ADDIS ABABA UNIVERSITY
COLLEGE OF DEVELOPMENTAL STUDIES
DEPARTMENT OF POPULATION STUDIES

Research Title

META- ANALYSIS OF MATERNAL MORTALITY AND ITS ASSOCIATED FACTORS IN ETHIOPIA

By: Michael Araya (Reg. No. GSE/6015/12)

August 2022
Addis Ababa, Ethiopia

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By: Michael Araya (Reg. No. GSE/6015/12)
Advisor: Professor Nigatu Regassa

Research submitted to the department of population studies, in partial fulfillment of the requirements for the degree of masters of population studies with specialization in Reproductive Health

August 2022
Addis Ababa, Ethiopia

Declaration Statement

I, Michael Araya, the final report of research titled "META- ANALYSIS OF THE STUDY OF MATERNAL MORTALITY AND ITS ASSOCIATED FACTORS IN ETHIOPIA" is my original work and has not been submitted for any previous degree or institution. The research document has also complied with the regulations of the university and meets the accepted standards with respect to originality and quality.

Signed by the Examining Board

External examiner (Name)	Signature	Date
Internal examiner (Name)	Signature	Date
Advisor (Name)	Signature	Date

Acknowledgements

I am pleased to thanks Professor Nigatu Regassa, my research Advisor, for his unreserve support and willingness to give his time and commitment in my engagement on this research paper. In addition, my special thanks to my family especial my mother (Jemanesh Abebe) and Aunt (Eshet Abera) for their support and word of encouragement and being by my side during all challenging times. Moreover, I want to extend my sincerely thanks to all ISHDO MULU KP Program Team colleagues for their overall support and encouragement.

List of Abbreviation and Acronyms

AMOR	Adjusted Median Odds Ratio
ANC	Ante Natal Care
AOR	Adjusted Odds Ratio
CDC	Center for Disease Control
CI	Confidence Interval
CSA	Central Statistical Agency
EDHS	Ethiopian Demographic Health Survey
EMDHS	Ethiopian Mini Demographic Health Survey
FP	Family Planning
HEW	Health Extension Worker
IUDF	Intra Uterine Fetal Death
JBI-MAStARI	Joanna Briggs Institute – Meta-Analysis of Statistics Assessment and Review Instrument
LICs	Low Income Countries
MCH	Maternal and Child Health
MDGs	Millennium Development Goals
MMEIG	Maternal Mortality Estimation Inter-Agency Group
MMR	Maternal Mortality Rate
NGO	Non-Governmental Organization
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RH	Reproductive Health
SDGs	Sustainable Development Goals
SBA	Skilled Birth Attendant
TBAs	Traditional Birth Attendants
UNICEF	United Nation Children Fund
USAID	United State Agency for International Development
WHO	World Health Organization

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ABSTRACT

Background

According to the World Health Organization, in 2017 the maternal death rate in Ethiopia was 401 for each 100,000 live births, which albeit essentially decreased from 2010 levels (1030, per 100,000 live births), is still high contrasted with worldwide pace of 211 for every 100,000 live births.

Objective

The main objective of the study was to examine the key determinants of maternal mortality in Ethiopia.

Methods

Data were entered into Microsoft Excel and then exported to STATA 16 software for further investigation. Random effect model was used, and the findings of meta-analysis is presented using forest plot, funnel plot, and meta regression table. Forest plots were used to present the combined estimate with 95% confidence interval (CI) of the meta-analysis.

Results

The factors significantly associated with maternal mortality are having Postpartum hemorrhage OR= 3.50 [2.86, 4.14] and antepartum hemorrhage OR=0.45 [0.14, 0.76]. The factors that have no significant association with maternal mortality are education, resident, Sepsis and Pregnancy induced hypertension overall effect size (Odds Ratio) with 95% CI of 2.09 [0.47, 3.70], 1.19 [0.44, 1.94], 0.90 [-0.33, 2.13] and 0.94 [-0.18, 2.07] respectively.

Conclusions

This meta-analysis study finding showed that physiological factors like Antepartum hemorrhage and postpartum hemorrhage have an impact on maternal mortality and highlights risk factors for maternal mortality in Ethiopia. It is also showed the importance of skilled person attended delivery, postnatal care, and maternal education on danger sign of pregnancy and actions to be taken to avoid the three delays that have huge impact on maternal mortality due to the effect of direct causes of occurrence.

Key words:

Maternal mortality, maternal health, Postpartum hemorrhage, antepartum hemorrhage, education, resident, Sepsis and Pregnancy induced hypertension.

CHAPTER ONE

1. INTRODUCTION

1.1 Background

A maternal death is characterized by the WHO as, "the death of a woman while pregnant or within 42 days of end of pregnancy, independent of the span and the site of the pregnancy, from any reason identified with or caused by the pregnancy or its administration, however not from unplanned or accidental causes" (Hovert, 2021). Maternal mortality causes are almost similar all across low- income countries, most of them obstetric origin and followed by obstructed labor, hypertensive disorders, infection problem, and hemorrhage (Berhan et. al., 2014). A woman's death during pregnancy, at birth, or after giving birth is a misfortune for her family and for the society as a whole (Cenrer for Disease Control, 2020).

Globally, roughly about 1,000,000 maternal mortalities happen each year (Berhan et. al., 2014). The larger portion of these mortalities in certain places of the world reflects disparities in admittance to quality wellbeing, administrations and features a huge gap among rich and poor. Maternal mortality is unacceptably high, where most of these mortalities (94%) happened in low-income settings, and most might have been forestalled (World Health Organization , 2019). Specifically, in the low-income nations, maternal pregnancy induced mortality are the significant reasons for death of women in the regenerative age bunch (Berhan et. al., 2014). In addition, they have higher life time risk because they are fertile, an in effect, they face repeated risk of maternal death. (Global Development commons, 2020).

Evidence suggest that maternal mortality has dropped significantly since the implementation of the MDGs, and the widespread maternal mortality decreased by 45% (from 380 to 210 maternal mortality for each 100,000 live births) between1990 and 2013 (Millennium Development Goals, 2016). Despite this, most of the low-income countries (LICs), especially in Sub-Saharan Africa, have not gained adequate headway to meet MDG 5a (Filipp et.al., 2016) Maternal mortality is also emphasized in Goal 3 of Sustainable Development Goals (SDGs) (Maternal Health Task Force at The Harvard Chan School Center of Excellence in Maternal and child health, 2021). Most governments have embraced this objective in their administration approaches and public procedures and pursuing and arriving at anticipated outcomes. Ethiopia's National Health Care

Quality Strategy for 2016-2020 set Maternal, Newborn and Child Health as vital with the driven objectives to decrease the maternal mortality proportion (MMR) from 412 to 199 for each 100,000 live births by 2020 (World Health Organization, 2021).

Even though there is an increase in focus for maternal mortality reduction by governments and development partners (including UN), there has been little knowledge around the levels of maternal mortality and morbidity and its causes (Filipp et.al., 2016). Furthermore, they are presenting and mainly focusing on maternal mortality immediate cause rather than focusing on many risk factors for maternal death that has begun long before delivery (Maternal Health Task Force at The Harvard Chan School Center of Excellence in Maternal and child health, 2021).

1.2 Statement of The Problem

Starting around the year 2000, Ethiopia is able to reduce maternal and youngster mortality significantly (Abebe, 2021). Ethiopia has likewise decreased maternal demise from 871 to 412 somewhere in the range of 2000 and 2016 (Agajie et.al., 2021). However, in absolute term, a maternal death pace of 412 for each 100,000 live births is still excessively high (Abebe, 2021). The critical additions made are because of the political responsibility and solid authority at all degrees of government, local area commitment and responsibility for programs, and the phenomenal help from improvement accomplices (Ethiopia Ministry of Health, 2015) Improving admittance to maternal wellbeing administration like antenatal consideration (ANC) and family arranging administrations is among the fundamental spaces of Health Extension Workers (HEW) projects' fruitful accomplishment somewhere in the range of 2003 and 2018 (Ayele et.al., 2021).

Ethiopia has recorded a significant decrease (71%) in maternal mortality, a little lower than the targets to accomplish the Millennium Development Goal (MDG) 5 objective of a 75% decrease (Chan et.al., 2021). Maternal mortalities are still high, with maternal mortality proportion of 412 maternal mortality for every 100,000 live births in 2016 (Chan et.al., 2021). According to the World Health Organization, in 2017 the maternal death rate was 401 for each 100,000 live births, which albeit essentially decreased from 2010 levels (1030, per 100,000 live births), is still high contrasted with worldwide pace of 211 for every 100,000 live births (Weldegiorgis et.al., Why Women in Ethiopia Give Birth at Home? A Systematic Review of Literature, 2021).

In Ethiopia, the proportion of women looking for care at a health facility during labor stays one of the lowest in the world. As indicated by the most recent Ethiopian Demographic Health Survey,

just 29% of women conceived an offspring at health facilities, while the rest receive support from TBAs (42%), No One (15%) and Family or Friend (14%) (Chan et.al., 2021). According to the 2016 Ethiopia Demographic and Health Survey, postnatal care service utilization was alarmingly low with just one has visiting health institutes for postnatal care services from five women that have got Institutional delivery service.

Like other parts of the world, the main reasons for maternal mortality in Ethiopia include obstructed labour and postpartum bleeding. A local study in Ethiopia has documented almost ¾ of maternal mortality happen during the post pregnancy time frame (Zeleke et.al., 2021) and larger part of the mortality happened at the age group of 20–29 years (Tessema et.al., 2017).

The key elements inferable for the maternal death are identified with low institutional delivery, helpless ability of suppliers, absence of crisis obstetric administrations at facilities, and wasteful reference frameworks for obstetric crises (Tessema et.al., 2017). In Ethiopia ANC utilization coverage, skilled delivery and postnatal care utilization were 35, 62, 28 and 17%, respectively. Even though home delivery remains high, primarily in hard-to-reach rural areas, there have been improvements in ANC service utilization and institutional delivery in Ethiopia (Harvard Chan School Center of Excellence, 2021) (Kiross et.al., 2021).

A systematic review with meta-analysis of causes of maternal deaths in Ethiopia between 1990 and 2016 with aim of documenting the causes of maternal deaths and risk factors contributing to deaths aggravated by pregnancy and its management in Ethiopia over the period 1990 to 2016has focuses on the review of Published and grey literature on the causes of maternal deaths during the period 1990 to 2016 in Ethiopia. This study has utilized the literature conducted at both the facility (15 studies) and community level (7 studies), and able to show the result of maternal mortality trends and its specific etiologies (Mekonnen et.al., 2018)

The study conducted by Berhan et.al (2014), a review of maternal mortality in Ethiopia during the past 30 years, has analyzed a total of 17 literatures that were conducted at different setting like community based – household survey (3 literatures), community based – verbal autopsy (3 literatures), hospital based – medical records (6 literatures) and other methods (2 literatures). It has analyzed and presented the trend of maternal mortality ratio in Ethiopia (1980-2010) based on the study conducted at community-based small-scale studies and hospital-based studies (Birhan et. al., 2014)

Almost all of the systematic analyses conducted on maternal mortality are five to six years old, and there is reasonable ground to believe that there have been significant changes observed on maternal mortality rate during the recent years. It has also noted that most previous studies used the mix of facility based and community-based studies which is usually poorly documented. Moreover, previous maternal mortality studies have focused more on estimation of and causation of maternal mortality based on a single health facility data at different places of the country rather than conducting systematic review of available studies. Thus, our understanding of the determinants (causes) of maternal mortality at country level is very low and concentrated on individual studies. Therefore, this meta-analysis is intended to examine the causal link (or key determinants) of maternal mortality in Ethiopia for the period 2000 to 2020.

1.3. Research Objectives

The main objective of the study was to examine the key determinants of maternal mortality in Ethiopia. The specific objectives are:

a) To assess the direct causes of maternal mortality in Ethiopia based on available evidences.
b) To identify and rollout the key socioeconomic factors that have causal link with maternal mortality in Ethiopia.

1.4. Research Questions

The leading research question for this study was "*what are the key determinants of maternal mortality in Ethiopia after the year 2000*"?

1.5 Significance of The Study

The rationale for conducting this study is two folds. First, as this study's primary focus is to examine the key determinants of maternal mortality, the findings may be useful on a national scale in informing health planners and policy makers the increased risk of maternal mortality and pregnancy, and appropriate measures to be taken thereof. Many non-governmental organizations (NGO), private organizations, and community-based organizations in Ethiopia will benefit from such a study for their planning, geographic targeting, and monitoring and evaluating programs. Secondly, results obtained from this study will add to the body of knowledge and contribute to the discourse on women health and mortality issues, guide response and recovery efforts to foster safer delivery. The findings could also help predict future public health challenges for individuals, families, communities and health care system at large.

1.6 Scope and Limitation of the Study

This study has primarily assessed causal inference on maternal mortality in Ethiopia based on meta-analysis of recent studies. While maternal death could include death due to a wide range of causes, this study is delimited to assess only deaths occurring due to pregnancy and related complications. The study has considered only women of reproductive age group (15-49) reported to have dead related to pregnancy and its complication during a certain reference period.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Conceptual Literature review

2.1.1 Global Context of maternal health

Maternal health is referring to the health of women during the period of pregnancy, childbirth and the postpartum (Kiross et.al., 2021). Each stage of the maternal health should have positive experience i.e. ensuring women and their babies reach their full capacity for health and well-being (World Health Organization, 2021). Maternal health has been a growing a worldwide public health concern because the lives of millions of mothers in the reproductive age group can be saved through maternal health care service utilization (Shudura et.al., 2020). Maternal and child health care service is the type of health service provided to mothers who are in their child bearing age and have children at the time of service seeking. All women in their reproductive age groups (15 – 49 years of age), children, school age population and adolescent girls are the targets for Maternal Child Health (MCH) service (Addisse, 2003). The maternity continuum of care is a continuous of maternal healthcare services includes antenatal care (ANC 4+ service), skill birth attendant, and postnatal care within 48 hours of delivery provision that a woman uses (Atnafu et.al., 2020). Maternal death mainly results from a pregnancy, delivery, postpartum complication; a chain of medical situations started by the pregnancy or delivery; the worsening of an unrelated condition because of the pregnancy or delivery; or other factors (National Institute of Health, NICHD, 2020). The lifetime risk of maternal death is the possibility of dying of a 15-year-old girl from complications of pregnancy or childbirth over her lifetime period; it considers both the maternal mortality ratio and the total fertility rate i.e. the average number of births per woman during her reproductive years under current age-specific fertility rates) (UNICEF/United Nation Children Fund/, 2019).Most the maternal morbidity and mortality can be prevented through service provided by qualified health professionals that is skilled birth attendants and maternal health service utilization at all level (Ombere, 2021); (Wanjala et. al., 2016). Maternal health care service utilization is critical issues to both maternal and child survival while reducing maternal mortality and morbidity and well improving the health situation of mothers and their children before, during and after birth (Wanjala et. al., 2016).

Maternal health issues remain a challenge in low-income countries and the numbers of women dying each year from maternity-related causes have remained high in these countries despite various efforts to bring them down (Ombere, 2021) . Increasing access to and utilization of Maternal health care services is not sufficient for improving maternal health outcomes and gain. The quality of maternal health care a woman receives during pregnancy, delivery and postpartum will affects her health, the health of her child and the likelihood that she will seek care in the future (Harvard Chan School Center of Excellence, 2021). Political commitment and will to invest in strong health systems by prioritizing mothers and newborns, and reach the poorest and most marginalized can make a significant difference, even though resources are limited and unavailable. If mothers and babies had access to timely and affordable maternal health care service, millions of lives could be saved every year (Organization, 2019).

Community-based care is a widely known concept in maternal and newborn health care worldwide and an important component of providing a continuum of care for low income and resource communities (Guta et.al, 2018)& (Black et.al., 2016). It encompasses encouraging healthier practices and care seeking among communities and families; recruiting and training of the local community members to work with trained health care professionals; and also a community member involvement in service provision, diagnosis, treatment, and referral (Black et.al., 2016). Facility-based delivery is also one of the maternal health services that are supported by skilled birth attendants within the healthcare facility, and accepted as intermediation to advance maternal health that could handle delivery complications (Zenbaba et.al., 2021) . Maternal service Quality of care is one of the strategies and mandatory step on the path to reaching the Sustainable Development Goals and Universal Health Coverage (PITTROF et.al., 2001)& (Goyet et.al., 2019). Maternity services High quality of care involves providing a minimum level of care to all pregnant women and their newborn babies and a higher level of care to those who need it (Goyet et.al., 2019). Sustainable Development Goals (SDGs) to reach by 2030, it has clearly indicated that efforts should have to be directed towards better quality of care service, in addition to the further expansion of health services coverage (PITTROF et.al., 2001). Experience in countries that have achieved low maternal mortality suggests that access to good-quality care is a critical issue to be focused. In addition, understanding what good quality of care is and how it is best evaluated is critical points to improving maternity services (PITTROF et.al., 2001).

Since the 1990s, the international community has implemented important initiatives to reduce maternal and newborn infants' morbidity and mortality. Improving women's health and reducing maternal mortality has been a global public health priority for the United Nations international development agenda (Tesfaye et.al., 2018). The major Global initiatives that have influenced maternal health service sector are MDG (2000-2015) goal 5, SDG (2015-2030) goal 3, and Global Strategy for Women's, Children's and Adolescents' Health (2016–2030) (World Health Organization, 2021). The initial main improvement strategy has focused on health services access and increasing the number of health facilities births, as well as the number of births attended by qualified health personnel (Saturno-Hernández et.al., 2019). Achieving the SDG target of a global Maternal Mortality Rate of lower than 70 maternal deaths per 100,000 live births by the end of 2030 will require continued and collaborated investment in maternal health research, programs and policy at the global level and very focused action at the level of country. Although important progress has been made in the last two decades across the world, about 295 000 women died during and post pregnancy, and at birth in 2017. The most common maternal morbidity and mortality causes are direct causes such as excessive blood loss, infection, high blood pressure, unsafe abortion and obstructed labour, and an indirect cause such as anemia, malaria, and heart disease (Kiross et.al., 2021).

2.1.2 Maternal Mortality Prevalence in world and Low-Income Countries

Globally, the maternal mortality ratio has declined by 44 percent, from 385 maternal deaths per 100,000 live births in 1990 to 216 in 2015 which is an average annual decline of 2.3 percent (The International Bank for Reconstruction and Development / The World Bank, 2016). The risk of a woman dying during her lifetime due to a maternal-related cause in a low-income country is about 130 times higher compared to a woman living in a high-income country (Fund, 2013) that is the lifetime risk of dying from pregnancy-related complications is 1 in 4,700 in the industrialized world and 1 in 39 in an African country. Maternal mortality is a health indicator that shows very wide gaps between rich and poor and between countries in the world (Fund, 2013). Most of these deaths are preventable, with hemorrhage accounting for over 27 percent of maternal deaths in developing regions and about 16 percent in the developed regions. Other complications leading to death are pregnancy related high blood pressure, infections, unsafe abortion, and delivery complications.

Despite the progress that has achieved for long time, 57 percent of all maternal mortality occur on the continent, giving Africa the highest maternal mortality ratio in the world and its rates vary across many different countries (Fund, 2013). In sub-Saharan Africa only, nearly 550 women die every day from preventable causes related to pregnancy complications and childbirth- accounting for 66% of pregnancy and childbirth related deaths across the globe. Among the developing countries, sub-Saharan Africa alone accounts for approximately 66% and followed by Southern Asia 22% of maternal deaths worldwide (Sara et.al, 2018). Sixteen other countries, all are in sub-Saharan Africa except for one (Afghanistan), had very high MMR in 2017 (i.e., estimates ranging between 500 and 999). Only three countries in sub-Saharan Africa had low MMR: Mauritius (61), Cape Verde (58) and Seychelles (53) (World Health Organization , 2019). Countries with high mortality rates across the African continent range from 119 deaths per 100,000 live births in South Africa, to much higher in countries like Sierra Leone (1,360 deaths per 100,000 live births), South Sudan (800 deaths per 100,000 live births), and Democratic Republic of Congo (473 deaths per 100,000 live births) (Rodriguez, 2021). Many women who experience maternal death in sub-Saharan Africa live in poverty and do not receive adequate care in time to address complications. Other contributing factors include high rates of child marriage and unintended pregnancies (Rodriguez, 2021).

2.1.3 Maternal Morbidity and Mortality in Ethiopia

Health in Ethiopia has improved from the last decades to then through the major achievement in areas of health service delivery by making health system accessible, affordable and acceptable at different level for the beneficiaries and put different efforts to provide quality health services care. Maternal health is one of the areas where an attention given and different efforts and initiatives were being implemented with strong political will and commitment (Wikipedia, 2021). Maternal mortality ia still high in Ethiopia even though it has a remarkable achievement with an estimated maternal mortality ratio of 412 maternal deaths per 100,000 live births in 2016 and far reaching the global target of 70 maternal death per 100,000 by 2030 (Ayele et.al., 2021) & (Mekonnen et.al., 2018). Based the Internationally comparable MMR estimates by the Maternal Mortality Estimation Inter-Agency Group (MMEIG), the remarkable achievement was attained between year 2000 and 2017 from 1030 to 401per 100,000 live birth respectively (Inter-Agency Group (MMEIG), 2019). This mortality rate is still high compared with the global rate of 211 per 100,000 live births (Tessema et.al., 2017) . The data collected from Ethiopian Demographic and Health Survey

(EDHS) conducted on 2000, 2005, 2011, 2016 and 2019 show that there is improvement on key maternal health service utilization at government as well as private health institutions even though there were inter regional disparities and among rural and urban resident (Central Statistical Agency Ethiopia and ICF, 2016) & (Central Statistical Agency (CSA) Ethiopia and ICF, 2019). The study conducted at national level in Ethiopia on Association between maternal mortality and caesarean section in Ethiopia has shown a report of significant regional maternal mortality ratios variation that is ranging from 74 (95% CI: 51–104) per 100,000 livebirths in Tigray region to 548 (95% CI: 251-1,037) in Afar region (Geleto et.al., 2020).

Table 2.1:Maternal Health Service Utilization among Key Indicators

Indicator	**EDHS 2000**	**EDHS 2005**	**EDHS 2011**	**EDHS 2016**	**EMDHS 2019**
Antenatal Care	27	28	34	62	74
ANC visit at least 4 visits			19	32	43
Birth attended at health facility	5	6	10	26	48
Delivery with the assistance of a trained health professional	6	6	10	28	50
Postnatal care	3	5	7	7	34
Delivery by cesarian section				2	5
Maternal Mortality Ratio	891	673	676	412	
Lifetime risk of pregnancy-related death (per 1000)			36	21	

Source: Ethiopian Demographic Health Survey 2000, 2005, 2011, 2016 and EMDHS 2019.

With regards of the determinants, a study conducted in a Pastoralist Area of Borena Zone of Oromia Region of Ethiopia has reported 51 direct obstetric causes of maternal mortality (86%) i.e. hemorrhage (45%), pregnancy related hypertensive (23%), and direct causes of obstructed labour (18%). It was also found that those who did not attend ANC were 5 times more at risk of mortality than those who attended (AOR 5.3, 95% CI 2.3–12.1). Mothers who delivered at home were two

times at risk of dying compared to those who had their deliveries at health facility (AOR 2.6, 95% CI 2.4–6) (Sara et.al, 2018).

The study conducted at Kersa health and demographic surveillance system, eastern Ethiopia on Magnitude, trends and causes of maternal mortality among reproductive aged women shows the result of 72 (23.2%) of 311 total maternal mortality were during pregnancy or within 42 days of delivery during the study period with postpartum hemorrhage (46.5%) was the most common cause of maternal mortality, followed by hypertensive disorders of pregnancy (16.3%) (Tesfaye et.al., 2018).

According to Maternal Death Review at Saint Paul's Hospital Millennium Medical in Ethiopia, direct causes of maternal death accounted for 90% (n=36) including pregnancy related hypertension (n=13, 32.5%), postpartum hemorrhage (n=10, 25%), sepsis (n=4, 10%), pulmonary thromboembolism (n=3, 7.5%) and amniotic fluid embolism (n=3, 7.5%) (Shiferaw et.al, 2020).

Based on study of prevalence and risk factors associated with maternal mortality conducted in Mizan Aman Hospital in Bench Maji of Southwest Ethiopia, about 13(3.39%) of cases died from obstetrical complications such as obstructed labor 3 (0.78%), Puerperal sepsis 2(0.52%), multi-pregnancy 1(0.26%), hypertensive problem 1(0.26%), hemorrhage 1(0.26%), IUFD 1(0.26%) and by non-frequent causes in 4(1.04%) from a total of 384 maternal delivery at the institution during the study period. Ward of referral Hospital from February to April 2014 (Weyesa et. al., 2015).

Another study conduct in Jimma University Specialized Hospital has shown a result of more than two third (68%) of death occurred during post-partum period and their death are due to being from rural area (AMOR = 2.594, 95%CI (1.001,6.726)), prolonged labour (AMOR=37.141,95%CI (13.296,103.750)), comorbidities (AMOR=9.631,95%CI (3.135, 29.588), referred cases from health center (AMOR=4.011, 95% CI (1.113, 14.464) and other health institution (AMOR=6.029, 95%CI (1.565, 24.626)) (Legese et.al, 2016).

A study conducted to see the trends and causes of maternal mortality in Ethiopia during 1990–2013 from the Global Burden of Diseases findings has shown the result of Maternal Mortality Ratio (MMR) in Ethiopia was still high in the study period that is a total of 16,740 maternal mortality (95% UI: 14,197, 19,271) in 1990 whereas 15,234 maternal mortality (95% UI: 11,378, 19,871) in 2013.However, there was insignificant change of MMR with annual change rate -1.6 (95% UI: -2.8 to -0.3) over these years. This study has also showed the top five causes of maternal mortality in 2013 were other direct maternal causes such as complications of anesthesia, embolism (air, amniotic fluid, and blood clot), and the condition of peri-partum cardiomyopathy amounts 25.7%, abortions

complications accounts 19.6%, maternal hemorrhage accounts 12.2%, hypertensive disorders accounts 10.3%, and maternal sepsis and other maternal infections like influenza, malaria, tuberculosis, and hepatitis (9.6%) (Tesfaye et.al., 2018).

Another study conducted to review maternal mortality history of past 30 years trend in Ethiopia shows that there has been no significant change in maternal mortality over the last three decades, However, Atat Hospital 22-year cohort analysis have only shown a very significant drop of maternal mortality among mothers who were kept in the maternity waiting area before the onset of labor (Berhan et. al., 2014).

The study conducted on causes of maternal mortality mainly on abortion related death in Ethiopia has reported four top most causes of maternal mortality between1980-1999: abortion related complications (31%), obstructed labor/uterine rupture (29%), sepsis/infection (21%) and hemorrhage (12%). However, the top four causes of maternal mortality in the last decade were obstructed labor/uterine rupture (36%), hemorrhage (22%), pregnancy related hypertension (19%) and sepsis/infection (13%) (Berhan et. al., 2014).

A systematic review with meta-analysis study conduct to assess the causes of maternal death in Ethiopia between 1990 and 2016 found that the main maternal mortality direct causes in Ethiopia are obstetric complications such as hemorrhage (29.9%; 95% CI: 20.28%-39.56%), obstructed labor/ruptured uterus (22.34%; 95% CI: 15.26%-29.42%), pregnancy-induced hypertension (16.9%; 95% CI:11.2%-22.6%), puerperal sepsis (14.68%; 95% CI: 10.56%- 18.8%), and unsafe abortion (8.6%; 95% CI: 5.0%-12.18%) with anemia (10.39%; 95% CI: 4.79%-15.98%) and malaria (3.55%; 95% CI: 1.50%-3.30%) as indirect causes. For recent years, the study has shown hemorrhage as the leading then followed by pregnancy related hypertension while obstructed labor and abortion have decreased over the period (Mekonnen et.al., 2018).

2.2 Conceptual Framework of the Study

Maternal mortality has happened across all continuum that starts from pregnancy to postpartum in different proportion i.e., Pregnancy (25%), delivery (16%) and postpartum (61%) (Tsegaye et. al., 2021). Traditionally, maternal mortality causes have been classified as direct (70%–80%) and indirect (20%–30%) contributing to the total (Berhan et. al., 2014). Most of direct causes of maternal mortality are hemorrhage, hypertension, abortion, and sepsis, and indirect cause contribution to maternal death is increasing all across the world (Filipp et.al., 2016). Maternal mortality main Direct causes were obstetric complications that are hemorrhage (29.9%), obstructed labor/ruptured uterus

(22.34%), pregnancy-induced hypertension (16.9%), puerperal sepsis (14.68%), and unsafe abortion (8.6%), and indirect causes were anemia (10.39%) and malaria (3.55%) for long time in Ethiopia. (Mekonnen et.al., 2018) Access to basic antenatal, delivery and postnatal care have an impact on preventing maternal mortality. (Srivastava et.al., 2014). In addition, other studies show that inadequate and poor-quality maternal health care services are associated with high maternal and child mortality rates. (Tarekegn et. al., 2014)

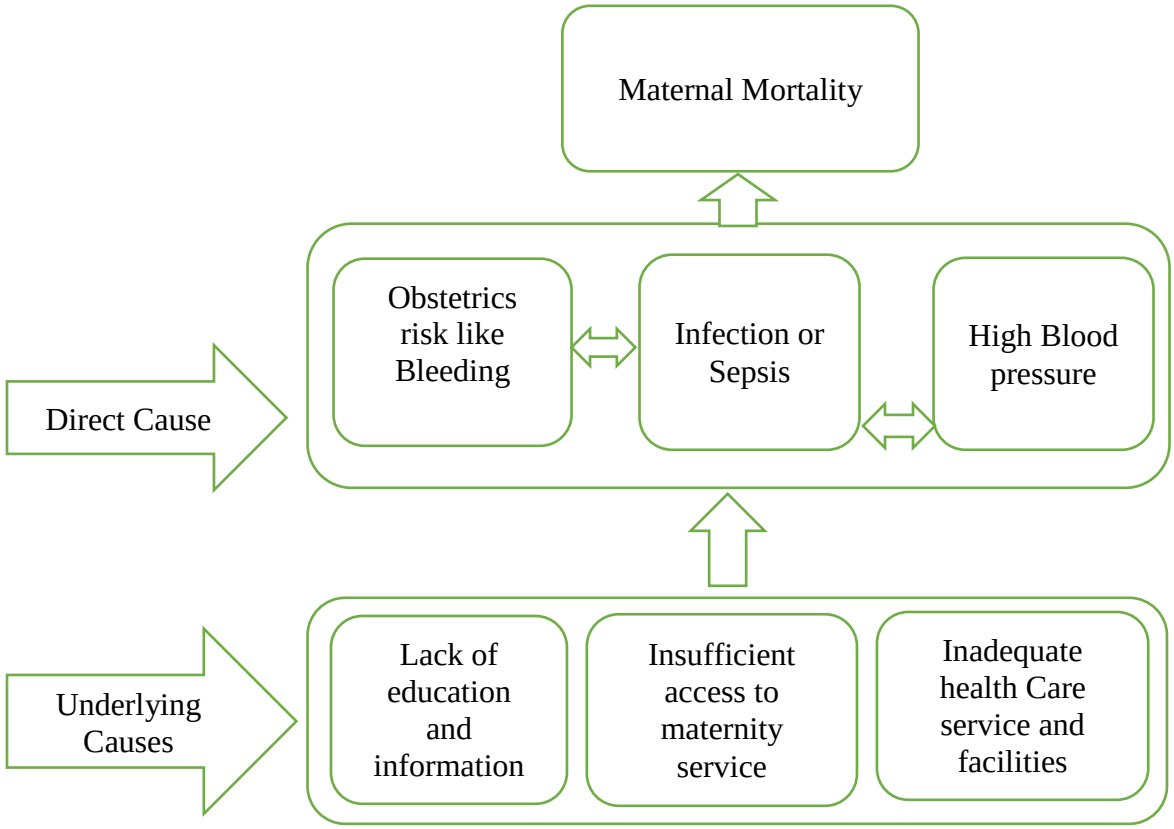

Figure 2.1: Conceptual Frame Work Linkage of Causes of Maternal Mortality

Source: Adopted and amended UNICEF 2013 Conceptual Frame Work Maternal and Neonatal Mortality and Morbidity

CHAPTER THREE

3. METHODS

3.1 Research Approach and Design

A meta-analysis of publish and unpublished studies were used to determine the causal link of selected variables with maternal mortality in Ethiopia. The review included research paper that employed quantitative research method with cross-sectional and case control study designs.

3.2 Search Strategy for The Systematic Review/Meta-Analysis

Review of all published and unpublished studies were done in PubMed, Cochrane Library, Google Scholar databases, and Addis Ababa University, Haromaya university, Gonder University, Bahirdar university, Hawassa university and Jimma University repository. The searches for published studies were restricted by time, and all published articles up to December 31, 2021 were included into the review. Search of the reference list of already identified studies to retrieve additional articles were done. The search terms that were used in PubMed included (mortality OR "maternal mortality" OR "maternal mortality among pregnant women" OR "death of women" OR "death among women of reproductive age" AND ("determinants of maternal mortality" OR "associated factors of maternal mortality") AND (Ethiopia OR "Ethiopian region"). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline were strictly followed when conducting this review.

3.3 Inclusion and exclusion Criteria

The inclusion and exclusion criterions of this research were

- Peer reviewed research papers that utilize quantitative methods
- Research with cross-sectional and case-control design
- Studies mainly on retrospective study and cohort study.
- Research that was conducted on maternal mortality and associated factors in Ethiopia.
- Research conducted at an institutional/facility level and community level
- Papers with proper control of confounding factors
- Only materials written in English

3.4 Outcome Variable

The primary outcome variable of this study was maternal mortality, measured as reported deaths occurring due to pregnancy and related complications during the reference period.

3.5 Study Selection and Data Abstraction

After identifying relevant studies based on the inclusion criteria stated above, the researcher extracted the main parameters of each study including name of authors, study period, study location, study design, sample size, reported odds ratio, maternal deaths number and proportion, major conclusion drawn related to causes of maternal deaths, and causes specific and case fatality rates reported.

3.6 Strategy for the Synthesis

The synthesis was conducted following series of steps. The first step was searching of published research paper on different online database sequentially. The second step was collecting all the searched and identified papers together and sees their relevance to the searching criteria and check for their duplicates. Then, the third step was identifying and selecting the papers based on the inclusion criteria. Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) was used for critical appraisal of the articles/studies.

3.7 Methods of Analysis

Data were entered into Microsoft Excel and then exported to STATA 16 software for further investigation. Random effect model was used, and the findings of meta-analysis is presented using forest plot., funnel plot, and meta regression table. Forest plots were used to present the combined estimate with 95% confidence interval (CI) of the meta-analysis. Funnel plots were used to assess the publication bias due to small studies.

3.8 Definition of terms

Ante-partum hemorrhage: the maternal genital bleeding after the 24^{th} week of pregnancy and before delivery of the baby.

Institutional delivery: the delivery that is conducted at any medical facility staffed with skilled delivery service professional or provider.

Maternal mortality: the woman death while pregnant or within 42 days of end of pregnancy, independent of the span and the site of the pregnancy, from any reason identified with or caused by the pregnancy or its administration, however not from unplanned or accidental causes”

Obstructed labor: it is a situation where the fetus does not exit the pelvis during vaginal delivery period due to being physically blocked even though there are adequate uterine contractions for vaginally delivered.

Post-partum hemorrhage: it is a serious bleeding condition that could lead to death and occur after immediately or within 12 weeks after delivery time.

Pregnancy induced hypertension: is a type of hypertension that is caused or happened after 20 weeks of gestation and during the period of pregnancy on the women who has a normal blood pressure.

PRISMA: is an evidence-based minimum set of items for reporting of reviews in systematic reviews and meta-analyses with focuses on the reporting of reviews evaluating the effects of interventions. It can also use as a basis for reporting systematic reviews with objectives.

Ruptured uterus: the tearing of uterus that is partially or completely during vaginal delivery and the fetus slips into her abdomen. It causes maternal bleeding and fetus distressed.

Safe motherhood: It is provision and confirming of all women receive maternal health services they need has to be safe and healthy throughout pregnancy, child bearing and the postnatal period of time.

Sepsis: it is a life-threatening condition that happens due to body's response to an infection and consequence of widespread swelling in the body, and causes damages on its own tissues.

CHAPTER FOUR

4. RESULTS

4.1. Description of selected studies

On the first stages of searching on PubMed, Cochrane Library, Google Scholar databases and Ethiopian Universities repositories like Addis Ababa, Jima, Gonder, Hawassa and Haromaya University, A total of 87 research are identified. Of which, 74 were excluded due to their non-relevance to the topics and the study areas which is Ethiopia as a general focus area of the research. 13 of the remaining research were checked for having important data that relevant to the analysis, and of which 7 of the research found to be relevant on the final stages of selection and identification due to their study design, area of focuses and having important indicators and data for the analysis. They are finally examined using this research quality checklist prepared to evaluate the quality of the studies included.

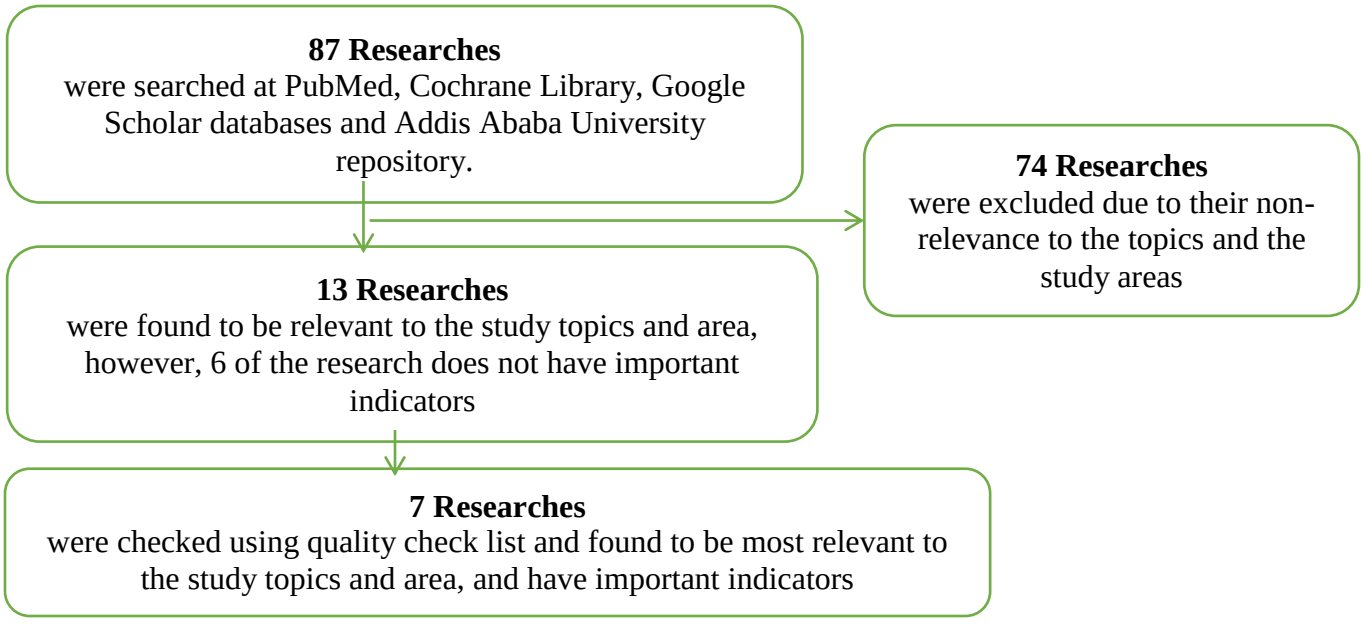

Figure 4.2: the process of selecting appropriate studies for meta –analysis/systematic review

These the final 7 identified studies are eligible and found to be qualified studies are from different parts of Ethiopia. Out of the total research finally selected, 3 of them are case control studies, and the remaining are retrospective cross-sectional studies. (Table 1)

Author	Study Title	Research methods	Country/ Region	Year
Hagos Godefay et.al	Risk Factors for Maternal Mortality in Rural Tigray, Northern Ethiopia	community-based case-control	Tigray	May 2012 to August 2013
Dereje Tolesa et.al.	Prevalence and Associated Factors with Maternal Near-Miss among Pregnant Women at Hawassa University Comprehensive Specialized Hospital	cross-sectional study	Sidama	May to June 2020
Fikadu Nugusu Dessalegn et.al	Factors Associated with Maternal Near Miss among Women Admitted in West Arsi Zone Public Hospitals	Unmached case control study	Oromia	Mar 1 to Apr 30, 2019
Birhanu Jikamo Bago,	Prevalence and Its Associated Factors among Women Undergone Operative Delivery at Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia	Retrospective record review study	SNNPR	June 2014-June 2016
Ayele Geleto et.al	Magnitude of direct obstetric complications and associated maternal death among hospitals in Ethiopia	a national cross-sectional study	All regions	2015
Girma seboka et.al	Maternal Mortality and its Determinants among Women Utilized Obstetrics and Gynecologic Services in Asella Teaching and Referral Hospital. Oromia Region, Ethiopia	retrospective cross-sectional	Oromia	2018
Tegene Legesse et.al	Trends and causes of maternal mortality in Jimma University Specialized Hospital, southwest Ethiopia	case–control study	Oromia	January 2010 to December 2014

Table 4.2: detailed description of finally selected List of studies

These finally identified lists of research, 7 researches, were evaluated and checked using the quality checklist tool and each study has evaluated using the Criteria or Quality Assessment points and scores are provided and documented well. Each score which has yes result (represented by Y) have got 1, and No (represented by N) and Not Applicable (represented by NA) have got 0. The total result calculated based the number of responses per each Criteria or Quality Assessment Checklists and the total score of the study which have got from 0 to 5 was measured poor quality, 6 to 9 as fair quality, and 10 to 14 as good quality (Table 2).

S. N	Criteria or Quality Assessment Checklists	Studies included in the review						
		S1	S2	S3	S4	S5	S6	S7
1	Was the research question or objective in this paper clearly stated?	Y	Y	Y	Y	Y	Y	Y
2	Was the study population clearly specified and defined?	Y	Y	Y	Y	Y	Y	Y
3	Was the participation rate of eligible persons at least 50%?	Y	Y	Y	N	Y	Y	Y
4	Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?	Y	N	N	N	N	N	N
5	Was a sample size justification, power description, or variance and effect estimates provided?	Y	Y	Y	Y	Y	N	Y
6	For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Y	Y	Y	Y	Y	Y	Y
7	Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Y	Y	Y	Y	Y	Y	Y
8	For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Y	Y	Y	Y	Y	Y	Y
9	Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y
10	Was the exposure(s) assessed more than once over time?	N	N	Y	N	N	N	N
11	Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y
12	Were the outcome assessors blinded to the exposure status of participants?	Y	Y	Y	Y	Y	Y	Y
13	Was loss to follow-up after baseline 20% or less?	NA	NA	NA	NA	NA	NA	NA
14	Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	N	N	N	N	N	N	N
	Total score	11	10	11	9	10	9	10
	Quality assessment status	Good	Good	Good	Fair	Good	Fair	Good

Table 4.3: Selected Studies Quality Checklist assessment with result

4.2. Education

The weight of each study was calculated based on the individual effect size of Odds Ratio and sample size, and the actual weight is 52.92%, 14.67% and 32.40% for Hagos Godefay et.al, Dereje Tolesa et.al and Fikadu Nugusu Dessalegn et.al, respectively. The overall pooled effect of the maternal mortality among the non-educated mother was Odds ratio of 2.27 with 95% CI (0.47, 3.70) as compared to educated mothers who are given birth and included in the studies. This meta-analysis result showed no significant association between education and maternal mortality. There is some heterogeneity observed within the studies as a result of finding of heterogeneity test of I2=58.16%. In addition, the test for homogeneity of the studies is rejected because we have the result of a chi-squared test(Q2) statistic of 8.11 and a p-value of 0.02 which is above the significance level of p value 0.05. (Figure 3)

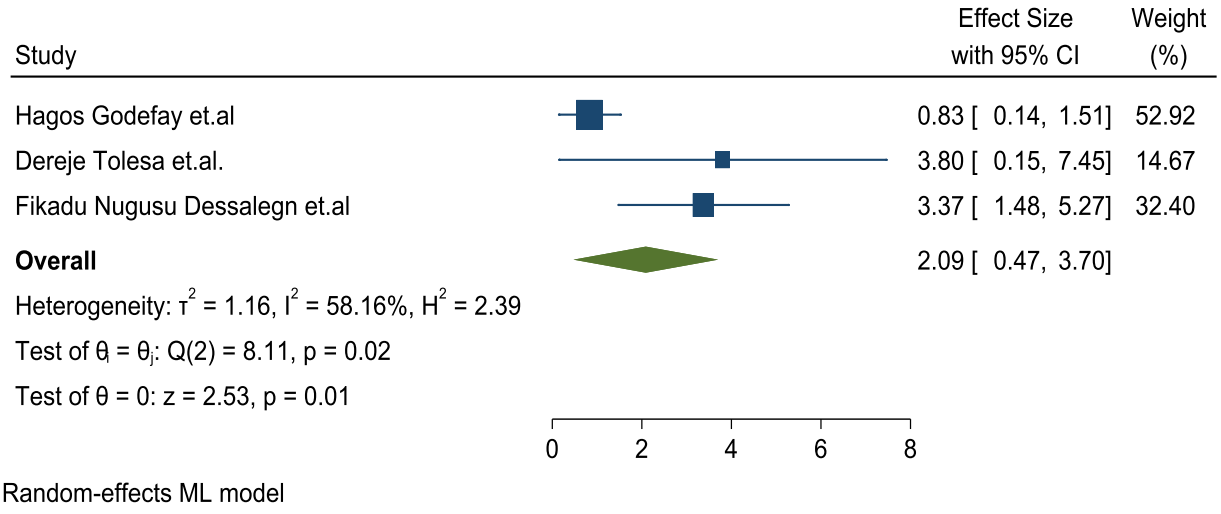

Figure 4.3: Forest plot of three studies on the effect of education on maternal mortality

It was observed that there is varied effect size among the studies and medium heterogeneity level of 58.16%. Meta regression calculation is done to explore the heterogeneity existence due to the relationship between moderators i.e. sample size and study effect sizes i.e. the Odds ratio. There is a positive relationship (coef. of 0.22) between sample size and effect size with heterogeneity I2(%) = 0 and it is statistically significant with P value 0.006. There is heterogeneity detected due to relationship between sample size and study effect.

```
  Effect-size label:  Effect Size
        Effect size:  OR
          Std. Err.:  _meta_se

Random-effects meta-regression                  Number of obs  =         3
Method: ML                                      Residual heterogeneity:
                                                           tau2 = 3.3e-09
                                                        I2 (%) =    0.00
                                                            H2 =    1.00
                                                R-squared (%) =  100.00
                                                Wald chi2(1)   =      7.53
                                                Prob > chi2    =    0.0061
```

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	.2277724	.0830308	2.74	0.006	.0650349	.3905098
_cons	-69.53176	25.78779	-2.70	0.007	-120.0749	-18.98863

```
Test of residual homogeneity: Q_res = chi2(1) =  0.58    Prob > Q_res = 0.4456
```

Table 4.4: meta-regression of three studies on the effect of education on maternal mortality

Publication bias was checked by using funnel plot asymmetry. The funnel plot looks asymmetrical because the funnel plot intercept on the X-axis deviated from zero and it reach to 1 to the right, and the number of studies at the left and right side of the funnel plot is not the same or equal in number. Thus, it is indicating that there is a publication bias (Figure 4). However, the varied effect size among the studies and medium heterogeneity level would also causes asymmetrical funnel plot of pyramidal and inverted funnel shape that have broaden base. Besides, the Random-effects analysis allow for heterogeneity to give an average treatment effect across studies and it will in turn causes funnel plot asymmetry.

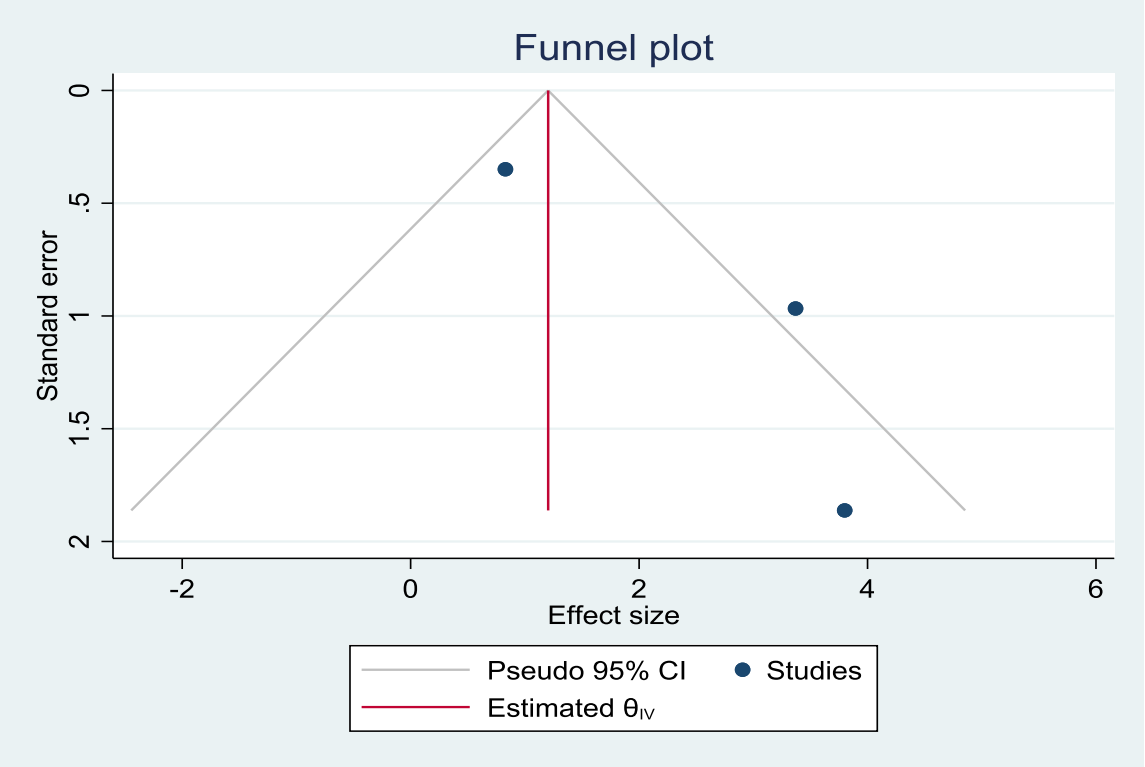

Figure 4.4: publication bias Funnel plot for the assessment of three studies

The Regression-based Egger test for small-study effects was done to see the publication bias due to small study effect and sample size. The result showed us that beta1 coefficient of 1.29 with no statistically significant level of p value of 0.44. This indicates that the publication bias may not be a serious problem and all the studies with varied effect size and sample size will be included in the review or meta-analysis. (Table 5)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
            beta1 =      1.29
      SE of beta1 =     1.693
                z =      0.76
       Prob > |z| =    0.4456
```

Table 4.5: Regression based Egger test small study effect of four studies of education

4.3. Residence

The weight of each study was calculated based on the individual effect size of odds ratio and sample size, and the actual weight is 27.57%, 4.10%, 45.87% and 22.45% for Hagos Godefay et.al, Dereje Tolesa et.al, birhanu Jikamo bago and Fikadu Nugusu Dessalegn et.al, respectively. The overall pooled effect of the maternal mortality among mothers of the rural resident was OR=1.19 with 95% CI (0.44, 1.94) compared to urban resident mothers who gave birth and included in the studies. This meta-analysis result showed no significant association between resident and maternal mortality. There is some heterogeneity observed within the studies based on the finding of heterogeneity test of I2=56.63%. The test for homogeneity of the studies is rejected because we have the result of a chi-squared test(Q3) statistic of 11.76 and a *p*-value of 0.01 and this means that it is not statistically significant. (figure 5)

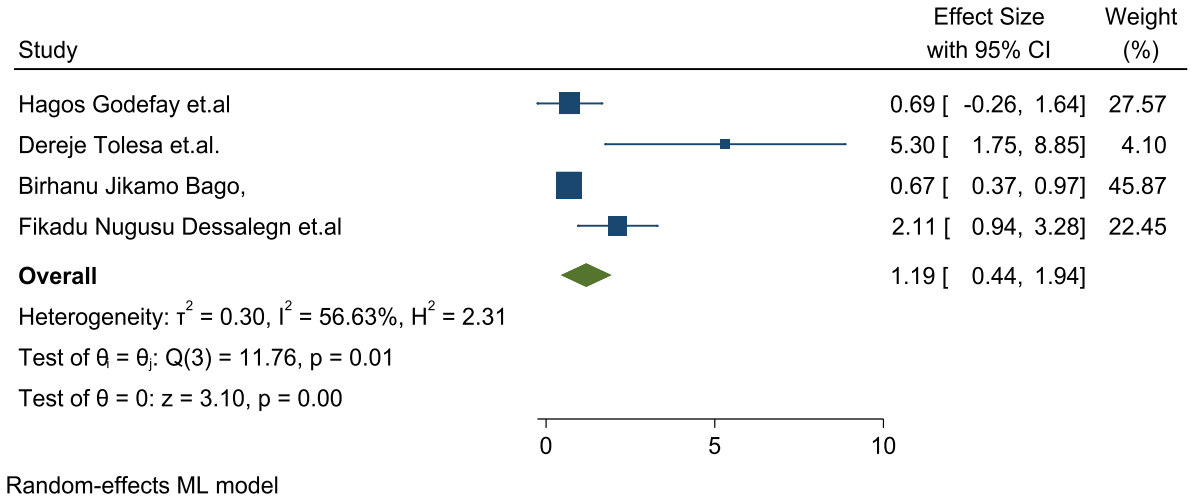

Figure 4.5: Forest plot of four studies on the effect of Residence on maternal mortality

We have observed that there is a varied effect size among the studies and medium heterogeneity level of 56.63%. We have done meta regression calculation which is often used to explore the heterogeneity existence due to the relationship between moderators i.e. sample size and study effect sizes i.e. the Odds ratio. There is a negative relationship (coef. of -0.006) between sample size and effect size with heterogeneity I2(%) = 0 and it is statistically significant with P value 0.078. There is heterogeneity detected due to relationship between sample size and study effect. (Table 6)

```
  Effect-size label:  Effect Size
        Effect size:  OR
          Std. Err.:  _meta_se

Random-effects meta-regression                  Number of obs  =          4
Method: ML                                      Residual heterogeneity:
                                                           tau2 = 1.6e-08
                                                         I2 (%) =     0.00
                                                             H2 =     1.00
                                                R-squared (%) =   100.00
                                                Wald chi2(1)   =       3.10
                                                Prob > chi2    =     0.0784
```

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	-.0069816	.0039665	-1.76	0.078	-.0147559	.0007926
_cons	3.567902	1.591447	2.24	0.025	.4487228	6.687081

Test of residual homogeneity: Q_res = chi2(2) = 8.66 Prob > Q_res = 0.0132

Table 4.6: Meta-regression of three studies on the effect of residence on maternal mortality

Publication bias was checked using funnel plot asymmetry. The funnel plot looks asymmetrical because the funnel plot intercept on the X-axis deviated from zero and it near to 1 to the right. Thus, it is indicating that there is a publication bias (Figure 6). However, the varied effect size among the studies and higher heterogeneity level would also causes asymmetrical funnel plot of pyramidal and inverted funnel shape that have broaden base. Besides, the random-effects analysis allow for heterogeneity to give an average treatment effect across studies and this will in turn causes funnel plot asymmetry.

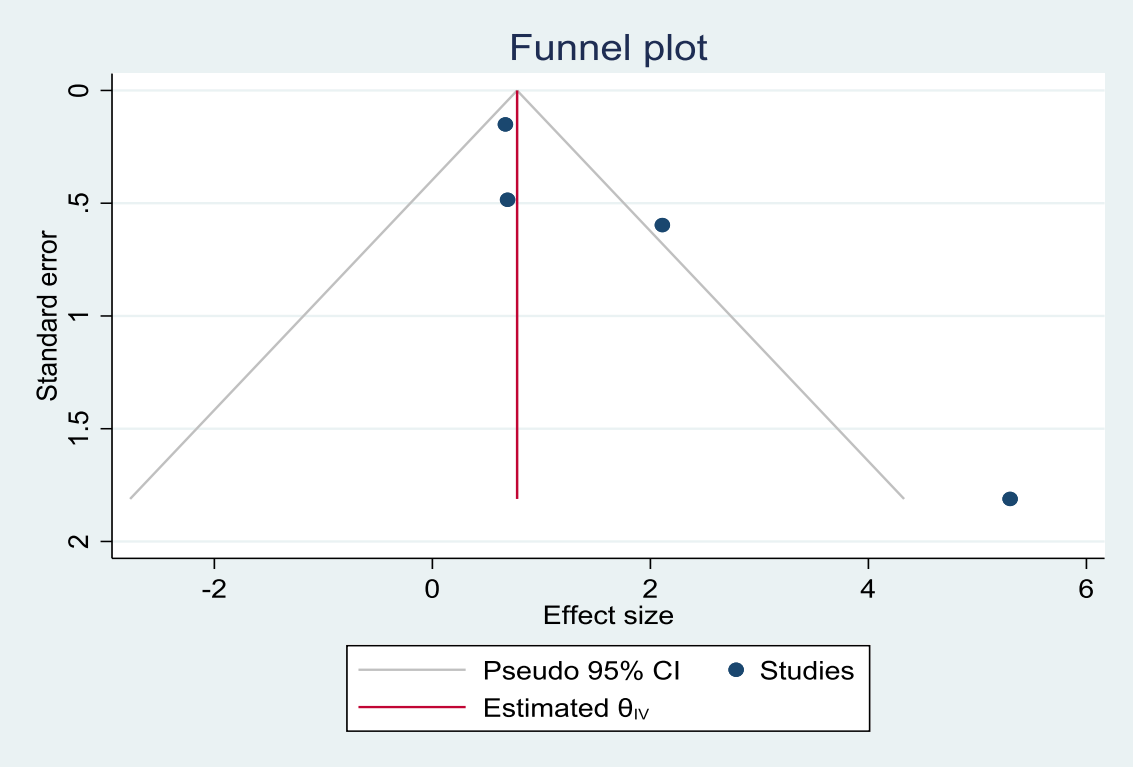

Figure 4.6: Funnel plot for the assessment publication bias of four studies of the resident

The Regression-based Egger test for small-study effects was done and the result has shown beta1 coefficient of 3.66 with statistically significant level of p value of 0.0075. there is a publication bias due to small study effect. (Table 7)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
            beta1 =      3.66
      SE of beta1 =     1.370
                z =      2.67
       Prob > |z| =    0.0075
```

Table 4.7: Regression based Egger test small study effect of four studies of resident

4.4. Ante-Partum Hemorrhage

The weight of each study was calculated based on the individual effect size of odds ratio and sample size, and the actual weight was 46.69%, 0.25% and 53.06% for Ayele Geleto et.al, Girma Seboka et.al and Tegene Legesse et.al, respectively. The overall pooled effect of the maternal mortality among the mother who have antepartum hemorrhage during birth was an OR=0.45 with 95% CI (0.14,0.76) compared to mothers who have noantepartum hemorrhage. This meta-analysis result showed a significant association between Ante-Partum Hemorrhage and maternal mortality. There is some heterogeneity observed within the studies as a result of finding of heterogeneity test of I2=66.54%. In addition, the test for homogeneity of the studies is rejected because the result of a chi-squared test(Q2) statistic of 13.12 and a p-value of 0.00 which is above the significance level of p value 0.05. (Figure 7)

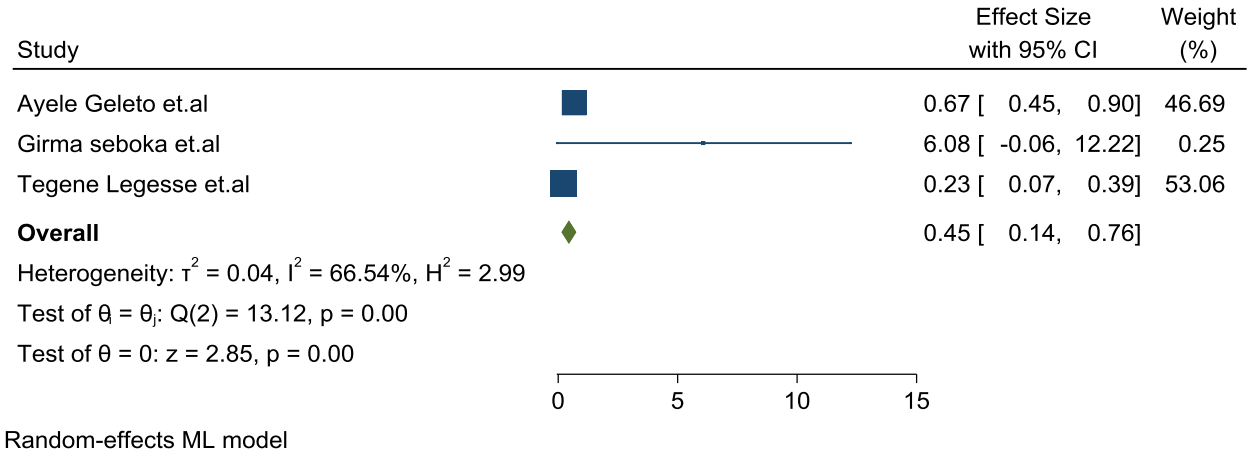

Figure 4.7: Forest plot of three studies on the effect of Ante-Partum hemorrhage on maternal mortality

There is a varied effect size among the studies and medium heterogeneity level of 66.54%. Meta regression was done to explore the heterogeneity existence due to the relationship between moderators i.e. sample size and study effect sizes i.e. the odds ratio. There is a positive relationship (coef. of 6.51) between sample size and effect size with heterogeneity I2(%) = 0 and it is statistically significant with P value 0.002. There is heterogeneity detected due to relationship between sample size and study effect. (Table 8)

```
  Effect-size label:  Effect Size
        Effect size:  OR
          Std. Err.:  _meta_se

Random-effects meta-regression                  Number of obs  =         3
Method: ML                                      Residual heterogeneity:
                                                           tau2 = 7.6e-08
                                                        I2 (%) =    0.00
                                                            H2 =    1.00
                                                R-squared (%) =  100.00
                                                Wald chi2(1)   =      9.63
                                                Prob > chi2    =    0.0019
```

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	6.51e-06	2.10e-06	3.10	0.002	2.40e-06	.0000106
_cons	.2271676	.083368	2.72	0.006	.0637692	.3905659

```
Test of residual homogeneity: Q_res = chi2(1) =  3.49    Prob > Q_res = 0.0618
```

Table 4.8: Meta-regression of three studies on the effect of Antepartum hemorrhage on maternal mortality

Publication bias was checked by using funnel plot asymmetry. the funnel plot looks a symmetrical because the funnel plot intercept on the X-axis has little shift from zero. Thus, it is indicating that there is a publication bias (Figure 8). However, the varied effect size among the studies and medium heterogeneity level would also causes asymmetrical funnel plot of pyramidal and inverted funnel shape that have broaden base. Besides, the Random-effects analysis allow for heterogeneity to give an average treatment effect across studies and it will in turn causes funnel plot asymmetry.

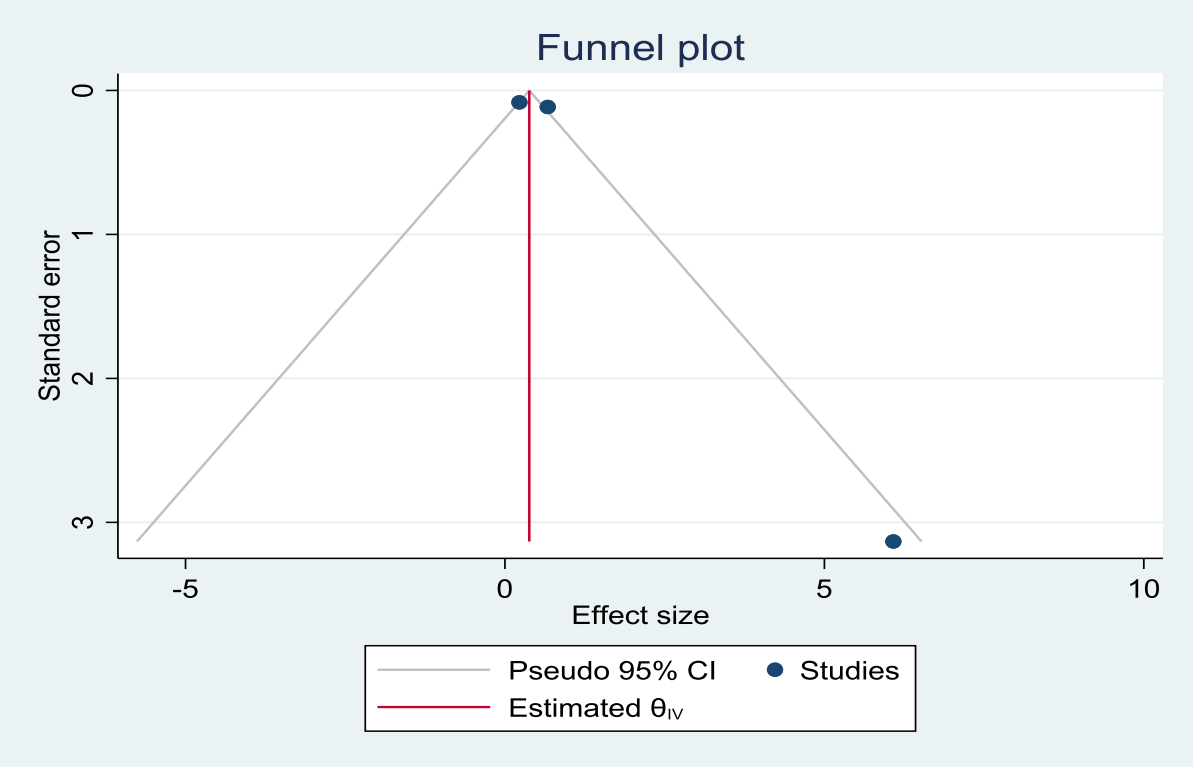

Figure 4.8: publication bias Funnel plot for the assessment of three studies

The Regression-based Egger test for small-study effects was done to see the publication bias due to small study effect and sample size. The result showed beta1 coefficient of 1.92 with statistically significant level of p value of 0.061 and there is a publication bias due to small study effect. (Table 9)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
            beta1 =      1.92
      SE of beta1 =     1.027
                z =      1.87
       Prob > |z| =    0.0618
```

Table 4.9: Regression based Egger test small study effect of three studies of ante partum hemorrhage

4.5. Post-Partum Hemorrhage

The weight of each study was calculated based on the individual effect size of Odds ratio and sample size, and the actual weight is 99.98% and 0.02% for Ayele Geleto et.al and Girma Seboka et.al respectively. The overall poled effect of the maternal mortality among mothers who have post-Partum hemorrhage during birth was an Odds ratio of 3.50 with 95% CI (2.86, 4.14) as compared to mothers who have no postpartum hemorrhage problem. This meta-analysis result showed a significant association between post-partum hemorrhage and maternal mortality. There is no heterogeneity observed within the studies as a result of finding of heterogeneity test of I2=0% with P of 0.0 which is no statistically significant result. the test for homogeneity of the studies is rejected because we have the result of a chi-squared test(Q2) statistic of 8.11 and a p-value of 0.02 which is above the significance level of p value 0.05. (Figure 9)

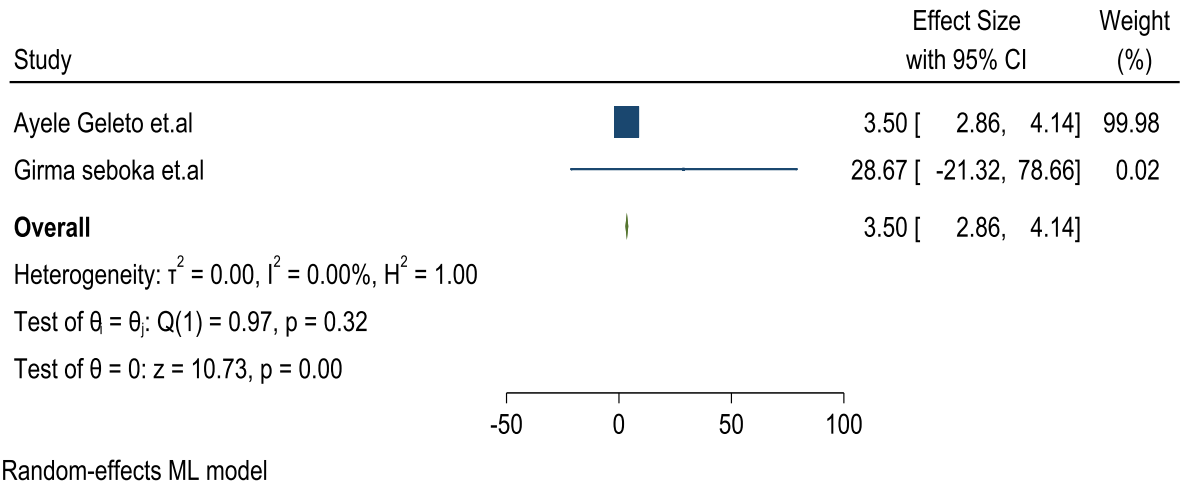

Figure 4.9: Forest plot of two studies on the effect of post-partum hemorrhage on maternal mortality

We have observed that there is no varied effect size among the studies and medium heterogeneity level of 0%. Meta regression calculation is often used to explore the heterogeneity existence due to the relationship between moderators i.e. sample size and study effect sizes i.e. the Odds ratio. Meta regression has done and negative relationship (coef. of -0.00037) between sample size and effect size with heterogeneity I2(%) = 0 and there is no statistically significant with P value 0.324. There is no relationship between sample size and study effect on have no effect on heterogeneity. (table 10).

Random-effects meta-regression — Number of obs = 2
Method: ML — Residual heterogeneity:
tau2 = 2.9e-09
I2 (%) = 100.00
H2 = .
R-squared (%) = 95.03
Wald chi2(1) = 0.97
Prob > chi2 = 0.3238

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	-.0003732	.0003782	-0.99	0.324	-.0011145	.0003681
_cons	28.87636	25.71726	1.12	0.262	-21.52854	79.28126

Test of residual homogeneity: Q_res = chi2(0) = -0.00 Prob > Q_res = .

Table 4.10: meta-regression of three studies on the effect of postpartum-hemorrhage on maternal mortality

Publication bias was checked by using funnel plot asymmetry. the funnel plot looks asymmetrical because the funnel plot intercept on the X-axis has little shift from zero. Thus, it is indicating that there is a publication bias (Figure 10), however, the varied effect size among the studies and medium heterogeneity level would also causes asymmetrical funnel plot of pyramidal and inverted funnel shape that have broaden base. Besides, the Random-effects analysis allow for heterogeneity to give an average treatment effect across studies and it will in turn causes funnel plot asymmetry.

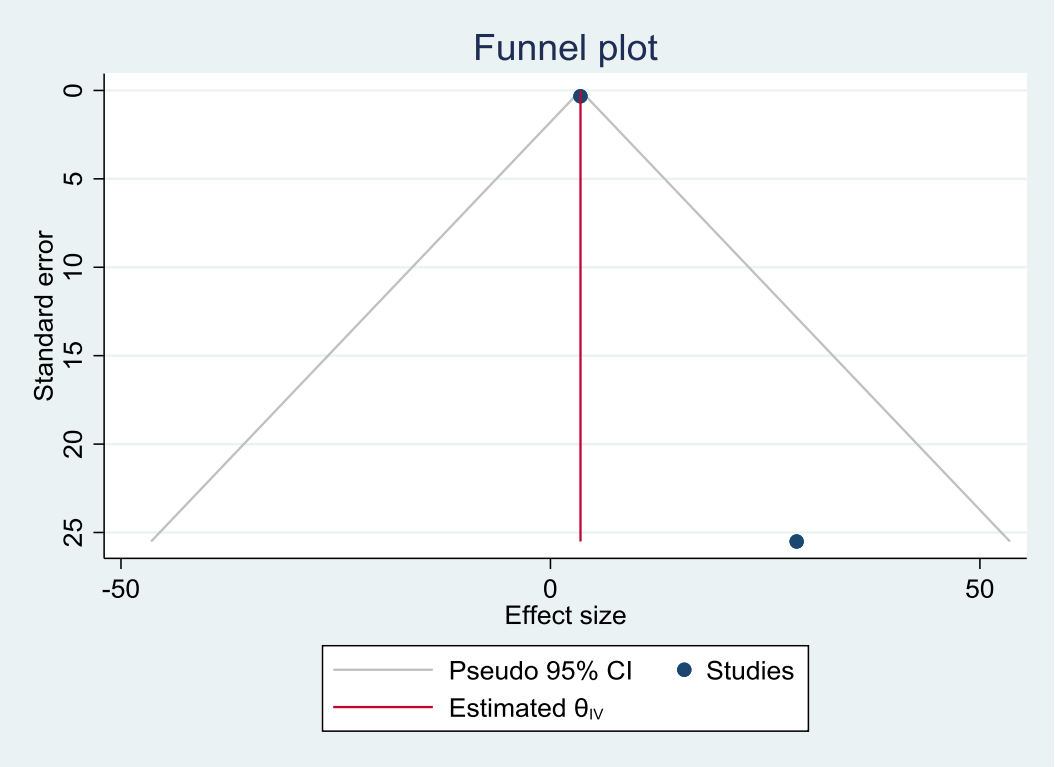

Figure 4.10: publication bias Funnel plot for the assessment of two studies

The Regression-based Egger test for small-study effects was done to see the publication bias due to small study effect and sample size. The beta1 coefficient has 0 result and there is no small study effects observed. So that the publication bias may not be a problem. (Table. 11)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
            beta1 =      0.00
      SE of beta1 =         .
                z =         .
       Prob > |z| =         .
```

Table 4.11: Regression based Egger test small study effect of four studies of postpartum hemorrhage

4.6. Sepsis

The weight of each study was calculated based on the individual effect size of Odds ratio and sample size, and the actual weight is 46.94 %, 0.52 % and 52.54 % for Ayele Geleto et.al, Girma Seboka et.al and Tegene Legesse et.al respectively. The overall poled effect of the maternal mortality who have sepsis during birth was OR= 0.90 with 95% CI (-0.33, 2.13) compared to mothers who had no sepsis problem. This meta-analysis result showed no significant association between sepsis and maternal mortality. There is some heterogeneity observed within the studies based on heterogeneity test of I2=89.18%. The homogeneity test of the studies is rejected because we have the result of a chi-squared test(Q2) statistic of 35.82 and a p-value of 0.00 which is above the significance level of p value 0.05. (Figure 11)

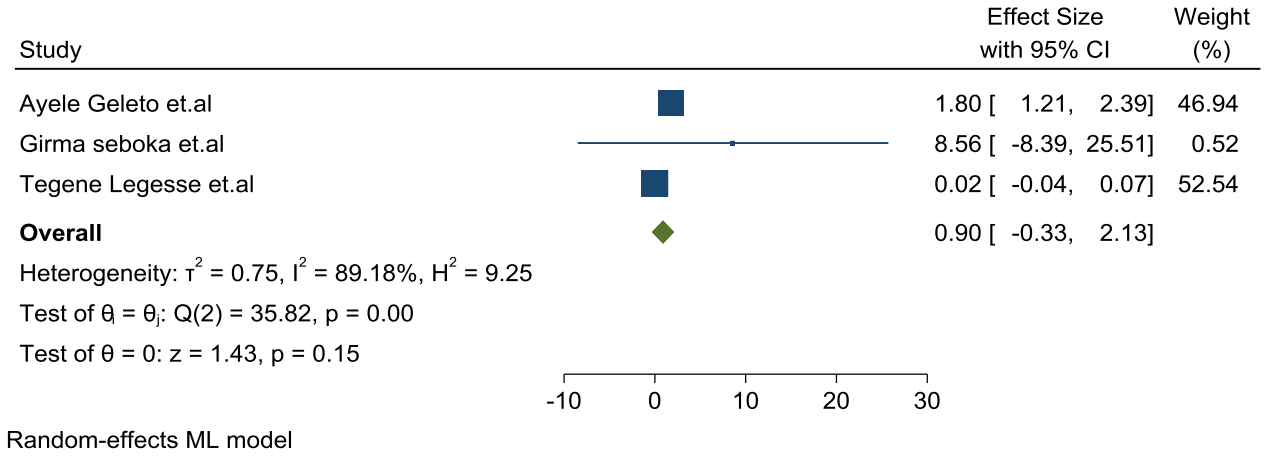

Figure 4.11: Forest plot of three studies on the effect of sepsis on maternal mortality

There is a varied effect size among the studies and higher heterogeneity level of 89.18%. There is a positive relationship (coef. of 0.00002) between sample size and effect size with heterogeneity I2(%) = 0, and it is not statistically significant with P value 0.0. There is no heterogeneity detected due to relationship between sample size and study effect. (table 12)

Random-effects meta-regression — Number of obs = 3
Method: ML — Residual heterogeneity:
tau2 = 8.3e-08
I2 (%) = 0.00
H2 = 1.00
R-squared (%) = 100.00
Wald chi2(1) = 34.84
Prob > chi2 = 0.0000

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	.0000265	4.48e-06	5.90	0.000	.0000177	.0000353
_cons	.000202	.0271586	0.01	0.994	-.0530279	.0534319

Test of residual homogeneity: Q_res = chi2(1) = 0.98 Prob > Q_res = 0.3231

Table 4.12: meta-regression of three studies on the effect of Sepsis on maternal mortality

Publication bias was checked by using funnel plot asymmetry. the funnel plot looks symmetrical because the funnel plot intercept on the X-axis is exactly on zero and thus, it is indicating that there is no a publication bias (Figure 12).

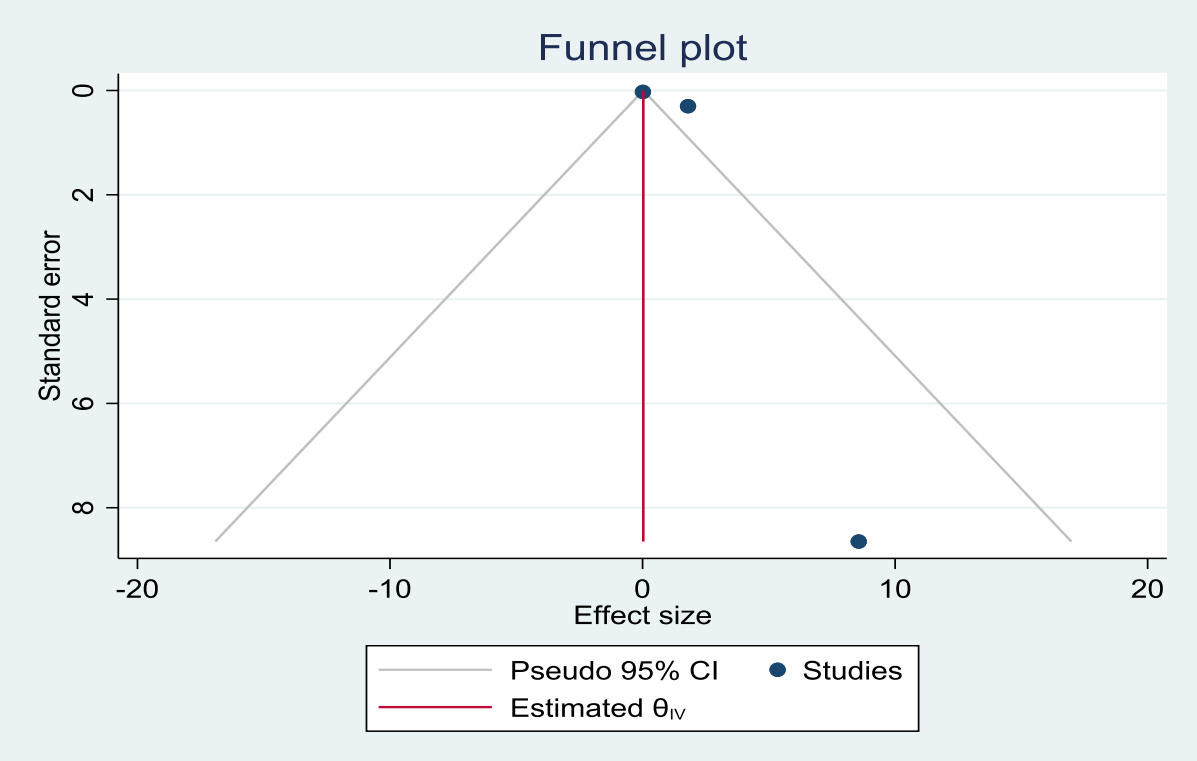

Figure 4. 12: publication bias Funnel plot for the assessment of three studies

The Regression-based Egger test for small-study effects was done to see the publication bias due to small study effect and sample size. The result showed that beta1 coefficient of 0.99 with no statistically significant level of p value of 0.32 and so that there is no publication bias due to small study effect. (Table. 13)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
             beta1 =      0.99
       SE of beta1 =     1.003
                 z =      0.99
          Prob > |z| =    0.3231
```

Table 4.13: Regression based Egger test small study effect of four studies of sepsis

4.7. Pregnancy Induced Hypertension

The weight of each study was calculated based on the individual effect size of Odds ratio and sample size, and the actual weight is 48.17 %, 2.30 % and 49.53 % for Ayele Geleto et.al, Girma Seboka et.al and Tegene Legesse et.al respectively. The overall poled effect of the maternal mortality among the non-educated mother who have sepsis during birth was OR= 0.94 with 95% CI (-0.18, 2.07) compared to mothers who have not sepsis problem during birth. This meta-analysis result showed no significant association between pregnancy induced hypertension and maternal mortality. There is high heterogeneity observed within the studies as a result of finding of heterogeneity test of I2=97.03%. In addition, the test for homogeneity of the studies is rejected because we have the result of a chi-squared test(Q2) statistic of 125.37 and a p-value of 0.000. (Figure 13)

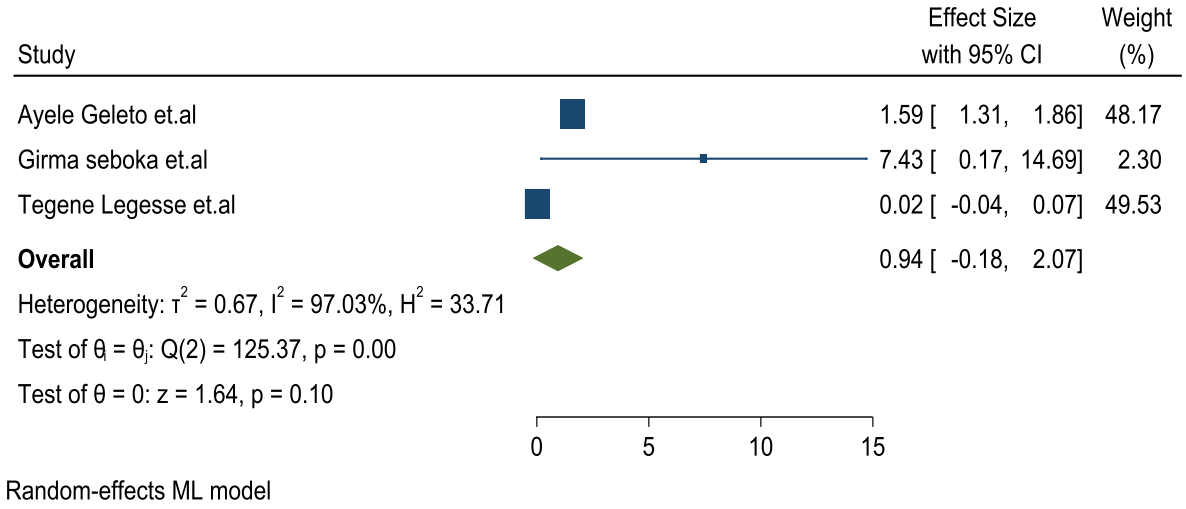

Figure 4.13: Forest plot of three studies on the effect of Pregnancy induced hypertension on maternal mortality

There is a varied effect size among the studies and high heterogeneity level of 97.03%. We have done meta regression calculation which is often used to explore the heterogeneity existence due to the relationship between moderators i.e. sample size and study effect sizes i.e. the Odds ratio. There is a positive relationship (coef. of 0.00023) between sample size and effect size with heterogeneity I2(%) = 0 and it is not statistically significant with P value 0.0. There is no heterogeneity detected due to relationship between sample size and study effect. (Table 14).

```
Random-effects meta-regression                  Number of obs   =         3
Method: ML                                      Residual heterogeneity:
                                                           tau2 = 1.6e-07
                                                        I2 (%)  =    0.00
                                                            H2  =    1.00
                                                R-squared (%)   =  100.00
                                                Wald chi2(1)    =  121.36
                                                Prob > chi2     =  0.0000
```

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
N	.0000233	2.12e-06	11.02	0.000	.0000192	.0000275
_cons	.0023807	.0270557	0.09	0.930	-.0506476	.055409

```
Test of residual homogeneity: Q_res = chi2(1) =  4.01    Prob > Q_res = 0.0452
```

Table 4.14: meta-regression of three studies on the effect of Pregnancy induced hypertension on maternal mortality

Publication bias was checked by using funnel plot asymmetry. the funnel plot looks symmetrical because the funnel plot intercept on the X-axis is on zero. Thus, it is indicating that there is no publication bias (Figure 14). Besides, the Random-effects analysis allow for heterogeneity to give an average treatment effect across studies and it will in turn causes funnel plot asymmetry.

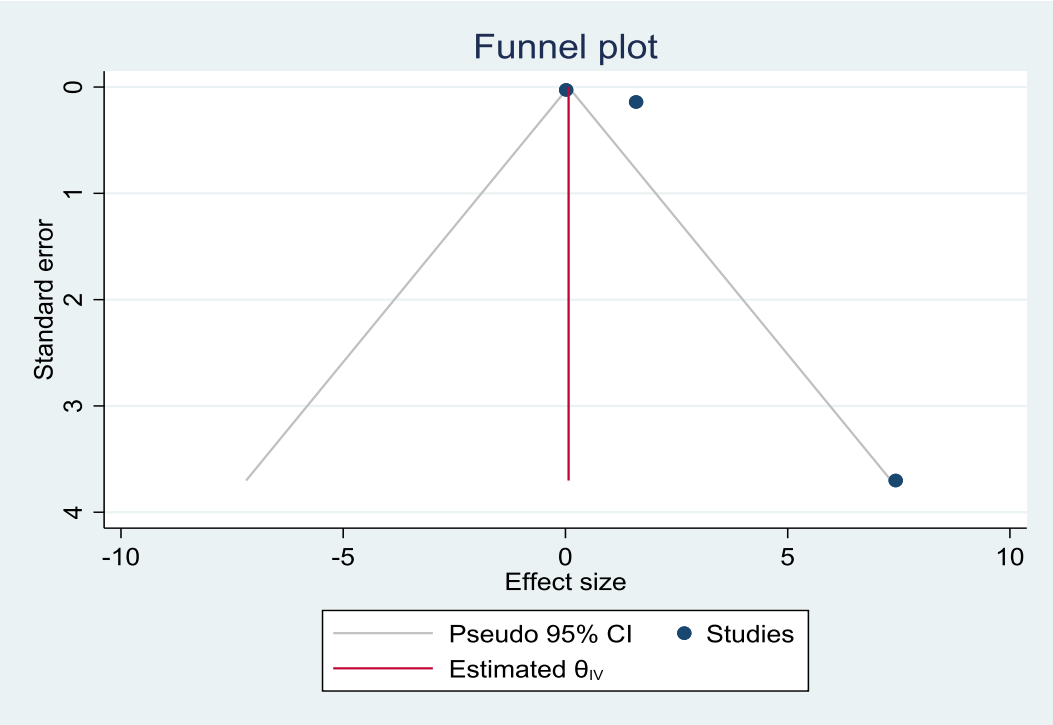

Figure 4.14: publication bias Funnel plot for the assessment of three studies

The regression-based Egger test for small-study effects was done to see the publication bias due to small study effect and sample size. The result showed us that beta1 coefficient of 2.02 with no statistically significant level of p value of 0.045, indicating no publication bias may not be a problem. (Table 15)

```
Regression-based Egger test for small-study effects
Random-effects model
Method: ML
Moderators: N

H0: beta1 = 0; no small-study effects
            beta1 =       2.02
      SE of beta1 =      1.007
                z =       2.00
        Prob > |z| =     0.0452
```

Table 4.15: Regression based Egger test small study effect of four studies of pregnancy induced hypertension

The summery result of overall effect of all factor with their corresponding 95% confidence interval (table 16)

Factors affecting Maternal mortality	**Overall effect size (OR)**	**With 95% CI**
Education	2.09	[0.47, 3.70]
Resident	1.19	[0.44, 1.94]
Antepartum hemorrhage	0.45	[0.14, 0.76]
Postpartum hemorrhage	3.50	[2.86, 4.14]
Sepsis	0.90	[-0.33, 2.13]
Pregnancy induced hypertension	0.94	[-0.18, 2.07]

***Table 4.16*: Study effect (Odds ratio) of all factors**

CHAPTER FIVE

5.1. Discussions

This meta-analysis has assessed the pooled effect of six factors affecting maternal mortality in Ethiopia. Of which, 2 of the factors i.e. Ante-partum hemorrhage and Postpartum hemorrhage are indicated a significant positive association with maternal mortality. The Overall effect size (OR) with 95% CI of ante-partum and Postpartum hemorrhage are 0.45 [0.14, 0.76] and 3.50 [2.86, 4.14], respectively. In addition, the meta regression calculated to identify the source of variation in the estimated effect showed that there is a strong relation of sample size increase in educational and antepartum hemorrhage factors with an increase effect estimate. This meta-analysis finding showed women who have developed post- partum hemorrhage have a risk of 3.50 times higher than women have no post-partum hemorrhage during their post-natal period. It has also a finding showed women who have antepartum hemorrhage have a lower risk of 0.45 times lower risk than women have no ante- partum hemorrhage during their ante-natal period, however, this could be because of heterogeneity detected due to positive relationship between sample size and study effect, and the Regression-based Egger test for small-study effects has showed a publication bias with significant level of small study effect.

Of the remaining 4 factors, education, resident, Sepsis and Pregnancy induced hypertension The Overall effect size (OR) with 95% CI of are 2.09 [0.47, 3.70], 1.19 [0.44, 1.94], 0.90 [-0.33, 2.13] and 0.94 [-0.18, 2.07] respectively. These factors have no significant association with maternal mortality.

This meta-analysis postpartum hemorrhage result finding has a similarity of result of OR= 27.50 (95% CI:8.40-90.13) of significance association with maternal mortality on the study conducted on maternal mortality among women who had a caesarean section delivery in Kenya. (Dindi et. al.) This meta-analysis pregnancy related hypertension and educational result findings have a different result compared to the result of hypertension factor of OR= 10.7(95% CI 2.7–43.4) and educational factor of OR= 3.3, 95% CI (1.1-10.4) that have a significance associations with maternal mortality on the study conducted on Risk factors for maternal mortality in a Tertiary Hospital in Kenya. (Yego et.al., 2014)

One of the limitations of the study is that the findings were based on few studies. There has been substantial publication bias including English language bias).

5.2. Conclusions

This meta-analysis study finding showed that physiological factors like Antepartum hemorrhage and postpartum hemorrhage have an impact on maternal mortality and highlights risk factors for maternal mortality in Ethiopia. It is also showed the importance of skilled person attended delivery, postnatal care, and maternal health education on danger sign of pregnancy and actions to be taken to avoid the three delays that have huge impact on maternal mortality due to the effect of direct causes occurrence. In addition, it is important to empower women to take a decision-making role on their own health and providing access to skilled professional health care service during pregnancy, at birth and postnatal period.

5.3. Recommendations

The prevention and early detection and treatment of postpartum hemorrhage is crucial and the main focus areas on decreasing maternal death as well. Quality maternal health service that is equipped with necessary equipment and staffed with skilled personnel must be accessible and available to all. and follow up of maternal health situation after birth be close to where women live. Working on the availability of postnatal service and timely provision of the service to all women who have given birth and encouraging utilization of postnatal service is vital to decrease maternal mortality and improve the health of women. Educating women on the importance of and attending postnatal care service is key and important to avoid maternal death occurred during the postnatal period. The policy makers and government strategy implementers have to work on increasing and strengthening training skilled birth attendant's and engaging well in service for all Ethiopian population at rural and urban.

These actions and intervention will not be successful without the involvement of the community, religious institutions and leaders, government and non-governmental organizations including private sectors. The planning, implementation, mobilization and coordination effort on stakeholders' involvement to bring change are challenging, however, it will have a huge impact on the identified problems and challenge that will bring improvement on the reduction of maternal death. Finally, the summery of the meta-analysis shows that working on the identified factors that significant relevance has bring change on maternal mortality and will have an effect on their child and family.

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ANNEX: Quality Assessment Checklist

S.N	Criteria or Quality Assessment Checklists	studies included in the review		
		S1	S2	S…
1	Was the research question or objective in this paper clearly stated?			
2	Was the study population clearly specified and defined?			
3	Was the participation rate of eligible persons at least 50%?			
4	Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?			
5	Was a sample size justification, power description, or variance and effect estimates provided?			
6	For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7	Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8	For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9	Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10	Was the exposure(s) assessed more than once over time?			
11	Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12	Were the outcome assessors blinded to the exposure status of participants?			
13	Was loss to follow-up after baseline 20% or less?			
14	Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

Total score			
Quality assessment status			