ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE, SCHOOL OF MEDICINE DEPARTEMENT OF ANATOMY

PATTERN AND ASSOCIATED RISK FACTORS OF ANORECTAL MALFORMATION AT SELECTED GOVERNMENTAL HOSPITALS IN ADDIS ABABA, ETHIOPIA, 2023

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AN MSc THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF ANATOMY, IN PARTIAL FULFILMENT OF THE REQUIRMENT FOR DEGREE OF MASTER IN HUMAN ANATOMY

December, 2023

ADDIS ABABA, ETHIOPIA

Declaration

This is to certify that the thesis prepared by Samrawit Solomon, entitled: The Pattern of Anorectal Malformation and associated risk factors at selected governmental hospitals in Addis Ababa, Ethiopia and submitted in partial fulfillment of the requirements for degree of Masters of science in Anatomy complies with the regulation of the University and meets the accepted standards with respect to originality and quality. This thesis has not been presented for degree any other University, and that all sources of materials used for the thesis have been fully acknowledged.

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DURATION OF THE PROJECT	FEBRUARY 2022- MAY 2023
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ACKNOWLEDGMENTS

I would like to express my sincere appreciation to my primary advisors, Professor Girma Seyoum and my co-advisor Dr. Fisseha Temesgen Dr. Hanna Abebe, for their invaluable guidance and helpful recommendations throughout the entire process, starting from the proposal development. Additionally, I am grateful to my dedicated team of data collectors and the study participants for their cooperation, time, and willingness to participate, even during challenging and stressful moments

I would like to extend my gratitude to Addis Ababa University, College of Health Sciences, for providing me with the opportunity to pursue this thesis. Additionally, I would like to express my appreciation to all the faculty and staff members of the Department of Anatomy and Pediatric Surgery for their support and assistance. I am also thankful to Dilla University for sponsoring my master's study. I am deeply honored to acknowledge the unwavering moral support, encouragement, and care of my family and friends throughout the duration of my work.

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LIST OF ABBREVIATIONS

ARM :Anorectal malformation

CA : congenital anomaly

GIT : Gastrointestinal tract

GLI2: GLI family zinc finger 2

HIC : High- income countries

HOXD12: Homeoboxd12

HrQoL: Health-related quality of life

IRB: Institutional Review Board
LIC: Low -income countries
MIC Middle-income countries

OR Odds ratio

PCSK5 Proprotein Convertase Subtilisin/Kexin Type 5

SHH : Sonic hedgehog

SPMHMC : St Paul's Hospital Millennium Medical College

TCF4: Transcription Factor 4

WNT :Wingless/Integrated

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ABSTRACT

Introduction

ARM is a birth defect that encompasses a wide range of abnormalities involving the anus, rectum, and genitourinary system in both males and females. These abnormalities can vary from minor issues affecting the skin to complex defects accompanied by other anomalies.. Its occurrence at birth varies geographically and annually, with a prevalence ranging from 1 in 1500 to 1 in 5000 globally. The Aim of this study is to evaluate the patterns and risk factors of anorectal malformation at governmental hospitals in Addis Ababa.

Methods and Materials: A hospital-based unmatched case-control study was conducted at TASH and SPHMMC in Addis Ababa from August 2022 to January 2023. The study involved 68 cases (patients with anorectal malformations) and 136 controls to investigate associated risk factors. Additionally, an institution-based retrospective cross-sectional study was conducted to assess the pattern of anorectal malformations. The study included all patients admitted to the pediatric surgery unit from January 2019 to January 2022. Data collection was performed using a structured questionnaire with the Open Data Kit (ODK) tool, and the data was exported to SPSS version 26 for management and analysis. Both descriptive and analytic statistics were calculated, and bivariable and multivariable binary logistic regression analyses were conducted to determine the association between independent variables and anorectal malformations. The multivariable model computed adjusted odds ratios (AOR) with 95% confidence intervals, and statistical significance was defined as a p-value less than 0.05.

Result: During a three-year period, a total of 273 cases of ARM were recorded. The male to female ratio was 1:1. Only 15% of the patients presented within the first day of their life. The prevalent type of ARM in male patients was recto-perineal fistula, accounting for 35.5% (48 cases), followed by recto-urethral fistula at 31.8% (43 cases). Among female patients, vestibular fistula was the most prevalent, observed in 54.3% (75 cases). Approximately 59% of the patients had isolated ARM.Certain factors were found to be associated with the occurrence of ARM. the chance of having newborns with ARM was 5 times more for women who had a history of alcohol consumption and taking unspecified medication during the first trimester of the pregnancy compared to their counterparts (**AOR** = 4.707; 95% CI: 1.705, 12.97).and (**AOR** = 4.857; 95% CI: 1.288, 18.318) respectively, furthermore low birth weight, unplanned pregnancy, advanced maternal age, of pregnancy and history of birth defect in first and second generation were associated with occurrence of ARM (**AOR** = 4.318; 95% CI: 1.199, 15.551), (**AOR** = 3.701; 95% CI: 1.551, 8.828), (**AOR** = 4.222; 95% CI: 1.214, 14.689) and (**AOR** = 6.15; 95% CI: 1.237, 30.582) respectively.

Conclusion: ARM was equally distributed among male and female patients. Among males, perineal fistula was the most common sub-type, while among females; vestibular fistula. Delayed presentation was common in our set up. Isolated cases of ARM were more prevalent than cases associated with syndromes. Advanced maternal age, unspecified medication intake in the first trimester of pregnancy, low birth weight, and alcohol consumption, family history of congenital malformations and unplanned pregnancy appeared to increase the risk of ARM.

CHAPTER ONE

1. INTRODUCTION

1.1 Background of study

Anorectal malformation is a congenital anomaly that encompasses a wide spectrum of defects involving the anus and rectum along with the genitourinary system in both sex , ranging from minor anomalies only involving the skin to complicated defects with associated anomalies (1, 2).

Anorectal malformation occurs due to abnormalities in the development of the hindgut, which is responsible for forming the descending colon, rectum, upper part of the anal canal, as well as the urethra and bladder. During normal human embryology, the hindgut's terminal part forms a structure called the cloaca. Around the seventh week of development, the cloaca splits, creating the ventral opening of the urogenital sinus and the anal opening of the hindgut. The severity of the anorectal defect is related to the extent of the division within the posterior angle of the cloaca. (3-5).

The birth prevalence of ARM ranges from 1/1500-1/5000 around the globe having geographical and yearly fluctuation (6). According to a research done in south Africa it's birth prevalence ranges 1.79/ 10000 -3.06 / 10000 with male predominance in male to female ratio. Many literatures in Africa distinguish anorectal malformation as the commonest cause of neonatal obstruction and also the leading congenital anomaly among congenital pediatric surgery cases in Africa(1). In Ethiopia 56 % of early neonatal intestinal obstruction is caused by ARM (7).

According to the new krickenbeck classification anorectal malformation is classified as major clinical group and rare variation. The major clinical group are further classified as perineal fistua, anal stenosis, rectourethral fistula, , cloacal malformation, rectovesical fistula patients with no fistula and vestibular fistula . The rare variants are subclassified as rectal stenosis, , rectovaginal fistula, H-type fistula and pouch colon (8). The most frequent ARM subtype in male is rectourethral fistula and vestibular fistula in female . About 48%-78% ARM are associated with other anomalies (9, 10).

ARM has been a notable problem since Aristotle described it for the first time in the early third century but the etiology is still equivocal even in the 21 century (4). Researches done on it's etiology indicated that it is a multifactor with a contribution from both a genetic factors and environmental factors. In human embryology SHH,WNT, CDX, TCF4 are important in the development of digestive tract , animal experiments show any problem in this genes or signaling pathways results ARM (11). Environmental risk factors like maternal smoking, maternal obesity, maternal diabetes, multiple pregnancy, previous miscarriage, maternal chronic disease are described in different literatures(12, 13).

1.2 Statements of the problem

ARM is the most prevalent congenital anomalies in the globe from those affecting the gastrointestinal tract accounting 25.7 %(14). Its births prevalence ranges from 0.2-0.6/1000 among birth defects of the digestive system.ARM is one of the major paediatric surgery burden even in the developed countries its birth prevalence in Germany is 3.59 per 10,000 and 3.09 per 10,000 in Italy (2, 15). In developing nations like Africa where the paediatrics surgery is not well organized incidence of ARM being 1.79/ 10000 -3.06 / 10000 is resulting catastrophic damage this is evident by researches done Nigeria and Uganda in which ARM is the leading surgical case among congenital anomalies ,21.2% and 19% respectively. It is also responsible for 67% of neonatal emergency surgical procedure in Africa (1, 16-18).

In Ethiopia there is no research conducted on the birth prevalence and incidence of ARM but there are few researches that shows its burden on the paediatric surgery units in the country, Anorectal malformation is responsible 19% of neonatal paediatric surgical cases and 24% of all congenital anomalies involving GIT in TASTH. and it is the second common cause of paediatric surgery accounting 8.9% of the total paediatric surgery case. This number should ring a bell because there is an increase in its trend from 4%-8.9%(19, 20) .ARM is also the third most common congenital anomaly (9%) preceded only by spinal bifida (14.6%) and club foot (12.56%) as shown in a research done Jimma (21).

Although ARM is classified as a rare disease entity, even in this time of highly innovative medical technology era it remains to be a medical challenge as its managements multidisciplinary involving specialized surgical and nursing team with long time rehabilitation and follow up but this seems to be far from happening when 67 % of world population doesn't have accesses to general surgery let alone paediatrics surgery, in regions like sub-Sahara and southeast Asia the number raise up to 95 % , the density of general surgeons in this region ranges from 0.13-1.57 per 100,000. In Africa the density of paediatric surgeons ranges from 0.06 -1.5/1,000,000 (22). In Addis Ababa in 2016 there were only 5 pediatric surgeons this one of the main reason for the high burden of ARM on the paediatric surgery unit in Africa as well as Ethiopia (23).

The mortality and rate of ARM has decline in the past decade due to advancement in its surgical management and continuous follow up but there is still higher rate of mortality in LIC and MIC compared to HIC where mortality in HIC is 1.7 %, MIC 12.1 % and 20 % in LIC. In Africa the number goes as high as 31% in Kenya(14, 24).

The other thing that magnify the problem is even after surgical management, they might have poor functional outcome and develop post operative complication, literatures shows that after surgery 77 % of the patients experience fecal incontinence, 87 % chronic constipation, 30% urinary incontinence and according to a research done Netherlands 37% of female patients and 9% of the male patient experience sexual dysfunction in addition to this child birth rate of patients with ARM is only 27% (25). In Africa a research done in Nigeria shows 21.6% post operative complication and 26% post operative complication in Ethiopia(26, 27).

The effect of ARM goes beyond physical health it also affect the patients psychological health and social life leading to mental health problem throughout their life where 58% of adults between 25-34 years among individuals who underwent surgical intervention during childhood, a significant proportion received a mental health diagnosis, with depression being the most prevalent (82%), followed closely by anxiety (81%).and as they grow up their physical HrQoL might improve while their psychosocial HrQoL worsen due to self perception of the disease(25).

The burden of ARM is not limited to the children who are born with it and are suffering with unbearable pain but also lead to devastating psychosocial problems for the parents who were in lots of joy to have their baby. Having a baby with ARM is going affect every domain of quality of life including social relation, physical, psychological and environmental domain. Providing for the health cost of ARM is another challenge for the family ,which is estimated to be ($273K, 95% CI:$163K-$378K), similar to health cost of premature patients (28, 29).

here is a significant knowledge gap regarding the prevalence and risk factors associated with anorectal malformations (ARM), particularly in developing countries like those in Africa where data scarcity is prevalent (4).. This study aims to investigate the pattern of ARM and its associated risk factors among patients who sought medical care at selected governmental hospital Pediatric surgery units in Addis Ababa, Ethiopia. It is crucial to evaluate the strength and direction of the association between risk factors and ARM, as there is currently a lack of literature addressing this relationship in Ethiopia, as well as in Africa as a whole. (1).

1.3 Significance of the Study

ARM is one of the leading case in the pediatric surgery unit, thus having a sufficient information of the risks is necessary to reduce its occurrence; there is scarcity of data that assess the factors predisposing to the development of ARM. Therefore, the study aim to assess pattern of anorectal malformation and risk factor at governmental hospitals in Addis Ababa as there is no research and review about this subject in Ethiopia as well as in Africa.

- In general this study will help in reduction of morbidity, mortality and cost of health care that are related to the problem at hand and may also stimulate and motivate researches to do more detailed research in the field in the future especially going to the level of community.
- The study also increase the sensitivity of health professionals in detecting and intervening on the problem as early as possible, to have good outcome and decrease complications.
- Moreover, the findings of this study will provide supplementary information for advisors, policymakers, educators, and other relevant stakeholders.
- Additionally, this study will promote awareness regarding the significance of prenatal care for expectant mothers during pregnancy.

CHAPTER TWO

LITERATURE REVIEW

2.1 Over view

2.1.1 .Definition and classification of anorectal malformation

Anorectal malformation (ARM) is a congenital abnormality that arises from the abnormal development of the distal part of the gastrointestinal tract, including the anus and rectum, as well as the genitourinary system. This developmental anomaly occurs during the early stages of embryonic development, typically between the sixth and tenth week. The severity of anorectal malformations varies across a spectrum, depending on the extent of disruption to the anorectal canal and associated caudal distortion. (30).

According to the new krickenbeck classification anorectal malformation is classified as major clinical group and rare variation. The major clinical group are further classified as rectovesical , perineal, rectourethral , vestibular fistula, cloacal malformation, no fistula and anal stenosis. The rare variants are subclassified as rectal stenosis, H-type, rectovaginal fistula, pouch colon and others (8).

Table 1. International ARM classification of Krickenbeck (31).

Male	Female
Perineal fistula	Perineal fistula
Rectourethral (bulbar) fistula	Rectovestibular fistula
Rectourethral (prostatic) fistula	
Rectovesical (bladder neck) fistula	Cloaca
No fistula	No fistula
Rectal Atresia / Stenosis	Rectal Atresia / Stenosis
Rare variant	Rare variant

Imperforate Anus without Fistula is a type of ARM lesion where perineum is completely covered with no identifiable opening while Rectoperineal Fistula is characterized by the rectum being mostly located in its typical position within the muscular structures, while the distal part of the rectum is anteriorly positioned. The opening of the fistula can be found anywhere from a slightly forward position compared to the usual location of the rectum along the midline, extending all the way to the penis shaft, and even encompassing the median raphe of the scrotum. In an alternate type of condition, the rectum ends above the bulbospongiosus muscle, and the fistula can take the form of either a narrow connection to the urethra or be positioned slightly higher with a wider fistula. This specific condition is referred to as Rectourethral Fistula Conversely, when the fistulous tract penetrates into the bladder; it results in the development of Rectovesical fistula in patients. The Most frequently observed defect in female patients is Rectovestibular fistula. In this condition, the rectum typically ends above the pubococcygeal lineA short fistula, measuring 1 to 2 cm in length, will penetrate the posterior part of the vestibule. (4). The most intricate anomaly among all is cloaca

malformation, which shares a common characteristic: the fusion of the rectal fistula, vagina, and urethra into a single cloaca, resulting in a singular orifice located on the perineum. (4). In case of anal stenosis .The anal canal appears normal externaly, Nevertheless, a blockage is present at a distance of approximately 1–2 cm from the surface of the anal skin. (32)

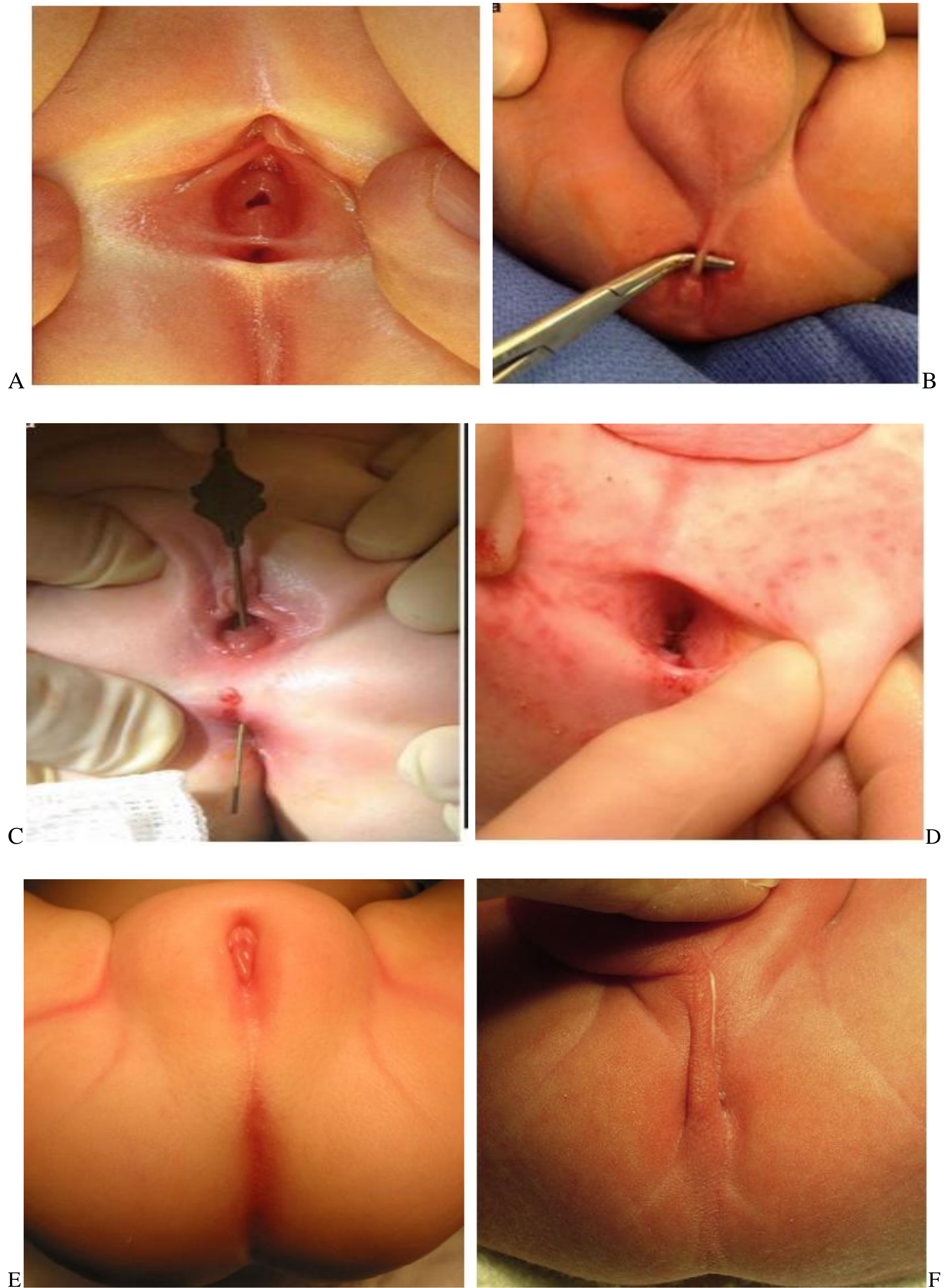


Figure 1.Anorectal malformation Type, A. Rectovestibular fistula, B. Rectoperineal fistula, C. Rectovaginal fistula, D.Skin-lined funnel appearance of the anus, E. Persistent cloaca F.Bucket handle deformity (4, 31, 32).

2.1.2 Embryology

In the course of normal human embryology, the hindgut plays a crucial role in the development of various anatomical structures. These include the lower segment of the transverse colon, the descending colon, the sigmoid colon, the rectum, the upper region of the anal canal, and the inner lining of the bladder and urethra. These structures originate from the endoderm layer of the hindgut. (3).

Irregularities in the development of the hindgut lead to the occurrence of anorectal malformations. The hindgut combines with the dorsal region of the cloaca, which is a fetal cavity lined with endoderm on its ventral side and ectoderm in other regions. The meeting point of the endoderm and ectoderm is known as the cloacal membrane. As development progresses, the area between the hindgut and the allantois divides the urorectal septum, ultimately forming the perineal body.(4).

During early development, the yolk sac contains a bulge known as the allantois, which consists of specialized mesenchyme and is located near the cloaca. As development progresses, the allantois eventually develops into the umbilical cord. Around the seventh week of development, the cloacal membrane undergoes division, resulting in the formation of a ventral opening for the urogenital sinus and an anal opening for the hindgut. Between these two openings, the perineal body forms. Initially, the posterior aspect is sealed by ectoderm, but after approximately two weeks, it undergoes recanalization, enabling the formation of a passageway.(33).

Several theories have emerged to explain the causes of these defects, and our understanding continues to evolve. Based on current embryologic evidence, it is suggested that imperforate anus occurs when recanalization fails to take place during the ninth week of gestation, and the anal opening ends up in an abnormal position within the cloaca. The severity of the anorectal defect is related to the degree of development in the posterior angle of the cloaca. Smaller defects manifest as more distal issues, like imperforate anus and anocutaneous fistula, whereas larger defects result in more proximal abnormalities, like urogenital fissure or cloacal malformation.(34).

2.1.3. Epidemiology

The birth prevalence of ARM ranges from 1/1500-1/5000 around the globe having geographical and yearly fluctuation (6). In Europe research done in Germany reports birth prevalence of 1:2784 and another research done in Italy state 3.09/10000 birth prevalence(2, 15). The only researches in Africa are done in south Africa indicating a birth prevalence ranging from 1.79/ 10000 -3.06 / 10000 but there is no literature about its birth prevalence in Ethiopia (1).

ARM is the most prevalent congenital intestinal anomaly [2]. Research conducted in Saudi Arabia describe ARM as the most common congenital anomaly among congenital anomalies of the GIT accounting 44% of the cases and it also accounts for the 25.3% of neonatal emergency cases in India(6, 35). Researches done in Nigeria and Uganda claim ARM as the leading surgical case among congenital anomalies, 21.2% and 19% respectively and it is also the leading cause of intestinal obstruction in Africa accounting 57-67%(1, 16, 17).

Researches done in Ethiopia emphasis on the burden of ARM on the paediatric surgery units in the country, 24 % of neonatal paediatric surgical cases among the total GIT lesion in neonates are due to ARM which is the leading cause and it accounts 8.9% of the total paediatric surgery cases which is the second common cause of all the cases.ARM is also the third most common congenital anomaly (9%) preceded only by spinal bifida (14.6%) and club foot (12.56% according to a research conducted in Jimma (19-21).

2.2. Associated risk factors

2.2.1 Genetic factors

The precise role of genetic variants in the development of anorectal malformations (ARM) remains uncertain and has not been conclusively established. The animal model commonly used to study the influence of genetic variations on ARM has evolved and been refined over time. In the majority of ARM cases, there are multiple pathological factors at play, with genetics playing a primary role, but environmental factors also (12).

The contribution of genetic factors is evident as 4%-11% of patients with ARM have chromosomal abnormalities and also high risk of ARM is seen in first or second degree relatives of probands (OR,40.3;95%CI,4.8,342.8) (36-38). In animal models number of genes (WNT3A, PCSK5, TCF4, GLI2, HOXD12, and BMP4) are recognized as being involving in the pathogenesis of anorectal malformation and literatures indicate normal functioning of SHH pathway is critical for normal hind gut development(11).

2.2.2 Maternal factors

There is scarcity of data regarding the associated risk factors for ARM but there are few researches suggesting association of different maternal factors with ARM however the association is inconsistence from one study to another study some factors which show strong association might have no association in other studies (12).

According to one meta analysis consistently increasing risk is observed for maternal pre-gestational diabetes (OR: 4.5, CI [2.55 to 7.97]), gestational diabetes (OR: 1.8, CI [1.23 to 2.65]) over weight (OR: 1.25, CI [1.07 to 1.47]), obesity (OR: 1.64, CI [1.35to 2.00])(12). Another research conducted in Dutch point out association of higher occurrence of fever in the first trimester And Overweight (BMI >25 kg/m2) before pregnancy with development of ARM (OR: 5.1; CI[0.9, 28.1]),(OR, 1.8; CI, [1.1, 2.8]) respectively but chronic illness like diabetes had poor association in this research (38). Anemia during pregnancy is another factor that is also associated with ARM(OR, 5.69; 95% CI, 1.01-32.07) (39).In addition to the above mentioned factors in Europe 5 times increased risk of developing ARM with mothers having a history of epilepsy and another research consider previous miscarriage as maternal risk factor (OR: 1.2; 95% CI: 0.7-2.1) (13, 40). There is no research conducted in this topic in Africa as well as in Ethiopia but a research done on the risk factor for congenital anomalies in southeast Ethiopia show high risk in mothers with maternal illness (OR: 6.1, 95% CI: 2.39, 15.57) (41).

2.2.3 Environmental factors

Many environmental factors have been studied in the few studies that are done on the etiology and risk factor of ARM but the results are heterogonous and inconsistent with one another. One of the factor which show consistent risk is maternal occupational exposure (42). A meta-analysis indicates that there is a notable increase in the risk of anorectal malformations (ARM) among pregnant women working as janitors and cleaners (with an odds ratio of 1.82 and a 95% confidence interval of 1.06 to 3.10). Similarly, maternal occupation as scientists also shows a significantly higher risk of ARM (with an odds ratio of 2.38 and a 95% confidence interval of 1.24 to 4.55).(12).

Another research conducted in Dutch also found association between maternal exposure to industrial cleaning agents which increase the risk 3 times (OR: 2.9, 95% CI, 0.9-9.3) (38). Other factors is maternal medication intake from all medication increased risks were seen for anti-asthma medication, and benzodiazepine (OR: 1.64 , 95% CI[1.22–2.21]), and (OR: 2.43, 95% CI [1.03–5.73]), respectively and urogenital infection (OR, 2.67; 95% CI , 1.11-6.38) and Maternal upper respiratory tract infection ([OR], 2.44; 95% [CI], 1.29-4.63) in the first trimester are also associated (39, 43).

A study conducted in China has put forth the suggestion that taking folic acid supplements before conception might potentially lower the risk of ARM (44). A Japanese study suggests that consuming alcohol during the early stages of pregnancy is identified as a potential risk factor for isolated ARM. (45) and additional factors like maternal caffeine intake and Cigarette smoking are found to be associated with ARM as suggested by a research conducted in USA (46).

Researches conducted in Ethiopia on the risk factors for congenital anomalies also point out association between maternal exposure to chemicals and ARM with AOR = 9.964; 95% and CI = 1.238-80.193, chemicals like pesticides and medication use during early pregnancy increase the risk 5 time furthermore, maternal alcohol consumption with (AOR = 2.394; 95% CI: 1.212-4.726, P-value = 0.012),and chewing chat (OR: 4,95% CI: 1.49-10.65) are also factors associated with congenital anomalies in Ethiopia but risk factors which are specific to ARM have not been identified in Ethiopia as well as in Africa.(41,47,1)

2.2.4 Gestational age and birth weight

Preterm delivery and low birth weight are among the factors which shows consistent association with anorectal malformation.(42) Patients with ARM were more often prematurely born (<35 weeks with AOR 4.81 95%, CI 3.42-6.75 and 35-36 weeks AOR 2.96 95%, CI 2.13-4.11) or small for gestational age with (AOR 3.82 95% CI 2.66-5.50) (48).

2.3 Patterns of ARM according to age, sex and type

Identifying the pattern is very crucial in the management of ARM and also in the management outcome of the patient however the pattern changes from one society to another. According one meta analysis done Overall median age of presentation was 4.4 days (IQR: 1.8–211.7 days) and 60.5% patients were neonates. Median age for Bangladeshi and Iranian patients were 14.6 days (IQR: 1.8 days–2 years) and 2.9 days (IQR: 1.8–21.9 days) (9). In UK the median age for their first surgery is 159 days (range 2 days-2.65 years of age, IOR: 19.5-234 days) (49).

Delayed presentation and diagnosis is one of the problems encountered in Africa, a research conducted in South Africa indicates delay in 57.9% of children's with ARM this is due to poor referral system as 55.1% of babies born in community health center have delayed presentation this research also shows age of diagnosis ranging from 2 days-5 years (50). In another research done in Rwanda only 43.5% of the patients are diagnosed in the first week of delivery, 17.4% are diagnose 2-4 week, 26.1% are diagnosed 5-24 week and the rest 13% are diagnosed after 24 weeks (51). In Africa due to the stigma in the community parents hide their children this can be evident in case that is shown in Uganda where a 15 years female patients is present to a hospital who had stayed for 15 years without intervention for ARM (52).when we come to the context of Ethiopia only 6% of the patients are diagnosis in the early neonatal period(26).

The male to female ratio varies in different geographical areas some researches show a slight dominancy of male cases but the first result of European multi-central registry of patients with anorectal malformation shows 1:1 male to female ratio beside this another research also show the same 1:1 male to female ratio however a research conducted in Bihar, India point out 3.01:1 male to female ratio similar with literatures in China (6, 53, 54). This is supported in many researchers conducted in Africa shows male predominance including research done Nigeria showing 2:1 male to female ratio and 1.3:1 male to female ratio in Kenya, 1.6:1 male to female ratio in south Africa(16, 24). However some show a little female dominance in Uganda M:F is 1:1.2 and 0.76:1 in one research conducted on TATH Ethiopia (26, 55).

The pattern of ARM in by its type is different around the globe in according research conducted in In Europe, the prevalence of anorectal malformations (ARM) varies by gender. In males, the most common type of ARM is perineal fistula, accounting for 43% of cases, followed by urethral fistulas at 29%. Among females, perineal fistulas are the most common, observed in 41% of cases, followed by vestibular fistulas at 28%. It is worth noting that in 15% of males and 4% of females, no fistulas were detected. Additionally, a smaller percentage of cases (9%) were identified as rare types of ARM, with 4% occurring in males and 14% in females. However, these frequency distributions may not remain consistent across different regions. For instance, research conducted in India reveals that rectourethral fistula is the most prevalent type of ARM in males, accounting for 54.4% of cases, with rectobulbar fistula and rectoprostatic fistula occurring in 76.2% and 23.8% of those cases, respectively. Furthermore, 17.4% of female patients presented with perineal fistula in the Indian study(6, 53).

Among boys in various regions of Africa, there is some variation in the spectrum of anorectal malformations (ARM). In Kenya, the most common type observed is imperforate anus without fistula, accounting for 31-42% of cases (24). However, in countries like Nigeria, Ethiopia, and Uganda, ARM with rectourethral fistula is the prevailing type in boys.In contrast, the pattern is more consistent among females in these African regions. Vestibular fistula is the most common subtype in Kenya (78%), Uganda (32.5%), and Ethiopia. (70%) (1).

The literature extensively describes the association of anorectal malformations (ARM) with a diverse range of other congenital abnormalities. It has been reported that approximately 48% to 78% of ARM cases are accompanied by additional anomalies.(9). According to research conducted in Singapore, the most commonly observed malformations associated with anorectal malformations (ARM) were genitourinary anomalies, accounting for 28% of cases, followed by spinal anomalies at 26%. On the other hand, in China, the most frequent malformation found in conjunction with ARM was cardiovascular malformation, particularly atrial septal defect, which accounted for 48.9% of cases. This was followed by urogenital defects, which were present in 18.2% of cases. (10). In Africa, a prevalence rate of 38% for associated anomalies in cases of anorectal malformations (ARM) has been observed. The most frequently encountered anomalies were genitourinary in nature, constituting 26% of cases. These anomalies included conditions such as renal agenesis, multicystic kidney, and hydronephrosis. The VACTERL group of anomalies, which encompasses vertebral, anorectal, cardiac, trachea esophageal, renal, and limb abnormalities, was the next most common. This group included vertebral anomalies (14%), esophageal atresia (13%), cardiac anomalies (13%), and skeletal anomalies (10%) (18).

2.4. Conceptual framework

In this study, the researchers utilized the following independent variables to evaluate the potential risk factors associated with anorectal malformation.

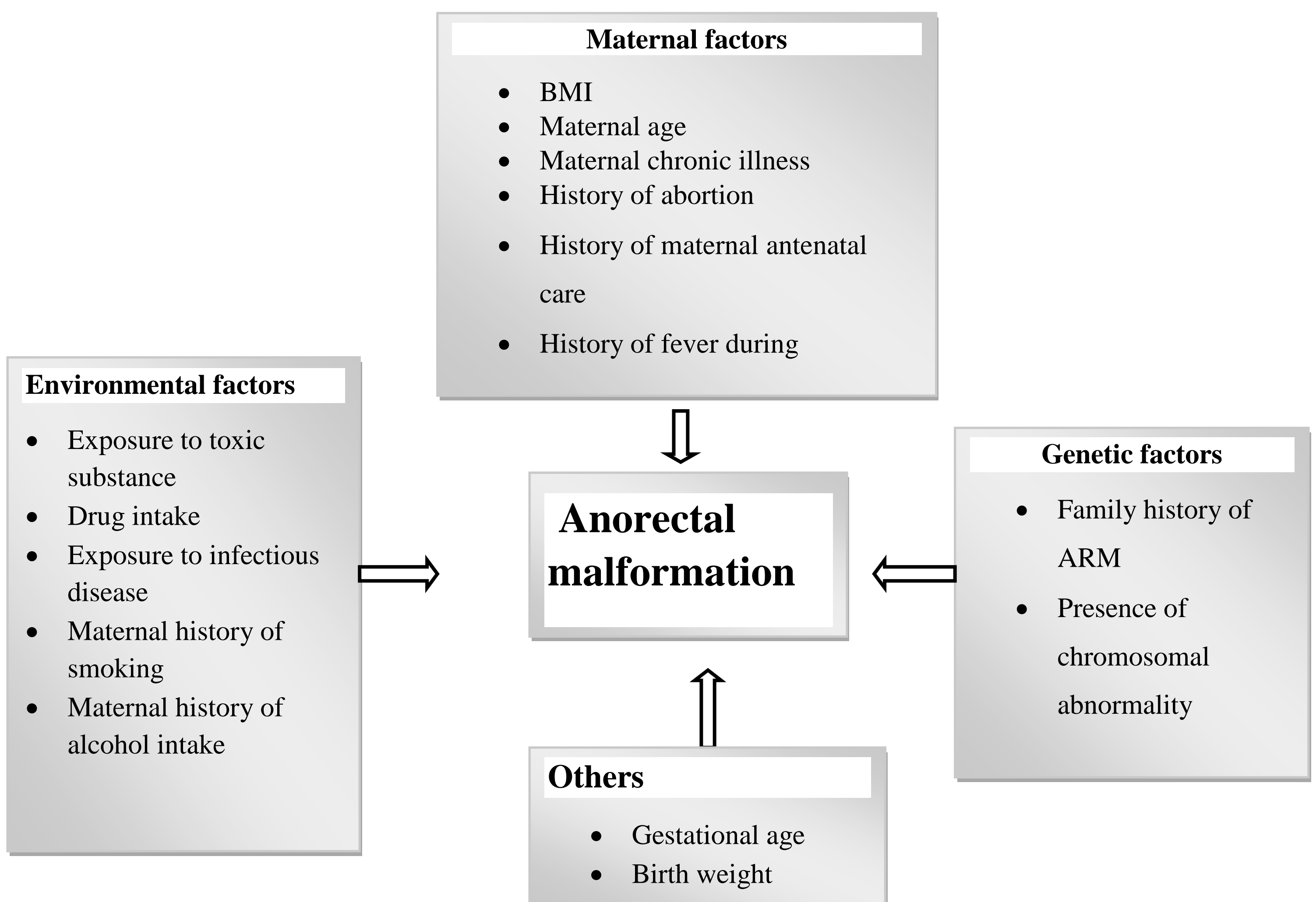


Figure 2. Conceptual frame work for the assessment of pattern and associated risk factors of anorectal malformation at selected governmental hospitals in Addis Ababa, Ethiopia, 2023

CHAPTER THREE

3. OBJECTIVES

3.1 General Objective

- To assess the patterns and associated risk factor of anorectal malformation at selected governmental hospitals in Addis Ababa, Ethiopia 2023

3.2 Specific objectives

- To assess the pattern of ARM according to age, sex, and type at selected governmental hospitals in Addis Ababa, Ethiopia 2023
- To identify different types of associated anomalies and their association with sex and type of ARM
- To identify the associated risk factors of anorectal malformation at selected governmental hospitals in Addis Ababa, Ethiopia 2023

CHAPTER FOUR

4. METHODS AND MATERIALS

4.1 Study area and Study Period:

4.1.1 Study area

The research took place in specific government hospitals located in Addis Ababa. Addis Ababa serves as the capital city of the Federal Democratic Republic of Ethiopia, positioned at the heart of the country. It is the largest city in Ethiopia, covering an estimated area of 530 square kilometers. It is located at an elevation of 2200 to 3000 meters above sea level and experiences an average temperature of 22.9 °C. The annual average rainfall in Addis Ababa is approximately 1,180.4mm.

In Addis Ababa, there are a total of 51 hospitals, out of which 11 are governmental. Among the governmental hospitals, only four have a pediatric surgery unit. Additionally, there are 40 non-governmental hospitals in the city. For the purposes of this study, two tertiary hospitals, Tikur Anbessa Specialized Hospital (TASH) and St. Paul's Hospital Millennium Medical College (SPHMMC), were selected. These two hospitals were chosen because they are the largest and oldest governmental hospitals with a pediatric surgery unit among the four available in Addis Ababa. Furthermore, they serve as referral centers for anorectal malformations and handle a significant number of cases not only in Addis Ababa but also in Ethiopia as a whole.

TASH holds the distinction of being the largest hospital in Ethiopia. It offers comprehensive medical services to both the local population and referred patients from other areas. Moreover, TASH stands out as one of the few specialized hospitals in the country that specifically caters to pediatric surgical needs. The pediatric surgery unit operates under the Department of Surgery within the School of Medicine at Addis Ababa University. Within TASH, there are 40 dedicated beds allocated for pediatric surgical cases.

Located in the northwestern part of Addis Ababa, SPHMMC is a prominent tertiary hospital in the city. The Department of Surgery, one of the larger departments within the hospital, comprises 90 beds dedicated to inpatient care and also provides outpatient surgical services. The Department of Surgery at St. Paul's Hospital is organized into three units, with the pediatric surgery unit being one of them.

4.1.2 Study period

- The research was carried out from August 2022-January 2023 G.C

4.2 Study design

This study used two study designs:-

To assess the associated risk factors:- A hospital-based unmatched case-control study was undertaken involving individuals who were designated as cases., presented to pediatric surgery unit with ARM and controls, patients presented to pediatric unit without any congenital anomaly in the study period at TASH, SPHMMC Addis Ababa, Ethiopia, 2023 GC.

To assess the pattern:- A retrospective cross-sectional descriptive study was conducted to analyze the registration records of all patients who presented to pediatric surgery unit with ARM from January 2019 – January 2022 at TASH, SPHMMC Addis Ababa, Ethiopia,2022 GC.

4.3 Population and sample

4.3.1 Source population.

To assess the pattern:

- All patients who presented to Pediatric surgery unit of TASH and SPMMC from January 2019 – January 2022

To assess the associated risk factors:

- All patients who visited Pediatric unit of TASH and SPMMC from August 2022-January 2023 G.C

4.3.2. Study Population:

To assess the pattern:

- All new patients who presented to Pediatric surgery unit of TASH and SPMMC diagnosed with ARM who fulfill the inclusion criteria from January 2019 – January 2022

To assess the associated risk factors:

- All patients visiting Pediatric unit of TASH and SPMMC diagnosed with ARM who fulfill the inclusion criteria during the study period (August 2022-January 2023 G.C,).

4.3.3. Study unit

For risk factor: - all mother of both control and casel groups and medical charts

For pattern: - medical charts

4.4. Eligibility criteria

4.4.1 Inclusion Criteria

To assess the associated risk factors:

- Case-All mothers of children with ARM who presented to TASH and SPHMMC Pediatric unit in the study period were included.
- Control- All mothers of patients who presented to TASH and SPHMMC Pediatric unit without any congenital anomalies in the study period were included

To assess the pattern:

- All new patients with ARM who presented to paediatric unit of TATH and SPHMMC from January, 2019 – January, 2022

4.4.2. Exclusion Criteria

To assess the associated risk factors:

- The study excluded children who were admitted with a caregiver other than their biological mother.
- A control group consisting of children with other congenital anomalies was excluded

To assess the pattern:

- Charts lacking a registration number or containing incomplete information were excluded from the study.
- Patients diagnosed before the study period and who are on follow up were excluded
- Chart which are lost during data collection period

4.5 Sample size and Sampling Techniques:

4.5.1 Sample size

The sample size for the study was determined separately for both the pattern and associated risk factors of ARM. To assess the pattern, medical records with a Medical Record Number (MRN) from January 2019 to January 2022, meeting the inclusion criteria, were reviewed. The study involved a retrospective review of patient charts from TASH and SPHMMC Pediatric Surgery Unit. All patients with ARM who presented during the study period were included. A total of 287 patients attended during the study period, and 273 patient charts that met the inclusion criteria were reviewed.

In order to evaluate the associated risk factors, the sample size was determined by Epi Info 7 statistical software packages. The calculation was conducted using the double population formula, which is expressed as : $\boldsymbol{n = \frac{r+1}{r}(p(1-p))(Z\beta - Z\alpha/2)^2\,(P1 - P2)^2}$. The study is based on sever assumptions, including a two-sided significance level of α=5%, a power (1-β) of 80% to detect the difference in exposure between cases and controls, a 95% confidence level, and a control-to-case ratio of 2:1. Previous research suggests that a larger sample size is needed for examining the family history of ARM compared to other exposures. The estimated exposure status is 7.2% for cases and 0.2% for controls. Accounting for a 5% non-responding rate, the sample size calculation yields 68 cases and 136 controls, resulting in a total of 204 participants.

4.5.2. Sampling procedure

Two tertiary governmental hospitals in Addis Ababa are included in the study. To assess patterns of ARM the MRN of all patients who presented to pediatric surgery unit was collected from the pediatric surgery unit HMIS registration book within the specified period. A total of 287 new patients were treated for ARM at the two centers, TASH and SPHMMC from the January 2019 to January 2022 from this 273 charts which fulfilled the inclusion criteria are reviewed and to assess the risk factors The sample size was distributed proportionally between the two centers, taking into account the total number of ARM patients TASH and SPHMMC from the January 2019 to January 2022 and convenient sampling technique was used among patients presenting to pediatric surgery unit in the study period until required sample size is reached.

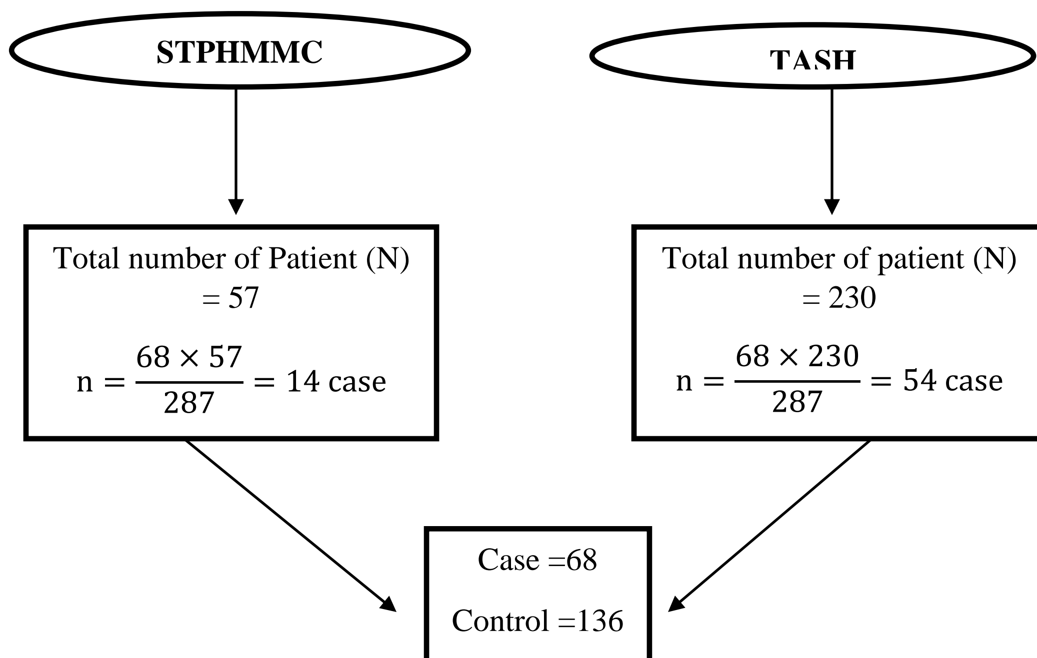


Figure 3: Schematic representation of sampling procedure in governmental territory hospitals, Addis Ababa, Ethiopia

4.6 Study variables

4.6.1 Independent variable

4.6.1.1 Maternal factor

- Maternal age
- Maternal BMI
- Socioeconomic status
- Educational background
- History of abortion
- History of maternal chronic illness
- Maternal antenatal care follow up

4.6.1.2 Genetic factor

- Family history of ARM
- Chromosomal abnormality

4.6.1.3 Environmental factor

- Maternal exposure to infection
- Maternal exposure to chemicals and pesticides
- Maternal exposure to Khat
- History of maternal smoking
- History of maternal alcohol intake
- Previous history of maternal drug intake

4.6.1.4 Other

- Gestational age
- Birth weight

4.6.2 Dependent variables

- Anorectal malformation

4.7. Data -Collection Instruments and Techniques:

Data was gathered by utilizing a structured checklist which is adopted from similar studies and through critical thinking and prepared in the English version. Variables included in the checklist are: social and demographic factors, clinical diagnosis, maternal-related factors, environmental factors, and genetic factors**.** Data will be collected using **Open Data Kit (ODK) version 1.25.2 software**.

To asses pattern of ARM

Two nurses with a BSc degree were designated to collect the data. from medical charts from January 2019 –Jauaery 2022 and one BSc degrees in public health was assigned to supervise data collectors in the process of data collections

To asses associated risk factor of ARM

Two nurses with a BSc degree were assigned to conducted face to face interview with parents and one BSc degrees in public health was assigned to supervise data collectors in the process of data collections.

4.8 Data quality control and management

In order to ensure the quality of data, the principal investigator recruited and trained data collectors. The training included an overview of the research objectives, data collection techniques, and the utilization of data collection tools. To ensure the reliability of the questionnaire, a pre-test was conducted on 5% of the total sample size of patient cards prior to the actual data collection at TASH and SPHMMC. Corrections were made to the questionnaire based on the findings and feedback obtained during the pre-test. To ensure data accuracy and reliability, an Excel template designed for ODK was prepared with suitable restrictions and necessary commands. This template underwent testing before the commencement of data collection. Throughout the data collection period, the principal investigator conducted daily reviews and checks of the collected data for any omissions, legibility issues in handwriting, as well as assessing completeness and consistency.

4.9 Data analysis:

Following the completion of data collection, the collected data was subjected to validation and subsequently exported to SPSS version 26 for further management and analysis. Descriptive statistics, such as frequency and percentage, were computed for categorical data. These statistics were then presented using tables, bar graphs, and pie charts to facilitate a clear and comprehensive representation of the data. Continuous variables will be summarized by using means, medians, and standard deviation after checking the distribution. To assess multicollinearity, VIF was utilized, whereby a VIF value greater than 10 was considered indicative of multicollinearity.. A binary logistic regression model was applied to the data. Bivariable binary logistic regression analysis was conducted to examine the association of each independent variable with the occurrence of anorectal malformation (ARM). Variables with a p-value less than 0.25 in the bivariable analysis were included in the multivariable analysis. In the multivariable logistic regression analysis, adjusted odds ratios (AOR) with 95% confidence intervals (CI) were calculated. Variables with a p-value less than 0.05 were considered statistically significant factors associated with the occurrence of

ARM. The fitness of the model was assessed using the Hosmer and Lemeshow model fitness test, where a p-value greater than 0.05 indicated a good fit for the model.

4.10 Ethical consideration:

Approval for the study was obtained from the Departmental of Research Ethics Review Committee (DRERC) at the Department of Anatomy, School of Medicine, AAU, as well as from the Institute of Review Board (IRB) at SPHMMC, ensuring compliance with ethical guidelines.

4.11. Dissemination and Utilization of Results

Following the completion of the research, the study results were presented during the thesis defense. The final outcome was submitted to the Department of Anatomy at AAU School of Medicine. Moreover, the final report will be shared with the Addis Ababa Regional Health Bureau, TASH, SPMMC Institute of Review Board, and other pertinent organizations. The study outcomes will be communicated to a broader audience through the publication of research articles and the delivery of presentations at scientific conferences and workshops. This dissemination approach aims to ensure that the study findings reach a wide range of individuals and contribute to the advancement of knowledge in the field

4.12 Operational definitions

- **Imperforate anus:** Absence of an anal opening in most ARM as diagnosed by physician
- **Alcohol Consumption:**-Average of three or more drink per week had significant to risk factors ARM
- **Smoking:** exposure to smoking of one or more than one cigarette per day.
- **Cases: -** for this study patient diagnosed as ARM occurring either independently or coexist with other congenital abnormalities.
- **Control :-** children without any congenital anomaly who visited pediatric surgery unit during the study period
- **Preterm: babies:** born alive before 37 weeks of pregnancy are completed
- **Age of diagnosis:** the first age at which the patient is diagnosed with ARM even if its outside of the study area
- **Age of presentation:** age by which the patients presented to the study area
- **Delayed Presentation :** presentation after 24 hour of delivery
- **Rare variant :** rectal stenosis, pouch colon, rectovaginal fistula, H-type fistula as diagnosed by physician

CHAPTER FIVE

RESULT

General characteristics of the patients

Two hundred and eighty seven patients with ARM were treated at the two hospital during the study period from this patients charts of two hundred and seventy three patients were retrieved. Out of this, there were 50.55% females (n=138) and 49.45% males (n=135) making male to female ratio 1:1.Age of presentation ranges from 1 hour to 12 years with a median age of presentation 18 days. We considered 15.02% (41/273) patients who presented within 24 hours after birth to have early presentation, the rest 84.98% (232/273) were considered to have delayed presentation and 67/273 (24.54%) of the patients were from Addis Ababa while the rest 206/273 (75.56%) patients were from the other regions of the country majority of them being from the from Oromia regional state accounting for 117(42.86%).Of these 273 patients, 260 (95.2%) were referred to the study areas from a health facility.

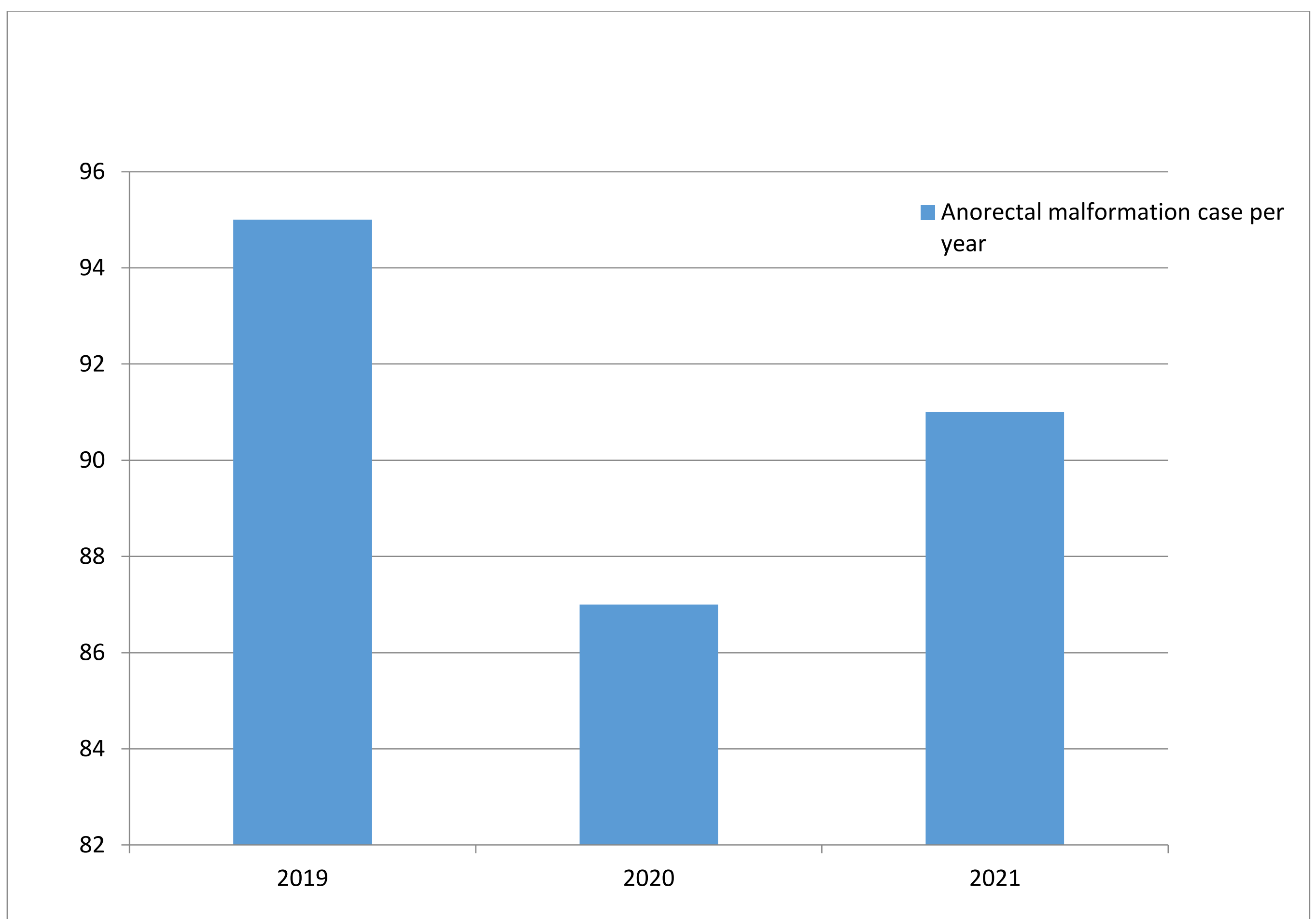


Figure 3. ARM case per year distribution at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

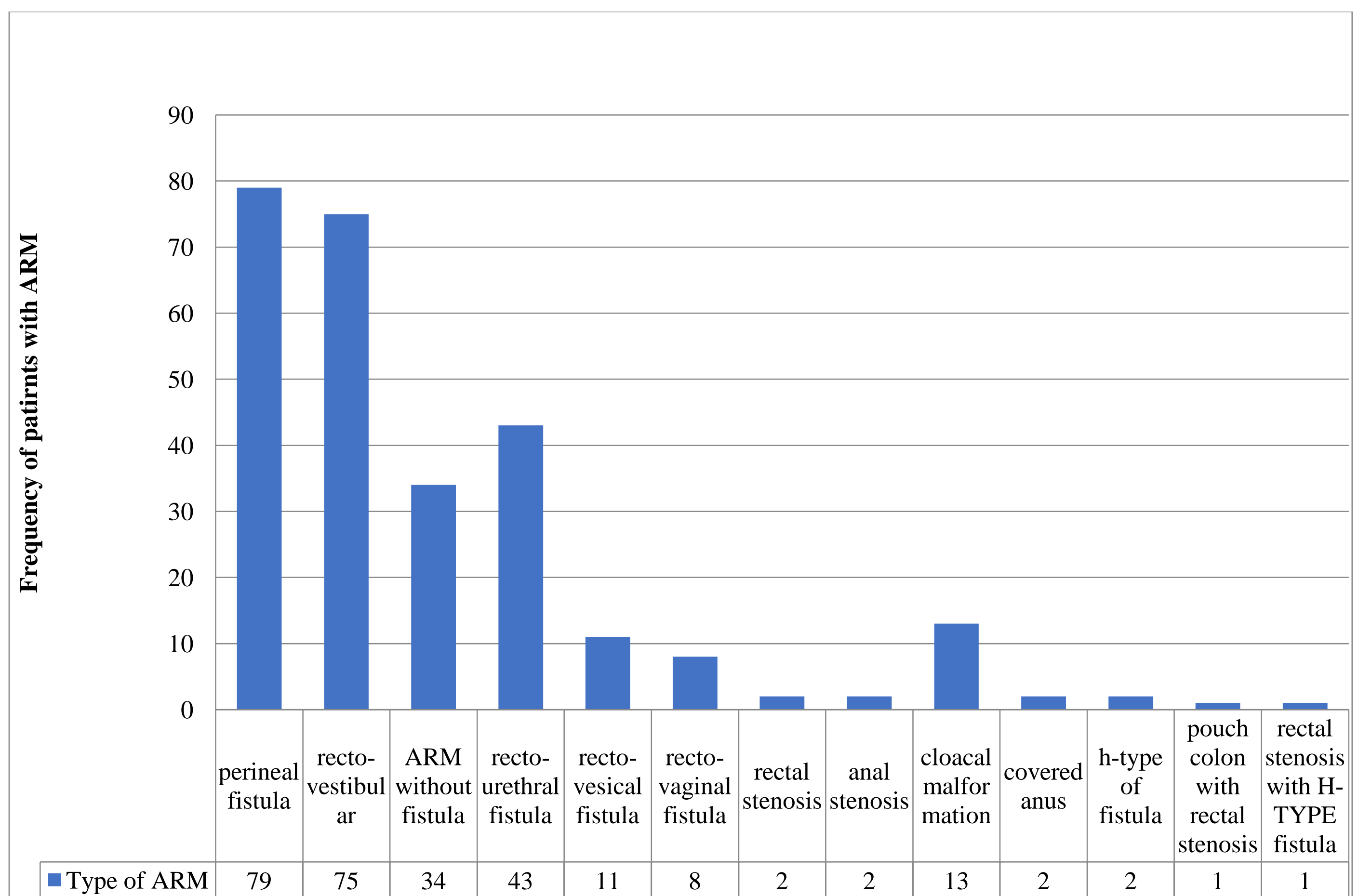
Table 2. General characteristics and Age distribution of ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

	Category	Frequency	Percentage	Cumulative percentage
Sex	Male	135	49.45	49.45
	Female	138	50.55	100
Total		273	100%	
Age of presentation	Within the first 24 hour	41	15.0	15.0
	25 hour-72 hour	43	15.8	30.8
	4 day -30 days	68	24.9	55.7
	31 day-6 month	74	27.1	82.8
	6 month-12 month	31	11.4	94.1
	1 year -5 year	13	4.8	98.9
	5 year -14 years	3	1.1	100
Total		273	100%	
Age of first diagnosis	Within the first 24 hour	54	19.8	19.8
	25 hour-72 hour	63	23.1	42.9
	4 day -30 days	62	22.7	65.6
	31 day-6 month	59	21.6	87.2
	6 month-12 month	27	9.9	97.1
	1 year -5 year	5	1.8	98.9
	5 year -14 years	3	1.1	100
Total		273	100%	
Residency	Oromia	117	42.9	42.9
	Addis Ababa	67	24.5	67.4
	Amhara	41	15.0	82.4
	SNNPR	23	8.4	90.8
	Harari	11	4.0	94.8
	Diredewa	6	2.2	97.0
	Somalia	4	1.5	98.5
	Afar	4	1.5	100
Total		273	100%	
Referral	Referred from health facility	260	95.2	95.2
	Without referral	13	4.8	100
Total		273	100%	

Types of anorectal malformation

From the total 273 ARM cases 79(28.9%) patients presented with Perinea (cutaneous) fistula which makes it the most common sub type in our set up from those affecting both sex. From 138 female patients seventy five (54.3%) female patients presented with recto-vestibular fistula making it the commonest type of ARM in female patients followed by perinea (cutaneous) fistula 31(22.5%) and cloacal malformation 13 (9.4%) among this 5 (38.5%) had short channel,2(15.4%) had long channel the rest 6(46.1%) was not specified .From the rare variants recto-vaginal fistula in females accounts 8(5.8%).

The most prevalent type of ARM in male patient was perinea (cutaneous) fistula 48/135 (35.5%) followed by recto-urethral fistula 43/135(31.8%) in which 26/43 (60.4%) patients were with recto-bulbar fistula, 10/43(22%) patients had recto-prostetic fistula and 8(18.6%) were unspecified. Twenty eight (20.75%) male patients had ARM without fistula and 11(8.2%) with recto-vesical fistula. Among the 273 patients two (0.7%) patients had complex multiple types of ARM at the same time one rectal atresia with H- type of fistula and other rectal atresia with pouch colon.



	perineal fistula	recto-vestibular	ARM without fistula	recto-urethral fistula	recto-vesical fistula	recto-vaginal fistula	rectal stenosis	anal stenosis	cloacal malformation	covered anus	h-type of fistula	pouch colon with rectal stenosis	rectal stenosis with H-TYPE fistula
Type of ARM	79	75	34	43	11	8	2	2	13	2	2	1	1

Figure 4 . Type of Anorectal malformation among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Table 3. Type of Anorectal malformation in female among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Type	Frequency	Percentage (%)
Vestibular fistula	75	54.3
Perinea fistula	31	22.5
Cloacal malformation	13	9.4
Recto vaginal	8	5.8
ARM without fistula	6	4.4
H-type of fistula	2	1.5
Rectal stenosis	1	0.7
Covered anus	1	0.7
Rectal stenosis with H-type of fistula	1	0.7
Total	138	100%

Table 4 . Type of Anorectal malformation in Male among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Type	Frequency	Percentage (%)
Perinea fistula	48	35.5
Recto- urethral	43	31.8.
ARM without fistula	28	20.75
Recto-vescical	11	8.2
Anal stenosis	2	1.5
Rectal stenosis	1	0.75
Covered anus	1	0.75
Rectal stenosis with pouch colon	1	0.75
Total	135	100%

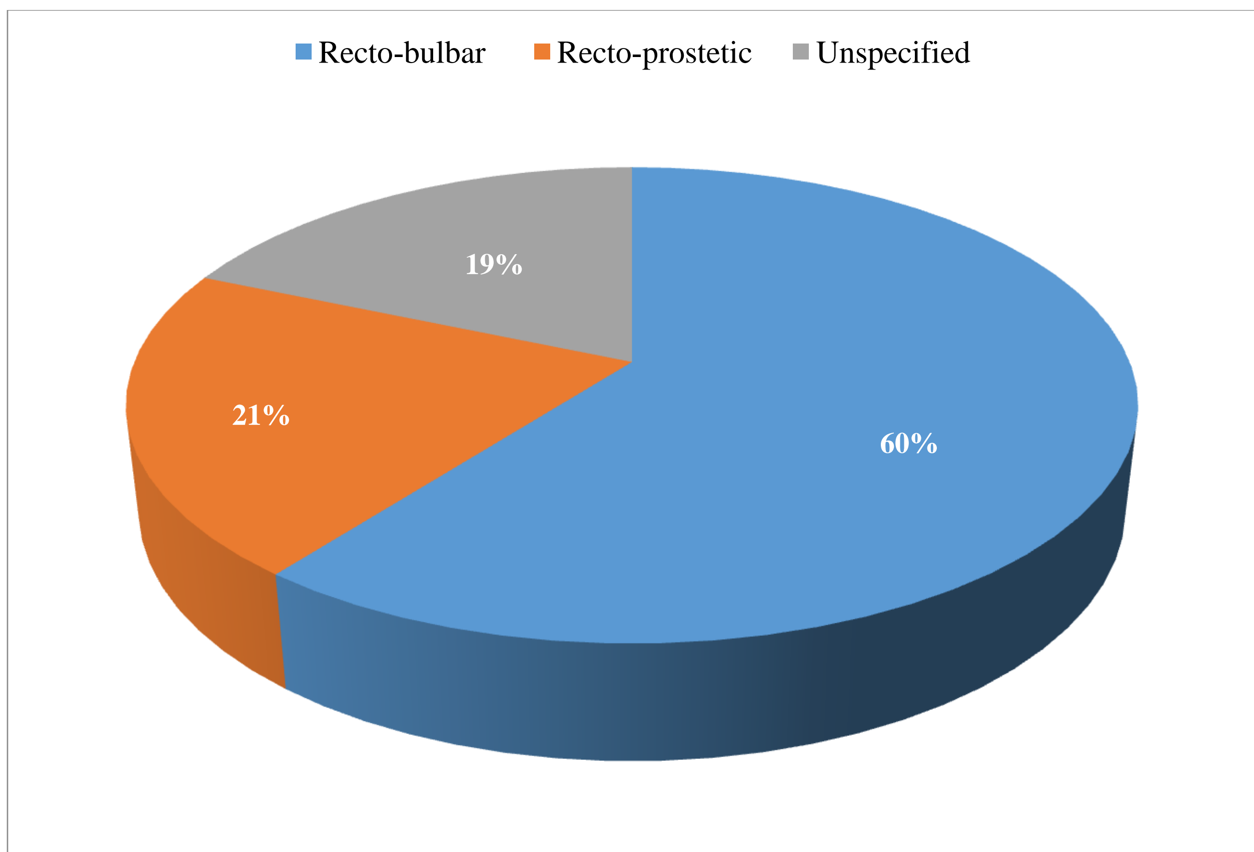


Figure 5 . Type of Recto-Urethral fistula in Male among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Associated congenital anomalies

Over all 58.6% (160/273) patients had isolated Anorectal malformation, whereas the remaining 41.4% (113/273) patients had at least one associated congenital anomalies from this 53.1% (60/113) were male the rest 49.9% (53/113) were female but no statistical significant association was not seen . Genitourinary and cardiovascular system anomalies were predominant among patients with associated anomalies. Twenty two percent (61/273) of the patients with ARM had genitourinary system anomalies (Ectopic kidney (15), renal agenesis (18), Hydronephrosis (11) Undecided testis (10), followed by cardiovascular system and musculoskeletal system anomalies accounting 12.1% (33/273) and 8% (22/273) respectively. Among cardiovascular system anomalies ASV and VSD were predominant type anomalies each affecting 19 patients and club foot was the most common type of musculoskeletal anomaly representing 3.7% (10/273) of all the cases.

Among the syndromes VACTERL was the commonest affecting 7.7% (21/273) of patients with ARM of whom 66.7% (14/21) were male, 33.3% (7/21) female, 57.1%(12/21) had three of anomalies and 42.9% (9/21) had four anomalies. Down syndrome was seen in 6.6% (18/273) and was the only chromosomal anomaly found among ARM patients in this study and it was diagnosed predominantly in patients with ARM without fistula 83.3% (15/18).

Among the subtypes of ARM, Recto-vesical fistula patients had the highest percentage of associated anomalies (82%, 9/11) followed by ARM without fistula (64.7%, 22/34), and cloacal malformations(53.8%, 7/13) and Recto-vaginal fistula (50%, 4/8) in contrast to this patients with perineal fistula sub type had less percentage of associated anomalies 25.3%(20/79) followed by vestibular fistula 40%(30/75)

In our study Significant association was noticed among sub types of ARM like Recto-vesical fistula, ARM without fistula, and perineal(cutaneous) fistula with presence of associated congenital anomalies. The result shows that patients with Recto-vesical fistula are 6 times more likely to develop associated congenital anomalies in comparison with those who doesn't have Recto-vesical fistula (OR, 6.315; 95% CI, 1.39–30.24) and patients with ARM without a fistula increases the likelihood of developing associated congenital anomalies by 2.6 times compared to individuals who does not have ARM without fistula (OR, 2.6; 95% CI, 1.19–5.585Conversely, patients with perineal fistula are less likely to have associated congenital anomalies with (OR, 0.467; 95% CI, 0.26–0.87)

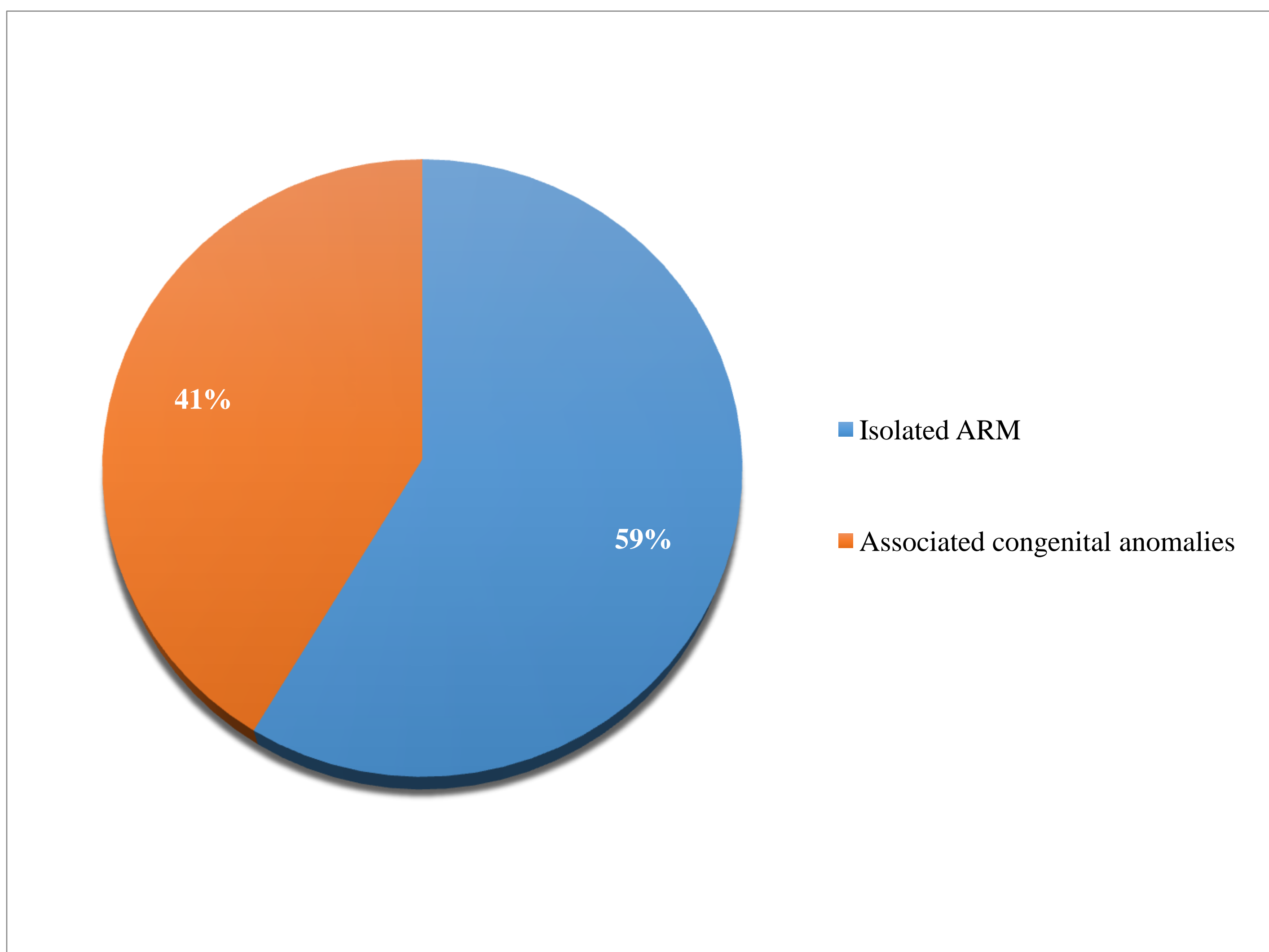


Figure 6 . Percentage of associated congenital anomalies among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Table 5. Type of associated congenital anomalies among ARM patients treated at selected governmental hospitals Addis Ababa, Ethiopia, 2023

Type of associated Anomaly	Frequency	Percentage From total cases	Percentage from Associated anomalies
Genitourinary system	61	22.3%	54%
Ectopic kidney	15	5.5%	13.3%
UDT	10	3.6%	8.8%
Renal agenesis	18	6.6%	15.9%
Hydronephrosis	11	4%	9.7%
Hypospadia	8	2.9%	7%
Bladder extrophy	3	1%	2.6%
Multicystic kidney disease	2	0.7%	1.8%
Genital anomalies	9	3.3%	8%
Urethral duplication	2	0.7%	1.8%
Other	7	2.6%	6.2%
Cardiovascular system	33	12.1%	29.2%
ASD	19	7%	16.8%
VSD	19	7%	16.8%
PDA	11	4%	9.7%
TOF	3	1%	2.6%
Other	6	2.2%	5.3%
Musculoskeletal system	22	8%	19.5%
Club foot	10	3.6%	8.8%
Scoliosis	5	1.8%	4.4%
Sacral agenesis	3	1%	2.6%
Hemi vertebrae	3	1%	2.6%
Polydactyl	2	0.7	1.8%
Other	5	1.8%	4.4%

Table 5. Type associated congenital anomalies among ARM patients treated at selected governmental hospitals Addis Ababa, Ethiopia, 2023

Type of associated Anomaly	Frequency	Percentage From total cases	Percentage from Associated anomalies
CNS	13	4.8%	11.5%
Spinal bifida	8	2.9%	7%
Hydrocephalus	3	1%	2.6%
Tethered chord	2	0.7%	1.8%
Corpus collosum agenesis	1	0.4%	0.9%
Fused thalamus	1	0.4%	0.9%
Other	3	1%	2.6%
GIT system	11	4%	9.7%
TEF	4	1.5%	3.5%
Umbilical hernia	3	1%	2.6%
Omphalocele	1	0.4%	0.9%
HSD	1	0.4%	0.9%
Other	4	1.5%	3.5%
Craniofacial	5	1.8%	4.4%
Cleft palate	1	0.4%	0.9%
Choanal stenosis	1	0.4%	0.9%
Microphthalmia	1	0.4%	0.9%
Microtia	1	0.4%	0.9%
Respiratory system	2	%	%
Laryngeomalesia	2	0.7%	1.8%
Chromosomal	18	6.6%	15.9%
Down syndrome (Trisomy 21)	18	6.6%	15.9%
Syndrome	22	8%	19.5%
VACTER	21	7.7%	18.6%
IEOS cloacal syndrome	1	0.4%	0.9%

Age of presentation

The result show great discrepancy between median Age of first diagnosis which is 6 days and median age of presentation to the two hospitals which is 18 days. We considered 41(19.8%) patients who presented within 24 hours after birth to have early presentation, the rest 232(84.98%) were considered delayed. .Majority of the patients presented to the two centers from 31 days- 6 month of age representing 27.1% of the total 273 patients while the commonest age group for age of first diagnosis was patients from 25 hour-72 hours. From 41(19.8%) patients with early presentation 28(68.3%) were from Addis Ababa and 10(24.4%) from Oromia regional state and 193(83.2%) of the patients with late presentation were from outside of Addis Ababa

From 41(19.8%) patients with early presentation the two most common sub type of Anorectal malformation were ARM without fistula and Recto- Urethral fistula accounting 12/41(29.3%) and 11/41(26.3) respectively. Among Patients who presented late cases with fistula such as Recto vestibular fistula and Perinea (cutaneous) fistula had high rate of delayed presentation accounting 69(29.7%) and 73(31.5%) from a total of 232(84.98%) patients who had delayed presentation. In Regard to patients with associated anomalies 25/41(61%) of the patients with early presentation were patients with associated anomalies the remaining 39% of the patients were diagnosed with Isolated ARM in the contrary majority of the cases with late presentation were patients with Isolated ARM accounting 144/232 (62.1%) of patients who had delayed presentation.

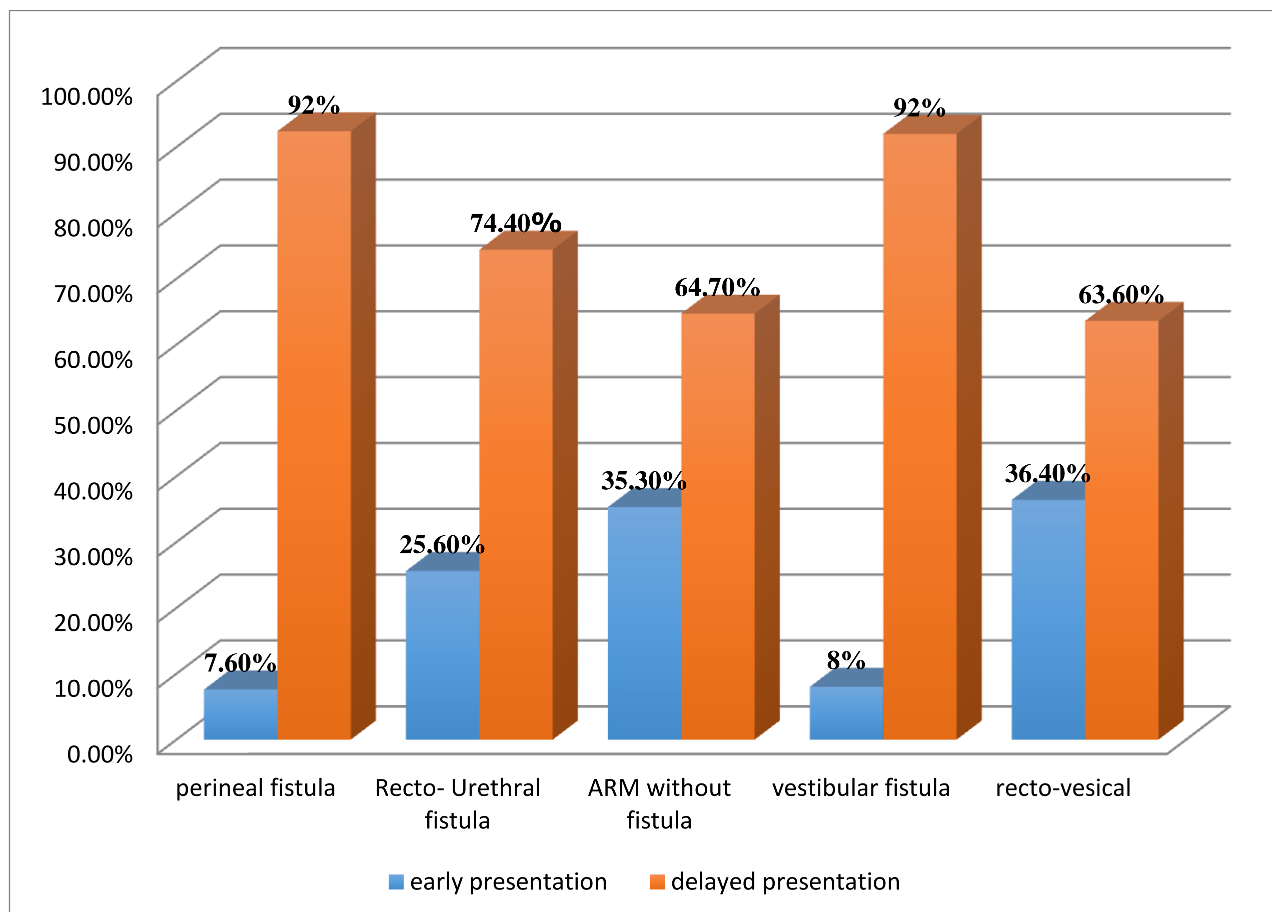


Figure 7.Age of presentation according to types of ARM among ARM patients treated at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Assessment of determinants of ARM:

Socio-demographic characteristics

A complete of 204 mothers, comprising 68 cases and 136 controls, were successfully interviewed at various departments including pediatrics surgery OPD, pediatrics OPD, NICU, and pediatrics inpatients, achieving a response rate of 100%. Table 6 shows that approximately 87.5% of the control group and the majority of the cases (76.4%) belonged to the age group of 20-34. he predominant religious affiliation among women participating in the study was Orthodox, accounting for 54.4% of cases and 57.3% of controls. Following Orthodox, the next most common religious affiliation was Muslim, representing 33.8% of cases and 30.9% of controls. In terms of the educational background of the mothers, 35.3% of cases and 39.7% of controls had completed high school. Regarding residency, the majority of cases (67.6%) and controls (94.8%) resided in urban areas, with 38.2% of cases and 60.3% of controls specifically originating from Addis Ababa. The majority of mothers identified as housewives, accounting for 69.8% of cases and 57.3% of controls.

Reproductive and obstetric characteristics

In our study, a significant proportion of women were multigravida, with 79.4% of cases and 61% of controls falling into this category. Additionally, 35.3% of the controls and 29.4% of cases were second-order births. Approximately half of the pregnancies among the cases (44.1%) and 13.2% of the controls were unplanned. Furthermore, a significant majority of both cases and controls (89%) were born at 37 weeks gestation or later, while a small percentage of cases (4.4%) and controls (7.3%) were born before 37 weeks. Around 12% of cases and 5.9% of controls had a history of previous abortions. In terms of previous history of children with congenital anomalies, 13.2% of cases and 2.9% of controls reported a family history of such anomalies. It is worth noting that no controls had a family history of anorectal malformation (ARM), whereas two cases (2.9%) reported a family history of ARM.. Among the study participants only few percent of controls (3%) and 11.8% of cases did not attend Antenatal care follow up. Forty three percent (29) of case and 81.6 %(111) of control were taking folic acid supplementation during their pregnancy , from this only Twenty two percent (15) of mothers of children with ARM and 46.7 %(64) of control mothers took folic acid supplementation in the first trimester of the pregnancy,

Table 6. General characteristics of cases and controls at selected governmental hospital, ADDIS ABABA,ETHIOPIAN, 2023

Characteristics		Case		Control	
		Frequency	%	Frequency	%
Child Mother Age	<20 years	0	0	10	7.3
	20 – 34 years	52	76.5	119	87.5
	>34 years	16	23.5	7	5.1
Religion	Orthodox	37	54.4	78	57.3
	Muslim	23	33.8	42	30.9
	Protestant	8	11.8	16	11.8
Child Mother Education	Illiterate	22	32.4	3	2.2
	Can read and write	3	4.4	14	10.3
	Elementary education	10	14.7	36	26.5
	High school education	24	35.3	54	39.7
	Higher education	9	13.2	29	21.3
Child Mother Occupation	Housewife	39	57.3	95	69.8
	Student	1	1.5	2	1.5
	Government employee	13	19.1	15	11
	Private	10	14.7	22	16
	Farmer	5	7.4	2	1.5
Residency of the mother	Urban	46	67.6	129	94.9
	Rural	22	32.4	7	5.2
Region of the mother	Addis Ababa	26	38.2	82	60.3
	Oromia	30	44.1	33	24.3
	Amhara	8	11.8	11	8.1
	SNNP	3	4.4	7	5.1
	Afar	1	1.5	0	0
	Somalia	0	0	3	2.2

Table 7 . Reproductive and obstetric history of cases and controls who presented at selected governmental hospital, ADDIS ABABA, ETHIOPIAN, 2023

Characteristics		Case		Control	
		Frequency	%	Frequency	%
Gravidity	Multigravida	54	79.4	83	61
	Primigravida	14	20.6	53	39
Gestational age at delivery	Preterm	3	4.4	10	7.3
	Term	61	89.7	122	89.7
	Post term	4	5.9	4	3
Birth weight	Very low BW	0	0	0	0
	Low birth weight	11	16.2	8	5.9
	Normal birth weight	54	79.4	114	83.8
	Macrosomia	3	4.4	14	10.3
ANC follow up	Yes	60	88.2	132	97
	No	8	11.8	4	3
Folic acid intake during pregnancy	Yes	29	42.6	111	81.6
	No	39	57.4	25	18.4
History of previous abortion	Yes	12	17.6	8	5.9
	No	54	79.4	128	94.1

Maternal and environmental factors

In our study maternal medical illness during pregnancy was seen in 30 (44%) mothers who had children with anorectal malformation and 22(16.2%) of mothers whose children were not affected with anorectal malformation. Out of this the commonest medical illnesses were Urinary tract infection, anemia and hypertension. Out of the study participants, unidentified medication use in early pregnancy was noticed in 15(22.1%) of mothers who had children with ARM and 8(5.9%) of the controls. About 8(11.8%) of the cases and 3(2.2%) of the controls had genetic relationships with their partner. Majority of the study participants ad normal body mass index (93(68.4% of the controls and 40(59%) cases) and 28% of the cases and 24% of the controls were overweight.

Alcohol conception during pregnancy was reported in about 21(30.9%) of case mothers and 13(9.6%) of control mothers. Passive smokers were observed only in 4 (5.9%) of cases and 1(0.7%) of controls. About 12(17.6%) of case mothers and 4(2.9) % of control mothers were exposed to chemicals like pesticides at the time of pregnancy and exposure to industrial cleaning agents was seen in 7(10.3%) of case mothers and 9(6.6%) of control mothers

Risk factors associated with Anorectal malformation

Binary logistic regression analyses revealed significant associations between anorectal malformation and various factors. These factors included alcohol consumption, drug use in the first trimester passive smoking during pregnancy, maternal illness, , exposure to pesticides and herbicides, insufficient folic acid supplementation in the first trimester, low birth weight, advanced maternal age, unplanned pregnancy, attendance of antenatal care, history of abortion, and family history of birth defects. However, factors such as maternal education, occupation, gravidity, birth order, previous history of anorectal malformation in a child, stillbirth, smoking during pregnancy, maternal obesity, radiation exposure during pregnancy, genetic relationships with the partner, and exposure to industrial cleaning agents were not found to have a statistically significant association with anorectal malformation

In the multivariable logistic regression analysis, the variables that were found to be statistically significant in the binary logistic regression were included to determine the factors associated with anorectal malformation. The results showed that women who consumed alcohol during pregnancy were five times more likely to give birth to newborns with anorectal malformation compared to those who did not drink alcohol (AOR = 4.707; 95% CI: 1.705, 12.97). Similarly, women who had a history of taking unspecified medication during the first trimester of pregnancy had a fivefold increased likelihood of having newborns with anorectal malformation (AOR = 4.857; 95% CI: 1.288, 18.318).

This study found that a mother having advanced maternal age during pregnancy had an increased risk of having a child with anorectal malformation with (AOR = 4.222; 95% CI: 1.214, 14.689). Additionally, low birth weight and unplanned pregnancy were also associated with the occurrence of anorectal malformation, with AORs of 4.318 (95% CI: 1.199, 15.551) and 3.701 (95% CI: 1.551, 8.828) respectively. Furthermore, mothers with a family history of birth defects in both the first and second generations were six times higher chance of having a child with anorectal malformation compared to those without such family history (AOR = 6.15; 95% CI: 1.237, 30.582).

Table 8 . Risk factors associated with anorectal malformation at selected governmental hospitals, ADDIS ABABA, ETHIOPIAN, 2023

Characteristics		Case N (%)	Control N (%)	COR (95% CI)	AOR (95% CI)	p-value
ANC follow up	Yes	60(88.2)	132(97.1)	0.0.227(0.066,0.784)	0.742(0.120, 4.593)	0.744
	No	8(11.8)	4(2.9)	1	1	
Advanced maternal age	**Yes**	**16(23.5)**	**7(5.1)**	**5.670(5.670,14.585)**	**4.222(1.214, 14.689)**	**0.024***
	No	52(76.5)	129(94.9)	1	1	
Low Birth weight	**Yes**	**11(16.2)**	**8(5.9)**	**3.088(1.179, 8.086)**	**4.318(1.199, 15.551)**	**0.025***
	No	57(83.8)	128(94.1)	1	1	
History of Maternal illness	Yes	30(44.1)	22(16.2)	4.091(2.111, 7.926)	2.265(.894, 5.718)	0.085
	No	38(55.9)	114(83.8)	1	1	
Unspecified medication use	**Yes**	**15(22)**	**8(5.9)**	**4.528(1.812, 11.361)**	**4.857(1.288, 18.318)**	**0.02***
	No	53(78)	128(94.1)	1	1	
Family history of birth defect	**Yes**	**9(12.2)**	**4(2.9)**	**5.034(1.490, 17.002)**	**6.150(1.237, 30.582)**	**0.026***
	No	59(86.8)	132(97.1)	1	1	
Passive smoking	Yes	4(5.9)	1(0.7)	8.437(0.924,77.022)	6.85(0.322, 43.385)	0.292
	No	64(94.1)	135(99.3)	1	1	
Exposure to Pesticide	Yes	12(17.6)	4(2.9)	9.500(2.581, 34.967)	2.526(0.495, 12.896)	0.265
	No	56(82.4)	132(97.1)	1	1	
Lack Folic acid intake in the First trimester	Yes	53(77.9)	72(52.9)	3.141(1.616, 6.106)	2.309(0.983, 5.420)	0.055
	No	15(22.1)	64(47.1)	1	1	
Unplanned pregnancy	**Yes**	**30(44.1)**	**18(13.2)**	**5.175(2.598, 10.311)**	**3.701(1.551, 8.828)**	**0.003***
	No	38(55.9)	118(86.7)	1	1	
History of abortion	Yes	12(17.6)	8(5.9)	3.429(1.328, 8.086)	1.442(.441, 4.722)	0.545
	No	54(79.4)	128(94.1)	1	1	
Alcohol conception during pregnancy	**Yes**	**21(30.9)**	**13(9.6)**	**4.617(2.107,10.119)**	**4.707(1.705,12.997)**	**0.003***
	No	47(69.1)	123(90.4)	1	1	

Note: COR: Crude odds ratio, AOR:Adjusted odds ratio, CI: Confidence interval, * indicates statistical significance at $P< 0.05$.

CHAPER SIX

DISCUSSION

ARM is a congenital abnormality that covers a broad range of defects affecting the anus, rectum, and the genitourinary system in both males and females. These defects can vary from minor anomalies that only affect the skin to defects that are associated with additional anomalies. Our study examined 273 patients with ARM to determine the subtypes of ARM based on Krickenbeck classification, as well as the distribution of cases by gender and age, and the presence of associated anomalies. Additionally, we conducted a case-control study with 68 cases and 136 controls to identify the factors associated with ARM in Addis Ababa, Ethiopia..

Gender distribution

The gender distribution of patients with ARM varies across different studies. The initial findings from the European multi-central registry of ARM patients, along with studies conducted in Iran and Bangladesh, revealed a 1:1 male to female ratio, which aligns with the results of our study. This suggests that the observed gender distribution may reflect the actual incidence of ARM in the general population. While certain types of ARM may be more prevalent in one gender compared to the other, the overall occurrence of ARM appears to be relatively consistent between males and females. However, a study conducted in Bihar, India, reported a higher incidence among males, which is in line with findings from literature in Kenya. (6,9,24 53,). On the other hand, some studies, such as one conducted in Uganda and another at TATH Ethiopia, reported a slight tendency towards a higher proportion of females or a close to equal ratio of males to females (26, 55). This difference in gender distribution could be due to the sample size, as these studies had smaller sample sizes compared to our study.

Relative Incidence of ARM Subtypes

Although the distribution of ARM varies by subtype across different regions of the world, perineal fistula consistently appears to be the most common subtype based on various studies (9). In our research, we also found that perineal fistula was the most frequent subtype in males, followed by recto-urethral fistula, which is consistent with the findings of Cassina M (2) and the initial results of the European multi-central registry of patients with ARM this could be the fact that perineal fistula is the least severe form of ARM and often results from a relatively minor disruption in fetal development. (53) However, our research findings were not in agreement with previous studies conducted in TASH, where recto-urethral fistula was found to be the most common subtype in male patients who underwent surgical management, and in Nigeria, where recto-urethral fistula was also the predominant subtype in male patients. Additionally, in Kenya, ARM without fistula was considered to be the most common type, but in our study, we found it to be the third most common subtype in male patients. (1,24,26,).

The reason for the difference in results between our study and previous research at TASH and in Nigeria may be due to the fact that we included all new patients with ARM, including those who did not undergo surgical management and were lost during follow-up. This group of patients mostly comprised of those with perineal fistula. Additionally, the study conducted at TASH calculated the percentage of bucket handle deformity separately from perineal fistula, resulting in a lower percentage of perineal fistula cases. On the contrary, the difference between our study and the one conducted in Kenya could be attributed to their methodology, which only included neonates in their study, while we included patients aged one day to twelve years. This difference in study methods may have led to a variation in results, as neonates who do not pass meconium may be clinically misdiagnosed with ARM without fistula. Moreover, our research findings and those of other studies suggest that many patients with perineal fistula present late, which further supports the difference in results between our study and the one conducted in Kenya(1,24,26,).

In females its more consistent, vestibular fistula being the commonest sub-type in different studies including those conducted in Italy, India, Kenya, Uganda, and Ethiopia (1,2,6) which goes in line with our study where vestibular fistula is by far the commonest ARM subtype in females followed by perineal fistula which is also similar with studies in Bangladesh and Iran(9) on the contrary perineal fistula was the most common cause of ARM in female patients according to the first European multi-central registry of patients with ARM which different from our study this could be due to socio-demographic difference between the two study areas(53).

In our study, the occurrence of rare types of ARM made up 5.1% of all cases, which was lower than the 9% reported in a study in Europe, but higher than the rate found in a study conducted in Italy and TASH Ethiopia. The difference in rates could be attributed to the varying sample sizes used in the studies. (2,26, 53,). The commonest among the rare anomalies was recto-vaginal fistula similar with global reports (6, 9)

The study revealed an interesting finding that two patients had a complex type of ARM, with one patient presenting with an H-type fistula and rectal stenosis and the other Rectal stenosis with pouch colon. This is a noteworthy finding because it suggests that these anomalies can occur simultaneously, which to our knowledge, has not been reported in Africa before. Previous research on the variants of H-type fistula has indicated that anorectal stenosis is the most common association observed in H-type fistula patients, in line with our study. (56,57). Rectal stenosis with pouch colon is also a very rare association which is only reported on few case reports like the one reported by Barolia DK and another by Parelkar S (58,59).

Age distribution of patients

One of the primary factors contributing to complications related to ARM, such as intestinal obstruction, sepsis, and perforation, is delayed presentation. In our study, 85% of patients had delayed presentation to the study areas, which is comparable to a study conducted in Nigeria where 86% of patients presented after 24 hours of their birth but lower rate of delayed presentation was seen compared to a pervious study conducted at TASH where only 6% presented on the early neonatal period this difference in result might attribute to the increased pediatrics surgery service all over the country in the past years resulting early detection and early referral to the health facilities. on the other hand, studies conducted in developed nations like Germen have reported lower rates of delayed presentation (27.3%). (1, 26, 60). A study conducted at TASH in Ethiopia revealed that ARM is the primary cause of intestinal obstruction in neonates, and this can be attributed to delayed patient presentation. The higher rate of delayed presentation may be due to inadequate referral systems, luck of access to healthcare facilities and transportation issues in Africa, including Ethiopia (7). This theory is supported by our study's findings, as most patients with delayed presentation came from outside of Addis Ababa, and there was a significant difference between the median age of first diagnosis and the age at which patients presented to our study areas. Additionally, late presentation may be attributed to poor knowledge about the treatability of the condition and stigma in the community toward patients and their families. This is evidenced in our study by cases where patients were as old as 12 years without having sought medical treatment before.

Among Patients who presented late cases with Recto vestibular fistula and Perinea (cutaneous) fistula had high rate of delayed presentation which was similar with studies conducted in United Kingdome and TASH this could be due to the fact that this patients didn’t develop intestinal obstruction as a result of enough fistula size compared to patients without fistula and recto-urethral fistula which had lower rate of delayed presentation in our study in line with the above mentioned studies (26,29)

Associated anomalies

Our study found a lower incidence of associated anomalies (41.4%) compared to studies conducted in Singapore (78%), Europe (72%). Germany (68.1%), and (65%) Korea (10,53,60,61), but consistent with many studies conducted in Africa, such as a study at TASH where associated anomalies were reported in 44% of patients, 20% in Uganda, and 20.5% in Rwanda (17,51). Generally, lower incidence rates of associated anomalies are reported in African countries, including our study, compared to developed countries. This could be due to a poor screening system for associated anomalies and the low economic status of patients, which may limit their ability to afford different investigation modalities in Africa, Additionally in developed countries, there are more advanced diagnostic tools available to detect associated anomalies, such as prenatal ultrasound and genetic testing. This can lead to earlier detection and a higher reported incidence of associated anomalies in ARM patients (1)

Many studies have reported that the genitourinary system is the most commonly affected system with associated anomalies in patients with ARM. Similarly, in our study, genitourinary system congenital anomalies (22%) were the most prevalent among patients with associated anomalies, which is consistent with findings from studies conducted in India, Germany, Singapore, Italy,korea and Kenya (2,10,60,61). This may be due to the close relationship between the genitourinary system and the hind gut during fatal development as the hindgut and the urogenital tract develop from the same embryonic structure called the cloaca in addition to this SHH pathway plays a critical role in the development of the anorectal canal and the genitourinary system, and disruptions in this pathway can result in a spectrum of malformations, at the same time including ARM and genitourinary anomalies(36-38). However, research conducted in China, Bangladesh and Iran indicated that cardiovascular anomalies were the most common associated anomalies, which is opposite to our findings where CVS anomalies (12%) were the second most common system affected after the genitourinary system(9,54). The first European multi-central registry of patients with ARM identified musculoskeletal system anomalies as the most common system affected, whereas in our study it was considered it the third most common system affected(53). These differences may be due to various factors such as socioeconomic status, environmental factors, genetic factors, referral systems, and institutional differences in screening protocols for additional anomalies.

Currently, the best approach for classifying cases based on the group of anomalies and symptoms they present is to classify them into syndromes. This approach helps to identify possible associations between anomalies, including ARM. Trisomy 21 and VACTERL association are the most commonly reported syndromes associated with ARM, but there is no single study conducted in Ethiopia that demonstrates this association. In our study, VACTERL association was observed in 7.7% of patients with ARM, which is similar to the prevalence reported in France (8%). However, the prevalence of VACTERL association varies across different geographic locations, ranging from 3% in India and 5% in Singapore to higher rates of eleven percent is reported in countries such as Italy, Iran, and Bangladesh and 16% in Korea(6,9,10,61). The variation in prevalence of VACTERL association may be due to several factors, including differences in diagnostic criteria, variability in patient populations based on geographic location, ethnicity, or socio-economic status, genetic and environmental factors since VACTERL association is believed to have a genetic component and may also be influenced by environmental factors. Additionally, diagnosing VACTERL association can be challenging, as it requires the identification of multiple congenital anomalies, and some anomalies may go undetected or be misdiagnosed (9).

other syndrome that was identified in our research was IEOS cloacal syndrome which is one of syndromes that has been identified in ARM patients in different researches similar with ours this association could be due to , a mutation on 1p36 as hypothesized by Chen Wang et al(10,37).

The contribution of genetic factors is evident as 4%-11% of patients with ARM have a chromosomal abnormality, which goes in line with our study, where 6.6% of the patients had chromosomal anomaly and all were trisomy 21 and it was diagnosed predominantly in patients with ARM without fistula 83.3% which is consistent with other studies. Overall, the association between trisomy 21 and ARM without fistula highlights the complex genetic and developmental mechanisms underlying these conditions and the need for further research to better understand their underlying causes and implications(2,10,36,) .

Research has demonstrated that as the complexity of anorectal malformation (ARM) decreases, the incidence of associated anomalies also tends to decrease. Our findings align with this pattern, as we observed that the perineal fistula group had the lowest occurrence of associated anomalies. On the other hand, the recto-vesical fistula group had the highest percentage (82%) of associated anomalies, followed by ARM without fistula (64.7%), cloacal malformations (53.8%), and recto-vaginal fistula (50%).This is because complex ARM involves more extensive disruptions in embryonic development, which can affect multiple organ systems and result in a wider range of associated anomalies. Overall, the increased incidence of associated anomalies in complex ARM highlights the need for comprehensive evaluation and management of affected patients, including evaluation of other organ systems and multidisciplinary care involving specialists in various fields (2,10,32,61).

Associated risk factors for Anorectal malformation

This study extensively investigated various maternal risk factors associated with ARM in children. The findings revealed significant associations between ARM and factors such as a family history of birth defects, alcohol consumption during pregnancy, use of unspecified medications in the first trimester, advanced maternal age, as well as low birth weight and unplanned pregnancy..

The exact cause of ARM remains incompletely understood. due to limited research on its etiology. However, existing literature suggests that it is multifactorial condition, involving both genetic and environmental factors in its pathogenesis. Genetic factors have been highlighted in many studies on ARM, including a case-control study conducted in the Netherlands, Germany which found a higher risk of ARM in individuals with a family history of birth defects, including ARM, in their first and second-degree relatives (12,38, 60). Our own research supports this theory, as we found that individuals with a family history of birth defects, including ARM in their first and second-degree relatives, were six times more likely to develop ARM than those without such a family history. This increased risk of ARM in families with a history of birth defects can be explained by genetic a mutation which is believed to play a role in the etiology of this condition in different studies including those conducted in china. Various genes, such as those involved in the SHH signaling pathway, have been identified as potential candidates in the development of ARM. Another gene that may be involved is Wnt5a, which encodes a protein involved in the Wnt signaling pathway that is essential for proliferation, migration, adhesion, and tissue differentiation. Wnt5a is prominently expressed in the rectum during embryonic development, particularly in the circular muscle and

myenteric plexus, suggesting its role in normal anorectal development. Mutations in these genes can interfere with normal embryonic development, leading to a range of ARM (36-37).

Several environmental factors have been investigated in studies on the etiology and risk factors of ARM, but the results have been inconsistent and heterogeneous. Our research suggests that maternal alcohol consumption during early pregnancy may increase the risk of ARM, which is consistent with studies conducted in Japan on ARM and Ethiopia on congenital anomalies (41,45). This may be due to the fact that alcohol exposure can disrupt normal embryonic development processes such as cell proliferation, migration, and differentiation by crossing the placental membrane. However, studies conducted in Germany, the Netherlands, and Sweden has not found a significant association between alcohol consumption and the occurrence of ARM (38, 48, 61). One possible explanation for these conflicting results is that the effects of alcohol on embryonic development are dependent on the dose, timing, duration, and pattern of exposure. Additionally, cultural differences in alcohol consumption patterns in different communities may also play a role. For example, In Ethiopia, alcoholic beverages like "areki" and "tella," which are produced locally, are regularly consumed by both Sex, especially in rural areas. (41).

This study highlighted the possibility that medication use during the first trimester of pregnancy could be a risk factor ARM. his finding aligns with previous studies, including a meta-analysis on maternal drug use and ARM occurrence, which found associations with various drug groups such as anti-asthma, anti-pain, and anti-depressant medications, as well as thyroid medication and other drug groups (43). A research study conducted in Ethiopia on congenital anomalies also reported this association (41). However, some reports, such as those by Melanie Kapapaet al and Iris A. L. M. van Rooij et al, did not find a significant association between medication use during pregnancy and ARM (38, 60). The conflicting results in the literature may be due to various factors, such as differences in study design, sample size, and the specific medications investigated. Additionally, the effects of medication use during pregnancy may be influenced by other factors, such as maternal health and underlying medical conditions. It is important for pregnant women to discuss any medication use with their healthcare provider, weighing the benefits and risks of medication use during pregnancy (12).

The study found that patients with ARM had significantly lower birth weights in comparison with the control group. These results align with a prior study by Anna Svenningsson et al , which also found a significant relationship between low birth weight and the occurrence of ARM (48). Two other studies by Wijers et al and Stoll C et al proposed that placental insufficiency during early pregnancy could be implicated in both the development ARM and the occurrence of low birth weight., which may explain the relationship between the two. It is also possible that LBW may be a marker for underlying fetal growth restriction, which could also affect the formatio of the anorectal canal and related structures. Additionally, Various congenital malformations, including but not limited to ARM, have been demonstrated to increase the likelihood of premature birth and growth restriction. (42, 62).

In our literature search, we were unable to find a study that specifically demonstrated a link between ARM and factors such as advanced maternal age and unplanned pregnancy. However, many Research studies have documented a link between advanced maternal age and the occurrence of congenital anomalies including a research conducted in ethiopia, which is consistent with our own study. We found that both advanced maternal age and unplanned pregnancy were associated with a higher risk of developing ARM. Prior studies have also shown that older mothers have a higher risk of genetic mutations and an increased incidence of aneuploidy, which could potentially contribute to the development of ARM. (63, 64,65).

Previous studies have shown that unplanned pregnancies are significantly associated with adverse birth outcomes; there is no clear evidence to suggest that unplanned pregnancy directly causes an increased risk of ARM. However, unplanned pregnancy can indirectly contribute to the risk of ARM by increasing the likelihood of certain risk factors that have been associated with the condition, such as low birth weight. Additionally, unplanned pregnancies may be associated with a lack of access to prenatal care, which can lead to undetected and untreated issues that could potentially contribute to the development of ARM or other birth defects. It is important to note that the risk of ARM and other birth defects is influenced by a complex interplay of factors, and unplanned pregnancy is just one of many potential risk factors that may contribute to the development of these conditions (66, 67).

Our study found that several factors, including maternal BMI, maternal medical illness during pregnancy (such as diabetes), folic acid intake, maternal smoking, and passive smoking, did not have a relevant association with the incidence of ARM. This contrasts with previous studies conducted in Germany, the Netherlands, Sweden, China, and Japan, where different variables were found to be associated with ARM in different areas, resulting in heterogeneous results (38, 44, 48, 60). The variation in results across different studies may be due to differences in study design, such as variations in the definition and classification of ARM, sample size, recruitment strategies, and methods used to collect and analyze data. In addition, differences in healthcare practices and access to prenatal care may also contribute to heterogeneity in the results. For example, limited access to prenatal screening and diagnostic tests in some areas of the world could affect the detection and reporting of ARM cases. Furthermore, differences in cultural and socioeconomic factors may also play a role in the heterogeneity of results. For instance, cultural practices or beliefs may influence the reporting or diagnosis of ARM cases, and socioeconomic factors like poverty or lack of access to healthcare may increase the risk of ARM (12).

7. Strengths and limitations of the study

7.1. Strengths

- Two different study designs were used
- Face to face interview was conducted with the study participants for the case control study
- We used the two largest territory hospitals in Addis Abeba for this study.
- Representative sample size was taken

7.2 Limitations

- Since the case control study was it was based on recall ability of study participants might be prone to recall bias
- Since it is hospital based study we might have missed patients who did not seek medical treatment.
- Since we used two territory hospitals we might have missed case with lower anomalies which could have been treated at referral hospitals.
- Due to the lack of a standardized institutional screening protocol, it is possible that some patients with associated malformations were not detected and may have been missed.

8. Conclusion and Recommendation

Conclusion

Our study found that anorectal malformations (ARM) were equally distributed among male and female patients. Among males, perineal fistula was the most common sub-type, while among females; vestibular fistula was the most common. Delayed presentation was common in our set up. Isolated cases of ARM were more prevalent than cases associated with syndromes. Genitourinary tract anomalies were found to be the most common associated anomaly in ARM cases. Associated anomalies are more common in high anomalies.Our study also suggested that advanced maternal age, unspecified medication intake in the first trimester of pregnancy, low birth weight, and alcohol consumption during the first trimester of pregnancy may contribute in the etiology of ARM. In addition, a family history of congenital malformations and unplanned pregnancy appeared to further increase the risk of ARM. However, further studies are needed to confirm these findings before definitive conclusions can be drawn.

Recommendation

Based on the findings of this study, the following recommendations have been proposed :-

Ministry of health

- Prepare trainings for health professionals, to widen their understanding about patterns of anorectal malformation and identified risk factors associated with ARM
- Increasing pediatrics surgery service in different hospitals all over the country

For health care providers

- Creating awareness on the control of the above listed risk factors
- Creating awareness on the treatability of the case and importance of immediate medical intervention that can go long way in decreasing the occurrence of ARM
- Neonatal screening for imperforated anus immediately after delivery is recommended to avoid delayed presentation in the study settings
- Screening for associated congenital anomalies patients is recommended for all patients with ARM
- Using Krickenbeck classification for diagnosis of ARM is recommended in all patients

For the researcher

- Further population based studies study shall be conducted to assess the prevalence of ARM
- Further population based studies are needed to assess the role of genetics and environmental factors involved in the causation of ARM

For the hospital

- Proper medical record keeping and digitalization of the records shall be done

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ANNEXES:

Annex I. Information sheet

Title: pattern and associated risk factors of anorectal malformation, in selected governmental hospitals in Addis Ababa, Ethiopia, 2023.

Investigator: Samrawit Solomon (BSc, MSc candidate)

Organization: AAU

Sponsor: DU

Introduction: This information sheet is prepared for TASH, Saint Pauli's Hospital Melinieum Medical College. These Governmental Hospitals are selected to conduct the proposed study " on the pattern and associated risk factors of anorectal malformation".

I kindly request permission from your office to carry out the proposed study in this hospital. Please review the following information to gain a better understanding:

Purpose of the study: To assess pattern and associated risk factors of anorectal malformation,in in selected governmental hospitals in Addis Ababa, Ethiopia, 2023.

Procedure: To conduct the study and fulfill the aforementioned objectives, the required information will be collected from records, patient files, and through face-to-face interviews. A checklist will be used to gather socio-demographic and clinical data from ARM patients admitted to the pediatric surgery unit.

Risk and benefit: The study poses no risks to the participants involved. The outcomes of the study will assist the responsible organization in identifying associated factors, thereby facilitating improvements in prevention and treatment services related to the identified issue.

Confidentiality: The confidentiality of all data obtained from the logbook, patient files, and interviews with mothers will be strictly maintained. No personal information of the patients will be documented. The study records will be securely stored in a locked file, and only the Principal Investigator will have authorized access to them.

Contact

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Annex II.

Hospital consent form

This study will take place at TASH and SPHMMC hospitals. The primary aim of this research is to evaluate the patterns and associated risk factors of ARM among patients admitted to the pediatric surgery unit. The results obtained from this evaluation will play a vital role in formulating preventive and therapeutic strategies for ARM. These approaches will be developed based on precise epidemiological data that is specific to both our region and the nation as a whole. Furthermore, the information gathered will assist the pediatric surgery department in implementing suitable management techniques for ARM. Currently, there is limited knowledge about the pattern and associated factors of ARM in Ethiopia. Therefore, the participation and collaboration of the hospital in this study are highly valuable in gathering the necessary information, and your support would be greatly appreciated.

To conduct this study, data will be collected retrospectively from the patients' medical record cards. No personally identifiable information, such as patient names, will be recorded, and the results will be presented in an aggregated format. The utmost confidentiality will be maintained throughout the study, with strict measures in place to prevent unauthorized access to personal information.

Lastly, the hospital reserves the right to decline participation in this study at any time. If you have any questions or need further clarification about the planned study, please do not hesitate to seek information from the principal investigator or the institution using the provided contact details.

Principal Investigator: Samrawit Solomon (BSc, MSc candidate)

Cell-phone: 0911804235

If you agree to participate in this study, please confirm your consent by signing here. Thank you very much.

Participant Hospital: ___________________________

Principal Investigator: _________________________

Mother Consent Form

The study aims to evaluate the prevalence, patterns, and associated risk factors of anorectal malformation (ARM) in specific governmental hospitals located in Addis Ababa, Ethiopia, in the year 2023.

Good morning/afternoon. My name is [---------------]. I am from Addis Ababa University, College of Health Sciences, School of Medicine, Department of Medical Anatomy. Ms. Samrawit Solomon, the principal investigator, is conducting this study as part of her Master's degree in Medical Anatomy. We kindly request your cooperation in answering a few questions related to the study. As part of the study, you have been selected to participate as a representative of the sample population. You have been given this interview questionnaire because you meet the required criteria for sampling. The goal of this interview is to gather pertinent data for my research study. I want to assure you that any information obtained from this interview will be used exclusively for research purposes and will be treated with the utmost confidentiality. Your name will not be included in any records, and there will be no possibility of linking your individual responses to the overall findings of the study..

our participation in this study carries no risks to you or your family, aside from a maximum time commitment of 30 minutes. If you come across any issues or concerns pertaining to the research, you can reach out to the responsible individual using the contact details provided below. It is important to note that you have the right to decline to respond or withdraw your participation at any point. However, your involvement is highly valued and crucial for the successful attainment of my research objectives. With great respect, I kindly request your cooperation and willingness to participate in this interview.

Please indicate your agreement to participate in this study:

Yes, (Continue) ------ No, (Stop) -------.

Thanks a lot!

Annex III. checklist

Addis Ababa University

College of health science, school of medicine

Department of human anatomy

Data Collecting Format for the assessment of pattern of Anorectal malformation at selected governmental hospitals in Addis Ababa, Ethiopia, 2023

Code ----------------------

MRN----------------------

Characteristics of the child from patient medical charts			
NO	**Question**	**Coding category**	**Skip**
1	Age of presentation		
2	Age of first diagnosis by health professional		
2	Sex	1. Male 2. Female	
3	Year of presentation		
4	Is there Diagnosis anorectal malformation?	1. Yes 2. No ⇩	Next part
5	what type of anorectal malformation	1.Perineal fistua, 2.Rectovesical fistula, 3.Rectourethral fistula, 4.Vestibular fistula 5. Cloacal malformation, 6. No fistula 7. Anal stenosis 8. other--------------------	
6	Is there associated congenital anomaly	1. Yes 2. No ⇩	
7	Type of associated anomaly	----------------------------	
8	Is there any chromosomal syndrome	1.Yes 2. No ⇩	10
9	What type of chromosomal abnormality		

Data Collecting Format for the assessment of risk factors associated with ARM of Anorectal malformation at selected governmental hospitals in Addis Ababa, Ethiopia, 2022			
Socio-demographic characteristics of the mother			
1	Age of a mother at pregnancy	------------------------------	
2	Residency	1.urban 2.rural	
3	Educational status	1.Ilitrate 2.Can read and write 3.Elementary school 4. High school graduate 5.Higher education	
4	Occupation	1.government 2. student 3.farmer 4.private 5.other	

Maternal reproductive and obstetric history			
No	**Question**	**Coding category**	**Skip**
1	The index pregnancy was	1. single tone 2. multiple pregnancy	
2	Gravidity	3.	
3	Gestation age at delivery	1.Term 2. Preterm	
4	Birth weight of child	--------------------------	
5	Did you have any of this in your previous pregnancies?	1.Abortion 2.Still birth 3.Early neonatal death 4. More than one specify	
6	Had ANC follow up?	1 . yes 2. No	
7	If yes to No 5 how many follow-ups did you attend?	1.1 2.2 3.3 4.4	
8	Was the pregnancy planned	1. yes 2. No	
Genetic Factors			
1	Previous history of congenital anomaly in the family?	1.Yes 2.No ⇩	
	How is that person related to this child?	First degree relative 2.Second degree relative 3. Third degree relative	
2	Previous history of anorectal malformation in the family?	1.Yes 2.No ⇨ ⇩	3
3	How is that person related to this child?	1.First degree relative 2.Second degree relative 3. Third degree relative	
4	Do you have genetically relationship with your husband?	1 . yes 2. No	
Maternal Medical And Drug History			
1	Is there any history of maternal chronic disease	1. yes 2. No ⇨ ⇩	3

2	What type of disease	1.Diabetes mellitus 2.Anemia 3.Epilepsy 4.urinary tract infection 5. Other -----------------------	
3	History of medication intake during pregnancy	1.Yes 2. No ⇨ ⇩	Next part
4	What type of medication	---------------------------------	
5	At what gestational age		
6	How long did she use it	-----------------------------------	
	Maternal nutritional and folic acid consumption		
1	History of folic acid intake during the pregnancy?	1.Yes 2.. No ⇨ ⇩	Skip
2	If yes, when did she start using them?	1. Before pregnancy (specify)……………………………… 2. . After conceiving (specify gestation age)………………………..	
3	For how long did the mother use folic acid?		
4	What was your weight and height during pregnancy	weight (Kg)__________ height (meter)__________	
	Maternal Chemical Exposure and maternal lifestyle		
1	History of alcohol intake during pregnancy?	1. yes 2.. No ⇨ ⇩	4
2	alcohol intake per day and how often		
3	During which month of pregnancy?		
4	History of smoking cigarette during pregnancy?	1.yes 2.. No ⇨ ⇩	8
5	the amount of cigarette per day		
6	At which gestation age		
7	Was the mother staying with the cigarette smoker during pregnancy	1.Yes 2.No	
8	Was the mother exposed to theaputic/diagnostic radiation during pregnancy?	1.yes 2. No ⇨ ⇩	11
9	Type and gestation age of radiation exposures did she had?	------------------------------	
10	At what estimated gestation age		

11	Use of pesticides (insecticides, herbicides or fungicides) at home /work place?	1. Yes 2. No	
12	exposure to industrial cleaning agents and solvents	1. Yes 2. No--------------	