Collage of Health Science

School of Medicine

Department of Pediatric and Child Health

Pattern and Factors associated with Congenital Anomalies among NICU admitted Neonates in TASH: Case-Control study

By: Hewan Asfaw (MD, Pediatric and Child Health Resident)

Advisor:

Dr. Edomgenet Tesfaye (M.D ,Assistant Professor of Pediatric and Child Health)

This research thesis is submitted to the Research and Community service office in partial fulfillment of the requirements for the Specialty for Certificate in Pediatrics and Child Health

March, 2024

ADDIS ABABA ETHIOPIA

Abstract:

Background: Congenital anomalies have imposed a sizable burden on global mortality, disability and medical cost worldwide. Several studies have investigated the risk factors attributed to lethal congenital anomalies

Objective: To assess pattern and associated factors of congenital anomalies, in neonatal intensive care unit, Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia 2023

Methodology: The case-control study was employed to investigate factors associated with congenital anomalies at Tikur Anbesa Specialized hospital. Cases included all newborns with congenital anomalies admitted to the ICU, while controls were randomly selected unmatched newborns without congenital anomalies. The normal distribution of continuous variables was assessed using Shapiro-Wilk test. The mean and standard deviation calculated for normality distributed data while median and interquartile range calculated for skewed data. A univariate and multivariate binary logistic regression analysis was performed to examine the factors associated Congenital anomalies. The results of logistic regression reported as adjusted odds rations (OR) with 95% confidence intervals and p-value < 0.05 are considered statistically significant.

Results: An analysis involving 131 cases and 128 controls revealed that the median age of mothers stood at 28(±IQR= 6) years. Respiratory anomalies were identified as the most common, accounting for 21.4 % of the cases, followed by multiple congenital anomalies at 20.6 %, and gastrointestinal anomalies at 19.8 % of cases. After adjusting for all variables in the multivariate analysis, folic acid supplementation was found to have a significant impact on preventing congenital anomalies (AOR=0.58, 95% CI 0.3, 0.99, p=0.032). Further analysis of the data revealed that maternal age over 35 years (AOR=2.3, 95% CI 0.8, 6.5, p=0.12), maternal smoking (AOR=6.7, 95% CI 0.8, 58.1, p=0.08), a history of previous congenital anomalies (AOR=2.1, 95% CI 0.4, 11.8, p=0.4), exposure to environmental toxins (AOR=0.2, 95% CI 0.3, 3.8, p=0.78), maternal alcohol consumption (AOR=2.4, 95% CI 0.6, 9.6, p=0.21), and maternal chronic medical conditions (AOR=1.8, 95% CI 0.7, 4.4, p=0.23) were non-statistical positive association with congenital anomalies.

Conclusion: Numerous factors have been linked to the occurrence of congenital anomalies. The pattern of these anomalies differed from those found in other local studies and global evidence, despite similar contributing and aggravating factors.

Acknowledgment

I would like to express my deepest gratitude to Addis Ababa University College of Health Sciences, Department of Pediatrics and Child Health for allocating the budget and giving me the chance to do this research. I would like to express my respect to my advisor Dr. Edomgenet Tesfaye M.D (Assistant professor of pediatrics and child health) for invaluable comments throughout the development of this proposal and her interest and readiness to help me until the end of the study.

Contents

List of Tables

Abbreviations and Acronyms

BDs	Birth Defects
Cas	congenital anomalies
CHD	congenital heart disease
CNS	Central nerves system
GIT	Gastrointestinal system
GUT	Genitourinary system
MCEE	maternal and child epidemiology estimation group
MRN	Medical record number
MSS	Musculoskeletal system
NICU	Neonatal intensive care unit
NTDs	Neural tube defects
OFAs	Oro facial anomalies
SPSS	Statistical package for social science
SS	Sub-Saharan Africa
WHO	World health organization

CHAPTER ONE: INTRODUCTION

1.1. Background

Congenital anomalies are a wide range of functional, behavioral, structural or metabolic anomalies that occur during prenatal development, which manifest prenatally, at birth, or even later in infancy(1, 2). Congenital anomalies stood as the fourth most prominent cause of death among children under age of 5 globally, representing for approximately 10% of all cases in 2019(3). This statistic underscores the profound impact of these anomalies, not only in terms of immediate mortality but also their tendency to result in long-term disabilities(1). The distribution of congenital anomalies displays a diverse pattern across different geographic regions and populations. Several studies have investigated the risk factors attributed to lethal congenital anomalies. According to the World Health Organization (WHO), factors such as genetic, environmental factors, sociodemographic factors, infections and unknown causes have all been identified as key contributors to the development of congenital anomalies(1). Nevertheless, around 50% of congenital disorders cannot be attributed to a specific cause(4). Other evidences stated that congenital anomalies (CAs) can result from genetic, multifactorial, or environmental influences. Approximately 20% of CAs are attributed to genetic factors, 10% to external factors, and the remaining 70% have a multifactorial origin(5). A meta-analysis of observational studies examined the associations between congenital anomalies and factors such as maternal folic acid supplementation, maternal illness, and maternal history of medication use during pregnancy(6). Many researchers examined on a set of significant birth abnormalities that are largely avoidable. These include congenital rubella syndrome, spina bifida and anencephaly preventable with folic acid, fetal alcohol syndrome, Down syndrome, and rhesus hemolytic disease of the fetus and newborn(7).

1.2. Statement of the problem

Congenital anomalies have imposed a sizable burden on global mortality, disability and medical cost worldwide(8). Studies analyzed the global burden of disease reported that the global incidence cases of congenital anomalies were approximately 8.5million in 2019, which was decreased by 0.44% for the last three decades(8). According to WHO reports in 2023, congenital birth disorder responsible for causing approximately 240,000 newborns globally within the first 28 days of life each year, and further these disorders were responsible for causing around 170,000 deaths among children aged 1 month to 5 years old(1). The impact and burden of congenital anomalies have disproportionately affected low and middle-income countries(1, 8, 9). Approximately 90% of children born in serious congenital disorder in low-middle income countries(1, 10, 11). An analysis of 25 studies conducted across in nine sub-Saharan African countries found that prevalence of birth defects was estimated to be around 20 per 1,000 births(6). Around 3-6% of newborns are born with congenital anomalies (CAs), which are a significant contributor to fetal death, infant mortality, and morbidity. It is estimated that approximately 21-25% of infant mortality cases are linked to congenital anomalies(5). Congenital anomalies pose a significant financial burden due to their disproportionately high medical costs, hospitalization rates, and impact on productivity(12, 13). This burden extends beyond just healthcare expenses, affecting various aspects of society and the economy(12, 13).

1.3. Significance of the study

The study on congenital anomalies and associated factors holds significant implications for various stakeholders in the healthcare sector, health equity advocates, policymakers, and researchers. The findings of this study are important for Healthcare Providers to understand the factors contributing to congenital anomalies can aid healthcare providers in improving the early detection, management, and treatment of affected individuals. This knowledge can enhance patient care, leading to better outcomes and quality of life for those with congenital anomalies. It is also important for Health Equity Advocators of Congenital Disease to identifying the factors associated with congenital anomalies, advocators can work towards ensuring that all individuals, regardless of socio-economic status or geographical location, have access to timely and appropriate healthcare services. This can help reduce disparities in the diagnosis and management of congenital anomalies. Healthcare Advocators of Congenital Anomalies Prevention can use the result of this study to promote preventive measures to reduce the incidence of congenital anomalies. This may include raising awareness about the importance of prenatal care, genetic counseling, and lifestyle modifications to minimize the risk of congenital anomalies. Policymakers can use the research findings to develop evidence-based policies and programs aimed at preventing and managing congenital anomalies. This may involve implementing screening programs, improving access to healthcare services, and allocating resources to support research and education initiatives related to congenital anomalies. The study also contributes valuable insights into the epidemiology and risk factors associated with congenital anomalies, providing a foundation for further research in this area. Researchers can build upon these findings to explore new avenues for prevention, treatment, and management of congenital anomalies, ultimately advancing the field of congenital anomaly research

CHPTER TWO: LITERATURE REVIEW

2.1. Burden of Congenital anomalies

Congenital anomalies are a wide range of functional, behavioral, structural or metabolic anomalies that occur during prenatal development, which manifest prenatally, at birth, or even later in infancy(1, 2). Congenital anomalies have imposed a sizable burden on global mortality, disability and medical cost worldwide(8). Studies analyzed the global burden of disease reported that the global incidence cases of congenital anomalies were approximately 8.5million in 2019, which was decreased by 0.44% for the last three decades(8). According to WHO reports in 2023, congenital birth disorder responsible for causing approximately 240,000 newborns globally within the first 28 days of life each year, and further these disorders were responsible for causing around 170,000 deaths among children aged 1 month to 5 years old(1). This data underscores the devastating impact of congenital disorders on infant and child mortality rates, highlighting the urgent need for continued efforts to address and prevent these tragic outcomes(1). Congenital anomalies stood as the fourth most prominent cause of death among children under age of 5 globally, representing for approximately 10% of all cases in 2019(3). This statistic underscores the profound impact of these anomalies, not only in terms of immediate mortality but also their tendency to result in long-term disabilities(1). The burden imposed by congenital anomalies extends far beyond individuals, affecting families, healthcare systems, and societies, highlighting the need for comprehensive strategies to address both the immediate and long-lasting effects of these conditions(1, 3). The impact and burden of congenital anomalies have disproportionately affected low and middle-income countries(1, 8, 9). Approximately 90% of children born in serious congenital disorder in low-middle income countries(1, 10, 11). An analysis of 25 studies conducted across in nine sub-Saharan African countries found that prevalence of birth defects was estimated to be around 20 per 1,000 births(6). Within high-income countries, the introduction of prenatal counseling, screening services, and the provision of termination of pregnancy for fetal anomalies (TOPFA) have played a crucial role in lowering the incidence and adverse outcomes of infants with congenital anomalies(11).Congenital is one health condition which need some surgical intervention. Congenital anomalies contribute to 9% of the surgical disease burden and pose a significant threat of morbidity and mortality to an estimated 150

million children globally if left untreated(9). It is noted that half of these congenital deformities can be remedied through surgical interventions(4). These nations often face significant challenges in terms of access to quality healthcare, diagnostics, and treatment options for congenital anomalies(1).

2.2. Pattern of congenital anomalies

The distribution of congenital anomalies displays a diverse pattern across different geographic regions and populations. The Global Burden of Disease analysis conducted in 2019 highlighted the significant impact of congenital birth defects on a global scale. Among these defects, Congenital heart anomalies emerged as the most prevalent category, representing a substantial portion of total incident cases and deaths at 36.63% and 39.49%, respectively. Following closely behind were congenital musculoskeletal and limb anomalies, which accounted for 26.99% of incident cases, and neural tube defects, which contributed to 24.19% of deaths related to congenital birth defects(8). A comprehensive meta-analysis spanning nine sub-Saharan African countries highlighted that musculoskeletal system defects had a combined prevalence of 3.9 per 1,000 births, ranking them as the most common anomalies. This was followed by neural tube defects at 2.98 per 1,000, cardiovascular system defects (CVSDs) at 2.8 per 1,000, and gastrointestinal defects at 1.50 per 1,000 births(6). Moreover, a separate meta-analysis conducted in low- and middle-income countries (LMICs) identified congenital heart disease, neural tube defects, and cryptorchidism as significant anomalies within these regions(9). The varying prevalence rates of these anomalies underscore the importance of understanding the unique epidemiological profiles of congenital anomalies in different settings, informing targeted interventions and public health strategies to address these conditions effectively. Research conducted at Jimma medical center in Ethiopia, involving 754 born neonate, found that Central nervous system accounted for 45% of cases, orofacial anomalies for 26%, and musculoskeletal anomalies for 13%(14). A study examining 1,518 children with congenital anomalies in Amhara and Addis Ababa revealed that the prevalence of neural tube defects accounted for 40%, orofacial clefts for 23%, musculoskeletal system anomalies for 23%, and syndromic disorders for 23%. The variation in the distribution of various patterns of congenital anomalies can be attributed to differences in the distribution of risk factors.

2.3. Risk factors

Several studies have investigated the risk factors attributed to lethal congenital anomalies. According to the World Health Organization (WHO), factors such as genetic, environmental factors, sociodemographic factors, infections and unknown causes have all been identified as key contributors to the development of congenital anomalies(1). Nevertheless, around 50% of congenital disorders cannot be attributed to a specific cause(4). A meta-analysis of observational studies examined the associations between congenital anomalies and factors such as maternal folic acid supplementation, maternal illness, and maternal history of medication use during pregnancy(6). A systematic review and meta-analysis involving 32 studies conducted in Africa, encompassing a total of 626,983 participants, revealed significant associations between various factors and congenital anomalies. The study highlighted that factors such as non-utilization of folic acid, maternal history of illness, maternal drug use, maternal age, alcohol consumption, khat chewing, and urban residency were notably correlated with the occurrence of congenital anomalies(15). In a study involving a total of 754 neonates at Jimma Medical Center found that factors associated with the presence of overt congenital anomalies included unknown medication use during early pregnancy, maternal history of khat chewing in early pregnancy, and maternal chronic illness before conception(14). The study also noted that the use of folic acid during the periconception period had a protective effect against overt congenital anomalies(14).

CHAPTER THREE: OBJECTIVES

3.1 General Objectives

- To assess pattern and associated factors of congenital anomalies, in neonatal intensive care unit, Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia 2023

3.2. Specific Objectives

- To identify patterns of congenital anomalies in NICU of TASH.
- To determine associated factors with congenital anomalies.
- To determine the outcome of neonates with congenital anomalies.

CHAPTER FOUR: METHODOLOGY

4.1. Study area and setting

The study was conducted at Tikur Anbessa specialized hospital at Neonatal intensive care unit Addis Ababa, Ethiopia. Tikur Anbessa Specialized Hospital, School of Medicine, College of Health Sciences, Addis Ababa University is the largest referral hospital in Ethiopia. It was established in 1964, and is now the main teaching center for both clinical and preclinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. The various departments, faculties and residents under specialty training in the School of Medicine provide patient care in the hospital. In addition, almost all regional and federal hospitals in Addis Ababa are affiliated to the School of Medicine as clinical services and training sites. NICU of this hospital has total of 41 beds and currently have provide treatment for around 2000 pt per year.

4.2. Study design

The case-control study was employed to investigate factors associated with congenital anomalies. Cases included all newborns with congenital anomalies admitted to the ICU, while controls were randomly selected unmatched newborns without congenital anomalies.

4.3. Study Period

- The study was conducted at TASH NICU from The study was conducted from July 1, 2023 - Dec 30, 2023

4.4. Population

4.4. 1. Source population:

- All neonates admitted to NICU during the study period

4.5 Study Population

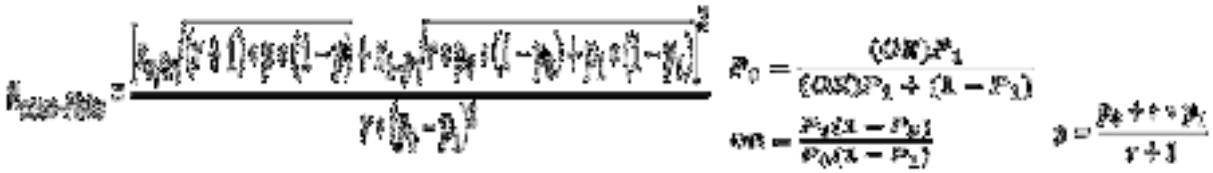
- Cases included all newborns with congenital anomalies admitted to the ICU, while controls were randomly selected unmatched newborns without congenital anomalies.

4.6. Sampling method:

The study employed a case-control design to explore factors related to congenital anomalies. Cases comprised all neonates with congenital anomalies admitted to the ICU during the study period. Controls were randomly selected without matching on the same day as the cases throughout the study period.

4.7. Sample size determination

A case-control study is being planned to investigate the relationship between factors and congenital anomalies. The study was comparing a sample of newborns admitted to the ICU with newly diagnosed congenital anomalies to newborns admitted to the ICU without congenital anomalies, who will serve as controls. The study comprised an equal number of cases and controls (r=1), with a sample size sufficient to detect an odds ratio of 2 (OR=2). Past studies have indicated that around 35.5% of cases utilize folic acid supplementation (p1=0.355). To achieve 80% power (1-β=0.8) at a significance level of 5% (α=0.05), the necessary sample size for both cases and controls was calculated to be 262 (131 cases and 131 controls).



P0 = The proportion for cases

P1 =The proportion for controls

OR = The calculated odds ratio

r = The ratio of case-control (1 case/r controls)

NFleiss = Required sample size for cases using Fleiss's formula

4.8. Inclusion and exclusion criteria

4.8.1. Inclusion criteria

- All neonates with external and internal congenital anomalies whether the anomalies were major or minor who were admitted during the study period

4.8.2. Exclusion criteria

- primary caregiver/parent who are not willing to participate in the study

4.9. Data collection and measurement

The structured questionnaire utilized in the study was crafted based on existing literature and encompassed sections on Sociodemographic data, associated risk factors and clinical profile. Prior to the primary data collection, the questionnaire underwent a pretest with 5% of the sample size to ensure the clarity and relevance of the questions. Data collection was conducted through face-to-face interviews. The principal investigator, one designated resident and 2 trained data collectors who received a brief explanation, carried out the data collection. The questionnaire covered sociodemographic characteristics, exposure to risk factors, and reproductive history.

4.10. Study Variables

4.10.1. Independent Variables

- Maternal age
- Paternal age
- Maternal chronic illness
- Maternal exposure for pesticides,
- Maternal alcohol
- Maternal tobacco smoking
- Parity
- Gestational age
- Sex of neonate

- Birth weight of the neonate
- Birth order

4.10.2. Dependent Variables

- **Case-control**

4.11. Data Analysis

The categorical variables in the study were presented with using frequency, percentage, and compared between groups using the chi-square test. The normal distribution of continuous variables was assessed using Shapiro-Wilk test. The mean and standard deviation calculated for normality distributed data while median and interquartile range calculated for skewed data. Multicollinearity test performed for categorical, continuous and binary variables. Multicollinearity measured by variance inflation factor (VIF) and tolerance. When a VIF was below five and tolerance was above 0.1, variables were forwarded to multivariable binary logistic regression analysis. Variables with a VIF score of ≥ 5 to 10 and tolerance below 0.1 were excluded from the final model. A univariate binary logistic regression analysis was performed to examine the factors associated Congenital anomalies. Variables with p-value 0.25 or less in the bivariate analysis were entered into the multivariable ordinal logistic model. A multiple binary logistic regression model was performed to assess independent association between factors and congenital anomalies. The results of logistic regression reported as adjusted odds rations (OR) with 95% confidence intervals and p-value < 0.05 are considered statistically significant.

4.12. Ethical Consideration

Ethical clearance to conduct this study was obtained from the pediatrics and child health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, Addis Ababa University. Confidentiality has been fully maintained during Data collection and further analysis and dissemination of results.

CHAPTER FIVE: RESULT

5. RESULT

In a comprehensive analysis involving 131 cases and 128 controls, several noteworthy patterns emerged. The examination of parental demographics revealed that the median age of mothers stood at 28(±IQR= 6) years, whereas fathers had a slightly higher median age of 31(±IQR-5) years. Gender distribution among neonates showcased a dominance of male infants, constituting 57.1% of the cases and a significant 83.8% of the individuals studied were urban residents. Delving into pregnancy-related insights, the analysis pointed out that multigravida, denoting women with multiple pregnancies, represented a substantial 69.5% of the cases. Furthermore, term pregnancies accounted for a notable 82.2% of the cases, indicating a prevalence of full-term gestations within the cohort. Respiratory anomalies emerged as the most prevalent, comprising 21.4 % of the cases, shedding light on the significance of respiratory health in the population under scrutiny. Multiple congenital anomalies were detected in 20.6 % of the cases, hinting at the complexity of certain cases involving multiple anomalies. Concurrently, 19.8 % of cases exhibited gastrointestinal anomalies, highlighting the presence of diverse gastrointestinal -related conditions within the studied population.

Table 1:Sociogemography characteristics and clinical profile of study participants at TASH, Ethiopia, 2024

Variable	Response	Frequency	Percentage
Age	Median ±IQR(Mother)	28±6	
	Median ±IQR(Father)	31±5	
Gende of neonate	Female	111	42.9
	Male	148	57.1
Residency	Rural	42	16.2
	Urban	217	83.8
Pregnancy type	Multiple	20	7.7
	Single	239	92.3
Parity	Multigravida	180	69.5
	Primigravida	79	30.5
History of previous congenital anomaly	No	251	96.9
	Yes	8	3.1
Environmental toxin exposure	No	238	91.9
	Yes	21	8.1
History of abortion or miscarriage	No	200	77.2
	Yes	59	22.8
Smoking	No	251	96.9
	Yes	8	3.1
Gestational age	post term	9	3.5
	preterm	37	14.3
	Term	213	82.2
ANC	No	28	10.8
	Yes	231	89.2
Folic acid	No	175	67.6
	Yes	84	32.4
Maternal alcohol	No	247	95.4
	Yes	12	4.6
Medication	No	242	93.4
	Yes	17	6.6
Outcome	Dead	39	15.1
	Improved	220	84.9

Table 2: Pattern of congenital anomalies in admitted in ICU at TASH, Ethiopia 2024

Congenital anomaly system		Frequency	Percentage
Cardiac		17	13
Multiple		27	20.6
CNS		7	5.3
GUT		9	6.9
GIT		26	19.8
Oropharyngeal		14	10.7
Respiratory		28	21.4
Chromosomal abnormality		3	2.3
Total		131	100
Multiple	Multiple	27	20.6%
Cardiac(N=17)	ASD	2	1.5
	AVSD	2	1.5
	ASD+VSD	3	2.3
	VSD+TGA	1	0.8
	PDA+ASD+TGA	2	1.5
	Other cardiac lesion	7	5.3
Respiratory (N=28)	TEF	26	19.8
	Tracheomalacia	1	0.8
	Diaphragmatic hernia	1	0.8
GIT(N=26)	ARM	4	3.0
	Gastroschisis	2	1.5
	Omphalocele	8	6.1
	Small intestine abnormalities	9	6.9
	HSD	3	2.3
CNS(N=7)	Spinal bifida	7	5.3
GUT(N=9)	PUJ	3	2.3
	Hypospadias's	3	2.3
	Blader exstrophy	1	0.8
	PPV	1	0.8
	Hydronephrosis	1	0.8
Oropharyngeal (N=14)	Cleft lip and Cleft Palat	6	4.6
	Conal atresia +Largomalcia	8	6.1
Chromosomal abnormalities	Chromosomal abnormalities	3	2.3

In the pursuit of unraveling factors linked to congenital anomalies, a thorough investigation employing both univariate and multivariate logistic regression analyses was conducted. In the initial phase of univariate analysis, various factors were considered, including maternal age, paternal age, maternal smoking, alcohol consumption, residency type, exposure to environmental toxins, folic acid supplementation, and chronic maternal health conditions. Following this preliminary screening, specific factors were chosen for further evaluation through multivariate analysis. Upon adjusting for all variables in the multivariate analysis, the impact of folic acid supplementation emerged as notably significant in preventing congenital anomalies (AOR=0.58 (95% CI 0.3, 0.99), p=0.032). Conversely, residing in a rural area exhibited a statistical association with neonates being born with congenital anomalies (AOR=2.5(1.1,5.8), p=0.03). Further exploration of the data revealed that maternal age exceeding 35 years (AOR=2.3, 95% CI 0.8, 6.5, p=0.12), paternal age over 40 years (AOR=1.5, 95% CI 0.7, 3.3, p=0.4), maternal smoking (AOR=6.7, 95% CI 0.8, 58.1, p=0.08), a history of previous congenital anomalies (AOR=2.1, 95% CI 0.4, 11.8, p=0.4), exposure to environmental toxins (AOR=0.2, 95% CI 0.3, 3.8, p=0.78), maternal alcohol consumption (AOR=2.4, 95% CI 0.6, 9.6, p=0.21), and maternal chronic medical conditions (AOR=1.8, 95% CI 0.7, 4.4, p=0.23) exhibited positive associations with congenital anomalies. However, these associations did not reach statistical significance, underscoring the intricate interplay of various factors in the development of congenital anomalies

Table 3: Univariate and multivariate binary logistic regression analysis to identify factors associated with congenital anomalies at TASH, Ethiopia 2024

Variable	Response	Cases	Control	COR	P	AOR	P
Mother age	below 35	109	119	1		1	
	above 35	22	9	2.7(1.2,6.05)	0.02	2.3(0.8,6.5)	0.12
Father age	Below 40	96	111	1		1	
	above 40	35	17	2.4(1.3 4.6)	0.008	1.5(0.7,3.3)	0.4
Residency	Rural	29	13	2.5(1.2,5.1)	0.01	2.5(1.1,5.8)	0.03*
	Urban	102	115	1			
Gender	Female	56	55	1			
	Male	75	73	1.0(0.62,1.7)	0.99		
Type of pregnancy	Multiple	12	8	1.5(0.6,3.8)	0.38		
	Single	119	120	1			
Hx of congenital	No	125	126	1		1	
	Yes	6	2	3.0(0.6 15.1	0.18	2.1(0.4,11.8)	0.4
Environmental toxin	No	116	122	1		2	
	Yes	15	6	2.6(1.0,7.1)	0.05	1.2(0.3,3.8)	0.78
Alcohol	No	122	125	1		1	
	Yes	9	3	3.1(0.8,11.6)	0.098	2.4(0.6,9.6)	0.21
Hx of abortion	No	94	106	1		1	
	Yes	37	22	1.9(1.04,3.4)	0.035	1.4(0.7,2.7)	0.32
Smoking	No	124	127	1			
	Yes	7	1	7.2(0.9,59.2)	0.02	6.7(0.8,58.1)	0.08
GA	Post term	5	4	1			
	Preterm	21	16	1.0(0.24,4.5)	.948		
	Term	105	108	0.8(0.2,2.9)	.714		
Folic acid	No	98	77				
	Yes	33	51	0.5(0.3,0.8)	0.012	0.58(0.3,0.99)	0.032*
Chronic illness	No	116	119	1			
	Yes	15	9	1.7(0.7,4.1)	0.22	1.8(0.7 4.4)	0.23
Birth order	1	38	41	1			
	2	40	46	0.8(0.4,1.7)	.557		
	3	32	23	0.7(0.34,1.6)	.448		
	4 and above	21	18	1.2(0.5,2.7)	.676		
Weight of neonate	LBW	43	31	1.5(0.9,2.6)	0.16	1.6(0.8,2.9)	0.14
	Normal	88	97	1			

CHPTER SIX: DISCUSSION AND RECOMMENDATION

6.1. Discussion

This case-control study delves into the patterns and associated risk factors that play a role in the development of congenital anomalies. Our research highlights that respiratory anomalies were the most frequently observed, followed by gastrointestinal congenital and cardiac anomalies. These results diverge from previous studies conducted in Ethiopia(16), meta-analyses from sub-Saharan Africa(6), and global evidence(8), underscoring the need for further investigation and understanding of the factors contributing to these birth abnormalities. According to a global burden analysis, congenital heart anomalies, musculoskeletal and limb anomalies, and neural tube defects were the most common congenital anomaly cases worldwide in 2019 (8). Research conducted at Jimma medical center in Ethiopia, involving 754 born neonate, found that Central nervous system accounted for 45% of cases, orofacial anomalies for 26%, and musculoskeletal anomalies for 13%(14). A study examining 1,518 children with congenital anomalies in Amhara and Addis Ababa revealed that the prevalence of neural tube defects accounted for 40%, orofacial clefts for 23%, musculoskeletal system anomalies for 23%, and syndromic disorders for 23%(17).

The geographical differences in the prevalence of congenital anomalies may be attributed to variations in the distribution of risk factors and environmental influences. These factors can play a significant role in shaping the occurrence and severity of congenital anomalies across different regions. Several studies have investigated the risk factors attributed to lethal congenital anomalies. According to the World Health Organization (WHO), factors such as genetic, environmental factors, sociodemographic factors, infections and unknown causes have all been identified as key contributors to the development of congenital anomalies(1). The results of this research indicated a significant role of folic acid supplementation in preventing congenital anomalies. These findings are in line with studies conducted in Ethiopia, Africa, and globally. A systematic review and meta-analysis of 32 studies involving 626,983 participants in Africa demonstrated significant links between various factors and congenital anomalies. The study

emphasized that the lack of folic acid utilization was associated with an increased occurrence of congenital anomalies (15). The case-control study conducted in seven hospitals in southwestern Ethiopia, involving a total of 1138 participants, revealed that folic acid supplementation was associated with a 57% reduction in the risk of congenital anomalies compared to those who did not take folic acid(16). Numerous observational studies and meta-analyses have highlighted the critical role of folic acid supplementation in preventing congenital anomalies, especially neural tube defects. These findings have led to strong international recommendations advocating for the supplementation of folic acid to reduce the risk of these birth defects. Our research findings suggest that advanced maternal and paternal age, maternal smoking, a history of prior congenital anomalies, exposure to environmental toxins, maternal alcohol consumption, and maternal chronic medical conditions may be linked to congenital anomalies. While our study did not find statistical associations between these factors and congenital anomalies, previous observational studies and meta-analyses have demonstrated significant statistical associations between these important factors and an increased risk of congenital anomalies(6, 15, 16, 18)

Conclusion: Numerous factors have been linked to the occurrence of congenital anomalies. The pattern of these anomalies differed from those found in other local studies and global evidence, despite similar contributing and aggravating factors.

6.2. Recommendation

It is crucial for healthcare providers to be aware of the varied patterns of congenital anomalies in different populations and regions. They should stay informed about the different factors that can contribute to the development of these anomalies, in order to provide appropriate care and support to affected individuals and their families. Healthcare equity advocators should also work towards ensuring that all individuals, regardless of their background or geographical location, have access to high-quality healthcare services and resources to prevent and manage congenital anomalies. They should advocate for policies and programs that address the specific needs of diverse populations in relation to congenital anomalies. Policy makers play a key role in shaping the healthcare system and implementing public health initiatives. They should consider the varied patterns of congenital anomalies and the different factors that contribute to their development when designing policies and programs aimed at preventing and managing these conditions. Policies should be inclusive and address the specific needs of diverse populations. Researchers should continue to investigate the factors that contribute to the development of congenital anomalies and explore the varied patterns observed in different populations. By advancing our understanding of these conditions, researchers can help inform healthcare providers, health equity advocates, and policy makers on effective strategies for prevention, early detection, and management of congenital anomalies. Collaboration between researchers and other stakeholders is essential to drive progress in this field.

Reference

1. WHO. Congenital disorders[Accessed Feb 223,2024:https://www.who.int/news-room/fact-sheets/detail/birth-defects/].
2. Al-Dewik N, Samara M, Younes S, Al-Jurf R, Nasrallah G, Al-Obaidly S, Salama H, Olukade T, Hammuda S, Marlow N, Ismail M, Abu Nada T, Qoronfleh MW, Thomas B, Abdoh G, Abdulrouf PV, Farrell T, Al Qubaisi M, Al Rifai H. Prevalence, predictors, and outcomes of major congenital anomalies: A population-based register study. Sci Rep. 2023 Feb 7;13(1):2198. doi: 10.1038/s41598-023-27935-3. PMID: 36750603; PMCID: PMC9905082.
3. GBD 2019 Under-5 Mortality Collaborators. Global, regional, and national progress towards Sustainable Development Goal 3.2 for neonatal and child health: all-cause and cause-specific mortality findings from the Global Burden of Disease Study 2019. Lancet. 2021 Sep 4;398(10303):870-905. doi: 10.1016/S0140-6736(21)01207-1. Epub 2021 Aug 17. PMID: 34416195; PMCID: PMC8429803.
4. WHO.Congenital disorder.[Accessed Feb 24, 2024. https://www.who.int/health-topics/congenital-anomalies#tab=tab_1].
5. Süüden EL, Muru K, Põder K, Rull K. The prevalence of congenital anomalies: nationwide study in 2020 in Estonia. J Matern Fetal Neonatal Med. 2023 Dec;36(2):2259050. doi: 10.1080/14767058.2023.2259050. Epub 2023 Sep 24. PMID: 37743247.
6. Adane F, Afework M, Seyoum G, Gebrie A. Prevalence and associated factors of birth defects among newborns in sub-Saharan African countries: a systematic review and meta-analysis. Pan Afr Med J. 2020 May 14;36:19. doi: 10.11604/pamj.2020.36.19.19411. PMID: 32774596; PMCID: PMC7388615.
7. Kancherla V, Oakley GP Jr, Brent RL. Urgent global opportunities to prevent birth defects. Semin Fetal Neonatal Med. 2014 Jun;19(3):153-60. doi: 10.1016/j.siny.2013.11.008. Epub 2013 Dec 14. PMID: 24333206.
8. Kang, L., Cao, G., Jing, W. et al. Global, regional, and national incidence and mortality of congenital birth defects from 1990 to 2019. Eur J Pediatr 182, 1781–1792 (2023). https://doi.org/10.1007/s00431-023-04865-w.
9. Toobaie A, Yousef Y, Balvardi S, St-Louis E, Baird R, Guadagno E, Poenaru D. Incidence and prevalence of congenital anomalies in low- and middle-income countries: A systematic review. J Pediatr Surg. 2019 May;54(5):1089-1093. doi: 10.1016/j.jpedsurg.2019.01.034. Epub 2019 Feb 2. PMID: 30786990.
10. Sitkin NA, Ozgediz D, Donkor P, Farmer DL. Congenital anomalies in low- and middle-income countries: the unborn child of global surgery. World J Surg. 2015 Jan;39(1):36-40. doi: 10.1007/s00268-014-2714-9. PMID: 25135175; PMCID: PMC4300430.
11. Anane-Fenin, B., Opoku, D.A. & Chauke, L. Prevalence, Pattern, and Outcome of Congenital Anomalies Admitted to a Neonatal Unit in a Low-Income Country—a Ten-Year Retrospective Study. Matern Child Health J 27, 837–849 (2023). https://doi.org/10.1007/s10995-023-03591-x.
12. Swanson J, Ailes EC, Cragan JD, Grosse SD, Tanner JP, Kirby RS, Waitzman NJ, Reefhuis J, Salemi JL. Inpatient Hospitalization Costs Associated with Birth Defects Among Persons Aged <65 Years - United States, 2019. MMWR Morb Mortal Wkly Rep. 2023 Jul 7;72(27):739-745. doi: 10.15585/mmwr.mm7227a1. PMID: 37410666; PMCID: PMC10328482.
13. Jordan C. Apfeld, Zachary J. Kastenberg, Alexander T. Gibbons, Ciaran S. Phibbs, Henry C. Lee, Karl G. Sylvester, The disproportionate cost of operation and congenital anomalies in infancy,

Surgery, Volume 165, Issue 6, 2019, Pages 1234-1242, ISSN 0039-6060, https://doi.org/10.1016/j.surg.2018.12.022. (https://www.sciencedirect.com/science/article/pii/S0039606019300078).

14. Bekalu Getachew, Tilahun Alemayehu, Soressa Abebe, Niguse Hamba, Solomon Tesfaye, Tesema Etefa, Ruth Tilahun, Prevalence of overt congenital anomalies and associated factors among newborns delivered at Jimma university medical center, southwest Ethiopia, 2018: A cross-sectional study, International Journal of Africa Nursing Sciences, Volume 18, 2023, 100513, ISSN 2214-1391, https://doi.org/10.1016/j.ijans.2022.10051(https://www.sciencedirect.com/science/article/pii/S2214139122001202).
15. Moges N, Anley DT, Zemene MA, Adella GA, Solomon Y, Bantie B, Fenta Felek S, Dejenie TA, Bayih WA, Chanie ES, Getaneh FB, Kassaw A, Mengist Dessie A. Congenital anomalies and risk factors in Africa: a systematic review and meta-analysis. BMJ Paediatr Open. 2023 Jul;7(1):e002022. doi: 10.1136/bmjpo-2023-002022. PMID: 37429669; PMCID: PMC10335447.
16. Abebe S, Gebru G, Amenu D, Mekonnen Z, Dube L. Risk factors associated with congenital anomalies among newborns in southwestern Ethiopia: A case-control study. PLoS One. 2021 Jan 28;16(1):e0245915. doi: 10.1371/journal.pone.0245915. PMID: 33508017; PMCID: PMC7843017.
17. Taye M, Afework M, Fantaye W, Diro E, Worku A. Congenital anomalies prevalence in Addis Ababa and the Amhara region, Ethiopia: a descriptive cross-sectional study. BMC Pediatr. 2019 Jul 11;19(1):234. doi: 10.1186/s12887-019-1596-2. PMID: 31296186; PMCID: PMC6625051.
18. Taye M, Afework M, Fantaye W, Diro E, Worku A. Factors associated with congenital anomalies in Addis Ababa and the Amhara Region, Ethiopia: a case-control study. BMC Pediatr. 2018 Apr 25;18(1):142. doi: 10.1186/s12887-018-1096-9. PMID: 29699508; PMCID: PMC5921791.