MEKELLE UNIVERSITY

COLLEGE OF HEALTH SCIENCE

DEPARTMENT OF MIDWIFERY

DETERMINANTS OF EXTERNALLY VISIBLE BIRTH DEFECTS AMONG NEWBORNS DELIVERED IN PUBLIC GENERAL HOSPITALS OF TIGRAY, ETHIOPIA, 2024/25 G.C

BY: BIREY YEMAR

MAY, 2025

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PRINCIPAL INVESTIGATOR: BIREY YEMAR (BSC, MSC CANDIDATE)

A RESEARCH THESIS TO BE SUBMITTED TO THE DEPARTMENT OF MIDWIFERY, COLLEGE OF HEALTH SCIENCES OF MEKELLE UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE MASTER OF SCIENCE IN CLINICAL MIDWIFERY

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We, the undersigned, members of the Board of Examiners of the final open defense by "_Birey Yemar" have read and evaluated his/her thesis "Determinants of externally visible birth defects among newborns in public general hospitals of Tigray, Ethiopia 2024/25" and evaluated the candidate. This is therefore to certify that the thesis has been accepted in partial fulfillment of the requirements for the Master's Degree in clinical midwifery.

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Approval of the Major Advisor

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Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATION AND ACRONYM

ANC……Antenatal Care

CDC……Center of Disease Controls

CKD……Chronic Kidney Disease

CNS……Central Nervous System

DM…….Diabetes Mellitus

EUROCAT……European Registration of Congenital Anamolies and Twins

HIV/AIDS…….Human Immune Virus/ Acquired immune Deficiency Syndrome

HTN……..Hypertension

ICBDSR…….International Clearinghouse for Birth Defects Surveillance and Research

ICD……International Classification of Diseases

IUFD……Intra Uterine Fetal Deaths

LBW……..Low Birth Weight

LMIC……Low and Middle Income Countries

NTD……..Neural Tube Defect

SDG…….Sustainable Development Goal

WHO…….....World Health Organization

ABSTRACT

Background: Birth defects are a series of functional and structural abnormalities resulted from disruption of the normal human embryonic development. Regardless of the interventions and targets to reduce neonatal mortality, the burden of birth defects remains high especially in low and middle income countries such as Ethiopia. In Tigray the neonatal mortality showed significant increment during the war crisis and birth defects takes a significant role with limited studies before the war and no studies conducted after the war. Studies on determinants of birth defects are timely essential to manage their burden and will be a guide on the postwar health care reform.

Objective: To asses determinants of externally birth defects among newborns delivered in public general hospitals of Tigray, Ethiopia, 2024/25

Methodology: Institutional based unmatched case control study design was conducted from December 1 to December 30, 2024 among 388 subjects (97 cases and 291controls) in public general hospitals of Tigray. Subjects were selected using systematic random sampling method after proportional allocation to each randomly selected five hospitals. Cases and controls were newborns that had at least one visible minor or major birth defect and without externally visible birth defect, respectively delivered from November 1, 2023-Octeber 30, 2024 in the selected public general hospitals. A structured checklist was used to extract data from maternal medical charts. Data was entered through Epi data and transported to SSPS version 25 for analysis. Multivariate Logistic regression model was used to identify factors associated with birth defects at p value less than 0.05. **Results;** more than half the mothers (51.5% and 58.4% of cases and controls respectively) fall in between 25 and 35 age category). Rural residence [AOR=1.95; 95% CI:(1.04, 3.667);p-value=0.037], lack of folic acid intake [AOR=2.77;95%CI: (1.464,5.24); p-value=0.002], history of acute illnesses[AOR=5.118;95%CI:(1.389,18.865);p-value=0.014],male sex [AOR=2.4;95%CI:(1.322,4.364);p-value=0.004],and Prematurity [AOR=11.74; 95%CI :(2.598, 53.05); p-value=0.001] were significant predictors of birth defects. **Conclusion and recommendations;** Rural residence, lack of folic acid intake, acute illnesses, newborn sex and prematurity, were significant predictors of birth defects. So that it's vital to address the modifiable factors such as folic acid intake, acute illnesses, awareness creation and service delivery in rural setting.

Keywords; Birth defects, Determinants, Newborns

1. INTRODUCTION

1.1. Background

Human development is a progressive change from a single cell formation through embryogenesis (period of organ formation) and differentiation during the fetal period later in pregnancy. The process of embryologic and fetal development is a critical period which is of susceptible and vulnerable to factors and conditions that causes alteration of the normal development(1). Birth defects are a variety of functional and/or structural abnormalities originated from disruption of the normal embryonic period or fetal development which can be identified prenatally, at birth or later in life(2).

They are described in different nomenclatures such as, “Congenital anomalies “, “congenital abnormalities”, “congenital malformations”, and “birth defects” interchangeably; can be classified as minor congenital anamolies (those with relatively little or no impact on physical and psychosocial health) and major anomalies (serious conditions affecting the infant’s life threatening health status, physical and psychosocial functioning) , as single or multiple and can externally visible or internal (3,4).

An estimated 134 million births are reported to occur per year, of which 8.5 million (6%) of them are born with at least one serious birth defect in 2019(5). The burden of birth defects is notably high in low-and middle-income countries, at which about of 64.2 defects per 1000 live births comparing to 47.2 per 1000 live births in high-income countries and majority of countries with the highest burden are in Africa (6).

Even though sustainable Development Goal (SDG) aimed to eliminate neonatal deaths due to preventable causes by 2030 and to lower neonatal mortality to less than 12 per 1000 live births in each country globally, reports show that more than 60 countries won’t fulfill the target. most of them are in Southern Asian and sub-Saharan African countries, particularly in sub-Saharan African countries, 30% of the global birth defect case and 38% of global under-five deaths attributed to birth defects are confined the region (7,8).

In Ethiopia, according to Ethiopian Demographic Health Survey (EDHS) 2019, neonatal mortality accounts 33 deaths per 1000 live births and 11% of neonatal mortality are due to birth defects (9,10). The pooled prevalence of birth defects in Ethiopia was estimated to be 2%

showing variation as low as 0.95% in Bahirdar and as high as 18.5% southwest Ethiopia (11–13).

As a measurement to improve perinatal outcome, WHO recommend a pregnant women that a minimum of eight antenatal care visits, daily oral iron and folic acid supplementation with 30mg to 60mg of elemental iron and 0.4mg folic acid to reduce adverse birth outcomes, an early ultrasound scan at least before 24 weeks' gestation and health care provider counseling regarding medications, substance use and history of risk factors aiming at improving perinatal outcome(14). However, lack of pre conception care follow up, poor access to prenatal screening, exposures to chemicals such as pesticides and herbicides in the farming community and micronutrient deficiencies worsens the problem mainly in low and middle income countries(7).

1.2. Statement of the problem

Birth defects are still the most common causes of infant mortality , morbidity and life time physical and mental disability(15). Despite of the advances in medical technology and prenatal care, The global prevalence of birth defects remains high which is around 2%–3% with variable prevalence from one region to another(16).

Around 6.3 million perinatal deaths are estimated every year and birth defects are the fifth leading causes of death(10). According to World Health Organization (WHO) estimation, around 240,000 neonatal deaths(about 7% of all neonatal deaths) and 3.3 million children die before five years of age due to birth defects every year (17,18). In addition birth defects are a cause for more than half of spontaneous abortions and 15-20% of stillbirths (19,20).

The impact of birth defects in addition to the negative pregnancy outcome includes a wide range of long-term physical, emotional, and psychosocial challenges to the survivors. Studies suggest that children with birth defects are suffering the risk of poor academic achievement and lower cognitive ability with special education needs compared to children of the same age and with their classmates (21).

In addition these defects can also cause developmental disabilities such as mental and physical impairments which leads to serious problem to care and raise raising the defected child (22). Psycho-social challenges for the parents and children also arise for infants and families. There

could be increased parenting stress in caring and due to sociocultural problems and dependency of a child on parents and caregivers (23).

Furthermore, to take care, raise and treat a child with birth defect also possess socioeconomic problem to families and the community. It needs higher cost of health care for defected children due to lifelong physical and mental disabilities and long term consequences(24). As a consequence of 3.2 million survivors worldwide who can suffer health problems and disabilities, birth defects constitute about 15–30% of all hospital admissions among children ; which needs care relatively higher cost than other hospital admission cases that highly affects the individual, family and the community(25). Birth defects are also a cause for around 25.3–38.8 million disability-adjusted life-years (DALYs) worldwide(26).

Even though, more than half of the birth defects are considered to be of unknown causes, multifactorial inheritance, environmental teratogens and mixed factors are thought to be causes of birth defects(27). Risk factors investigated to be correlated to birth defect i.e. age, life style habits such as alcohol consumption, chat chewing and smoking, folic acid supplementation, maternal illnesses, drug intake, exposure to chemicals and lack of ANC follow-up (13,28).

In Ethiopia, the government in collaboration with NGOs, is working to reduce birth defects, primarily neural tube defects which has notably highest burden, by designing prevention strategies such as folic acid supplementation, food fortification and awareness creation but birth defects still remains high and a very low number of women are reported to be prescribed with folic acid(10,29).

Tigray region which is the northernmost part of Ethiopia has an estimated total population of 7.3 million with 80.5% of the population living in rural area. The region was on civil war from 2020-2023. In the region relatively low neonatal mortality rate of ten deaths per 1000 live births were estimated before the war with prevalence 3.1% but the neonatal mortalities during the war found to be 28 neonatal deaths per 1000 live birth which is around three times higher than prewar estimate(30,31). The contribution of birth defects is high accounting about11% of admissions to neonatal intensive care unit according to estimations in 2019(32). This may be due to the health care system damage during the war and the health care coverage was also affected. Before the war there are limited studies conducted about the burden of birth defects but there are no studies that investigate the determinants factors. Hence, studies on factors advocate the postwar reform

the health care system and to deliver evidence based prevention strategies and health service deliveries are needed to address the gap. Thus, this study aims to assess the determinant factors of birth defect in Tigray region.

1.3. Significance of the study

The study of birth defects is essential as these conditions have a significant impact that affects individual, families, community and health care system and collectively being a public health concern worldwide. This study is particularly significant and timely for its study area and population because the region was recently in a war crisis and there are limited studies conducted before the crisis with no studies conducted after the war. Even though, causes and factors that induce the occurrence of birth defect have been studied, most of the cases have no clear specific cause or inducing factors yet with some of the study's findings being contradictory in some factor. Hence, this case control study is found timely essential to assess predictors of birth defects.

Findings of this study related to the more local and current knowledge will be a scientific guide and reference for stake holders to develop effective prevention, intervention policy and service delivery that fits the local setting to contribute in neonatal mortality reduction, morbidities and disabilities. In addition findings will also be used as an input in the postwar reform of the health care system. Furthermore this study will provide a base for subsequent researches and scientific innovations.

In general, this study underscores the crucial significance of scientific understanding of birth defects highlighting several key findings with extreme implications for public health, clinical practice, and research advancement. Moreover, this study has incredibly significant contribution for Tigray region which was in a destructive war which causes a turn back in the health care system and socioeconomic disruptions.

2. LITERATURE REVIEW

2.1. Determinants of birth defects

Most cases of birth defects have no identified causes yet. Studies showed different associations which is variable in different setting. Research articles were accessed from different webs such as Google scholar and PubMed by using key words. The review was organized from global to local level by including literatures mostly conducted with in the past five years.

2.1.1. Maternal socio demographic characteristics

Studies have revealed different degrees of associations of the maternal socio demographic characteristics with the occurrence of birth defects. One study conducted in Brazil showed that neonates from single mothers were at higher risk to have birth defects than neonates from married mothers. The Brazilian study revealed that the odds of having a neonate with birth defects in single mothers were 1.23 times (OR=1.23; 95%CI=1.04-1.45) higher than married mothers(33).

Most of the studies found that significant association of advanced maternal age with the occurrence of birth defects. A systemic review and meta-analysis in Korea aimed to assess the relationship of maternal age and birth defects found that the odds having a neonate with birth defects was 1.64(times higher in older ages (34). In addition, one study conducted in China on a Multivariate logistic regression analysis of risk factors for birth defects, a study from population-based surveillance data found that mothers with <20 years and >35 years maternal age were 2.2 times (OR=2.20, 95%CI: 1.19–4.09) and 1.5 (OR=1.56, 95%CI) times more likely to give to a neonate with birth defects, respectively (35).

In contrary a study conducted in Pakistan shows that mothers aged 19-30 had a higher risk(4). Another retrospective observational study conducted in Brazil maternal age showed significant association with congenital anomalies(2). On the other hand one matched case control study conducted in Bangladesh revealed that neonates from mothers aged 20-29 years old were 4 times (AOR= 4.69; 95% CI:1.078, 20.448) more likely to have birth defects(22).

A retrospective cross-sectional study conducted in Sudan also found significant association between advanced maternal age (> 35 year) and birth defects. In this study rural residence also shows significant association(26). Against The finding of Sudanese study one analytic cross sectional study carried out in Egypt which demonstrated that urban residence puts mothers at risk

of having birth defects(19). The Sudanese study, regarding maternal age, is advocated by a study conducted in Oromia, Ethiopia mothers with >35 years of age were 6.5 times (AOR =6.5; 95% CI ; 2.4–18) at higher risk to have a neonate with birth defects(36).

Moreover, one case control study carried out in Eastern Ethiopia on determinants of congenital anomalies in neonates admitted to public hospitals also revealed that the odds of congenital anomalies in neonates born to rural women were 1.73 times (AOR: 1.73, 95% CI: 1.04–2.85) higher than neonate born to urban women(37).

In contrary a case control study conducted in Gojjam, Northwest Ethiopia on determinants and seasonality of structural birth defects founds significant association between maternal urban residence and structural birth defects. This study showed that neonates born from women of urban residence were found to be about six times(AOR=6.4; 95% CI: 1.9–21.7) more likely to develop birth defect as compared to those neonates born from women of rural settings(18). One additional cross-sectional study in Bahirdar shares the finding of the study in northwest Ethiopia by revealing that urban resident mothers were two times(AOR=2.1; 95%: CI 1.28–3.55) more likely to have a neonate with birth defects(11).

2.1.2. Pregnancy and ANC related characteristics

Pregnancy and ANC characteristics found to play role in the occurrence of birth defects in different studies. One hospital based Case-Control study carried out in Bangladesh found that poor ANC follow-up was a significant predictor of birth defect. This study included less than four antenatal care visits as a variable and the odds having a neonate with birth defects for mothers with less than four ANC visits found to be ten times higher AOR=10.07; 95% CI 2.816, 36.0) (22).

Folic acid intake before and in early pregnancy was found to be a protective factor in most studies. A systemic review and meta-analysis in a resource limited settings regarding prevalence and associated factors of structural congenital anamolies revealed that never using folic acid was strongly associated. The review found that pregnant women who did not use iron foliate were 6 times (OR = 6.01; 95% CI: 2.87–14.89) higher than women who used folic acid during and before pregnancy to have neonates with structural congenital anamolies. This review also showed unidentified drug use during pregnancy is significant a predictor. Women with history of unidentified drug use during pregnancy were 2.83 times (OR = 2.83; 95% CI: 1.19–4.46) more

likely to have structural CA compared to women with no history of drug use during pregnancy(38).

One systemic review and meta-analysis on the effect of folic acid intake on congenital anamolies resulted a pooled relative risk of congenital anomalies for children born to mothers who took folic acid was 0.23 times (OR= 0.23; CI: 0.16–0.32) lower than for children born to mothers who did not take folic acid, indicating that taking supplements of folic acid prior to conception (at least 4 weeks) and during pregnancy until 12 weeks significantly reduces the risk of congenital anomalies by 77%(39).

Medication intake during pregnancy was found to be significant predictor of birth defects in different studies. One systematic review and meta-analysis in Sub Saharan African countries revealed drug intake during pregnancy showed significant association with birth defect. The Meta analysis displayed that neonate of mothers with history of drug intake during pregnancy found to be 7.54 times (AOR= 95% CI: 3.88, 14.66) more likely to have birth defect. In addition mothers who didn't use folic acid were also 3.92 (AOR=3.92; 95% CI; 1.95, 7.88) times more likely to have a neonate with birth defects than mother who used, in this review(28). In addition another systemic review and meta-analysis undertaken in Ethiopia also showed medication use during pregnancy found to be statistically significant. This review shows mothers who took teratogenic medication during pregnancy and who didn't take folic acid were 2.58 times (pooled OR= 2.58; 95% CI: 1.03–6.47) and 2.8 times (pooled OR= 2.83; 95% CI: 1.09–7.36) more likely to have a neonate with birth defect, respectively (13). Furthermore, one case control study conducted in south west Ethiopia also resulted drug use during the first trimester of pregnancy (AOR = 3.435; 99% CI: 2. 012–5.863), and folic acid supplementation (AOR = 0.428; 99% CI: 0.247–0.740) were also strongly associated with the occurrence of birth defect(40).

2.1.3. Maternal health characteristics

In some studies history of illnesses in the index pregnancy is mentioned as a significant predictor for the occurrence of birth defects. one case control study conducted in Iran and a study carried out in Iraq revealed that history of maternal disease during pregnancy was a significant predictor of birth defects(41,42).

According to a cross sectional study carried out in Baghdad, Iraq, anemic mother and hypertensive mothers had higher likelihood of having a neonate with birth defects.(43) This study is supported by another study conducted in Iran which shows significant association of maternal diseases HTN, DM, hyperthyroidism and hypothyroidism) with occurrence of birth defects. The Iranian study implicated that the odds of having a neonate with birth defects is 4.42 times higher in mothers who are positive for medical diseases than mothers negative for maternal disease during pregnancy(41). This association is also supported by One systemic review and meta-analysis undertaken in Africa which resulted that mothers with history of illnesses during pregnancy had 2.44 times higher likelihood of giving birth to a neonate with birth defects(44).

A cross-sectional study conducted in Jimma university medical center, southwest Ethiopia, also found strong positive association between presence of maternal chronic illness (Hypertension, Diabetes, and Hypertension with diabetes) and birth defects. The strength of association in this study shows mothers who had a chronic illness were 4.3 times more likely to have a neonate with birth defect than those mothers who hadn't chronic illness(45). This study also supported by a cross-sectional study conducted in North West Ethiopia which shows a strong association between maternal history of chronic disease (diabetic mellitus, hypertension, HIV/AIDS and chronic kidney disease) and birth defects. In this study neonates born from mothers with history of chronic disease during pregnancy were 4 times (AOR = 4.05, 95% CI: 2.27-7.21) more likely to have birth defects compared to neonates born from mothers without history of chronic disease(46).

Furthermore, one case control study undertaken in Eastern Ethiopia revealed that the likelihood to give birth to a neonate with birth defect is four times higher (AOR= 4.37; 95% CI: 2.48–7.69) in women who had history of anemia during index pregnancy(37). In addition, a case control study conducted in Arsi, Ethiopia found that the likelihood of having a newborn with birth defect was 6 times (AOR = 6.10; 95%CI: 2.39, 15.57) higher for women who had maternal illnesses(47). Another case control study carried out in North West Ethiopia revealed that mothers who had history of fever during pregnancy are three times (AOR: 3.4, 95% CI 1.3–11.6) more likely to give birth to a newborn with birth defects(18).

2.1.4. Obstetric characteristic

An ecological study design carried out in Brazil showed that multiple pregnancy and cesarean type of delivery were significantly associated(33). This finding is supported by one case control study conducted in Hamadan Iran that showed emergency C-section was also the most frequent mode of delivery for neonates with birth defects(48). On the other hand a study conducted in china revealed that multiple births had 1.4 times (OR=1.44, 95%CI: 1.18–1.76) higher odds of having birth defects than singleton(35). But against the Chinese study, one analytic cross sectional study in Egypt revealed that birth defects were frequent among singleton pregnancies.(19)

According to a study conducted in Brazil Midwest revealed previous history of child with birth defect was significantly associated with birth defect. The strength of association of previous birth defects in this study showed that women who had previous delivery history of birth defects were 3.85 times (AOR=3.85; 95% CI: 1.11–13.27) more likely to have a neonate with birth defect than those women with no history of birth defects(49). Another population-based case-control study in Brazil but in different city also showed previous history of a child with birth defects is associated with subsequent occurrence of birth defect. This study also resulted that mothers with previous miscarriage had 2.9 times higher odds of giving subsequent birth to a neonate with birth defects (OR=2.93; 95% CI:1.51,5.69) birth (50).

Multiparty was also mentioned as significant predictor in some studies. One cross-sectional study undertaken in Egypt and a study in morocco displays a strong association between Multiparty and birth defects(51,52). Moreover, In a study conducted in Oromia, Ethiopia neonates with birth order above three and singleton pregnancies were 8.4 (AOR= 8.4; 95% CI:3.4–20.7) times and 6.4 (AOR = 6.4; 95%CI:2–18.9) times more likely to have birth defects respectively(36).

In one case control study conducted Adama, Ethiopia previous history of birth defects was significantly associated with reoccurrence of birth defect. Women with previous history of birth defects were about 4.853 (AOR=4.853; 95% CI: 1.492, 15.788) times more likely to have a neonate with birth defects than those women with no previous history of birth defect. In this study strong association between previous history of still birth and subsequent occurrence of

birth defects was also found. Mothers with previous history of still birth found to be 3.967 times (AOR=3.967; 95% CI: 1.772, 8.88) more likely to have a neonate with birth defects(10).

2.1.5. Newborn characteristics

Regarding the newborn characteristics, some studies show contradictory findings especially in sex of the newborn. For instance, one study conducted in Kerman, Iran female neonates show higher risk than males. According to the study male neonate were 0.42 times less likely to have birth defects(24). In contrary, another study in Hamadan, in the same country Iran shows a result that contradicts the above statement. The study resulted being male had significant association with birth defect(48). In an ecological study carried out in Brazil showed male sex and low birth weight were significantly associated with birth defects(33).

In addition, a study in Qatar revealed that the odds of birth defects were four times (AOR=4.17; 95%: CI 2.75–6.32) and 5.8 times (AOR=5.88; 95%: CI 3.92–8.82) higher for prematurity and low birth weight respectively(53). This is supported by One cross-sectional study conducted in Nigeria also shows low birth weight (birth weight between 1.5–2.49 kg) was associated with birth defects and shows 30% higher risk(54). In contrary a study conducted in neonatal intensive care unit in Egypt, revealed that full term had higher risk than preterm neonates(19).

One longitudinal study conducted in Tanzania revealed that prematurity and being male takes the higher odd for the occurrence of birth defects specifically musculoskeletal defects. This study showed that 1.86 (AOR = 1.86, 95% CI = 1.53–3.66) and 1.67 (AOR = 1.67, 95% CI = 1.23–1.89) times higher odds of having birth defects or premature and male neonates, respectively(55). A study carried out in Addis Ababa, Ethiopia also found that low birth weight and male sex were significantly associated with birth defects. In this study the odds of having birth defects in male infants was 1.3 times (OR = 1.3; 95% CI = 0.9-2.8 higher than females(56). This finding is also supported by a study conducted in Bahirdar which found that a lower risk for females neonates (AOR=0.59; 95% CI 0.37–0.95)(11). Another study in Oromia, Ethiopia also shows an association of low birth weight and birth defects (36).

Moreover ,one cross-sectional study conducted in Tigray region, Ethiopia also found that low birth weight and prematurity were significantly associated(31). Another prospective cohort study carried out in Tigray in Mekelle general hospital and Ayder specialized and comprehensive

referral hospital regarding on Birth weight by gestational age and congenital malformations also revealed that, low birth weight, gestational age less than 35 weeks, male sex, were strongly associated with birth defects. This study implies the possibility of having birth defects shows decrement after 35 weeks of gestation and those with <35 weeks of gestation found to be at higher risk(57).

In general the review tried to explore literatures of different setting. Studies with different limitations in terms of study area, study period, study populations, inclusion criteria and methodology aspects resulted variations from region to region and from study to study. Variables found to be a risk factor that increase the occurrence of birth defects in some studies found to have a protective effect or a factor that lower the chance of occurrence of birth defects in other studies. On the other hand variables which shows strong association with the occurrence of birth defects, found to have no significant association in other studies. Reviewing these literatures leads to increase the intention and commitment to study further about the problem and fill the gap with adequate knowledge in our local setup.

2.2. Conceptual frame work for determinants of externally visible birth defects

The framework in the next page shows the association of variables mainly the dependent and independent variables which is adapted from different literatures (Fig. 1).

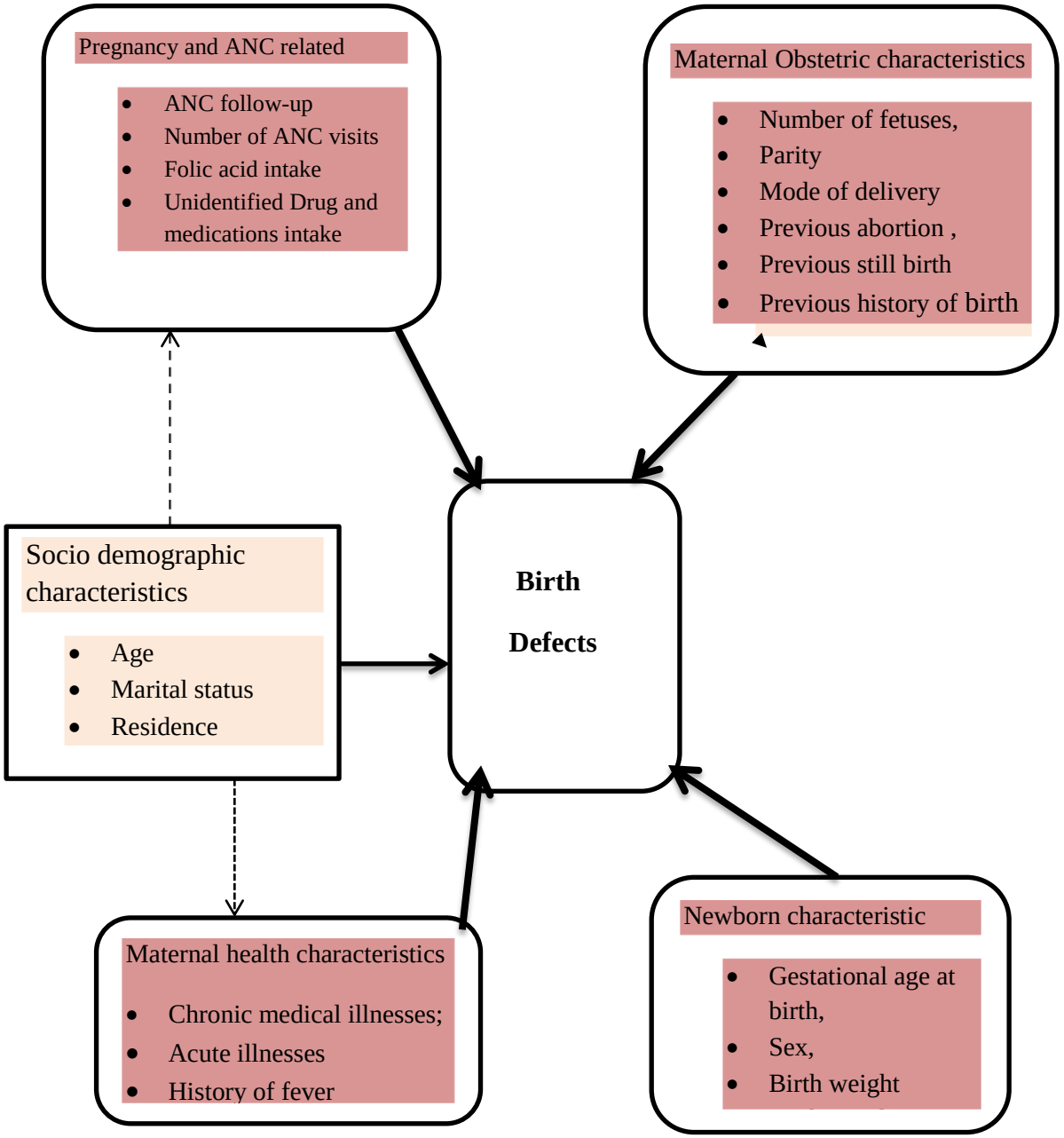

Fig 1 .conceptual frame work for determinants of externally visible birth defects among newborns in public general hospitals in Tigray, Ethiopia 2024/25, adapted from different litterateurs

3. OBJECTIVE

3.1. General objective

To assess determinants of externally visible birth defects among newborns delivered in public general hospitals of Tigray, Ethiopia 2024/25

3.2. Specific objective

To identify determinants of externally visible birth defects among newborns delivered in public general hospitals of Tigray, Ethiopia

4. METHODS AND MATERIALS

4.1. Study area and period

The study was conducted from December 1to December 30, 2024 in public general hospitals in Tigray region. Tigray Region is one of the twelve regions in Ethiopia found in northern part of Ethiopia and its capital city is Mekelle. Tigray is bordered by Eretria to The north, Sudan to the west, Afar region to the east, and the Amharic region to the south and southwest. The region has a total population of around 7.3 million people and is administratively divided into 7 zones, 88 Woredas and 814 Kebeles. In Tigray region there are 2 comprehensive specialized hospitals, 14 general hospitals, 25 primary hospitals, 228 health centers, 712 health posts and over 500 private health facilities(58). The fourteen general hospitals are named as Alameta, Korem, Kahsay Abera, Mearg, Lemlem Karl, Quiha, Suhul, Axum Saint Mary, Adwa, and Adigrat, wukro, Abiadi and Mekelle general hospitals.

4.2. Study Design

Institutional based unmatched case control study design was to asses determinants of birth defects among newborns in public general hospital of Tigray.

4.3. Source population

All newborns delivered in public general hospitals of Tigray

4.4. Study population

Cases; all newborns delivered with at least one minor or major externally visible birth defects between November 1, 2023- October 30, 2024 in the selected public general hospitals of Tigray

Controls; all newborns delivered without externally visible birth defects between November 1, 2023- October 30, 2024 in the selected public general hospitals of Tigray

4.5. Study units

All cases and controls included in the study

4.6. Eligibility criteria

4.6.1. Inclusion criteria

Cases; newborns (both live and still births, singleton and multiple births) who had at least one minor and/or major externally visible birth defects delivered after 28 weeks of gestation via all modes of delivery from November 1, 2023 - October 30 2024 in the selected public general hospitals

Controls; newborns who hadn't any externally visible birth defects delivered after 28 weeks of gestation via all modes of delivery from November 1, 2023 - October 30 2024 in the selected public general hospitals

4.6.2. Exclusion criteria

Those newborns with incomplete maternal medical records

4.7. Variables

4.7.1. Dependent variable

Externally visible birth defects

4.7.2. Independent variables

Maternal Socio demographic factors; Age, Marital status, and residence

Pregnancy and ANC related factors; ANC follow-up, number of ANC visits, folic acid intake, medications intake

Maternal health characteristics; chronic illnesses such as DM, HTN, HIV/AIDS, CKD and hypo/hyperthyroidism, Acute illnesses i.e. Anemia, malaria, acute febrile illnesses and history of fever

Maternal obstetric characteristic; parity, number of fetuses, mode of delivery, previous history of birth defects, previous history of abortion, previous history of still birth

New born related characteristics; gestational age at birth, sex, birth weight

4.8. Sample size determination

The sample size was calculated using Epi info version 7 Statcalc for unmatched case control study Fleiss with continuity correction factor formula with assumptions of percent of controls exposed and percent of cases with exposure from associated factors obtained from previous

literatures and considering 1:3 cases to controls ratio. anemia during pregnancy, antenatal care follow-up from a study conducted in Eastern Ethiopia and medication intake from a study in (37) were significant determinants. In addition medication use in early pregnancy showed significant association according to a study conducted in south west Ethiopia.(40) The sample size computed is summarized in the following table (Table 1).

Table 1; sample size calculation for determinants of externally visible birth defects among newborns delivered in public general hospitals in Tigray, 2024/25

Variables	% of controls exposed	% of cases exposed	AOR	cases	Controls	Total sample size	10% incomplete records	Final sample size
Anemia during pregnancy(37)	15.1	36.4%	4.37	47	140	187	19	206
medication use(40)	8.7	22.7	3.09	73	218	291	29	320
Antenatal care follow-up(37)	27.1	12.4	0.38	88	264	352	35	387

The highest sample size is 387 and rounding up the decimals to Adjust the1:3 cases to control ratio which is 97cases and 291 controls, finally the total sample size, NF=388.

4.9. Sampling procedure

There are ten accessible pubic general hospitals in Tigray region during the data collection period. Adwa general hospital, Maichew Lemlem Karl general hospital and Adigrat general hospital were selected using lottery method. In the selected five hospitals 20,554 newborns (Suhul general hospital= 5,728, Axum general hospital= 4,047, Adwa general hospital=3,859, Adigrat general hospital=4,543, and Maichew general hospital=2,377) without externally visible birth defects and 172 newborns (Suhul general hospital=45, Axum general hospital= 31, Adwa general hospital= 35, Adigrat general hospital=32 and Maichew general hospital=29) with

externally visible birth defects were delivered in one year duration from November 1, 2023 – October 30, 2024.

Proportional allocation was used according to the number of cases and controls deliveries in the selected time duration. Samples are included as 1:3 cases to controls ratio. Cases and Controls were selected using systematic random sampling method by determining k for cases and controls. Where, K=N/n, N= total number of newborns delivered in each hospital with birth defects for cases and newborns without birth defects for controls, n = number of cases and controls to be selected in each hospitals by systematic random sampling. K was ~2 for cases and ~71 for controls. For cases every other recorded newborn with birth defects were selected and for controls every 71th unit according to their order in the delivery unit registration book excluding the case from the frame. The first unit was selected randomly by lottery method from the interval 1-K. The steps in sampling procedures are summarized in the following diagram (Fig 2).

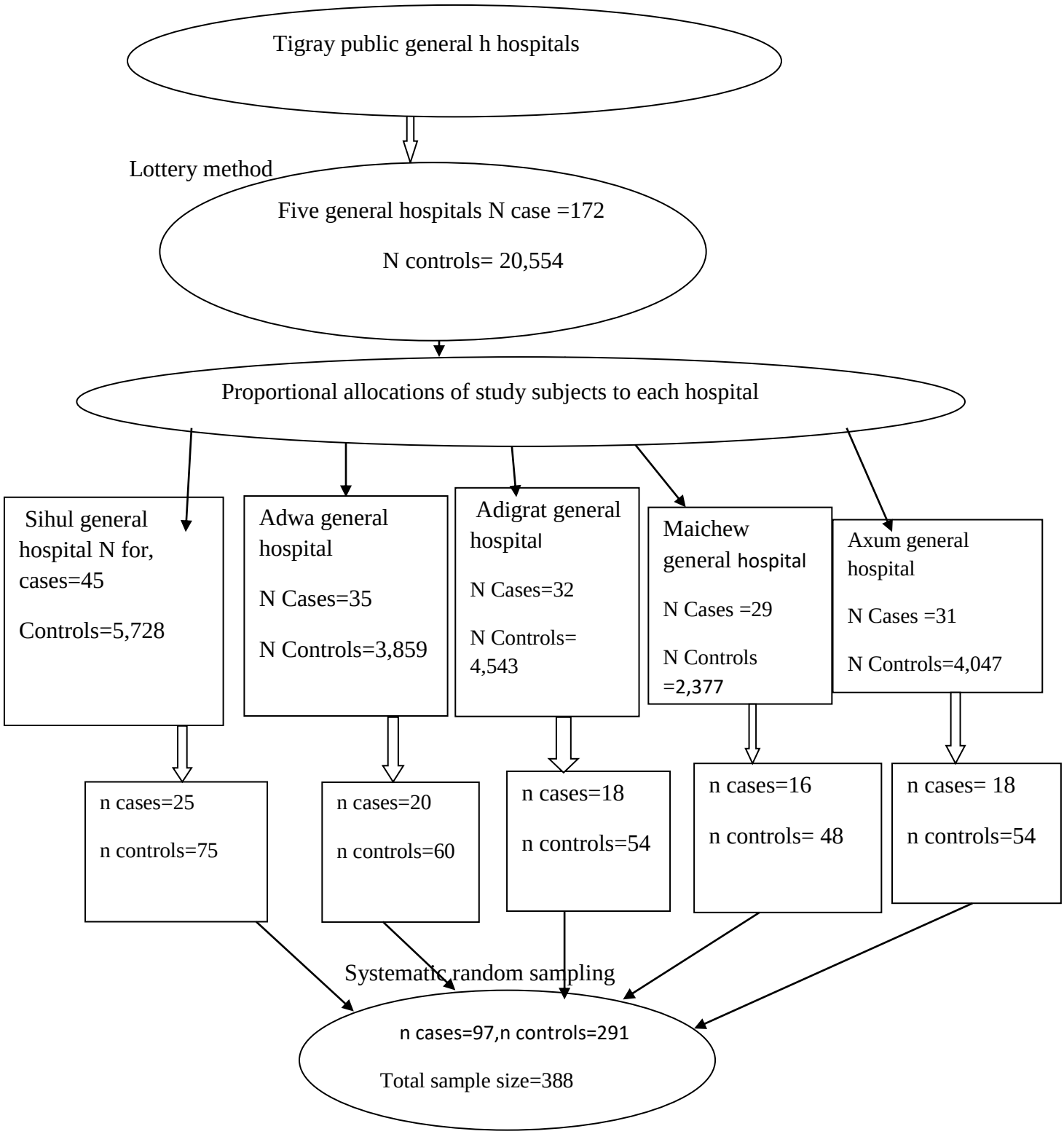

Fig2. Diagrammatic presentation of sampling procedure and sampling technique for determinants of externally visible birth defects among newborns in public general hospitals in Tigray, Ethiopia 2024/25

4.10. Operational definition

Anemic; a mother with Hemoglobin <11g/dl found recorded in the lab results, a history of anemia in the antenatal care follow-up and history sheets which is concomitant to the that pregnancy.

Birth defects; externally visible birth defect which is recorded in the registration books and maternal records i.e. neural tube defects, gastrointestinal defects, down syndrome , musculoskeletal defects

Cases; new born (live birth or stillbirth) with any externally visible birth defects who ascertained by registry based ascertainment

Chronic illnesses; health conditions that last longer in life that requires ongoing medications and treatments i.e. diabetic mellitus, chronic hypertension, HIV/AIDS, epilepsy etc. for this study previously diagnosed before pregnancy, still continuing with pregnancy and recorded in the medical record of a mother.

Controls; new born (live birth or stillbirth) without any externally visible birth defects who ascertained by registry based ascertainment

Externally visible birth defects; A type of anomaly that can be identified by inspection and physical examination registered by the delivery attending health personnel (3).

Incomplete medical records; maternal charts that lacks birth defect status of the new born, records without labour admission history (medical and obstetric history) and ANC follow up history

Low birth weight neonate; a neonate with a birth weight of less than 2.5 k.g(59).

Major birth defects; structural and /or functional abnormalities defects that cause substantial medical, social and cosmetic consequences, have higher result of mortalities and morbidities and needs surgical intervention i.e. hydrocephalus, spinal bifida, anencephaly(3).

Medication use; documented, prescribed medication during early pregnancy, written medication intake which is documented in admission history and documented treatment for chronic or acute illnesses.

Minor birth defects; defects with no significant health problem and of limited social and cosmetic results(3).

Preterm neonate; A neonate delivered beyond 28 weeks of gestation but less than 37 weeks of gestation(59)

Unspecified defects; those defects that are recorded as "congenital anomolies, congenital malformations, congenital abnormalities" without specification in the record and a thick or symbol under the congenital anamolies section of the registry

4.11. Data collection tool

A structured pretested data collection checklist was adapted after a comprehensive literature review and was modified according to the context of the study to suit for secondary data extraction (60). The data collection checklist was used to grasp socio demographic, pregnancy and ANC characteristics, maternal health, obstetric characteristics, and newborn characteristics from the maternal record. 5% pretest was conducted out of the study area and changes made accordingly.

4.12. Data collection procedures

Data was collected from December 1 to December 30, 2024 by one MSc holder supervisor and five trained and oriented BSc midwives. Cases and controls were ascertained first according to the delivery unit registry book. Maternal medical records were accessed through the registrations in the labor and delivery wards then accessed from record office. The ANC follow up sheet and antenatal histor**y**, admission history, delivery summary, chronic illnesses follow up history and medication sheets in early pregnancy was reviewed in each medical record of a mother. Diagnosis of chronic and acute illnesses in the medical records was cross checked with the timing of pregnancy. Prescribed medications written in the medical records were also crosschecked with timing to define medication intake that could be missed in admission history. Folic acid supplementation was checked from ANC checklists and from admission history. Presence or absence of birth defects was first checked in the delivery room registry log book and next reviewed in the ANC and ultrasound screening, admission diagnosis and delivery summary of maternal record.

4.13. Data quality and management

The data collection tool was properly designed and adapted from previous literatures and checked by senior researchers. 5 % Pretest was conducted before starting the actual data collection and changes made accordingly. A one day Training was given for supervisors and data collectors on every step how to access medical records, how to grasp data from patient fills and selections of cases and controls. Data collectors were BSc midwives and the supervisor was MSc holder in clinical midwifery. There was close follow up of the principal investigator with supervisor and data collectors. Privacy and confidentiality was secured.

4.14. Data analysis procedures

Data was carefully checked for completeness and consistency. Questionnaires was checked visually, cleaned, coded and entered through Epi data version 3.1 and transported to SPSS version 25 for analysis. Errors, inconsistencies and missing data was checked and corrected with appropriate handling. Descriptive statistics such as cross tabulations were used and presented in the form of texts and tables.

All independent variables entered into bivariate logistic regression analysis and independent variables which shows association in bivariate analysis with p value less than or equal to 0.05 with a 95% CI entered in to multivariate logistic regression model to assess association by controlling the potential confounders. Hosmer and lemshow test was bused to assess the goodness of fit of the model and resulted a p value =0.7. A Collinearrity diagnostic variance inflation factor was used to assess multicollinearity. The odds ratio was used to measure the strength of association between the dependent and independent variables. 95% confidence interval was used to assess the significance of the association at p value less than 0.05. Tables and figures were used to present the result of the study.

4.15. Ethical consideration

Ethical clearance was obtained from Mekelle University, College of health science, institution review board and permission letter was also obtained from Tigray region health bureau. A formal letter for permission and support was written to the selected hospitals and Permission was obtained from the administrative of each selected hospitals to get access to logbooks and patient cards. Confidentiality about information collected from the study subject's cards was kept and card was returned appropriately to the record office after the completion of the data collection.

4.16. Dissemination of result

The result of the study is to be presented during the thesis defense and submitted to Mekelle University College of health science department of midwifery. Efforts will be done to present the result at an annual work ship. Efforts will also be made to publish in scientific journals.

5. RESULTS

5.1. Socio-demographic characteristics

In this study 388 newborn (97 were case and 291 controls) included from delivery unit registration book by selecting using predefined criteria. 388 mothers whose newborn are included ranged from 18 to 42 years of age. More than half of the mothers age [170(58.4%) of controls and 24(51.5%) of cases] fall into an age category between 25 and 35. 23(23.7%) of cases and 87(29.9%) controls were below 25 years of age. On the other hand, about 34(11.7%) of controls and 24(24.7%) cases of had mothers with ≥35 years old. Regarding maternal residence about 123(42.3%) of controls and 71.1% of cases were from rural area. Moreover, the majority of the mothers, about 273(94.5%) of controls and 90 (92.8%) of cases were married (table 2).

5.2. Pregnancy and ANC characteristics

In this study about 10(3.4%) mothers of the controls and 19(19.6%) of cases had no history of ANC follow up. About 29(10.3%) of controls and 2(2.6%) of mothers of cases had more than four visits. Regarding folic acid intake 204(70.1%) mothers of the controls and 32(33%) mothers of cases were supplemented with folic acid (table 3).

Table 2; Pregnancy and ANC characteristics of study participants for determinants of externally visible birth defects birth defects among newborns in public general hospitals of Tigray, Ethiopia 2024/25

Variable	Category	Cases n(%)	Controls n(%)	Total n(%)
ANC follow up	Yes	78(80.4)	281(96.6)	359(92.5)
	No	19(19.6)	10(3.4)	29(7.5)
Number of visits	1-3 visits	60(76.9)	160(56.9)	220(61.3)
	Four visits	16(20.5)	92(32.7)	108(30.1)
	>4 visits	2(2.6)	29(10.3)	31(8.6)
Maternal folic acid intake	Yes	32(33)	204(70.1)	236(60.8)
	No	65(67)	87(29.9)	152(39.2)

Maternal Medication intake	Yes	9(9.3)	9(3.1)	18(4.7)
	No	88(90.7)	281(96.9)	369(95.3)

5.3. Maternal health characteristics

According to this study, newborns of mothers with a record of chronic illness (asthma, hepatitis B, etc.) accounts about 1% of cases and controls. In addition 15(15.5%) mothers of cases and 10(3.4%) mothers of controls had experienced acute illnesses such as malaria and typhoid fever (table 4).

Table 3; maternal heath characteristics of study participants for determinants of externally visible birth defects among newborns in public general hospitals in Tigray, Ethiopia 2024/25

Variable	category	Case n(%)	Controls n(%)	Total n(%)
Maternal Chronic illnesses	Yes	1(1)	3(1)	4(1)
	No	95(99)	288(99)	383(99)
	Missing	1	-	1
Maternal Acute illnesses	Yes	15(15.5)	10(3.4)	25(6.4)
	No	82(84.5)	281(96.6)	363(93.6)
Maternal Fever	Yes	3(3.1)	5(1.7)	8(2.1)
	No	94(96.9)	286(98.3)	380(97.9)

5.4. Obstetric characteristics

This study resulted that majority of mothers were multiparous (mothers with more than two but less than five previous births) accounting 60(61.9%) of cases and 183(62.9%) of controls. Grand multiparous mothers (≥5 previous births) also constitute about 9(9.2%) of cases and 8(2.7%) of controls. Regarding the mode of delivery around 89(91.8) cases and 240(82.5%) were vaginal deliveries (table 5).

Table 4; Obstetric characteristics of study participants for determinants of externally visible birth defects among newborns in public general hospitals of Tigray, Ethiopia 2024/25

Variable	Category	Case n(%)	Controls (%)	Total
Parity	Primiparous	28(28.9)	100(34.4)	128(33)
	multiparous	60(61.9)	183(62.9)	243(62.6)
	Grand multiparous	9(9.2)	8(2.7)	17(4.4)
Number of neonates	Singleton	94(96.9)	281(96.6)	375(96.6)
	Twin	3(3.1)	10(3.4)	13(3.4)
Mode of delivery	Vaginal	89(91.8)	240(82.5)	329(84.8)
	Cesarean	8(8.2)	51(17.5)	59(15.2)
Maternal History of abortion	Yes	10(10.3)	14(4.8)	24(6.2)
	No	87(89.7)	277(95.2)	364(93.8)
Maternal History of still birth	Yes	2(2.1)	6(2.1)	8(2.1)
	No	95(97.9)	285(97.9)	380(97.9)
Maternal History of birth defect	Yes	2(2.1)	2(0.7)	4(1)
	No	95(97.9)	289(99.3)	384(99)

5.5. Newborn characteristics

From the total 388 newborns 32(34.4%) of cases and172 (59.1%) of controls were females. On the other hand premature neonates (<37weeks) account 39(40.2%) of cases and 11(3.8%) of controls. Regarding birth weight 32(33%) of cases and 7(2.4%) of controls were recorded for

low birth weight (<2500 gram). In terms of birth outcome, 41(42.3%) of cases were recorded as stillbirths (table 6).

Table 5; Newborn characteristics of study participants for determinants of externally visible birth defects among newborns in public general hospitals of Tigray, Ethiopia 2024/25

Variable	Category	Cases n(%)	Controls n(%)	Total n(%)
Sex	Female	32(34.4	172(59.1)	204(53.1)
	Male	59(63.4)	119(40.9)	178(46.4)
	Missing	6	_	0.5%
Gestational age	<37 weeks	39(40.2)	11(3.8)	50(12.9)
	>37 weeks	58(59.8)	280(96.2)	338(87.1)
Birth weight	<2500 g	32(33)	7(2.4)	39(10.1)
	>2500g	65(67)	284(97.6)	349(89.9)
Birth outcome	Alive	56(57.7)	284(97.6)	340(87.6)
	Still birth	41(42.3)	7(2.4%)	48(12.4)

5.6. Types of birth defects

From the total 97 cases majority of them were neural tube defects accounting 55(56.7%) of the registered defects. Among the neural tube defects hydrocephalus were most common accounting 47.3% of the neural tube defects (table 7, see next page).

Table 6; classification of externally visible birth defects by organ system of study subjects in public general hospitals of Tigray, Ethiopia 2024/25

Classification of birth defects	frequency	Percentage
Neural tube defects	56	57.7%
Unspecified in registry	18	18.5%
Musculoskeletal defects	14	14.4%
Chromosomal	5	5.2%
Genitourinary	2	2.1%
Digestive system defects	2	2.1%

5.7. Determinants of birth defect

Binary logistic regression analysis was used to identify predictors of birth defects. All Variables were first analyzed in bivariate logistic regression model to assess association of each independent variable with the occurrence of birth defect. As a result of the bivariate logistic regression model maternal age, residence, parity, ANC follow up, number of ANC visits, maternal folic acid intake, maternal medication intake, maternal history of acute illnesses, newborn sex, gestational age and birth weight variables were significantly associated. Then variables which found statistically significant in the bivariate logistic regression model entered into the multivariate logistic regression mode to identify independent predictors.

According to the result of multivariate logistic regression analysis rural residence, maternal folic acid, maternal history of acute illnesses, sex and gestational age of the new born were statistically significant at p-value less than 0.05. For mothers of rural residence the odds of giving birth to a newborn with externally visible birth defects is 1.9 times higher than mothers of urban residence **[**AOR= 1.953; 95% CI: (1.04, 3.667)]. Newborns from mothers who didn't take

folic acid had 2.77 times higher odds of having externally visible birth defect compared to newborns from mothers who took folic acid[AOR= 2.77; 95%CI: (1.464, 5.240)].

In addition newborns from mothers with history of acute illness i.e. anemia, malaria, typhoid fever were five times more likely to develop externally visible birth defects compared to newborns from mothers without history of acute illnesses during pregnancy [AOR= 5.118; 95% CI: (1.389, 18.865)]. Furthermore, male newborns were 2.4 times more likely to develop externally visible birth defects than females [AOR= 2.4; 95% CI: (1.322, 4.364)]. The odds of having externally visible birth defects for preterm neonates were 11 times higher than term neonates [AOR= 11.74; 95%CI: (2.598, 53.05)].

Table 7; Bivariate and multivariable logistic regression analysis of determinants of externally visible birth defects among newborns in public general hospitals of Tigray 2024/25

Variable		Birth defects				
	category	Cases n(%)	Control%	COR(95%CI)	AOR(95%CI)	P-value
Maternal Age	18-25	23(23.7)	87(29.9)	1	1	
	25-35	50(51.5)	170(58.5)	1.113(0.637-1.942)	0.92(0.343-2.468)	0.689
	>35	24(24.7)	34(11.7)	2.67(1.331-5.355)	1.72(.494-5.991)	0.394
Residence	Rural	69(71.1)	123(42.3)	3.366(2.048-5.532)	1.953(1.040-3.667)	**0.037***
	Urban	28(28.9)	168(57.7)	1	1	
Parity	Primiparous	28(28.9)	100(34.4)	1	1	
	Multipara	60(61.9)	183(62.9)	1.7(0.7-1.951)	0.927(0.361-2.382)	0.875
	Grand multiparous	9(9.3)	8(2.7)	4.018(1.419-11.373)	1.681(0.338-8.357)	0.526
ANC follow-up	Yes	78(80.4)	281(96.6)	1	1	
	No	19(19.6)	10(3.4)	6.845(3.058-15.322)	2.492(0.816-7.609)	0.109

Maternal Folic acid intake	Yes	32(33)	204(70.1)	1	1	
	No	65(67)	87(29.9)	4.763(2.912-7.791)	2.770(1.464-5.240)	**0.002****
Maternal Medication intake	Yes	9(9.3)	9(3.1)	3.193(1.229-8.293)	1.088(0.234-5.049)	0.915
	No	88(90.7)	281(96.9)	1	1	
History of Acute illnesses	Yes	15(15.5)	10(3.4)	5.14(2.226-11.872)	5.118(1.389-18.865)	**0.014***
	No	82(84.5)	281(96.6)	1	1	
Sex	Female	32(34.4)	172(59.1)	1	1	
	Male	59(63.4)	119(40.9)	2.665(1.633-4.349)	2.402(1.322-4.364	**0.004****
Gestational age	<37 weeks	39(40.2)	11(3.8)	17.116(8.278-35.390)	11.740(2.598-53.049)	**0.001****
	>37 weeks	58(59.8)	280(96.2)	1	1	
Birth weight	<2500g	32(33)	7(2.4)	19.974(8.443-47.252	0.992(0.168-5.848)	0.992
	>2500g	65(67)	284(97.6)	1	1	

Note: - 1 Reference category,***** p value less than 0.05, **p value less than 0.01, CI=Confidence interval COR=Crude odds ratio, AOR=adjusted odds ratio

6. DISCUSSION

This is a study conducted in public general hospitals of Tigray aiming to assess the determinants of externally visible birth defects and most of its findings are consistent with previous studies with some inconsistent findings with some of the previous studies.

Regarding the independent predictors, in this study mothers who live in rural areas were 1.95 times more likely to give birth to a newborn with externally visible birth defects compared to mothers of urban residence. This result is also strongly supported by a study conducted in eastern Ethiopia which showed that the odds of congenital anomalies in neonates born to rural women were 1.73 (95% CI) times higher than neonates born to urban women(37).

This finding is also in accordance with a study conducted in Sudan which revealed significant association of rural residence with occurrence of birth defects(26). The possible justifications for the association could be lack of access to health related information, unidentified exposures from the living environment that exacerbates the occurrence of birth defects, nutritional and micronutrient deficiency(26,37). This similarity in finding among these studies may be due to closeness in study time, similarity in the living environment of study participants and similarity in socioeconomic level. In contrary, studies carried out in Gojjam and Bahirdar, Ethiopia contradicts the finding of this study revealing that neonates born from women of urban residence were found to be about six times(95%CI) and two times more likely to develop birth defect as compared to those neonates born from women of rural settings, respectively(11,18). Another additional study carried out in Egypt is also against this study which demonstrated that urban residence had significant association(19). This contradiction could be differences in sources of data mainly with the studies in Gojjam, Ethiopia and Egypt, time differences and there may also be similarities in awareness level even though participants are from opposite residence that may result discrepancies of findings.

In accordance with this study, studies of different settings found folic acid intake as a protective factor. In this study newborns from mothers who didn't take folic acid were 2.77 times more likely to have externally visible birth defects compared to newborns from mothers who took folic acid. This finding is supported by systemic review and meta-analysis on the effect of folic acid conducted in Ethiopia which revealed for newborns born to mothers who took folic acid the risk

of birth defects is reduced by 77%(39). In addition like the finding of this study, one systemic review and meta-analysis carried out in a resource limited setting revealed that pregnant women who did not use folic acid were six times higher to have neonates with structural congenital anamolies than women who used folic acid during and before pregnancy(38). This association could be due importance of folic acid is for the proper formation and development of neural tube, as it is recommended by WHO for pregnant women to take daily folic acid to prevent neural tube defects(39).

In this study newborns delivered from mothers with history of acute illnesses (anemia, malaria, typhoid and infection) in early pregnancy had five times higher risk to develop externally visible birth defects than newborns delivered from mothers without history of acute illnesses. The justification for the significant association of acute illnesses with the occurrence of birth defect is poor dietary intake that can leads to nutritional deficiencies and effect on placental function and illnesses such as malaria and typhoid fever can cause anemia with folic acid depletion which is important for organ formation and development. This is supported by a study conducted in Arsi, Ethiopia which revealed mothers with history of illnesses had six times higher likelihood of giving birth to a neonate with birth defects than mothers without maternal illnesses(47). This finding is also in accordance with a study carried out in eastern Ethiopia which indicated that for anemic mothers in the index pregnancy the odds of having a neonate with birth defects were four times higher than non-anemic mothers(37).

A systemic review and meta-analysis in Africa also supports the significant association of maternal illnesses with the occurrence of birth defect. The systemic review revealed that neonates from mothers who had illnesses during pregnancy were 2.44 times more likely to have birth defects(44). Another study consistent with these finding is, a study in Iraq that showed significant association of anemia with the occurrence of birth defects(43). The possible explanation for this finding is that anemic mothers will also lack folic acid which is important in neural tube development because the cause of anemia could be due to folic acid deficiency which is essential nutrient for producing healthy red blood cells(37).

Unlike studies conducted in Jimma and North West Ethiopia, this study found no significant association between chronic illnesses and occurrence of birth defects. The studies carried out in Jimma and North west Ethiopia showed mothers who had a chronic illness were 4 times more

likely to have a neonate with birth defect than those mothers who hadn't chronic illnesses(45,46). It is also inconsistent with a studies conducted in Iran which found significant association between chronic illnesses and birth defects(41). The difference in finding could be due to a difference in the source of data in which this study used secondary data that the probability to miss chronic illnesses due to documentation challenges is high.

According to this study male neonates had 2.4 times higher likelihood of developing externally visible birth defects. This is in agreement with studies conducted in Addis Ababa, Bahirdar and in Tigray which revealed being male is significantly associated with occurrence of birth defects(11,56,57). The similarity in finding could be a result of socio economic, ethnic and cultural similarity of participants. This study is also supported by studies in Tanzania , Hamadan Iran and brazil that showed higher risk of males for development of birth defects(33,48,55). But another Iranian study contradicts this finding, revealing females were at higher risk(24). This contradicting finding can be a result of the differences in delivery time in which this Iranian study includes registration of births of five years which is from this study.

Furthermore, the odds of having externally visible birth defects were eleven times higher for premature neonates in this study. This is supported by one cross-sectional and one cohort studies conducted in Tigray which also showed significant association of prematurity and birth defects(31,57). In addition this finding is also in line with studies in Nigeria, Tanzania and Qatar showing prematurity is significantly associated with birth defects(53–55). This strong association could be resulted due to inclusion of newborns (live births and stillbirths) after 28 weeks of gestation and those terminated due to major defects are more likely to be premature. However, this study is inconsistent with a study conducted in Egypt which revealed that term neonates were at higher risk than preterm neonates(19). This discrepancy can be a result of discrepancies in the inclusion criteria's of the studies because this study includes terminations of pregnancies for birth defects after 28 weeks of gestation and still births, so that, those cases are more likely to be premature. But the Egyptian study includes only live births in which many premature birth defects cases are more likely not to be excluded.

7. STRENGTHS AND LIMITATIONS OF THE STUDY

7.1. Strengths

This study addressed the time consuming nature and feasibility issues of the problem as a solution by using existing data even though it has its own demerits. In addition, the study includes all public general hospitals in the region with random selection of five hospitals that can help for reasonable generalizability of results. Furthermore, secondary data usage in this study eliminates the challenges to interview emotionally and depressed mothers after birth of a neonate with birth defect but this would have been challenging in primary data or interview.

7.2. Limitations

The study is based on secondary data of medical records in which incompleteness and inaccuracy of data can create bias on findings. Second, characteristics related to socio economic level, environmental exposures, lifestyle and behavioral characteristics are not included due to unavailability of data which can leads to differences in findings. In addition this study only includes birth defects that are externally visible and can be diagnosed immediately in the labour ward. Hence, internal defects that can be diagnosed through further investigations and later in life are excluded.

8. CONCLUSION

Central nervous system defects were most commonly recorded anamolies. Rural residence, folic acid intake, history of acute illness such as anemia, male sex, and prematurity were significant predictors of birth defects.

9. RECOMMENDATIONS

For stakeholders

Stalk holders should promote awareness creation for women of child bearing age to consume folic acid rich foods and early treatment of illnesses to keep healthy pregnancy, especially for mothers in rural setting.

For Tigray regional health bureau

Focus should be given in providing measures to enhance folic acid intake by promoting folic acid supplementations and food fortifications. Ensure access to information and deliver adequate health care services to cure any illnesses for women of child bearing age is also essential for positive perinatal outcome.

For health care providers

Proper and timely supplementation of folic acid and counseling about its uses to encourage intake should be under attentive consideration. In addition Health care providers should promote regular health care check-ups for early diagnosis and treatments of acute illnesses especially in early pregnancy to promote healthy pregnancy.

For research community

Additional prospective and long term follow up studies are required to address all aspects that can be missed in secondary data sources **.**Further studies that include the functional defects are also essential for more detailed findings and generalizability of results.

For women of child bearing age

Women of child bearing age should have preconception care and take folic acid properly according to the instruction given by health care provider. In addition, Mothers should take care of their nutritional and health status must early seek health care service for any illnesses especially during pregnancy.

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11. ANNEXES

Annex A: participant Information sheet

Study title: DETERMINANTS OF EXTERNALLY VISSIBLE BIRTH DEFECTS AMONG NEWBORNS DELIVERED IN PUBLIC GENERAL HOSPITALS OF TIGRAY, ETHIOPIA, 2024

Investigator; Birey Yemar

Introduction

Hello, I am Birey Yemar. I am the principal investigator student of a study to be conducted in partial fulfillment of Master of Science in clinical midwifery at Mekelle University, college of health science. I am here today to collect data on determinants of birth defects among newborns delivered in public general hospitals of Tigray. The objective of this study is to assess determinants of birth defects among newborns delivered in public general hospitals of Tigray from December 1- December 30. I kindly request you to permit this study take part on behalf of your institution and cooperate with your staff until the completion of this study. Your cooperation and willingness to take part in this study is greatly helpful in identifying and accessing information related to determinant factors of birth defects. Data will be collected retrospectively from cards of women who gave birth in your hospital from November 1, 2023 to October 30, 2024. It needs about a week to access log books and maternal medical records. There is no direct benefit and possible risk factor associated with permitting and cooperating with the study and also there is no benefit and possible risk factors for subjects of the medical records. The information extracted from medical record will be kept strictly confidential. Your cooperation is voluntarily and you are not obliged to give any access and information you don't allow to access.

Purpose

The overall purpose of this study is to assess the determinants of externally visible birth defects among newborns delivered in public general Hospitals of Tigray region. The study aims in identify the factors associated with the occurrence of birth defects. With this information I will be able to give information to Tigray regional health bureau and share with governmental and non-governmental organizations to come up with possible interventions.

Procedure and participation

You will receive the information sheet and consent form to read until you completely understand it. If you are in a condition that you can't read that will not be a problem because I will provide you oral briefing so that maximum understanding and clarity will be created. After consent declared on behalf of your institution, maternal medical records will be accessed through their registration in the logbooks of labour wards and operation theatre. Then, maternal records will be accessed to extract information using data collection checklist which contains 35 question lists that is prepared in advance. Data will be extracted for each question in the checklist from maternal records. Finally logbooks and medical record cards will be returned to their ordinary place appropriately.

Confidentiality

I strongly assure that names of mothers will not appear in the checklist and medical record numbers will be changed to codes. Any information acquired from the medical records will not be disclosed to any one out of the study and it will only be used for the purpose of the study. Overall confidentiality is strictly kept.

Risks and Benefits of the study

Permitting data collection for this study and your cooperation is voluntary. There is no direct benefit for you, for the hospital, and for the study subjects (patients with the included medical records) that you can get from this study, unless you will contribute to the generation of new knowledge on birth defects and its determinants which help to improve perinatal outcome in your institution and the health care system in general. The result of this study will be shared for governmental and non-governmental responsible bodies. I strongly want to assure you that your participation will not involve any risks to you and study subjects only it takes a little time for cooperating staffs.

Inducement, incentive and compensation

There will be no monetary payment linked with participation of study subjects in this study.

Result dissemination

Findings from this study will be submitted to Mekelle University, college of health science department of midwifery and presented during thesis defense presentation. Results will also be submitted to Tigray regional health bureau and may also presented in conferences and workshops. Efforts for publication and share the international community will be made.

Rights and Freedom to withdraw

If any violation of ethical rules and conduct seen throughout study, your health institution has full right to withdraw and stop study. Your support and cooperation in this study is completely voluntary and if you are in uncomfortable conditions to help this study's requirement you can quit and interrupt.

Person to contact

If you have any question regarding this study or would like to be informed about the result of the study you can contact the principal investigator via the following address

Principal investigator; Birey Yemar

Cell phone; 0960817014

Email; breyyemar19@gmail.com

Annex B. Consent form

I have read the information sheet very well. I have got clear understanding of the nature of the study the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, the rights and the contact address for any quires. I am aware that the health institution has the right to stop the study in a case of certain misconduct and unethical procedures are observed during the data collection process in the `health institution premises. In addition, I understand that the health institution has the right to use the result of the study as public property. Therefore, I declare my voluntary consent on behalf of the health institution to allow you to collect your data.

1. Yes, of course permission given ☐
2. No. ☐

Name of Hospital: ---------- Date: ----------

Name of data collector: ---------- Signature: ----------

Annex C: Data Collection tool, structured checklist English version

Instruction: for each of the following questions, please carefully review the charts and provide answers as appropriate. (For number categories, circle the number of coding categories and for open categories, write the information needed in the provided space).

Name of data collector: ---------- Signature: ----------

MRN: ---------- Date: ----------Hospital: ----------

Case ☐ Control ☐

Part 1: Socio-demographic data

No	Question	possible response	Remark
S01	Age in years	_____	
S02	Residence	a. Rural b. Urban	
S03	marital status	A. Single B. Married C. divorced D. widowed	

Part 2; Obstetric related characteristics

O01	Parity	_____	
O02	Number of neonates in the current delivery	1. Single 2. Twin 3. Multiple	
O03	What was the current mode of delivery	A. Vaginal B. Cesarean	
O04	Did she have history of abortion?	A. Yes B. No	
O05	Did the mother have history of still birth?	A. Yes B. No	
O06	Have she ever given birth to a neonate with birth defects?	A. Yes B. No	

Part 3: pregnancy and ANC related characteristics

P01	Did she have antenatal care follow-up during pregnancy time of this neonate?	A. Yes B. No, skip to Q#P03	
P02	If the response is yes for Q#P01, how many visits?	A. Once B. Twice C. Three E four times B. Above	
P03	Did the mother take folic acid prior to conception and early in the first trimester of pregnancy?	A. Yes B. No	
P04	Did she take any medication while she was pregnant in the first 3 months of pregnancy?	A. Yes B. No, skip to Q#M01	
P05	If the response for P04 is yes, what kind of medication it was?	A. Identified B. Unidentified	
P06	If your response is "identified" for P05 what kind of medication it was?	A. Ant pains B. Antiepileptic drug C. Anti-malarial D. Anti-hypertensive E. Anti-Asthmatic medications F. Others _____specify	

Part 4: Maternal health characteristics

M01	Have she ever experienced any chronic illnesses before pregnancy and still had continued?	A. Yes B. No, skip to M03	

M02	If your response for M01 is yes which type of chronic illness it is?	A. Diabetic mellitus B. Hypertension C. Epilepsy D. Chronic kidney disease E. Hypothyroidism F. hyperthyroidism G. HIVAIDS H. Others_____specify	
M03	Does the mother ever experience any acute illnesses early before and during pregnancy?	A. Yes B. No, skip to M05	
M04	If the Response For M03 is yes what kind of acute illness it was?	A. Anemia B. Malaria C. Typhoid D. Urinary tract infection E. Others_____specify	
M05	Does the mother experienced fever during pregnancy?	A. Yes B. No	

Part 5. New born characteristics

N01	Does the new born has birth defects	A. Yes B. No ,skip to N03	
N02	If yes for N01what kind of birth defect it is? Specify!	A. Anencephaly B. Hydrocephalus C. Spinal bifida D. Club foot	

		E. Down syndrome F. Cleft lip and palate G. Unspecified in the registry H. Others specify _____	
N03	Birth outcome	A. Alive B. Still birth	
N04	Sex	A. Female B. Male C. Ambiguous genitalia	
N05	Gestational age at birth	_____in weeks	
N06	Birth weight	_____in grams	