)	2.48 (0.73-8.47)	0.15
Others (healthy and diseased)	130 (87.2%)	154 (97.5%)	1	

*=adjusted for residence, educational status, occupation, alcohol use, tobacco use/smoke, gestational hypertensions, abruptio placenta, pre-labor rupture of membranes, preterm labor, fetal distress, oligohydramnios.

**=adjusted for maternal age, residence, ethnicity, educational status, occupation, marital status, alcohol use, tobacco smoke, ANC visits, gestational hypertension, maternal anemia, MUAC, abruptio placenta, pre-labor rupture of membranes, preterm labor, placental weight.

*****=**adjusted for maternal age, residence, education status, occupation status, alcohol use, tobacco smoke, ANC visits, MUAC, BMI, oligohydramnios, placental abruptio, true knots in umbilical cord.

5.2.18 **Mediation analysis results**

The mediation analysis results of khat chewing during pregnancy and selected pregnancy outcomes were detailed in table 22 and figure 6 and 7. Khat chewing during pregnancy was significantly associated with preterm birth (path n, β=0.37, p<0.001). More importantly significant associations were also observed between khat chewing during gestation and gestational hypertension (path k, β=0.15, p=0.001), gestational hypertension and cesarean delivery (path l, β=0.08, p<0.05), cesarean delivery and preterm birth (path m, β=0.09, p<0.05). After adjusting for gestational hypertension and cesarean delivery, the regression coefficient of khat chewing during pregnancy has been decreased in size from path n, β=0.37, p<0.001 to path n', β=0.15, p<0.005 (Figure 6). Hence, the present study revealed that the effect of khat chewing during pregnancy on preterm birth was partially mediated by gestational hypertension and cesarean delivery.

A statistically significant association was obtained between khat chewing during pregnancy and low birth weight (path q, β=0.4, p<0.001). More importantly significant associations were also observed between khat chewing during gestation and gestational hypertension (path k, β=0.15, p=0.001), gestational hypertension and cesarean delivery (path l, β=0.08, p<0.05), cesarean delivery and preterm birth (path m, β=0.13, p<0.05), preterm birth and low birth weight (path n,

β=0.29, *p*<0.001). At last, significant associations were also observed between khat chewing during pregnancy and maternal anemia (path o, β=0.19, *p*<0.001), and maternal anemia and low birth weight (path p, β=0.024, *p*<0.05). After adjusting for gestational hypertension, cesarean delivery, preterm birth and maternal anemia, the regression coefficient of khat chewing during pregnancy has been decreased in size from path q, β=0.4, *p*<0.001 to path q', β=0.2, *p*<0.001 (Figure 7). Hence, this finding revealed that the effect of khat chewing during pregnancy on low birth weight was partially mediated by gestational hypertension, cesarean delivery, preterm birth and maternal anemia.

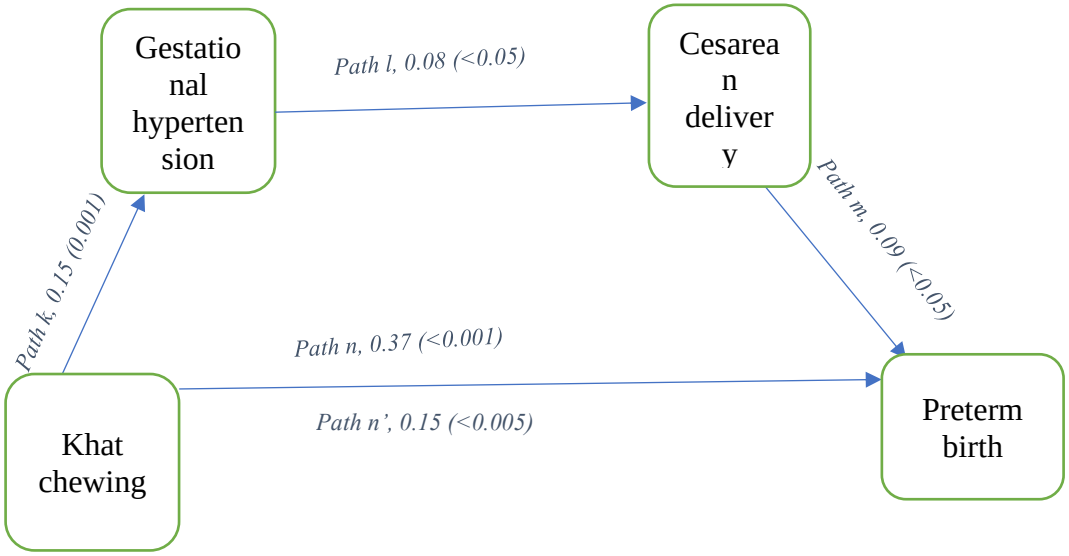
Table 22: The relationship between khat chewing during pregnancy, potential mediators and selected pregnancy outcomes of the study cohorts in eastern Ethiopia, 2022 (N=320): A generalized structural equation modeling analysis.

Model		**β*(95% CI)**	***p*-value**
Preterm birth	Khat use effect on gestational hypertension	0.15 (0.06-0.24)	0.001
	Gestational hypertension effect on emergency cesarean delivery (c/s)	0.08 (0.04-0.20)	<0.05
	Emergency cesarean delivery effect on preterm birth	0.09 (0.01-0.19)	<0.05
	Khat use effect on preterm birth before adjustment for gestational hypertension and cesarean delivery	0.37 (0.27-0.46)	<0.001
	Khat use effect on preterm birth after adjustment for gestational hypertension and cesarean delivery	0.15 (0.04-0.25)	<0.005
Model		**β**(95% CI)**	***p*-value**
Low birth weight	Khat use effect on gestational hypertension	0.15 (0.06-0.24)	0.001
	Gestational hypertension effect on emergency cesarean delivery (c/s)	0.08 (0.04-0.29)	<0.05

Emergency cesarean delivery effect on preterm birth	0.13 (0.02-0.25)	<0.05
Preterm birth effect on low birth weight	0.29 (0.16-0.42)	<0.001
Khat use effect on maternal anemia	0.19 (0.094-0.39)	<0.001
Maternal anemia on low birth weight	0.024 (0.009-0.11)	<0.05
Khat use effect on low birth weight before adjustment for gestational hypertension, cesarean delivery, preterm birth and maternal anemia	0.4 (0.3-0.49)	<0.001
Khat use effect on LBW after adjustment for gestational hypertension, cesarean delivery, preterm birth and maternal anemia	0.2 (0.08-0.32)	<0.001

*=adjusted for residence, educational status, occupation, alcohol use, tobacco use/smoke, abruptio placenta, pre-labor rupture of membranes, preterm labor, fetal distress, oligohydramnios.

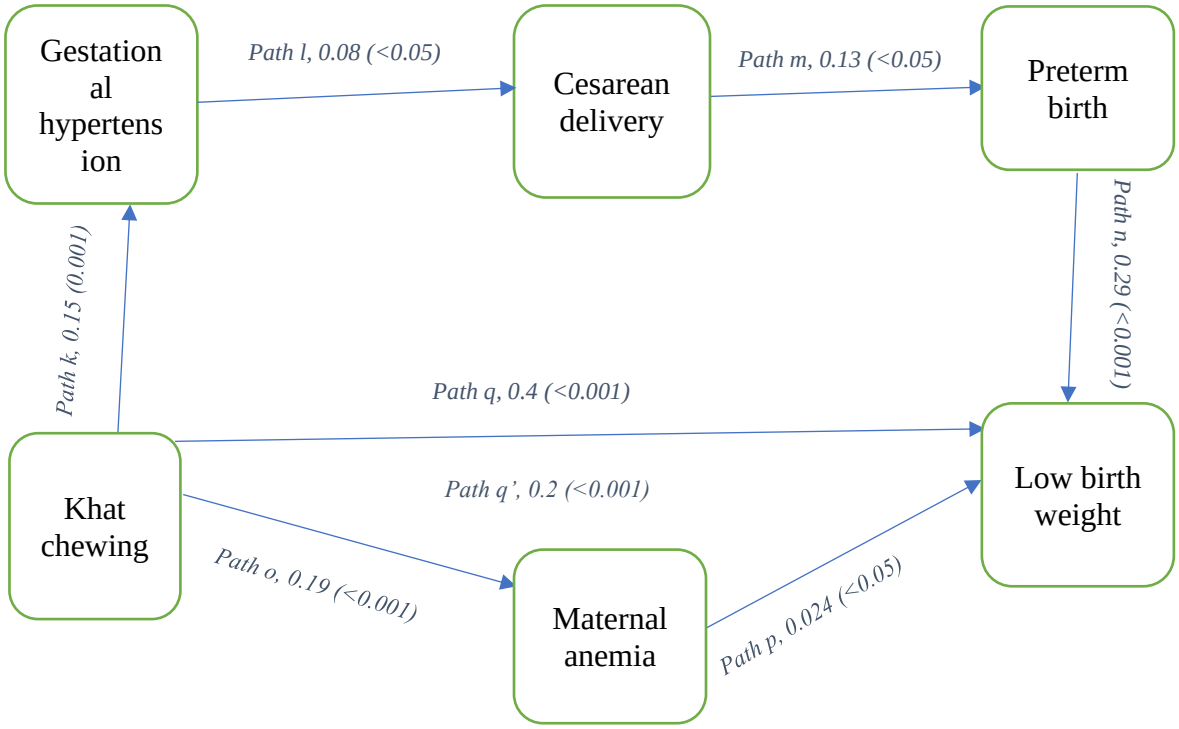
**=adjusted for maternal age, residence, ethnicity, educational status, occupation, marital status, alcohol use, tobacco smoke, ANC visits, MUAC, abruptio placenta, pre-labor rupture of membranes, preterm labor, placental weight.



β(p-value) of path k, l and m is the indirect effects of khat chewing during pregnancy on preterm birth through gestational hypertension and cesarean delivery.

β(p-value) of path n and n' is the direct effects of khat chewing during pregnancy on preterm birth before and after adjusting for gestational hypertension and cesarean delivery respectively.

Figure 6: Revealed the adjusted effect sizes of khat chewing during pregnancy on preterm birth via the consecutive mediators.



β(p-value) of path k, l, m, n, o and p is the indirect effects of khat chewing during pregnancy on low birth weight through gestational hypertension, cesarean delivery, preterm birth and maternal anemia.

β(p-value) of path q and q' is the direct effects of khat chewing during pregnancy on low birth weight before and after adjusting for gestational hypertension, cesarean delivery, preterm birth and maternal anemia respectively.

Figure 7: Revealed the adjusted effect sizes of khat chewing during pregnancy on low birth weight through the possible mediators.

Furthermore, khat chewing duration has been marginally associated with fetal growth restriction, preterm birth and low birth weight as shown in figure 8. In same way, the amount of khat

consumed has been associated with the occurrence of fetal growth restriction, preterm birth and low birth weight as presented in figure 9.

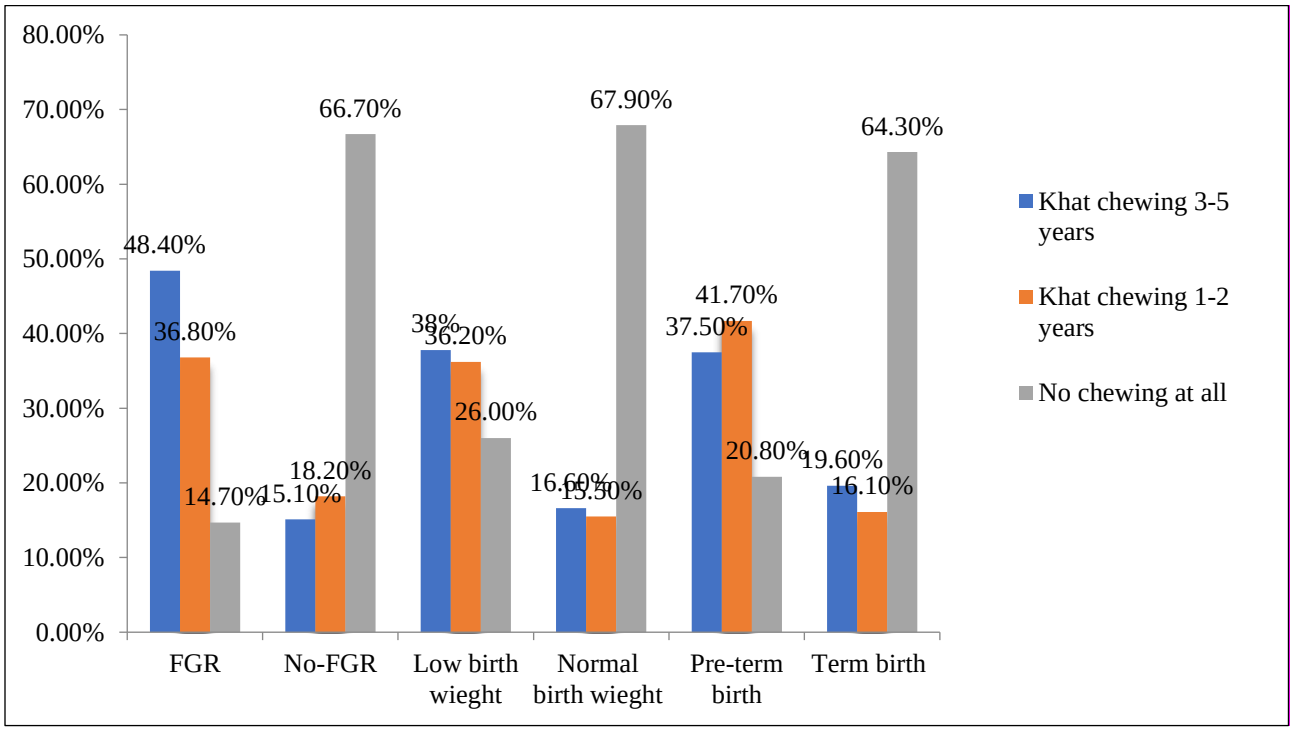


Figure 8: Revealed khat chewing duration association with fetal growth restriction, preterm birth and low birth weight among the study cohorts in eastern Ethiopia, 2022 (N=320).

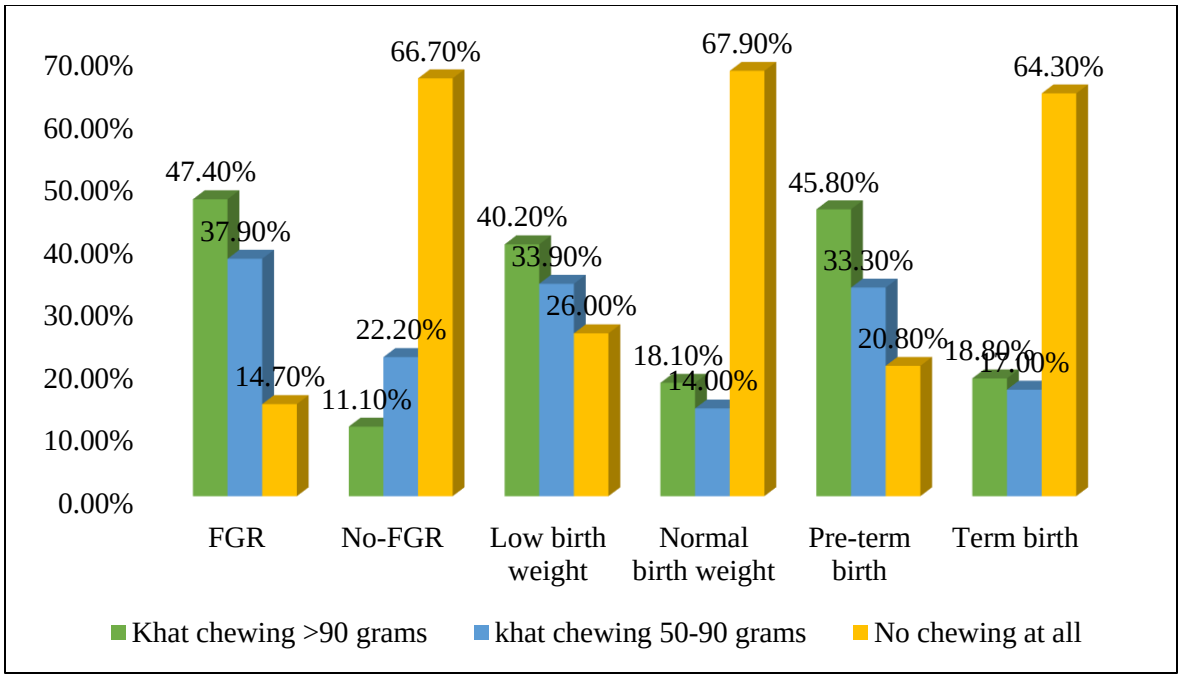


Figure 9: Revealed khat chewing amount association with fetal growth restriction, preterm birth and low birth weight among the study cohorts in eastern Ethiopia, 2022 (N=320).

5.3 Histopathologic changes in placenta and umbilical cord associated with chewing khat during pregnancy

The overall mean age of the study participants and birth weight of the newborn were, respectively 25.68 years with standard deviation of 6.53 years and 2600 gram with standard deviation of 662.16 gram. The mean age, the parity, mean birth weight of the newborn and mean placental weight among chewer and non-chewer study participants were as shown in table 23.

Table 23: Maternal and newborn characteristics of the study participants by their chewing status in eastern Ethiopia, 2022 (N=40).

Variables measured	**Chewing characteristics of study participants**		***p*-value**
	Chewers	**Non-chewers**	
Mean ±SD age of participants (in years)	27.4kg±6.95years	23.95kg±5.74years	0.095
Parity			
Primipara	8 (40%)	10 (50%)	0.53
Multipara	12 (60%)	10 (50%)	
Mean birth weight of fetuses (in gram)	2375±600.77	2825±657.65	0.03
Mean placental	434±63.69	527.2±55.17	<0.001

weight (in gram)			
Fetal growth restriction			
Yes	15 (75%)	3 (15%)	<0.001
No	5 (25%)	17 (85%)	

The placental histopathologic findings identified in the present study were placental hypoplasia, increased syncytial knots, villous hemorrhage/thrombosis, villous hyalinization and villous calcification. The aforementioned findings were described by khat chewing status of the study participants in table 24 and figure 10, 11, 12 and 13. Moreover, in the present histopathologic study of umbilical cord of the two comparison study groups, there were no abnormal findings observed. The histopathologic parameters studied include number of vessels, the presence of venous and arterial hemorrhage/thrombosis, the presence of Wharton's jelly edema and hemorrhage, and the venous and arterial wall and lumen status (see details in figure 14).

Table 24: Placental histopathologic study findings by khat chewing status of the study participants in eastern Ethiopia, 2022 (N=40).

Parameters studied	**Khat chewing status of the study participants**		**Total**	**Effect size**	***p*-value**
	Chewers No (%)	**Non-chewers No (%)**			
Trophoblasts proliferation					
No significant proliferation	20	20	40	----	----
Extensive proliferation	0	0	0		
Villous hypoplasia					
Present	17 (85%)	4 (20%)	21	0.65	<0.001
Absent	3 (15%)	16 (80%)	19		
Syncytial knots					
Present in excessive amount	12 (60%)	4 (20%)	16	0.41	0.01
Not present in excessive amount	8 (40%)	16 (80%)	24		
Villous/intervillous hemorrhage/thrombosis					
Present	14 (70%)	3 (15%)	17	0.56	<0.001
Absent	6 (30%)	17 (85%)	23		
Villous edema					
Present	5 (25%)	2 (10%)	7	0.19	0.21
Absent	15 (75%)	18 (90%)	33		
Villous hyalinization					

Present	10 (50%)	2 (10%)	12	0.44	0.006
Absent	10 (50%)	18 (90%)	28		
Villous calcification					
Present	8 (40%)	2 (10%)	10	0.35	0.028
Absent	12 (60%)	18 (90%)	30		
Villous infarction/necrosis					
Present	0	0	0	----	----
Absent	20	20	40		
Villous fibrosis					
Present	2 (10%)	0	2	0.22	0.20
Absent	18 (90%)	20 (100%)	38		
Fibrinoid necrosis in placenta					
Present	0	0	0	----	----
Absent	20	20	40		
Vascularity of placenta					
Present	2 (10%)	1 (5%)	3	0.09	0.55
Absent	18 (90%)	19 (95%)	37		
Lumen of villi vessels					
Dilated	2 (10%)	1 (5%)	3	0.09	0.55
Non-dilated	18 (90%)	19 (95%)	37		
Width of intervillous space in micrometer (mean+/-SD)	38.85±1.23	18.25±1.29	40	16.40	<0.001

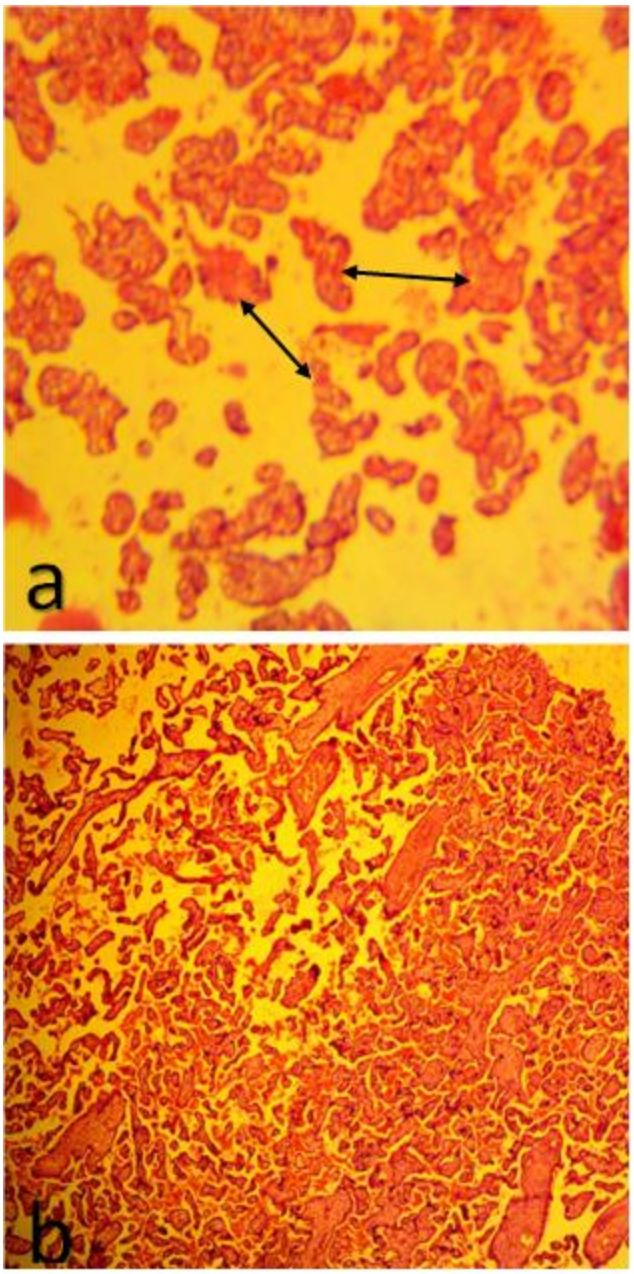


Figure 10: Photomicrograph of placenta from khat chewers placenta (a) as compared to those of non-khat chewers (b) in eastern Ethiopia revealing villous hypoplasia. Note the small sized terminal villi with elongated stem villi appearing together and decreased in number and the widely spaced villi (↔), in (a); H & E staining, 10X.

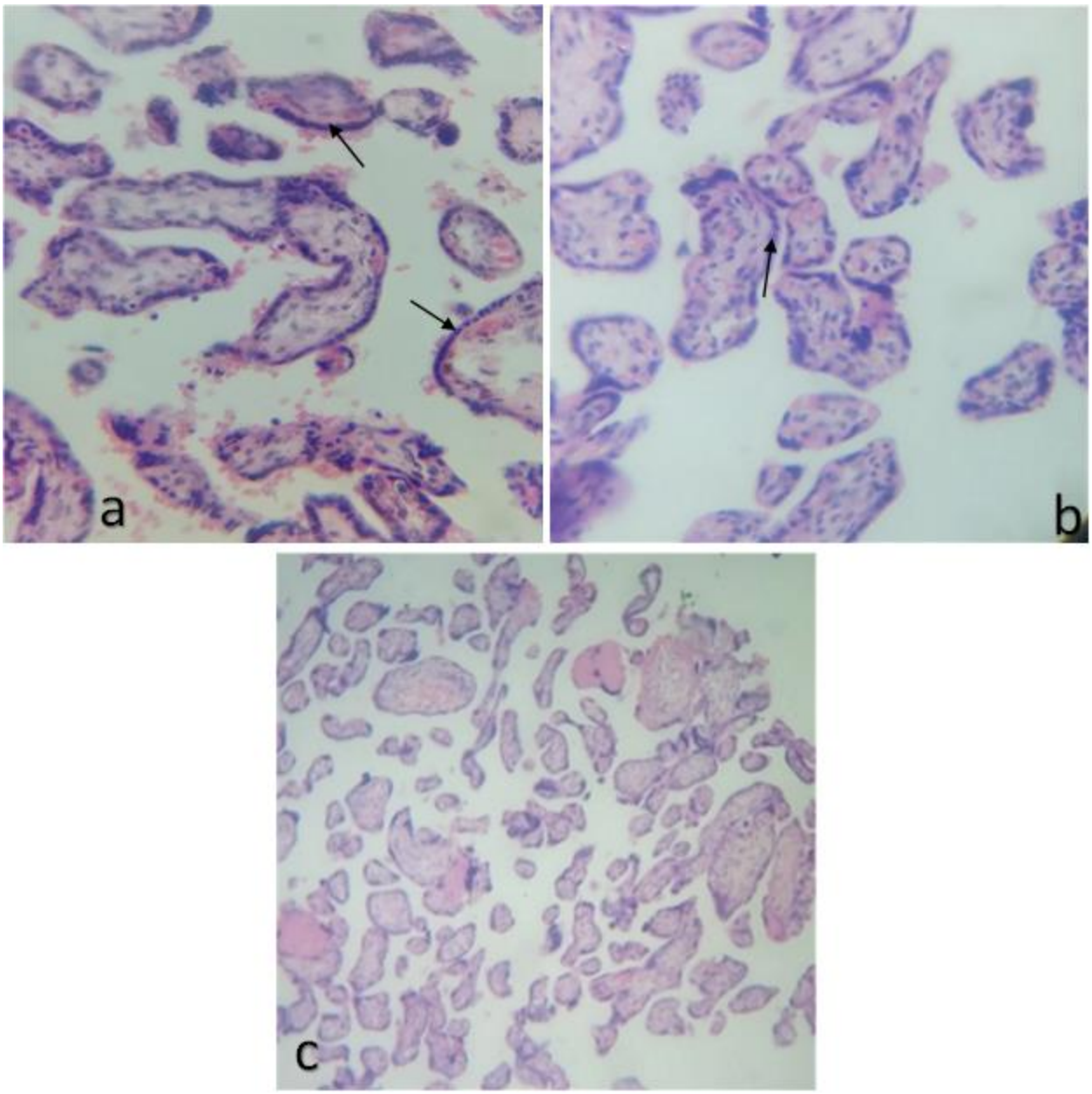


Figure 11: Photomicrograph revealing mainly increased syncytial knots (black arrow), in khat chewer placenta (a and b) compared to non-khat chewer placenta (c) in eastern Ethiopia; Stains used were H & E, 10X.

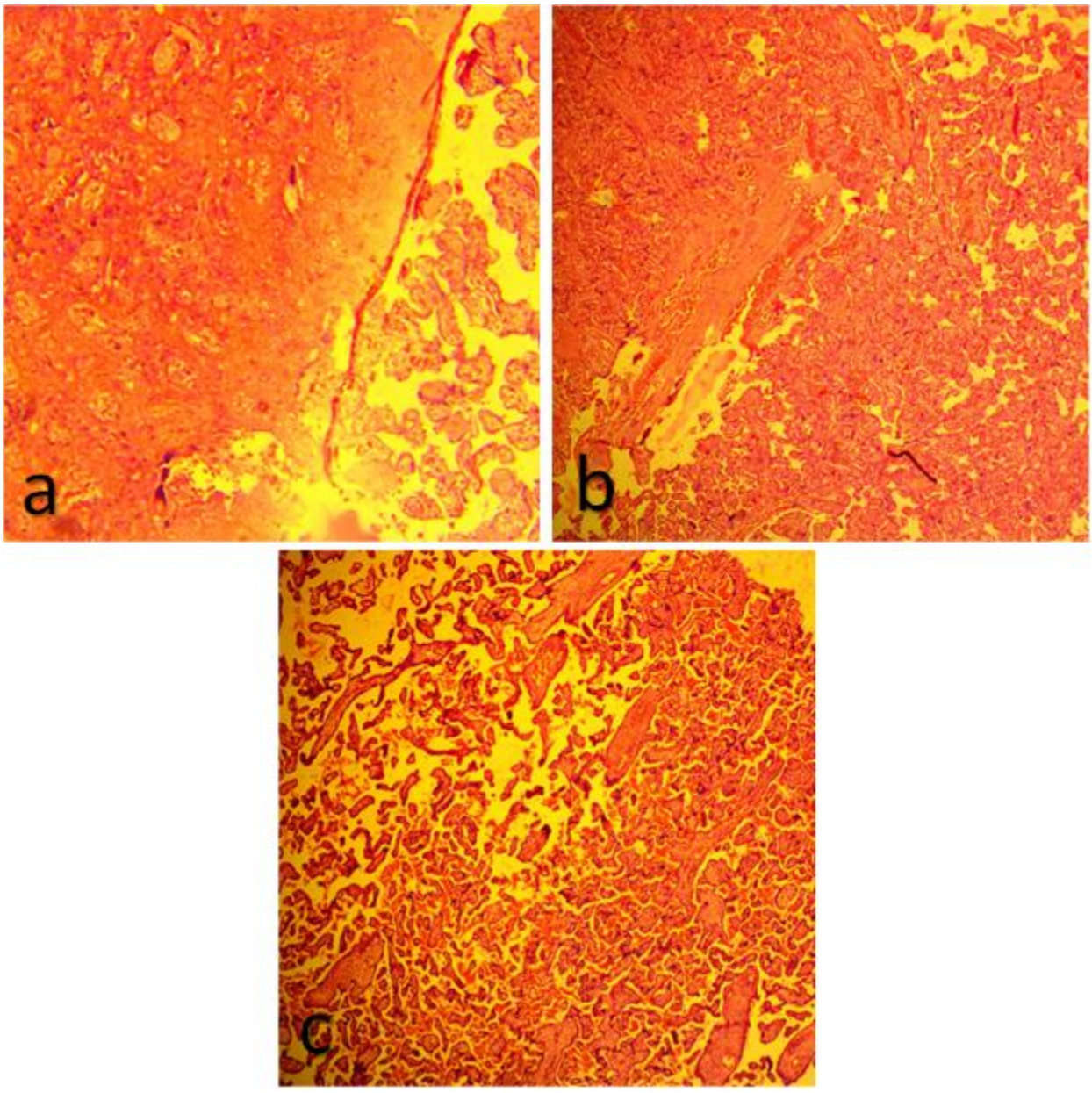


Figure 12: Photomicrograph revealing mainly more villous hemorrhage/thrombosis with congestion, in khat chewer placenta (a and b) compared to non-khat chewer placenta (c) in eastern Ethiopia; Stains used were H & E, 10X.

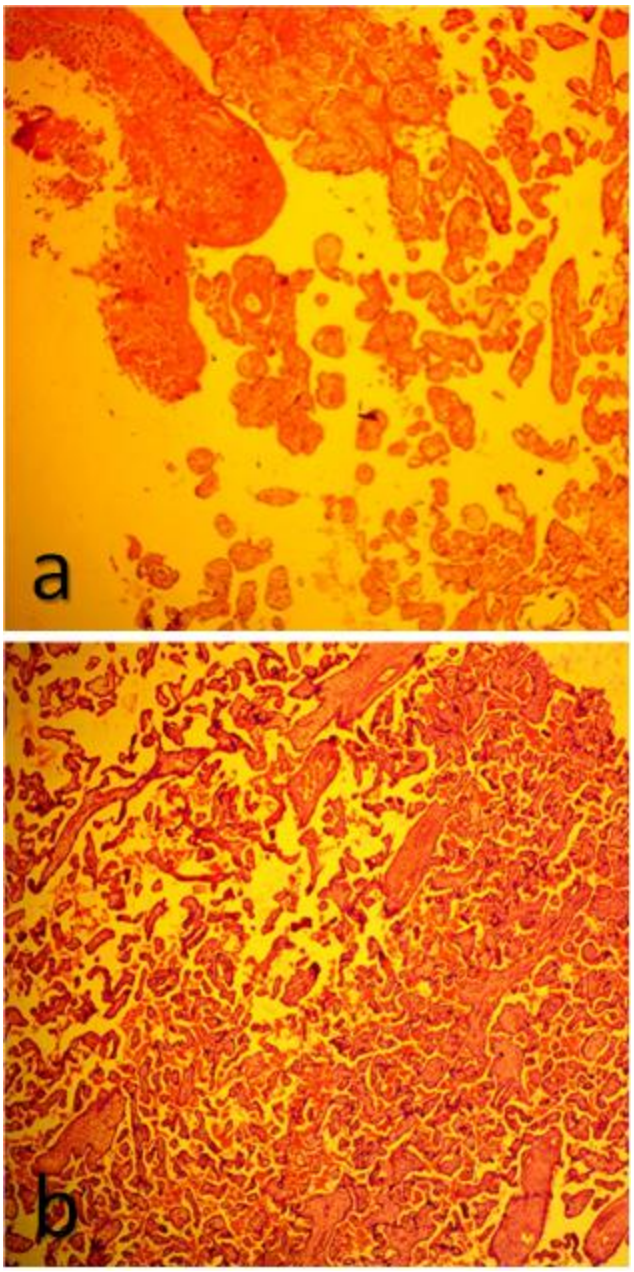


Figure 13: Photomicrograph revealing mainly increased villous hyalinization, in khat chewer placenta (a) compared to non-khat chewer placenta (b) in eastern Ethiopia; Stains used were H & E, 10X.

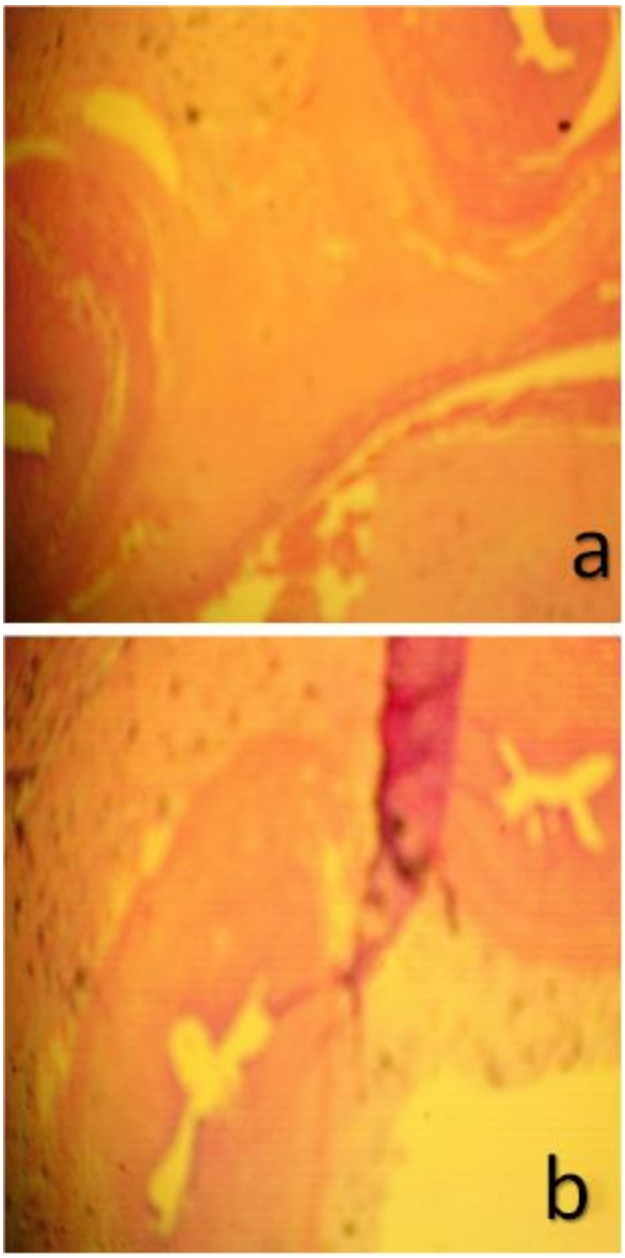


Figure 14.1: Photomicrograph showing umbilical vessels and wharton's jelly of the participants in eastrern ethiopia; stains used H & E, 10X.

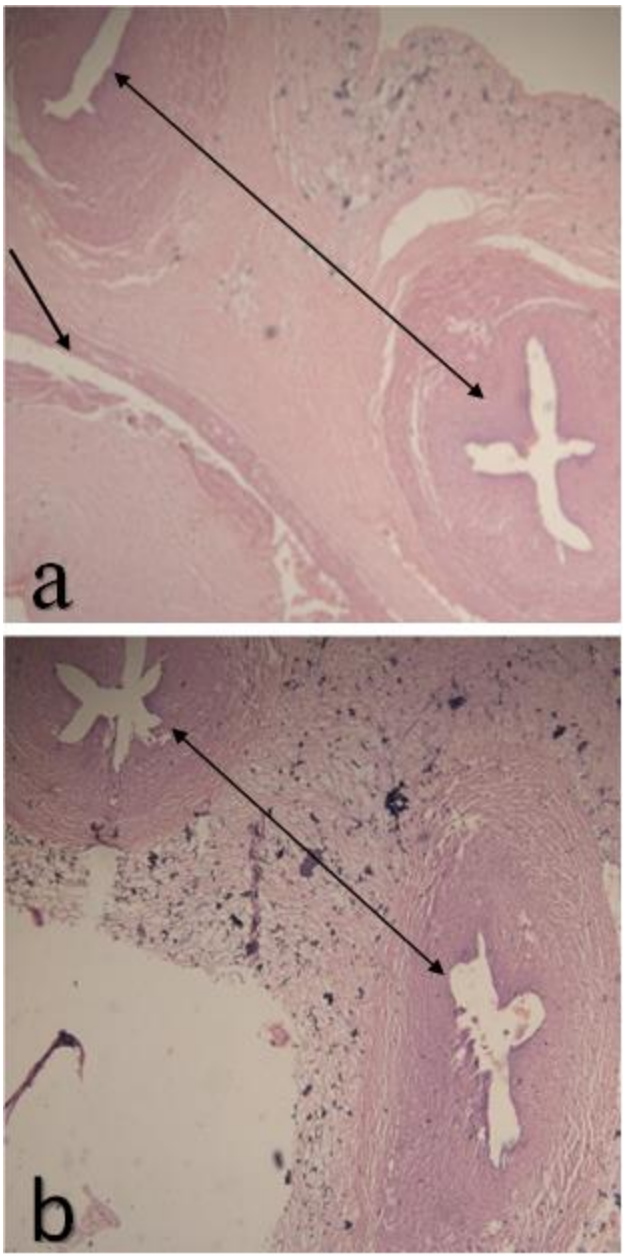


Figure 14.2: Photomicrograph showing mainly umbilical vein (⟶) umbilical artery (⟷) and wharton's jelly with amnion of the study participants in eastrern ethiopia; stains used H & E, 10X.

In further analysis, the present study revealed a significant association between placental histopathologic findings and selected fetal outcomes, as indicated in table 25.

Table 25: The association between placental histopathologic findings and selected fetal outcomes in eastern Ethiopia, 2022 (N=40).

Placental	**Fetal outcome**	**Effect size**	***p*-value**

histopathologic parameters	Fetal growth restriction present	Fetal growth restriction absent		
Villous hypoplasia				
Yes	18 (100%)	3 (13.6%)	0.86	<0.001
No	0	19 (86.4%)		
Syncytial knots				
Present in excess amount	12 (66.7%)	4 (18.2%)	0.49	0.002
Not present in excess amount	6 (33.3%)	18 (81.8%)		
Villous hyalinization				
Present	11 (61.1%)	1 (4.5%)	0.61	<0.001
Absent	7 (38.9%)	21 (95.5%)		
Villous/intervillous hemorrhage/thrombosis				
Present	12 (66.7%)	5 (22.7%)	0.44	0.005
Absent	6 (33.3%)	17 (77.3%)		
Placental histopathologic parameters	**Fetal outcome**		**Effect size**	***p*-value**
	Low birth weight (<2.5kg)	**Normal birth weight (>=2.5kg)**		
Villous hypoplasia				
Yes	15 (75%)	6 (30%)	0.45	0.004
No	5 (25%)	14 (70%)		
Syncytial knots				
Present in excess amount	11 (55%)	5 (25%)	0.31	0.049
Not present in excess amount	9 (45%)	15 (75%)		
Villous hyalinization				
Present	10 (50%)	2 (10%)	0.44	0.006
Absent	10 (50%)	18 (90%)		
Villous/intervillous hemorrhage/thrombosis				
Present	12 (60%)	5 (25%)	0.35	0.025
Absent	8 (40%)	15 (75%)		

6. Discussion

Magnitude and associated factors of chewing khat during pregnancy

The magnitude of chewing khat among pregnant mothers in the present study was 27.4%. This magnitude is lower than studies conducted in Yemen, which reported 41% magnitude of chewing khat during pregnancy[39] and 29.6% prevalence of khat chewing in adult women[97]. The variability may be attributed to study area, study population and sociocultural variability. Similarly, the current finding is lower than local studies: a study in Jimma reported 37.8% magnitude of khat chewing[98] in general populations, a study in Harar reported 53% prevalence of khat chewing[8] in general populations, and studies in Butajira, Ethiopia found 50% prevalence of chewing khat [99] in general population and 35.8% prevalence of khat chewing during pregnancy[40]. The variability may be due to the differences in the study area, study period, study populations and approach. In most areas of Ethiopia females participation in khat chewing practices are low as compared to males[100] due to cultural taboo and restrictions. A previous study reported that 27% of men and 12% of females in Ethiopia are khat chewers[9]. But in some areas of Ethiopia females' involvement in khat chewing practices is not culturally and socially prohibited.

On the other hand, the present magnitude of chewing khat during pregnancy is higher than previous local studies which reported 20% prevalence in a systematic review and meta-analysis in Ethiopia[26], 19.6% magnitude[27] and 9.9% prevalence of chewing during pregnancy[41]. This variability may be attributed to sociocultural variations. Even though the participation of females in khat chewing practices in most parts of Ethiopia are limited due to sociocultural taboo, the involvement of women in khat chewing in Harar, eastern Ethiopia is culturally as well as socially accepted practice as seen in the current study and this finding is in agreement with a previous report[101]. Hence, the study participants may freely report their chewing practice at time of interview and there is a less chance of underreporting of their chewing practices. In the present study 63.5% of study participants were chewing khat for socialization, and 60.5% of the study participants practiced khat chewing to obey tradition. These findings can also be supported by the qualitative findings obtained thorough an in-depth interview of pregnant mothers. A 27 years old 7 months pregnant study participant at in depth interview reported, "*Chewing khat hear in Harar is a common traditional daily practice of the population which I have seen in my day-*

to-day life. As part of this community, I consumed khat daily because I received it from the population, and I feel proud of my chewing and hence, I can say chewing khat in Harar is our culture."

Another 27 years old 6 months pregnant study participants explained, *"Being living in Harar, it is impossible to live without chewing. Chewing khat is a highly valued traditional practice in the community, in which the chewing practices are transmitted from elders to our generation. Hence, I have consumed khat because it is my community's and as well my family's cultural practices."*

Moreover, 32 years old 8 months pregnant mother also explained the condition in Harar as follows: *"Life in Harar is unique. Because every individual whether rich or poor, older or young, male or female all participates in khat chewing practices, preferably in groups. Everybody is buying his/her own khat and comes together to chew and to discuss different issues related to the community. Hence, in order to participate in the discussion of community issues and to live together in the community chewing of khat is a must. Otherwise, you are not counted as part of the community. The majority of the community sees you, as you are not accepting the culture and tradition of the community. Hence, I used chewing khat for many years."*

In the present study participants with relatively older age, being living in rural area, being illiterate, having chewer husbands and other family members were significantly consumed khat during their current pregnancy.

Participants aged 26 and above years were a significantly increased risk of chewing khat during their current pregnancy as compared to those aged less than 26 years. The finding is consistent with previous studies[39, 97, 102], which reported statistically significant khat chewers were aged between 25 and 49 years. This could be due to the fact that young mothers are more likely to depend on others for their livelihood and may be in lack of income which may greatly decrease their involvement in khat chewing. In addition, older age mothers may have gradually developed the habit through the years. In this study, 54 (23.5%) of the study participants were housewife. Of this, 37 (68.5%) of them were aged 26 and above years. In addition, young mothers may be under control of their family that may decrease their involvement in khat chewing practices. More importantly, younger women may fear the harm of khat chewing on unborn child as compared to older mothers, as older mothers may have previous children born healthy.

In the present study participants living in rural area were at significant risk of chewing khat during pregnancy compared to those living in urban areas. This result is in line with previous studies[8, 39, 103]. This may be due to the fact that participants living in rural area may be in lack of access to healthcare services to be advised on healthy practices as compared to urban residents. It has been highlighted that access to health services was variable in rural and urban areas in Ethiopia[104]. In addition, rural residents could lack means to get information about healthy practices as compared to urban residents. More importantly, since khat is mostly farmed in rural areas, the study participants in rural area are more accessible to the product.

Lack of education of study participants were at significantly increased risk of khat chewing during pregnancy compared to educated study participants. The finding is consistent with previous study findings[26, 39, 105]. The possible justification for this could be due to the fact that illiterate mothers may be in lack of information and knowledge about the negative health impacts of khat chewing on unborn child and mothers compared to educated mothers. In addition, health seeking behaviors of educated mothers may be greater as compared to illiterate mothers and may visit the health institutions and hence, may be advised on the harm of chewing khat on themselves and on their unborn child. In the present study out of the total 74 study participants having only one ANC visit at 7 and greater months of gestation, 39 (52.7%) were illiterate. On the other hand, out of the total 88 study participants having 4 ANC visits at 7 and greater months of gestation, 62 (70.5%) were having primary and above levels of education. A previous study also reported literate mothers are more likely utilized appropriate antenatal care than illiterate mothers[106].

Participants having khat chewer husbands in the present study were at significantly increased risk of chewing khat during current pregnancy as compared to those participants having no chewer husbands. The result is in line with previous studies conducted elsewhere[26, 27, 41, 97, 103]. The possible justification for the finding could be khat chewer husbands' may encourage and influence their wives to involve in khat chewing practices and hence, women may share the practice. In the present study 30.2% of the study participants chewed khat to cope up with their partner's pressure. A qualitative finding obtained through in-depth interview of pregnant women also strengthens this finding. A 34 years old 9 months pregnant respondent explained the role of her husband in her khat chewing practices as follows, *"I was primarily not in Harar. I was born in an area and family where chewing of khat is highly forbidden. I came to Harar due to*

marriage when my current husband joined the area as a government employee. Then after, we were displaced from my birth area to Harar. When I joined Harar, my husband encouraged and enforced me to start chewing khat to be part of the community and hence, I began chewing a few sticks with sugar and now I become a regular chewer of khat."

Another 29 years old 6 months pregnant study participants also explained the role of her husband in her khat chewing practices as follows, *"In my khat chewing experience, my husband plays a great role. At first, I feared khat chewing since I saw my neighbor's elder man become manic which I think is related to his long-time chewing practices of khat. But my husband reassured me, as the case of our neighbor man was related to his family rather than his chewing practices. And told and repeatedly encouraged me to start and enjoy chewing khat to be a healthy thinker and to have a joyful family. Now I enjoyed chewing of khat."*

In the current study respondents with khat chewer family members were at significantly increased risk of chewing khat during pregnancy as compared to those having no chewer family members. The present finding is in agreement with previous studies conducted elsewhere[27, 102, 103]. This could be due to the fact that participants living with chewer family members will be more likely to be influenced by their chewing behaviors. In this study 25.4% of study participants chewed khat to cope up with their family pressures. This result is also supported by qualitative findings obtained through an in-depth interview of pregnant mothers. An in-depth interview of 27 years old pregnant respondents said*, "I practiced chewing khat since almost all except the children of my family members are khat chewers. Without chewing khat I feel I will not be part of the family members and not to be alone I began chewing khat. Now I am a daily consumer of khat."*

On an in depth interview a 32 years old 7 months pregnant study participant added, "*In our family, our elders are practiced khat chewing being in groups. They encouraged us to begin chewing khat by providing a small amount and also told us on how to use it the first time. Now I enjoyed chewing khat. That is how I began chewing khat."*

Maternal, pregnancy and neonatal outcomes following consumption of khat during pregnancy

The current study, determining the effects of khat chewing during gestation on maternal, pregnancy, birth, neonatal, umbilical cord and placental outcomes in a longitudinal follow up approach, as well as revealing its effect in histopathologic methods is the first-time report in Ethiopia. It is to mean that previous literature documented the relationships between khat chewing during gestation and a few pregnancy outcomes even in any approaches are limited and almost nil similar to the present study approach (design and analysis). Because of these, comparison of the current study findings with comparable study populations and study approaches becomes a difficult task. Hence, in reading of comparisons made in the current study, the aforementioned intrinsic literature limitation needs to be considered.

Khat chewing and maternal outcomes

In the current follow up study the total level of anemia among pregnant cohorts was 38.8%; with higher proportion and as well increased adjusted relative risk of anemia among khat chewer cohorts; and hence noticed to be a public health problem[107]. The current whole magnitude of anemia is inferior than the prevalence reported in a previous study done in eastern Ethiopia[108], but in lineage with the current finding this previous study found an increased risk of occurrence of anemia in regular khat chewers as evaluated to non-regular chewers. The present finding is higher than the global prevalence of anemia (38.2%)[107], the amount of anemia reported in a previous local study (33.1%)[109], and a pooled prevalence reported in a study (26.4%)[110]. However, the current study finding is lower than the amount of anemia reported in African region (46.3%)[107], and a finding (41%) from further analysis of EDHS 2016 data[111]. These differences in magnitude may be due to variations in study area, study period, study population, study design, variations in culture, lifestyle, dietary practices, and socioeconomic status.

A relatively higher proportion and as well increased relative risk of anemia among khat chewer study cohorts in the current study may be due to mainly their lifestyle and dietary practice differences. It has been reported that khat chewing may greatly influences the appetite of pregnant mothers and hence, may greatly reduce their daily intake[112] and thereby leading to anemia and undernutrition. In support of this an experimental animal study also revealed khat intake greatly reduced the food consumption of rats [32] and guinea pigs[113]. A study reported

poor dietary intake during pregnancy significantly increased the risk of anemia during pregnancy[114]. In addition, khat chewer cohorts may give priority to buying khat even from the poor households rather than buying nutritious food items[112], which again will affect their dietary intake leading to increased development of anemia and undernutrition. In support of this, the current study revealed a relatively low monthly household income among chewer cohorts compared to non-chewer cohorts. Moreover, the mean Hgb concentration in the present study (11.25±2.12g/dl) was lower than the mean global Hgb concentration (11.4g/dl)[107] and higher than the mean African region Hgb concentration (11.1g/dl)[107] reports. A relatively low mean Hgb concentration was observed among khat chewer cohorts compared to non-khat chewers in the present study. This finding is in line with a previous case control study reported in Yemen[45].

The present study noticed a significantly higher magnitude and increased relative risk of occurrence of gestational hypertension among khat chewer cohort mothers compared to non-khat chewer counterparts. In line of this finding, a case control study in Yemen[45] reported a significantly increased risk of gestational hypertension among khat chewer pregnant mothers compared to non-chewers. In addition, the present study found a significantly higher mean systolic blood pressure among khat chewers ($p<0.05$) and a marginally significant higher mean diastolic blood pressure among khat chewers ($p=0.067$). Even though the study populations, study area and design made difficult to compare the present finding, a previous study reported a significantly higher mean systolic and diastolic blood pressure among khat chewers[115] and also another study reported a significantly higher mean diastolic blood pressure among khat chewers[116]. Even though controlled in the analysis and the consumed levels per week is not significantly different among the study cohorts, a relatively an increased conception of alcohol was observed among khat chewers which may be associated with a significantly higher occurrence of gestational hypertension among khat chewers. Lastly, the most important factor associated with the significant increased occurrence of gestational hypertension among khat chewer cohorts may be due to a sympathomimetic activity of the active ingredients of khat, mainly cathinone, causing increased heart rate and vasoconstriction leading to bigger heart output and then increased blood pressure[117].

Khat chewing and pregnancy outcomes

In the present follow-up study, the overall magnitude of fetal growth restriction among the study cohorts was 29.7%. Moreover, the overall magnitude of small for gestational age at birth among the present study cohorts was 31.3%. Although, the study populations and the study approaches are not comparable to discuss, a lower prevalence of FGR (23.5%) and SGA (19.7%) have been reported in a previous local study[118].

A significantly higher magnitude and increased relative risk of fetal growth restriction was observed among khat chewer participants as compared to their non-khat chewer counterparts in the present follow up study. The possible explanations for this finding may be associated with extrauterine and intrauterine factors. The extrauterine environment may be a factor in the following ways. One, there may be differences in daily dietary intake of chewers and non-khat chewers. It was reported[112] that chewing khat may decrease the food appetite of pregnant mothers and hence, chewer pregnant mothers may consume less which may greatly decreases the nutrient quantity needed for unborn fetus and then will affect its growth. In addition, since chewer pregnant mothers, even the poor, may give priority for buying khat, chewer pregnant mothers may be in lack of nutritious foods at household and then consume less food that may not satisfy the need of unborn fetus and as result will affect its growth[112]. In agreement with these elaborations' further mediation analysis in the present study found a significant association between khat chewing during pregnancy and maternal anemia and maternal anemia and fetal growth restriction. The other, an increased relative risk of fetal growth restriction may be associated with an intrauterine environment such as placental and umbilical cord abnormalities. An experimental animal study has reported a decrease in placental blood flow due to vasoconstriction in the uteroplacental vessels among khat fed animals as compared to controls[119] and then this may lead to fetal growth restriction. In line with this finding further mediation analysis of the present study found a significant association between khat chewing during pregnancy and gestational hypertension and gestational hypertension and fetal growth restriction. Normal growth of unborn fetus in the intrauterine life greatly depend on the healthy growth and appropriate attachment of umbilical cord to the placenta[120, 121]. In the present study abnormal cord insertion (marginal), abnormal umbilical cord coiling (both hypo and hyper coiling) and umbilical cord true knots were significantly higher among births of khat chewer cohorts compared to births of non-khat chewer counterparts. Cord abnormalities are highly related with abnormalities in development and function of the placenta[122]. In addition,

impaired vascular development in placenta is closely associated with cord abnormalities[123, 124]. As reported in a previous study[125] the peripheral cord insertion compared to central cord insertion was significantly associated with fetal growth restriction. This may be due to the fact that central insertion of cords to the placenta will enables vessels to be stable and hence, will shelter from rotational and pressing forces[85] which will interrupt the blood flow, unlike with that of peripheral insertions. In addition, central cord insertions will better enable a sizeable distribution and flow of blood in different placental parts, that will then enable for better growth of the fetus[125]. Previous studies documented both hypo-coiled[83, 85, 126] and hyper-coiled[84, 86] umbilical cord being significantly associated with the occurrence of fetal growth restriction. The possible justification could be due to the fact that, hypo-coiling may be associated with solidity of cord and hyper-coiling may lead to rotation of the cord; in both cases may be associated with interfering to fetoplacental blood flow which in turn leads to fetal growth restriction.

In the current study, a significantly higher magnitude and increased relative risk of abruptio placenta was observed among khat chewer study cohorts as compared to non-chewers. Even though no previous study in the same or related study population to compare and to explain the association; this significantly higher occurrence of abruptio placenta among khat chewers may be due to a significant increased occurrence of PROM among khat chewers compared to non-khat chewers. More importantly, in the present study the occurrence of abruptio placenta among PROM mothers was significantly higher (aRR=2.62; 95%CI 1.31-5.25) ($p<0.005$) than those mothers without PROM. In line with this finding a study has demonstrated significant increased occurrence of abruptio placenta among those birth who had experienced PROM[127]. This previous study also found PROM together with oligohydramnios were significantly associated with the occurrence of abruptio placenta. Similar with this previous finding, the present study found a significantly higher occurrence of oligohydramnios among khat chewers compared to non-chewers. Another, study also reported PROM as an independent significant risk factor for the occurrence of abruptio placenta[128]. This significant occurrence of abruptio placenta in association with PROM may be due to reduction in uterine volume[129].

In the present follow up study, the magnitude and relative hazard of pre-labor rupture of membranes among khat chewer cohorts were significantly higher compared to non-khat chewer cohorts. The present study is in lineage with former studies; one case control study in Yemen[45]

found a 2.05 times increased hazard of chewers for pre-labor rupture of membrane and another cross sectional study in Ethiopia reported, 23.5% proportion of PROM and 1.5 times increased risk of khat chewers for PROM as compared to non-khat chewers[46]. Even though no previous related findings explained the association; the significantly increased occurrence of PROM among khat chewer cohorts compared to non-chewers in the present-day study may be due to the immunosuppression effects of the active ingredients of khat which is cathinone[130], an amphetamine like substance. It has been reported that synthetic amphetamine (structurally and functionally similar with cathinone) has a role in suppression of B and T cell production and as well suppress production of interleukin-2 (IL-2)[131] which are necessarily for the control of infections and inflammations. Hence, this leads to increased susceptibility to different infections including infections of fetal membranes that will lead to weaking of membranes and rupture. In addition, it has been also reported that khat initiates cell death through stimulation of cysteine proteases[132, 133]. These activated enzymes are responsible for weakening of fetal membranes[134], leading to rupture of membranes. Besides, in the present-day study a significantly increased occurrence of PROM was observed among mothers who had experienced gestational hypertension (aRR=1.0089 95%CI 1.0087-1.0093) (p<0.001) compared to those moms who had not experienced gestational hypertension. This result is in agreement with a previous finding who had reported significantly increased occurrence of PROM among mothers experienced gestational hypertension compared to those not experienced gestational hypertension[135]. This may be due to the circumstance that gestational hypertension may be associated with decreased uteroplacental perfusion due to wrong cytotrophoblast invasion of uterine arterioles leading to endothelial dysfunction and then placental ischemia and finally to premature rupture of membranes[136]. Lastly, in the present-day study a significantly increased occurrence of PROM was observed on those mothers who had BMI<18.5kg/m^2 (aRR=2.96;95%CI 1.64-5.34) (p<0.001) than those mothers who had greater BMI. In line with this finding similar findings are documented elsewhere[137, 138].

Khat chewing and birth, neonatal, umbilical cord and placental outcomes

In the current cohort study, the magnitude as well as the relative risk of occurrence of preterm birth was significantly higher among khat chewer participants compared to births of non-khat chewer cohorts. More importantly, the average gestational age at birth of khat chewer cohorts (36.46±2.34weeks) is significantly lower than the average gestational age at birth of non-khat

chewer cohorts (38.10±1.66weeks). Similarly, a case control study conducted in Yemen[45] found significantly increased risk of preterm birth among khat chewer participants compared to non-khat chewers. Even though, the study finding is not in comparison of study participants with khat chewing status, a cross sectional study conducted in Jimma, Ethiopia[139] reported a 25.9% prevalence of preterm births and another cross sectional study conducted in Gondar, northwest Ethiopia[118] reported a 23.2% prevalence of preterm births. Moreover, a comprehensive review and metanalysis study in Ethiopia[140] also reported a 37.2% pooled prevalence of preterm births using 2 studies that reported preterm births magnitude which have been conducted on those mothers attended ANC and it is not known whether those mothers were using khat while pregnant. Such significantly increased relative risk of occurrence of preterm birth among khat chewers, may be associated with significantly increased occurrence of preterm labor among khat chewer cohorts compared to non-chewers in the presents study. A previous study had reported that khat chewing during pregnancy cause labor induction[45], which may be preterm labor and then preterm birth. In addition, a significantly increased relative risk of preterm birth among khat chewers in the present study may be due to a significantly increased occurrence of gestational hypertension, fetal growth restriction, abruptio placenta, and PROM among khat chewers which resulted in significantly increased rates of emergency cesarean delivery compared to non-chewers. This emergency cesarean delivery may end in preterm birth. In line with this finding, further mediation analysis of the present study found a significant association between gestational hypertension and emergency cesarean delivery and emergency cesarean delivery and preterm birth. It has been stated that fetal growth restriction, abruptio placenta and gestational hypertension may end in surgical procedures and preterm birth[141]. In addition, in line with the present study, previous studies reported a significant association between PROM and preterm birth[142, 143]. More importantly, PROM is greatly associated with a significant occurrence of oligohydramnios among khat chewers in the present study, which in turn may be associated with the significant occurrence of preterm birth. In line with the present finding previous studies reported a significantly higher circumstance of preterm birth associated with oligohydramnios[143, 144].

Moreover, the total average gestational age at birth in this study (37.3±2.18weeks) is lower than 38.8±1.1weeks[145], 39.6±1.7weeks[146], and 39.6±1.3weeks[147] documented in northwest Nigeria, south eastern Nigeria, and Switzerland respectively. These variations in findings may be

due to differences in lifestyle, culture, socioeconomic status, educational level, dietary practices and policy of the countries.

The current cohort study found a significantly higher magnitude and increased relative risk of occurrence of low birth weight among khat chewer participants. This finding is in support of a case control study conducted in Yemen[45] and cross sectional studies conducted in Yemen[35, 44] and a case control study conducted in Ethiopia[38], which reported a significantly increased risk of low birth weight among births of khat chewers compared to non-khat chewer counterparts. In addition, the mean birth weight among khat chewers in the present study is significantly lower compared to non-khat chewers. In agreement with the present finding, low mean birth weight among khat chewers as compared to non-chewers has been reported in a systematic review[148]. Additionally, in line with the present finding experimental studies[32, 43] revealed decreased birth weight among khat extract administered rats compared to non-administered controls. The possible justification for this finding may be related to extrauterine and intrauterine factors. Decreased daily intake of food as demonstrated in both experimental animals[32, 113] and as well in human study[112] may be highly associated with the significant occurrence of low birth weight among khat chewers. This may be due to the fact that khat chewing may greatly influences the appetite of pregnant mothers and hence, may greatly reduce their daily intake[112] and thereby leading to maternal anemia and undernutrition which in turn has an impact on fetal birth weight. In line with this explanation further mediation analysis of the present study found a significant association between maternal anemia and low birth weight. The other is intrauterine factors. A decrease in placental blood flow as demonstrated from experimental study[119] and abnormal cord insertion in human placenta[125] have been associated with a significant occurrence of low birth weight. In agreement with the previous findings, in the present study aberrant cord insertions were significantly observed among khat chewer cohorts as compared to non-khat chewers and then this may be a factor for this significant occurrence of low birth weight. Moreover, this significant occurrence of low birth weight among khat chewer cohorts may be due to a significant occurrence of preterm birth among them compared to the occurrence on non-chewers. In further mediation analysis significant relationships were detected between chewing khat and preterm delivery and as well between preterm birth and low birth weight. Even though no similar study exists to compare and explain the association, a previous comprehensive review and metanalysis aimed in identifying

determinants of low birth weight using those studies conducted on births of general population, reported preterm birth as one of the factors which significantly associated with low birth weight[149].

In addition, the mean birth weight of the newborn in the current study (2717.81±739.29grams) is lower than 3275±469grams[145], 3400±500grams[146], 3398±484grams[150], and 3036±478grams[151] documented in north western Nigeria, south-eastern Nigeria, Ukraine and Asian populations respectively. These variations of findings may possibly be due to differences in culture, lifestyle, dietary patterns, study area, sample size, study design, and mode of delivery.

The mean placental weight of births of cohort mothers in this study (490.73±75grams) is higher than 475±103.4grams reported in southern Ethiopia[152], 470±88grams reported in Ukraine[150] and 442±105grams reported in New York[153]. But the current result is inferior than 590±82grams[145], 630±110grams[146], and 588±128grams[151] revealed in north western Nigeria, south-eastern Nigeria, and Asian populations respectively. The variability of these findings may be due to variations in mode of delivery, lifestyle, dietary practices, and as well the technique of preparing to weigh placentas.

In the present study, the mean birthweight is significantly higher among non-khat chewers whereas placental weight is lower. However, the average placental weight is higher among khat chewers compared to non-khat chewers. The possible explanation may be in khat chewers there may be placental hypertrophy as an adaptation for maternal poor nutrition[154]. The other main likely justification for this finding may be mode of delivery. In the current study khat chewer cohorts significantly delivered through emergency cesarean section compared to non-chewers. Similar finding of a significantly low average birth weight and high average placental weight have been reported elsewhere[147] among those cesarean section deliveries as compared to vaginal deliveries. It is suggested that, in cesarean section delivery umbilical cord clamping is relatively early compared to vaginal delivery[155]. So early clamping will cause early decrement of flow of nutrient to the fetus compared to vaginal delivery. On the contrary, in cesarean delivery unlike vaginal delivery contraction of uterus is almost nil, hence intervillous space is more filled with maternal blood. But in vaginal delivery due to contraction maternal blood may pushed out of the placental tissues and then, may decrease its weight.

The mean placental-to-birth-weight ratio in the present study (19.71±7.35%) is comparable to those documented in Asian populations (19.5%)[151]. However, the present finding is relatively

higher than those documented in north western Nigeria (18.2%)[145], in Switzerland (17.6%)[147] and Ukraine (13.9%)[150].

In the present study the occurrence of still birth and neonatal death was not significantly different among khat chewers and non-khat chewer study cohorts. This finding is in line with previous study findings reported elsewhere[35, 45]. But a statistically significant increased fetal loss was observed in experimental animal studies[30-33]. These variations may be attributed to behavioral and physiological differences, differences in dose, and differences in study period. In fact, the present study found a significantly higher magnitude of previous spontaneous abortion history among khat chewer study cohorts compared to non-khat chewer counterparts. Hence, khat chewing may highly be associated with abortion (early pregnancy loss) in human pregnancy and since, the present study starts in the late second and early third trimester those having early loss may be missed.

In the present study, a significantly low 1- and 5-minute Apgar score (<7 score) were observed among khat chewer cohorts compared to non-khat chewer cohorts. In line with this finding a previous cross-sectional study conducted in Jimma, Ethiopia reported a significantly low 5-minute Apgar score among khat chewers compared to non-chewers[156]. The possible justification for the present finding may be due to the facts that, a significantly increased occurrence of preterm birth was noticed among khat chewer cohorts compared to non-chewers. Low Apgar score has been greatly related with preterm birth[157, 158]. Low Apgar score may possibly be linked with low fetal oxygen levels that may be related with impaired placental function[159]. The low fetal oxygen concentrations which latter leading to low Apgar count at delivery may possibly be due to sympathomimetic action of cathinone, one of the active ingredients of khat[45]. It has been documented in an experimental animal study is that, khat chewing during gestation leads to distortion of neural tube development and undifferentiated brain vesicles and then leading to imperfect closure of brain flexures[33] that may end in low Apgar score. Lastly, it has been elaborated in literature is that, low Apgar score was related with high placental weight[160, 161]. In line with these study findings, a significantly high placental weight was observed among khat chewer study cohorts compared to non-chewers.

The present study found 71.9%, 17.8% and 10.3% central, eccentric and marginal umbilical cord insertion respectively. A previous study[162] conducted in Gondar, northwest Ethiopia reported a lower magnitude of marginal cord insertion (6.4%) and 53.3% and 40.3% magnitude of

eccentric and central cord insertions respectively. On the other hand, another study conducted in India reported a higher marginal cord insertion (16.4%) and higher normal cord insertion (75.5%)[163]. Another study conducted elsewhere[125] reported a 65%, 25.8% and 8.3% magnitude of central, eccentric and marginal umbilical cord insertions respectively. In line with the current finding a 71% magnitude of central cord insertion is reported elsewhere[164]. Overall, our finding is in line with a report of nearly 90%[87] central and eccentric umbilical cord insertion to placenta.

The mean umbilical cord length in the present study (53.59±14.59cm) is almost similar with 52.87±13.49cm reported in India[126]. But higher than a previous report in southern Ethiopia (46.34±10.72)[165]. In similar pattern, 79.1%, 12.8% and 8.1% magnitude of normo, hypo and hyper coiled umbilical cord respectively in the present study, is almost comparable to 78.3%, 11.7% and 10% magnitude of normo, hypo and hyper coiled umbilical cord respectively, which have been reported in India[126].

Khat chewing and placental histopathologic findings

The present histopathologic study of the placenta revealed a significant association between khat chewing during pregnancy and placental hypoplasia, increased syncytial knots, villous hemorrhage/thrombosis, villous hyalinization and villous calcification ($p<0.05$). The current finding of a significant occurrence of placental hypoplasia among chewer mothers may possibly be due to vasoconstriction of uteroplacental vessels. It has been explained that the active constituents of khat, mainly cathinone is responsible for the sympathomimetic activity, thereby resulting in vasoconstriction[117]. Constriction of vessels may lead to ischemia which in turn leads to uteroplacental insufficiency and then underdevelopment of the placenta[166]. In line with the current study a previous experimental animal study registered a decrease in uteroplacental circulation among khat consumed compared to non-khat consumed experimental animals[119]. Moreover, it has been stated that an increased syncytial knot is the indication of uteroplacental insufficiency[167, 168]. The main factor associated with increased syncytial knots among chewer study participants may possibly be due to ischemia which in turn leads to hypoxia. It has been stated that increased syncytial knots were highly associated with hypoxia as it may lead to cell death[169].

Placental histopathologic findings and fetal outcomes (mainly fetal growth restriction and low birth weight)

In further, analysis of the present study revealed a significant relationship between placental histopathologic findings such as villous hypoplasia, increased syncytial knots, villous hyalinization and villous hemorrhage/thrombosis and fetal outcomes such as fetal growth restriction and low birth weight ($p<0.05$). Even though not compatible to compare and explain the association, previous studies also registered a significant relationship between villous hypoplasia, increased syncytial knots and villous hyalinization and restricted fetal growth and low birth weight[170-173]. The possible justification is that the normal development of the placenta is one of the vital factor for the normal development and growth of the fetus[174]. Hence, villous hypoplasia is highly associated with decreased uteroplacental circulation or ischemia which in turn leads to uteroplacental insufficiency and finally low birth weight[170]. Moreover, villous hypoplasia as well as increased syncytial knots could be highly associated with hypoxia of the fetus and then growth restriction of the fetus[170]. It has been also stated that fetal growth restriction may be associated with a reply to oxygen scarcity or hypoxia[175]. Additionally, in track with the present study finding, a previous study has reported the association between increased placental hemorrhage/thrombosis and low birth weight[176].

7. Strengths and limitations of the study

The cross-sectional nature of the first study did not reveal temporal relationships between the dependent and independent variables. But being a multi-centered study and conducted using both the quantitative and qualitative methods are the major strengths of the present study.

The main limitations of the present cohort study may be the recruitment time of the study being in late second and early third trimester of pregnancy, which may miss those early outcomes associated with practices of chewing khat during pregnancy. In fact, considering late second and early third trimester of pregnancy for the beginning time of the study is due to the fact that most of the Ethiopian mothers start to visit the health institutions for seeking ANC in the second trimester of their pregnancy [177]. Thus, the main factor is this feasibility issue. The other, the present study established an association between chewing khat during gestation and selected maternal, pregnancy, birth and neonatal outcomes, but the association may not be causal. Moreover, other limitation may be inability of measuring exposure status of participants using biological tests. So, relaying on self-reported data in research may have a risk of underreporting of their exposure status due to fear of prohibition or stigmatization and hence, underestimating its associated effects. But, since khat chewing practice on current study area is culturally and socially accepted phenomenon[101], the chance of misreporting is unlikely. Moreover, excluding cohorts with maternal anemia and gestational hypertension for histopathologic study may be the limitation for the present study. Hence, in the interpretations of the present findings the aforementioned limitations must be considered. But the present study has strengths. The first is being prospective cohort, as it establishes temporal relationships between chewing khat during gestation and the selected maternal, pregnancy, birth and neonatal outcomes studied. In addition, being a prospective cohort, the chance of missing data would be highly minimized. More importantly, up to the researcher's knowledge the present study is the first to demonstrate a model by which selected variables mediate the association between chewing khat during gestation and selected pregnancy outcomes, thereby explaining the mechanism by which khat chewing during pregnancy can influence these selected pregnancy outcomes. Lastly, up to the researcher's knowledge the present study is first in its nature, especially to demonstrate the impacts of khat chewing practices during pregnancy on selected maternal, pregnancy, birth, neonatal, umbilical, and placental outcomes in a prospective approach and also to demonstrate

the impacts of chewing khat during gestation on umbilical cord and placenta in a histopathologic way.

8. Conclusion

In the present study, a relatively higher proportion of mothers chewed khat during their current pregnancy. Bing older age, living in rural area, being illiterate, having khat chewer husbands and other family members were statistically significant variables associated with khat chewing during pregnancy.

Moreover, in the current follow-up study, four in every ten cohort mothers was diagnosed with maternal anemia; of these about forty-nine percent were among khat chewer cohorts and twenty nine percent were among non-chewers. One in every five cohort mothers was diagnosed with gestational hypertension; of these about twenty nine percent were among the khat chewer cohorts and fourteen percent were among non-chewers. Likewise, almost one in every three cohort mothers delivered newborns with fetal growth restriction; of which about fifty two percent were among khat chewer cohorts and about nine percent were among non-khat chewers. In additional analysis, the effect of khat chewing during pregnancy on fetal growth restriction has been partially mediated by gestational hypertension and maternal anemia. In the present study, the magnitude of oligohydramnios, preterm labor, pre-labor rupture of the membranes and abruption placenta were higher in proportion among the khat chewer study cohorts as compared to cohort mothers with no practice of khat chewing. Moreover, nearly one in every three cohort mothers delivered preterm newborns; of which about forty-nine percent were among the khat chewer cohorts and twelve percent were among non-chewers. In the present follow up study, the occurrence of low birth weight was one in every ten cohort mothers with sixty percent occurrence among khat chewer cohorts. Furthermore, in the present study, the magnitude of small for gestational age at birth, a low 1-minute Apgar score, a low 5-minute Apgar score, and the mean placental-to-birth-weight ratio were higher in proportion among khat chewer study cohort mothers as compared to study cohort mothers with no practice of khat chewing. More importantly, further analysis of the present study found that the effect of khat chewing during pregnancy on preterm birth was partially mediated by gestational hypertension and emergency cesarean delivery. In the same way, the effect of chewing khat during gestation on low birth

weight was partially mediated by gestational hypertension, emergency cesarean delivery, preterm birth, and maternal anemia.

The present histopathologic study of placenta found a significant association between khat chewing during pregnancy and placental hypoplasia, increased syncytial knots, villous thrombosis and villous hyalinization. Moreover, the aforementioned placental findings were significantly associated with fetal growth restriction and low birth weight. Overall, the present study discovered that chewing khat is not only a worry of the current population but also a public health concern of the generation affecting unborn fetuses.

9. Recommendations

Based on the current findings, the following possible ways of tackling the problem are recommended. One, the health professionals working in the area should highly engage in creation of awareness on harm of chewing khat during pregnancy while providing other healthcare services during antenatal care visits of mothers in the current study area. In addition, creation of awareness of the harm of chewing during gestation out of health institutions, at household and community levels including conducting of campaign is highly required using probably health development armies as an agent in the present study area. The local medias of the country should also work in awareness creation for the community regarding the harms of chewing khat during pregnancy on their unborn child through invitations of health professionals or invitations of trained community volunteers using local languages or through invitations of religious leaders. The religious leaders are highly recommended to work on how to stop the chewing practice especially during pregnancy. For example, the religious leaders can work on averting consideration of chewing by the community as culturally accepted practices. Health policy makers of the country should design policies and strategies that prohibit use of khat during pregnancy. This is because the effectiveness of every health intervention needs legal framework and government concern. The ministry of health and the respective zonal health offices and woreda health bureaus should provide emphasis on uncontrolled use of khat by pregnant women and should even communicate with the concerned government body so as to stop chewing of mothers while pregnant. The concerned government bodies especially local leaders should design the strategies of how to minimize or even stop chewing of khat during pregnancy in order to have healthy population. Moreover, non-governmental organizations working on community welfare should also work on how to decrease or stop use of khat during pregnancy. Lastly, we highly recommend further large-scale histopathologic study.

10. References

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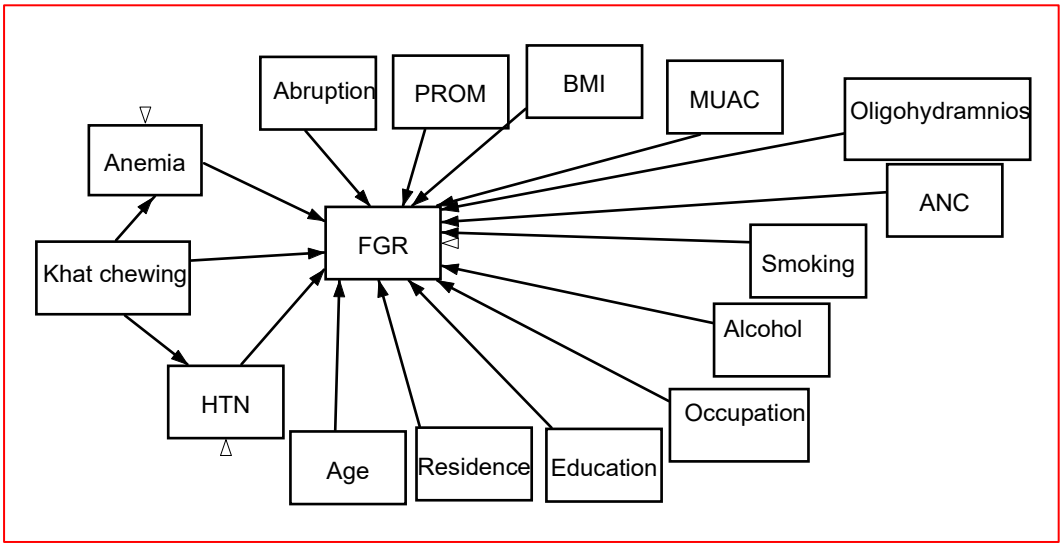
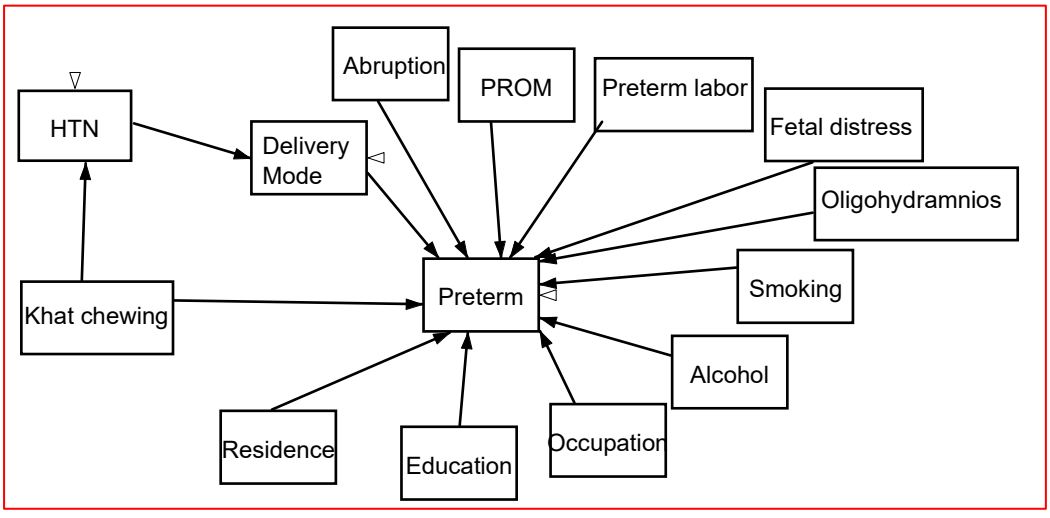
Annexes

Annex 1: Hypothetical GSEM model for FGR, Preterm birth and LBW.

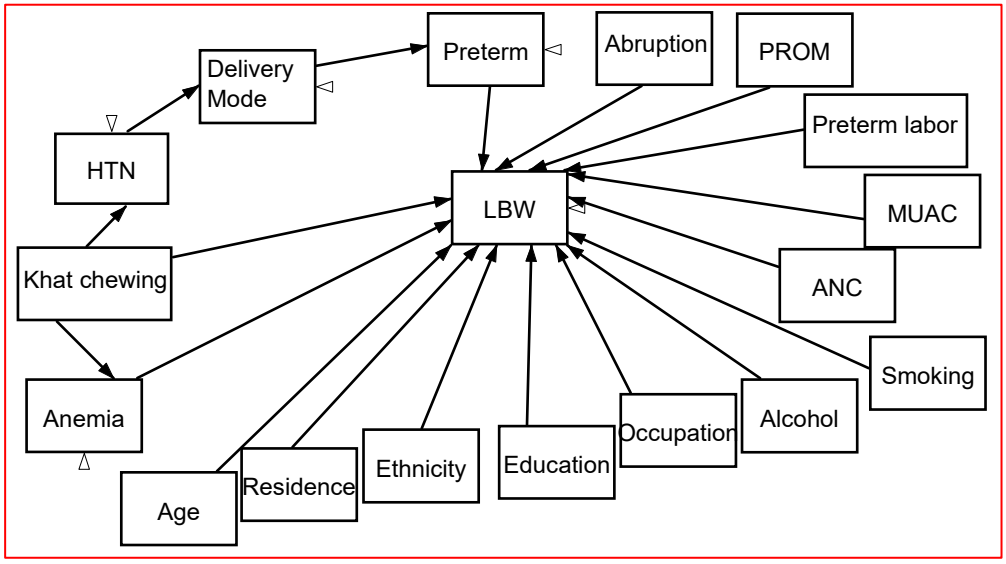
Hypothetical GSEM model for FGR.



Hypothetical GSEM for preterm birth



Hypothetical GSEM model for LBW



Annex 2: Processing protocol used for paraffin infiltration of human placenta and umbilical cord, adapted from previous work[178].

Activities	Steps	Solutions used	Time spent	Remark
Fixation	1	10% neutral buffered formalin	48-72 h	
Dehydration	2	40% alcohol	1:30 h	
	3	70% alcohol	1:30 h	
	4	80% alcohol	1:30 h	
	5	95% alcohol	1:30 h	
	6	95% alcohol	1:30 h	
	7	100% alcohol	1:30 h	
	8	100% alcohol	1:30 h	
Clearing	9	Xylene 1	1:30 h	
	10	Xylene 2	1:30 h	
	11	Xylene 3	1:30 h	
Infiltration/embedding	12	Paraffin (60 °C)	1:30 h	
	13	Paraffin (60 °C)	1:30 h	
	14	Paraffin (60 °C)	1:30 h	

Annex 3: Staining protocol used for paraffin-embedded placental and umbilical cord sections, adapted from previous work [178].

Activities	Steps	Solutions used	Time spent	Remark
Dewax/deparaffinization	1	Xylene 1	5 min	

	2	Xylene 2	5 min	
	3	Xylene 3	5 min	
Rehydration	4	100% alcohol	2 min	
	5	100% alcohol	2 min	
	6	90% alcohol	2 min	
	7	80% alcohol	2 min	
	8	70% alcohol	2 min	
	9	60% alcohol	2 min	
	10	Running tape Water	1 min	
Staining	11	Hematoxylin	10 min	
	12	Running water	5 min	
	13	Acid alcohol (alcohol with HCL)	2 dips	
	14	Running water	3 min	
	15	Bluing solution (Scott's tape water)	2 min	
	16	Running tape water	3 min	
	17	Eosin	5 min	
	18	Water	2 dips	
Dehydration	19	70% alcohol	2 dips	
	20	80% alcohol	2 dips	
	21	90% alcohol	2 dips	
	22	100% alcohol	2 min	
	23	100% alcohol	2 min	
Clearing	24	Xylene 3	5 min	
	25	Xylene 2	5 min	
	26	Xylene 1	5 min	
Mounting in DPX				

Annex 4: English Version Tools

Information sheet and Consent form

A. Information Sheet

Greetings! My name is _____, I am living in this area. Now I am collecting data from mothers on ante natal care follow up for the research being conducted to assess **Magnitude and associated factors of chewing khat during pregnancy and its Impact on maternal, pregnancy and neonatal outcomes in eastern Ethiopia, 2022: Cross Sectional, Prospective Cohort and Histopathologic Study** by Ato Amsalu Taye who is a PhD student in Addis Ababa University. The study will be used directly\indirectly to reveal magnitude of the problem and associated contributing factors for the occurrence of the problem and to know its impact on maternal and neonatal health outcomes and thereby its impact on the general health of the society. In addition, it is unclear if pregnant women who had practiced chewing have higher rates of pregnancy-related complications or health issues in their newborn. The evidence is expected to be used by governmental and non -governmental organizations working on substance use in order to inform policy makers and medical practitioners. The data which is necessary for the study will be taken from your response. Therefore, your willingness to respond to the list of questions in this study will be helped to achieve the stated benefits of the study and participation in the study is seen as vital citizenry and societal opportunities as well as contributions.

If you have any questions about this study, you may ask me or the principal investigator.

Principal investigator: Amsalu Taye Tel: 0921815441

E-mail: 50amsalu@gmail.com

Advisors: 1. Professor **Mekbeb Afework** (Tel: 0911411285) 2. **Dr. Miressa Bekana** (Tel: 0913281302).

B. Consent Form

Based on the purpose and objectives of the study, you are selected as one of study subject by chance. The investigator employed me for this data collection to maintain your data strictly confidential. As the study will be conducted through face-to-face interview and as well via measurements, it will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, and participation is totally voluntary. Your name and other personal identifiers will not be recorded on data collection form and the information that you give us will be kept confidential and will also be used for this study purpose only. You have

full right to leave/to refuse to take part at any stage of the interview. But your participation in this study will be essential to achieving the stated objectives that cannot be achieved without the participation of you. You will not face any problem if you do not volunteer to give information. On the other hand, generating new knowledge from your information will produce benefits for yourselves, for other persons or for society as a whole, or for the advancement of knowledge. More importantly, at the end of pregnancy when you come for childbirth, we will also ask to take a small portion of the placenta and umbilical cord.

Are you willing to let your information to be used for this study?

1. **Not** willing to extract data_____

   (End the session with thanks)

2. **Yes,** willing to extract data _____

   (Appreciate and proceed to extract data)

Signature of the data collector which shows that the respondent has consented (verbally) to take part in the study _____

Date of interview_____

Name of interviewer_____

Questionnaire ID (identification number) _____

የአማረኛ ቃለ መጠይቅ ቅጽ; መረጃ ስለመስጠትና የፈቃደኝነት ቅጽ

ሀ. መረጃ ስለመስጠት

ሰላምታ! ስሜ _____ እባላለሁ፣ የምኖረው በዚህ አካባቢ ነው። አሁን በእርግዝና ወቅት ጫት የመቃም መጠንን እና ተያያዥ ምክንያቶች እና በእርግዝና፣ በእናቶች እና በአራስ ሕፃናት ላይ ያለው ተጽእኖ ለመገምገም ለሚደረገው ጥናት የቅድመ ወሊድ እንክብካቤ ክትትል ከሚያደርጉ እናቶች *መረጃ* እየሰበሰብን ነው። ጥናቱ በዋናነት የሚካሄደዉ በአዲስ አበባ ዩኒቨርሲቲ የዶክትሬት ተማሪ የሆነው በአቶ አምሳሉ ታዬ ሲሆን ጥናቱ የችግሩን መጠን እና ተያያዥነት ያላቸውን ለችግሩ መከሰት እና አሁን በህብረተሰቡ ላይ ያለውን ተፅእኖ ለማሳየት በቀጥታ\በተዘዋዋሪ ጥቅም ላይ ይውላል። ማስረጃው ፖሊሲ አውጪዎችን እና የህክምና ባለሙያዎችን ለማሳወቅ በአደንዛዥ እፅ አጠቃቀም ላይ የሚሰሩ መንግሥታዊ እና መንግስታዊ ያልሆኑ ድርጅቶች ሊጠቀሙበት እንደሚችሉ ይጠበቃል። ለጥናቱ አስፈላጊ የሆነው መረጃ ከእርስዎ ምላሽ ይወሰዳል። ስለዚህ በዚህ ጥናት ውስጥ ላሉት ጥያቄዎች ዝርዝር ምላሽ ለመስጠት ፈቃደኛ መሆን በጥናቱ የተዘረዘሩትን ጥቅሞች ለማሳካት ይረዳል እና በጥናቱ ውስጥ መሳተፍ እንደ አስፈላጊ የዜጎች እና የህብረተሰብ ዕድሎች እንዲሁም አስተዋፅኦዎች ይታያል ።
ስለዚህ ጥናት ማንኛውም አይነት ጥያቄ ካሎት እኔን ወይም ዋናውን ተመራማሪ ልትጠይቁ ትችላላችሁ::

ዋና ተመራማሪ አምሳሉ ታዬ ስልክ ቁጥር 0921815441
ኢሜል፡ 50amsalu@gmail.com
አማካሪዎች፡ 1. ፕሮፌሰር መክብብ አፈወርቅ (ስልክ፡ 0911411285) 2. ዶ/ር መሬሳ በቃና (ስልክ፡ 0913281302).

ለ. የስምምነት ቅጽ
በጥናቱ አላማ እና አላማ ላይ በመመስረት በአጋጣሚ የጥናት ርዕሰ ጉዳይ ሆነው ተመርጠዋል። መረጃዎን በጥብቅ ሚስጥራዊ ለማድረግ ተመራማሪው ለዚህ መረጃ አሰባሰብ ቀጠረኝ። ጥናቱ የሚካሄደው ፊት ለፊት በቃለ መጠይቅ እና እንዲሁም በመለኪያ አማካኝነት ስለሆነ, ምስጢራዊነቱ እስከሚጠበቅ ድረስ ምንም አይነት ጉዳት አያስከትልም. ፈቃድ ሲሰጡ መረጃው ይወሰዳል፣ እና ተሳትፎ ሙሉ በሙሉ በፈቃደኝነት ነው። የእርስዎ ስም እና ሌሎች የግል መለያዎች በመረጃ መሰብሰቢያ ቅጽ ላይ አይመዘገቡም እና እርስዎ የሚሰጡን መረጃ በሚስጥር ይጠበቃል እና ለዚህ ጥናት ዓላማ ብቻ ጥቅም ላይ ይውላል። በማንኛውም የቃለ መጠይቁ ደረጃ ላይ ለመሳተፍ ለመተው/ለመቃወም ሙሉ መብት አልዎት። ነገር ግን በዚህ ጥናት ውስጥ ያለእርስዎ ተሳትፎ ሊሳኩ የማይችሉትን አላማዎች ለማሳካት በዚህ ጥናት ውስጥ ያለዎት ተሳትፎ ወሳኝ ይሆናል። መረጃ ለመስጠት ፈቃደኛ ካልሆኑ ምንም አይነት ችግር አይገጥምዎትም። በሌላ በኩል፣ ከመረጃዎ አዲስ እውቀት ማፍለቅ ለራሳችሁ፣ ለሌሎች ሰዎች ወይም ለህብረተሰቡ በአጠቃላይ ወይም ለእውቀት እድገት ጥቅማጥቅሞችን ያመጣል።

መረጃዎ ለዚህ ጥናት እንዲውል ለመፍቀድ ፈቃደኛ ነዎት?
1. ለመሳተፍ ፈቃደኛ አለመሆን_____
(ክፍለ ጊዜውን በምስጋና ጨርስ)
2. አዎ፣ ፈቃደኛ _____
(አመስግኑና ይቀጥሉ)
በጥናቱ ላይ ለመሳተፍ (በቃል) መስማማቱን የሚያሳይ የመረጃ ሰብሳቢው ፊርማ
የቃለ መጠይቁ ቀን _____
የጠያቂው ስም _____
መጠይቅ መታወቂያ (የመታወቂያ ቁጥር) _____

Gaafilee Afaan Oromoo.

A. Unka odeffannoo:

Nagaan isiniif haa ta’u. Maqaan kiyya _____ jedhama. Jiraataa naanoo kanaati. Ani amma qorannoo Baha Itiyoopyaatti mata duree “Babaliina jimaa qama’uu haadhoolee ulfa fi dhibbaa fayyaa inni haadhoolii fi daa’imman reefuu dhalataan irratti fiduu” kan jedhu irratti odeeffannoo sassaabaa jira. Qorannon kuni kan godhamuu barataa digrii sadaffa (PhD) Yunvarsiitii Addis Ababaa/Finfinnee kan ta’e obbo Amsaaluu Taayyeetiin dha. Qorannoon kuni kallattiif al-kallattidhan rakkoo jimaa qama’uun hadhoolii fi daa’imman reefuu dhalatan irratti inni qabu agarsiisuuf faydaa qaba. Arggannoon qorannoo kanaa qaamni moottummaa fi dhabbattota kan moottumma hin ta’iin (NGO) imaammata fi hojii fayyaa hadhooliif daa’immanii foyyeessuuf ni gargaara. Kanaafiis odeffannoon sirii isin biraa dhufa. Gaafilee armaan gadiitti jiraniif fedhii keessaniin hirmmaannaa gochuun keessan qorannoon kun akka galma ga’u murtteessadha. Kana gochuu kessaniinis dirqama hawwaasumma fi rakkoo akka

kanaa hiikuu keessatti ga'ee kessan ni baatu. Gaaffii yoo qabaattan ana yookiin qorataa muummichaa gaafachuu dandeessu.

1. Qorataa muummichaa: Obbo Amsaaluu Taayyee. Bilbila: 0921815441.
   E-mail: 50amsalu@gmail.com
2. Gorssitoota qorannoo:
   1. Prooffeessor Makbib Aaffewoorq: Bilbila: 0911411285
   2. Doctoor. Mirreessaa Baqaanaa. Bilbila: 0913281302.

B. Unka eyyamaa:

Qorannoo kanaaf kan atti filamte carraadhan qofa. Odeeffannoo atti kennitu icittiin isaa kan eegame ta'a. Qorannoon kun gaafilee deebisu fi qaama keessan safaaruu(measurement) qofaan waan raawwatuuf miidhaa isin irra fidu hin qabu. Odeeffannoon kan isin irraa fudhatamu yoo isin feetan qofa. Maqaan keesaan fi wanti eenyumaa dhunfaa keessan kan mul'isu unka kana irratti hin guutamu. Ragaa atti laattu icittiin isaa kan eegame yoo ta'u, qorannoo kana qofaaf tajaajila. Yoo barbaadde yeroo kamitti iyyuu hirmmanna kee addan kuttu ni danddeessa. Garuu hirmmaannan kee kayyoo qorannoo kanaaf baayyee barbaachisa. Yoo hirmaachuu didde rakkoon si irra ga'u hin jiru. Hirmmaannaan kee arggannoo haaraa yookiin beekumsa gabbisuu irratti bu'aa guddaa qaba.

Odeeffanno/Ragaa kee qorannoo kanaaf akka fayyadamnu in eeyyamtaa?

1. Lakki eyyamamaa miti?
   (Galateefadhaati addaan kuta).
2. Eeyyee.
   (Galattefadhaatti raga sasaabaa)
   Mallatoo kan nama ragaa sassaabe_____
   Guyyaa ittin ragaan sassaabame_____
   Maqaa nama nama ragaa sassaabe_____

Kooddii gaafilee(Questionaire code)_____

Xaashida Warfaafinta iyo Foomka Oggolaanshaha

A. Xaashida Warfaafinta

Salaan! Magacaygu waa _____, waxaan ku noolahay aaggan. Hadda waxaan hooyooyinka ka ururinayaa xog ku saabsan daryeelka dhalmada hore ee daba-galka cilmi-baadhista la samaynayo si loo qiimeeyo baaxadda iyo arrimaha la xidhiidha cunista qaadka xilliga uurka iyo saamaynta uu ku leeyahay uurka, natiijada hooyada iyo dhallaanka ee bariga Itoobiya, 2022: Isku-tallaabta, Kooxda Mustaqbalka iyo Cilmi-baarista Histopathology oo uu diyaariyay Ato Amsalu Taye oo PhD ka dhiga Jaamacadda Addis Ababa. Daraasadda waxa loo isticmaali doonaa si toos ah\n si dadban si loo muujiyo baaxadda dhibaatada iyo arrimaha la xidhiidha ka qayb qaadashada dhacdada dhibaatada iyo hadda saamaynta ay ku leedahay bulshada. Caddaynta waxaa la filayaa inay adeegsadaan hay'adaha dawliga ah iyo kuwa aan

dawliga ahayn ee ka shaqeeya isticmaalka muqaadaraadka si loogu wargaliyo siyaasad dejiyaasha iyo dhakhaatiirta caafimaadka. Xogta lagama maarmaanka u ah daraasadda waxaa laga soo qaatay jawaabtaada. Sidaa darteed; Rabitaankaaga inaad ka jawaabto liiska su'aalaha daraasaddan ayaa lagu caawin doonaa si loo gaaro faa'iidooyinka la sheegay ee daraasadda iyo ka qaybqaadashada daraasadda waxaa loo arkaa inay tahay fursadaha muwaadinka iyo bulshada muhiimka ah iyo sidoo kale wax ku biirinta.

Haddii aad wax su'aalo ah ka qabto daraasaddan, waxaad i waydiin kartaa aniga ama baaraha maamulaha

Baaraha maamulaha: Amsalu Taye Tel: 0921815441

E-mailka: 50amsalu@gmail.com

La-taliyayaasha: 1. Professor Mekbeb Afework (Tel: 0911411285) 2. Dr. Miresa Bekana (Tel: 0913281302)

B. Foomka Oggolaanshaha

Iyada oo ku saleysan ujeedada iyo ujeedooyinka daraasadda, waxaa laguu doortaa mid ka mid ah maadada daraasadda si nasiib ah. Baaraha ayaa ii shaqaaleysiiyay xog ururintan si aan xogtaada ugu ilaaliyo si adag. Maaddaama daraasadda lagu samayn doono waraysi fool ka fool ah iyo sidoo kale iyada oo la cabbirayo, ma keenayso waxyeello ilaa inta sirta la hayo. Macluumaadka waxaa la qaadan doonaa marka aad fasax bixiso, ka qaybqaadashaduna gebi ahaanba waa ikhtiyaari. Magacaaga iyo aqoonsiyada kale ee gaarka ah laguma qori doono foomka xog ururinta macluumaadka aad na siisona waxa lagu hayn doonaa sir waxaana sidoo kale loo isticmaali doonaa ujeedada daraasaddan oo keliya. Waxaad xaq buuxda u leedahay inaad ka baxdo/ diiddo inaad ka qayb qaadato marxalad kasta oo waraysiga. Laakin ka qaybqaadashadaada daraasaddan waxay noqon doontaa lama huraan si loo gaaro ujeedooyinka la sheegay ee aan la gaari karin ka qaybqaadashadaada la'aanteed. Ma la kulmi doontid wax dhibaato ah haddii aadan si tabaruc ah u bixin macluumaadka. Dhanka kale, abuurista aqoonta cusub ee macluumaadkaaga waxay kuu soo saari doontaa faa'iidooyin naftiinna ah, dadka kale ama bulshada guud ahaan, ama horumarinta aqoonta.

Ma doonaysaa in macluumaadkaaga loo isticmaalo daraasaddan?

1. Aan rabin in la soo saaro xogta_____

(Ku dhammee fadhiga mahadsanid)

2. Haa, diyaar u ah inuu soo saaro xogta _____

(Mahadsanid oo sii wad si aad xogta u soo saarto)

Saxeexa xog ururiyaha kaas oo tusinaya in jawaab-bixiyuhu ogolaaday (af ahaan) inuu ka qayb qaato daraasadda _____

Taariikhda wareysiga _____

Magaca waraystaha_____

Aqoonsiga xog-ururinta (lambarka aqoonsiga) _____

Participants ANC follow up card ID_____

Date of Assessment/Extraction_____

Participant background characteristics at enrollment to the study during ANC follow up.

Part I: Sociodemographic and economic characteristics of participants			
No	**Variables**	Coding category	Remark
101	Age	----------in years	
102	Are of residence	1. Urban 2. Rural	
103	What is your ethnicity?	1. Oromo 2. Harari 3. Somali 4. Amhara 5. Others, specify_____	
104	What is your religion?	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 5. Others, Specify……	
105	Educational status (What is the highest level of schooling attained)	1. No formal education 2. Primary education (grade 1-8) 3. Secondary education (grade 9-12) 4. College/University completed 5. Post-graduate degree	
106	Occupation status	1. House wife/ Homemaker 2. Farmer 3. Government employee 4. Non-government employee 5. Self-employed/ Merchant 6. Student 7. Daily laborer 8. Unemployed 9. Other specify	
107	Marital status	1. Never married/single 2. Currently married 3. Divorced/separated 4. Widowed	
108	Monthly income of the HH?	_____	
Part II: Substance use status during current pregnancy			
201	Have you ever used	1.Yes 2. No	

	any kind of substance during current pregnancy?		
202	Which kind of substance?	1. Khat 2. Alcohol 3. Tobacco product like cigarette 4. Others	
203	How often do you chew *khat?*	1. Daily 2. More than one day per week 3. Once per week 4. Less than once per week	
204	During chewing how many times and how many grams/packs do you chew?	How many times per day_____ How many grams_____ or how many packs per day_____ How many hours spent per chewing _____	
205	Have you consumed any alcohol within the past 30 days?	1. Yes 2. No	
206	Type and amount of alcohol used	1.beer ☐ yes ☐ no how many bottle 2.wine ☐ yes ☐ no how many glass 3.home made alcoholic drinks/specify	
207	Do you currently smoke tobacco products	1. Yes 2. No	
208	How often do you smoke tobacco products*?*	1. Daily 2. More than one day per week 3. Once per week 4. Less than once per week	
209	Why did you use these substance/es?	1. Unaware of pregnancy ☐ Yes ☐ No 2. Unaware of its harm ☐ yes ☐ no 3. For excited way of life ☐ yes ☐ no 4. Socialization ☐ yes ☐ no 5. To manage life pressure ☐ yes ☐ no 6. To cope up peer pressure ☐ yes ☐ no 7. To cope up partner pressure ☐ yes ☐ no 8. To cope up family pressure ☐ yes ☐ no 9. To obey tradition ☐ yes ☐ no 10. others	
210	Is your partner use any type of substance?	1.Yes 2. No	
211	Which type?	1.Khat ☐ yes ☐ no 2.Alcohol ☐ yes ☐ no 3.Tobacco product ☐ yes ☐ no 4.Other/specify	
212	Is there anyone using substance in your family?	1.Yes 2. No	
213	Which type?	1.Khat ☐ yes ☐ no 2.Alcohol ☐ yes ☐ no 3.Tobacco Product ☐ yes ☐ no	

		4.Other/Specify	
Part III: Past and current obstetric related characteristics			
301	How many times ever be pregnant?	----------	
302	How many children do you have?	----------	
303	Number of vaginal deliveries	----------	
304	Number of cesarean deliveries	----------	
305	History of spontaneous abortions	1. Yes 2. No	
306	History of still birth	1. Yes 2. No	
307	History of previous congenital anomalies	1. Yes 2. No	
308	Do you have family history of congenital anomalies?	1. Yes 2. No	
309	How many months pregnant are you now?	----------	
310	Have you planned this pregnancy?	1. Yes 2. No	
311	How many ANC visits did you have?	_____	
Part IV: Medical history and current medicine/drug use status			
401	Have you experienced diseases conditions prior to current pregnancy:	1. Yes 2. No	If yes, specify (eg. Heart diseases, lung diseases, liver diseases, kidnney diseases, DM, HTN, HIV/AIDS, malaria etc)
402			1. 2. 3.
403	Are you currently using medications?	1. Yes 2. No	If yes, specify (eg. Antihypertensives, anti-diabetic, antipain, antibiotics etc.)
404			1. 2. 3.

Measurement evidence to be filled during ante natal care follow up፤ participant ANC follow up card ID_____

Part 5: ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ ልኬት እና ዉጤቱ /physical examination & results done at ANC visits **(1st, 2nd, 3rd, 4th)**/			
No	**የተደረገ ልኬት**	**ውጤት (Results)**	**Remark**
501	Weight	**_____kg**	
502	Height	**_____meter**	
503	MUAC	**_____cm**	
504	Body temperature	_____degree Celsius	
505	Respiratory rate	_____ breaths/minute	
506	Heart rate	_____beats per minute	
507	Urinary Glucose	1. (+) 2. (++) 3. (+++) 4. Negative	
508	Urinary Protein	1. (+) 2. (++) 3. (+++) 4. Negative	
509	Blood pressure	_____/_____m mHg	
510	Pulse oximetry	_____%	
511	Fetal heart rate	_____beats per minute	
Part 6: **ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ የላቦራቶሪ ምርመራ ዉጤት/lab result at ANC visits**			
No	**የተደረገ ምርመራ**	**ውጤት (Results)**	**Remark**
601	Haemoglobin		
602	Haematocrit		
603	WBC Count		
604	Platelets		
605	Blood glucose		
Part 7: **ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ የአልትራሳዉንድ ምርመራ ዉጤት/ U/S results at ANC visits/**			
No	**የተደረገ ምርመራ**	**ዉጤት**	**Remark**
701	Fetal growth restriction (fetal weight is below 10th percentile for gestational age) BPD_____ HC_____ AC_____ FL_____	1. Yes 2. No	Gestational age at u/s investigation _____ LMP_____ Date at investigation_____ SFH (cm)_____
702	Oligohydramnios (SDP <2cm)	1. Yes 2. No	If "Yes", specify

	SDP; Single deepest pocket in cm_____		gestational age_____
703	Polyhydramnios (SDP >8cm)	1. Yes 2. No	If "Yes", specify gestational age_____
704	Echogenic bowel	1. Yes 2. No	If "Yes", specify gestational age_____
705	Ventriculomegaly (≥ 10 mm)	1. Yes 2. No	If "Yes", specify gestational age_____
706	Effusion	1. Yes 2. No	If "Yes", specify gestational age_____
707	Cardiomegaly	1. Yes 2. No	If "Yes", specify gestational age_____
708	Ascites	1. Yes 2. No	If "Yes", specify gestational age_____
709	Hydrops fetalis	1. Yes 2. No	If "Yes", specify gestational age_____
710	Any congenital anomalies identified	1. Yes 2. No	If "Yes", specify gestational age_____
711	Type of congenital anomalies seen		
Part 8: ቅድመ ወሊድ ክትትል ለሚደርጉ እናቶች በተደረገ ምርመራ የታወቁ በሽታዎች ወይም ምልክቶች/ችግሮች (Diseases identified at ANC visits).			
No	**የበሽታዉ/ችግሩ አይነት**	**መልስ (Responses)**	Remark
801	Gestational diabetes (የእርግዝና ስኩዋር በሽታ)	1. Yes 2. No	
802	Gestational hypertension (High blood pressure)	1. Yes 2. No	**If yes, specify** 1. Non-proteinuric hypertension 2. Pre-eclampsia / eclampsia
803	Low blood pressure	1. Yes 2. No	
804	Anemia (Hb < 11 g/dL)	1. Yes 2. No	
805	Hyperemesis/ ከባድ ማቅለሽለሽ እና ማስታወክ	1. Yes 2. No	
806	Fetal growth restriction/ የፅንስ እድገት ገደብ	1. Yes 2. No	
807	Placental previa (attachment to cervix)	1. Yes 2. No	
808	Placental abruption (premature separation)	1. Yes 2. No	
809	Vaginal watery discharge	1. Yes 2. No	
810	Vaginal bleeding	1. Yes 2. No	
811	Preterm labor	1. Yes 2. No	
812	Preterm premature rupture of	1. Yes 2. No	

	membranes (< 37weeks) (PPROM)		
813	Headaches	1. Yes 2. No	
814	Vision changes	1. Yes 2. No	
815	Right upper quadrant (abdominal) pain	1. Yes 2. No	
816	Decreased or no fetal movement	1. Yes 2. No	
817	Hemorrhage (>500ml of blood loss)	1. Yes 2. No	
818	Other, diseases/symptoms	1. Yes 2. No	

Maternal outcomes at delivery or pregnancy termination form
Participant ANC follow up card ID_____

Part 9: **Clinical measurement information during admission for delivery**			
No	**የተደረገ ልኬት**	**ውጤት (Results)**	**Remark**
901	Weight	**_____kg**	
902	Height	**_____meter**	
903	MUAC	**_____cm**	
904	Body temperature	_____degree Celsius	
905	Respiratory rate	_____ breaths/minute	
906	Heart rate	_____beats per minute	
907	Urinary Glucose	1. (+) 2. (++) 3. (+++) 4. Negative	
908	Urinary Protein	1. (+) 2. (++) 3. (+++) 4. Negative	
909	Blood pressure (Systolic / Diastolic)	_____/_____mmHg	
910	Pulse oximetry	_____%	
911	Fetal heart rate	_____ beats per minute	
Part 10: Laboratory measurements results during admission for delivery			
No	**የተደረገ ምርመራ**	**ውጤት (Results)**	**Remark**
1001	Haemoglobin		
1002	Haematocrit		
1003	WBC Count		
1004	Platelets		
1005	Blood glucose		
Part 11: **Diseases or symptoms/complications, identified during delivery/TOP period (regardless of their chewing status)**			
No	**የበሽታዉ/ችግሩ አይነት**	**መልስ (Responses)**	**Remark**
1101	Gestational diabetes	1. Yes 2. No	
1102	Gestational hypertension (High blood pressure)	1. Yes 2. No	**If yes, specify** 1. Non-proteinuric hypertension 2. Pre-eclampsia /

			eclampsia
1103	Low blood pressure	1. Yes 2. No	
1104	Anemia (Hb < 11 g/dL)	1. Yes 2. No	
1105	Hyperemesis	1. Yes 2. No	
1106	Fetal growth restriction (fetal weight is below 10th percentile for gestational age)	1. Yes 2. No	
1107	Placental previa	1. Yes 2. No	
1108	Placental abruption	1. Yes 2. No	
1109	Vaginal bleeding	1. Yes 2. No	
1110	Vaginal watery discharge	1. Yes 2. No	
1111	Headaches	1. Yes 2. No	
1112	Vision changes	1. Yes 2. No	
1113	Right upper quadrant (abdominal) pain	1. Yes 2. No	
1114	Uterine contractions	1. Yes 2. No	
1115	Decreased or no fetal movement	1. Yes 2. No	
1116	Fetal distress (የጽንስ መታፈን አለ)	1. Yes 2. No	
1117	Fever	1. Yes 2. No	
1118	Hemorrhage (>500ml of blood loss)	1. Yes 2. No	
1119	Others,	1. Yes 2. No	Specify_____
Part 12: Presentation and delivery outcomes			
No	Variables	Responses	Remark
1201	Indication for childbirth (የወሊዱ ምክንያት ምንድን ነዉ)	1. Spontaneous labor (በራሱ ጊዜ ምጥ በመጀመሩ) 2. Premature rupture of membranes 3. Fetal distress 4. Preeclampsia/gestational hypertension 5. Vaginal bleeding 6. Post-dates (የእርግዝና ጊዜዉ በማለፉ) 7. Fetal growth restriction 8. Other, specify_____	
1202	Mode of Delivery	1. Normal vaginal delivery 2. Instrumental (vacuum/forceps) 3. Planned Cesarean delivery 4. Emergency Cesarean delivery	
1203	Fetal presentation at delivery	1. Cephalic 2. Transverse 3. Breech	
1204	Amniotic fluid at delivery	1. Clear	

		2. Meconium-stained	
1205	Pregnancy outcomes	1. Live birth 2. Still birth	
1206	Maternal status at the end of delivery	1. Discharge 2. Referral 3. Admission 4. Death	
1207	If maternal death, what was underlying cause of death?	Specify,	

Neonatal outcomes assessed between birth and end of 4th week of birth form
Participants ANC/Delivery card ID_____

Part 13: **Childbirth and after birth information**			
No	Variables	Results	Remark
1301	Sex of newborn	1. Male 2. Female	
1302	Gestational age at birth	_____ Weeks	LMP (D/M/Y)_____ DOB (D/M/Y)_____ SFH (cm)_____
1303	Birth weight	_____grams	
1304	Apgar scores at	1. 1 min_____ 2. 5 min_____	
1305	Temperature	_____ degree Celsius	
1306	Respiratory rate	_____***breaths/min***	
1307	Heart rate	_____ ***beats/min***	
1308	Pulse oximetry (Peripheral O2 saturation (SpO2)	_____%	
1309	Did the child have any of the following problems at time of birth?	1. Poor feeding 2. Convulsions or fits 3. Fast breathing 4. Severe chest indrawing 5. Not moving spontaneously/by self 6. Temperature >37.5C 7. Temperature <35.5C 8. Jaundice or yellow colour in skin or eyes 9. Nasal congestion/runny nose 10. Vomiting 11. Diarrhea 12. Seizures 13. Sepsis	

		14. Skin rash 15. Skin peeling from hands, feet, or lips 16. Enlarged lymph nodes 17. Red eyes 18. Discharge or fluid coming from eyes 19. Any other symptoms	
1310	Can we say that the new born is in the respiratory distress?	1. Yes 2. No	
1311	Are there noticed congenital anomalies at birth?	1. Yes 2. No	
1312	If yes, types of congenital anomalies noticed:	1. Neural tube defects 2. Microcephaly 3. Congenital malformations of ear 4. Suspected congenital heart defects 5. Orofacial clefts 6. Congenital malformations of digestive system 7. Congenital malformations of genital organs 8. Abdominal wall defects 9. Suspected chromosomal abnormalities 10. Reduction defects of upper and lower limbs 11. Talipes equinovarus/clubfoot 12. Others, specify	
1313	Neonatal status at the end of delivery	1. Healthy 2. Referral 3. Admitted 4. Death	
1314	Neonatal status at the end of 4th week	1. Healthy 2. Admitted 3. Death	
1315	If neonate died, what was the primary cause of death?	1. Preterm birth 2. Low birth weight 3. Birth asphyxia 4. Congenital anomalies /birth defects 5. Birth trauma 6. Other, specify	
1316	Age at death of		

	neonates (in days)		

ቅድመ ወሊድ ክትትል (ANC) ለሚያደርጉ እናቶች የሚደረግ መጠይቅ፡

የመጠይቁ ተሳታፊ መለየ_____ መጠይቁ የተከናወነበት ቀን/ወር/አ.ም/_____

ክፍል 1፡ የተሳታፊዎች ማህበራዊ እና ኢኮኖሚያዊ ባህሪዎች			
ተ.ቁ	**የባህሪዎች ዝርዝር**	ኮድ መስጫ ምድብ	ምርመራ
101	እድሜ በአመት	----------(በአመት)	
102	የመኖሪያ አድራሻ	1. ከተማ 2. ገጠር	
103	ብሄር?	1. ኦሮሞ 2. ሀረሪ 3. ሶማሌ 4. አማራ 5. ሌላ, ይጥቀሱ_____	
104	ሀይማኖት?	1. ሙስሊም 2. ኦርቶዶክስ 3. ፕሮቴስታንት 4. ካቶሊክ 5. ሌላ, ይጥቀሱ……	
105	የትምህርት ሁኔታ	1. ማንበብና መጻፍ የማትችል 2. አንደኛ ደረጃ (grade 1-8) 3. ሁለተኛ ደረጃ (grade 9-12) 4. ኮሌጅ/ዩኒቨርሲቲ የጨረሰች 5. ሁለተኛ ዲግሪ የጨረሰች	
106	የስራ ሁኔታ	1. የቤት እመቤት/House wife 2. ገበሬ 3. የመንግስት ሰራተኛ 4. መንግስታዊ ያልሆነ ድርጅት ሰራተኛ 5. ነጋዴ 6. ተማሪ 7. የቀን ሰራተኛ 8. ስራ ፈላጊ 9. ሌላ፣ ይጠቀስ----------	
107	የጋብቻ ሁኔታ	1. ያላገባች 2. ያገባች 3. የተፋታች 4. የሞተባት	
108	የቤተሰብ ወርሃዊ ገቢ	_____	
ክፍል 2፡ በአሁኑ እርግዝና ጊዜ እጾችን ከመጠቀም ጋር በተያያዘ መጠይቆች			
201	በአሁኑ እርግዝና ወቅት እጾችን ተጠቅመው ያውቃሉ?	1.አውቃለሁ 2.አላውቅም	2→ክፍል 3
202	የትኛውን አይነት እጽ?	1.ጫት	→203

		2. የአልኮል መጠጥ	→205
		3.ሲጋራ /የትምባሆ ምርት	→207
		4. ሌላ / ይግለጹ	
203	በየስንት ጊዜው ይቅማሉ?	1.በየቀኑ 2. በሳምንት ከአንድ ቀን በላይ 3.ቢያንስበሳምንትአንዴ 4.በሳምንትከአንድጊዜባነሰ	
204	በሚቅሙበት ወቅት ስንት ጊዜ እና ምን ያህል ግራም ይቅማሉ	በቀን ስንት ጊዜ_____ስንት ግራም_____ለምን ያህል ስአት_____	
205	ላለፉት 30 ቀናት የአልኮል መጠጥ ተጠቅመዉ ያቃሉ	1.አውቃለሁ 2.አላውቅም	
206	የተጠቀሙትየመጠጥአይነት	1.ቢራ አዎ አይ ስንት ጠርሙስ 2.ወይን አዎ አይ ስንት ብርጭቆ 3.በቤትውስጥየሚዘጋጅ/ይጠቀስ	
207	ሲጋራ ወይም ሌላ የትምባሆ ምርት አጭሰዉ ያቃሉ	1.አውቃለሁ 2.አላውቅም	
208	በየስንትጊዜውይጠቀማሉ?	1.በየቀኑ 2. በሳምንት ከአንድ ቀን በላይ 3.ቢያንስበሳምንትአንዴ 4.በሳምንትከአንድጊዜባነሰ	
209	እነዚህን እጾች የተጠቀማችሁበት ምክንያቶች?	1.ነፍሰጡርመሆኔንባለማወቄ አዎ አይ 2.የሚያስከትለውንጉዳትባለማወቄ አዎ አይ 3 የደስታ ስሞት እንዲሰማኝ አዎ አይ 4. ለማህበራዊ ኑሮ አዎ አይ 5 የኑሮን ጫና ለመቀነስ አዎ አይ 6. የጉዋደኞን ግፊትለመቋቋም አዎ አይ 7. የባለቤትዎን ግፊትለመቋቋም አዎ አይ 8 የቤተሰብወን ግፊትለመቋቋም አዎ አይ 9. ባህልስለሆነ አዎ አይ 10. ሌሎች / ይግለጹ	
210	ባለቤትዎ እጽ ይጠቀማል?	1.አዎ 2.የለም	
211	የትኛውን አይነት እጽ?	1. ጫት አዎ አይ 2. የአልኮል መጠጥ አዎ አይ 3.የትምባሆ ምርት አዎ አይ 4. ሌላ / ይግለጹ	
212	በቤተሰብ ውስጥ እጽ የሚጠቀም ሰው አለ?	1.አዎ 2.የለም	
213	የትኛውን አይነት እጽ?	1. ጫት አዎ አይ 2. የአልኮል መጠጥ አዎ አይ 3. የትምባሆ ምርት አዎ አይ 4. ሌላ / ይግለጹ	
ክፍል 3፡ ከእርግዝና እና ወሊድ ጋር የተያያዙ ባሕርያት			
301	ምን ያህል ጊዜ አርግዘሽ ታውቂያለሽ?	----------	

302	ስንት ልጆች አሉሽ?	----------	
303	በምጥ የተወለዱ ህጻናት ቁጥር	----------	
304	በቀዶ ህክምና (C/S) የተወለዱ ህጻናት ቁጥር	----------	
305	ድንገተኛ ውርጃ ተከስቶ ያቃል	አዎ አይ	
306	ሞቶ የተወለደ ህጻን ነበረ (still birth)	አዎ አይ	
307	የአእምሮ ወይም የአካል እድገት ችግር ያለበት ልጅ ወልደው ያቃሉ	አዎ አላቅም	
308	በቤተሰባችሁ የአእምሮ ወይም የአካል እድገት ችግር ያለበት ልጅ ተወልዶ ያቃሉ	አዎ አያቅም	
309	አሁን የስንት ወር እርጉዝ ነሽ ?	---------- -	
310	እርግዝናሽ የታቀደ ነበር?	1.አዎ 2.አይደለም	
311	እስካሁን ምን ያህል የእርግዝና ክትትል አድርገሻል?	---------- -	
ክፍል 4፡ የጤና ሁኔታ እና አሁናዊ የመድሃኒት አጠቃቀም ሁኔታ			
401	ከአሁኑ እርግዝና በፊት የተለያዩ በሽታዎች አጋጥሞዎታል	1.አዎ 2.አይ	ካጋጠመወት የትኛዉ በሽታ፡ የልብ፣ የሳንባ፣ የጉበት፣የኩላሊት፣ ስኩዋር፣ደም ግፊት፣ ኤች.አይ.ቪ፣ወባ...
402			1. 2. 3.
403	በአሁኑ ጊዜ መድሃኒቶችን እየተጠቀሙ ነው?	1.አዎ 2.አይ	አዎ ከሆነ የትኛዉን መድሀኒት፡የግፊት፣ የስኩዋር፣የቁርጥማት፣ የሙቀት፣ antibiotics…
404			1. 2. 3.

ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የሚሞላ ጥናታዊ መረጃ፤ መለያ ኮድ_____

ክፍል 5፡ ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ ልኬት እና ዉጤቱ /physical examination & results done at ANC visits (1st, 2nd, 3rd, 4th)/			
No	**የተደረገ ልኬት**	**ውጤት (Results)**	**Remark**
501	Weight	**_____kg**	
502	Height	**_____meter**	
503	MUAC	**_____cm**	
504	Body temperature	_____degre e Celsius	
505	Respiratory rate	_____ breaths/minute	

506	Heart rate	_____beats per minute	
507	Urinary Glucose	1. (+) 2. (++) 3. (+++) 4. Negative	
508	Urinary Protein	1. (+) 2. (++) 3. (+++) 4. Negative	
509	Blood pressure	_____/_____ _____mmHg	
510	Pulse oximetry	_____%	
511	Fetal heart rate	_____beats per minute	
ክፍል 6፡ ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ የላቦራቶሪ ምርመራ ዉጤት/lab result at ANC visits			
No	**የተደረገ ምርመራ**	**ውጤት (Results)**	**Remark**
601	Haemoglobin		
602	Haematocrit		
603	WBC Count		
604	Platelets		
605	Blood glucose		
ክፍል 7፡ ቅድመ ወሊድ ክትትል ለሚያደርጉ እናቶች የተደረገ የአልትራሳዉንድ ምርመራ ዉጤት/ U/S results at ANC visits			
No	**የተደረገ ምርመራ**	**ዉጤት**	**Remark**
701	Fetal growth restriction (fetal weight is below 10th percentile for gestational age)	1. Yes 2. No	If "Yes", specify gestational age_____
702	Oligohydramnios (SDP <2cm)	1. Yes 2. No	If "Yes", specify gestational age_____
703	Polyhydramnios (SDP >8cm)	1. Yes 2. No	If "Yes", specify gestational age_____
704	Echogenic bowel	1. Yes 2. No	If "Yes", specify gestational age_____
705	Ventriculomegaly (≥ 10 mm)	1. Yes 2. No	If "Yes", specify gestational age_____
706	Effusion	1. Yes 2. No	If "Yes", specify gestational age_____
707	Cardiomegaly	1. Yes 2. No	If "Yes", specify gestational age_____
708	Ascites	1. Yes 2. No	If "Yes", specify gestational age_____
709	Hydrops fetalis	1. Yes 2. No	If "Yes", specify gestational age_____
710	Any congenital anomalies identified	1. Yes 2. No	If "Yes", specify gestational age_____
711	Type of congenital anomalies seen		

ክፍል 8፡ ቅድመ ወሊድ ክትትል ለሚደርጉ እናቶች በተደረገ ምርመራ የታወቁ በሽታዎች ወይም ምልክቶች/ችግሮች (Diseases identified at ANC visits)			
No	**የበሽታዉ/ችግሩ አይነት**	**መልስ (Responses)**	Remark
801	Gestational diabetes (የእርግዝና ስኩዋር በሽታ)	1. Yes 2. No	
802	Gestational hypertension (High blood pressure)	1. Yes 2. No	**If yes, specify** 1. Non-proteinuric hypertension 2. Pre-eclampsia / eclampsia
803	Low blood pressure	1. Yes 2. No	
804	Anemia (Hb < 11 g/dL)	1. Yes 2. No	
805	Hyperemesis/ ከባድ ማቅለሽለሽ እና ማስታወክ	1. Yes 2. No	
806	Fetal growth restriction/ የፅንስ እድገት ገደብ	1. Yes 2. No	
807	Placental previa (attachment to cervix)	1. Yes 2. No	
808	Placental abruption (premature separation)	1. Yes 2. No	
809	Vaginal watery discharge	1. Yes 2. No	
810	Vaginal bleeding	1. Yes 2. No	
811	Preterm labor	1. Yes 2. No	
812	Preterm premature rupture of membranes (< 37weeks) (PPROM)	1. Yes 2. No	
813	Headaches	1. Yes 2. No	
814	Vision changes	1. Yes 2. No	
815	Right upper quadrant (abdominal) pain	1. Yes 2. No	
816	Decreased or no fetal movement	1. Yes 2. No	
817	Hemorrhage (>500ml of blood loss)	1. Yes 2. No	
818	Other, diseases/symptoms	1. Yes 2. No	

መዉለድ ለሚመጡ እናቶች የሚሞላ ጥናታዊ መረጃ /Maternal outcomes at delivery/፤ መለያ ኮድ_____

ክፍል 9፡ በወሊድ ወቅት ለእናቶች የተደረገ ልኬት እና ዉጤቱ /physical examination and results/			
No	**የተደረገ ልኬት**	**ውጤት (Results)**	**Remark**
901	Weight	**_____kg**	
902	Height	**_____meter**	
903	MUAC	**_____cm**	
904	Body temperature	_____degree Celsius	
905	Respiratory rate	_____ breaths/minute	
906	Heart rate	_____beats per minute	
907	Urinary Glucose	1. (+) 2. (++) 3. (+++) 4. Negative	

908	Urinary Protein	1. (+) 2. (++) 3. (+++) 4. Negative	
909	Blood pressure (Systolic / Diastolic)	_____/_____mmHg	
910	Pulse oximetry	_____%	
911	Fetal heart rate	_____ beats per minute	
ክፍል 10፡ መዉለድ ለመጡ እናቶች የተደረገ የላቦራቶሪ ምርመራ ዉጤት			
No	**የተደረገ ምርመራ**	**ውጤት (Results)**	**Remark**
1001	Haemoglobin		
1002	Haematocrit		
1003	WBC Count		
1004	Platelets		
1005	Blood glucose		
ክፍል 11፡ መዉለድ ለመጡ እናቶች በተደረገ ምርመራ የታወቁ በሽታወች/ምልክቶች/ Diseases identified at delivery			
No	**የበሽታዉ/ችግሩ አይነት**	**መልስ (Responses)**	**Remark**
1101	Gestational diabetes	1. Yes 2. No	
1102	Gestational hypertension (High blood pressure)	1. Yes 2. No	**If yes, specify** 1. Non-proteinuric hypertension 2. Pre-eclampsia / eclampsia
1103	Low blood pressure	1. Yes 2. No	
1104	Anemia (Hb < 11 g/dL)	1. Yes 2. No	
1105	Hyperemesis	1. Yes 2. No	
1106	Fetal growth restriction (fetal weight is below 10th percentile for gestational age)	1. Yes 2. No	
1107	Placental previa	1. Yes 2. No	
1108	Placental abruption	1. Yes 2. No	
1109	Vaginal bleeding	1. Yes 2. No	
1110	Vaginal watery discharge	1. Yes 2. No	
1111	Headaches	1. Yes 2. No	
1112	Vision changes	1. Yes 2. No	
1113	Right upper quadrant (abdominal) pain	1. Yes 2. No	
1114	Uterine contractions	1. Yes 2. No	
1115	Decreased or no fetal movement	1. Yes 2. No	
1116	Fetal distress (የጽንስ መታፈን አለ)	1. Yes 2. No	
1117	Fever	1. Yes 2. No	
1118	Hemorrhage (>500ml of blood loss)	1. Yes 2. No	
1119	Others,	1. Yes 2. No	Specify_____
ክፍል 12፡ እናቶች ለመዉለድ ከመጡ በሁዋላ የወለዱበት አግባብ እና ዉጤቱ			
No	Variables	Responses	Remark
1201	Indication for childbirth	1. Spontaneous labor (በራሱ ጊዜ ምጥ	

	(የወሊዱ ምክንያት ምንድን ነዉ)	በመጀመሩ) 2. Premature rupture of membranes 3. Fetal distress 4. Preeclampsia/gestational hypertension 5. Vaginal bleeding 6. Post-dates (የእርግዝና ጊዜዉ በማለፉ) 7. Fetal growth restriction 8. Other, specify_____	
1202	Mode of Delivery	1. Normal vaginal delivery 2. Instrumental (vacuum/forceps) 3. Planned Cesarean delivery 4. Emergency Cesarean delivery	
1203	Fetal presentation at delivery	1. Cephalic 2. Transverse 3. Breech	
1204	Amniotic fluid at delivery	1. Clear 2. Meconium-stained	
1205	Pregnancy outcomes	1. Live birth 2. Still birth	
1206	Maternal status at the end of delivery	1. Discharge 2. Referral 3. Admission 4. Death	
1207	If maternal death, what was underlying cause of death?	Specify,	

ህፃናት በተወለዱበት ቀንና ከተወለዱ በሁዋላ ባሉት 30 ቀናት ዉስጥ የተመዘገቡ አካላዊና ተግባራዊ ልኬትና ዉጤቶች መረጃ (የተወለዱ ህጻናት መረጃ- Neonatal outcomes between birth and end of 4th weeks of birth)፤ መለያ ኮድ_____

ክፍል 13፡ በወሊድ ጊዜ እና ከወሊድ በሁዋላ ህጻኑን በሚመለከት የተከናወኑ ልኬቶች እና ዉጤት			
No	Variables	ዉጤት (Results)	Remark
1301	**Sex of newborn**	**1. Male 2. Female**	
1302	Gestational age at birth	_____ Weeks	
1303	Birth weight	_____grams	
1304	Apgar scores at	1. 1 min_____ 2. 5 min_____	
1305	Temperature	_____ degree Celsius	
1306	Respiratory rate	_____***breaths/min***	
1307	Heart rate	_____ ***beats/min***	
1308	Pulse oximetry	_____%	
1309	Did the child have any of the following problems at time of birth?	1. Poor feeding 2. Convulsions or fits 3. Fast breathing	

		4. Severe chest indrawing 5. Not moving spontaneously/by self 6. Temperature >37.5C 7. Temperature <35.5C 8. Jaundice or yellow colour in skin or eyes 9. Nasal congestion/runny nose 10. Vomiting 11. Diarrhea 12. Seizures 13. Sepsis 14. Skin rash 15. Skin peeling from hands, feet, or lips 16. Enlarged lymph nodes 17. Red eyes 18. Discharge or fluid coming from eyes 19. Any other symptoms	
1310	Can we say that the new born is in the respiratory distress?	1. Yes 2. No	
1311	Are there noticed congenital anomalies at birth?	1. Yes 2. No	
1312	If yes, types of congenital anomalies noticed:	1. Neural tube defects 2. Microcephaly 3. Congenital malformations of ear 4. Suspected congenital heart defects 5. Orofacial clefts 6. Congenital malformations of digestive system 7. Congenital malformations of genital organs 8. Abdominal wall defects 9. Suspected chromosomal abnormalities 10. Reduction defects of upper and lower limbs 11. Talipes equinovarus/clubfoot 12. Others, specify	
1313	Neonatal status at end of delivery	1. Healthy 2. Referral 3. Admitted 4. Death	
1314	Neonatal status at end of 4th week	1. Healthy 2. Admitted	

		3. Death	
1315	Age at death of neonates (in days)		
1316	If neonate died, what was the primary cause of death?	1. Preterm birth 2. Low birth weight 3. Birth asphyxia 4. Congenital anomalies /birth defects 5. Birth trauma 6. Other, specify	

Gaafilee/kooddii hirmaataa_____
Guyyaa ragaan itti sassabame_____
Odeeffannoo waliigalaa (Bacground information):
Kuttaa 1: Haala hawwaassummaa fi dinaagdee hirmaattootaa

Lakk.	**Vaariiablii/gaaffii**	**Koodii/garee**	**Hubachiisa davbalataa**
101	Umuriin kee wagaa meeqa?	----------	
102	Iddoo itti jiraatan?	1. Magaala 2. Baadiyaa	
103	Qomoon kee maal?	1. Oromoo 2. Hararii 3. Soomaalee 4. Amaara 5. Kan biraa(ibsi)----------	
104	Amantiin kee maal?	1. Islaama 2. Ortodoxii 3. Protestaantii 4. Kaatoolikii 5. Kan bira(ibsi)----------	
105	Sadarkaa barumsa kee inni olaanaa kutaa meeqa?	1. Mana barumsaa hin galle 2. Sadarkaa 1^{ffaa}(kutaa 1-8) 3. Sadarkaa 2^{ffaa}(kutaa 9-12) 4. Kolleejii/digrii tokkoffaa 5. Digrii lammaffaa fi isa oli	
106	Hojiin keessan maal?	1. Giiftii manaa 2. Qonnaan bula 3. Hojjetaa moottummaa 4. Hojjetaa NGO 5. Hojii dhunfaa/dalddaalaa 6. Barataa 7. Hojii humnaa/ Daily laborer 8. Kan hin qacaramne	

		9. Kan bira(ibsi)----------	
107	Haala gaa'ilaa	1. Hin fuune/hin eerumne 2. Kan fuudhe/kan eerumte 3. Walk kan hiike/tte 4. Kan jalaa du'ee/widowed	
108	Galiin akka maattiitti isin ji'aan argattan meeqa ta'aa?	----------	
Kutaa 2: Haala fayyadama araada Yeroo ulfaa tti godhamu			
201	Yeroo ulfa kannatti araada kammiyyuu fayyadamtee beektaa?	1, Eeyyee 2, Lakki	
202	Eeyyee yoo jette, araada gosa kami?	1. Jimaa/caatii 2. Dhugaatti 3. Tamboo kan akka sigaaraa 4. Kan bira(ibsi)----------	
203	Yeroo ammamiif jimaa/caatii qamaata?	1. Guyyaa guyyaatti 2. Torbanitti yeroo tokko kan caalu 3. Torbanitti yeroo tokko 4. Torbanitti yeroo tokko gadii	
204	Yeroo qamaatu, yeroo meeqaa fi giraamaa meeqa qamaata?	Guyyaatti yeroo meeqa____ Giraamaa meeqa_____	
205	Guyyootaa 30 darbaniitti alkoolii kamiyyuu fayyadamtee beektaa?	1, Eeyyee 2, Lakki	
206	Gosa alkoolii fayyadamte?	Biiraa 1, Eeyyee 2, Lakki Woyinii 1, Eeyyee 2, Lakki Kan bira (ibsi)----------	
207	Yeroo ammamiif tamboo fayyadamta?	1. Guyyaa guyyaatti 2. Torbanitti yeroo tokko kan caalu 3. Torbanitti yeroo tokko 4. Torbanitti yeroo tokko gadii	
208	Yeroo ammamiif taboo fayyadamta?	1. Guyyaa guyyaatti 2. Torbanitti yeroo tokko kan caalu 3. Torbanitti yeroo tokko 4. Torbanitti yeroo tokko gadii	
209	Araada kana maallif fayyadamta?	1. Ulfa ta'u koo hin beeku 1, Eeyyee 2, Lakki 2. Miidhaa isaa hin beeku 1, Eeyyee 2,	

		Lakki 3. Gamachuu argachuuf 1, Eeyyee 2, Lakki 4. Hawassumaaf 1, Eeyyee 2, Lakki 5. Dhiibbaa jirenyaa mo'achuuf 1, Eeyyee 2, Lakki 6. Dhiibbaa hir'aa 1, Eeyyee 2, Lakki 7. Dhiibbaa aantee 1, Eeyyee 2, Lakki 8. Dhiibbaa maatii 1, Eeyyee 2, Lakki 9. Aadaa eeguuf 1, Eeyyee 2, Lakki 10. Kan bira (Ibsi)----------	
210	Wara manaa kee araada fayyadamuu?	1, Eeyyee 2, Lakki	
211	Gosa kami?	1. Jimaa/caatii 2. Dhugaatti 3. Tamboo kan akka sigaaraa 4. Kan bira(ibsi)----------	
212	Maatii kee keessaa namnii araada fayyadamuu jira?	1, Eeyyee 2, Lakki	
213.	Gosa kami?	1. Jimaa/caatii 2. Dhugaatti 3. Tamboo kan akka sigaaraa 4. Kan bira(ibsi)----------	
Kutaa 3: Halaa da'umsa kana dura waliin wal qabatu			
301	Kana dura yeroo meeqaf ulfooftee beekta?	----------	
302	Ijoollee meqa qabda?	----------	
303	Lakkofsa da'umsaa kara gadameessa	----------	
304	Lakkofsa da'umssa operaashinii(C/S)	----------	
305	Ulfi sii irra ba'ee beeka?	1, Eeyyee 2, Lakki	
306	Mucaan garaatti miidhamte dhalattee beeka(still birth)?	1, Eeyyee 2, Lakki	
307	Kana dura mucaan garaatti qaama midhamaa kan ta'e jira?	1, Eeyyee 2, Lakki	
308	Maatii keessan	1, Eeyyee 2, Lakki	

	keessa dhibeen akka kanaa mudatee beeka?		
309	Ulfi kee ammaa ji'a meeqa?	_____	
310	Ulfa kana karooraan godhattee?	1, Eeyyee 2, Lakki	
311	Yerroo meeqaf horddooffi tajaajila hadhooli ulfaaf kennamu argatte?	----------	
	Kuta 4: Seenaa Medikaalaa fi qorichaa fayyadamuu		
401	Ulfa kana dura dhibee/dhukkuba sii mudatee jira?	1, Eeyyee 2, Lakki	Eeyyee yoo jette gosaa isaa ibsi
402			1. 2. 3.
403	Yeroo kana qoricha kan fayyadamtu jira?	1, Eeyyee 2, Lakki	Eeyyee yoo jette gosaa isaa ibsi
404			1. 2. 3.

APGAR Score

At one minute after birth

APGAR sign	0	1	2	Examination value (0, 1, 2)
Activity/muscle tone	Limp	Some extremity flexions	Active	
Pulse (heart rate)	Absent	<100BPM	>=100BPM	
Grimace (Reflex irritability)	None	Grimace	Sneeze/cough	
Appearance/color	Blue/pale	Blue extremities, pink body	All pink	
Respirations/breathing	Absent	Irregular/slow	Good/strong crying	
			Total score	

At five minute after birth

APGAR sign	0	1	2	Examination value (0, 1, 2)
Activity/muscle tone	Limp	Some extremity flexions	Active	
Pulse (heart rate)	Absent	<100BPM	>=100BPM	
Grimace (Reflex irritability)	None	Grimace	Sneeze/cough	
Appearance/color	Blue/pale	Blue extremities, pink body	All pink	
Respirations/breathing	Absent	Irregular/slow	Good/strong crying	
			Total score	

የጥናት ተሳታፊዉ መለያ ኮድ_____

Macroscopic examination checklist for umbilical cord and placenta

Umbilical cord:

Insertion: 1. Central 2. Eccentric 3. Marginal 4. Velamentous

Length:_____cm Average diameter:_____cm Number of vessels:__

Twists: 1. Under coiled 2. Normal 3. Hyper twisted

True knot: 1. Yes 2. No

Other abnormalities, specify_____

Placenta:

Trimmed weight:_____gm

Shape: 1. Round 2. Oval 3. Irregular 4. Other_____

Fetal surface: any abnormality:_____

Maternal surface: 1. Complete 2. Incomplete 3. Other

Any other abnormality_____

Focal lesion: 1. Yes 2. No %_____

If yes describe_____

Diffuse lesion: 1. Yes 2. No %_____

Specimen collection for histopathology preparation.

Histopathologic procedures/steps
Specimen processing steps used

Specimen staining steps used

Histopathologic results
Routine light microscope visualization results with different magnification power.

Parameters for placental histopathologic observation

Slide code	Parameter type	Possible finding choices	Remark
	Trophoblasts proliferation		
	Villous edema		
	Villous hypoplasia		
	Villous hyalinization		
	Villous infarction/necrosis		
	Villous calcification		
	Villous fibrosis		
	Villous/intervillous hemorrhage/thrombosis		
	Fibrinoid necrosis in placenta		
	Syncytial knots		
	Lumen of villi vessels		
	Width of intervillous space		
	Any new findings noticed		

Parameters for umbilical cord histopathologic observation

Slide code	Parameter type	Possible findings	Remark
	Number of vessels		
	Vein lumen		
	Vein wall		
	Venous thrombosis		
	Venous hemorrhage/hematoma		
	Artery lumen		
	Artery wall		
	Arterial thrombosis		
	Arterial hemorrhage/hematoma		
	Wharton’s jelly wall		

	Wharton's jelly hemorrhage		
	Wharton's jelly edema		
	Any other new findings		

Interview guide for qualitative data collection (for chewer pregnant mothers)

Age

Residence

GA at interview_____ number of visits at interview_____.

How are your experiences of chewing?

Do you know khat? Have you practiced of chewing ever? For how long you chewed? How much chewed (local measurements) per single chewing session? How long it takes per single chewing session? How many times you chewed per week?

Why you chew khat?

What is your experience on cultural, traditional, religious, family, partner and peer influences for starting khat chewing?

Importance/value of chewing khat?

How does chewing impacted/influenced your life/daily living and health status?

Do you know the impacts of chewing on pregnancy and unborn child? If yes, could you mention?

Annex 5: <u>Curriculum Vitae of Principal Investigator and Advisors respectively.</u>

<u>CV of Principal Investigator</u>

1. **Personal information**

- Name — Amsalu Taye Wondemagegn
- Date of birth — January 13, 1987
- Sex — Male
- Address — **mobile: 09-21-81-54-41**
  Email: 50amsalu@gmail.com
- Nationality — Ethiopian
- Physical condition — Normal

2. Educational Background and Qualification

No	Year	Award	Name of Institution
1.	**July, 2010**	**Bachelor of Science in *Public health***	**Hawassa University**
2	**February, 2013**	**Master of Science in Anatomy**	**Addis Ababa University**
3	**June, 2016**	**Master of public health in reproductive health (MPH)**	**Wollega University**
4	**March 16, 2020**	**Assistant Professor of Medical Anatomy**	**Debre Markos University**

3. Language

- Fluent in listening, speaking, reading and writing English and Amharic.
- English language was the formal medium of instruction for teaching-learning for high school, preparatory school, bachelor and master's degree.

4. Computer skill

- I have good computer skill including Basics and analysis of data using different application soft wares like **Excel**, **Epi-info, SPSS, STATA, SAS, R** and others.

5. Qualification

- ***BSc in Public Health,***
- ***MSc in Anatomy***
- ***MPH in RH***
- **Assistant Professor of Medical Anatomy**

6. Work Experience and skills

- ✓ I have teaching and research experience by working in Debre Markos University since September 2015 as staff member of biomedical sciences department, school of medicine. I also served as a unit leader and head, department of biomedical sciences, and as vice dean of school of medicine. Previously I also served being staff member of public health department (from 2011 to 2014) in Wollega university.

7. Research experience

- I had worked in systematic review and meta-analysis on the following topic which had been published on different peer reviewed journals as elaborated below:
    - ✓ Is protease inhibitors based antiretroviral therapy during pregnancy associated with an increased risk of preterm birth? Systematic review and a meta-analysis, published on Biomed central reproductive health journal;
    - ✓ Effects of antenatal care follow up on neonatal mortality: A systematic review and meta-analysis, published on Public Health Reviews journal;
    - ✓ Prevalence of diabetes mellitus among tuberculosis patients in Sub-Saharan Africa: a systematic review and meta-analysis of observational studies, published on BMC Infectious Diseases
    - ✓ Household latrine utilization and its association with educational status of household heads in Ethiopia: a systematic review and meta-analysis, Published on BMC Public Health
- I had worked on original research articles being principal investigator, co-investigator and advising students and can be elaborated as follows;
- I had worked being **principal investigator** on the following original research article topics:
    - Undernutrition and related factors among children aged 6-59 months in Gida Ayana district west Ethiopia, **published on nutrition and food sciences journal**
    - Perceived psychological, economic and social impact of khat chewing among adolescents and adults in Nekemte town, west Ethiopia, **published on Biomed research international journal**
    - Undiagnosed diabetes mellitus and related factors in east Gojjam northwest Ethiopia, published **on journal of public health research**
    - Predictors of chronic undernutrition (stunting) among under five children in rural east Wollega, west Ethiopia: **a community-based case - control study,** published on **Journal of Nutritional Health & Food Engineering**

- Prevalence of diagnosed and newly diagnosed diabetes mellitus and its related factors in east Wollega zone, west Ethiopia, published on **World Journal of Advance Healthcare Research**
- Evaluation of Pattern of Community Engagement in District Health Care in East Wollega: Qualitative Study, published on **Journal of Community Medicine & Health Education**

- I had worked being co-investigator and being advising undergraduate students; and a few of the topics includes:
  - Long acting contraceptive method utilization and associated factors among reproductive age group female health worker at Debre Markos hospital, 2018
  - Determinants of stunting among under five children at east Gojjam zone Amhara region: A case control study, 2018
  - Patterns of road traffic accident and related factors in east Wollega, west Ethiopia
  - Mothers' perception on antenatal care services and institutional delivery in east Wollega, Oromia west Ethiopia
  - The prevalence and factors associated with delayed treatment seeking behavior of mothers/care givers for under five pneumonia in Diga District, west Ethiopia
  - Assessment of knowledge, attitude and practice of mothers towards child respiratory tract infection and its management in Bako Tibe town, west Ethiopia
  - Breast self-examination among adolescents in Debre Markos town, northwest Ethiopia, 2017.

8. Publication:

I have **16 publications** which also includes systematic review and meta-analysis in which the titles are given below, hence please confirm online:

1. Yonatan Moges Mesfin, Kelemu Tilahun Kibret and **Amsalu Taye**. Is protease inhibitors based antiretroviral therapy during pregnancy associated with an increased risk of

preterm birth? Systematic review and a meta-analysis. Reproductive Health (2016) 13:30. DOI 10.1186/s12978-016-0149-5.

2. **Wondemagegn, A.T**., Alebel, A., Tesema, C. *et al.* The effect of antenatal care follow-up on neonatal health outcomes: a systematic review and meta-analysis. *Public Health Rev* **39,** 33 (2018) doi:10.1186/s40985-018-0110-y.
3. Alebel, A., **Wondemagegn, A.T.**, Tesema, C. *et al.* Prevalence of diabetes mellitus among tuberculosis patients in Sub-Saharan Africa: a systematic review and meta-analysis of observational studies. *BMC Infect Dis* **19,** 254 (2019) doi:10.1186/s12879-019-3892-8.
4. Leshargie, C.T., Alebel, A., Negesse, A. *et al.* Household latrine utilization and its association with educational status of household heads in Ethiopia: a systematic review and meta-analysis. *BMC Public Health* **18,** 901 (2018) doi:10.1186/s12889-018-5798-6.
5. Chego M, Adeba E, **Taye A** (2018) Evaluation of Pattern of Community Engagement in District Health Care in East Wollega: Qualitative Study. J Community Med Health Educ 8:612. DOI: 10.4172/2161-0711.1000612
6. **Taye A**, Wolde T, Seid A (2016) Under-nutrition and Related Factors among Children Aged 6-59 Months in Gida Ayana District, Oromiya Region, West Ethiopia: A Community Based Quantitative Study. J Nutr Food Sci 6: 543. doi: 10.4172/2155-9600.1000543.
7. **Amsalu Taye Wondemagegn**, Melese Chego Cheme, and Kelemu Tilahun Kibret. Perceived Psychological, Economic, and Social Impact of Khat Chewing among Adolescents and Adults in Nekemte Town, East Welega Zone, West Ethiopia. BioMed Research International Volume 2017, Article ID 7427892, 9 pages https://doi.org/10.1155/2017/7427892.
8. **Amsalu Taye Wondemagegn**, Habtamu Mellie Bizuayehu, Dagninet Derebe Abie, Getachew Mengistu Ayalneh, Tenaw Yimer Tiruye, Mequanint Taddele Tessema. Undiagnosed diabetes mellitus and related factors in East Gojjam (NW Ethiopia) in 2016: a community-based study. Journal of Public Health Research 2017; volume 6:834.
9. **Wondemagegn AT**, Cheme MC, Gerbi EA (2017) Predictors of Chronic Undernutrition (Stunting) among Under Five Children in Rural East Wollega, Oromiya Region, West

Ethiopia: A Community Based Unmatched Case - Control Study. J Nutr Health Food Eng 7(2): 00233. DOI: 10.15406/jnhfe.2017.07.00233

10. Binalfew Tsehay, Desalegn Shitie, Akilog Lake, Erimiyas Abebaw, **Amsalu Taye** & Enatinesh Essa. Determinants and seasonality of major structural birth defects among newborns delivered at primary and referral hospital of East and West Gojjam zones, Northwest Ethiopia 2017–2018: case–control study. *BMC Res Notes* **12,** 495 (2019). https://doi.org/10.1186/s13104-019-4541-4.
11. **Wondemagegn AT**, Afework M. The association between folic acid supplementation and congenital heart defects: Systematic review and meta-analysis. SAGE Open Medicine. 2022 Mar;10:20503121221081069.
12. **Wondemagegn AT**, Mulu A. Effects of Nutritional Status on Neurodevelopment of Children Aged Under Five Years in East Gojjam, Northwest Ethiopia, 2021: A Community-Based Study. Int J Gen Med. 2022 Jun 8;15:5533-5545. doi: 10.2147/IJGM.S369408. PMID: 35707740; PMCID: PMC9189147.
13. **Wondemagegn AT**, Seyoum G. A multicenter study on practices and related factors of traditional medicinal plant use during pregnancy among women receiving antenatal care in East Gojjam Zone, Northwest Ethiopia. Front Public Health. 2023 Apr 17;11:1035915. doi: 10.3389/fpubh.2023.1035915. PMID: 37139367; PMCID: PMC10149730.
14. **Wondemagegn AT**, Tsehay B, Mebiratie AL, Negesse A. Effects of dietary diversification during pregnancy on birth outcomes in east Gojjam, northwest Ethiopia: A prospective cohort study. Front Public Health. 2022 Dec 5;10:1037714. doi: 10.3389/fpubh.2022.1037714. PMID: 36544806; PMCID: PMC9760662.
15. **Wondemagegn AT**, Bekana M, Bekuretsion Y, Afework M. **Magnitude and associated factors of chewing khat during pregnancy in Eastern Ethiopia, 2022: a mixed method cross-sectional study.** Pan Afr Med J. 2023 Oct 24; 46:66. doi: 10.11604/pamj.2023.46.66.39872. PMID: 38282772; PMCID: PMC10822099.
16. **Wondemagegn AT**, Bekana M, Bekuretsion Y, Afework M. **The effect of possible mediators on the association between chewing khat during pregnancy and fetal growth and newborn size at birth in Eastern Ethiopia. BMC Pregnancy Childbirth. 2024 Jan 13; 24(1):63.** doi: 10.1186/s12884-024-06243-2. PMID: 38218789; PMCID: PMC10787403.

9. Leadership experiences

I have been working as head of department of biomedical sciences for around 5 months and as a vice dean of school of medicine for more than 3 years at Debre Markos University.

10. Trainings attended and professional certificate

- I had taken different trainings organized and given by governmental and non-governmental organizations like: -
  - ✓ Successfully completed and certified on Higher Diploma Program (HDP) given by Debre Markos University (issued date June, 30/2018 G.C).
  - ✓ Training on STATA, SAS and R soft wares organized by Federal Ministry of Health, Amhara regional health Bureau in collaboration with Debre Markos University.
  - ✓ Training on Human and Financial resource Management for different professionals organized by Federal Ministry of Health of Ethiopia in collaboration with Adama Hospital Medical College.
  - ✓ Training of trainer (TOT) on Problem Based Learning (PBL) organized by Federal Ministry of Health in collaboration with Jhpiego with funding from USAID.
  - ✓ Certificate for successful completion of public health emergency management training organized by Ethiopian public health institute.
  - ✓ Certificate for participation as external examiner of second year medical students in Wollo University held from February 3-10/2018.
  - ✓ Certificate for participation as external examiner of first year medical students in Hawassa University held from march 4-7/2019.
  - ✓ Certificate for participation as external examiner of second year medical students in Wolaita Sodo University held from march 18-22/2019.
  - ✓ Certificate for participation as external examiner of second year medical students in Wolaita Sodo University held from march 18-22/2019.
  - ✓ Certificate for recognition as external examiner of second year medical students in Mizan Tepi University held from January, 2022.

- ✓ Certificate for recognition as external examiner of second year medical students in Debre Birhan University held from February 12 to 14, 2024.
- ✓ Certificate of participation as presenter at national nutrition research conference held in Addis Ababa, Ethiopia, December 8-10, 2021; organized by EPHI.
- ✓ Certificate of presentation at 9th annual national research conference held on February 15, 2024, at Dire Dawa University.
- ✓ Certificate of participation on a conference in improving medical education held at Bishoftu, March 12-13, 2020, organized by AHMC and AKU, CHS-CSH in collaboration with FMOH, Ethiopia and Maastricht University, the Netherlands
- ✓ Training on effective teaching and performance assessment organized by project-Jhpiego- Ethiopia.
- ✓ Training on doctors as teachers course organized by university of Exeter medical school, 2015.
- ✓ Attending workshop on the Ethiopian health care challenges, organized by Albert Einstein college of medicine, NYC, USA, Malaria consortium Ethiopia and Hawassa health sciences college, Hawassa university.
- ✓ Active learning, continuous assessment, classroom management.

Curriculum vitae of Professor Mekbeb Afework, BSc, MPhil, PhD, HDP

Professor of Histology,
Department of Anatomy,
School of Medicine, CHS, AAU, Ethiopia.
Consultant, Health Sciences Specialist, Ministry of Health, Ethiopia

BIOGRAPHICAL DATA

- Name: **Mekbeb Afework Kidane-Mariam**
- Date of birth: 12 February, 1962
- Place of birth: Nekempte, Ethiopia
- Nationality: Ethiopian
- Language: Amharic, Oromiffa and English
- Sex: Male
- Marital status: Married, with one daughter and two sons.
- Address: Department of Anatomy, School of Medicine, College of Health Sciences, Addis Ababa University, P.O.Box 2888, Addis Ababa, Ethiopia.
  Tel: + 251-11-555 7967(Off), + 251-911-411285 (Mobile)
  Fax: + 251 1 551 3099
  E-mail: mekbebafework@yahoo.co.uk, m.afework@yahoo.com
  P.O. Box: 2888, Addis Ababa, Ethiopia

HIGHER EDUCATION:

LEVEL	INSTITUTE	DATE
1. BSc degree in Biology major & Chemistry minor with distinction	Department of Biology, Faculty of Science, Addis Ababa University, Ethiopia	Sept 1979- July 1983
2. MPhil degree in Human Morphology University of Nottingham, U.K.	Department of Human Morphology, Faculty of Medicine,	Jan 1987- Aug 1988
3. PhD degree in Anatomy, Developmental Biology & Neuroscience	Department of Anatomy & Developmental Biology, Faculty of Science, University College London, U.K.	Sept 1991- Sept 1995
4. Higher Diploma Program (HDP) in Pedagogy	Addis Ababa University, Ethiopia	Mar 2015- July, 2015

AWARDS

1. **Certificate of recognition of promotion** to the academic rank of full professor of Histology. College of Health Sciences, Addis Ababa University, September 30, 2021.
2. **Letter of Appreciation** dated February 9, 2015 by Dr Abebe Bekele, Associate Dean School of Medicine, CHS, AAU, to the huge contribution as the Head of Department of Anatomy to the school of Medicine, CHS, AAU
3. **Letter of Appreciation** dated February 2, 2015 by Dr Mahlet Yigeremu, Dean School of Medicine and CEO Tikur Anbessa Specialized Hospital, CHS, AAU, to the great contribution as the head of Department of Anatomy and a member of Academic Commission during April 2012-February 2015 to the school of Medicine, AAU
4. **Letter of Appreciation** dated April 20, 2011 by Dr Miliard Derbew, Dean School of Medicine and A/Executive Director, CHS, AAU, to the unreserved support and commitment as the Head of Department of Anatomy during April 2007-April 2011 to the school of Medicine, AAU
5. **Letter of appreciation and prism award** December 21, 2014 for dedicated long years of service of over 30 years to the School of Medicine, CHS, AAU
6. **Best Teacher of the year**, School of Medicine, Addis Ababa University, 2012
7. **IBRO travel Award** for the 4th International Conference of the Society of the Neuroscientists of Africa (SONA 99), April 12-16, 1999, Dakar, Senegal.
8. **IBRO travel Award** for the 3rd International Conference of the Society of the Neuroscientists of Africa (SONA 97), April 21-25, 1997, Cape Town, South Africa.
9. The following three awards for postgraduate study leading to a PhD degree in Neuroscience 1991-1995
    a. **Overseas Research Students' award**, University College London, U.K.
    b. **Dean's Scholarship award**, Faculty of Medical Sciences, University College London, U.K.
    c. **Research Studentship award,** Department of Anatomy & Developmental Biology, University College London, U.K.
10. **British Council Scholarship** Award for Postgraduate Study leading to an MPhil degree in Anatomy, 1987-1988.

PROFESSIONAL SOCIETY MEMBERSHIP

1. Member International Brain Research Organization (IBRO) since 1995.
2. Member International Society for Neurochemistry (ISN) since December 7,1998.
3. Member Society of Neuroscientists of Africa (SONA) since 1999.
4. Member Ethiopian Biological Society since January 14 1999.
5. Member Family Guidance Association of Ethiopia since February 02, 2016
6. Founding Member of Anatomical Society of Ethiopia since January 2016

WORK EXPERIENCE:

A. Ranks and Posts held at School of Medicine, College of Health Sciences, Addis Ababa University
    1. Full Professor of Histology (since July 2021).
    2. Head, Department of Anatomy, Faculty of Medicine, Addis Ababa University (on three

occasions, respectively during: May, 1998 – Jan, 2001; February, 2003 – December 2005; March 2009 – January 09, 2017).
3. Consultant, Health Sciences Specialist, Ministry of Health, Ethiopia, since March 2008
4. Acting Head, Department of Anatomy, Faculty of Medicine, Addis Ababa University (on three occasions, respectively during: February 28 – March 09, 2001; June 25 – July 27, 2007; February 19 – February 22, 2008).
5. Associate Professor of Anatomy (since Oct 2000-July 2021).
6. Assistant Professor of Anatomy (Oct 1995 - Oct 2000).
7. Lecturer in Anatomy (Aug1988-Sept 1991).
8. Assistant Lecturer in Anatomy (Feb 1985 - Jan 1987).
9. Graduate Assistant in Anatomy (Sept 1983 - Feb 1985).

B. Taught the following Courses/Modules for over 27 years (during 1984-1987; 1988-1991; and since 1995 to date) at School of Medicine, College of Health Sciences, Addis Ababa University

1. Histology course for Preclinical Students of Doctor of Medicine (MD) and Doctor of Dental Medicine (DDM) degrees
2. Embryology course for Preclinical Students of Doctor of Medicine (MD) and Doctor of Dental Medicine (DDM) degrees
3. Clinical Histology and Embryology courses for Residents from Surgery, Obstetrics & Gynaecology and Orthopaedic Surgery
4. Cytology, General Histology and Histological Techniques for MSc students in Anatomy
5. Systemic Histology and Histophysiology for MSc students in Anatomy
6. General Embryology and Teratology for MSc students in Anatomy
7. Gross Anatomy, including Neuroanatomy for Preclinical Students of Doctor of Medicine (MD) degree
8. Anatomy for BSc in Pharmacy students
9. Anatomy for BSc in Nursing students
10. Demonstrator of Gross Anatomy Dissections and CNS to 1st year Medical students.

C. Part-time Instructor of:

- Histology and Embryology courses for Preclinical Students Doctor of Medicine (MD) and Doctor of Dental Medicine (DDM) degrees at**:**
  1. **Hayat Medical College**, Addis Ababa, Ethiopia, since 2007
  2. **Bethel Medical College**, Addis Ababa, Ethiopia, since 2012
  3. **Africa Medical College**, Addis Ababa, Ethiopia, 2014-2016
  4. **Sante Medical College**, Addis Ababa, Ethiopia, since 2015

D. Gust Lectureship/Visiting Scientist Abroad and Outside Addis Ababa University

1. Taught Embryology & Histology I Course for Year I Medical Students at the **A.M. Dogliotti College of Medicine, Monrovia University of Liberia**, during December 1-31, 2015.
2. Visiting Associate Professor at the Faculty of Medicine, **Adama University, Assella, Ethiopia**, **Jan 15- 21, 2012**. Taught Histology course for year I Medical Students.
3. Visiting Associate Professor at the Faculty of Medicine, **Adama University, Assella,**

Ethiopia, **Jan 25-Feb 1, and Feb 15-20, 2013** Taught Embryology course and Special Histology for year I Medical Students

4. Visiting Associate Professor at the Department of Anatomy, Faculty of Medicine, **National University of Rwanda, Rwanda** (on two occasions, respectively during: Oct. 1-23, 2005, and Sept 18-27, 2009). Taught:
   a. Gross Anatomy of the Upper & Lower Limbs, Thorax and Peripheral Nervous System, for Year I Medical Students, Oct. 1-23, 2005.
   b. Embryology course for Year II Medical Students, Sept 18-27, 2009.
5. Honorary Senior Research Fellow, Honorary Research Fellow and Visiting Scientist at **Autonomic Neuroscience Institute and Department of Anatomy & Developmental Biology, Royal Free Hospital Medical School, University of London**, London, U.K. (on three occasions, respectively during: July 1 - September 30, 1998; Sept 30 – Dec 22, 2001; Aug 1 - Oct 30, 2003).
6. Visiting Associate Professor of Anatomy at **Hayat Medical College, Addis Ababa, Ethiopia** (1st December, 2005 – 31st December, 2006); and Acting Assistant Dean (on four occasions, respectively during: Feb 20 -24, 2006; July 1 -23, 2006; Sept 02 – 07, 2006; Feb 28-March 09, 2008).
7. Visiting Associate Professor at the Faculty of Medicine, **Bahir Dar University, Bahir Dar, Ethiopia**, March 1-15, 2009. Taught Special Histology course for year I Medical Students.
8. Guest Lecturer **Gondar College of Medical Sciences, University of Gondar, Gondar, Ethiopia** (April 29-May 29, 1990). Taught Gross Anatomy, Histology and Embryology of the Head and Neck to 1st year Medical students.
9. Visiting Associate Professor at the **Atlas University College**, Addis Ababa, Ethiopia, 2016-2008

E. **Supervised MSc theses**

1. Amenu Tolera (2004) The effect of *Ricinus communis* and *Jatropha curcas* seed aqueous extracts on the histology of uterus and ovary in mice. Addis Ababa University.
2. Jickssa Mulissa (2004) Age-related Changes in Pre-aortic Ganglion cells of the Rat. Addis Ababa University.
3. Abebe Muche (2005) Effect of Ethanol and Khat (*Catha edulis*) on Cerebellar Cortex of the Rat. Addis Ababa University.
4. Gezahegne Mamo (2005) Studying human responses to antigens of *Mycobacterium uberculosis* relevant to non-replicating persistent uberculosis in an endemic population of Ethiopia. Addis Ababa University.
5. Solomon Tibebu Antifertility (2006) Effect of *Rumex stedulii*. Histological study on the uterus and ovary of rats. Addis Ababa University.
6. Hayelom Kebede (2009) Toxicological investigation of chronic treatment with *Clerodendrum myricoides* on blood, liver and kidney tissue of mice. Addis Ababa University.
7. Tilahun Alemayehu Investigation of toxic effects of chronic treatment with *Gnidia stenophylla* Gilg root extracts on some hematological and biochemical composition of blood and histopathology of liver and kidney in mice. Addis Ababa University.

8. Sintayehu Kebede Chronic toxicological investigation of fractionated extracts of *Asparagus a fricanuslam* root on some hematological and biochemical parameters of blood and histopathology of liver and kidney in mice. Addis Ababa University.
9. Getachew Chane (2013) "Investigation of toxic effects of subchronic treatment with*Maesa Lanceolata* Forsk fruit ethanolic extract on Some hematological and biochemical parameters of blood and histopathology of liver and kidney in mice." Addis Ababa University.
10. Mekonnen Debebe (2015) Study on the toxic effects of sub-chronic treatment with *Albizia gummiefera* and *Millettaia ferruguinea* seeds aqueous extract on histopathology of liver, kidney, intestine and heart in rats and in mice, respectively. Addis Ababa University.
11. Nigatu Debelo (2015) The histopathological effects of *Thymus serralatus* and *Thymus schimperi* on heart, liver and kidney, intestine and heart in rats and some blood parameters of rats and mice, respectively. Addis Ababa University.
12. Ketema Mekonen (2015) Evaluation of the acute and subacute toxicity of aqueous extract of *Artemisia afra* on brain, heart and superarenal glands of mice. Addis Ababa University.
13. Lemessa Debela (2015) Evaluation of the sub-chronic toxicity of aqueous extracts of leaves of *Moringa stenopetala* on some blood parameters and histopathology of thyroid gland, pancreas and adrenal glands in rats. Addis Ababa University.
14. Mengistu Ayele (2015) Evaluation of acute and sub-chronic toxicity of aqueous extract of *Maytenus gracilipes celastraciae* (Kombolcha) on some blood parameters and histopathology of liver and kidneys in mice. Addis Ababa University.
15. Nikodimos Eshetu (2015) Evaluation of the acute and sub-chronic toxic effects of aqueous extracts of *Artemisia afra* on Liver, Kidney and some blood parameters in rats. Addis Ababa University.
16. Yared Wasihun (2015) Hepatoprotective activity of aqueous and ethanol extract of *Lippia adoensis* leaf against carbon tetrachloride-induced hepatotoxicity in mice. Addis Ababa University.
17. Binalfew Tsehay (2016). Assessment of reliability of Greulich and Pyle (GP) method for determination of age of children at Debre Markos referral Hospital, East Gojjam zone. Addis Ababa University.
18. Molla Getu (2016). Evaluations of sub-chronic toxicity of hydro-ethanolic seed extracts of albizia gummifera and millettia ferruginea on blood, heart and small intestine of albino wistar rats. Addis Ababa University.
19. Biniam Endale (2017). Acute and sub-chronic toxicity of a formulation comprising *cymbopogon citratus* essential oil and *jatropha curcas* fixed oil in swiss albino mice. Addis Ababa University.
20. Fikre Bayu (2018) Evaluation of the effects upon chronic administration of aqueous leaf extract of *Moringa stenoptela* on blood parameters and histopathology of liver and kidney of Wistar rats. Addis Ababa University.
21. Shewit Gebre (2018) Toxicity study of anti ecto-parasitic industry scale based formulation comprising *Eucalayptus globules* on the histopathology of liver, kidney and some blood parameters in mice. Addis Ababa University.

22. Yesuf, Elsabet Mohammed (2019) Gross And Histomorphologic Study of Umbilical Cord and its Vessels in Preeclampsia . Addis Ababa University.
23. Destaye Tirit (2020) Prevalence and associated factors of digital ridge pattern types and palmar crease pattern types among high school students in Dessie town, Northeast Ethiopia. Addis Ababa University.
24. Yihun Tefera (2020) Prevalence of dermatoglyphic patterns and palmar creases among diabetic and non-diabetic patients at governmental hospitals, East Gojjam Zone, North West Ethiopia. Addis Ababa University.
25. Ephrem Fisseha (2020) Evaluation of the acute and sub-chronic toxicity of aqueous extracts of seeds of *Moringa stenopetala* on kidneys, liver, and some blood parameters of Wistar rats. Addis Ababa University.
26. Tsega-Ayehu Bazezezw Determinants of Placental Abruption among Pregnant Women Attending Government Hospitals in Addis Ababa, Ethiopia: an Unmatched case-control study. Addis Ababa University, ongoing.
27. Dureti Godanna Correlation between magnetic resonance imaging findings and clinical features in patients with low back pain due to lumbar degenerative disc disease attending orthopedic and neurology outpatient clinic in Tikur Anbessa Specialized Hospital, Addis Ababa. Addis Ababa University, ongoing.
28. Samrawit Ayalew Prediction of fetal sex by placental location in Dessie Referal Hospital, Ethiopia. Addis Ababa University, ongoing.
29. Dagnachew Mulugeta Prevalence of nonunion healing and associated factors after long bone fracture in Ethiopia, black lion hospital orthopedic clinic in 2021, *ongoing.*
30. Seble Mesfin Assessment of factors influencing distribution of vernix caseosa on the skin surface of newborns delivered at, Adama Hospital Medical Collegue, Oromia Regional State, Ethiopia, 2021, *ongoing.*
31. Hussen Aman Possible Determinants of Birth Defects Responsible for Perinatal Mortality in Adama Hospital, *ongoing.*
32. Hailemariam Zeleke Prevalence and associated factors of carpal tunnel syndrom among manual weavers in Addis Ababa, Ethiopa, *ongoing.*
33. Agumas Shibabaw Prevalence and associated factors of traumatic brain injury among patients admitted in emergency department at selected governmental Hospitals, Addis Ababa, Ethiopia, *ongoing.*

H. Supervised PhD Thesis

1. Mola Taye, Birth Defects in Central and Northwest Ethiopia: Magnitude, Associated Factors, Knowledge, Beliefs, Opinions, and Attitudes. Addis Ababa University. Completed, July 2017.
2. Mihretu Jegnie, Acute, sub-chronic and teratogenic effect evaluation of the methanolic extracts of leaves of *Justicia schimperiana* and roots of *Cucumis ficifolius* used in the treatment of rabies, *ongoing.*
3. Amsalu Taye, Magnitude and associated factors of chewing khat during pregnancy and the Impact of chat chewing during pregnancy on embryonic and fetal development and maternal and fetal birth outcomes as well as its effect on placenta and umbilical cord

changes in eastern Ethiopia: Cross sectional study and 13 Month Prospective Cohort Study and histopathologic study, *ongoing.*

I. Supervised Project Papers for MSc degree in Anatomy

1. Abdulekerim Dedefo (2011) Toxic Effect of Mercury (Hg) on Tissue of Liver and Kidney. Addis Ababa University.
2. Girmay G/Hiwot (2011) Toxic Effect of Lead (pb) on |Tissue of Liver and Kidney. Addis Ababa University.
3. Abdu Mohammed (2012) Effect of microwave from GSM mobile phones on the blood-brain barrier. Addis Ababa University.
4. Habtamu G/Senbet (2012) The roles of stem cells in the therapy of disease resistant to conventional medicine. Addis Ababa University.
5. Amsalu Taye (2013) The risk of birth defects related with anti HIV drugs exposure during pregnancy. Addis Ababa University.
6. Birhan Alem (2013) Histological and functional effect of aluminium chloride in cerebral cortex of brain. Addis Ababa University.
7. Elias Wondim (2013) Teratogenic Effects of Retinoic Acid on Limb Development in Animal Modeles. Addis Ababa University.
8. Workineh Diriba (2014) Oral Contraception and Congenital limb reduction defect. Addis Ababa University.
9. Birhanu G/Meskel Hepatoprotective effect of moringa on the histology of liver
10. Desta Gebeya Histopathological effects of liver and kidney exposed to cadmium and protective roles of Spirulina
11. Endeshaw Yilma Teratogenic effects of environmental estrogen on the development of reproductive system

PARTICIPATION IN PROFESSIONAL RELATED ACTIVITIES

A. **External Examiner of Anatomy** for preclinical MD student, BSc Pharmacy students and BSc Medical Laboratory Technology students at the **Department of Anatomy**, **Faculty of Medicine, University of Malawi, Malawi** (two times 2008, 2009).

B. **External Examiner of Histology and Embryology courses** for preclinical MD students at:
   1. **Jimma Institute of Health Sciences, Jimma, Ethiopia** (fourteen times in 1999, 2000, 2001, 2002, 2006, 2009-17).
   2. **Gondar College of Medical Sciences, Gondar, Ethiopia** (thirteen times in 1999, 2000, 2004, 2005, 2007-15).
   3. **College of Health Sciences, Mekelle University, Mekelle, Ethiopia.** (eight times in 2005, 2007, 2009-12, 2004-2005).
   4. **College of Health Sciences, Haramaya University, Haramaya, Ethiopia** (2009).
   5. **College of Health Sciences, Arbaminch University** (2013)
   6. **College of Health Sciences, Adigrat University**(two times 2014-2015).
   7. **Africa Medical College, Ethiopia.** (two times 2013 and 2014)

C. **Examined the following MSc theses**:

1. Girmay Amare (2009) Chronic effects of *Syzygium guineese* on some blood parameters and histopatholoy of liver and kidney of mice. Addis Ababa University.
2. Solomon Adane (2009) Histological and biochemical effects of *Achyranthes aspera* leaf extract on the ovary and uterus of mice. Addis Ababa University.
3. Worku Abie (2015) Sub-chronic study of the aqueous extract of *Maesa lanceolata* seed on the histopathology of liver, kidney, small intestine and spleen in rat.
4. Berhanu Mebrahte (2014) Determination of anatomical variations in the position and length of vermiform appendix of stillbirth and adult cadavers in selected universities of Ethiopia, University of Gondar
5. Hafte Teklay (2014) Assessment of congenital clubfoot treatment and its outcome in Mekelle hospital among patients who started treatment in 2003 E.C, Tigray National Regional State, Northern Ethiopia, University of Gondor
6. Merhawit Reda (2016) Effectof methanolic extract of *croton macrostachys* leaves on the histopathology of the liver,packed cell volume and body weight of albino mice, Mekelle University
7. Reda Abrha G/Hiwet (2016) The variation of umbilical cord insertion to placenta in ayder referral hospital, tigrayethiopia and its clinical implication, Mekelle University
8. Mohammed Yesuf (2018) The effects of sub-acute treatment of hydromethanolic leaf extract of Ocimum lamiifolium (dama-kassie) on liver and kidney of swiss albino mice, Mekelle University
9. Haile G/slassie (2018) Effect of Ricinus communis leaf extract administration on liver, kidney and some biochemical parameters in mice, Mekelle University
10. Bekalu Getachew (2018) Birth Prevalence of Overt Congenital Anomalies and Associated Factors Among Newborns Delivered at Jimma University Medical Center, South West Ethiopia.
11. Diliab Desta (2018) Ultrasonographic Investigation of Kidney Size, and Associated Factors Among Diabetic Patients at Jimma University Medical Center, Southwest Ethiopia, Jimma University.
12. Mekdes Bekele (2018) An Assessment of the Knowledge, Attitude, and Willingness Towards Body and Cadaveric Organ Donation and Their Associated Factors Among Health Care Professionals Working an Jimma University Medical Centre.
13. Tesema Etefa (2018) Prevalence and Predictors of Cognitive Impairment Among Hypertensive Patientsinjimma University Medical Center, Southwest, Ethiopia, 2018
14. Berhe Baymot (2019) Sub-acute hepato-renal toxicity of fenugreek (T*rigonella foenum-graecum*) seeds aqueous extract in Swiss albino mice, Mekelle University, Ethiopia.
15. Helen Beyene (2019) Toxicological investigation of *Aloe megalacantha* baker leaves latex in Swiss albino mice, Mekelle University, Ethiopia.
16. Seid Abdelkadir (2019) Effect of sub-chronic administration of methanolic leaf extract of Ruta chalepensis (tena'adam) on testis histopathology and hormonal assay in Swiss albino mice, Mekelle University, Ethiopia.
17. Atalo Agemas (2019) Computed Tomographic Measurement of Normal Lumbar Spinal

Canal Diameters of Adults in University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, University of Gondar, Ethiopia.

18. Daniel Gashaneh (2019) Prevalence and associated factors of palmar crease pattern types among Students of University of Gondar, Northwest Ethiopia., University of Gondar, Ethiopia.
19. Misganaw Gebrie (2019) Sonographic measurement of normal common bile duct diameter and associated factors at the University of Gondar Comprehensive Specialized Hospital and one private imaging center in Gondar town, Northwest Ethiopia, University of Gondar, Ethiopia.

D. **Peer Reviewed Scientific articles** for:
   1. BMC Pediatrics
   2. BMC Research Notes
   3. Ethiopian Journal of Health Sciences
   4. F1000 Research
   5. Cell and Tissue Research
   6. Journal of Anatomy

E. **Evaluated Teaching Materials** entitled:
   1. Brief Human Anatomy, by Dr Massresha Abuhay from Gondar College of Medical Sciences, Gondar, Ethiopia (1999).
   2. Anatomy for Students of Health Sciences Part I by: Cherinet, Muluneh, Al Hassan, Selamawit and Mihretu. The Carter Center, Addis Ababa, Ethiopia. (2005).
   3. Anatomy For Students of Health Sciences Part II by Cherinet, Asegedech, Yimaj and Muluneh. The Carter Center, Addis Ababa, Ethiopia. (2005).
   4. Text Book of Anatomical and Histological Techniques, by Dr Abebe Muchei from Gondar College of Medical Sciences, Gondar, Ethiopia (2015).

WORK IN PROFESSIONAL RELATED COMMITTEES

Standing:

1. Member Academic Commission, Faculty of Medicine, Addis Ababa University May, 1998 – Jan, 2001; February, 2003- Dec 2005; March 2009-Jan 09, 2017.
2. Secretary Academic Commission, Faculty of Medicine, Addis Ababa University May 2000 – Jan 2001; Sept 2015 – Sept 2016.
3. Member Faculty Graduate Commission, Faculty of Medicine, Addis Ababa University May, 1998 – Jan, 2001.
4. Member Departmental Graduate Committee since 1995.
5. Secretary Departmental Staff Meetings 1995-1998.
6. Secretary Departmental Graduate Committee Oct 2007-March 2009.
7. Member and Secretary Students Welfare Committee, Faculty of Medicine, Addis Ababa University Sept. 1996 – Feb. 2002.
8. Member and Secretary of Academic Commission, Hayat Medical College, Addis Ababa December, 1995 – December, 1996

9. Member of MSc Research Proposal Review Committee, as appointed by the Associate Dean for Postgraduate & Research, Faculty of Medicine, Addis Ababa University January, 2004- Jan 2006.
10. Member of Committee on College of Health Sciences, AAU E-learning and Health Care as of November 4, 2012.
11. Member of Quality Assurance Committee, Hayat Medical College as of October 25, 2013 as appointed by the Dean of the college.
12. Member of Exit Examination Board, School of Medicine, College of Health Sciences, Addis Ababa University, April 2016 – October, 2016
13. Chairman, Exit Exam committee, Department of Anatomy, School of Medicine, AAU, since March, 2018

Ad-Hoc:

1. Member of Teaching Load Study Committee, Faculty of Medicine, Addis Ababa University 1996.
2. Member of Self-Assessment Committee, Faculty of Medicine, as appointed by the President of Addis Ababa University 1997.
3. Member of Self-study Committee for Strategic Planning Steering Committee, 1997, Faculty of Medicine, Addis Ababa University, since Jan 2004.
4. Representing the Department of Anatomy in the Preparation of the 5 year Strategic Plan of the Faculty of Medicine, Addis Ababa University. February, 2007.
5. Member of a committee to work on a proposal for expansion of Medical Intake, Faculty of Medicine, Addis Ababa University as appointed by the Associate Dean for the Undergraduate Studies, Faculty of Medicine, Addis Ababa University, 2009.
6. Member of a committee to work on a proposal for expansion of Medical Intake, Faculty of Medicine, Addis Ababa University as appointed by the Associate Dean for the Undergraduate Studies, Faculty of Medicine, Addis Ababa University, 2008.
7. Member of a committee that facilitate the formation of College of Health Sciences, Addis Ababa University as appointed by the President of Addis Ababa University, 2009.
8. Member of the screening Committee for Associate Dean for School of Medicine and Head/Chairmanship/ for the various Departments of the College of Health Sciences, AAU, as appointed by the CED, May 2012.
9. Member of the screening Committee for medical director of the Black Lion Hospital, College of Health Sciences, AAU, as appointed by the CED, May 2012.
10. Member of a committee delegated to study the issue of the planned expansion for TASH as per the vision of individual Department in the newly allocated grounds as appointed by the School of Medicine AC on its 761th meeting and the Dean of School of Medicine & CEO, TASH, May 2013.
11. School of Medicine entrance exam committee since 2020

ACTIVE PARTICIPATION ON CONFERENCES AND/OR WORKSHOPS/TRAININGS

1. PhD curriculum Review in a national workshop held from November 2-3, 2018
2. Workshop on the medical curriculum review Hayat Medical College, Ethiopia, Oct 12,

2018

3. Workshop on the curriculum development for an MSc program in Anatomy by School of Medicine, Jimma University, Ethiopia, July 30-31, 2015.
4. Training on the requirements of Medical Education Partnership Initiative (MEPI) – Intensive Grant Writing Workshop, held during January 20-23, 2015. At Addis Ababa University, Addis Ababa, Ethiopia.
5. Participated on Leadership, Management & Governance training workshop for AAU College of Health Science and Black Lion Hospital workforce organized by MSH/LMG project in-collaboration with AAU Health Science College, during March 18-21, 2014 at Black Lion Hospital, Addis Ababa, Ethiopia.
6. Workshop on the curriculum development of "hybrid innovative medical curriculum" organized by Debre Tabor University in collaboration with Jhpiego Ethiopia held at Debre Tabor University during October 1-2, 2013. Debre Tabor, Ethiopia.
7. Participated on a "Scientific Literature Searching, Online Learning & Communication Strategies' Training" organized by Center for eHealth, SoM & CHS, AAU, held during January 29-31, 2014. Addis Ababa, Ethiopia.
8. Participated on a "Research Ethics and Good Clinical Practice (GCP)" organized by Institutional Review Board of College of Health Sciences, AAU in collaboration with Medical Education Partnership Initiative (MEPI) Consortium and CDC, held during January 29-31, 2014. Addis Ababa, Ethiopia.
9. Participated on a workshop on Undergraduate modular curriculum finalization workshop organized by School of Medicine, College of Health Sciences, held during January 1-2, 2014 at Nazreth, Ethiopia.
10. Participated on a Scientific Review Workshop on the findings of the ongoing efficacy and safety investigational efforts of medicinal plants claimed for various human and animal ailments organized by Traditional and Modern medicine Research Directorate of Ethiopian Health and Nutrition Research Institute (ENHRI) held during November 15-16, 2013 at Ambo, Ethiopia.
11. Workshop on the curriculum development for an MSc program in Anatomy by School of Medicine, Mekelle University, January 23, 2013.
12. A two day meeting to deliberate on the way forward of the Changes Agenda at CHS and come up with tangible action plan, held at the Ethiopian Red Cross Society Training Center, during December, 25-26, 2012, Addis Ababa, Ethiopia.
13. Leadership Training organized by Leadership and Management Capacity Development Project of College of Health Science s, Addis Ababa University during November 18 – 20, 2011 in Adama, Ethiopia.
14. Participated on a "Effective Teaching Skills Training for Addis Ababa University Medical Faculty Instructors" organized by Jhpiego Ethiopia in collaboration with the Medical Faculty, Ministry of Health and Ministry of Education, PEPFAR and CDC held during February 9-13, 2009. Addis Ababa, Ethiopia.
15. Workshop on the curriculum development for an MSc program in Anatomy by School of Medicine, Gondar University, August 18-19, 2007, Gondar, Ethiopia.
16. Workshop to finalize the 5 year strategic plan of the Faculty of Medicine, Addis Ababa University. March 27, 2007, Addis Ababa, Ethiopia.
17. Workshop on the "curriculum review of the Doctor of Dental Medicine Degree

Program", Atlas University, on May 27, 2006, Addis Ababa, Ethiopia.

18. Workshop in Management Principles (Planning) September 28 - 30, 2000, Faculty of Medicine, Addis Ababa University, Ethiopia.
19. 10th Annual Conference of the Biological Society of Ethiopia, February 2- 4, 2000, Addis Ababa, Ethiopia. Presented an abstract.
20. 4th International Conference of the Society of the Neuroscientists of Africa (SONA 99), April 12-16, 1999, Dakar, Senegal. Presented an abstract.
21. 3rd International Conference of the Society of the Neuroscientists of Africa (SONA 97), April 21-25, 1997, Cape Town, South Africa. Presented an abstract.
22. Anatomical Society of Great Britain and Ireland and the Nederlands Anatomen Verenigeng, July 22 - 24, 1992, Nottingham, England. Presented an abstract.
23. Qualification improvement programme for teachers of Biology in institutions of higher learning, July 25 - August 25, 1983, Debrezeit, Ethiopia.

PUBLICATIONS:

A) Dissertations

1. **Afework, M** (1995) *Distribution of Nitrergic Nerves in the Rat Adrenal Gland: Plasticity in Aging and Disease.* A thesis submitted to the University of London for the degree of Doctor of Philosophy at the University College London.
2. **Afework, M** (1988) *The Sensory Innervation of Rat Adrenal Gland: A Retrograde Study*. A thesis submitted to the University of Nottingham for the degree of Master of Philosophy.
3. **Afework, M** (1983) *The Prevalence and Identification of Human Hookworm Species in Filiklik*. A thesis submitted to Addis Ababa University in partial fulfilment of the degree of Bachelor of Science in Biology.

B) Full papers in reputable journals

1. Abebe M, **Afework M,** Emamu, B and Teshome, D (2021) Risk Factors of Anencephaly: A Case–Control Study in Dessie Town, North East Ethiopia. *Pediatric Health, Medicine and Therapeutics*, 12: 499–506; https://doi.org/10.2147/PHMT.S332561
2. Gebremickael, A., **Afework, M**., Wondmagegn, H. and Bekele, M (2021) Renal vascular variations among kidney donors presented at the national kidney transplantation center, Addis Ababa, Ethiopia. *Translational Research in Anatomy 25 (2021) 100145; pp 1-4;* https://doi.org/10.1016/j.tria.2021.100145
3. Jegnie, M and **Afework, M** (2021) Prevalence of self-reported work-related lower back pain and its associated factors in Ethiopia: A systematic review and meta-analysis. *Hindawi, Journal of Environmental and Public Health* Volume 2021, Article ID 6633271, 19 pages, https://doi.org/10.1155/2021/6633271
4. Abebe MS, **Afework M** and Abaynew Y (2020) Primary and secondary infertility in Africa: systematic review with meta-analysis. *Fertil Res Pract* 6:20, 1-11. https://doi.org/10.1186/s40738-020-00090-3.
5. Mekonen K, **Afework M**, Makonnen E, Debela A, Ergete W and Tolessa T (2020) Evaluation of Acute and Sub-Acute Toxicity of Aqueous Extracts of *Artemisia afra* Leaves on Brain, Heart and Suprarenal Glands in Swiss Albino Mice. *Ethiop J Health Sci*. 30(6):981.doi:http://dx.doi.org/ 10.4314/ejhs.v30i6.16

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C) Abstracts

1. Muche, A, Makonnen, E, Kinfu, Y and **Afework, M** (2009) The Effect of Ethanol and Khat (*Catha Edulis Forsk*) on the Cerebellar Cortex of Early Postnatal Rats. Presented for the European Science Foundation in Linkoping, Sweden. Oct 5-9, 2009.
2. **Afework, M** and Burnstock, G (2000) Occurrence of P2X (nucleotide) receptors in the rat Adrenal gland. Presented at the 10th Annual Conference of the Biological Society of Ethiopia, February 2-4, 2000, Addis Ababa, Ethiopia.
3. **Afework, M** and Burnstock, G (1999) Developmental Expression of P2X5 purinoceptors in the rat Adrenal Gland. Presented at the 4th International Conference of the Society of the

Neuroscientists of Africa (SONA 99), April 12-16, 1999, Dakar, Senegal.

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5. Parker, TL, Kesse, WK and **Afework, M** (1993) The Innervation of the Adrenal Medulla. *J Anat* 182**,** 122.
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Curriculum Vitae

Personal information

First name/ Surname	**Miressa Bekana Hirpa**
Address	Haramaya university, College of health sciences, School of medicine, department of Obstetrics and Gynecology Harar, Ethiopia
Telephone	+251913281302
E-mail	miressabekana@gmail.com
Nationality	Ethiopian
Date of birth	08-10-1989
Gender	Male

Personal Statement

- I am obstetrician and gynecologist actively involved in clinical service and teaching activity at Haramaya University.
- I am compassionate and skilled physician fully committed to improve obstetrics and Gynecology care at outpatient, emergency unit,and wards.
- I am actively performing diagnostic and therapeutic procedures including Delivery service, Cesarean delivery, Family planning service and General Gynecologic surgery.
- I have been teaching and supervising medical students and residents of obstetrics and Gynecology
- I have special interest to pursue further training in Family planning and Reproductive health.

Educational background

MPH on epidemiology
Starting from December 2020 to present I am taking class on weakened

Title of qualification awarded	**Specialty in Obstetrics and Gynecology**
Dates	January 2016- December 2019
Name and type of organisation providing education and training	Addis Ababa University, Addis Ababa

Principal skills acquired	• I have acquired knowledge and skills of thoroughly evaluating and providing evidence based treatment for patients coming to various units of obstetrics and Gynecology. • I have demonstrated excellent clinical and leadership skills during my residency. • I was responsible for Monitoring and evaluating junior residents.
	Medical Doctorate degree
Title of qualification awarded	September 2007- December 2013
Dates	Haramaya University, Harar
Name and type of organisation providing education and training	• I was dedicated and hardworking medical student determined to be excellent clinician. I have acquired basic science knowledge and clinical skills and completed my undergraduate medical study with great distinction.
Principal skills acquired	
Professional History	• Assistant professor of obstetrics and Gynecology, Haramaya University, Harar.
Job title	December 2019-present
Dates	• I am working as an educator responsible for teaching medical students and residents delivering lectures and bedside teachings. I am currently working as post graduate coordinator of residency program in Obstetrics and Gynecology Department.

Job title	• Lecturer of Obstetrics and Gynecology, Haramaya University, Harar.
Dates	December 2013- December 2016 • My duties and responsibilities were delivering Obstetrics and Gynecology lectures for Health officer students and running staff OPD of Hiwot Fana hospital
Awards won	• 2013- Certificate of recognition as **best performing Obstetrics and Gynecology intern** by Department of Obstetrics and Gynecology. • 2013- Certificate of recognition as **best performing pediatrics intern** by Department of pediatrics and child health.
Trainings and Workshops attended	• Ethiopian society of obstetrics and Gynecology scientific meetings 2016-present • Ethiopian medical association annual conference 2013-present • TOT on HIV AIDS • Different training on family planning • I trained midlevel health professional five times with IPAS collaboration
Personal skills and competences Social skill	• Good communication and interpersonal skill. Able to adjust to new cultures and customs.

	Organisational skill	• Supervising and coordinating both clinical and academic activities.
	Computer skill	• Good knowledge of SPSS, Microsoft office, internet
	Language skills	Afan Oromo and Amharic – Native Speaker; **English - I can communicate thoroughly**
activities	**Research**	Worked as principal investigator in a paper titled client satisfaction on ANC in public and private health service ,a comparative study "" unpublished data yet to be completed. • . • I am interested in research in the area reproductive health rights.
References		**1. Dr shiferaw Negash Associate professor of obstetrics and Gynecology, gynecologic oncologist, Addis Ababa University.** **Phone: +251 911141082 email: shiferaw-negash@yahoo.com** **2. Dr Esayas Birhanu, Assistant professor of obstetrics and Gynecology, gynecologic oncologist , Addis Ababa university** **Phone: +251 89825805**

ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES (IRB)
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Institutional Review Board

ANNEX 3
Form AAUMF 03-008

IRB's Decision

Meeting No: 03/2022 Meeting Date: March 23, 2022
Protocol number: 021/22/Anatomy

Protocol Title: Magnitude and associated factors of chewing khat during pregnancy and its Impact on pregnancy, maternal and neonatal outcomes in eastern Ethiopia, 2022: Cross-Sectional, Prospective Cohort, and Histopathologic Study.		
Principal Investigator:	Amsalu Taye	
Institute:	College of Health Sciences, AAU	
Elements Reviewed (AAUMF 01-008)	☑ Attached	☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of the Previous review:	
Decision of the meeting:	☑Approved ☐ Approved with Recommendation ☐Resubmission ☐ Disapproved	

I. Elements approved- 1. Protocol Version No: 2
2. Protocol Version Date:
3. Informed consent Version No. 2
4. Informed Consent Version Date:

II. Obligations of the PI-
1. Should comply with the standard international & national scientific and ethical guidelines
2. All amendments and changes made in protocol and consent form need IRB approval
3. The PI should report SAE within 10 days of the event
4. End of the study, including manuscripts and thesis works should be reported to the IRB
5. The PI should report non-compliance and unanticipated events

III. TO NERC ☐

Institution Review Board (IRB) Approval: Period from July 11, 2022, to July 10, 2023
Follow up report expected in 3 Months __✔__ 6 months ___ 9 months____ one year____

Chairperson, IRB
Dr. Adamu Addissie

የአዲስ አበባ ዩኒቨርስቲ Institutional Review Board Office (IRB) Faculty of Medicine ADDIS ABABA UNIVERSITY

Signature _____
Date: **July 11, 2022**

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V/President Office

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Ref. R/T/T/V/PO 300/ 267 / 2016

Date: January 31 /2024 G.C

To: Mr. Amsalu Taye
Email: 50amsalu@gmail.com;
Mobile No: 0921-815441
Addis Ababa University

Subject: Acceptance of Your Paper for Oral Presentation at DDU 9th Round Annual National Research Conference

Dear Mr. Amsalu,

We are pleased to inform you that your paper titled ***"The histopathologic changes in placenta associated with chewing khat during pregnancy and its correlation with fetal outcomes in eastern Ethiopia: A Comparative Study."*** has been accepted for oral presentation at the 9th Round Annual National Research Conference organized by Dire Dawa University under Grand theme of **"Synergizing Business, Health, and Technology and Engineering for Sustainable Development."** The conference, with the major Theme of ***"Health Innovations for Sustainable Development,"*** is scheduled to take place on February 15, 2024, at the Red Hall of Dire Dawa University.

We congratulate you on your acceptance and kindly request you to prepare a PowerPoint presentation that lasts between 15 to 20 minutes. Your presence and contribution to the conference will provide an excellent opportunity for collaboration and the sharing of experiences.

To ensure your comfort during your stay in Dire Dawa, we will make suitable arrangements for your accommodation at a hotel, provide meal services, and arrange for round trip air flight transportation from Addis Ababa to Dire Dawa. Our team of conference organizers will strive to make your visit as pleasant as possible. We sincerely hope that you will accept this invitation and join us at the conference event. We look forward to welcoming you to the Queen City of the Deseret, Dire Dawa, Ethiopia.

Should you have any questions or require further information, please do not hesitate to contact us. Thank you for your valuable contribution, and we eagerly anticipate your participation.

Best regards,

Temam Awel (Ph.D)
Research & Technology Transfer
V/President

CC:
President Office

Oasis of Knowledge

CERTIFICATE OF PRESENTATION

This is to certify that

Mr. Amsalu Taye

has presented his paper entitled **"The Histopathologic Changes in Placenta Associated with Chewing Khat during Pregnancy and its Correlation with Fetal Outcomes in Eastern Ethiopia: A Comparative Study"** at the 9th Annual National Research Conference with the Grand Theme of **Synergizing Business, Health and Technology and Engineering for Sustainable Development**, held on February 15, 2024 at Dire Dawa University.

Ubah Adem (PHD)
President

President