INSTITUTE OF HEALTH

DEPARTMENT OF BIOMEDICAL SCIENCES

ANATOMY COURSE UNIT

PREVALENCE OF OVERT CONGENITAL ANOMALIES, AND ASSOCIATED FACTORS AMONG NEWBORNS DELIVERED AT JIMMA UNIVERSITY MEDICAL CENTER, SOUTHWEST ETHIOPIAFROM MAY 1 TO JUNE 30,2018

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A THESIS RESEARCH SUBMITTED TO THE DEPARTMENT OF BIOMEDICAL SCIENCES, INSTITUTE OF HEALTH, JIMMA UNIVERSITY,IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR MASTER'S DEGREE IN CLINICAL ANATOMY

NOVEMBER 2018

JIMMA, ETHIOPIA

PREVALENCE OF OVERT CONGENITAL ANOMALIES, AND ASSOCIATED FACTORS AMONG NEWBORNS DELIVERED AT JIMMA UNIVERSITY MEDICAL CENTER, SOUTHWEST ETHIOPIA FROM MAY 1 TO JUNE 30, 2018

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ABSTRACT

BACKGROUND: *Congenital anomalies, also known as birth defects, are structural, functional and metabolic disorders that occur during intrauterine life and can be identified prenatally, at birth or later in life. According to the World Health Organization, an estimated 270,000 deaths globally were attributable to congenital anomalies during the first 28 days of life. Neural tube defects are one of the most serious and most common of these anomalies. However, scientific data on the magnitude, contributing factors and health impact of birth defects in Ethiopia in general and in Jimma particularly is currently inadequate.*

OBJECTIVES: *To assess the prevalence of overt congenital anomalies and associated factors among neonates delivered at Jimma university medical center.*

METHODS: *An institutional based cross-sectional study was conducted from May 1 to June 30, 2018. Data was collected from 754 delivered neonates with their respective mothers using structured and interviewer administered questionnaire. Neonatal weight, head circumference and length were measured after birth. Mid upper arm circumference was measured to assess nutritional status of the mother. All data were cleaned, coded and entered into EPI data 3.1 and exported to SPSS software version 20:0 for analysis. Analysis included descriptive statistics and logistic regression. Multivariate logistic regression model was fitted to assess the association between the independent and dependent variables. Adjusted Odds ratios were calculated with 95% CIs and considered significant with a p-value <0.05.*

RESULTS: *A total of 754neonates were delivered from 754 mothers and participated in this study which yielded93.6% response rate. The study finding showed that the prevalence of overt congenital anomalies among live and still births neonates was 4.1%. From 31 cases, Majority of anomalies were isolated and major in 93.5% and 96.7% of cases respectively. Central nervous system anomalies had the highest prevalence 45.1% and followed by orofacial clefts 25.8% and musculoskeletal system defects 13%. Anencephaly was the most common central nervous system anomaly in 50% of cases followed by hydrocephalus 21.4%. Unspecified cleft palate with unilateral cleft lip and bilateral cleft lip were most prevalent*

forms of orofacial clefts in50% and 25% of the cases respectively. Unknown medication uses during early pregnancy (AOR = 15.1; 95% CI: 5.5-40.2, p-value=<0.00), history of maternal khat chewing in early pregnancy (AOR = 3.4; 95% CI: 1.462-7.95, p-value= 0.004), and maternal chronic illness before conception (AOR = 4.3; 95% CI = 1.65-11.37, p-value=0.031), were independent predictors of congenital anomalies. Folate use (AOR = 0.18; 95% CI: 0.02-0.92, p-value=0.003) during periconception had a protective effect from congenital anomaly.

CONCLUSION AND RECOMMENDATION: *The Prevalence of overt congenital anomalies among the study participants was high. Unknown medication use, maternal chronic illness and history of maternal khat chewing were independent predictors of congenital anomalies. Folic acid supplementation, prevention and treatment of chronic medical illness and provision of health education regarding impact of khat chewing and unknown medication use should be recommended.*

KEY WORDS: *Congenital anomalies, Newborns, Live birth, Stillbirth, Risk factors, Delivered mothers, Neonates, Periconception, Maternal khat chewing*

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ACKNOWLEDGEMENTS

Above all, I would like to thank almighty GOD to help me do this thesis. I would like to express my deepest gratitude to my advisors Mr. Tilahun Alemayehu (M. Sc, Assistant professor of Anatomy) and Mr. Niguse Hamba (M.Sc.) for their Constructive and stimulating advice, I would also thank them for their interest, unreserved guidance and consistent effort made in supervising my thesis work.

I am also very grateful to Jimma University for sponsoring me for this master's study. My sincere thanks go to department of biomedical sciences and staff members for their direct or indirect support.

I would like to say thanks to Jimma University Medical center hospital administrators, pediatricians and staff members who largely helped me for the realization of the study through providing relevant information related to the study. I am also grateful to my family members and friends for their unreserved support.

My deepest thanks shall go to the study participants, without whom the study would have been impossible.

ACRONYMS/ABBREVIATIONS

ANC	Antenatal care
AOR	Adjusted Odds ratio
BD	Birth defect
CA	Congenital anomalies
CDC	Communicable disease control
CI	Confidence interval
CNS	Central nervous system
COR	Crude Odds ratio
C/P	Clinical presentation
CS	Cesarean section
DHFR	Dihydrofolate reductase
DM	Diabetes mellitus
ETB	Ethiopian birr
Fig.	Figure
GIT	Gastrointestinal tract
g	gram
HBW	High birth weight
HC	Head circumference
hCG	Human chorionic gonadotropin
ICD-10	International classification of diseases 10^{th} revision
IRB	Institutional Review Board
JUMC	Jimma university medical center
Kg	Kilogram
LB	Livebirth
LBW	Low birth weight
MSS	Musculoskeletal system
MTHF	Methyl Tetrahydrofolate
MUAC	Mid upper arm circumference
NBW	Normal birth weight
NTDs	Neural tube defects
OFCs	Orofacial clefts
PGDM	Pre-gestational Diabetes mellitus
Rh	Rhesus
ROS	Reactive oxygen species
SB	Stillbirth
SD	Standard deviation
SVD	Spontaneous vaginal delivery
THF	Tetrahydrofolate

1. INTRODUCTION

1.1. Background of the Study

Human development is an on-going process that begins when an ovum is fertilized by a sperm. Cell growth, division, differentiation, and even cell death, transform the fertilized ovum into a multicellular human being. In early pregnancy, each body organ has a critical period of organogenesis. Interference during this early pregnancy with intrinsic and extrinsic factors can lead to different forms of birth defects(1).

Congenital anomaly (CA), also known as birth defect, is defined as a structural or a functional defect that may be detected during pregnancy or be visible at birth or later in life. It includes gross and microscopic malformations, inborn errors of metabolism, mental retardation and cellular and molecular abnormalities. CAs are the major causes of fetal death, neonatal mortality, infant and child morbidity and mortality, and adult disability ranking 17th in all causes of disease burden (2).Major abnormalities may be life threatening or have the potential to result in a tremendous physical, financial, and emotional burden on the affected families. Approximately, 270,000 newborns die during the first 28 days of life every year from congenital anomalies (3) Neural tube defects being one of the most serious and most common of these anomalies(4). About 2‑3% of newborns have a single major malformation, and0.7% have multiple major defects (5).

It is estimated that greater than 80% of malformed conceptuses are lost during the embryonic period, and more than 90% before birth, genes mutations and known teratogens can each be identified as a cause in about 7‑8% of malformations (4). Another 20‑25% of malformations fall into the group of multifactorial disorders (5).Globally, an estimated nine million infants, representing 7% of all births are born annually with a serious birth defect (6).Prevalence of congenital anomalies in different parts of the world varies considerably. Recent studies on prevalence of congenital anomalies from Europe, estimated a rate of 2.9% were in Norway, 1% in Portugal and 1.5% in Ireland (7).

In Western Australia, birth defects occur in4.5% to 5.7% of live births from 2005 to 2008 and in Kasur,6% to 9% of perinatal mortality is due to congenital anomalies, in 40% to 60%

malformed cases the cause is unknown,20% are due to multiple factors,7.5% are single gene defects,6% are due to chromosomal abnormalities, and 5% are due to maternal ailments (8).

It was reported that the prevalence of congenital anomalies to be low as 1.07% in Japan, as high as 4.3% in Taiwan, several surveys tried to estimate the prevalence of congenital anomalies around the world which varies greatly among different populations and about 2% in England, 2-3% in the United States and 3.65% in India (9). In many cases, the causes of congenital anomalies are unknown; however, several factors known to be associated are genetic factors and environmental factors including infections agents like rubella, cytomegalovirus, Zika virus, *Toxoplasmagondi* and syphilis, drugs like thalidomide, streptomycin, phenytoin, smoking, irradiation, maternal age, geographical factors and dietary factors (10). The prevalence of neural tube defects in England and Wales was 38.0per 10,000 live births (11).

In Central Africa, including Gabon, very little is known about the occurrence of birth defects. The only data available indicates that birth defects occur at a relatively high level of 3.5% in urban areas (12). Some of the rare studies on congenital anomalies have reported prevalence of 1.5% in Egypt (13) and about 0.7% in north west Nigeria (14). A five years descriptive retrospective study in central and north west Ethiopia showed that the prevalence of birth defect to be 1.9% (15) and similar hospital based study from Addis Ababa indicated the prevalence rate of NTD to be 63.4 per 10,000 births (16).

1.2. Statement of the Problem

According to WHO, birth defects are estimated to affect one in every 33 infants globally and at least 3.3 million of children less than five years of age die from CAs each year and an additional 3.2 million remain with different degrees of disabilities, It is estimated that about 20–30%of infant deaths occur due to CAs(13)severe CAs occur in 3% of live (17) and 20% of still births (18).Congenital anomalies represent an especially challenging problem for the developing countries where more than 94% of serious congenital malformations and 95% of deaths from such malformations occur (19).

In India an estimated 511,900 births may have been affected with a congenital anomaly (20).In the United States of America, congenital anomalies reportedly affect 2-5% of all live birth, in Asia it has been shown to vary with reported incidences of 2.5% in India and 1.3% in China (21).Birth defects account for 12% of all pediatric hospitalizations and a significant portion of health care costs in the United States (22).The burden of birth defects goes beyond childhood because it is responsible for 2.3% of cases of premature death and disability, as measured by disability-adjusted life years, among the United States population (23).

In Iran prevalence of congenital anomalies among infants is 2.3% (24).In the middle east, where marriage between relatives is common, major congenital anomalies were most prevalent (2–2.5%) (25).Prevalence of birth neural tube defects in developing countries is still high, with reported incidence as high as 130 per 10,000 births (26).About 60% of the causes of congenital anomalies in humans is still unknown, indicating a complex interaction between genetic and environmental risk factors (27).Drug utilization studies reveal that most women use medications during pregnancy with estimations varying from 44% to 99% (28). Congenital anomalies are also preventable in 60% cases (8).

Substance use during pregnancy is one of the risk factors that can affect the fetus both directly passing through placental barrier and indirectly through poor maternal health habits and environmental conditions. Prenatal alcohol exposure can result in major organ birth defects, growth disorders and damage to multiple structures in the brain resulting in

permanent and lifelong disabilities (29). The prevalence of substance use among pregnant in Nigeria women was 10.8%, with alcohol the most used substance 5.4% (30).

About 55.2% pregnant mothers in Ethiopia were prescription medications users, 15% were obtained without prescribers' order. Self-medication reported to be common among pregnant women due to varieties of pregnancy related ailments such as back pain, headache, heartburn, nausea, vomiting, and hemorrhoids (31). Across sectional study conducted in North east Ethiopia showed that the prevalence of visible birth defects was8.4% (32).Based on a recent study done in Jimma, the overall prevalence of substance use among pregnant women was 37.9%, with khat chewing predomination 65.8% followed by alcohol consumption 29.7%and cigarette smoking 2.7% (33).

Another study conducted in Bahir-Dar, Northwest Ethiopia, showed that the prevalence of alcohol use during pregnancy was 34% (34) Because of the lower living standard and low antenatal diagnosis and termination of pregnancy (35) the incidence of NTDs in developing countries have been reported to be up to fourfold higher than in developed ones (36).In Ethiopia, 33% of women had a deficiency of folic acid, suggesting that these women are at a higher risk of giving birth to a baby with NTDs and the prevalence of folic acid usage at the recommended time in Adama was found to be low as 1.92% (37).

In our culture, child birth is a major and welcome event thus a mother giving birth to a malformed baby poses a great dilemma not only to her immediate family but also the entire community. The mother of such babies would feel unfulfilled, humiliated sometimes ostracized from the community. A parent giving birth to an abnormal baby is seen as a reproductive failure and may be saddled with high cost of taking care of such a child. The child faces an uncertain in a highly competitive society, thus a child born in developing countries like Ethiopia would be abandoned.

Even though there are some researches done on factors that contribute to adverse pregnancy outcome like still birth, low birth weight there was lack of data on the magnitude and associated risk factors of congenital anomalies. Hence, this research will fill the gap by determining the prevalence and factors associated with overt congenital anomalies among neonates delivered at Jimma university medical center.

1.3. Significance of the study

Knowing the risk factors would ease its overall impact, since it was the first study done in Jimma it helps to estimate the burden. The research will help health institutions for mobilizing more resources for optimal and timely management, rehabilitation of patients for appropriate referral services. It also enables health care providers to give health education that aims at creating awareness about the risk factors. Policy makers will also benefit from this study by planning, implementing and evaluating healthcare strategies, and the integration of data into the decision-making process to help prevent birth defects, additionally it will also be used as baseline for further researchers. Above all pregnant mothers will be benefited by which they will lead a healthy life.

2. LITERATURE REVIEW

2.1. Prevalence and types of congenital anomalies

The prevalence rate of birth defects was 5.48%(548.3 per 10,000 births) in Korea (9). Another study in similar country showed that prevalence of orofacial clefts in the total live births was 11.09 per 10,000 births accounting for 3.9% of all birth defects (38). According to a one year descriptive study done in Nepal, the incidence of congenital malformation were found to be 0.42% (39). Data from a hospital-based study in Pakistan reported a frequency of congenital anomalies at 2.91% (40).In China, the prevalence rate of birth defects was 156.1 per 10,000 births, the most common anomalies detected are those of the urinary system 15.9% followed by genital and chromosomal anomalies. central nervous system (CNS) anomalies of neural tube defect (NTD) origin were found to be the highest, 20.1 per 10,000 births (41).

A recent Danish study found, a high total rate of hypospadias 4.6% in a large prospective cohort of 1072 newborn boys (42). Another, a prospective analysis showed that, scrotal hypospadias was found with unilateral and bilateral undescended testis in 27(45.0%) and 9(15%) cases respectively whereas scrotal hypospadias with unilateral undescended testis was seen in 18(30.0%) cases while scrotal hypospadias with bilateral undescended testis was evident in 6(10%) cases (43).With regard to association individual anomalies of orofacial group such as cleft lip and palate, an Iran study reported cleft lip without cleft palate in 11.4%, versus cleft lip with cleft palate in 16.2% and cleft palate only in 20.7% (44). About 80% of cleft patients had no associated anomalies (45).

A cross sectional study done in Brazil showed that the prevalence of nervous system abnormalities, of which hydrocephalus was 27% and spina bifida were the most prevalent in 25% of cases. Prevalence of polydactyl was 32%, and congenital deformities of the feet accounts 27% ,cleft palate, 21% and genital abnormalities, with a higher prevalence of hypospadias at 47% (46). In SriLanka, CNS anomalies were the most common in almost 58% of cases. some cases of hydrocephalus were found in patients with spina bifida (47).

The most prevalent defect in Russia were congenital malformations and deformations of the musculoskeletal system, which represented 35.4% of all birth defects (48). Based on the

finding from Egypt, the musculoskeletal system was the most commonly affected in 23% of cases, followed by the central nervous system (CNS) and gastrointestinal system (GIT) in 20.3%, 16.2% cases respectively. In the same country, involvement of more than one system was observed in 28.6% of cases (49).

In Ghana, the majority 69.4% of clefts were unilateral (50). A retrospective based study showed that the most common cleft type was isolated cleft lip, constituting 49.2% of all cleft deformities with the left side 43.7% predomination, followed by right side 28.8% and bilateral in 18.3% cases (51).A study done in Jordan showed that the prevalence rate of neural tube defect to be 62.9 per 10,000 births (52).The overall birth prevalence of birth defects in Tanzania was 28.3 per 10,000 live births (53).A cross sectional study done in south east Nigeria showed that the birth prevalence of birth defect to be 2.8% (54).According to report from Asia region, prevalence of NTDs was 199.4 per 10,000 births in west pacific, 87 per 10,000 births in china (55) 9.8 per 10,000 births, in South Africa (56) In Kenya, about 33.9% of anomalies involves the musculoskeletal system (57).

2.2. Factors associated with congenital anomalies

Among uneducated women in Pakistan, 78% received no antenatal care during pregnancy (58). Lower maternal education status has been associated with higher risk of neural tube defects (59) .In Poland, the prevalence of congenital malformations of the extremities, and Down syndrome increases with female population over 35 years and paternal age (≥ 40 years) there is also positive association between advanced paternal age and hypospadias (60). Early maternal ages (up to 20 years) are associated with gastroschisis (61).BD is more frequently observed in premature children and those weighing less than 2500 g and measuring less than 45 cm at birth (62). According to population based studies, about 54.9% male neonates were affected by congenital anomalies (63).In California, Male births were observed to have an overall malformation prevalence that was 28.6% higher than females (64).

A hospital-based study in Iraq showed that among 22,487 births, Males comprised 65.2% of anomalies (65) but In north Iran, from the total births, 53.6% of female neonates were majorly affected (24).As a study done in China, there might be several possible reasons for

the higher risk of birth defects observed in families living in rural areas those women who are working on agricultural activities in rural areas are prone to have a baby with congenital anomaly especially Fever or hypothermia in the first trimester of pregnancy are risk factors for the occurrence of congenital anomalies, particularly anencephaly, spina bifida, hydrocephalus, congenital undescended testicle and cleft lip (66).

Folic acid supplementation can reduce the overall occurrence of congenital abnormalities and neural-tube defects. Emerging evidences show that, low blood folate status results in higher levels of homocysteine in plasma (67)which may be caused by folate deficiency. Several hypotheses have been proposed to explain how increased levels of homocysteine, or the accompanying decreased methionine levels, could cause a neural tube defect (68). Almost half of the pregnancies in the USA are unintended so that many women expose their unborn children to drugs before they know they are pregnant Furthermore, prescription drug use is common during pregnancy in many other countries as well, with prevalence estimates ranging from 44 to 79% in several European countries (12).

Similarly, it has been proposed that exposure to high levels of estrogen during pregnancy may reduce the number of Leydig-cells (clusters of testosterone secreting cells in the testis), which may impair masculinization of the reproductive tract and genitalia resulting in hypospadias. Also, a recent study found that higher estrogen levels in first- time mothers are significantly correlated with the risk of gastroschisis (69).Mothers having their first birth had modest, yet statistically significant increases in the risk of having an infant affected by 24 of the 65 birth defects in the study compared with women having their second birth (70).

Different lifestyles and habits of mother in taking nutrition supplements may differ between rural and urban areas and only 15% of the mothers of young infants had used folic acid during the first trimester of pregnancy and that nonuse folic acid was significantly associated with congenital anomalies (71). women having their third, fourth or higher order birth had significantly decreased odds ratios for six birth defects (hypospadias, obstructive congenital hip dislocation, and sacrococcygeal anomalies (61).A study conducted in France showed that , that maternal hormone levels may act in similar ways on other organ systems resulting in birth defects (72). In Sweden , it is known that among women having their first birth, non-

pregnant uterus is smaller and have less vasculature compared with women having their second or higher birth (73).

The non-pregnant uterus of a woman who has not previously given birth is 7x3x 5 x3x 2cm^3 with convex inner walls, whereas the pregnant uterus of a woman who has given birth previously is 10x3x6x3x 2.5 cm^3 with concave inner walls making for a larger and more spacious cavity (74). According to a similar study done in California, about 63.6% of women reported at least one infection during pregnancy. Reports of infections were more common during pregnancy implying that a small increase in risk for birth defects than in the 3 months before pregnancy, nearly half 49.6% of women reported a respiratory infection, 20.5% reported a fever and 3.4% reported a sexually transmitted disease (75).

In Spain, multiparity seems to be another risk factor associated with congenital anomalies, as evidenced in 56.16% of cases, especially among multiparous women who had three or more births (40). Another study shows two-third of congenital malformations in newborns associates with maternal multigravida (76).A high frequency of birth defects was also reported in other studies that examined infants with low or very low birth weight, including premature infants (77). Antenatal care (ANC) frequency was also associated with CAs. In Brazil, none or ANC visits fewer than four have been associated with the occurrence of congenital anomalies (78).Data from the same country showed that low birth weight children were found to be associated with BDs (79).

The association between obesity and the occurrence of NTDs was similarly reported elsewhere .This may be because NTD-protective effect of folic acid supplementation is weaker in overweight/obese mothers (80) and obese women may require higher doses of folic acid supplementation to achieve similar serum levels (16).About 6% of cases with BD were stillborn with multiple and major BD. There is a lower risk of neural tube defect in children of multiparous women (62).

Maternal diabetes mellitus (DM) is also indicated as risk factor for CAs. Neonate of diabetic mothers in Romania had approximately twice the incidence of congenital malformations than those of mothers without DM. Thus, 4.82% of mother's cases were diagnosed with hyperglycemia or diabetes in the Romanian study the association between glycemic level and congenital anomalies is well documented because maternal obesity which is frequently

associated with maternal diabetes, seems to adversely affect organogenesis and favors the occurrence of birth defects such as spina bifida, heart defects, limb abnormalities, omphalocele and hypospadias (81).

Underweight mothers seem to have a higher risk for orofacial cleft (82). It is well known that maternal pathologies can induce malformations more commonly incriminated maternal infections are: rubella, cytomegalovirus and herpes simplex virus (83). An association between hypospadias and maternal hypertension(regardless of timing) were reported somewhere else (84).Consanguinity was present in 67.7% of cases with various CAs (40). A study performed in Iran demonstrated that CAs are 3.5 times more common in consanguineous marriages as compared to non-consanguineous marriages (85). Drinking alcohol was significantly associated with the risk of birth defects while no association was found between smoking and birth defects. Those mothers with a family history of birth defects were more likely to have birth to malformed babies than those without a family history (77).

According to a meta-analysis done in united kingdom (UK), there is an established fact that the risk of congenital malformation is significantly increased by passive second-hand smoke exposure during pregnancy anomalies occur due to the effects of carbon monoxide which reduces tissue oxygenation and nicotine stimulates the release of hormones that cause vasoconstriction in the uterus and placenta, so it carries less oxygen and fewer nutrients to the fetus (86).The most common perinatal risk factors that are associated with congenital anomalies are preterm labor (34%), polyhydramnios (24%) and breech presentation (22%).In 40%of cases, there was a history of one or more abortions in association with congenital anomalies (87).In Denmark, maternal use of oral contraceptive was associated with reported increased risks for specific defects including gastroschisis, limb defects, andurinarytractanomalies(88).InSwitzerland,exposuretoorganophosphates(pesticides)increases the risk of neural tube defects (89).

According to a study done in Nevada, women with an interpregnancy interval of 36 months or more are more likely to have infants with birth defects compared to those with an interpregnancy interval of 18 to23 months. It is found that an interpregnancy interval of 36 months or more was associated with down syndrome even if the mechanism is not well

known but some of suggested mechanism is “physiological regression” that may explain the adverse birth outcomes after along interpregnancy interval. During pregnancy, a woman’s body undergoes physiologic changes that are conducive for the optimal growth of the fetus. After birth, the body slowly returns to near normal and if conception does not occur soon enough, the physiologic characteristics may become similar to those of a primigravid and thus, adverse birth outcomes (90).

In Southern California, exposure to ambient Carbon monoxide during each of the first three months of pregnancy was examined and the results only showed the association between CO and increased risk of limb defects. The Possible mechanism of how pollutants result in anomaly is under investigation. Air pollutants might be involved in the development of skeletal malformation via hemodynamic, anoxic events, oxidative stress, and toxicity to certain cell populations during pregnancy (91).According to the study done in Egypt, the incidence of congenital malformations was significantly higher among the LBW babies in comparison to normal weight babies (13).Out of 10,163 deliveries in Nigeria, about 58.3% of males had congenital anomalies (14).

Based on an experimental study from Nigeria, X-rays radiation on embryo may cause some effects such as miscarriage, restriction of fetal growth, microcephaly, or lead to mental retardation (92).In Kenya, about 50% of women were reported of having some sort of chronic disease during pregnancy while severe anemia was the most common complication irrespective of pregnancy status (93).According to a case-control study done in Addis Ababa and Amhara region, no association was found between maternal age, previous history of abortion, stillbirth, infant death and congenital anomalies (94).

A study done in northeast Ethiopia showed that, mothers with a hemoglobin level less than 11 mg/dl were found to experience adverse birth outcomes when compared with those with Hgb level greater than 11 gm/dl. The possible reason could be linked to the effect of anemia on the oxygen- bearing capacity and its transportation to the placental site for the fetus. Similarly, mothers with MUAC less than 23 cm were also found to experience adverse pregnancy outcome like congenital anomalies when compared with those with MUAC greater than 23 cm (32).

2.3. Causes and mechanisms of birth defects

A particular birth defect may be caused by many different factors as well as by different mechanisms, whereas a specific pathogenic process may result in different outcomes depending upon such factors as duration of exposure, embryonic age, and dose of exposure and genetic susceptibility. Although the mechanisms by which drugs may cause birth defects are still not completely understood (95).

Folate, a water-soluble B vitamin, occurs in high concentrations in certain natural foods (fruits, leafy green vegetables, beans, and liver) as polyglutamate. The conversion of folate needs two reduction reactions by dihydrofolate reductase (DHFR) to the naturally bioactive form tetrahydrofolate (THF), which is converted into 5- methyl tetrahydrofolate (5-MTHF) monoglutamate. 5-MTHF is the main form of folate that circulates and transported by three routes: by membrane-associated receptors, by a carrier-mediated system, the reduced folate carrier, and by passive diffusion (96).

Since rapidly proliferating tissues require DNA synthesis, it is obvious that folate-dependent reactions are essential for fetal growth and development and that folate requirements increase during pregnancy. In addition, methylation of DNA is known to be involved in the epigenetic control of gene expression during development. Drug-related inhibition of folate metabolism may have a teratogenic effect by inhibiting of the folate methylation cycle. Some anti-epileptic drugs, such as carbamazepine and valproic acid, are generally known to increase the risk of folate-sensitive birth defects, such as neural tube defects, orofacial clefts and limb defects (97).

The neural crest is pluripotent cell population that originates in the neural folds. In the craniofacial region, various cell types and structures, including cartilage, nerves intramembranous bone, and muscles, are derived from the cranial neural crest. The truncal neural crest produces important components of the peripheral nervous system (98).Non-cardiovascular defects that have been proposed to be neural-crest related are craniofacial malformations (99).Proper induction, migration, proliferation and differentiation of neural crest cells are tightly controlled and regulated. A variety of receptors and molecular signals are implicated in neural crest cell development. Fibroblast growth factors may be involved

in the induction of neural crest cells (100). Integrins, a family of cell surface receptors, play a role in the interaction of neural crest cells with the extracellular matrix (101), whereas interactions between neural crest cells are mediated by N-cadherins (102).

However, one of the most important signaling molecules in neural crest cell development is retinoic acid, the biologically active form of vitamin A. Excesses as well as shortages of retinoic acid seem to cause neural crest-related malformations, indicating that proper retinoid homeostasis is necessary for normal development (100).Male development is more susceptible to endocrine disruption than female development because of its hormone dependence (103).Testosterone secretion is responsible for most of the masculinization process, including the development of the male reproductive tract and external genitalia. Therefore, compromised testosterone production may result in congenital anomalies of a male urogenital system such as in hypospadias. In addition, estrogen exposure also suppresses the production of insulin-like factor 3 by fetal Leydig cells. This peptide regulates the growth of the gubernaculum (104).

At cellular level, a teratogen may potentially affect embryogenesis by causing gene mutation, chromosome breakage or nondisjunction, depletion or inhibition of precursors or substrates, depletion of energy sources, changes in membrane integrity and inhibition of enzymes. These lead to cell death, reduced cell division, and failure of expected interaction between cells, interruption of cell migration, or mechanical disruption. Regardless of the initial mechanism, the ultimate result usually is an organ with too few cells. The critical mass necessary for induction or continuation of differentiation is lacking; thus, the particular organ system fails to develop, more ever, some anomalies such us (polydactyly) could result either from increased cell proliferation or from failure of localized cell degeneration (105).With regard to the molecular mechanisms of congenital anomalies, involvement of several growth factors, local hormones and/or their receptors and ligands is well established. For instance, in failure of midline fusion of the urethral folds in hypospadias, lack of growth factor expression is described (106).

Ephrin (Eph) receptors and their ligands, regulate a wide spectrum of pathophysiological processes, including cellular adhesion, migration or chemo-repulsion and tissue/cell boundary formation. Dysregulated Eph/ephrin signaling in the genital tubercle vascular

endothelia has been linked to the failure of midline fusion of the urethral fold. Similarly, fibroblast growth factor is an androgen-induced growth factor while epidermal growth factor is regulated by human chorionic gonadotropin (hCG) (107).

Although placental enzymes play a role in protecting the fetus against oxidative stress, the developing embryo is susceptible to high levels of reactive oxygen species (ROS) this because of its weak antioxidant defense, in particular in the early stages of organogenesis. Oxidative stress is postulated to be involved in the pathogenesis of a wide spectrum of birth defects, including skeletal malformations (108) limb defects (109) neural tube defects (110) cleft lip/palate and cardiovascular defects (111).

During embryogenesis, vascular disruption results in aberrant differentiation and distortion of contiguous tissues, loss of tissue and incomplete development of structures within the same or a secondary embryonic developmental field. Anomalies that result from vascular disruption during the fetal period are usually limited to the areas with disturbed blood supply, to which the peripheral vasculature is most susceptible. Therefore, most of the defects caused by tissue damage through vascular disruption occur in structures supplied by the most peripheral vasculature, such as the distal limbs and the embryonic intestine(112) Birth defects that were attributed to vascular disruption include terminal limb reductions (113)gastroschisis and Poland anomaly(114).

2.4. Conceptual framework

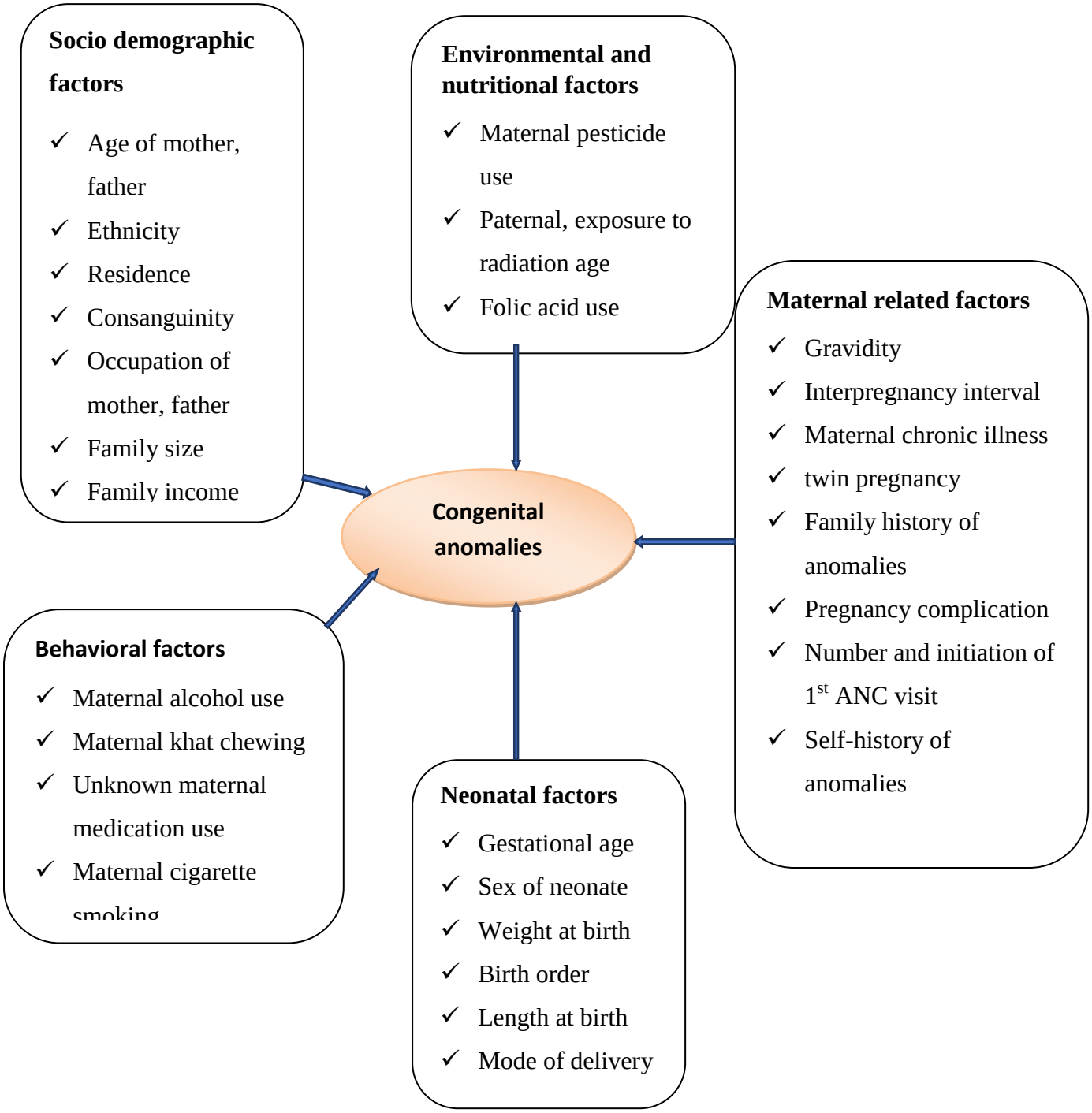

Figure 1:Conceptual frame work adapted by reviewing different literatures

3. OBJECTIVES

3.1. General Objective

- To assess the prevalence and factors associated with overt congenital anomalies among neonates delivered at JUMC, Southwest Ethiopia, from May 1 to June 30,2018

3.2. Specific Objectives

- To determine the prevalence of overt congenital anomalies.
- To identify types of congenital anomalies among neonates.
- To characterize the structural anomalies among neonates.
- To describe the factors associated with congenital anomalies.

4. METHODS AND PARTICIPANTS

4.1. Study Area and Period

This study was conducted in Jimma University Medical Center (JUMC)which is located in Jimma town, Jimma zone, 355 Km in the south west of Addis Ababa, the capital city of the Ethiopia. Jimma University medical center (JUMC) is 800 bedded teaching and referral hospital that give general and specialized clinical services including maternal and childcare for about 20 million populations in South-western part of Ethiopia. The Gynecology/Obstetric ward of the hospital has 45 maternity beds and five delivery tables, and provides 24-hour obstetrics and gynecology care to both direct and referral cases. Most of the deliveries and evaluations were made by senior obstetrician, gynecologists and pediatricians. The study was conducted from May 1- June 30, 2018.

4.2. Study Design

Institution based- cross-sectional study was conducted among neonates delivered at Jimma university medical center.

4.3. Source Population

All neonates delivered at Jimma university medical center, and their mothers.

4.4. Study Population

All neonates delivered at Jimma university medical center, and their respective mothers presented during data collection time. All neonates delivered in the labor rooms were examined for overt(external) anomalies within 48 hours soon after birth. The diagnosis was assured by a pediatrician after physical examination was performed.

4.5. Eligibility Criteria

4.5.1. Inclusion criteria

- All neonates delivered after 28 completed weeks of gestation irrespective of mode of delivery.
- Cases with external anomalies were included.

- A neonate with major and minor anomalies was counted once as having major anomalies.
- Cases with multiple anomalies were counted once in systemic classification.

4.5.2. Exclusion criteria

- Those mothers who were not willing to give information.
- Those mothers who were seriously ill.

4.6. Sample Size and Sampling Technique

The minimum sample size was estimated by a single population proportion formula with finite population correction. The following parameters were considered 50% prevalence, 95% confidence interval, 5% margin of error. The size of the source population obtained from the total deliveries in 2010 at JUMC was4796

$$n = \frac{(z_{\alpha/2})^2 \cdot pq}{d^2}$$

Where*; n* – sample size

$Z\,\alpha/_2$ – Confidence interval = 1.96

P – Prevalence = 50%

d – Margin of error = 5%

With the above assumptions, the calculated sample size was 384.

Since the estimated total population of annual deliveries was less than 10,000 we use correction formula.

$$nf = n/(1 + \frac{n}{N})$$

nf = final sample size for the targeted population

n= calculated sample size (384)

N= total targeted population (4796)

Then the final sample size according to these equation yields 356 and adding 10% for non-response (36) incomplete data, the minimum sample size required was 392. Consecutive sampling technique was used for selecting the study subjects.

4.7. Data Collection Tool and Procedure

Data was collected through face to face interviews with mothers in the immediate postpartum, by using a structured questionnaire adapted from the WHO birth defect surveillance tool (2). The data was gathered at delivery rooms/wards. Two B.Sc level midwives were recruited to collect the data. The tool generally had six parts [Annex-II] that was aimed for assessing sociodemographic factors (13 items), maternal and obstetric factors (27 items), nutritional factors (3 items), behavioral factors (6 items), environmental (4 items) and neonatal factors (7items).The type of CAs were classified as major and minor after they met the case definition set by WHO/CDC/ICBDSR in 2014 (2). Based on International classification of disease version 10 (ICD-10) the cases were classified by anatomical system. Neonates with morphological signs of a known syndrome were classified as having multiple anomalies. Proper codes were assigned after the pediatrician reviewed and confirmed the diagnosis

Newborn length was measured with readable measurement tape with the neonate placed on the side and measured from the head to the heel of the foot. Birth weight was also measured with a digital baby scale measuring device (**Model 8463, OIML EC Class III)** where newborn is lying down naked or with minimal clothing in the weighting pan. Head circumference (HC) of neonate was measured using non-stretchable tape meter. Occipital frontal circumference was measured over the largest circumference of the head, above eyes and ears. Measurement tape was positioned just above ears and eyebrows and around the biggest part of the back of the head (115). It was also assured that tape was straight. Classification of HC was done according to WHO child growth chart. Nutritional status of the mother was assessed by measuring of mid-arm circumference (MUAC) on left arm using a standard MUAC tape meter. The use of the left arm was random.

4.8. Study Variables

4.8.1 Dependent variable

- Congenital anomalies among neonates
  - **Prevalence of congenital anomalies** is defined as number of cases of live birth or still birth with overt congenital anomalies after 28 weeks of gestation (numerator) among a total number of live and still birth (denominator) over two-month period.

4.8.2 Independent Variables

Sociodemographic variables

- Age of the mother, father
- Family size
- Ethnicity
- Family income
- consanguinity
- Parental consanguinity
- Residence
- Marital status
- Occupational status of mother, father

Behavioral and nutritional variables

- Unknown medication use
- History of maternal khat chewing
- History of maternal cigarette smoking
- History of maternal alcohol use
- Folic acid use

Environmental and neonatal variables

- Maternal, paternal x ray Radiation exposure
- History of maternal Pesticide use
- Mode of delivery
- Gestational age
- Birth order
- Sex of neonate
- Weight at birth

Maternal and obstetric related variables

- Gravidity
- History of stillbirth
- History of Twin pregnancy
- Complication during pregnancy
- Chronic illness before conception
- Family history of CAs

- Self-history of CAs
- History of spontaneous abortion
- Interpregnancy interval
- History of anemia
- Number, initiation of 1st ANC visit
- Types of pregnancy complications
- Types of chronic illness

4.9. Operational Definitions of Terms

Alcohol intake: A mother who had history of alcohol intake on daily bases (> 30 drinks/ month), sometimes (5-15 drinks/month) and rarely (1-4 drinks/month)(116).

Maternal cigarette Smoking: A mother who lives with a smoker such as neighbors, family members are passive smokers. Whereas former smokers are those who were smoking one year back but stopped currently (within this year).

Maternal khat chewing: A mother who chew khat sometimes means more than two times and more per month whereas rarely is chewing once per month rather than on daily basis(117).

Vegetable and fruit consumption: If a pregnant mother consume rarely means1-2 servings per week, sometimes 3-4 servings per week and daily 5-7 days per week.

Preconception is used to refer to the preceding three months before conception, while **periconception** is used to refer to the period including three months before conception (preconception) and the first three months after conception (first trimester).

NTDs were defined as cases of anencephaly, spina bifida, and encephalocele based on ICD-10 criteria.

Live birth or stillbirth will be considered after 28 weeks of gestation or birth weight of 1,000 g and greater.

Major birth defects are defined as structural and functional congenital anomaly that have health and social impacts upon the affected person and need medical interventions**. Major structural birth defects** include neural tube defects (NTDs), hydrocephalus, orofacial clefts, upper and lower limb reduction defects; omphalocele, hypospadias, and downs syndrome these defects are considered severe, having adverse effects on the well-being and survival of children born with those anomalies while **Minor birth defects** such as polydactyly are anatomical

structural defects that have minimal social and health effects and require no medical interventions. **Single or isolated anomalies** are structural defects of only one system where as **multiple or associated** is when more than one system is involved(2).

Head circumference classified based on -2 to -1SD (32-32.9cm), -1 to 0 SD (33-34.9cm), 0 to1SD (35-35.9cm) and 1to2SD (36-37cm). According to WHO child health monitoring chart.

Unknown medication- could be obtained without physician order, it might be herbal medication.

Birth weight – if a newborn weight 1-1.49kg is very low birth weight (VLBW),1.5-2.49 kg is low birth weight (LBW), 2.5-3.99 kg is normal birth weight (NBW) and high birth weight (HBW) if ≥ 4 kg.

Elective termination of pregnancy for congenital anomalies is made after 12 weeks of gestations and diagnosis via ultrasonography.

Interpregnancy Interval- Interpregnancy interval was calculated as the time period between two consecutive deliveries (the index delivery and the most recent delivery) and subtracting the gestation age of the recent neonate.

Chronic illness- A mother who had hypertension, diabetes mellitus and both at a time.

Gestational age- An infant is said to be term if delivered between 37-42 completed weeks of gestation from first day of last menstrual period, preterm if delivered before 37 weeks and post term after 42 weeks.

Early pregnancy- The first three months of pregnancy.

4.10. Data Analysis

The collected data was checked for its completeness and then entered to Epi data version 3.1, then exported to SPSS version 20.0 for analysis. Frequencies, means, standard deviation and percentage were used for the descriptive analysis of data Bivariate analysis was done to select candidate variables for multivariate analysis. All variables with p-value < 0.25 on bivariate logistic regression were entered into multivariate logistic regression analysis. Odds ratio for the associated variables were calculated. Confidence interval of 95% and P-value < 0.05 were

considered statistically significant. Model fitness was checked by Hosmer Lemshow goodness of fit test (p=0.79).

4.11. Data Quality Management

Data was checked on daily basis by data collectors and further overseen by the principal investigator for completeness and correctness during collection periods. It was also rechecked during data entry. Training was given for two days on the purpose of data collection, techniques of data collection, and on ways of bias minimization. The questionnaires were prepared in English and translated in to Amharic and retranslated back to English to check its consistency.

4.12. Ethical Consideration

Ethical clearance was obtained from Institutional Review Board (IRB), of Jimma University. Supportive letter was written to Jimma University Medical center. The purpose of the study was explained to the neonate mothers briefly. Data collection was started after permissions was obtained from hospital managers/medical directors and after a written consent was obtained from children's mothers. Separate discussion was held with the mothers and father about the possibility of taking few photographs of their neonate. As a result, most parents welcomed and agreed and signed consent form [Annex-I]. After that one or two photographs of the cases were taken humanly with a great care by holding the camera at 90° to the fetus or neonate. To maintain confidentiality, no personal identification; instead coded identifications were used during image processing and throughout the study period. Nonetheless, all cases regardless of the photograph taken or not were still included in the study. Data that was collected from the participants were kept in secured and locked cabinets in order to maintain confidentiality.

4.13. Dissemination of the Results

After completion of the research, the result will be presented during thesis defense and submitted to Jimma university department of biomedical science. Then it will be disseminated to Jimma university research unit and ministry of health. Beside to this, the findings of the study will be disseminated through publications and may be presented in scientific conferences and workshops.

5. RESULTS

5.1. Sociodemographic Characteristics of participants

During the two-month study period (May 1—June 30, 2018) a total 805 births occurred at JUMC. All births were singletons. Out of the 805 deliveries, 754 mothers take part in the study, yielding a response rate of 93.6%. General characteristics of the study parents are shown in Table 1. The mean (±SD) age of the mothers and fathers was 27.3 (±5.7) and 35(±8.62) years respectively. Majority 392(52%) of the mothers were Oromo by their ethnicity, Muslim 326(43.2%) by religion and almost two fifth,302 (40.1%) of mothers were housewives. More than half 492(65.3%) of mothers were married, 234(31%) were illiterate and about 388(51.5%) of mothers were from rural area. The average size of family was > 3 in 446(59.2%) of participants. As indicated in Table 1, 745 (98.8%) parents had no blood relation and 236 (31.3%) of the fathers were governmental workers and 204(27.1%) of these earn average monthly income of 1001-2000 ETB.

Table 1: Sociodemographic characteristics of participants at JUMC, 2018

Variables (N=754)	Frequency (%)
Age of mother	
≤20 years	82(10.9)
21-34 years	574(76.1)
≥35 years	98(13)
Marital status	
Married	492(65.3)
Widowed	40(5.2)
Divorced	94(12.5)
Single	128(17)
Religion	
Muslim	326(43.2)
Orthodox	180(23.9)
Protestant	162(21.5)
Catholic	86(11.4)
Mothers education	
Illiterate	234(31)
Primary education	220(29.2)
Secondary education	198(26.3)
Collage and above	102(13.5)
Residence	
Urban	366(48.5)
Rural	388(51.5)

Table 2. Cont.	
Variables (N=754)	**Frequency (%)**
Mothers ethnicity	
Oromo	392(52)
Amhara	148(19.6)
Gurage	118(15.6)
Kaffa	82(10.9)
Others*	14(1.9)
Mothers occupation	
Housewife	302(40.1)
Farmer	118(15.6)
Government employee	182(24.1)
Non-governmental employee	54(7.2)
Merchant	98(13)
Blood relation of parents	
Yes	9(1.2)
No	745(98.8)
Age of father (Years)	
20-39	508(67.4)
40-59	236(31.3)
≥60	10(1.3)
Fathers occupation	
Farmer	208(27.6)
Merchant	158(21)
Government worker	236(31.3)
Non-governmental worker	72(9.5)
Daily laborer	80(10.6)
Religion of Husband	
Orthodox	144(19.1)
Muslim	342(45.4)
Protestant	170(22.5)
Catholic	98(13)
Family size	
≤3	308(40.8)
>3	446(59.2)
Average family income (ETB)	
≤1000	152(20.2)
1001-2000	204(27.1)
2001- 3000	192(25.5)
3001-4000	100(13.3)
≥4001	106(14.1)

*** Tigrie, Dawro**

5.2. General neonatal characteristics

A total of 754 neonates: 734 live and 20 stillborn neonates were involved in this study. Most of the neonates 392(52%) were females and more than half 502(66.5%) of them were delivered at term. About 348(46.1%) were expelled by spontaneous vaginal delivery. Normal birth weight was reported in 621 (82.3%) of participants, majority of 326(43.2%), 631(83.6%), 568 (76.5 %) of neonates were third order and above, had a length ≤ 50 cm and head circumference of 35-35.9 cm respectively. The birth weight of the neonates ranged from 1 to 4,5 kg with a mean ± SD of 3.28 ± 0.57 kg, Mean ± SD occipitofrontal (Head) circumference was 33.19 ± 1.05 cm, minimum of 32 cm, maximum 39 cm, and mean ± SD of birth length was 48.12 ± 3.06cm, ranging from a minimum value of 34 cm to maximum of 57 cm as indicated in Table 2.

Table 3: Characteristics of neonates delivered at JUMC,2018

Variables (N=754)	**Frequency(%)**
Sex of neonate	
Male	362(48)
Female	392(52)
Gestational age	
Term	502(66.5)
Preterm	129(17.1)
post term	123(16.3)
Birth weight	
VLBW	3(0.4)
LBW	46(6.1)
NBW	621(82.3)
HBW	84(11.1)
Birth order	
First order	184(24.4)
Second order	244(32.3)
Third and above	326(43.2)
Length at birth	
≤50 cm	631(83.6)
> 50 cm	123(16.3)
Head circumference	
32-32.9 cm	15(2)
33-34.9cm	71(9.5)
35-35.9 cm	568(76.5)
36-37 cm	88(11.8)
> 37cm	5(0.7)
Mode of delivery	
SVD	348(46.1)
Instrumental	198(26.2)
C/S	208(27.5)

5.3. Prevalence of congenital anomalies

Out of 754 neonates, 31 of them were born with one or more visible birth defect(s). The prevalence of overt congenital anomalies was therefore 4.1% (95% CI=2.8-4.7), 411 per 10,000 births. Almost half **(**52%) of the cases were male. Slightly more than half 17(54.8%) of deliveries with CAs were livebirths. Majority 29 (93.5%) of the anomalies were isolated (single system) and the rest 2(6.4%) were associated anomalies; and in 30 cases (96.7%) the defects were major anomalies; minor anomaly was observed in 1(3.2%) newborn only.

5.4. Types of congenital anomalies

The specific types of anomalies captured in this study were given in Table 3. Overall prevalence of central nervous system (CNS) anomaly was 1.86% [in 14 cases out of 754 births], while that of orofacial clefts and anomalies of musculoskeletal system were 1.06% and 0.5% respectively. Anomalies of genital organs and chromosomal abnormality accounted 0.26% each. The least frequent anomaly was gastrointestinal system in 0.13% of cases (Table 3).

From 31 neonates with birth defects, CNS anomalies were most prevalent, evident in 14 newborns accounting almost 45% of the cases. Majority (12/14, 85.7%) of neonates with CNS anomalies were stillbirths. Figure 2 consists of photographs of two neonates with different types of CNS anomalies captured in this study. Anencephaly was the most common type of nervous system anomaly in seven (7/14, 50%) cases in this study (Fig. 2a). Majority of neonates with anencephaly were females (5/7, 71.4%). Hydrocephalus was reported in three (21.4%) cases with male predomination. Almost two third (2/3,67%) of neonates with hydrocephalus were stillbirths. Spina bifida with hydrocephalus was also seen in two (2/14, 14.2%) cases. Typical example of Spina bifida cases was shown in Fig.2b. The average size of spina bifida in this case was in the lumbosacral region and measured about 3 cm x4 cm in size.

Orofacial clefts were the second common anomalies found in eight (8/31,25.8%) neonates. Among the cases of orofacial clefts even (7/8,87.5%) of them were livebirths. Majority (4/8,50%) of orofacial anomalies were cleft palate and lip. From the cases of cleft palate and lip, three (3/4,75%) of them were male and all had unspecified cleft palates with a unilateral cleft lip.

Table 4: Classification of External anomalies among neonates delivered at JUMC, 2018

Types of Anomalies	Sex		Number (Percent)	Type of birth		ICD-10 code
CNS anomalies (n=14, 1.9%)	Male	Female		**Livebirth**	**Stillbirth**	
Spina bifida (Lumbosacral)			2(14.2)			Q05
Meningocele	1	-		-	1	Q05.7
Myelocele	-	1		1	-	
LS Spina bifida (Myelocele)with hydrocephalus	1	1	2(14.2)	-	2	Q05.2
Anencephaly	2	5	7(50)	-	7	Q00
Hydrocephalus	2	1	3(21.4)	1	2	Q03
Orofacial clefts (n=8, 1.06%)						
Cleft lip			3(37.5)	2	1	Q36
Unilateral	-	1		1	-	Q36.9
Bilateral	-	2		1	1	Q36.0
Cleft palate and lip			4(50)	4	-	Q37
▪ Unspecified C/P with unilateral cleft lip	3	1	4	-	-	Q37.9
▪ Unspecified C/P with unilateral C/L and polydactyly	1	-	1(12.5)	1	-	Q89
Gastrointestinal system anomalies (n=1)						
Imperforate Anus	1	-	1(100)	1	-	Q42.3
Anomalies of genital organs (n=2)						
Hypospadias's			2(100)	2	-	Q54
First degree (Glanular)	1	-	1(50)	-	-	Q54.0
Second degree (sub coronal)	1	-	1(50)	-	-	Q54.1
Musculoskeletal system anomalies (n=4; 0.53%)						
Omphalocele	1	-	1(25)	1	-	Q79.2
Talipesequinovarus, bilateral		1	1(25)	-	1	Q66.0
Bilateral absence of thumb	-	1	1(25)	1	-	Q71.3
Polydactyly only	-	1	1(25)	1	-	Q69
Chromosomal abnormalities						
Downs syndrome (Probable)	1	1	2(50)	2	-	Q90
Total 16	15		31(100)		17(54.8)	14(45.2)

CP=cleft palate; LS- Lumbosacral

A photograph of unilateral cleft lip neonate with probable cleft palate captured in this study was shown in Fig. 3. More than one third (3/8, 37.5%) of neonates had cleft lip. All of neonates with cleft lip were females. Based on laterality, majority (2/3, 67%) of them had bilateral cleft lip. Unspecified cleft palate with unilateral cleft lip and polydactyly was reported to be a multiple anomaly.

Figure 2: Photographs of newborns with two different types of CNS anomalies anencephaly (a) and spina bifida (b) delivered at JUMC, Jimma, Southwest Ethiopia, 2018

The musculoskeletal system was the third commonly occurred anomaly in (4/31, 13%). Polydactyly (minor anomaly) of toes was found in one (1/4, 25%) case. A neonate with bilateral polydactyly of the lower limb, with six toes each was shown in Figure 4a, Anomalies of genital organs were seen in (2/31, 6.4%) of neonates. Two male neonates were diagnosed to have first and second-degree hypospadias. The locations were glandular and sub coronal respectively.

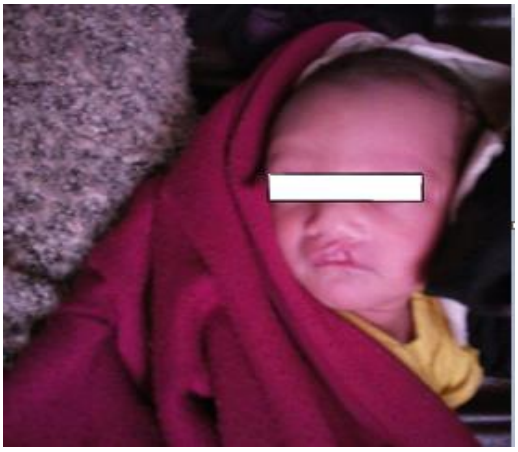

Figure 3: A photographs of a newborn with unilateral (left) cleft lip with unspecified cleft palate delivered at JUMC, Jimma, Southwest Ethiopia, 2018

Probably chromosomal anomaly was also observed in two (2/31, 6.4%) neonates: one female and one male. This was based on typical appearance of these infants with characteristic features of Down syndrome including low set small ears, long flat face, epicanthal folds, simian creases and diagnosed clinically to have downs syndrome (multiple anomaly).GI system anomaly (imperforate anus) was least observed in one (1/31, 3.2%) case only as indicated in Table 3.A male neonate with omphalocele measuring 5x6cm, covered by thin glassy membrane was also found. The photograph of this infant is shown below in Figure 4b.

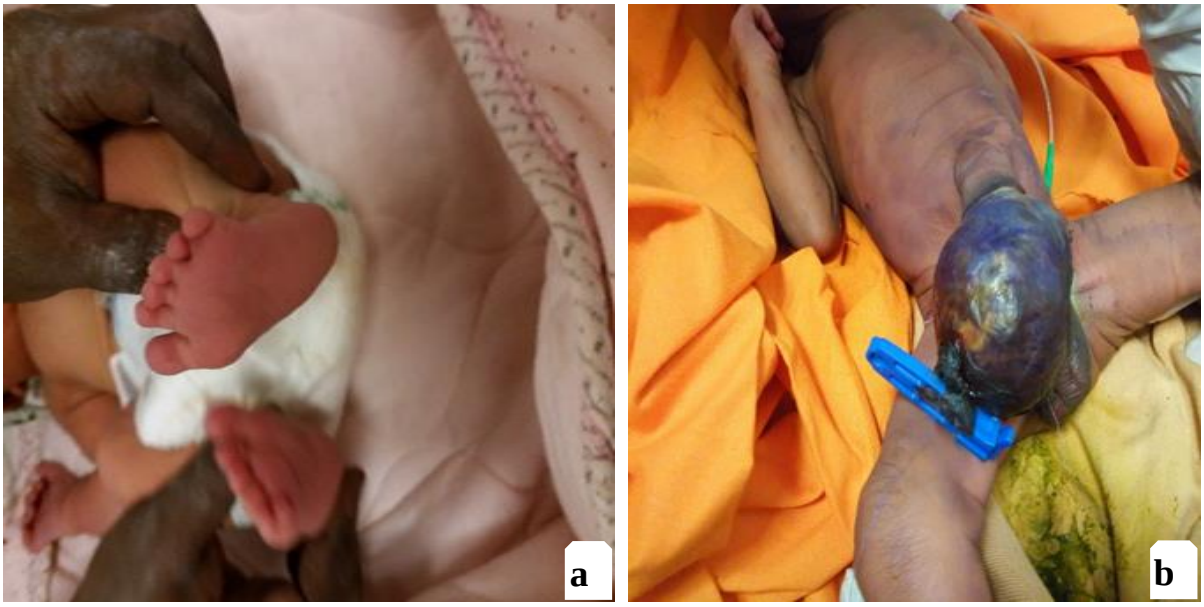

Figure 4: Photographs of newborns with typical example of musculoskeletal anomaly, Polydactyly (a) in this case, and GI anomaly specifically Omphalocele (b) delivered at JUMC, Jimma, Southwest Ethiopia, 2018

From the total 754 births, the prevalence of congenital anomalies varies greatly among live and still births. About 70% of anomalies were found in still births.

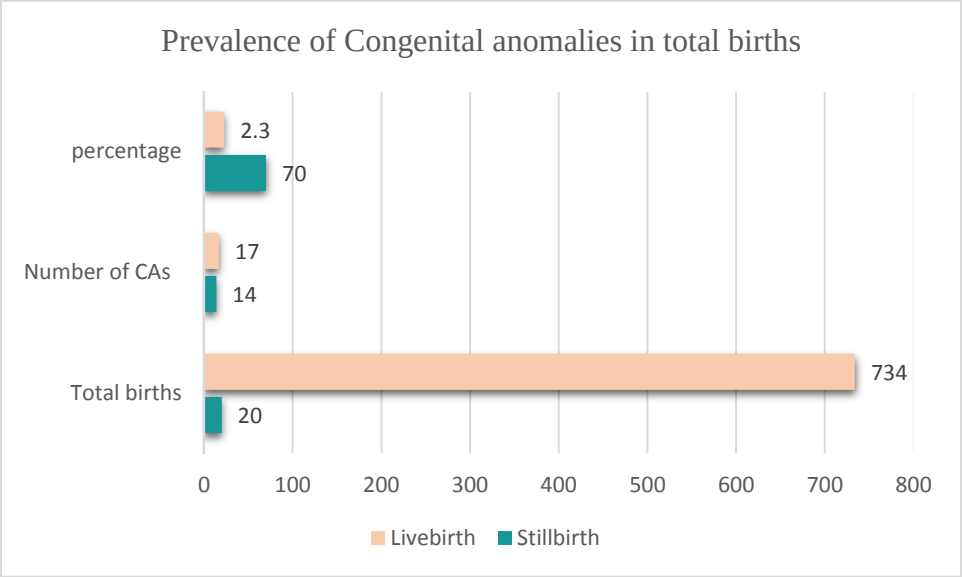

Figure 5: Distribution of overt congenital anomalies among neonates delivered at JUMC, 2018

5.5. Obstetric related maternal health characteristics

About three-fourth 570(75.6%) of mothers were multigravida. 546 (72.4%) of pregnancies were planned. Less than half 348 (46.2%) of deliveries were spontaneous. Only 6 (0.8%) and 60 (8%) of mothers had a previous self-history of congenital anomalies and a history of spontaneous abortion respectively. Mothers who had previous history of stillbirth, anemia were reportedly account 50(6.6%) and 60(8%) of cases respectively.

Only 160 (21.2%) and 108 (14.3%) of mothers had a complication during current pregnancy and chronic illness before conception respectively. Majority 119 (74.3%), 53(49%) of mothers had infections and hypertension with diabetes mellitus respectively. A family history of congenital anomalies was found in 15(2%) of mothers. About 30(4%) of mothers had previous history of twin pregnancy and 42(5.6%) had history of infant death. Majority 692 (91.8%) of mothers attended ANC visits. From those mothers about 386 (55.2%) of them attended two to three times, and majority 286 (41.3%) of them initiated their visit during the 1st trimester. High proportion 428(56.8%) of mothers had MUAC of <23cm.

Almost half 374 (54%) of mothers attended care in the health center. Total number of living children was 1-2 in 328(43.5%) of participants and almost 494 (65.5%) of mothers used

modern contraception before current pregnancy. Majority 451(91.2%) of mothers stopped to use contraceptive more than three months before pregnancy onset. Most 668(88.5%) of the mothers were Rh positive and Injectable were most widely used by 212 (43%) of mothers. Interpregnancy interval of 23 months and less was reported in 474(63%) of mothers. About 60 (8%) of mothers used unknown medications during early pregnancy as indicated in Table 4.

Table 5: Obstetric related maternal health characteristics at JUMC, 2018

Variables (N= 754)	**Frequency (%)**
Gravidity	
Primigravida	184(24.4)
Multigravida	570(75.6)
Condition of pregnancy	
Planned	546(72.4)
Unplanned	208(27.6)
Type of Birth	
Livebirth	734(97.3)
Still birth	20(2.7)
Past self-history of CAs	
Yes	6(0.8)
No	748(99.2)
History of elective termination	
Yes	2(0.3)
No	752(99.7)
History of spontaneous abortion	
Yes	60(8)
No	694(92)
Previous history of still birth	
Yes	50(6.6)
No	704(93.4)
Previous history of twin pregnancy	
Yes	30(4)
No	724(96)
History of infant death	
Yes	42(5.6)
No	712(94.4)
Total number of living children	
None	184(24.4)
1-2	328(43.5)
≥3	242(32.1)
ANC follow up	
Yes	692(91.8)
No	62(8.2)
No of ANC visits	
1 time	50(6.6)
2-3 Times	386(51.2)
≥4 times	256(34)

Table 4. Cont.

Variables (N= 754)	Frequency (%)
Complication during current pregnancy	
Yes	160(21.2)
No	594(78.8)
Types of complication	
	10(6.4)
Preeclampsia	119(74.3)
Maternal infection	31(19.3)
Antepartum hemorrhage	
Middle upper arm circumference	
<23cm	428(56.8)
≥ 23cm	326(43.2)
Maternal chronic illness	
Yes	108(14.3)
No	646(85.7)
Type of chronic illness	
Hypertension	34(31.4)
Diabetes	21(19.4)
Hypertension with diabetes	53(49)
Family History of CAs	
Yes	15(2)
No	739(98)
History of anemia in current pregnancy	
Yes	60(8)
No	694(92)
RH status of mother	
Positive	668(88.5)
Negative	86(11.4)
Modern contraceptive use before current pregnancy	
Yes	494(65.5)
No	260(34.5)
Type of FP used	
Injectables	212(43)
Pills	142(28.7)
Implant	50(10.1)
IUCD	34(6.9)
Others*	56(11.3)
When did you stopped using contraceptive method?	
0-3 months before pregnancy onset	43(8.7)
>3months before pregnancy onset	451(91.2)
Interpregnancy interval	
≤23 months	474(63)
> 23 months	280(37)
Unknown medication intake in early pregnancy	
Yes	60(8)
No	694(92)

* condom

5.6. Behavioral and nutritional characteristics

About 120(15.9%) of mothers had history of alcohol consumption during early pregnancy and from them 87(72.5%) of mothers drank alcohol sometimes and one tenth 78 (10.3%) of mothers were passive smokers. About 126(16.7%) of mothers had history of khat use and most 60(47.6%) of them chew khat sometimes. Only 160 (21.2%) of mothers had received folic acid during pregnancy. Less than half 290 (38.5%) of mothers consumed fruit daily and almost one-third 252 (33.4%) of them ate vegetables rarely as indicated in Table 5.

Table 6: Behavioral and nutritional characteristics of delivered mothers at JUMC,2018

Variables (N= 754)	Frequency (%)
History of maternal alcohol use during pregnancy	
Yes	120(15.9)
No	634(84.1)
How often mother drinks alcohol per month	
Daily	10(8.3)
Sometimes	87(72.5)
Rarely	23(19.2)
History of maternal smoking during Pregnancy	
Current	40(5.4)
Former	56(7.4)
Passive	78(10.3)
Never	580(76.9)
History of maternal Khat chewing during pregnancy	
Yes	126(16.7)
No	628(83.3)
How often did you chew?	
Sometimes	60(47.6)
Daily	20(15.8)
Rarely	46(36.6)
History of folic acid intake	
Yes	160(21.2)
No	594(78.8)
How often did you consume fruits?	
Sometimes	224(29.7)
Daily	290(38.5)
Rarely	222(29.4)
Not	18(2.4)
How often did you consume vegetables?	
Sometimes	250(33.2)
Daily	232(30.8)
Rarely	252(33.3)
Not	20(2.7)

5.7. Environmental characteristics

Only 96(12.7%) and 84(11.1%) of mothers and fathers had exposure to x- ray radiation respectively. Majority 408 (54.1%) of mothers used wood as a source of energy for cooking and about 84 (11.1%) of mothers had exposure to pesticide as indicated in Table 6.

Table 7:Environmental exposure characteristics of mothers and fathers at JUMC,2018

Variables(N=754)	Frequency (%)
Maternal exposure to x-ray radiation	
Yes	96(12.7)
No	658(87.3)
Paternal exposure to x-ray radiation	
Yes	84(11.1)
No	670(88.9)
Source of energy for cooking	
Coal	214(28.4)
Wood	408(54.1)
Stove	132(17.5)
Maternal exposure to pesticide	
Yes	84(11.1)
No	670(88.9)

5.8. Factors associated with congenital anomalies

Congenital anomalies were seen more commonly (6.5%) in the primigravida. The prevalence of congenitally anomalous babies born was 6.09% for mothers ≤20 years, 0.7% for 21-34years and 22.4% for ≥35 years. The proportion of congenital anomaly among very low birth weight neonates was higher (33%) but lower cases were observed among those who were post term (0.8%). From all neonates with overt anomalies, Majority (38.7%) of neonates with congenital anomalies were first order. Among all spontaneously delivered neonates about 7.1% of cases had birth defects.

The prevalence of CAs among those mothers who used folic acid was 1.25%. Cases of congenital anomalies were found to be 10.3% in khat chewers, about 5% in alcohol drinker mothers, 5.1% in passive smokers and about 21.6% in those who had history of unknown medication use in early pregnancy. Among all mothers with chronic illness about 15.7% of them gave birth to malformed babies.

Thirteen variables found to be associated in crude analysis variables and this factors were: Inter pregnancy interval (COR = 1.73, 95% CI :0.8,4.1), gravidity (COR=2.0, 95% CI: 0.91,4.1),number of ANC visits (COR = 4.22, 95% CI :1.39,12.77),initiation of 1st ANC visit (COR = 2.8, 95% CI :0.62,12.9),history of maternal exposure to pesticide (COR = 1.98, 95% CI :0.76,4.77),birth order (COR = 2.31, 95% CI :0.97,5.46),unknown medication use during early pregnancy (COR = 10.3, 95% CI :5.3,24.43), folic acid use (COR = 0.24, 95% CI :0.04,0.76), sex of neonate (COR = 1.16, 95% CI :0.75,3.25),history of maternal khat chewing in early pregnancy(COR = 3.9, 95% CI :2.09,8.91), maternal chronic illness(COR = 8.4, 95% CI :3.45,9.09) and total number of living children (COR = 0.51, 95% CI :0.19,1.31),mothers with hypertension and diabetes(COR = 1.7, 95% CI :0.51,2.31) as indicated in table 7.

5.9. Independent Predictors of congenital anomalies

After adjusting for all the variables in a logistics regression analysis, whose value was less than 0.25 in crude odds ratio were entered into the multivariable logistic regression model to observe exposure variables. Those with p-value < 0.05 were considered as statistically significant. The factors independently associated with congenital anomalies were: mothers who had history of unknown medication use during early pregnancy were 15.1 times more likely to have neonates with congenital anomalies compared to those who did not use unknown medication. (AOR = 15.1, 95% CI :5.51,40.2).

Mothers who had history of khat use during early pregnancy were 3.4 times more likely to have babies with congenital anomalies than non-chewers (AOR = 3.4, 95% CI :1.46,7.95) and mothers who had chronic illness were 4.3 times more likely to have malformed babies than those without illness (AOR = 4.3, 95% CI :1.65,11.37) and those mothers who took folic acid before and during pregnancy were 82% less likely to have babies affected by congenital anomalies compared to non-users (AOR = 0.18; 95% CI:0.02,0.92) as indicated in Table 7.

Table 8: Bivariate and multivariate analysis factors associated with congenital anomalies among neonates delivered at JUMC, 2018

Variables		Congenital anomalies		Bivariate Analysis		Multivariate analysis	
		Yes	No	COR (95% CI)	P- value	AOR (95% CI)	P-value
Maternal age (years)	≤ 20	5	77	1	1		
	21 ─34	4	570	0.53 (0.14-1.97)	0.335		
	≥ 35	22	76	1.06 (0.36-3.16)	0.912		
Birth weight	VLBW	1	2	2.1 (0.16-2.57)	0.572		
	LBW	9	37	5.8 (1.3-11)	0.271		
	NBW	19	602	3.4 (1.2-4.5)	0.314		
	HBW	2	82	1	1		
Type of chronic illness	Hypertension	8	26	1	1	1	1
	Diabetes	5	16	4.5(2.3-6.82)	0.682	2.5 (0.5-3.61)	0.542
	Both	18	35	3.2(1.2-4.1)	0.236	1.7 (0.5-2.31)	0.084
Interpregnancy interval	≤ 23months	23	451	1	1	1	1
	>23months	8	272	1.73(0.8-4.1)	0.158	0.37 (0.13-1.09)	0.075
Gestational age	Term	24	478	1	1		
	Preterm	6	123	1.1(0.4-2.5)	0.951		
	Post term	1	122	6.1(0.8-4.2)	0.702		
Gravidity	Primigravida	12	172	1	1	1	1
	Multigravida	19	551	2(0.91-4)	0.083	0.34 (0.01-11.12)	0.551
History of maternal cigarette smoking	Current	1	39	0.4(0.02-7.16)	0.298		
	Former	1	55	0.14(0.01-1)	0.332		
	Passive	4	74	0.89(0.01-1.31)	0.546		
	Never	25	555	1	1		
Mode of delivery	SVD	25	323	1	1		
	Instrumental	2	196	1.5(1.7-3.2)	0.622		
	C/S	4	204	3.9(1.35-11.5)	0.427		
No of ANC visits	1 time	5	45	4.22(1.39-12.77)	0.011	0.85 (0.31-2.31)	0.753
	2-3 times	16	370	3.15(1.17-8.47)	0.356	0.35 (0.08-1.54)	0.165
	≥ 4 times	10	246	1	1		1
Initiation of 1st ANC visit	1st trimester	11	275	1	1	1	1
	2nd trimester	16	258	0.7(0.32-1.52)	0.377	0.33 (0.06-1.77)	0.192
	3rd trimester	4	128	2.8(0.62-12.9)	0.175	0.21 (0.04-1.13)	0.071
Maternal exposure to pesticide	Yes	6	78	1.98(0.76-4.77)	0.165	12.9 (0.91-32)	0.064
	No	25	645	1	1		
Paternal age	20-39 years	21	488	1	1		
	40-59 years	8	227	1.22(0.53-2.79)	0.632		
	≥ 60 years	2	8	0.17(0.03-0.86)	0.331		
Birth order	First order	12	172	1.77(0.74-4.19)	0.355	0.03(0.001-1.29)	0.078
	Second order	10	234	2.31(0.97-5.46)	0.015	0.07(0.005-1.17)	0.066
	Third & more	9	317	1	1		1
Maternal alcohol use	Yes	6	114	1.28(0.49-3.1)	0.625		
	No	25	609	1	1		
Maternal medication use	Yes	13	47	10.3(5.3-24.43)	0.001	15.1(5.51-40.2)	<0.000*
	No	18	676	1	1		
Folic acid use	Yes	2	158	0.24(0.042-0.76)	0.023	0.18(0.02-0.92)	0.003*
	No	29	565	1	1		1
Sex of neonate	Male	16	346	1	1		1
	Female	15	377	1.16(0.75-3.25)	0.224	1.92(0.81-4.58)	0.114
Length at birth	≤ 50 cm	30	601	6.1(0.8-8.2)	0.328		
	> 50 cm	1	122	1	1		
Maternal khat chewing	Yes	13	113	3.9(2.09-8.9)	0.001	3.41(1.46-7.95)	0.004*
	No	18	610		1		1
Maternal chronic illness	Yes	17	91	8.43 (3.45-9.09)	0.071	4.3(1.65-11.37)	0.031*
	No	14	632		1		1
Total living children	None	7	177	1	1		1
	1-2	14	314	0.51(0.19-1.31)	0.178	2.5(1.12-8.79	0.072
	≥3	10	232	1.21(0.53-2.75)	0.642	3.14(0.06-5.24)	0.063

* value statistically significant (P-value< 0.05) AOR- Adjusted Odds ratio COR- Crude odds ratio CI-Confidence interval 1- reference

6. DISCUSSION

The study determines the prevalence and factors associated with overt congenital anomalies among neonates delivered at JUMC. From a total of 754 delivered neonates, 31 (4.1%, 95%CI,2.8-4.7) had overt anomalies. According to the current finding the overall prevalence of overt congenital anomalies was 4.1 %. This finding was higher than a study done in Nepal (0.42%),Pakistan (1.9%),China (1.56%),Tanzania (0.28%), Southeast Nigeria (2.8%)and central and north-west Ethiopia (1.9%) (15,32,39–41,53,54). The possible reason for high prevalenceof congenital anomalies in the presentstudy may be explained thatsince the study is conducted in a referral hospital, hospital-based studies tend to overestimate the prevalence and also thedifference could be due to that this study included both live and stillbirths but other studies might exclude stillbirths.

The current finding was lower than previous studies from Korea (5.8%) and Northeast Ethiopia(8.4%)(9,32).The reason could be related to subsequent abortion and preference of home delivery by mothers may also play a role. The current finding shows that CNS was the most affected system 45.1%, followed by orofacial anomalies 25.8% and musculoskeletal system defects in 13% of cases. This findings were comparable with the study done in SriLanka suggesting that about 58% of anomalies were CNS in origin (47).The reason would probably be due to low folic acid usage during pregnancy in this study and the other possible reason might be different lifestyles and habits of mother in taking nutrition.

On the other hand, inconsistent results were reported from Egypt showing that the musculoskeletal system was most commonly affected in 23% of cases (49).Similar a study from Kenya contradicts with the current study, suggesting that the musculoskeletal system defects were the most common 33.9%, followed by 28.1% of the central nervous system defects (57) and similarly a previous study from Russia also reported a higher prevalence (8.7%), of congenital malformations and deformations of the musculoskeletal system (48). The differences in the prevalence of body systems may be due to genetic factors or the existence of multifactorial effects in the countries the studies were carried out.

Among the orofacial clefts, a bilateral cleft lip was the most frequently observed defect in this study. These results are inconsistent with the findings from Ghana by which 28.6% of cleft lip

were unilateral (50). The variation may be a genetic difference between the study populations. In the current study, about 96.7% of anomalies were major. however, a study conducted in Brazil showed that 66% of the malformations were minor (78). These widespread differences may be due to racial difference and the variations in criteria of classifying anomalies .Most of the congenital anomalies in this study were isolated birth defects (90.3%)however, the result disagrees with that of a study conducted in Egypt showing that 28.6% were multiple anomalies (49). The variation could be explained that clinical observation was used to diagnose anomalies in current study where as sophisticated modalities were used to diagnose internal anomalies by other studies.

In the present study, majority of neonates with birth defects were males. These finding is congruent with study done in California and Iraq (64,65). But inconsistent results were reported from north Iran by which 53.6% of female neonates affected at birth (24). The variation could be attributed to hormonal factors that tend to affect development. In this study 14.3% of mothers had chronic illness before conception and significant associations were noted with congenital anomaly. Similar associations were reported from Romania and Brazil (80,81).

These findings support the hypothesis that the embryopathy that is associated with PGDM is nonspecific and increase the likelihood that different signal transduction pathways and morphogenetic processes might be disturbed A possible model for the association of maternal hyperglycemia and neural tube defects has been proposed recently on the basis of animal studies. According to this model, maternal hyperglycemia results in increased glucose levels in the embryo and, consequently, biochemical abnormalities that increase oxidative stress. Oxidative stress results in inhibition of the Pax3 gene, which is a gene that is required for neural crest development. Inhibition of expressions of the Pax3 gene leads to depression ofp53-dependent cell death, which results in impaired normal neural tube closure (118).On the contrary, in India, no significant associations were found between maternal diabetes and the occurrence of congenital anomalies (87).The difference could be variations in the level of maternal glycemic control in the countries were the study was carried out. Chronic hypertension whether treated or not results in uteroplacental insufficiency which can lead to compromised blood flow to the developing fetus which if present in early pregnancy may, in turn, increase the risk for certain types of malformations (119).

In this study, 8% of mothers had taken unknown medication in early pregnancy and taking medication was an independent predictor of congenital anomalies. A similar association was reported in a study from Addis Ababa and Amhara region (94). Drugs taken by pregnant women can affect the fetus by acting directly on it, causing damage, abnormal development or death. They can alter the function of the placenta by constricting blood vessels thus reducing the supply of oxygen and nutrients to the fetus from the mother. The result is underweight, underdeveloped and may be an abnormally developed baby (120).On the other hand, Study conducted in Pakistan was not consistent with the present study that medication intake during pregnancy had no any significant association with the presence of congenital anomalies (8).The possible reason might be differences in gene susceptibility.

The current findings indicated that maternal age, smoking, alcohol consumption and a family history of congenital anomalies were not associated with congenital anomalies but these factors have previously been reported as risk factors for the occurrence of congenital anomalies including orofacial clefts (121) Ascertainment bias could have also affected the results due to non-reporting of family history because of shame.

In this study, 16.7% of mothers had a history of khat chewing during early pregnancy. History of khat chewing during early pregnancy was significantly associated with congenital anomalies. These agree with a study done in Yemen (122).An experimental study in rats has recently proved that khat can affect intrauterine fetal growth by reducing total fetal fat and weight and by inducing changes in the chemical composition of fetal organs. This effect was attributed to depletion of carbohydrate material and suppression of DNA and protein synthesis in the fetal organs (123). Animal models reported that Khat had a genotoxic effect. They observed also retarded fetal growth and induced musculoskeletal abnormalities in a dose-dependent manner (124).

Even if only 21.2% of mothers were users of folic acid during pre or periconceptionally, folic acid use was found to be protective for the occurrence of congenital anomalies in this study. A Similar association was reported in the Tanzanian study (125). Several studies have shown that folic acid reduces the occurrence of some congenital anomalies such as neural tube defects, orofacial clefts, limb reduction defects, and omphalocele (126).

Folic acid is necessary for the growth and smooth function of human cells, as it is crucial for the biosynthesis and methylation of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)This is important for cell division, differentiation and regulation of gene expression, especially at a time of rapid cell division like during embryogenesis (127).

Limitation of the Study

- Inferring casual association is difficult due to the cross-sectional nature of the study.
- Only cases with visible birth defects were included by which internal anomalies may be missed.
- Different types of birth defects can have different causes and arise through several different biologic pathways and importantly anomalies of different systems may differ etiologically and biologically, the paternal and environmental characteristics associated with different clusters of anomalies were not assessed in this study;
- Institutional nature of the study over a shorter period of time may also hinder generalizability of the findings.

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

Based on the finding of this study, the prevalence of overt congenital anomalies was found to be 4.1%. Major and isolated birth defects predominate in the current study. CNS anomalies were the most prevalent followed by orofacial and musculoskeletal system defects. Unknown medication use, history of maternal khat chewing during early pregnancy and maternal chronic illness before conception were the identified risk factors for the occurrence of congenital anomaly. Folic acid use was found to be protective factor.

7.2. Recommendation

Based on the findings the following recommendations were made.

- Jimma university medical center should
  - ✓ Promote screening and treatment of pregnant mothers for chronic illness like hypertension and diabetes mellitus.
  - ✓ Place women with diabetes under strict glycemic control prior to conception continuing through gestation would be mandatory and encouraging risky hypertensive and diabetic mothers to frequently attend visits to health professionals.
  - ✓ Mobilize health professionals to give health education to mothers about impact of khat chewing during early pregnancy.
- Jimma town health office in collaboration with ministry of health should educate mothers about the risk of taking unknown medication during early/throughout pregnancy.
- Federal ministry of health should strictly follow health care professionals to stick to the recommended guideline of supplementation of folic acid as it is required to reproductive age groups, particularly around conception and during early pregnancy.
- The preliminary findings in the current study should be validated through multi-centered population based longitudinal studies

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ANNEX I: PARTICIPANT'SCONSENT FORM

Hello. My name is _____. I am data collector on research working on prevalence and factors associated with overt congenital anomalies among neonates delivered at Jimma university medical center. The information that we collect will help policy makers, and other stakeholders to plan and intervene on birth defects. The questions usually take about 15 to 20 minutes. All of the answers you give will be kept confidential and will not be shared with anyone. Photos of cases may be taken after an agreement was reached. You don't have to be in the survey, but we hope you will agree to answer the questions since your views are important. If I ask you any question you don't want to answer, just let me know and I will go on to the next question or you can stop the interview at any time. In case you need more information about the survey, you may contact the principal investigator whose number written on the bottom of the consent paper.

VOLUNTARYPARTICIPATION

Your participation in this study is voluntary. It is up to you to decide whether or not to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will not affect the relationship you have, if any, with the researcher. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

CONSENT

I have read and I understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study.

- Date of interview……. Signature ----------
- Interviewer name……. Code ----------

Bekalu Getachew

Tel no: +251920447821

Thank you for your participation!!

ANNEX II: ENGLISH VERSION QUESTIONNAIRE

Part I: Sociodemographic Characteristics			
Q1.	Age of the mother	…… ……..	
Q2.	Marital status	1. Married 2. Widowed 3. Divorced 4. Single	
Q3.	Religion of the mother	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 5. Others specify……	
Q4.	Mother's education	1. Illiterate 2. Primary education 3. Secondary education 4. Collage and above	
Q5.	Mother's ethnicity	1. Oromo 2. Amhara 3. Gurage 4. Kaffa 5. Others specify……..	
Q6.	Mothers occupation	1. Housewife 2. Farmer 3. Government employee 4. Non-governmental employee 5. Merchant	
Q7.	Residence	1. Urban 2. rural	
Q8.	Blood relation of parents	1. Yes 2. No	
Q9.	Fathers occupation	1. Farmer 2. Merchant 3. Government worker 4. Non-governmental worker 5. Daily laborer	
Q10.	Age of the father	……..……..	
Q11	Religion of husband	1. Orthodox 2. Muslim 3. Protestant 4. catholic	
Q12	Family size	…….	
Q13	Family income	……ETB	

	Part II: presence of overt Congenital anomalies		
Q14.	Is there visible birth defect	1. Yes 2. No	
	If yes to Q14, Specify on the types of anomalies		
	Encircle on the following listed anomalies		
Q15.	Congenital malformations of the nervous system		Detail description
		Craniorachischisis	
		Iniencephaly	
		Encephalocele	✓ Frontal ✓ Occipital
		Congenital hydrocephalus	
		Anencephaly	
		Spina bifida only ✓ Myelocele ✓ Meningomyelocele ✓ meningocele Spina bifida with hydrocephalus	Locations o Lumbar o Sacral o Cervical o Thoracic
Q16.	Orofacial clefts	Cleft palate only	✓ Cleft soft and hard palate ✓ Unspecified cleft palate ✓ Cleft hard palate
		Cleft lip only	o Unilateral o Bilateral
		Cleft palate and cleft lip	o Unspecified cleft palate with bilateral cleft lip

			○ Cleft soft and hard palate with unilateral cleft lip ○ Cleft hard palate with unilateral cleft lip
Q17.	Congenital malformations and deformations of the musculoskeletal system		✓ Talipesequinovarus ✓ Gastroschisis ✓ Omphalocele ✓ Polydactyl ✓ Reduction defects of upper limb ✓ Reduction defects of lower limb ✓ Reduction defects of unspecified limb
Q18.	Congenital malformations of genital organs		✓ Hypospadias ✓ Undescended testes ✓ Epispadias's
Q19.	Other malformations		

Part III: Maternal and obstetric related factors			
Q20.	Gravidity	1. Primigravida 2. Multigravida	
Q21.	Mode of delivery	1. VSD 2. Instrumental 3. Cesarean section	
Q22.	Condition of pregnancy	1. planned 2. unplanned	
Q23.	Type of birth	1. Livebirth 2. Still birth 3. Twin birth	
Q24.	History of Elective termination	1. Yes 2. No	If no, go to Q26
Q25.	If yes, to Q 24 mention the reason		
Q26.	Past self-history of congenital anomalies	1. Yes 2. No	
Q27.	History of Miscarriage (spontaneous abortion)	1. Yes 2. No	
Q28.	Previous history of still birth	1. Yes	

		2. No	
Q29.	Previous history of twin pregnancy	1. Yes 2. No	
Q30.	Previous neonate/infant/ child death	1. Yes 2. No	
Q31.	Total number of living children		
Q32.	ANC follow up	1. Yes 2. No	If no, go to 36
Q33.	No of ANC Visits	1. 1 time 2. 2-3 times 3. > 4 times	
Q34.	Time of 1st ANC visit	1. 1st trimester 2. 2nd trimester 3. 3rd trimester	
Q35.	Place of ANC follow up	1. Health center 2. Hospital 3. Health post	
Q36.	Complications during current pregnancy	1. Yes 2. No	If no go to, Q38
Q37.	If yes,	1. Pre-eclampsia 2. Oligohydramnios 3. Polyhydramnios 4. Maternal infections 5. Fever 6. Syphilis 7. Antepartum hemorrhage 8. Other specify	
Q38.	Maternal chronic illness before conception	1. Yes 2. No	
Q39.	If yes to Q38, type of illness	1. Hypertension 2. Diabetes mellitus 3. Both hypertension and diabetes 4. Others specify…..	
Q40.	Family history of anomalies	1. Yes 2. No	
Q41.	History of anemia during pregnancy	1. Yes 2. No	
Q42.	MUAC in cm		
Q43.	RH status	1. Positive 2. Negative	

Q44.	Modern contraceptive before current pregnancy	1. Yes 2. No	IF no skip to Q 47
Q45.	Type of family planning Used before current pregnancy	1. Injectable 2. Pills 3. Implant 4. IUCD 5. others	
Q46.	If yes to Q 45,when did you stopped using contraceptive	…….. Months	
Q47.	Inter pregnancy interval	……In months/years	
Part IV: Behavioral factors			
Q48.	History of maternal alcohol use during early pregnancy	1. Yes 2. No	If no, go to Q 50
Q49.	If yes to Q 48, how often did you drink	1. Daily 2. Occasionally 3. rarely	
Q50.	History of maternal Smoking during early pregnancy	1. Current 2. Never 3. Passive 4. former	
Q51.	History of maternal Khat chewing in early pregnancy	1. Yes 2. No	If no, go to Q 53
Q52.	If yes to Q 52, How often do you chew	1. Daily 2. Occasionally 3. rarely	
Q53.	History of unknown medication use in early pregnancy	1. Yes 2. No	
Part VI: Nutritional factors			
Q54.	Mother took folic acid during peri or preconceptionally	1. Yes 2. No	
Q55.	How often a mother consumes Vegetable per week	1. Sometime 2. Daily 3. Rarely 4. Not at all	
Q56.	How often a mother consumes Fruit per week	1. Sometimes 2. Daily 3. Rarely	

		4. Not at all	
Part VI: Environmental factors			
Q57.	History of maternal exposure to x ray radiation in early pregnancy	1. Yes 2. No	
Q58.	History of father exposure to radiation before conception	1. Yes 2. No	
Q59.	Source of energy for cooking	1. Coal 2. Wood 3. Stove 4. Others specify	
Q60.	History of maternal exposure to certain pesticides in early pregnancy	1. Yes 2. No	
Part VII: Neonatal factors			
Q61.	Weight at birth (kg)		
Q62.	Birth order	1. First order 2. Second order 3. Third and above	
Q63.	Sex of neonate	1. Male 2. Female 3. Ambiguous 4. undetermined	
Q64.	Length at birth (in cm)		
Q65.	Gestational age	1. Term 2. Preterm 3. post term	
Q66.	Head circumference (in cm)		
	Is photograph taken	1. Yes 2. No	
	If yes image no		

ANNEX III: AMHARIC VERSION CONSENT FORM

የመረጃ መሰብሰቢያ ቅጽ

በጅማዩኒቨርሲቲየሕክምናማዕከልውስጥበሚወለዱሕፃናትላይየልደትጉድለትዙሪያለሚያካሂዱየመረጃሰብስቦችእኔየጥሬመረ

ጃሰብሳቢነኝ. የምንሰበስበውመረጃበፖሊስአውጭዎች, እናሌሎችባለጉዳዮችየልደትጉድለትላይእቅድለማውጣትእናጣልቃለመግባትያግዛቸዋል. ጥያቄዎቹብዙውንጊዜየሚወስዱትከ 15 እስከ 20 ደቂቃዎችነው. የሚሰጧቸውሁሉምመልሶችበሚስጢርይጠበቃሉእናከማንምጋርአይጋሩም. በጥናቱውስጥመሆንየለብዎትም,

ነገርግንየእርስዎአመለካከቶችአስፈላጊስለሆኑጥያቄዎችዎንለመመለስመስማማትዎንተስፋእናደርጋለን.

ለመመለስየማይፈልጉትንማንኛውምጥያቄከጠየቅሁብቻያሳውቁኝእናወደሚቀጥለውጥያቄእሄዳለሁወይምቃለመጠይቁንበማ ንኛውምጊዜማቆምይችላሉ.

ስለጥናቱተጨማሪመረጃከፈለጉበስምምነትወረቀትግርጌስርየተጻፈውንቁጥርዋናውንመርማሪውንያነጋግሩ.

በዚህጥናትውስጥያለዎትተሳትፎበፈቃደኝነትነው. በዚህጥናትውስጥለመሳተፍወይምላለመሳተፍለመወሰንየእርስዎውሳኔነው. በዚህጥናትለመሳተፍከወሰኑ, የስምምነትቅጽላይእንዲፈርሙይጠየቃሉ. የስምምነትቅጹንከፈረሙበኋላ, በማንኛውምጊዜእናያለአለመጠይቅዎለመውጣትነጻነዎት. ከዚህጥናትመውጣት, ካለዎት, ከተመራማሪውጋርያለዎትንግንኙነትአይነካም.

የመረጃአሰባሰብከመጠናቀቁበፊትከጥናቱከወጡምመረጃዎወደእርስዎይመለሳልወይምይደመሰሳል.

ስምምነት

እኔአንብቤያለሁእናየቀረበልኝንመረጃተረድቻለሁእናምጥያቄየመጠየቅእድልአግኝቻለሁ.

የእኔተሳትፎበፍቃደኝነትመሆኑንእናምንምሳንጠይቅእናሳንወጣበማንኛውምጊዜለመውጣትነጻነኝ.

የዚህንየስምምነትቅጽቅጂእንደሚሰጠኝይገባኛል. በዚህጥናትለመሳተፍበፈቃደኝነትተስማምቻለሁ

የቃለመጠይቁቀን .....ፊርማ ----------

የመረጃሰብሳቢውስም.....ኮድ ----------

በቃሉጌታቸው

ስልክቁጥር: +251920447821

ለተሳትፎዎእናመሰግናለን !

ክፍልአንድ ፡ ማህበራዊትውፊታዊባህርያት			
ተቁ 1	የእናትእድሜ		
ተቁ2	የጋብቻሁኔታ 1. ያገባች 2. መበለት 3. የተፋታች 4. ያላገባች		
ተቁ3	ሃይማኖት 1. ሙስሊም 2. ኦርቶዶክስ 3. ፕሮቴስታንት 4. ካቶሊክ 5. ሌሎች		
ተቁ4	የእናትየትምህርትሁኔታ 1. ማንበብናመጻፍአልችልም 2. የመጀመሪያደረጃትምህርት 3. ሁለተኛደረጃትምህርት 4. ኮሌጅእናበላይ		
ተቁ5	የእናትብሄር 1. ኦሮሞ 2. አማራ 3. ጉራጌ 4. ካፋ 5. ሌሎች		
ተቁ6	የእናትሥራ 1. የቤትእመቤት 2. ገበሬ 3. የመንግስትሰራተኛ 4. ነጋዴ 5. ሌላ ካለ ይግለጽ		
ተቁ7	የመኖሪያአድራሻ 1. ከተማ 2. ገጠር		
ተቁ 8	የወላጆችየደምትስስርአለ 1. አዎን 2. አይ		
ተቁ9	የአባትሥራ 1. ገበሬ 2. ነጋዴ 3. የመንግስትሠራተኛ 4. መንግስታዊያልሆነሠራተኛ 5. የቀንሰራተኛ		
ተቁ 10	የአባትዕድሜ		
ተቁ 11	የአባትሃይማኖት 1. ኦርቶዶክስ		

	2. ሙስሊም 3. ፕሮቴስታንት 4. ካቶሊክ		
ተቁ 12	የቤተሰብብዛት		
ተቁ 13	የቤተሰብገቢ		
ተቁ 14	በግልጽየሚታይየወሊድጉድለት 1. አዎ 2. አይ		
ተቁ 15	የዋናው የነርቭ ስርአት የወሊድጉድለት 1. ክራንዬሲኖስቶሲስ 2. ኢንሴፋሎሰሌ 3. ኢእንሴፋሊ 4. አኒንከፋሊ 5. ስፓይናቢፊዳ ብቻ 6. ስፓይና ቢፊዳና ሀይድሮሴፋለ 7. ሀይድሮሴፋለስ		
ተቁ 16	የአፍና የፌት አካባቢ ጉድለት 1. የከንፈር መሰንጠቅ 2. የላንቃ መሰንጠቅ 3. የላንቃመሰንጠቅና የከንፈርመሰንጠቅ		
ተቁ 17	የስጋና አጥንት ተያያዠ የወሊድ ችግሮች 1. ታሊፕሰአኬኖቭረስ 2. ጋስትሮቺያሲስ 3. አምፋሎሰሌ 4. ፓሊዳክታሊት 5. የእጅ ጉድለት ችግር 6. የእግር ጉድለት ችግር 7. ያልታወቀ የእጅና እግር ችግር		
ተቁ 18	የብልት አካባቢ የወሊድ ጉድለት ችግሮች 1. ሀይፖስፓዲያሲስ		
ተቁ 19	ሌሎች የወሊድ ጉድለት ችግሮች		
ከፍል ሁለት : የእናትናከወሊድጋርየተገናኙጉዳዮች			
ተቁ20	አጠቃላይ የእርግዝና ሁኔታ 1. የመጀመሪያ 2. ባለብዙ		
ተቁ21	የወሊድ ዘዴ 1. በማህጸን 2. በመሳሪያ በመደገፍ 3. በአፕሬሽን		
ተቁ 22	የወሊድሁኔታ 1. የታቀደ 2. ያልታቀደ		
ተቁ 23	የወሊድአይነት 1. በህይወት ያለ		

	2. በህይወት የሌለ 3. መንታ		
ተቁ 24	የወሊድ የምርጫ ማቁረጥ 1. አዎ 2. አይ		አይ ከሆነ ወደ ተቁ 26 ይሂዱ
ተቁ 25	የየምርጫ ማቁረጥ ምክንያት		
ተቁ 26	የወሊድ ጉድለት ታሪክ 1. አዎ 2. አይ		
ተቁ 27	ከዚህ በፊት የጽንስ ማቋረጥ ታሪክ አለ 1. አዎ 2. አይ		
ተቁ 28	በህይወት የሌለ ልጅ ወልደዎያውቃሉ 1. አዎ 2. አይ		
ተቁ 29	ከዚህ በፊት መንታ ወልደውያውቃሉ 1. አዎ 2. አይ		
ተቁ30	ከዚህ በፊት ልጅ ሞቶቦት ያውቃል 1. አዎ 2. አይ		
ተቁ31	በህይወት ያሉ ልጆች ብዛት		
ተቁ 32	የወሊድ ክትትል አድርገሻል 1. አዎ 2. አይ		አይከሆነ፣ወደ 38ይሂዱ
ተቁ 33	የክትትል ብዛት 1. አንድ ግዜ 2. ከ ሁለት እስከ ሶስት 3. ከ አራት በላይ		
ተቁ 34	የመጀመሪያው ክትትል መቼ ጀመርሽ 1. መጀመሪያው ሶስት ወር 2. ሁለተኛው ሶስት ወር 3. ሶስተኛው ሶስት ወር		
ተቁ 35	በወሊድ ጊዜ ችግር ገጥሞሽ ነበር 1. አዎ 2. አይ		አይ ከሆነ፣ወደ 37 ይሂዱ
ተቁ 36	አዎ ከሆነ፣ 1. የደም ግፊት 2. የእሽልት ውሀ ማነስ 3. የእሽልት ውሀ መብዛት 4. አንፈከሽን 5. ትኩሳት 6. የአባላዘር በሽታ 7. ከወሊድ በፊት ደም መፍሰስ 8. ሌሎች		
ተቁ 37	የክትትል ቦታ 1. ጤና ጣቢያ 2. ሆስፒታል 3. ጤና ኬላ		
ተቁ 38	ተላላፊ ያልሆኑ በሽታዎች ታመው ነበር 1. አዎ		አይ ከሆነ ወደ ተቁ 40 ይሂዱ

	2. አይ		
ተቁ 39	የበሽታው አይነት 1. የደም ግፊት 2. ስኳር 3. የልብ ህመም 4. ሌሎች		
ተቁ40	በቤተሰብ የወሊድ ጉድለት ያለበት አለ 1. አዎ 2. አይ		
ተቁ41	በእርግዝናሽ ጊዜ የደም ማነስ አሞሽ ነበር 1. አዎ 2. አይ		
ተቁ42	ሙአክ (በሳሜ)		
ተቁ43	አርአች		
ተቁ44	ዘመናዊ የወሊድ መቆጣጠሪያ ተጠቃሚ ነዎት 1. አዎ 2. አይ		አይከሆነ፣ወደ47ይሂዱ
ተቁ45	የወሊድ መቆጣጠሪያ አይነት 1. መርፌ 2. የሚዋጥ ክኒን 3. በክንድ የሚቀበር 4. ማህጸን ውስጥ የሚቀመጥ 5. ሌሎች		
ተቁ46	ለ ጥያቄ ቁጥር 44፣አዎ ከሆነ፣ የወሊድ መቆጣጠሪያ መቼ መጠቀም አቆምሽ ወር/አመት		
ተቁ47	በእርግዝና መካከል ያለ ግዜ ወር/አመት		
ክፍል አራት: የስነምግባር ጉዳይ			
ተቁ48	እናቶችእርግዝናወቅትአልኮልይጠቀሙነበር 1. አዎ 2. አይ		አይከሆነ፣ወደ50ይሂዱ
ተቁ49	መልስዋለጥያቄቁ 48 አዎከሆነበየስንትጊዜይጠጡነበረ 1. በየቀኑ 2. አልፎአልፎ 3. ከስንትአንዴ		
ተቁ50	በእርግዝናዎትጊዜመቼሴጋራያጨሱነበረ 1. እስከአሁን 2. አጭሼአላቅም 3. በተዘዋዋሪ 4. ከዚህበፊት		
ተቁ51	በእርግዝናዎትጊዜጫትይጠቀሙነበረ 1. አዎ 2. አይ		አይከሆነ፣ወደ53ይሂዱ
ተቁ52	መልስዋለጥያቄቁ 51 አዎከሆነበየስንትጊዜይጠቀሙነበረ 1. በየቀኑ 2. አልፎአልፎ 3. ከስንትአንዴ		
ተቁ 53	በእርግዝናጊዜያልታወቁመድሀኒቶችንተተቀመሽነበር	1. አዎ 2. አይ	

ክፍልአምስት: የአመጋገብሁኔታዎች			
ተቁ54	በእርግዝናዎጊዜያልታወቁመድሃኒቶችወስደዋል. 1. አዎ 2. አይ		
ተቁ55	በእርግዝናዎጊዜፎሊክአሲድ / ቫይታሚንወስደዋል. 1. አዎ 2. አይ		
ተቁ56	እናቶችበእርግዝናጊዜአትክልትበየስንትግዜይመገቡነበር 1. አንድአንዴ 2. ቀንበቀን 3. ከስንትአንዴ 4. በፊጹም		
ተቁ57	እናቶችበእርግዝናጊዜፍራፍሬበየስንትግዜይመገቡነበር 1. አንድአንዴ 2. ቀንበቀን 3. ከስንትአንዴ 4. በፊጹም		
ክፍልስድስት:አካባቢያዊሁኔታዎች			
ተቁ58	እናት በእርግዝና ወቅት ለጨረር ተጋልጠው ነበር ı. አዎ 2. አይ		
ተቁ59	አባት ለጨረር ተጋልጠው ነበር ı. አዎ 2. አይ		
ተቁ60	ለምግብ ማብሰያ የሚጠቀሙት ı. ከሰል 2. እንጨት 3. የኤሌትሪክ ምድጃ		
ተቁ6ı	እናቶች በእርግዝና ጊዜ ለኬሚካል ተጋላጭ ነበሩ ı. አዎ 2. አይ		
ክፍልሰባት: የጨቅላ ህጻናት ሁኔታዎች			
ተቁ62	የህጻኑ ክብደት (በ ኪ.ግ)		
ተቁ63	የትውልድ ይዘት ı. የመጀመሪያ 2. ሁለተኛ 3. ሶስተኛ		
ተቁ64	የህጻኑ ጾታ ı. ወንድ 2. ሴት 3. አሻሚ 4. አልታወቀም		
ተቁ65	ርዝመት (ሳሜ)		
ተቁ66	የእርግዝና ጊዜ ı. በጊዜው የተወለደ 2. ከጊዜው ቀድሞ የተወለደ 3. ከጊዜው ካለፈ በኋላ የተወለደ		
ተቁ67	በወሊድ ጊዜ አቀራረብ		

	1. በጭንቅላት 2. በእግር 3. በፊት 4. በትከሻ		
ተቁ 68	የራስ ልኬት መጠን (ሳሜ)		
ተቁ 69	የወሊድ ጉድለቱ ፎቶ ተነስቷል 1. አዎ 2. አይ		
	የወሊድ ጉድለቱ ፎቶ ከተነሳ ቁጥር ይግለጹ		