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FACULTY OF HEALTH SCIENCES



A TEN-YEAR REVIEW OF NEONATAL CONGENITAL ABNORMALITIES AND PARENTAL PERCEPTIONS AT A TERTIARY HOSPITAL IN GHANA

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A Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Master of Science (Obstetrics and Gynaecology)

Johannesburg, 2022

DECLARATION

I, Dr. Betty Anane-Fenin, declare that this thesis is my own, unaided work. It is being submitted for the Degree of Master of Science (Obstetrics and Gynaecology) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



……

13th day of April 2022 in Johannesburg

DEDICATION

To

My family: Kwame, Paakofi, Maame Ama, Grace, my parents, siblings and inlaws for all the support given me during my period of study.

My supervisor and mentor: Professor Lawrence Chauke for his seasoned advice and encouragement

ABSTRACT

Prevalence of congenital abnormalities (CA) is highest in developing countries. For the first time in Ghana, the prevalence and spectrum of neonatal CA and their admission outcomes over a ten-year period, and the perceptions of parents on their acceptability of prenatal testing and termination of pregnancy for fetal anomaly (TOPFA) were determined in a tertiary hospital. Demographic, obstetric and clinical data were collected for all babies admitted to the Special Care Baby Unit between 1st January 2010 and 31st December 2019. Parents of new-borns diagnosed with CA in the hospital between 13th April and 13th October 2021 were also recruited to assess their perceptions on prenatal testing and TOPFA. A total of 236 admissions occurred over the decade, accounting for 2.8% of neonatal admissions and 8.6 per 1000 births. Mortality occurred in 31.4%, responsible for 4.6% of total neonatal deaths. Gravidity of $\geq$5 and place of delivery were statistically associated with mortality. Central nervous system anomalies were the most prevalent, followed by suspected chromosomal abnormalities, then cardiac defects. Neonates with cardiac defects were more likely to demise. There is a high acceptance rate for prenatal testing and TOPFA among parents of new-borns with CA. However, there is a significant lack of knowledge on prenatal testing. Strategies for the prevention and early detection of CA, including the creation of a CA register, are required. Education and introduction of prenatal testing in routine antenatal care is essential. Parental support is also key to the management of parents with affected foetuses or new-borns.

ACKNOWLEDGEMENTS

I would like to acknowledge Mr. Douglas Aninng Opoku for his guidance on the statistical tools.

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LIST OF ABBREVIATIONS AND SYMBOLS

A&D:	Admission and Discharges
CCTH:	Cape Coast Teaching Hospital
cFTS:	Combined first trimester screening
CHPS:	Community-based Health Planning and Services
DALYs:	Disability-related life years
DS:	Down syndrome
b-hCG:	Beta-human chorionic gonadotropin
ICD:	International Classification of Diseases
KATH:	Komfo Anokye Teaching Hospital
LMICs:	Low- and Middle-income Countries
OPD:	Outpatient department
NHIS:	National Health Insurance Scheme
NIPS:	Non-invasive Prenatal Screening
NIPT:	Non-invasive Prenatal Testing
PAPP-A:	pregnancy-associated plasma protein A
SBA:	Skilled birth attendant
SCBU:	Special Care Baby Unit
SDG-3:	Sustainable Development Goal 3
SSA:	Sub-Saharan Africa
TOPFA:	Termination of Pregnancy for Foetal Anomaly
VACTERL:	Vertebra, anorectal, cardiac, tracheoesophageal, renal and limb association
YLL:	Years of life lost

CHAPTER ONE - INTRODUCTION

1.1 GENERAL INTRODUCTION

The World Health Organization (WHO) defines congenital disorders as “any potential pathological conditions arising before birth, whether evident at birth or manifesting later in life”[1,2]. By this, congenital disorders can be put under two main groups: environmental and congenital disorders with principally endogenous causes or constitutional congenital disorders[3].

Congenital abnormalities can also be defined as ‘’structural, functional and/ or biochemical abnormalities that are present from birth”[4], but detection or diagnosis may be made before birth, at birth or later after birth. Congenital abnormalities are also referred to as birth defects, congenital malformations, congenital anomalies, or congenital disorders. The commonest of these defects are the structural (anatomic or morphological) abnormalities[5]. It is also known that about 70% of these abnormalities can be prevented or treated[6,7], thus, reducing overall mortality and disability.

Eighty percent (80%) of the global under-5 mortality burden lies in Sub-Saharan Africa and Southern and Central Asia[8]. Congenital abnormalities are among the top 5 causes of these deaths and 94% of the total congenital abnormalities worldwide come from LMICs[9]. They are also among the causes of child mortality that have seen a rather slow progress in its reduction when considering the global picture. This is due to the fact that unlike the western countries, which have instituted measures such as prenatal counselling and screening and succeeded in reducing their poor outcomes significantly, most developing countries virtually have no such system on prenatal screening and diagnosis in place. One major contributory factor is the paucity of data to even define and assess the problem as a first step.

Congenital anomaly registers are useful in determining the incidence/ prevalence, types and trends of birth defects in a community or population. This serves as relevant epidemiological information and an alert or warning sign for new teratogenic exposures that may be responsible for new malformations or atypical presentation of previously known malformations in a community. Again, a register enables researchers to identify the possible causes of congenital anomalies which leads to the

planning of health service delivery and the formulation of preventive measures. It also serves as a means for auditing prenatal screening and diagnostic practice. For example, it can provide data on the proportion of cases diagnosed prenatally and the proportion of screen-positives that become confirmed, the proportion of abnormalities that led to termination of pregnancy or resulted in intrauterine demise.

The management of babies born with congenital anomalies is financially, psychologically, emotionally and physically challenging for mothers or couples, their family, and the country as a whole[10] but elaborate knowledge on the perceptions and acceptability of prenatal screening/diagnosis, and termination of pregnancy for foetal anomaly is unavailable in Ghana.

Two studies have been conducted so far on congenital abnormalities in Ghana and both were in tertiary teaching hospitals[11,12]. However, these did not touch on the admission/perinatal outcomes of the affected babies and one of the studies concentrated on only external abnormalities.

This study sought to contribute to the knowledge about the prevalence, spectrum, admission outcomes and parental perceptions of prenatal testing and termination of pregnancy for fetal anomaly in Ghana. It will also be used to advocate for a detailed national policy on prenatal screening.

1.2 AIM AND OBJECTIVES:

To determine the prevalence, spectrum and pattern of congenital abnormalities in CCTH between 1st January 2010 and 31st December 2019, and parental perceptions on prenatal testing and termination of pregnancy for fetal anomaly between April and September 2020 in CCTH.

SPECIFIC OBJECTIVES:

a. To estimate the prevalence of congenital anomalies at the Special care Baby Unit (SCBU), the paediatric ward and outpatient clinic of the hospital over a ten-year period from 1st January 2010 to 31st December 2019.

b. To describe the spectrum and pattern of the anomalies observed between 1st January 2010 and 31st December 2019 among neonates in CCTH.

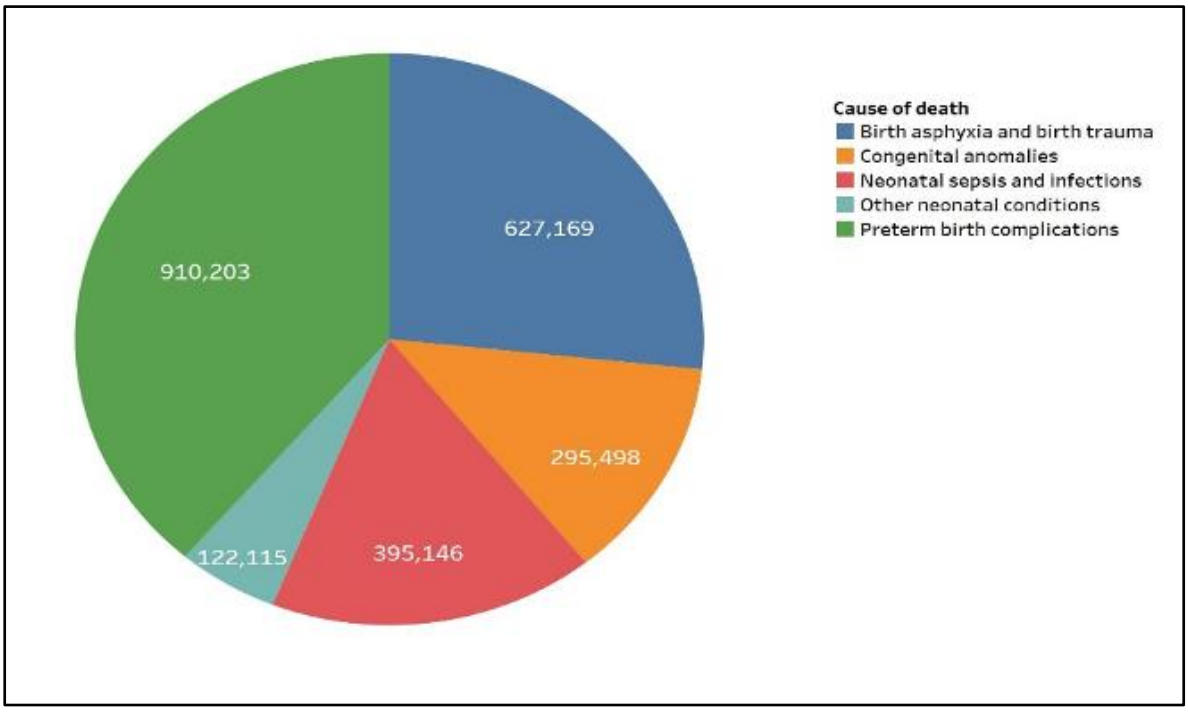
c. To determine the admission outcomes of babies who were diagnosed with at least one congenital abnormality in CCTH between 1st January 2010 and 31st December 2019.

d. To explore the experiences and perception about prenatal testing and termination of pregnancy among parents whose neonates (dead or alive) or aborted fetuses were diagnosed with a congenital anomaly between 13th April and 13th October 2021 in CCTH.

1.3 LITERATURE REVIEW

1.3.1 Overview and the global burden of congenital anomalies

Congenital abnormalities affect 1 in 33 babies[13], and responsible for 12.6% of neonatal deaths worldwide[14] (see Figure 1.1 below). In 2006, the March of Dimes reported that about 7.9 million children (6% of total global births) were born with serious functional or structural defects which were as a result of genetic abnormalities, and several hundreds of thousands abnormalities that were due to environmental causes like alcohol, maternal infections, nutritional deficiencies, and other teratogens[8]. Four years later, 510,400 deaths were attributed to congenital anomalies and ranked as the 23rd among all causes of deaths but because deaths due to congenital anomalies occur quite early in life (within the first month), they ranked worse at the 14th position when years of life lost (YLL) was considered[15]. In fact, in countries with low infant mortality rates, about 20% of the deaths are due to congenital anomalies[7].



Source: Adapted from WHO 2000-2016 child causes of death[16]

Figure 1.1: Leading causes of neonatal mortalities globally, 2016

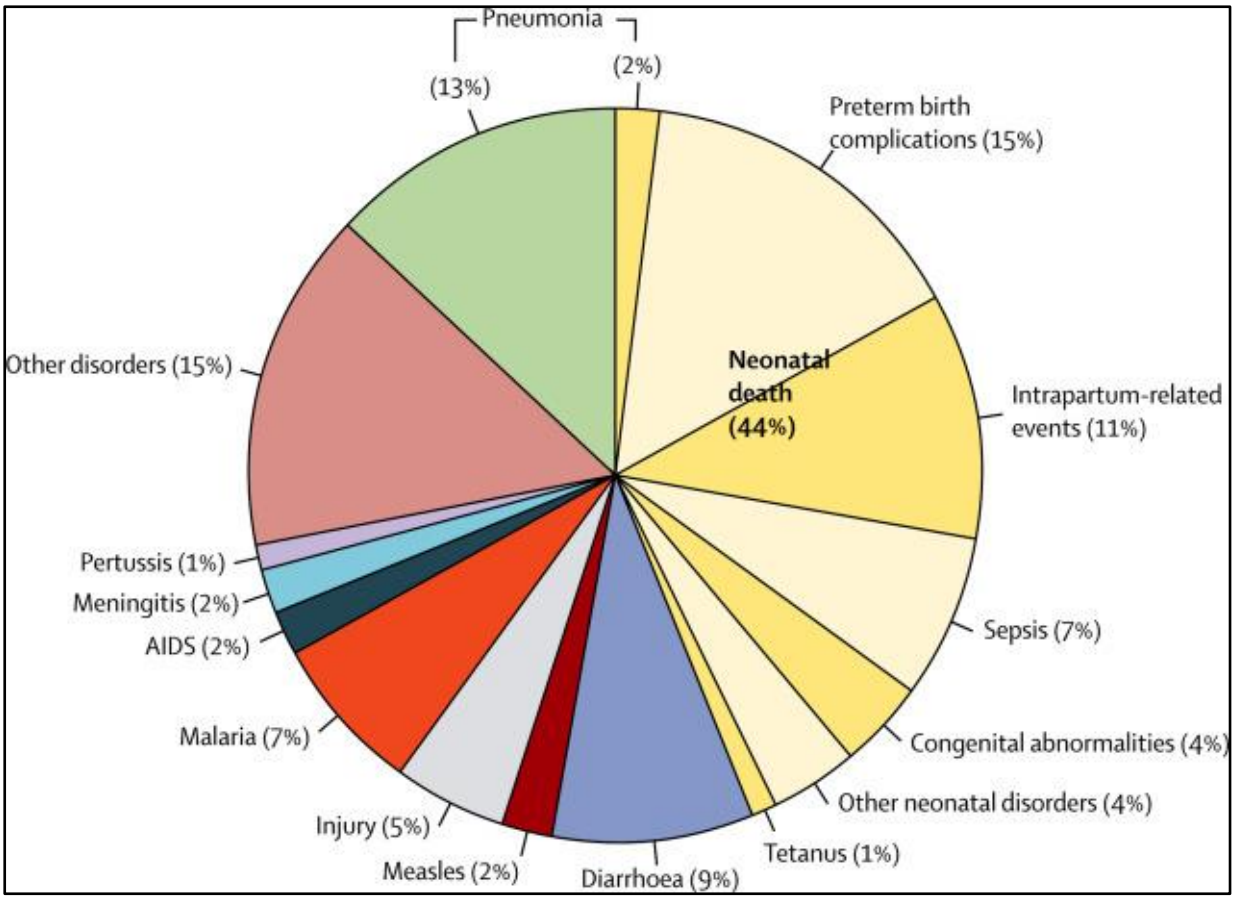
Projections from a 13-year review of global and regional child mortalities reveal that if current trends continue, congenital anomalies will be responsible for 4.4% of under-five mortalities in 2030, compared to 4% in 2013[17]. But if the global preventive strategies put in place are followed, then deaths from congenital anomalies could reduce considerably (see Figures 1.2 and 1.3 below). By the same projection, 30% of births and 60% of deaths will occur in Sub-Saharan Africa, as compared to 25% and 50% in 2013 respectively. Although the prevalence rate of congenital anomalies is underestimated in developing countries[18], figures available for Ghana in 2010 showed a prevalence of 66.6 per 1000 live births[15]. This figure obviously does not include the abnormally-formed foetuses that were miscarried or died in-utero and pregnancies that were terminated due to prenatally-diagnosed severe abnormalities. If all these are considered, then the denominator becomes *'informative offsprings'* instead of live births and the numbers will soar even higher.

In the same year that 510,400 deaths occurred form congenital anomalies, a little over 250,000 maternal deaths were also recorded[15].

Children born with congenital anomalies do need frequent hospital and rehabilitation visits throughout their lifetime, as their quality of life usually depends on these. Financial burden on affected families, society and governments, thus, increase. Coupled with the financial drain, parents of children with disability experience enormous psychological and emotional distress, including stigmatisation from society, especially when the anomalies are visible externally.

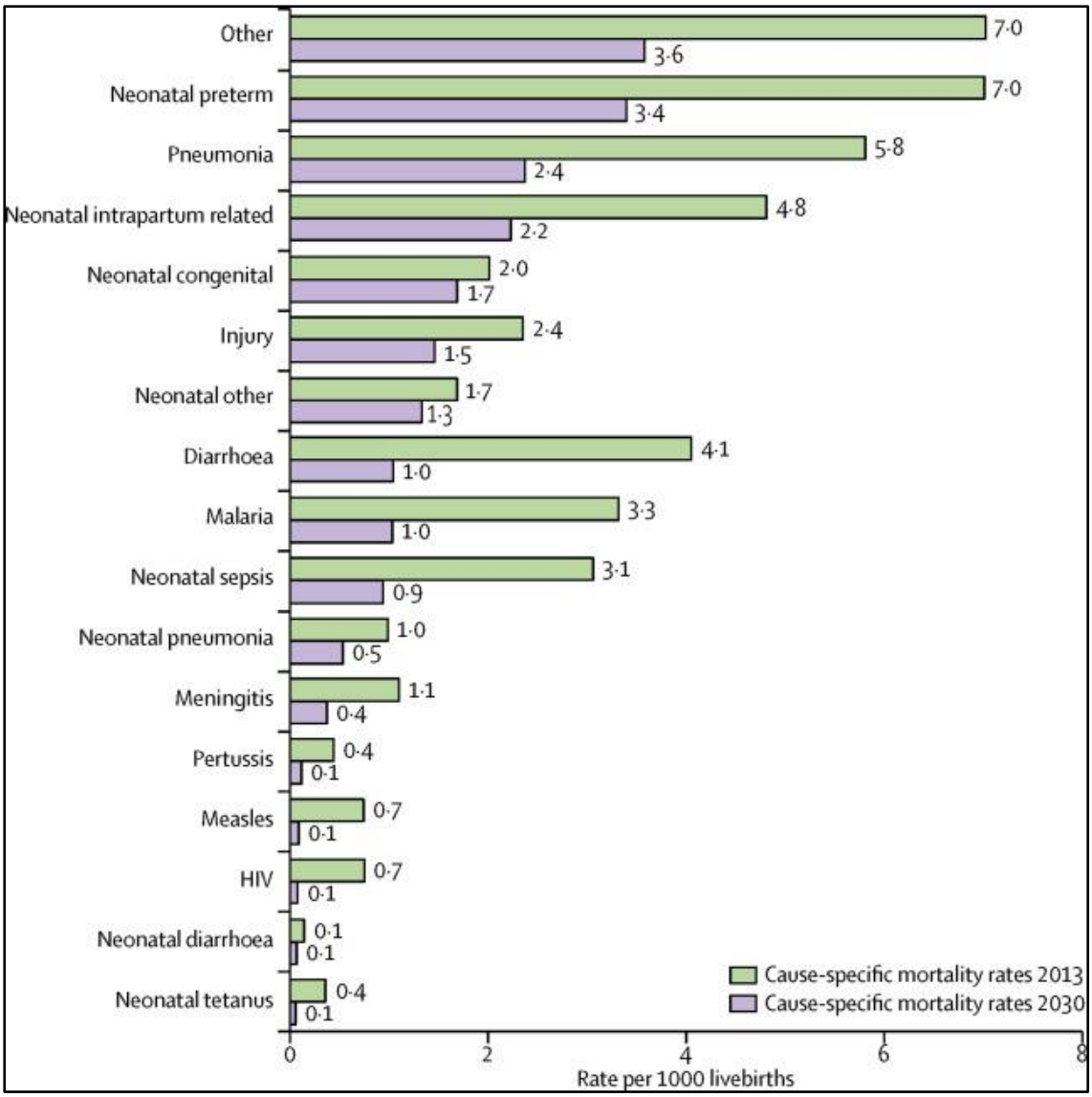
In spite of the above, congenital anomalies do not enjoy the same level of priority as maternal health, which may be partly due to the lack of epidemiologic data on the anomalies, especially in low-resource countries. The Modell Global Database (MGDb) was therefore, created to meet this need of providing national, regional and global data on the prevalence and outcomes of congenital anomalies. This helps to inform health policies and aid budgetary allocations in the health sector[19].

If congenital anomalies are also prioritised, as other areas such as HIV and Malaria, the burden of health service costs and deaths from these defects will reduce considerably and the closer we will get to achieving the Sustainable Development Goal 3 (SDG-3).



Source: Liu L et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: An updated systematic analysis. Lancet,Volume 385 Issue 9966, Pg. 430-440, January 31, 2015[20]

Figure 1.2: Causes of under-five mortality globally, 2000 – 2013



Source: Liu L et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: An updated systematic analysis. Lancet,Volume 385 Issue 9966, Pg. 430-440, January 31, 2015[20]

Figure 1.3: Global cause-specific under-five mortality in 2030 within the achievement scenario by comparison with cause-specific mortality in 2013

1.3.2 Prevalence and spectrum of Congenital Anomalies

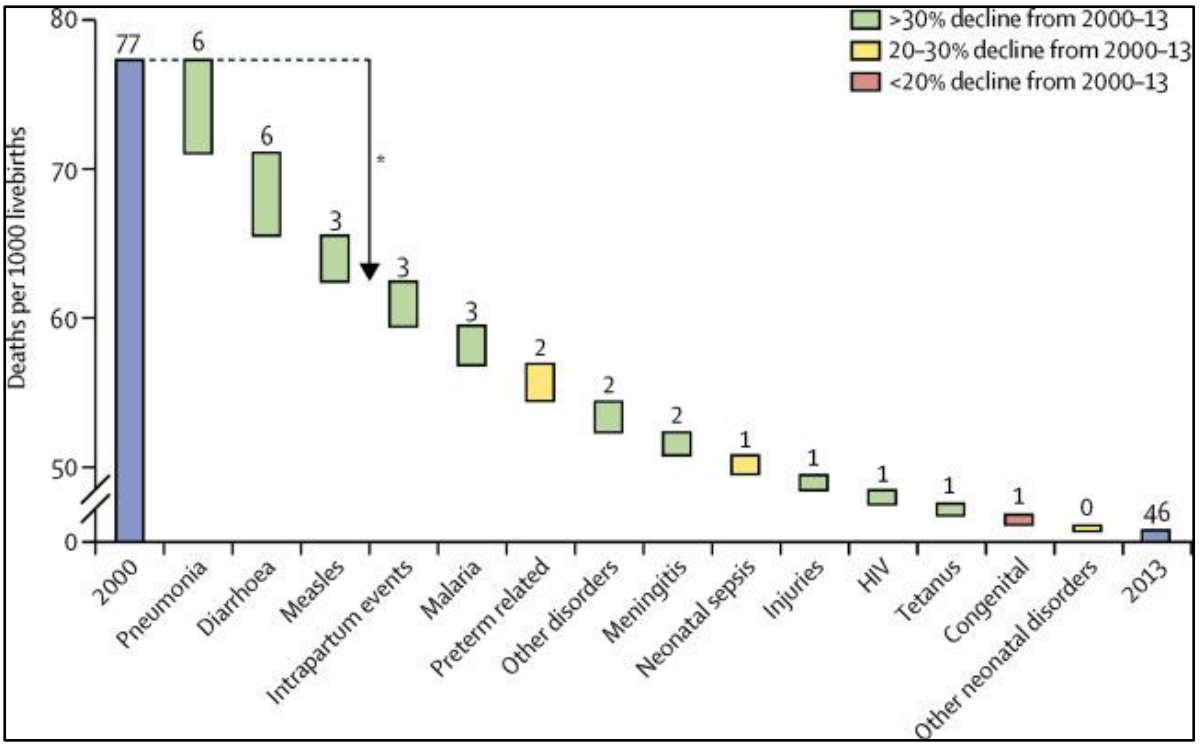
Global:

There is an estimated prevalence of 20-55 per 1000 live births worldwide with variations in the study population and its characteristics, the study design and the sample sizes used, thus rendering it inaccurate[21]. Deaths from congenital abnormalities increased from 276,000 to 303,000 in 2015 and 2016 respectively[22]. Congenital anomalies have risen from being in the top-seven causes of under-five mortality in 2015 to the top-five in 2016[17]. Although the global under-five mortality saw a 59% decline between 1990 and 2018, deaths from congenital defects did not reduce appreciably[17,23,24] (See Figure 1.4 below).

The prevalence rate for Europe is 23.9/1000 births and they contribute to 17-43% of infant mortality, with the higher rates in countries where termination of pregnancy for foetal anomaly (TOPFA) is illegal, like Ireland and Malta[25] (See Figure 1.5 below). Fourteen percent (14%) of these deaths are attributed to genetic causes, 11% from chromosomal causes, 15% from multiple malformations, and a little less than 4% for isolated malformations. Thirty-five per cent (35%) of babies with anomalies that are incompatible with life were stillborn, as compared to 4%–9% for the other categories[25].

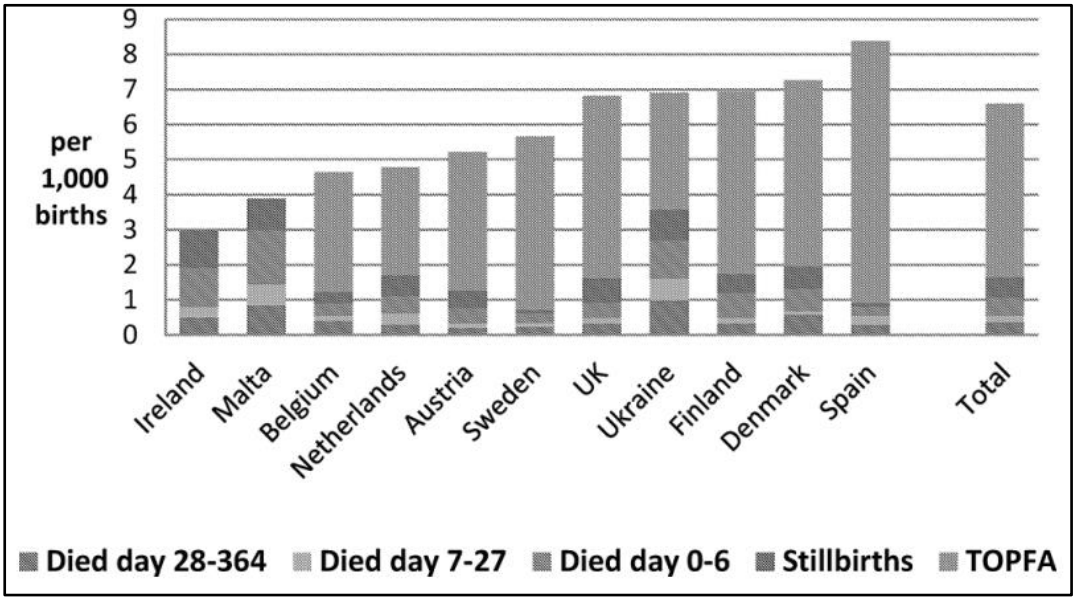
The prevalence in the United States of America is 28.9/1000 live births, with 4% representing genetic syndromes and cardiovascular defects being the majority[21]. Twelve percent (12%) of all paediatric hospitalisations are due to congenital anomalies.

In South Africa, even with a presumed under-reporting, 70 per 1000 live births are documented to be affected by a congenital disorder and they contribute to 14% of under-five mortalities[26]. The commonest disorders globally are cardiac abnormalities, neural tube defects and Down syndrome[14].



Source: Liu L et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: An updated systematic analysis. Lancet,Volume 385 Issue 9966, Pg. 430-440, January 31, 2015[20]

Figure 1.4: Global trends in cause-specific mortality rates in neonates and children aged 1–59 months, 2000–13



Source: Boyle B, et al. Arch Dis Child Fetal Neonatal Ed 2018;103:F22–F28[25]

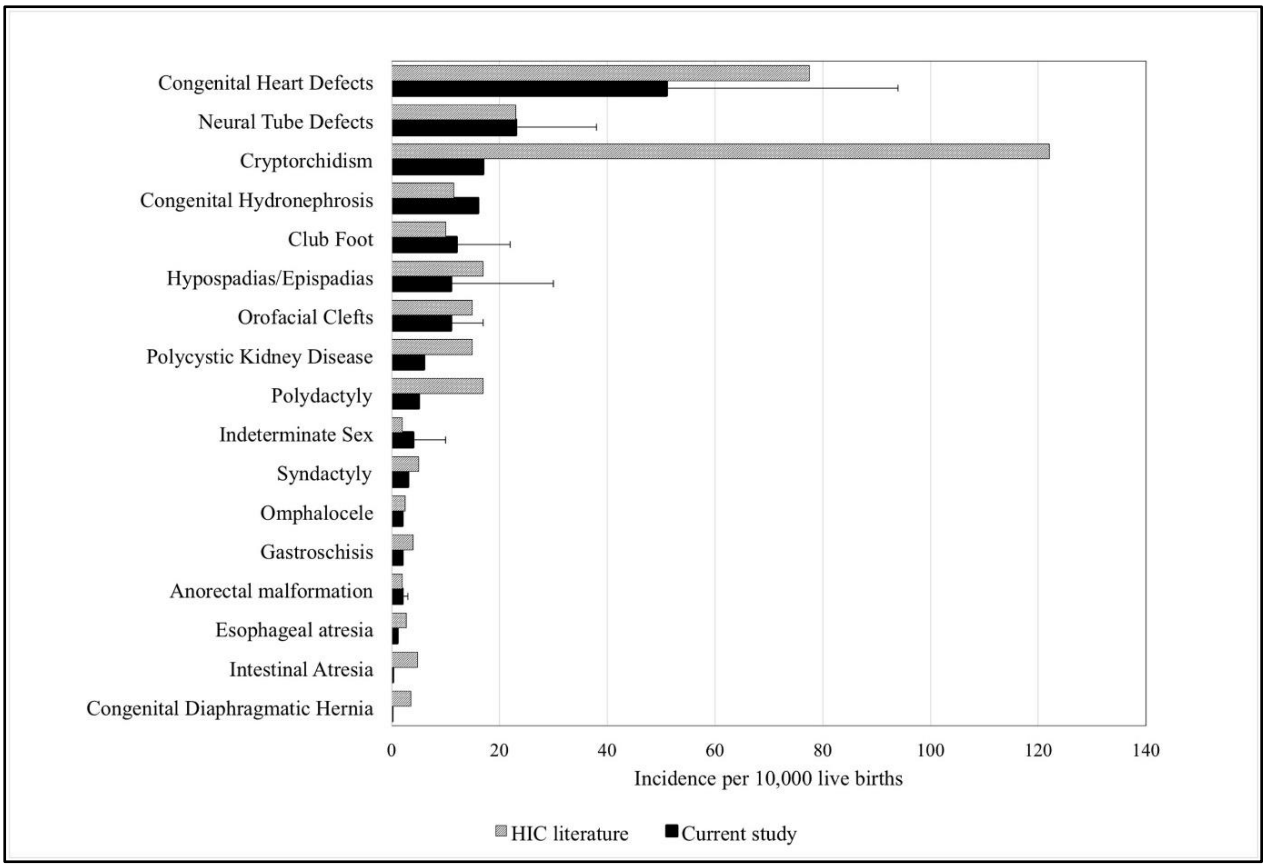
Figure 1.5: Prevalence per 1000 births of infant deaths with congenital anomaly, by age at death and country, for 19 EUROCAT registries in 11 countries, 2005–2009

Low- and Middle-Income Countries

Ninety-four percent (94%) of all birth defects occur in the low- and middle-income countries (LMICs) because higher fertility rate translates into higher birth rates, and hence higher numbers of abnormalities[9]. Another reason is the low rates of TOPFA in LMICs, resulting in higher live births with congenital anomalies than in countries where TOPFA is allowed. Apart from the lack of diagnostic facilities which makes accurate diagnosis difficult, babies born outside the hospitals with obvious physical anomalies may be stigmatised, leading to low self-reporting of anomalies, as families often hide them from public view. Some families even commit infanticide due to the remote belief that they are 'spirit' or 'water' babies and so must not live among humans[11]. Moreover, since a significant proportion of deliveries in developing countries occur outside the hospitals[27–29], hospital-based studies, which seems to be the best source of data, tend to underestimate the incidence.

Reports of the most-predominant congenital anomalies in LMICs appears to be inconsistent. A systematic review on surgically correctable congenital anomalies in low-income countries showed cardiovascular anomalies as the commonest, just as in the high-income countries[27]. Contrary to that, another review for Sub-Saharan Africa alone had musculoskeletal system anomalies in the lead[22]. In Malawi, the prevalence of congenital anomalies is about 7.7/1000 live births, 2-28/1000 in Nigeria and approximately 18.5 per 1000 in India, with musculoskeletal system in the lead, followed by central nervous system[30–33]. Not surprisingly, anomalies of the musculoskeletal system which are often not severe, (mostly talipes) are common among live births while those of the central nervous system (typically anencephaly) are seen more in stillbirths[31]. In Gabon, the prevalence is 2.29% of neonatal admissions, 55% of which are anomalies of the central nervous system[34].

Although underestimation in LMICs seems quite likely, estimates provided for LMICs in literature from high-income countries also appear exaggerated or overestimated[27] (see Figure 1.6 below).

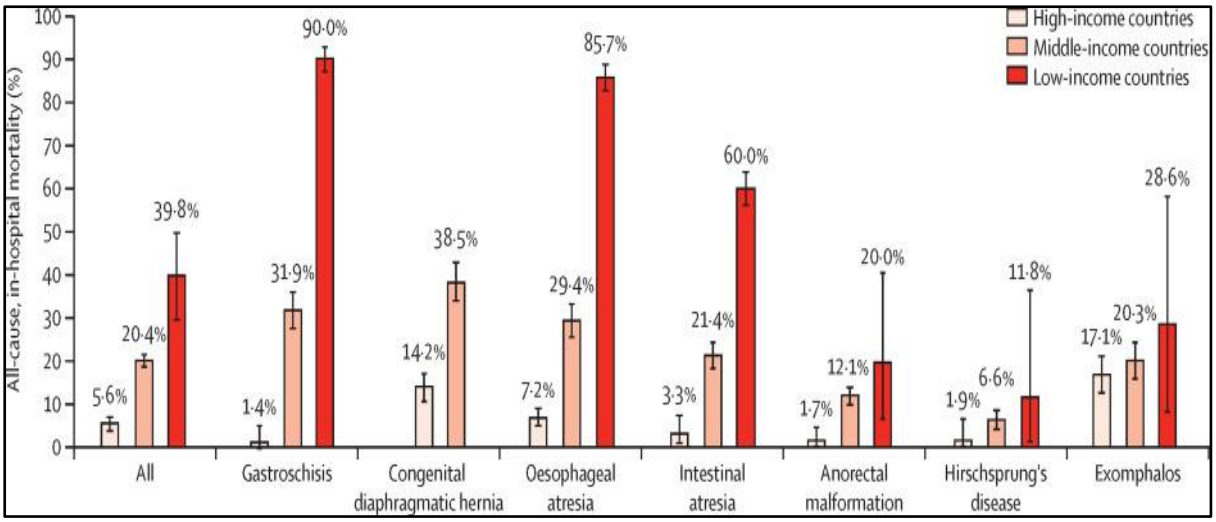


Source: Toobaie A, Yousef Y, Balvardi S, St-Louis E, Baird R, Guadagno E, et al. Incidence and prevalence of congenital anomalies in low- and middle-income countries: A systematic review. J Pediatr Surg 2019;54(5):1089–93[27]

Figure 1.6: Incidence rates of some common congenital anomalies in LMICs as compared to estimates provided in high-come countries' literature.

Prompt corrective surgery does reduce disability significantly, despite the wide disparity in surgical outcomes that exists between LMICs and high-income countries. Figure 1.7 gives a graphical representation of this disparity in surgical outcomes.

Surgically-correctable cardiac defects in LMICs are also believed to be more complex than in the advanced countries, thus offering a much lower disability-adjusted life-years (DALYS), even after surgery[35]. But on the whole, the burden from congenital anomalies lessens when paediatric surgery services are scaled up[36].



Source: Wright NJ, Leather AJM, Ade-Ajayi N, Sevdalis N, Davies J, Poenaru D, et al. Mortality from gastrointestinal congenital anomalies at 264 hospitals in 74 low-income, middle-income, and high-income countries: a multicentre, international, prospective cohort study. Lancet [Internet] 2021[36]

Figure 1.7: In-hospital mortality rates for some selected gastrointestinal anomalies, comparing high-, middle- and low-income countries

Ghana

Almost six decades ago, an audit of 286 autopsies of people of all ages (both adults and children) showed 199 congenital abnormalities, 5% of which were considered major, approximately 3.2% were potentially harmful, and 61.5% were incidental anatomic deviations[37]. In this audit, 61.3% were anomalies of the cardiovascular system whiles the lowest was in the central nervous system (1.4%). Subsequently, two hospital-based studies on the prevalence and spectrum of congenital anomalies have been conducted. There is also a handful of studies that looked at specific abnormalities but not a holistic picture for congenital anomalies. In the second biggest tertiary hospital whose catchment area includes the whole of the middle belt and the northern part of Ghana, congenital anomalies accounted for 7.22% (103.3/1000 births) of all neonatal admissions[11]. It should be noted that, this neonatal unit admits babies up to 3month-olds, and not only neonates. Musculoskeletal anomalies were in the majority (33.33%), just as observed in some other LMICs. The central nervous system anomalies followed with 22.8%. Ambiguous genitalia and congenital heart disease contributed equally (10.53%). Chromosomal abnormalities formed 1.77% of the total admissions and the commonest was Down syndrome (trisomy 21), followed by Patau Syndrome (Trisomy 13) and Turner syndrome (Monosomy X). The overall prevalence

of external structural abnormalities in another study was reported as 455 per 100,000 live births (4.55 per 1000 live births), of which abnormalities of the gastrointestinal (abdominal wall defects) and central nervous systems form about 77%[12]. Common anomalies considered included spina bifida, hydrocephalus, anencephaly, oro-facial defects, omphalocele, and imperforate anus.

The huge numbers of cardiovascular defects identified in the earliest study has therefore not been observed in the latter studies.

1.3.3 Causes and Risk factors of Congenital Anomalies

Variations in the pattern and prevalence of congenital abnormalities occur over time and may vary from one geographical location to the other. The cause of about 50% of congenital anomalies cannot be identified, but some genetic, environmental and other risk factors have been found to be associated with these abnormalities[14]. Per the WHO definition[1,2], the cause of congenital disorders fall under two main groups*:* *environmental congenital disorders* and *congenital disorders with principally endogenous causes* or *constitutional congenital disorders*. The first group includes disorders due to maternal exposure to infection, nutritional deficiencies, or teratogens[3]. The second group includes chromosomal disorders, congenital malformations, single-gene disorders, and disorders due to genetic risk factors.

In 2016, the Modell Global Database (MGDb) for congenital anomalies was proposed[19,38] The reason for this database is to generate epidemiological data on congenital abnormalities and their outcomes per country so as to foster preventive interventions. It puts congenital anomalies under five main groups: *chromosomal disorders*, *single-gene disorders*, *disorders due to common genetic risk factors* (hemolytic disease of the newborn and neonatal jaundice due to glucose-6-phosphate dehydrogenase deficiency), *congenital malformations*, and *environmental* disorders, which includes maternal exposure to infections and other teratogens. Only groups with relatively constant birth prevalence, without interventions, and those whose birth rates can be calculated were considered for this grouping system.

These environmental and endogenous causes of congenital anomalies interact with each other in a complex manner, thus, giving a multifactorial picture in some instances. The causes of congenital anomalies can therefore simply be grouped into three – *genetic*, *environmental*, and *complex* or *multifactorial*[5].

Genetic anomalies include the chromosomal abnormalities like Down syndrome and Patau syndrome and the single-gene defects (Mendelian disorders) like cystic fibrosis, Fragile X syndrome, and muscular dystrophy. This group forms about 25% of all congenital anomalies[39]. Advanced maternal age (>35 years) and consanguineous marriages have been identified as two major causes of genetic aberrations.

Disorders due to environmental causes are post-conception and contribute to about 15% of all congenital anomalies. They include maternal diseases like diabetes and thyroid disease, infections such as cytomegalovirus and rubella. Others include maternal nutritional deficiencies, smoking, the use of alcohol, drugs that are contraindicated in pregnancy, and other teratogenic chemicals.

The third group is the largest, contributing to about 60% of total congenital anomalies. This is when an abnormality is triggered by an environmental risk factor in a foetus that carries a genetic predisposition for that abnormality. These include conditions like orofacial clefts, hypospadias, and cardiovascular defects[40].

1.3.4 Classification of Congenital abnormalities

Congenital abnormalities can be classified according to the developmental mechanism, the clinical presentation, or the prognosis[5,39].

i. ***Developmental mechanism***[41]***:***

malformation*- defect in the structure of an organ or a part of an organ that can be traced back to an anomaly in its development (e.g. spina bifida, heart defects, cleft lip and palate);*

disruptive *- interruption of the normal development of an organ that can be traced back to outer influences (anomalies caused by teratogenic agents like chemicals and infections);*

dysplasia *- abnormal organization of the cells in a tissue (e.g. osteogenesis imperfecta, achondroplasia)*

deformation *- anomalies that occur due to outer mechanical effects on existing normal organs or structures (e.g. amniotic bands)*

ii. Clinical presentation in a child:

- ***Isolated –*** a stand-alone abnormality
- ***sequence****- a group of related abnormalities that are presumed to derive from a single primary anomaly or mechanical factor*
- ***multiple congenital abnormalities****- two or more unrelated defects occurring together*
- ***associations****- a set of anomalies that occur with a higher frequency than random but are neither a sequence or a syndrome, and*
- ***syndromes****- a pattern of abnormalities that occur together and are thought to derive from a single cause*

The International Classification of Diseases (ICD)[41] takes into consideration malformations, deformations, and chromosomal abnormalities, but not metabolic disorders. Per this classification, anomalies are to a large extent classified based on eleven (11) systems or organs that can be affected. The systems are the nervous, circulatory, respiratory, digestive, urinary, and musculoskeletal systems. The other parts are the eye; ear, face and neck; lip and palate, and genital organs. It also includes congenital abnormalities like situs invertus and asplenia, and congenital abnormalities not classified elsewhere, like the trisomies and microdeletions. This classification was employed and modified in the EUROCAT study to group the anomalies into subclasses[25].

There is yet another classification based on prognosis – lethal, severe, and mild[5].

The lethal abnormalities are those that cause stillbirths or infant deaths, or lead to termination of pregnancy after prenatal diagnosis. These include anencephaly and

alobar holoprosencephaly. The severe ones often end in severe morbidity or even death if medical intervention is not instituted. Examples include the cleft lip and palate. The mild ones have a good survival rate although they need medical intervention anyways. An example is an undescended testis.

Minor abnormalities and anatomic variants that do not carry severe medical or cosmetic consequences are not included in this classification.

1.3.5 Outcome of babies born with congenital abnormalities

Perinatal outcomes reflect both the severity of defects exhibited and the level of perinatal care. Societal and health sector support systems play a paramount role thereafter. Thus, survival rates are expected to be higher in developed countries than in the developing countries for similar anomalies.

Children born with birth defects are 13 times more at risk of dying than those born without, and this trend remains so even 10-15 years after birth[42]. Prematurity and low birth weight are strong risk factors for congenital anomalies and deaths from birth defects[21,42]. In addition, the number of defects also correlates directly with the risk of death.

As stated earlier, congenital abnormalities contribute to 17-43% of infant mortality according to The European Surveillance of Congenital Anomalies (EUROCAT)[25] (See figure 1.8 below). The prevalence is 23.9/1000 births, and 80% of babies with congenital abnormalities are born alive. However, early neonatal deaths occur in 2.5% of this number. Two percent (2%) are foetal deaths from 20 weeks gestation, and 17.6% are as a result of TOPFA[43].

Among the live births that had no chromosomal abnormalities, the most common defects were in the heart, followed by limb, urinary, and the central nervous system. This trend is not surprising as foetal cardiac defects usually manifest after birth and with the advancement in cardiothoracic surgery, the prognosis is quite promising. Also, the commonest central nervous system abnormalities are the neural tube defects, particularly spina bifida, which can be repaired either in-utero or immediately after delivery to minimise disability. Almeida et al. also observed that neonatal deaths are less frequently associated with central nervous system abnormalities[44]. With all this

knowledge, fetuses with cardiac and neural tube defects are unlikely to be aborted but allowed to be born alive. Urinary system abnormalities are also usually amenable to surgery postnatally with good outcomes, so TOPFA does not occur most of the time.

Table 1 Death from congenital anomaly (CA) in the first year of life (infant deaths), comparing EUROCAT data with that reported by WHO per country for selected years 2005–2009*

	WHO				EUROCAT				
Country	Years where WHO data are available	All infant deaths (n)	Deaths <1 year due to CA per 1000 live births	Infant deaths due to CA (%)	Country covered by EUROCAT (%)	Data source for infant deaths†	Liveborn CA cases registered (n)	Infant deaths with CA (n)	Deaths of infants with CA per 1000 live births‡
Austria, Styria	**2005–2009**	1464	1.01	27	13	(B)	1323	**41**	0.81
Belgium, Antwerp and Hainaut	**2005–2006**	**964**	0.98	24	27	(D)(E)	1217	**55**	0.87
Croatia, Zagreb	**2005–2009**	1121	1.80	34	16	(B)	**641**	**42**	1.26
Denmark, Odense	**2005–2006**	**506**	1.09	28	8	(B)	**290**	**11**	1.06
Finland	2005–2009	**825**	0.92	33	100	(A)	12 890	**353**	1.19
France - Ile de la Reunion*	**2005–2006**	**331**	1.23	17	100	(C)	**570**	**39**	0.84
Germany, Mainz and Saxony-Anhalt	**2005–2009**	12 679	0.96	26	3	(A)(B)	3014	**49**	0.47
Hungary*	2008–2009	1048	1.38	25	100	(D)	6209	**172**	0.89
Ireland, Cork and Kerry, Dublin and South East Ireland	**2005–2009**	1245	1.63	42	62	(A)(A)(B)	4166	**412**	2.05
Italy, Tuscany and Emilia Romagna	2006–2008	5987	0.93	26	13	(A) (C)	4051	**58**	0.27
Malta	**2005–2009**	**118**	2.56	43	100	(A)	**529**	**60**	3.02
Netherlands, North	**2005–2009**	3893	1.26	30	10	(B)	2014	**106**	1.21
Poland, Wielkopolska	**2005–2009**	11 564	1.93	32	10	(D)	4777	**138**	0.73
Portugal, South	2007–2009	1065	0.81	23	21	(D)	**545**	**7**	0.11
Spain-Basque Country	**2005–2009**	8523	0.93	26	4	(B)	1463	**84**	0.80
Sweden	2005–2009	1366	0.77	30	100	(A)	8492	**331**	0.63
Switzerland, Vaud	**2005–2007**	**926**	1.31	31	10	(B)	**650**	**20**	0.90
Ukraine	**2005–2006 2008–2009**	18 542	2.59	31	6	(A)	2383	**374**	2.75
UK, Wales, N England, EMSYCAR, Wessex, Thames Valley, SW England	**2005–2009**	18 571	1.15	23	32	(A)(B)(D)(D)(D)(D)	24 539	**1141**	0.95

Used with permission from Boyle B, et al. Arch Dis Child Fetal Neonatal Ed 2018;103:F22–F28[25]

Figure 1.8: Infant mortality rates from congenital anomalies, comparing EUROCAT data with that reported by WHO per country for 2005 – 2009

As far as cleft lip and palate, neural tube defects and congenital heart diseases are concerned, it is estimated that about 59% of the disability-adjusted life-years (DALYs) in LMICs can be averted through full surgical coverage[35]. In fact, 76% of the burden is averted following corrective surgery for neural tube defects, 62% for cleft lip and palate, and 52% for congenital heart anomalies. Reduction of burden from the correction of cleft lip and palate is highest in Sub-Saharan Africa (SSA). Greater burden reduction from corrected congenital heart defects also occurs in North Africa

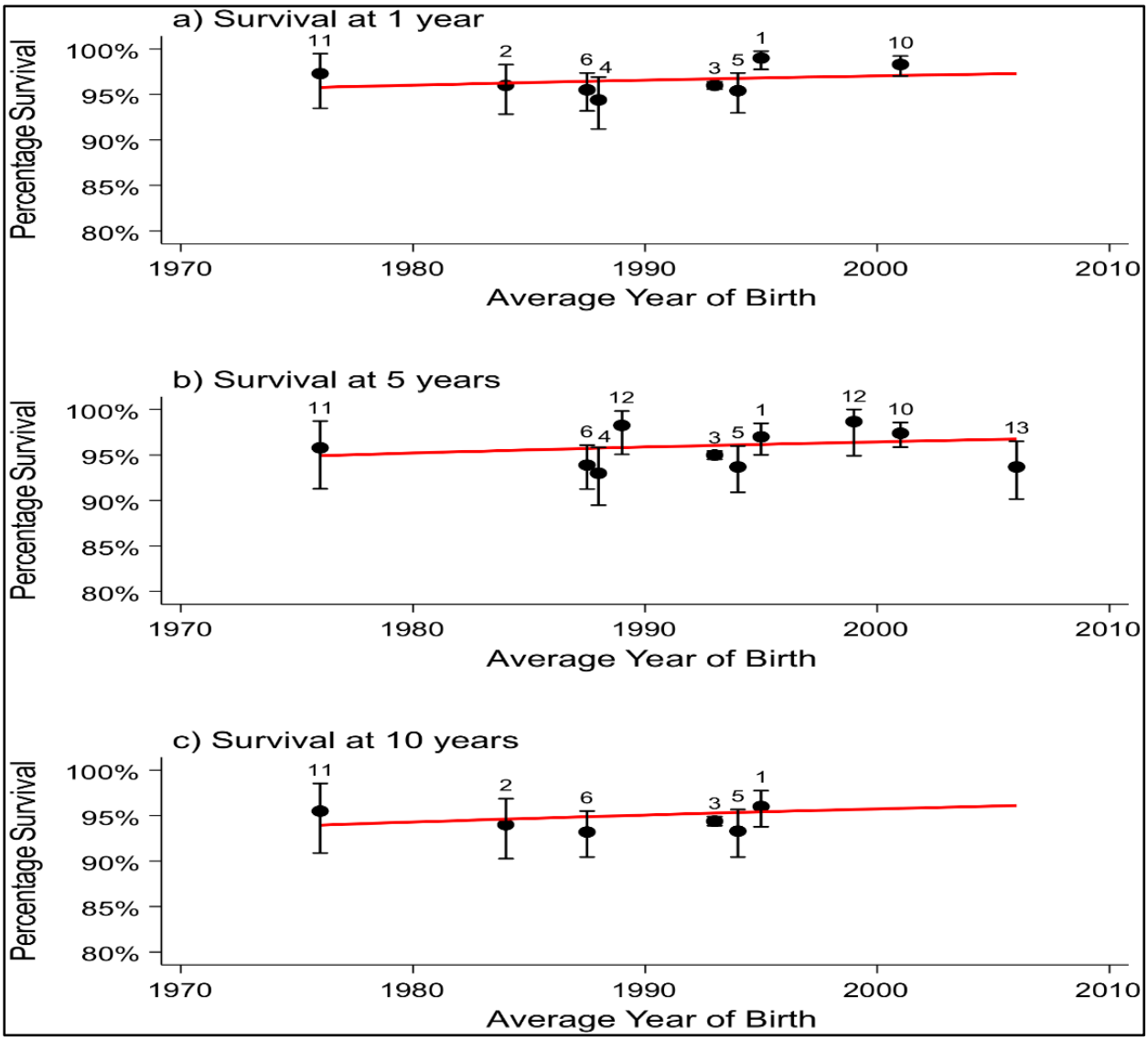
and the Middle East, and South Asia is for corrected neural tube defects. With SSA and South Asia having the lowest proportion of congenital heart abnormalities that are amenable to surgery, it may imply that the anomalies seen in these two regions are more severe, with the capacity to result in stillbirths, thus, not being accounted for when the burden of congenital anomalies is being estimated.

The 20-year survival rate of 85.5% for babies born with at least one congenital anomaly in the United Kingdom is reassuring[45]. Orofacial and urinary system anomalies are the least lethal – 97.6% and 93.2% respectively. About seventy-nine percent (79%) of those born with chromosomal anomaly actually survive up to at least 20 years. Survival for cardiovascular defects is 89.5% and the least is found among children with nervous system defects – 66.2%. The strength of this study is the fact that survival status was available for 99% of the babies born with anomalies within the study period. It is also estimated that about 57% of congenital abnormalities in LMICs are amenable to surgery and this intervention, when conducted on time could bridge the gap between outcomes in LMICs and the high-income countries (HICs)[9].

Similarly, a meta-analysis by Glinianaia and colleagues[46] showed impressive survival estimates for European babies born in the year 2020 with a congenital anomaly. Twenty-year survival rates for spina bifida, encephalocele, orofacial clefts were 89%, 71%, and >99% respectively. For disorders of the digestive tract, oesophageal atresia, congenital diaphragmatic hernia and gastroschisis, the estimated survival rates were 92%, 83%, and 92% respectively. Survival was consistently higher for gastroschisis than for omphalocele. With respect to the common trisomies, trisomy 13 and 18 had the poorest survival rates at 1 year: 12-21% for trisomy 13 and 2-20.6%. The 5- and 10-year survival rate for trisomy 18 were 14% and 13% respectively.

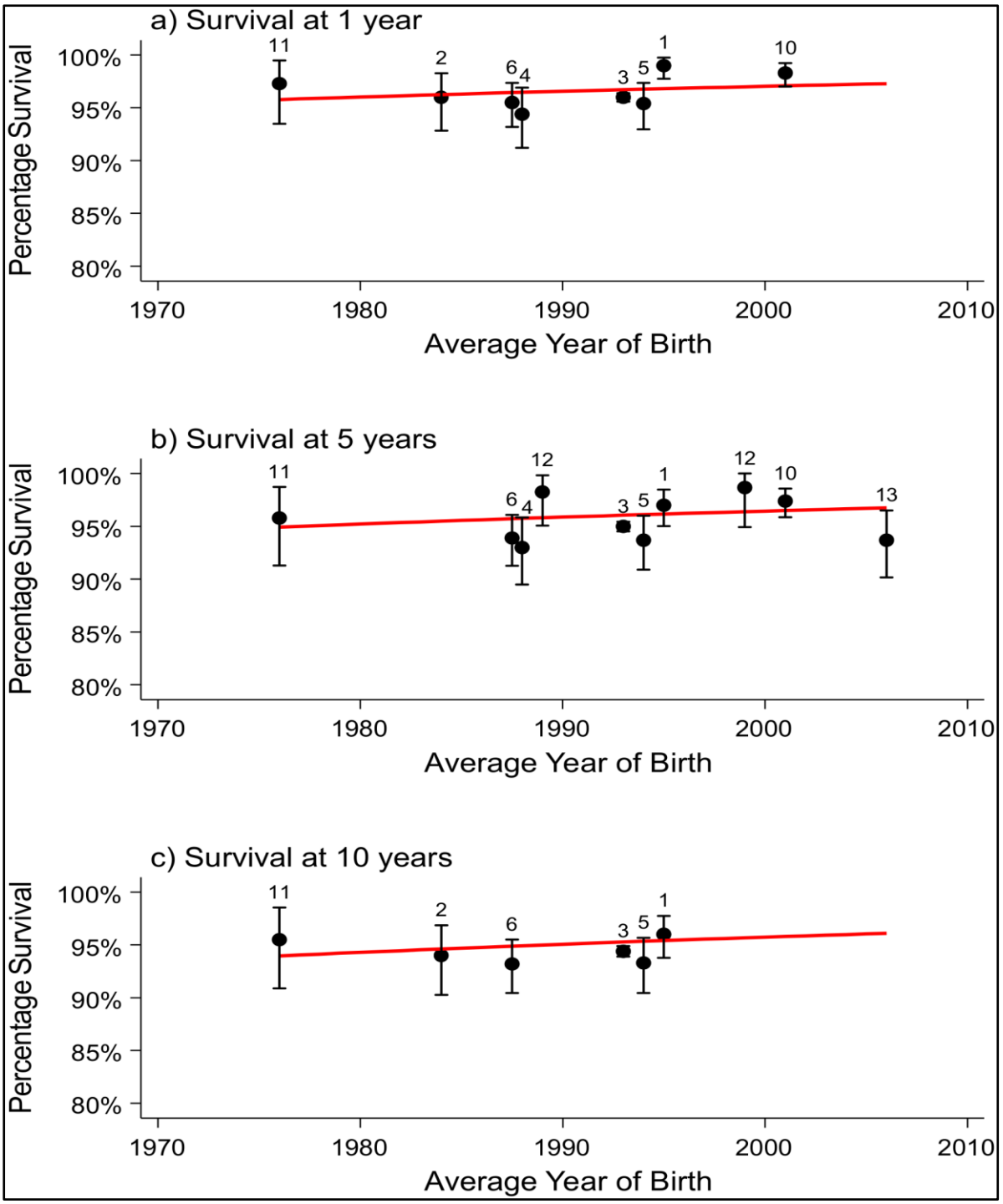
Trisomy 21 has the most encouraging survival rates among the trisomies, and this is irrespective of associated cardiac defects. The overall 20-year pooled estimate with or without a cardiac anomaly was 96%. Figures 1.9 and 1.10 give a pictorial representation of the survival rates, first for those without cardiac defects and then those who had.

This data also reflects the point of good support systems and early medical intervention being the mainstay for survival in children born with anomalies.



Source: Glinianaia S V., Morris JK, Best KE, Santoro M, Coi A, Armaroli A, et al. Long-term survival of children born with congenital anomalies: A systematic review and meta-analysis of population-based studies. PLOS Med [Internet] 2020[46]

Figure 1.9: Survival estimates of children with Down Syndrome associated with congenital heart defect at 1, 5, and 10 years of age over time (11 birth cohorts from 10 studies)



Source: Glinianaia S V., Morris JK, Best KE, Santoro M, Coi A, Armaroli A, et al. Long-term survival of children born with congenital anomalies: A systematic review and meta-analysis of population-based studies. PLOS Med [Internet] 2020[46]

Figure 1.10: Survival estimates of children with Down syndrome without congenital heart defect at 1, 5 and 10 years over time (11 birth cohorts from 10 studies)

1.3.7 Burden on Health Systems

Dealing with congenital anomalies puts a big strain on the finances and resources of the health systems. Most congenital anomalies in Ghana are diagnosed after birth due to lack of proper prenatal screening and diagnosis. Hence, a large number of babies with congenital anomalies are born alive. It is already estimated that about 94% of babies born with congenital anomalies are from LMICs[9]. Once born, these children require the health systems and strong family support for their survival and quality of life. They often need sophisticated imaging equipment like computer tomography, magnetic resonance imaging, echocardiography and other expensive diagnostic tests to assess the extent of the defects in order to guide their management. It is worth mentioning that in Ghana, these sophisticated tests are not covered by the National Health Insurance Scheme and so these services are limited to those who can afford. Financial constraints in this case, therefore delays definitive treatment for the babies and may lead to prolonged hospital stay, severe morbidity, and death.

Prolonged hospital stay may also be inevitable as most of the babies will need ventilatory support and other interventions until adequate resuscitation and stabilisation have been achieved. The abnormalities amenable to surgery require either a once-off corrective surgery or multiple surgeries to reduce the level of disability and morbidity. The admission sometimes requires at least one parent or family member to either be on admission with the child or at least pay frequent visits. There is therefore a reduction in workforce productivity due to parents' frequent absenteeism at work. The cost of surgeries also puts a toll on the finances of the family and the already-stretched health system. Moreover, prolonged hospital stay is associated with nosocomial infections which require resources to treat.

Lindower and colleagues[47] demonstrated that the length of stay for neonates with major congenital abnormalities in United States of America was almost twice that of those without (16 days versus 9 days). The cost of stay also doubled for those with major abnormalities (USD24,655 versus USD12,339). This study was conducted more than 20 years ago so costs are likely to have gone up over the years with the introduction of better and more sophisticated diagnostic machines and treatment options in this dynamic medical practice.

With the advances in surgery, mortality from congenital malformations has been reduced to less than 10%[48]. The downside of this is that morbidity has rather increased. Some survivors suffer life-long disabilities accounting for 25.3 to 35.8 million disability-adjusted life years (DALYs) worldwide[9]. Children with severe disabilities often require dependency on another person. This translates into the use of more healthcare services and higher health care expenses than their counterparts without disabilities. In an American study[49], there were significant differences in length of hospital stay (464 versus 55 days per 1000), non-physician professional visits (3.0 versus 0.6) and home health provider days (3.8 versus 0.04) for children with disabilities under 18 years than those without. Another important finding from the study was the vulnerability of low-income families to having greater financial burden due to more out-of-pocket expenses since most of them do not have health insurance cover. These factors highlight the financial burden on the health system and the families of such children. In some instances, this stress is escalated as some parents are compelled to abandon their income-generating jobs in order to dedicate time to cater fully for the physical and emotional needs of their special children. On the other hand, because of the inability to cope with the stress involved in giving their children a decent life, some parents may resort to the abandonment of these children, exposing them to societal dangers and even death.

1.3.8 Prevention of Congenital Abnormalities

About 70% of congenital abnormalities are said to be preventable or can be ameliorated[6]. Preventive measures are grouped into primary, secondary, and tertiary[5]. Primary prevention basically prevents the cause. It includes measures like folic acid supplementation and vaccination against conditions like rubella, and optimisation of blood glucose in diabetics. The secondary prevention entails early detection and intervention which will include training in prenatal diagnosis, training in the care of babies with congenital anomalies, and equipping of neonatal units. Tertiary prevention aims to reduce disability to the barest minimum through surgery. Based on these, the World Health Organization has enumerated ten (10) strategies for the primary prevention of congenital anomalies[14]. They are:

1. encouraging balanced diet and maintenance of healthy weight among adolescent girls
2. making sure adolescent girls and mothers take in adequate amounts of vitamins and minerals, particularly folic acid
3. avoidance of harmful agents such as tobacco and alcohol
4. pregnant women and women of child-bearing age to avoid travels to areas experiencing outbreaks of infection that are associated with congenital anomalies;
5. reducing exposure to dangerous substances, such as pesticides and heavy metals in pregnant women.
6. achieving optimum preconception and antenatal control of diabetes
7. ensuring the appropriate use of medication and medical radiation in pregnant women, using a risk versus benefit approach.
8. screening and treating infections, especially syphilis, varicella and rubella
9. vaccination for women and children (particularly the rubella vaccine) for children and women;
10. health staff education in promoting preventive strategies for congenital anomalies

Prenatal screening for infections and fetal anomalies plus neonatal screening for familial genetic conditions are the mainstay for early detection of congenital abnormalities (secondary prevention). In order to select high risk patients, a good patient history to identify risk factors such as maternal age, chronic medical illnesses and the use of tobacco is essential. Tertiary prevention is the offer of surgical services for anomalies that can be surgically corrected and the early initiation of treatment for the functional anomalies such congenital hypothyroidism and thalassemia.

The Participant Working Group of the Dar es Salaam Seventh International Conference on Birth Defects and Disabilities in the Developing World also summarises the strategies for the reduction of congenital abnormalities into four main areas – *improving data quality*, *reducing risk*, *improving care* and *empowering the public and civil society*[50].

1.3.9 Prenatal screening and diagnosis

In high-income countries, there are laid-down policies that guide prenatal screening for congenital abnormalities. The commonly investigated are the chromosomal anomalies, with Down syndrome (Trisomy 21) being major, and structural anomalies like cleft palate, gastroschisis and neural tube defects. The methods employed are ultrasound and maternal biochemical tests in the first and second trimesters, and non-invasive prenatal screening/ tests (NIPS/ NIPT), which is cell-free DNA testing using maternal blood sample[51,52]. Structural anomalies are generally screened for in both the first and the second trimesters, with a third one in the early third trimester for countries like Croatia. These countries also have clear laws on termination of pregnancies affected by major congenital anomalies. By this, mothers/ couples can opt for termination before a set gestational age, defined by the laws of their country. Foeticide is also permitted after the age of viability in advanced gestations when major abnormalities and lethal anomalies are present.

The detection rate of congenital malformation by prenatal ultrasound in Africa is only 20% and almost all were diagnosed late in the pregnancy[53]. In a study in India, congenital anomalies were detected in 7.6% of women going for prenatal ultrasound but only 1.6% of these abnormalities could be well diagnosed in the first trimester[54]. This brings to the fore the issue of ultrasonography in developing countries in view of limited resources. In fact, the benefit and feasibility of obstetric ultrasound as an integral part of antenatal healthcare has been adequately explained by some researchers[53–56]. In order to be able to maximise the benefit of this service, some conditions have been proposed - maintenance of good quality perinatal care, offering at least three scans as part of basic ANC, establishing first trimester screening, training of sonographers and standardising basic examination[56].

Building on the ultrasound, the combined first trimester screening (cFTS) for the common aneuploidies (Trisomies 21, 18, and 13), which comprises maternal age, maternal blood samples for pregnancy-associated plasma protein A (PAPP-A) , beta human chorionic gonadotropin (b-hCG), plus ultrasound scan for nuchal translucency, can also be employed as it shows satisfactory detection rates[57].

South Africa is one of the few African countries that have well-structured guidelines on prenatal screening for congenital anomalies and a comprehensive law on termination

of pregnancy, including fetocide. Ghana does not have a screening policy yet and the acceptability of prenatal screening and diagnosis in the population has not been explored. However, using the high rate of acceptance of prenatal diagnosis for sickle cell disease as a premise, it is likely for screening and diagnosis of other disorders to also be widely accepted in the country

In a cost-benefit analysis, Wanapirak and colleagues[58] identified independent screening plus NIPT (cell-free DNA) as cost-beneficial for the screening of Down syndrome in developing countries which are obviously resource-constrained and lack a widespread sonographic expertise on nuchal translucency measurements. Per this model, pregnant women who are seen in the first trimester (9–14 weeks) are screened with the first trimester maternal serum biochemical markers (pregnancy-associated plasma protein-A (PAPP-A) and serum beta-human chorionic gonadotropin (b-hCG)) and likewise, the second trimester biomarkers (alpha fetoprotein, b-hCG, unconjugated oestradiol, with or without Inhibin-A) for those seen in the early second trimester (15–20 weeks).The high-risk cases will be followed up with NIPT, and then, amniocentesis for the NIPT-positives. Since this model is only for the screening of Down syndrome, it is likely to give couples a false sense of security that their unborn baby is structurally normal; meanwhile it highlights only one aspect of prenatal screening and totally neglects the presence of structural defects which are only diagnosed on ultrasound, and not with biochemical tests. Therefore, the pressing need for developing countries to develop a holistic cost-effective programme that can detect aneuploidies, genetic syndromes as well as isolated structural defects cannot be overemphasised.

It should also be emphasised that prenatal screening is not devoid of disadvantages. There is evidence of parental anxiety before and after either ultrasound or other diagnostic tests are carried out. It has also been shown that procedures that have an impact on fetal health make women more anxious that those that have maternal health impact[59]. Hence, adequate counselling by qualified personnel is required before and after screening.

1.3.10 Parental experiences with having a child with a congenital anomaly

The expectation of every expectant couple is to have an uneventful pregnancy with a healthy baby. The diagnosis of congenital abnormalities is obviously devastating and leads to a negative pregnancy experience. The psychological distress, anxiety and fears that affected parents experience is enormous, and this increases with increasing severity of the abnormality[10,13,48,60]. A lot of this arises from the inability to attribute a specific cause for the occurrence of the anomaly most of the time, coupled with the strong traditional religious belief that such children are given to people as a form of punishment for a sin they have committed[61,62]. In Ghana, this belief is so deeply rooted that even the introduction of Christianity and Islam has not been able to eradicate it and the leaders of those religious bodies even hold on to this. Parents of children with an anomaly or disability who happen to be wealthy sometimes bear the greatest brunt of this societal prejudice as they are often branded as money ritualists who exchange the fortunes of their children for money. This judgemental premise is associated with stigmatization and isolation of such families. Without proper counselling and social support systems, parents of children with anomalies or disability become vulnerable to living with guilt, self-worthlessness, depression and other psychological problems.

Major congenital anomalies do not confer high mortality risk only to the child but to the mothers as well, compared to women without an affected child. Cohen and colleagues[63] highlighted this risk when they followed up 455,250 mothers of children with a major congenital anomaly. The causes of death were mainly cardiovascular disease, respiratory disease and other natural causes. The cardiovascular disease may arise from the physical, emotional, and psychological stress of caring for the child(ren). Suicide was not documented in the study.

1.3.11 Parental perceptions of TOPFA

Diagnosing a major congenital anomaly antenatally can be frustrating for the parents. They are often faced with their first parental decision which is to either continue or terminate the pregnancy. The decision-making is based on multiple factors – the attitude and communication style of the health worker who is breaking the bad news; the information they are given about the condition; the financial implications; the

availability of a support system, and their own personal and religious beliefs and socio-cultural background[13,64]. With respect to prenatal diagnosis of severe or lethal abnormality and Down syndrome (DS), the following factors are important in the decision to terminate or continue the pregnancy – maternal age and its implications on fertility, religion, gestational age, history of voluntary abortion, number of living children, financial implications, anticipated quality of life of the child after birth, societal perceptions of DS, and support from their significant others[13,64,65].

Although prenatal diagnosis has become an integral part of antenatal care in developed countries with a high level of acceptance, some couples prefer to opt out, mainly because termination of pregnancy is not an option for them[66]. In a four-year nationwide review of the Danish Fetal Medicine database, the acceptability of invasive testing after a screen-positive combined first trimester screening (cFTS) and termination of pregnancy for DS were 82.8% and 82.2% respectively[57]. The rate of pregnancy termination after the diagnosis of sickle cell in Nigeria is also about 70%[67].

Such vital information about acceptability of prenatal diagnosis for other congenital anomalies is non-existent in Ghana and most part of Africa. It is therefore important for adequate studies to be done on the perceptions about prenatal diagnosis in Africa to serve as a guide to stakeholders and policy makers in maternal and child health care.

It is also necessary to evaluate the perceptions of obstetricians on prenatal diagnosis and termination of pregnancy, as it has an impact on service delivery. Among British obstetricians in 1980 and 1993, it was noted that the proportion against termination of pregnancy had not changed over the 13-year period, although they all made exceptions for serious fetal anomalies[68]. However, over that period, the number of obstetricians that required an undertaking to terminate an affected pregnancy before performing an amniocentesis in 1980 had reduced by about half in 1993 and also more of them were comfortable with TOPFA and abortion for social reasons as well but less for termination of Down syndrome after 24 weeks.

CHAPTER TWO – METHODS AND MATERIALS

2.1 METHODOLOGY

2.1.1 Study Design

This was a combination of a retrospective quantitative study on all neonatal congenital abnormalities diagnosed between 1st January 2010 to 31st December 2019 in CCTH, and a six-month prospective qualitative study to explore the perceptions of parents whose neonates/ stillborns or aborted fetuses had been diagnosed with at least one congenital anomaly.

2.1.2 Setting

The study was conducted at the Cape Coast Teaching Hospital in the Central Region of Ghana. The hospital has existed for about 20 years now and was upgraded into a tertiary teaching hospital in 2014. It is the main tertiary referral centre for the Central, Western, and parts of the Ashanti and Greater Accra Regions of Ghana. From the 2010 Population and Housing Census, there were 2,201,863 people in Central; 3,093,201 in Western; 4,780,380 in Ashanti; and 4,010,054 in the Greater Accra Region. The hospital receives referrals from Community-based Health Planning and Services (CHPS) compounds, health centres, clinics, and hospitals. It also accepts walk-in patients. It is a 400-bed hospital which is endowed with specialists and sub-specialists. Paediatric surgery services are offered by a visiting specialist bi-weekly. But there is an on-site paediatric urologist. The hospital is one of the training centres for residents of the Ghana College of Physicians and Surgeons, and is accredited for housemanship training by the Medical and Dental Council. The Child Health Department has 6 resident paediatricians and other health cadres. It runs an outpatients' clinic on weekdays, but has a 24-hour emergency service. Neonates that need admission are put in either the neonatal unit, preferably called the Special Care Baby Unit (SCBU), or the main paediatric ward, if stable. Neonates can also be de-escalated from the SCBU to the paediatric ward. Data of such babies are captured in both the SCBU and the Paediatric Ward A&D books. It is mandatory for all babies born alive with congenital abnormalities in the hospital to be assessed at the SCBU for further management, irrespective of whether or not they need admission. Outside referrals for similar reasons are also received at the unit. Even stable babies with

congenital abnormalities who are born outside CCTH are sent to the SCBU to be attended to and not the paediatric outpatients' department (OPD).

Just as for live babies, stillborns are also examined at the delivery suite for external abnormalities after delivery but routine autopsy is not done for stillborns and neonatal deaths. Autopsies on stillborns who have a scan-diagnosis of an internal abnormality are considered on request by the attending obstetrician and/ or parents of the child. Parents of babies with congenital abnormalities are also taken through psychological counselling by the Psychology and Counselling Unit of the Hospital, as part of routine care.

The people of Central Region are from the Akan Ethnic group. It is the largest ethnic group in Ghana, forming 47.3% of the population, and comprising the Asante, Akyem, Kwahu, Akuapem, Fante, Bono, Adanse, Twifo, Assin (Asen), Fante, Akwamu, Sehwi, Awowin, Nzema and the Ahanta, and spread across 8 of the 16 regions. There are several languages within this group, including Twi, Fante, Akyem, Akuapem, Bono and Guan. The people of the Central Region speak Fante and Twi, with Fante being more predominant. The regional capital town is Cape Coast. According to the 2010 Population and Housing Census, the overall literacy rate in the Cape Coast Metropolis is 90%, and 67.2% can read and write in both English and a Ghanaian language.[69]

2.1.3 Study Population

***Population A*:** All babies within 28 days of birth, who were seen at the paediatric outpatients' clinic, or admitted at the SCBU or paediatric ward, with at least one documented congenital abnormality, from the 1st of January 2010 to the 31st of December 2019.

***Population B*:** Parents whose neonates or stillborns were diagnosed with at least one congenital abnormality between 13th April 2021 and 13th October 2021.

2.1.4 Sample Size

Population A: All neonates at SCBU with the diagnosis of a congenital abnormality in CCTH from 1st January 2010 to 31st December 2019 were included.

Population B: All parents whose neonates were diagnosed with a congenital abnormality, from 13th April 2021 to 13th October 2021 were approached at the delivery suite and the SCBU. Parents of stillborns at any gestational age who had a congenital abnormality, confirmed either by an antenatal ultrasound scan, physical inspection after delivery, and/or autopsy were included in this part of the study and were recruited at the delivery suite. Appropriate and uniform translation of the questionnaire from English into either Twi or Fante was done by the researcher and three research assistants so that parents who cannot read English can be assisted to fill the questionnaire. Only those who gave their consent to participate were made to fill the questionnaire and both parents of an affected baby could be recruited. All parents with affected babies were referred to the clinical psychology unit for counselling.

2.1.5 Inclusion Criteria

All neonates documented to have at least one congenital abnormality on admission at the SCBU from 1st January 2010 to 31st December 2019, and all parents with babies born dead or alive with at least one congenital abnormality between 13th April 2021 and 13th October 2021.

2.1.6 Exclusion Criteria

Retrospective study

Stillborns with congenital abnormalities and babies with ≥30% of their data missing from the records were excluded from the retrospective study.

Prospective study

Parents who declined participation

2.1.7 Data Collection and Tools

Retrospective Study Population*:* Available maternal and neonatal data was captured from the Admissions and Discharges (A&D) books of the SCBU.

All eligible babies were entered onto an Excel spreadsheet. The gestational age at delivery, the date of birth and age in days of neonates at the time of admission or consult, sex, birth weight, diagnosis, place and mode of delivery, and the maternal characteristics, which are name, age and parity were obtained from the SCBU A&D book. The admission outcomes (discharged alive, died, or referred) and the number of days spent on the ward were also documented for those that required admission. There was no anonymity but information was kept as confidential and only accessible to the researcher and the two research assistants.

2.1.8 Categorization of abnormalities using the EUROCAT subgroup classification system

The International Classification of Diseases coding system was not employed in the retrospective study. A modification of the EUROCAT subclassification system was used to group the various abnormalities. The original systems are nervous system; eye; ear, face, neck; cardiac; respiratory; orofacial; digestive; abdominal wall; urinary; genital; limb; chromosomal; multiple; and other anomalies/ syndromes. (Appendix 4 has the full list of abnormalities under each subclass)

In this study, the subclass ‘limb’ was replaced with ‘musculoskeletal’. Osteogenesis imperfecta was originally under the category ‘other anomalies/ syndromes’ but in this study, it was recategorized under musculoskeletal. This subgroup therefore comprises all limb abnormalities including polydactyly and talipes (club foot). Due to the unavailability and/or the lack of knowledge on confirmatory tests (karyotyping) in most parts of Ghana, the diagnosis of suspected chromosomal abnormalities was maintained as such since they were never confirmed. The suspicion was made on the basis of the presence of abnormalities typically associated with common chromosomal syndromes such as Trisomies 21, 18, and 13. For example, some of the typical abnormalities associated with trisomy 13 or Edward syndrome include holoproscencephaly, midfacial clefts, midline abdominal wall defects and cardiac defects. Similarly, trisomy18 or Patau’s syndrome has choroid plexus cysts and

strawberry-shaped head on ultrasound scan, micrognathia and clenched fingers as some of the typical manifestations. Neonates with malformations in more than one subgroup system but not perceived as syndromic or related to a particular association were classified as ‘Multiple’. The category ‘Others’ in this study were conjoint twins, Moebius syndrome and obvious VACTERL (vertebral, anorectal, cardiac, tracheoesophageal, renal and limb abnormalities).

The following are the specific diagnoses that were retrieved from the data source.

Abdominal wall abnormalities: omphalocele, gastroschisis

Cardiac abnormalities: congenital heart disease, cyanotic heart disease.

Digestive system abnormalities: oesophageal atresia, anorectal anomalies, rectal atresia, intestinal stenosis, imperforate anus, trachea-oesophageal fistula, duodenal atresia, Hirschsprung’s disease, diaphragmatic hernia

Eye abnormalities: congenital bilateral cataract

Respiratory system abnormalities: congenital laryngomalacia

Genital abnormalities: phallus anomalies, ambiguous genitalia, hypospadias

Musculoskeletal abnormalities: limb abnormalities, talipes, osteogenesis imperfecta (OI), achondroplasia

Nervous system abnormalities: hydrocephalus, spina bifida, meningocele, myelomeningocele, encephalocele, anencephaly, neural tube defect, Dandy-Walker with hydrocephalus, Dandy-Walker, microcephaly

Orofacial abnormalities: cleft palate and hare lip, bilateral cleft lip and palate, bilateral cleft palate, cleft lip

Urinary system abnormalities: polycystic kidney disease, imperforate urethral orifice, Prune belly syndrome, bladder exstrophy

Suspected chromosomal abnormalities: syndromic baby, down syndrome, Patau syndrome, Edward syndrome

Other anomalies/ syndromes: conjoint twins, Moebius syndrome, VACTERL

Prospective Study Population: A data collection tool (See Appendix 2) was used to assess the perceptions of parents with neonates born with congenital abnormalities, regarding prenatal screening/ diagnosis and termination of pregnancy. Parents of stillborns at any gestational age who have a congenital abnormality, confirmed either by an antenatal ultrasound scan or physical inspection after delivery were included.

The researcher and two research assistants adopted a uniform translation of the questionnaire from English into Fante and Twi. The translated questionnaire was pretested in March 2021 at two entry points – the SCBU and the delivery suite.

The research assistants were then allocated to the SCBU and the delivery suite. Parents who could not read English were therefore assisted to fill the questionnaire.

Anonymity was maintained but the data but coded.

2.1.9 Data analysis

Data was entered in Microsoft Excel, cleaned and exported onto STATA 14 (College Station, TX, USA) for analysis. Descriptive statistics were presented as frequencies, proportions, percentages, mean with standard deviation and median with range and charts. The outcome variable was the status of the baby upon exiting from the NICU, ward, or outpatients' department (alive, referred or dead). Pearson chi-square was used to determine association between independent variables and mortality in a univariate analysis. A p-value of <0.05 at 95% confidence level was considered statistically significant. The variables with significant p-values in the univariate analysis were entered into a Cox regression analysis for adjusted hazard ratios. Kaplan-Meier survival graphs were generated for comparison of survival among the different categories of the variables which are associated with mortality. For the prospective study, the demographic characteristics of study participants and their responses to the specific subjects were captured and drawn into a central them where possible.

2.2 ETHICS

Ethical clearance was sought from the Ethical Review Committee of the Cape Coast Teaching Hospital (**CCTHERC/EC/2020/081**) and the Wits Human Research Ethics Committee (**M2011122**)

2.3 FUNDING

The study was funded by the researcher. No external source of funding was required. One of the two research assistants involved in the data collection is an employee of the hospital. The second is a member of a research group, which the researcher is also part of. Hence, the research assistants were not remunerated.

2.5 CONFLICT OF INTEREST

No conflict of interest to declare.

CHAPTER THREE – RESULTS AND DISCUSSION

RESULTS

3.1 Background, demographic and clinical characteristics of study participants

There were 8346 neonates admitted to SCBU of CCTH during the study period and, there were 1593 total neonatal deaths at the SCBU. The total number of neonates with at least one congenital anomaly were 236. Therefore, the prevalence of congenital abnormalities at the SCBU during the study period was 2.8% (236/8346). The mortality rate among neonates with congenital abnormalities was 31.4% (n= 74), which accounted for 4.6% (74 out of 1593) of the total SCBU mortalities over the ten-year period. There were also 27,320 deliveries (both live and stillbirths) in the hospital during this period. The SCBU admissions rate in the hospital over the study period, therefore was 30.5% of total deliveries (305 per 1000 births).

Table 3.1 shows the demographic characteristics of the mothers and the newborns. Of the 236 mothers, 33.5% (n = 79) were between the ages of 25 – 35 years. For eighty-nine (89) mothers, the age was unknown, as reflected in Table 1. The mean age of the mothers was 26.8 (SD: 6.8) years with a minimum age of 15 and maximum age of 45 years. The median parity of the mothers was 1.5 (SD: 1.5) and the median gravidity of 2.6 (SD: 1.7). Almost two-thirds (65.7%; n = 155) of the neonates were delivered at term [Figure 3.1] and 47.5% of the neonates had normal weight [Figure 3.2]. About 13% (n = 31) were preterm, 1.3% (n= 3) postdate and missing data in this category accounted for about 20% (19.9%; n = 47). The mean age of the neonates at the time of admission was 0.9 (SD: 2.2) days with a range of 0 to 21 days. No name appeared twice. Male neonates constituted 58.9% (n = 139); four (4) neonates had ambiguous genitalia and sex was not indicated in seven (7). Majority (78.0%, n = 184) of the neonates were delivered in a hospital. Four neonates were documented as being twins but the names of their mothers were different; hence, those neonates were most likely from four different twin pregnancies.

Table 3.1: Demographic characteristics of study participants

Variable	Frequency, N = 236	ǂPercentage, % [Range]
Age of mother (years)		
< 25	53	22.5
25 – 35	79	33.5
> 35	15	6.4
Not indicated	89	37.7
Mean age (±SD)	26.8 (±6.8)	[15 – 45]
Age of neonate (days)		
0	154	65.3
1	38	16.1
2	8	3.4
3	9	3.8
4+	22	9.3
Not indicated	5	2.1
Mean age (±SD)	0.9 (±2.2)	[0 – 21]
Gender of neonate		
Male	139	58.9
Female	87	36.9
Undetermined	4	1.7
Not indicated	7	3.0
Place of delivery		
Clinic	4	1.7
Health centre	22	9.3
Home	16	6.8
Hospital	184	78.0
Not indicated	10	4.2
Parity		
Nulliparous	48	20.3
Primiparous	35	14.8
Multiparous	58	24.6
Not indicated	95	40.3
Median parity (±SD)	1.5 (±1.5)	[0 – 6]

Gravidity		
1 – 2	59	25.0
3 – 4	38	16.1
5+	13	5.5
Not indicated	126	53.4
Median gravidity (±SD)	2.6 (±1.7)	[1 – 8]

[Ŧ]Rounded to one decimal place

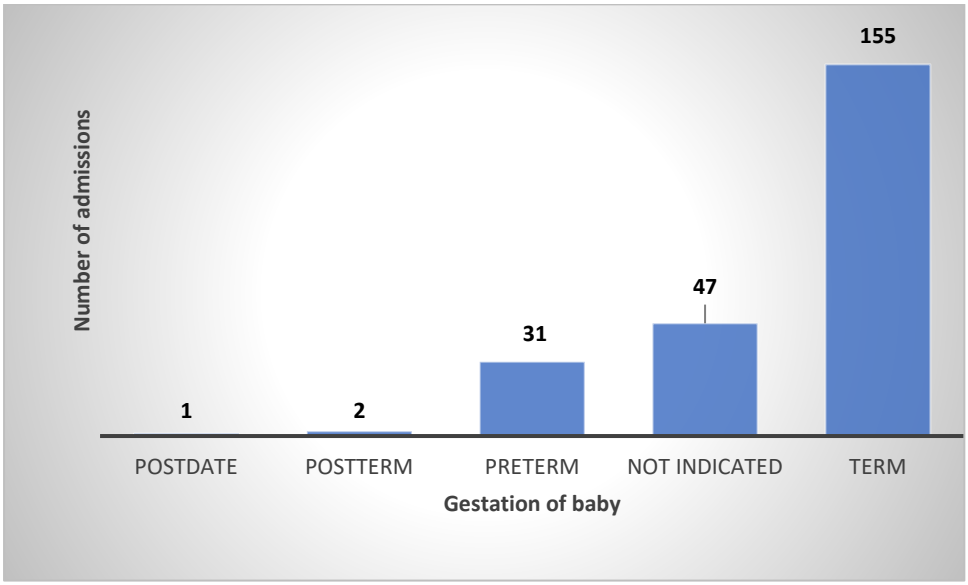


Figure 3.1 Gestational age

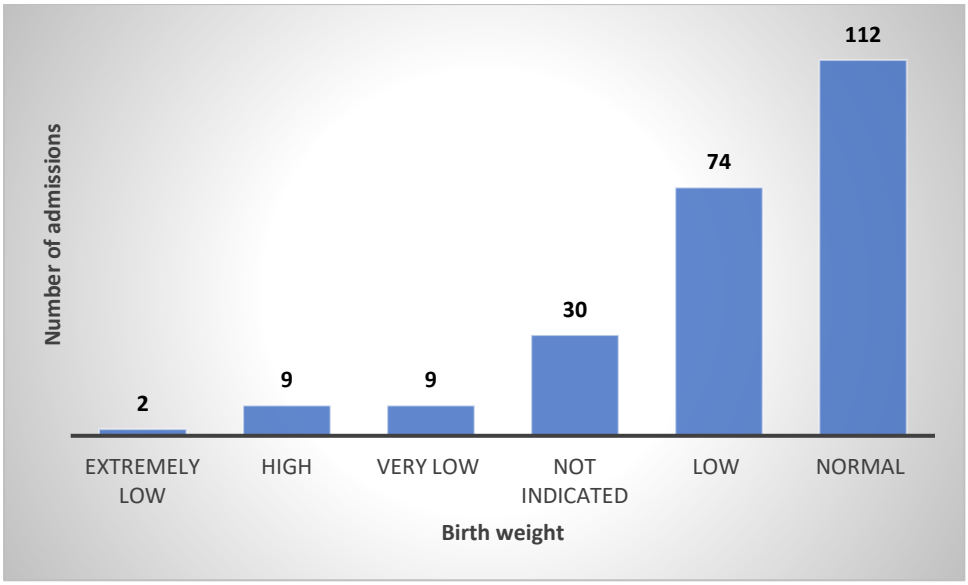


Figure 3.2 Birth weight of neonate

Table 3.2 shows the clinical characteristics of the neonates, specifically, the mode of delivery, duration of stay and the category of their abnormalities. Out of a total of 236 neonates, majority (89.0%, n = 124) were delivered vaginally. The median duration of stay of the neonates was 3.0 (SD: 7.2) days with a minimum stay of 1 day and a maximum of 43 days. The table also shows that abnormalities of the nervous system were the most common (n = 54; 22.9%), followed by suspected chromosomal abnormalities (n = 39; 16.5%), cardiac defects (n = 27; 11.4%) and abdominal wall abnormalities (n = 24; 10.2%). The least represented were the eye and the respiratory system abnormalities which had a prevalence of 0.4% (n = 1) each.

Table 3.2 Clinical characteristics of the neonates

Variable	**Frequency, N = 236**	**Ŧ Percentage, % [Range]**
Mode of delivery		
Ceasarean Section	86	36.4
Vaginal Delivery	124	52.5
Not indicated	26	11.0
Duration of stay (days)		
< 7	145	61.4

7 – 13	40	16.9
14 – 20	9	3.8
> 20	15	6.4
Not indicated	27	11.4
Median duration of stay (±SD)	3.0 (±7.2)	[1 – 43]
Category of diagnosis		
Abdominal wall	24	10.2
Cardiac	27	11.4
Digestive	21	8.9
Eye	1	0.4
Genital	3	1.3
Multiple	16	6.8
Musculoskeletal	19	8.1
Nervous	54	22.9
Orofacial	15	6.4
Respiratory	1	0.4
Suspected chromosomal	39	16.5
Urinary	8	3.4
Others	8	3.4

ǂRounded to one decimal place

3.2 Prevalence trend over the study period

Table 3.3 shows the trend in the prevalence of congenital abnormalities over the ten-year period, with the highest being recorded in 2014 to 2016 and 2019.

Table 3.3 Annual prevalence rates over the ten-year period

Year	Number of abnormalities	Total neonatal admissions	ǂPrevalence per 1000 admissions	Total births	ǂPrevalence per 1000 births
2010	12	1255	9.6	2307	5.2
2011	18	620	29.0	2104	8.6
2012	13	712	18.3	2635	4.9
2013	20	756	26.5	2656	7.5
2014	32	830	38.6	2618	12.2
2015	32	765	41.8	2854	11.2
2016	31	670	46.3	2904	10.7
2017	23	780	29.5	3055	7.5
2018	22	890	24.7	3160	7.0
2019	33	1068	30.9	3027	10.9
Total	**236**	**8346**		**27320**	

ǂRounded to one decimal place

3.3 Outcome of admission

About 64.8% (n= 153) of the neonates were alive at the time of discharge or referral while 31.4% (n = 74) died [Figure 3.3]. Of the 153 neonates that were alive, 70.6% (n = 108) were discharged home alive while the remaining 29.4% (n = 45) were referred for further management [Figure 3.4]. About 30% (n = 46) of the term neonates died [Figure 3.5]. The number of neonates that survived and died in each category of diagnosis have been presented in figure 3.6. The cumulative numbers per category in figure 3.6 are less than as documented in Table 3.2 and this is due to the undocumented outcome for some of the neonates. Table 3.4 shows the survivors and deaths in each subclass of abnormality.

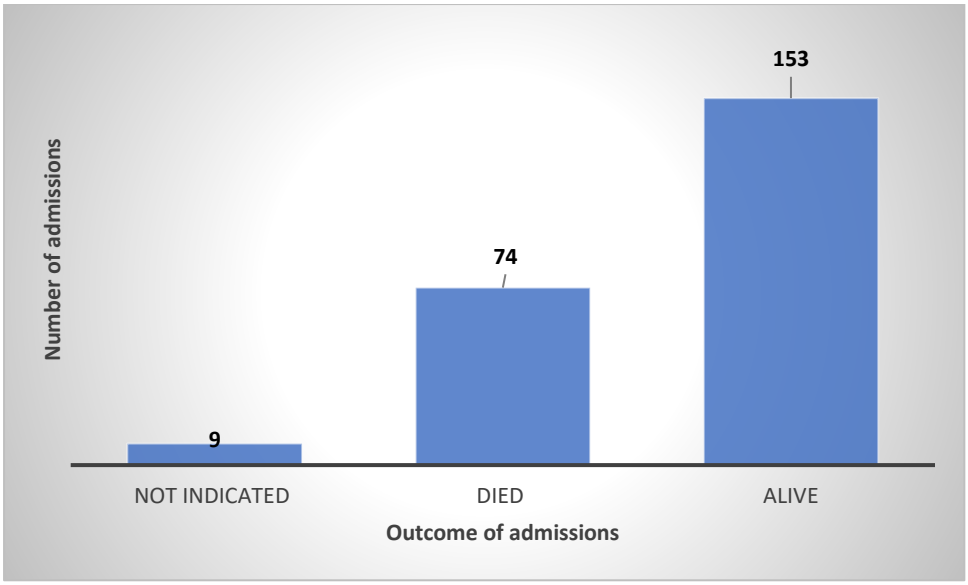


Figure 3.3 Outcome of admissions

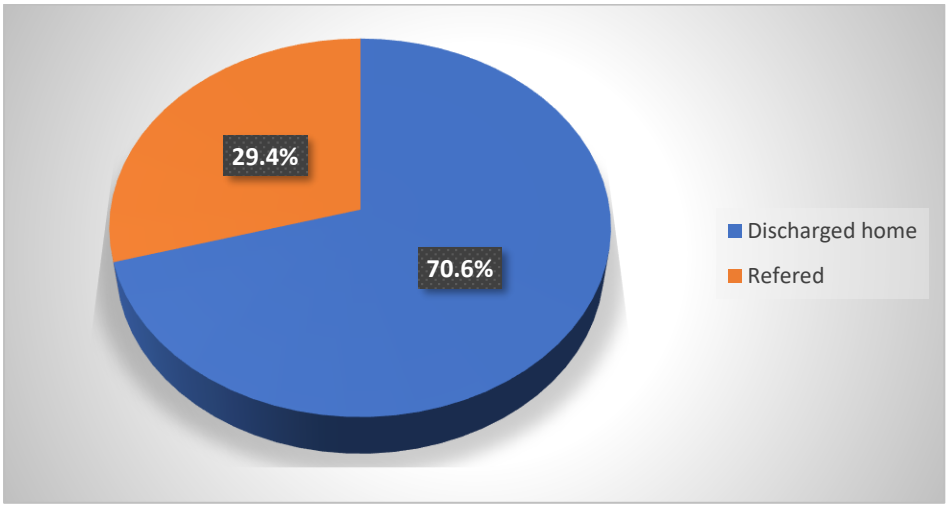


Figure 3.4 Outcome of survivors

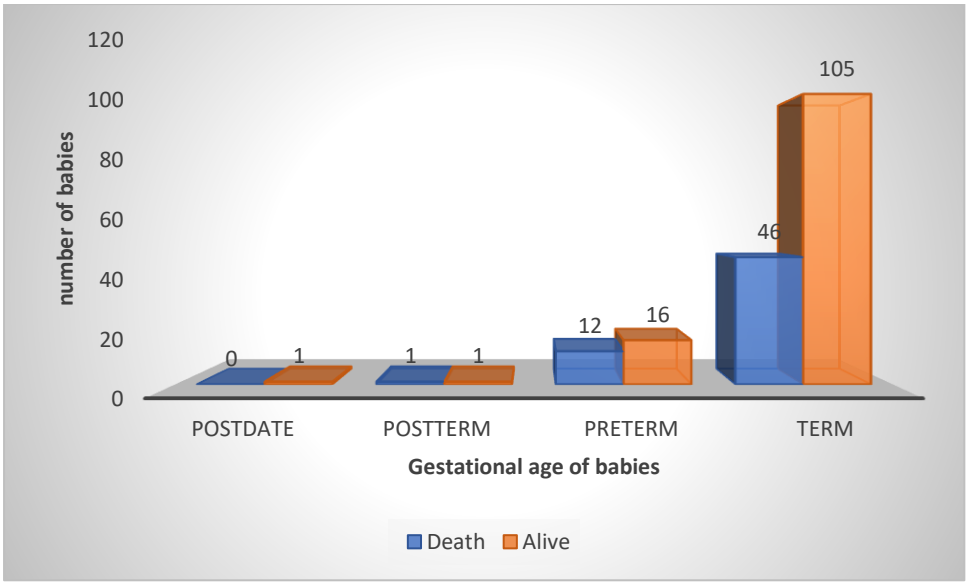


Figure 3.5 Gestational age and admission outcomes

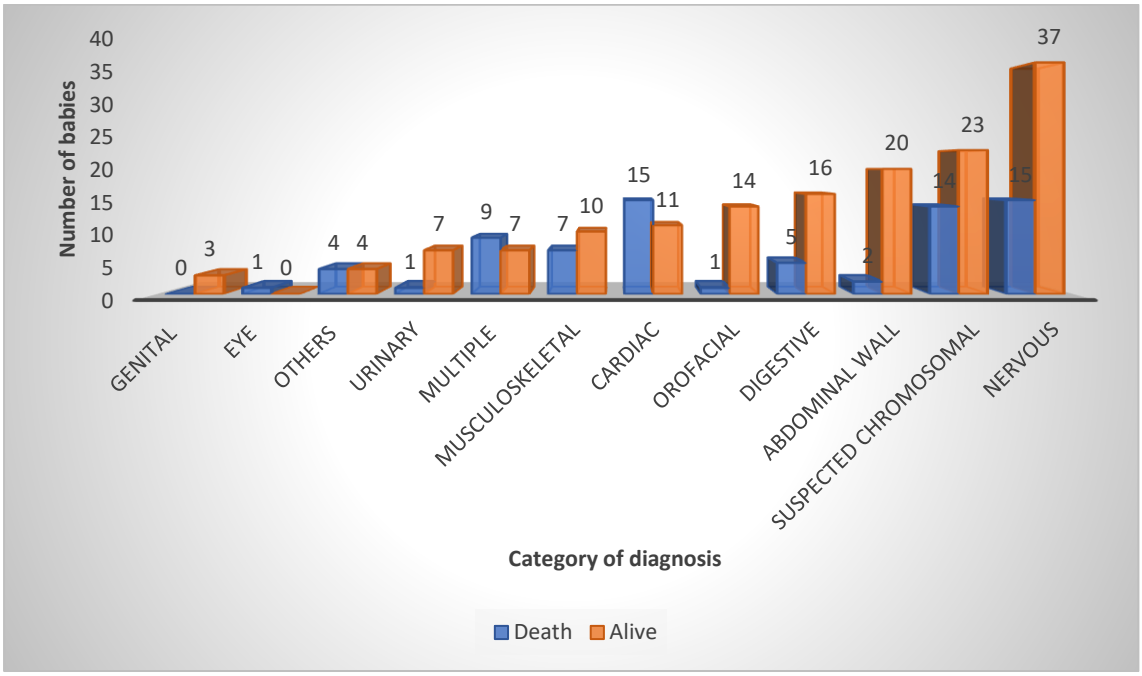


Figure 3.6 Category of abnormality and admission outcomes

The following are the specific diagnoses per category that were responsible for the deaths:

Abdominal wall: omphalocele, gastroschisis

Cardiac: cyanotic heart disease, congenital heart disease.

Digestive: duodenal atresia, congenital diaphragmatic hernia, imperforate anus, intestinal stenosis, anorectal malformations

Eye: bilateral congenital cataract

Multiple: arthrogryposis with ambiguous genitalia, hypospadias with anal atresia, omphalocele with cleft lip and palate, hydrocephalus with intestinal atresia

Musculoskeletal: osteogenesis imperfecta, limb abnormalities, achondroplasia, talipes

Nervous: anencephaly, encephalocele, dandy-Walker malformation, neural tube defects, hydrocephalus

Orofacial: cleft lip and palate

Suspected chromosomal abnormality: chromosomal abnormality, Down syndrome, Edward Syndrome, Patau syndrome. It is interesting to note that all six babies diagnosed as Down syndrome survived.

Urinary: prune belly syndrome

Others: conjoint twin, Moebius syndrome, VACTREL.

Table 3.4 Subclass mortality rate over the ten-year period

Subclass	Total number (N)	Survived (n^1)	Died (n^2)	Outcome not indicated	ŦSubclass mortality rate (%) (n^2/N x 100)
Abdominal wall	24	20	2	2	8.3
Cardiac	27	10	16	1	59.3
Digestive	21	16	5	1	23.8
Eye	1	0	1	0	100.0
Genital	3	3	0	3	0.0
Musculoskeletal	19	10	7	2	36.8
Multiple	16	7	9	0	56.3
Nervous	54	37	15	2	27.8
Orofacial	15	14	1	0	6.7
Respiratory	1	1	0	0	0.0
Suspected Chromosomal	39	23	14	2	35.9
Urinary	8	7	1	0	12.5
Others/ syndrome	8	4	4	0	50.0

ŦRounded to one decimal place

3.5 Contribution of congenital abnormalities to annual neonatal mortalities

Year	Total Mortalities (N)	Mortalities among neonates with congenital anomalies (n)	₸ Proportion of mortalities due to congenital anomalies (%) (n/N x 100)
2010	101	5	5.0
2011	131	6	4.6
2012	131	3	2.3
2013	143	7	4.9
2014	186	6	3.2
2015	173	11	6.4
2016	179	12	6.7
2017	155	9	5.8
2018	176	6	3.4
2019	218	9	4.1

*Missing data for outcome excluded from the calculation ₸ rounded to one decimal place

3.4 Factors influencing congenital anomalies admissions outcomes

Table 3.6 indicates the factors influencing admission outcomes in neonates with congenital abnormalities. Place of delivery and gravidity were significantly associated with death or survival in a univariate Cox regression analysis (crude hazard ratio). Neonates that were delivered in a hospital had about 5 times the risk of death (HR: 5.19, 95%CI: 1.62 – 1.66, $p < 0.001$) as those that were delivered in a clinic. Neonates that were delivered at home had about 7 times the risk of death (HR: 7.32, 95%CI: 1.94 – 2.77, $p < 0.001$) as those that were delivered in a clinic. This has been presented in the Kaplan Meier survival estimates graph [Figure 3.8].

Similarly, neonates born to mothers with at least five pregnancies were about 3 times more likely to die (HR: 2.61, 95%CI: 1.12 – 6.08, $p = 0.027$), compared with those whose mothers had had at most 2 pregnancies [Figure 3.7]. Neonates that were admitted due to a cardiac defect and multiple diagnosis had about 5 times (HR: 5.15, 95%CI: 1.18, 22.54, $p = 0.030$) and 6 times the risk (HR: 5.74, 95%CI: 1.24, 26.58, $p = 0.025$) of death respectively, compared with those that were admitted due to abdominal wall.

In a multivariate analysis, delivery in a hospital and gravidity of 5+ were the variables that were significantly associated with death (AHR: 2.61, 95%CI: 2.61, 9.55, p < 0.001) and (AHR: 3.29, 95%CI: 1.20 – 8.97, p = 0.020) respectively.

Table 3.6 Factors influencing congenital anomalies admissions outcomes

	Crude Hazard Ratio (HR)		Adjusted Hazard Ratio (AHR)	
Variables	**HR (95%CI)**	**P – value**	**AHR (95%CI)**	**P – value**
Age of mother (years)				
< 25	1.00			
25 – 35	1.03 (0.55 – 1.93)	0.923		
> 35	0.66 (0.22 – 2.00)	0.464		
Age of neonates (days)				
0	1.00			
1	1.42 (0.79 – 2.54)	0.241		
2	0.75 (0.18 – 3.10)	0.694		
3	1.69	1.000		
4+	1.40 (0.66 – 2.96)	0.380		
Gender of neonate				
Male	1.00			
Female	1.25 (0.78 – 1.99)	0.355		
Undetermined	1.01	1.000		
Place of delivery				
Clinic	1.00		1.00	
Health centre	2.51	-	3.02	1.000
Home	7.32 (1.94 – 2.77)	<0.001	1.06	-
Hospital	5.19 (1.62 – 1.66)	<0.001	2.61 (7.12 – 9.55)	<0.001
Parity				
Nulliparous	1.00			
Primiparous	1.78 (0.81 – 3.89)	0.150		
Multiparous	1.27 (0.61 – 2.64)	0.525		
Gravidity				
1 – 2	1.00		1.00	

3 – 4	0.96 (0.45 – 2.05)	0.915	1.06 (0.48 – 2.32)	0.889
5+	2.61 (1.12 – 6.08)	0.027	3.29 (1.20 – 8.97)	0.020
Gestational age of neonate				
Postdate	1.00			
Post-term	-	-		
Preterm	0.31 (0.04 – 2.43)	0.267		
Term	0.24 (0.03 – 1.76)	0.161		
Not indicated				
Weight of neonate				
Extremely low	4.81	1.000		
High	1.43 (0.44 – 4.71)	0.552		
Low	1.09 (0.63 – 1.91)	0.754		
Normal	1.00			
Very low	1.66 (0.59 – 4.72)	0.340		
Mode of delivery				
Caesarean Delivery	1.00			
Vaginal Delivery	0.87 (0.54 – 1.42)	0.585		
Category				
Abdominal wall	1.00		1.00	
Cardiac	5.15 (1.18 – 22.54)	0.030	2.70 (0.50 -14.64)	0.251
Digestive	2.20 (0.43 – 11.36)	0.345	0.62 (0.06 – 7.52)	0.706
Eye	9.11 (0.82 – 100.88)	0.072	-	-
Genital	1.05	1.000	2.27	1.000
Multiple	5.74 (1.24 – 26.58)	0.025	2.75 (0.41 – 18.37)	0.296
Musculoskeletal	3.19 (0.66 – 15.41)	0.148	1.19 (0.20 – 7.08)	0.845
Nervous	2.50 (0.57 – 10.97)	0.223	2.78 (0.55 – 14.13)	0.217
Orofacial	0.78 (0.07 – 8.56)	0.836	2.38	1.000
Respiratory	1.04	1.000	7.61	1.000
Suspected chromosomal	3.01 (0.68 – 13.27)	0.146	1.96 (0.36 – 10.54)	0.434
Urinary	1.20 (0.11 – 13.22)	0.884	2.94	1.000
Others	3.21 (0.59 – 17.60)	0.179	1.75 (0.22 – 14.17)	0.599

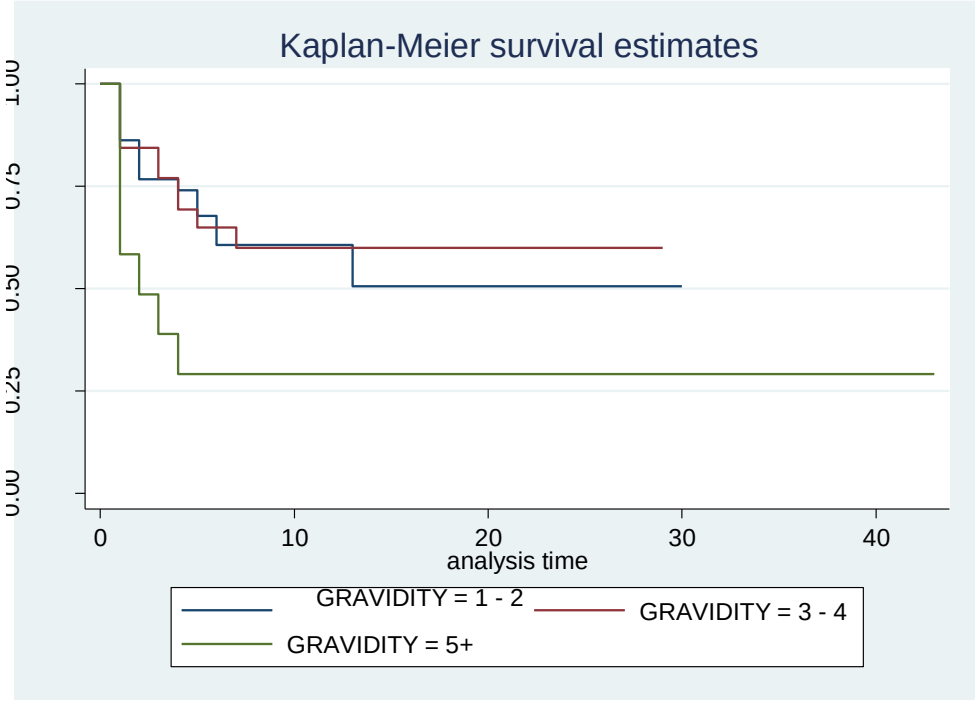


Figure 3.7 Survival estimates based on gravidity

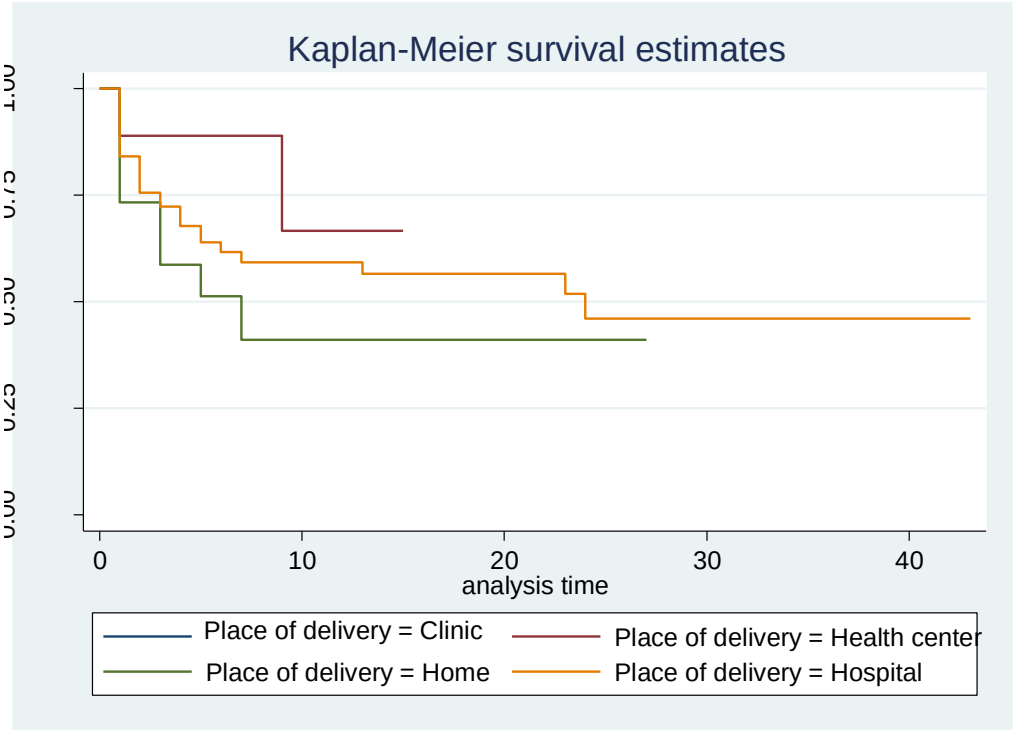


Figure 3.8 Survival estimates based on place of delivery

3.5 Background and demographic characteristics of parents with new-borns with congenital anomalies in the prospective study

A total of 28 parents whose new-borns had been diagnosed with a congenital anomaly between 13th April 2021 and 13th October 2021 responded. They were recruited at the delivery suite and the SCBU. Mothers formed the majority (68.9%; N = 19). Both parents of the same neonate were eligible to respond but their neonates were counted once. The ages of the parents ranged from 16 to 41 years, with a mean of 27.6 (±6.1). All respondents were Christians and their highest level of education for the majority (71.4%) was secondary/ vocational; 17.9% tertiary, and 10.7% primary. There were 21 cases of congenital anomalies during the six-month period and all neonates were born alive, hence sent to SCBU for assessment. All mothers had at least one obstetric scan during the index pregnancy. All respondents agreed that prenatal screening and diagnosis was a necessary addition to antenatal care.

Out of the 21 cases, 4 cases were detected antenatally using ultrasound and those cases were hydrocephalus, hydrancephaly, sacrococcygeal teratoma, and posterior urethral valve. The remaining 17 abnormalities were all detected after delivery.

The different abnormalities and categories are as follows:

Abdominal wall (1): gastroschisis

Cardiac (1): cyanotic heart disease

Digestive (3): intestinal obstruction, imperforate anus, duodenal atresia

Musculoskeletal (1): osteogenesis imperfecta

Nervous (6): hydrocephalus (4), hydrancephaly (1), myelomeningocele

Other (2): sacrococcygeal teratoma, thrombocytopenia-absent radius syndrome (TAR)

Respiratory (1): choanal atresia

Suspected chromosomal (3): Trisomy 18

Urinary (2): posterior urethral valve, bladder exstrophy

There were no cases of genital; eye; orofacial; multiple; and ear, neck, face

3.6 Acceptability of other methods of prenatal screening/ diagnostic methods aside ultrasound scan but including invasive testing

Almost two-thirds (64.7%) responded that if another test, including invasive testing, was indicated and offered in their subsequent pregnancies, they would opt for it.

'To help me know the extent of the abnormality and the treatment available'

'In order to give me more information concerning the baby and other possible genetic issues in the future for anticipation'

'So that the underlying condition of the baby can be known and the necessary intervention can be arranged'

'If the specialist is recommending it knows its importance so I will do it '

The reasons parents would not consider invasive testing were about their lack of adequate knowledge on the tests as at the time of response, and the fear of the procedure.

'Because I don't have any idea of such tests'

'Because I do not have the necessary knowledge to guide me to make that decision'

'Because this procedure looks scary'

'I am scared of this procedure'

On the whole, majority (92.9%; n = 26) of parents prefer to do an ultrasound scan first, then other tests, if indicated. The rest would want a scan only.

3.8 Acceptability of TOPFA

About 71% (n = 20) of parents said they would have considered termination of pregnancy if they had been offered; 17.9% (n = 5) were uncertain and 10.7% (n = 3) said they would not. Their responses can be put under three main themes- *'religion and ethics factor', 'the baby factor'* and '*the stress factor'*. Some of the responses for the first theme are found below:

'No, because abortion is against my religious values'

'It is against my beliefs and also I don't know what the baby will become in future'

'It is not in my power to determine who to live and who to die and also I don't know what the baby can become in future'

The second theme (baby factor) is based on the gestational age at which diagnosis is made and the third theme (stress factor) expresses their compassion for the babies as they see them go through pain, discomfort and disability and their own psychological, emotional and financial stress.

'It is dependent on the gestational age of the baby. If it is more than 6 months, terminating it will be like a murder'

'If only the pregnancy has not advanced'

'Because if the baby prognosis on this current condition is poor, then it would been better if it was terminated earlier to avoid going through all this stress'

'Because if this problem had been diagnosed early and termination was done, baby will not be going through this pain and I will also not be going through this psychological stress'

'It would have saved me from all these financial and psychological stress I am going through now'

'If doing it could prevent the psychological problem we are going through now, I would have considered it'

'This decision will lift a huge burden from me in relation to the stress associated with caring for such babies

'It would have saved us from this disturbing moment we are going through now'

DISCUSSION

Prevalence and clinical characteristics:

There is paucity of data on congenital abnormalities in Ghana and perceptions about invasive testing and TOPFA. This study comprises both a retrospective and a prospective study. It reports the prevalence, spectrum and trends of congenital abnormalities among neonates admitted to the neonatal unit (SCBU) in a tertiary hospital over a ten-year period, the admission outcomes of such neonates, and the perception of parents of newborns with a congenital anomaly about prenatal testing and termination of pregnancy for fetal anomaly (TOPFA). Congenital abnormalities constituted 2.8% (28 per 1000) of all neonatal admissions at the SCBU with an incidence of 0.86% (8.6 per 1000) of total births. Mortality among neonates with congenital abnormalities at the unit was 31.4%, contributing to 4.6% of the total mortalities at the unit over the ten-year period. Gravidity and place of delivery were significantly associated with admission outcomes among these neonates.

To accurately assess the prevalence of congenital anomalies, the following must be achieved: adequate clinical expertise, advanced diagnostics (including fetal anatomy scans and neonatal/paediatric postmortem examinations), registration of medical cause of death, and a robust notification system to national anomaly registries. These resources are almost non-existent in many low- and middle-income countries such as Ghana. Therefore, diagnosis is mainly based on physical examination, which can reliably diagnose only about 30% of congenital anomalies[70].

The global prevalence of congenital abnormalities is reported as 20-25 per 1000 live births, with higher prevalence and mortality rates seen in low-resource countries[21].

In the present study, congenital abnormalities contributed to 2.8% (28 per 1000) of neonatal admissions and 8.6 per 1000 births (both live and stillborns). The former is similar to that observed in two tertiary care neonatal units in Gabon and Nigeria[34,71] but higher that the 1.94% reported from Kenya[72]. It is however lower than the 7.22% that Ameyaw et al[11] reported from a similar facility in Ghana, which is the Komfo Anokye Teaching Hospital (KATH). The wide difference may be due to two reasons: firstly, the KATH neonatal unit admits babies up to three months of age and so their data was not only for neonates, and secondly, KATH has a wider coverage area than

CCTH since it provides services to the Ashanti region, which is one of the populous regions in Ghana with almost 6 million inhabitants as of the year 2021[73], similar to the Greater Accra region, where the national capital city is situated. KATH also serves the Bono, the Bono East and the Ahafo regions (collectively called Brong-Ahafo region in the recent past) and also parts of the Northern belt of Ghana.

Silesh and colleagues[74] found a higher rate in Ethiopia as well (5.95%). Several other studies focused only on either externally-visible abnormalities or major congenital malformations. In Malawi and India, for instance, the prevalence of congenital abnormalities among neonatal admissions are 7.5% and 9.41% respectively[33,75]. If all congenital abnormalities (from prenatal and postnatal diagnosis including postmortems, examination at delivery and at the time of admission), were to be included, these figures would be much higher.

Although believed to be an underestimation, congenital anomalies are estimated to occur in 4-12 per 1000 births in low- and middle-income countries[9] and the 8.6 per 1000 births from this study correlates well with this finding. Nigeria reports a wide range (2.2 – 20.73 per 1000 live births) of prevalence rates for neonatal congenital abnormalities and this is mainly attributed to the varying study designs[30,76]. For example, Akinmoladun et al.[32] concentrated only on major abnormalities that were prenatally diagnosed in a particular hospital, while Abbey et al.[76] studied only major abnormalities at delivery and others such as Obu et al.[71] focused on neonatal admissions which includes babies managed and delivered outside the study hospital. Most of the studies also used the number of deliveries (births) as the denominator, which suggests the inclusion of live birth (both viable and non-viable), stillbirths and abortuses. Yet these were reported as live births. Nonetheless, all these studies were hospital-based just like the present study. The interplay of peculiar environmental and geographical factors may also be responsible for the varying rates between these studies. For example, the high rates of 15.8 and 20.73 per 1000 births that were recorded in two of the Nigerian studies were conducted in Lagos and Port Harcourt respectively, which are considered multiethnic and industrialised cities, with the latter exposed to the risks of oil extraction, refinery and transport[76,77]. Cape Coast, the city where CCTH is located is noted for education and tourism but not much of industrialisation and this environmental difference could be the reason for the varying

prevalence, considering the similarities in the demographics and health systems of Ghana and Nigeria.

Civil wars have been shown to increase congenital abnormalities in Africa due to the exposure to uranium, the element used in manufacturing guns and other weapons of mass destruction. This is evident from the increased incidence of congenital abnormalities after wars, as demonstrated by researchers from Lybia, Iraq and the Democratic Republic of Congo[78].

Comparing the findings in this study to some high-income countries, this prevalence is significantly lower. In a tertiary hospital in Australia for instance, about 76 per 1000 admissions were due to congenital abnormalities[79]. Also, the EUROCAT study showed a congenital anomaly incidence of 26.9 per 1000 births from 11 European countries, which is exceedingly higher than the 8.6 per 1000 births reported in this study[25]. This difference in the trends may be attributed to better diagnostic systems in place both prenatally and postnatally, including autopsies. In that case, because of a good prenatal diagnosis service and fetal surveillance, majority of abnormalities can be diagnosed prenatally. This affords the clinician a better preparation in terms of timing of delivery, mode of delivery and to link babies to the appropriate specialties for continuous care. Hence, the rate of stillbirths are reduced and many fetuses survive through the intrauterine life and gets admitted to the neonatal unit after delivery. It is worth reiterating that karyotyping and other genetic tests are not offered in the government-owned hospitals in the country. Also, autopsies are not routinely done after unexplained neonatal deaths. Therefore, many internal defects and genetic or chromosomal abnormalities could have been missed in this study.

Trend in the prevalence of congenital abnormalities over the ten-year period

The prevalence of admissions due to congenital abnormalities in the hospital was highest during the 2014 to 2016 period and also in 2019. It was high for both per 1000 neonatal admissions and per 1000 births. Towards the end of 2013, the hospital was upgraded from a secondary level facility and a regional hospital to a tertiary teaching hospital capacity. Therefore, referrals may have increased afterwards and that can explain the influx of congenital abnormalities to the hospital. It is however unclear why

the rates dropped drastically for 2017 to 2018 and picked up again in 2019. This finding is slightly similar to that of Sanfaz et al.[78], who also reported 2016 as the year with the most abnormalities at the neonatal unit. They went further to demonstrate that the numbers were highest in the first quarter of each year, which appeared to correlate with a previous study but this seasonal variation of congenital abnormalities was later disproved[80,81]. The outbreak of Zika virus in 2015 and 2016 increased the incidence of congenital abnormalities, especially, microcephaly in countries that were hit, causing the World Health Organization to declare a Public Health Emergency of International Concern (PHEIC) after which several surveillance and preventative strategies were implemented in the affected countries[14]. However, Ghana did not record a single case of this infection although its Public Health personnel remained alert for it. Hence, it is unlikely to be the cause of the surge in congenital abnormalities between 2014 and 2016.

Relationship between patient characteristics and the prevalence of congenital abnormalities

Maternal age, gravidity and parity:

The association of maternal age of >35 years as a risk factor for congenital abnormalities, particularly the chromosomal anomalies and some specific abnormalities is well known. The non-chromosomal abnormalities are associated with younger maternal age, especially teenagers, but not with advanced maternal age[82,83]. Recent studies have also noted the increased incidence of congenital anomalies in younger women and also with young paternal age[84,85]. The particular mechanism responsible for this is unclear but it is thought to be multifactorial – an interaction of genetic and environmental factors. The association between increased parity and congenital anomalies have also been demonstrated in several studies around the world[30,78]. In this present study, there were significant proportions of missing data for maternal age (n = 89; 37.7%), gravidity (n = 126; 53.4%) and parity (n = 95; 40.3%). In view of this, it is difficult to validate findings involving age, gravidity and parity.

Nonetheless, considering the absolute figures, majority of the women whose age and parity had been documented were multiparous (having had two or more deliveries) (n

= 58;24.6%) and aged between 25 and 35 (n= 70; 33.5%) which is the age bracket that most women actually deliver and confirmed by Akinmoladun et al.[32]

Further studies are needed to properly assess the correlation between age, gravidity and parity in the Ghanaian population.

Mode of delivery and congenital abnormalities:

More than half of the neonates in this study were delivered vaginally (n = 124; 52.5%), with missing data in 11%. Therefore, the distribution does not support the findings by Sarkar et al.[86] in India which showed a strong association between congenital abnormalities and caesarean delivery. This may be due to the fact that majority of the abnormalities in this study were not prenatally diagnosed. Hence, delivery plans were not instituted, even for those who might have benefitted from it, and so women waited for spontaneous onset of labour. Caesarean section was most likely performed for obstetric indications in the majority of the study mothers.

Birthweight and gestational age

Majority (n = 112; 47.5%) of the neonates in this study had normal birthweight, 31.4% low birthweight (n = 74), 3.8% for each of very low birthweight and macrosomia, 0.8% extremely low birthweight and 12.7% missing data. Also, 65.7% (n = 155) of the neonates were delivered at term. The distribution of cases in this study is contrary to that shown in several studies that suggest an increased risk of abnormalities with low birth weight and prematurity[21,87]. Some fetal abnormalities predispose to complications that warrant preterm delivery. For example, gastrointestinal obstructions and conditions that lead to improper fetal swallowing or hydrops, for instance, can cause polyhydramnios which is a risk factor for preterm labour due to mechanical pressure on the cervix. It is also not strange for a preterm baby to have low birth weight as they have would have gained more weight if allowed to stay longer in-utero under favourable conditions. Prenatal diagnosis and optimum fetal surveillance may lead to early delivery of fetuses that are at risk of in-utero demise if pregnancy should be allowed to continue. The disparity in the distribution of cases as noted in this study compared with the other studies may stem from the lack of prenatal diagnosis and

delivery preparations. It might also be due to pregnancy interruption by clinicians once particular severe abnormalities are identified in-utero but before term in those other studies.

Sex of neonate

Male neonates constituted 58.9% (n = 139) in this study, correlating with existing literature which also show male predominance among neonates with congenital abnormalities[21,88,89]. Being female may be protective as some researchers believe but it may also mean that females are plagued with more lethal abnormalities which lead to stillbirths.

Duration of stay

The mean length of stay at the SCBU was 3.0 days which is significantly shorter than what have been recorded in other studies. In Australia, a study by Siddhisena et al.[79] showed a mean length of stay of 19.71 days for neonates with congenital anomalies, while Lindower and colleagues[47] in the United States of America reported a mean of 16 days for neonates with major congenital abnormalities and 9 days for those without. In the latter study, low birth weight, the need for ventilation, and surgical intervention contributed significantly to the variation in costs. Information about length of stay in neonates with congenital anomalies in Africa and other low-middle-income countries is scarce. The significantly shorter duration of stay at the SCBU may reflect the lack of ideal resources that are needed to sustain and prolong life or at least postpone death in these neonates. It might be simplistic to suggest that most of the abnormalities were less severe, as compared to the ones in the other studies. This disparity in the length of stay is also unlikely to be due to prematurity and low birth weight as most of the subjects in all three studies were of normal weight and delivered at term.

Spectrum of congenital abnormalities

Over the ten-year period, a wide range of congenital abnormalities were admitted to the neonatal unit of the Cape Coast Teaching Hospital.

The commonest abnormalities involved the nervous system, followed by suspected chromosomal abnormalities, cardiac and then abdominal wall. The observation that the specifics of the cardiac anomalies were not documented suggests that echocardiography had still not been done at the time of death or discharge.

Next are digestive, musculoskeletal, multiple and orofacial. Abnormalities of the urinary system and 'other anomalies/ syndromes' had equal number of cases. The subclasses with the least abnormalities in decreasing order are genital, eye and respiratory.

The finding that majority of abnormalities involved the central nervous system (CNS) correlates with several African studies in Nigeria, Tanzania and Kenya[32,74,76,90]. Two of these studies were not conducted among neonatal admissions but from prenatal diagnosis or from examination at birth. They also either focussed only on external structural abnormalities at delivery or major congenital abnormalities. Many studies across the continent, although did not observe CNS abnormalities as the commonest, reported CNS in their top three commonest systems involved in anomalies. Neural tube defects formed a significant proportion of these abnormalities. This highlights the need to strengthen education on folic acid supplementation and its compliance among pregnant women and other women in their reproductive age.

Contrary to this finding, two systematic reviews observed in developing countries had musculoskeletal defects and cardiac anomalies respectively, to be the most predominant among new-borns[22,27]. In the first (Adane et al.)[22], only Sub-Saharan African countries were studied whiles the second (Toobaie et al.)[27] involved all low-middle income countries. It is unclear whether the varying study designs alone is responsible for this disparity. Particularly, studies that use neonatal admissions, such as this present one, record less numbers of musculoskeletal abnormalities such as isolated polydactyly, syndactyly and talipes since most of them do not warrant admission. On the contrary, studies whose methodologies employed examination of babies at birth or prenatal diagnosis are likely to record more of these abnormalities that do not require admission[87,91].

Some studies from India and Libya report the commonest subclass for congenital abnormalities to be the cardiovascular or cardiac[75,78,92]. It is interesting to note that anomalies of the cardiovascular system appears to be quite common in studies done

in the western countries such as United States of America and Australia[21,79]. This may be due to better diagnostic techniques, both prenatally and postnatally, and the availability of correctional surgeries; thus, making TOPFA unattractive to parents.

Outcomes of neonatal admissions for congenital abnormalities

Almost two-thirds (64.8%) of the neonates with congenital abnormalities survived while 31.4% died. Other studies also report, with higher survival rates, that majority of neonates with congenital abnormalities are discharged alive from the neonatal units[75,79,93]. This shows that many of the abnormalities are not lethal. The level of neonatal care is also a factor to neonatal admission outcomes and that may explain the lower rates of survival in this study, as the neonatal unit in CCTH is below the level of a neonatal intensive care unit, hence, called a Special Care Babies Unit. For example, an Australian tertiary level neonatal unit with a congenital anomaly admission rate of more than 76 per 1000 neonatal admissions (compared to 28 per 1000 admissions in this study), had more than 92% of affected babies as survivors at the time of discharge or referral[79]. Similarly, in a neonatal intensive care unit in Nigeria, with a congenital anomaly admission rate of 63 per 1000 neonatal admission, the survival rate is reported as 89.6%; that is, 10.4% mortality among neonates with congenital abnormalities[93]. In both studies, cardiac defects, followed by digestive system anomalies were the top two predominant abnormalities. Singh et al.[75] also with cardiac defects in the lead, had a survival rate of more than 75% (72.61% discharged and 3.82% discharged against medical advice). Majority of the babies in all three studies were delivered at term with normal birthweights, just as in this study. Therefore, the relatively better survival rates cannot be attributed to significantly less prematurity or higher birthweights but rather more likely to be due to the severity of abnormalities and the level of neonatal care, including surgical intervention.

Annual mortality rates from congenital abnormalities

Although the prevalence rates were highest for 2014 to 2016 and 2019, the mortalities attributed to congenital abnormalities did not correlate with the trend. The highest mortalities were recorded in 2015 to 2017 (6.4%, 6.7% and 5.8% respectively). This was closely followed by 2010, 2013, 2011 and 2019. The lowest mortalities were noted

for 2012 and 2014 (2.3% and 3.2% respectively). Therefore, it was only in 2015 and 2016 that the increased number of admissions translated into more mortalities. The reason for this trend is unclear since 2014 and 2019 did not follow this pattern.

Mortality rates per subclass over the study period

The subclasses with the most mortalities over the ten-year period were eye, cardiac, multiple and other anomalies/ syndromes. It must be clarified though that there was only one admission for the 'eye' subclass over the whole ten years and that baby succumbed. The abnormality was bilateral congenital cataract, which suggests either a severe intrauterine infection or a genetic syndrome, both of which are likely to carry a poor prognosis.

More than half (59.3%) of neonates with cardiac defects demised. Those diagnosed as cyanotic heart disease were six (6) in total and all of them demised. This supports the belief that Sub-Saharan Africa may have much more cardiac anomalies that are not amenable to surgery due to their severity[35]. Existing studies such as Ajao et al., Singh et al. and Siddhisena et al.[79] which recorded high numbers of cardiac anomalies did not provide data on whether mortality was also higher in this subclass. There is a high likelihood that these anomalies were not detected antenatally and were only admitted to the SCBU when they began to show symptoms after delivery. Perhaps, if the defects were properly diagnosed antenatally, better antenatal follow-up, delivery preparation and arrangement for prompt referral may have improved their chances of survival.

Concerning surgically correctable gastrointestinal congenital anomalies, the Global PaedSurg Research Collaboration's multinational study highlights the role of surgery in the management of these conditions[36]. However, there is a wide disparity in mortality rates even after surgical interventions, comparing low-, middle- and high-income countries. A total of 39.8% deaths was reported for the low-income countries involved in the study, 20.4% mortality for the middle-income countries and 5.6 for the high-income countries. Although this study was conducted among all children younger than 16 years presenting for the first time with a correctable gastrointestinal congenital anomaly (and not only neonates), it brings out the need for optimum pre- and post-operative care as a key element for better outcomes.

There was no mortality from genital and respiratory abnormalities, which is expected as these abnormalities are usually not lethal and mostly amenable to surgery.

Factors affecting survival in children born with congenital abnormalities

In this study, place of delivery and gravidity were significantly associated with death or survival. Cardiac and multiple anomalies also conferred a higher risk of death, compared to abdominal wall defects but these two were not statistically significant. The findings in this study do not correlate with what existing literature reports[21,42,46], and there is limited information on the risk factors for mortality in the African studies. It is imperative that population-based studies are carried out across the continent to provide epidemiologic data in this area.

Globally, prematurity, low birth weight and the presence of additional anomalies are strong risk factors for death from birth defects[21,42,46]. Ethnicity and being an Aboriginal have also been inconsistently associated with either better survival or mortality for specific anomalies in the USA and Australia. Confounding factors such as low educational level, malnutrition and low-income status may be responsible for the poorer outcomes in offspring of blacks, Hispanics and the Aboriginals.

This study demonstrates that clinic delivery appears to proffer a better prognosis than hospital delivery. This data must be interpreted with caution, as only about 1.7% (n = 4) of the neonates were delivered at the clinic before being referred to the SCBU. A better interpretation will be to say that delivery in a health facility improves survival of neonates with congenital anomalies, as both hospital and clinic delivery showed better survival rates than home delivery.

Skilled birth attendant (SBA) hugely improves pregnancy outcomes as most maternal deaths occur during labour, delivery, or within 24 hours of delivery. It also gives room for better perinatal/ neonatal care. The World health Organization defines a SBA as '*an accredited health professional — such as a midwife, doctor or nurse — who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and*

newborns'[94]. Most deliveries in developing countries occur outside the health facilities although antenatal services may have been utilized to some extent[28,29,95]. In Ethiopia, SBA occurs in only 48% of deliveries, whiles Tanzania records 50%[96,97]. It is also known that SBA is higher in urban areas than in the rural areas[97,98].

Ghana has made giant strides in improving SBA as a means to reducing maternal and neonatal mortality. In 2005, the National Health Insurance Scheme (NHIS), which requires subscribers to pay a small premium annually, was introduced. The free maternal and childcare policy was also brought into effect in 2008. Again community-based health planning services (CHPS) compounds have been established to give rural folks constant access to basic health care. Health education has also increased across all media platforms and during antenatal care, to emphasize the importance of antenatal care (ANC) and delivery in a health facility. As at 2014, ANC utilisation and SBA in Ghana were 97% and 76% respectively[99,100]. It is therefore encouraging to see these interventions yield good results and this could explain the finding of only 9.3% home deliveries in this study. However, poor self-reporting of obvious congenital malformations by parents or families after home delivery, due to the reasons already discussed above, may also be a factor.

This is the first report that has identified gravidity ($\geq$5) as a significant risk factor for death in children born with congenital anomalies. Birth order above 3 (that is, parity of >3) has been cited as a risk factor for the occurrence of fetal anomalies, among others such as maternal age and low birth weight, but not as a risk factor for mortality[78,101]. It is unclear whether socio-economic factors underlie the high gravidity; in which case, the mortality risk could be better explained. Per the data set available for this study, it is difficult to assign a reason to this trend. It must be noted also that 53.4% of entries and 40.3% did not have record on gravidity and parity respectively, therefore caution with this interpretation is required until further studies also prove this.

The presence of additional anomalies (multiple anomalies) is also a recognised risk factor for mortality[21]. This is expected as each anomaly confers a certain degree of morbidity and mortality risk; a cumulative effect of which may translate into poorer coping capabilities and hence, death.

Congenital heart defects also carry a higher risk of death per this study, although not statistically significant. Heart defects are among the surgically-correctable anomalies and prognosis is better when diagnosed prenatally or soon after birth and prompt treatment offered. Although early surgical correction has substantially increased survivorship in children with heart defects, the mortality risk is still high. Heart defects remain one of the major causes of infant and childhood deaths, and the major and complex types such as transposition of the great arteries (TGA), hypoplastic heart syndrome (TOF), and common arterial trunk (CAT) carry the highest risk of death[102].

Pace and colleagues identified four (4) factors (3 of which are maternal) that affect survival in babies with congenital heart defects that involve both ventricles (biventricular defects); namely- maternal educational level, race and/ or ethnicity, marital status, and delivery at a heart centre.

The absence of specific diagnoses in the SCBU records suggests that echocardiography was probably not done before they left the unit. If this is the case, then it is obvious that early surgical correction could not have taken place for improved outcomes to occur. Prenatal diagnosis with proper fetal surveillance, appropriate delivery plans including referral to a centre with a paediatric cardiologist/ cardiothoracic surgeon and optimum neonatal intensive unit care are essential for the prevention of death from cardiac defects. It will be difficult to conclude that this study supports earlier speculations that congenital heart defects in developing countries may be more severe[9,35].

Experiences of parents of new-borns with congenital abnormalities

In regard to the perceptions of parents about prenatal testing and TOPFA, a high response rate was achieved over the 6-month study period. There was a palpable sense of frustration among the parents, mainly based on the pain they perceived their neonates to be enduring at the time, the fact that the children may grow up with a low quality of life due to disability, and their own psychological, emotional and financial stress. These perceptions are universal, as several studies across the globe have demonstrated this[10,13,48,60,67]. It proves also that it is a natural response in humans whenever expectations are not met. In fact, mothers are often the hardest-hit as they

have been shown to be less able to adjust to the situation than fathers[10]. Therefore, psychological counselling and support for these parents is an important part of patient care[60]. Once the fetal diagnosis is made, there must be a multidisciplinary team involving the relevant specialists (depending on the abnormality), genetic counsellors, social workers and midwives/ nurses in the management of the fetus and the mother. Counselling should also involve their husbands/ partners and parents' significant others such as the immediate family and people they trust, because social support is also required for a holistic management. Support should be continued to delivery and beyond[60]. These measures are able to ease the burden and enable them make informed decisions concerning their children.

Acceptability of prenatal testing

Almost two-thirds of the parents expressed interest in any test that can help with accurate diagnosis of fetal anomalies. Of these, 92.9% prefer ultrasound scan first, followed by invasive testing, if indicated. This correlates well with studies from some low-middle countries[67,103–109]. The widespread acceptance of the ultrasound as demonstrated in this study agrees also with findings in Nigeria[110]. In some upper-middle and high-income countries, prenatal testing is part of routine antenatal care, for which the states cover the costs. In others, the cost is not borne by the state but there are policies that grant pregnant women the opportunity to be tested. In Ghana, obstetric ultrasound has become an integral part of routine antenatal care. It does not only guide practitioners in the clinical management of patients, but also provides another platform for expectant couples to bond with their unborn child. The challenges of ultrasound use in LMICs have been clearly enumerated by several researchers[55,111–114]. This includes inadequate training of sonographers, misuse and abuse, and maintenance costs of the machines. There have also been concerns of it not improving maternal, perinatal and neonatal outcomes in LMICs but Wanyonyi and colleagues[113] opined that those experiences are often seen in places with minimal or no access to pregnancy ultrasound; an issue which is not captured in the analysis of such studies. Despite the above, ultrasound remains an essential, acceptable and safe tool in the prenatal diagnosis of fetal anomalies. The problem, however arises with the issue of unqualified persons who offer the service in Ghana and other LMICs, and the potential of missing detectable abnormalities on scan[112,114]. There is therefore the

need for a more robust monitoring system to clean up the practice for maximum benefit.

Similar to other developing countries, knowledge on the other methods of prenatal testing (aside ultrasound), such as non-invasive prenatal testing (NIPT) and invasive testing (amniocentesis, chorionic villus sampling (CVS) and cordocentesis) in Ghana is low, even among health workers[105]. This is possibly due to its almost non-existence in routine antenatal care, especially in the public sector, the general lack of knowledge about these tests, and the lack of expertise for conducting them among obstetricians. Hence, there has not been any advocacy for a related policy. In one Japanese study[109], although women over 35 years were willing to undergo these tests, especially for Down syndrome, their doctors did not encourage it. The underlying problem here could also be the lack of knowledge on prenatal tests among the doctors themselves. This current study highlights the unmet need for advanced prenatal testing education and services in the Ghanaian populace. This will be an effective way to increase acceptability and uptake of prenatal tests throughout the country, as demonstrated in China and other parts of the world[105,115]. Although healthcare costs are likely to increase with this, research has shown that its benefits outweigh the risks, even in low-resource countries[6]. Whiles increasing the knowledge base, a prenatal screening and diagnosis policy must also be advocated for, considering all relevant cultural, religious and socioeconomic factors.

Acceptability of termination of pregnancy for fetal anomaly (TOPFA)

There is a presumed high acceptance for termination of pregnancy for fetal anomaly, although this response remains conditional for a few. The two main conditions considered by these women are gestational age at which diagnosis of the anomaly is made, and the severity of the anomaly. Pregnancies that are not considered to be advanced, and anomalies that are not lethal are unlikely to be terminated. Closely related to one's religious beliefs, is the feeling of unworthiness to decide who should live or die. The fact that they are given very limited time to decide, particularly in countries whose laws do not permit termination beyond a certain gestational age, is also another source of discomfort for some parents. For the majority though, the experience of having to see their babies struggle to survive or live with substantial disability, coupled with their own psychological and financial stress, termination of

pregnancy would have been their best decision if it had been offered. These responses, especially the high acceptance for TOPFA are quite similar to what other researchers have already reported on[60,67,104,107] but may also be due to the uniqueness of the study population. Ghana has had a relatively liberal abortion law, which includes TOPFA, since 1985. Abortion is legal when performed by a registered and trained health personnel in an approved facility in cases of rape, defilement, incest, fetal abnormality or disease, or to protect physical or mental health[116]. Due to the stressfulness of this decision-making process and the period beyond, a multidisciplinary team made up of the relevant specialists, clinical psychologists, genetic counsellors, social workers and midwives/ nurses must always be available to offer adequate information about the condition and appropriate counselling and support as soon as diagnosis is made. Counselling should also involve their significant others, as described above[60].

Strengths and Limitations of study

This is the first study in the region to document the prevalence and spectrum of neonatal congenital abnormalities. It is also the first in the country to report on the admission outcomes of neonates with congenital abnormalities, the experiences of parents with neonates born with congenital anomalies, and parental perceptions about prenatal testing and termination of pregnancy for fetal anomaly. Another strength of this study is the use of a large number of neonates affected with congenital anomalies and the decade-long study period. Undoubtedly, this is a useful epidemiological data, upon which further studies can arise, in order to better understand the aetiology, management and prevention of these anomalies among the Ghanaian population.

It also has the capacity to generate public interest and discussions on prenatal testing and termination of pregnancy for fetal anomaly.

The retrospective aspect of the relied solely on information that had already been collected. Missing portions of data, therefore, could not be retrieved. Again, detailed maternal risk factors such as chronic medical conditions, vaccinations, folate supplementation and whether or not the congenital anomaly was detected on ultrasound before delivery could not be assessed. To emphasize, data for the study

was obtained only from the SCBU record due to the documentative challenges encountered at the paediatric ward, delivery suite and the outpatients' department (OPD). Firstly, stable neonates with congenital anomalies that were admitted directly to the paediatric ward but not as transfers from SCBU were excluded since their missing data were more than 30% less of what the SCBU A&D book captured. Secondly, the few neonates that may have been attended to at the OPD but did not require admission were not accounted for because the consulting room book does not record patient diagnoses and all the relevant information required by the study. Thirdly, stillborns and abortuses with congenital abnormalities that were delivered at the delivery suite could not be properly accounted for because of poor documentation. Finally, neonates with minor defects such as isolated talipes or polydactyly, that were examined at the SCBU after delivery, were not captured in the records. Thus, this study is only among neonates that were admitted at the SCBU between the study period. Therefore, it may not be a true reflection of the spectrum of abnormalities in the hospital.

Due to the unavailability of karyotypic and genetic testing in the public health service in Ghana, it was not possible to confirm suspected chromosomal or genetic abnormalities.

Admission outcomes of cases could also be determined only up to the time of discharge, referral, or death. Those that were discharged home or referred to a higher centre could not be followed to determine the actual survival rate.

Due to the small sample size and the use of parents whose new-borns already have a congenital anomaly, the prospective study may not be a true reflection of the collective perceptions of Ghanaians on prenatal diagnosis and TOPFA.

CONCLUSION AND RECOMMENDATIONS

This was a ten-year hospital-based review of neonatal congenital abnormalities. The anomalies contribute significantly to neonatal admissions and mortality. Central nervous system anomalies, particularly, neural tube defects, were the commonest, followed by suspected chromosomal abnormalities, then cardiac defects. Mortalities occurred more frequently among those with cardiac anomalies. However, gravidity of five or more and place of birth were the most significant factors for mortality.

Parents of neonates born with abnormalities do experience enormous psychological, emotional and financial stress. This is the basis for the high acceptance of prenatal testing and termination of pregnancy for fetal anomaly in the majority. Ultrasound is a safe and well-accepted tool in pregnancy and useful for prenatal testing. However, there appears to be a general lack of knowledge on the other methods of prenatal testing.

Based on the above, the following recommendations would be useful in reducing the Ghanaian burden due to congenital abnormalities:

1. Intensification of education on preconception and antenatal folic acid supplementation to prevent neural tube defects.
2. Introduction of prenatal screening and diagnosis into routine antenatal care to promote early detection, prompt referrals and interventions for fetal malformations and genetic conditions. In order to increase the detection of fetal anomalies, at least 3 scans must be advocated for throughout pregnancy – 1st trimester at 11-13^{+6} weeks, 2nd trimester at 18-23^{+6} weeks and 3rd trimester at 28-32 weeks. The first two are specialised scans and must therefore be performed only by ultrasound practitioners with high expertise on fetal anomalies. Ultrasound practice should also be monitored by a robust system that ensures adequate qualification of practitioners and the adherence to a standardised scanning protocol so that ultrasound-detectable fetal anomalies will not be missed. There must also be clear referral guidelines for all ultrasound practitioners.
3. Investing in fetal surgery, paediatric surgery, paediatric cardiology/ cardiothoracic surgery and neonatal intensive care in order to prevent or minimise severe morbidity in children born with major congenital anomalies.
4. The creation of a national congenital anomalies database, using the Modell Global Database as a guide and making congenital abnormalities a notifiable condition.
5. Providing parents with adequate specialised information about newly-detected fetal abnormalities and initiating a multidisciplinary team management right away to offer optimum medical and psychological services to the parents and their significant others, which must continue even after delivery.

6. Further population-based studies on the prevalence, spectrum and outcome of neonates with congenital anomalies, and the factors associated with their incidence and survival, for health planning purposes. A wider study on the perceptions about prenatal testing and TOPFA is also needed.

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APPENDIX

Appendix 1: Data Collection Tool – Retrospective Study

CHARACTERISTICS OF INFANTS WITH CONGENITAL ABNORMALITIES AND THE MATERNAL BIODATA

CODE:.....

MATERNALDATA

1. Age (in years).....
   ☐ Not documented

2. Parity (number of deliveries after 28 weeks of pregnancy)
   ☐1 ☐2 ☐3 ☐≥4 ☐ Not documented

BABY

3. Date of admission.....
   ☐ Not documented

4. Age of baby at the time of admission or consultation
   ☐Day 0 ☐Day 1 ☐Day 3 ☐≥Day 4
   ☐ Not documented

5. Sex
   ☐Male ☐Female ☐Ambiguous ☐Not documented

6. Is baby from a multiple pregnancy (e.g. twin, triplet pregnancy)?
   ☐ Yes ☐ No

7. Gestational age at the time of birth.....
   ☐ Not documented

8. Birth weight (g).....
   ☐ Not documented

9. Mode of delivery ☐Vaginal delivery ☐Caesarean Section
   ☐ Not documented

10. Place of delivery?
    ☐Hospital ☐Clinic ☐Health Centre/ CHPS compound

1

☐ Home/ Traditional birth attendant ☐ Not documented

11. Diagnosis……

12. Outcome ☐ Discharged ☐ Referred ☐ Died
☐ Not documented

13. Date of Outcome ……

☐ Not documented

14. Number of days spent at SCBU

☐ <24 hours

☐ 1-3 days

☐ 4-7 days

☐ 1-2 weeks

☐ >2 weeks

☐ Date of admission or date of outcome not documented

Appendix 2: Data Collection Tool – Prospective Study

PARENTAL PERCEPTIONS OF CONGENITAL ABNORMALITIES

CODE:.....

PERSONAL DATA

1. Relationship to baby ☐ Mother ☐ Father
2. Date of birth .....day.....month.....year
3. Religion
   ☐ Christian ☐ Muslim ☐ Traditional ☐ Other
4. Educational level
   ☐ None ☐ Primary ☐ Secondary ☐ Tertiary
   ☐ Vocational
5. Occupation
   ☐ Formal ☐ Artisan (informal) ☐ Trader ☐ Farmer
6. Parity (number of deliveries, irrespective of outcome) of baby's mother
   ☐ 1 ☐ 2 ☐ 3 ☐ >4
7. Did you (the mother) or your partner (if mother not the one answering) take folic acid supplements in the first trimester of this pregnancy?
   ☐ Yes (most days) ☐ Yes (sparingly) ☐ No

DIAGNOSIS OF BABY

8. What is your current child's diagnosis?
   .....
9. When did you become aware of your child's condition?
   ☐ During pregnancy ☐ After delivery
10. How was the diagnosis made?

1

☐ Ultrasound findings during pregnancy

☐ By the doctor after delivery

☐ Other……

11. If this diagnosis was **NOT** made during the pregnancy by an ultrasound scan, would you have opted for a scan from hindsight, if the opportunity had been offered?

☐ Yes ☐No

12. Not all abnormalities can be detected on ultrasound scan. If an abnormality is as a result of a chromosomal or genetic condition, the prognosis or outcome is dependent on the underlying condition. So if your baby's diagnosis was, or had been made during the pregnancy by an ultrasound scan, would you have opted for another test through the sticking of a needle into your abdomen, and/or a blood test on you to confirm a chromosomal or genetic condition in your baby?

☐ Yes ☐No

13. May you please give reason(s) for your answer above?

……

……

14. Would you have considered termination of pregnancy if you had been given the opportunity?

☐ Yes ☐No ☐Maybe

15. May you please give reason(s) for your answer above?

……

……

16. If you fall pregnant in the future, would you prefer to have screening for congenital abnormalities during pregnancy?

☐ Yes ☐No

17. May you please give reason(s) for your answer above?

……

……

18. If you answered 'Yes' to question 16 above, which of the following would you prefer?
    - ☐ Ultrasound scan only
    - ☐ Ultrasound scan, then invasive testing, if indicated
    - ☐ Never an invasive test
    - ☐ None of the above

19. Who is the main person you often consult when you need to make major decisions, including pregnancy-related decisions?
    - ☐ Parent(s)
    - ☐ Spouse
    - ☐ Sibling(s)
    - ☐ Religious leader (E.g. Pastor, Imam)
    - ☐ Friend
    - ☐ Nobody
    - ☐ Other.....

Thank you.

Appendix 3: Informed Consent

INFORMED CONSENT

TITLE OF RESEARCH: A ten-year review of neonatal congenital abnormalities and parental perceptions at a tertiary hospital in Ghana

INVESTIGATOR: Dr Betty Anane-Fenin

INSTITUTIONAL CONTACT: Department of Obstetrics and Gynaecology
Cape Coast Teaching Hospital
P.O.Box CT 1363
Cape Coast

1. INTRODUCTION AND PURPOSE OF STUDY

Congenital abnormalities or birth defects occur in 1 in 33 of babies. Some are severe, whiles others are intermediate or mild, with respect to outcomes. Birth defects are responsible for about 6% of deaths in children globally, and about 95% of these defects occur in developing countries like Ghana. This study seeks to determine the perceptions of parents who have given birth to babies with a birth defect, on birth abnormalities in general and also on antenatal diagnosis of the defects.

2. DESCRIPTION OF RESEARCH

When you decide to participate in this research, you will be interviewed with a questionnaire in a language that you are most comfortable with.

3. SUBJECT PARTICIPATION

Parents of babies born with birth defects will be approached and selected.

4. POTENTIAL RISKS AND DISCOMFORT

There are no known risks associated with your participation.

5. POTENTIAL BENEFITS

You will be able to express your views on the topic

6. CONFIDENTIALITY

Questionnaires will NOT bear the names of the participants or telephone numbers. Questionnaires will have codes instead. Findings of this study will be shared with University of the Witwatersrand, the Child Health and Obstetrics and Gynaecology departments of Cape Coast Teaching Hospital, the Research and Development Unit (RDU) of the hospital, and then subsequently published in a medical journal.

7. COMPENSATION

Participants will not be remunerated.

8. VOLUNTARY PARTICIPATION AND AUTHORISATION

Your decision to participate in this study is completely voluntary. If you decide not to participate, it will not affect the care, services, or benefits which you are entitled to as a patient in this hospital. You will be given a copy of the consent form for safe-keeping.

9. WITHDRAWAL FROM THE STUDY

If you decide to participate in this study, you can withdraw your participation at any time without penalty.

10. COST

You will not be required to pay any fees to participate in this study.

I voluntarily agree to participate in this research program.

□ Yes

□ No

I understand that I will be given a copy of this signed Consent Form.

Name of Participant (Print)……

Signature…… Date……

Name of Witness (Print)…… Signature…… Date……
Name of Person Obtaining Consent (Print)…… Signature…… Date……
Name of Interpreter, if any (Print)…… Signature…… Date……

Appendix 4: Distress protocol

Distress Protocol

Due to the sensitive nature of discussing a deceased child or a live-born with congenital abnormalities, a high level of emotional risk or discomfort is anticipated.
The following is provided as a means of preparation should a participant become distressed during the time of the filling of the questionnaire.

Strategies to assist those distressed during the written interview.

Should a participant become uncomfortable or distressed while discussing their experience of having a child with a congenital abnormality, the following actions will be taken by the allocated research assistant:

1. The research assistant will suggest that it is appropriate that the interview be terminated.
2. If the participant wishes for this to happen, the interview will be ended, and participant sent to the Psychology and Counselling Unit of CCTH, irrespective of whether they have already received professional psychological counselling as part of the routine care.
3. If the participant wishes to finish filling the questionnaire nonetheless, he/she will be given time to calm down before continuing. During this time, the research assistant will offer emotional support. After the questionnaire is completed, the participant will be sent to the Psychology and Counselling Unit, irrespective of whether they have already received professional psychological counselling as part of routine care.
4. A follow-up phone call will be made by the research assistant or researcher the following day to ensure that the participant is feeling better.

Contact details provided to participants

The location of the Psychology and Counselling Unit of the hospital will be given to all study participants. The phone number of the Unit will also be provided.

Conclusion

Although it is unlikely that the questionnaire will result in severe emotional distress for the participant, it is the researcher and research assistants' duty of care to ensure that these strategies are put in place prior to administering the questionnaire.

Adapted from University of Sydney's Distress protocol.

Appendix 5: EUROCAT subgroup classification

eurocat
european surveillance of congenital anomalies

EUROCAT Guide 1.4 and Reference Documents

	Includes Chromosomal Cases				Excludes Chromosomal Cases			
	No of LB	No of FD	No of TOPFA	Total Cases	No of LB	No of FD	No of TOPFA	Total non-chromosomal cases
All Anomalies								
Nervous system								
Neural Tube Defects:								
Anencephalus and similar								
Encephalocele								
Spina Bifida								
Hydrocephalus								
Severe microcephaly								
Arhinencephaly / holoprosencephaly								
Eye								
Anophthalmos / microphthalmos Anophthalmos								
Congenital cataract								
Congenital glaucoma								
Ear, face and neck								
Anotia								
Congenital Heart Defects								
Severe CHD								
Common arterial truncus								
Double outlet right ventricle								
Transposition of great vessels								
Single ventricle								
VSD								
ASD								
AVSD								
Tetralogy of Fallot								
Triscuspid atresia and stenosis								
Ebstein's anomaly								
Pulmonary valve stenosis								
Pulmonary valve atresia								
Aortic valve atresia/stenosis								
Mitral valve anomalies								
Aortic atresia/interrupted aortic arch								
Hypoplastic left heart								
Hypoplastic right heart								
Coarctation of aorta								
Total anomalous pulm venous return								
PDA as **only** CHD in term infants (LB and GA 37+ weeks)								

	Includes Chromosomal Cases				Excludes Chromosomal Cases			
	No of LB	No of FD	No of TOPFA	Total Cases	No of LB	No of FD	No of TOPFA	Total non-chromosomal cases
Respiratory								
Choanal atresia								
Cystic adenomatous malf of lung								
Oro-facial clefts								
Cleft lip with or without cleft palate								
Cleft palate								
Digestive system								
Oesophageal atresia with/without tracheo-oesophageal fistula								
Duodenal atresia or stenosis								
Atresia or stenosis of other parts of small intestine								
Ano-rectal atresia and stenosis								
Hirschsprung's disease								
Atresia of bile ducts								
Annular pancreas								
Diaphragmatic hernia								
Abdominal wall defects								
Gastroschisis								
Omphalocele								
Urinary								
Bilateral renal agenesis including Potter syndrome								
Multicystic renal dysplasia								
Congenital hydronephrosis								
Bladder exstrophy								
Posterior urethral valve and/or prune belly								
Genital								
Hypospadias								
Indeterminate sex								
Limb								
Limb reduction defects								
Club foot - talipes equinovarus								
Hip dislocation and/or dysplasia								
Polydactyly								
Syndactyly								

	Includes Chromosomal Cases				Excludes Chromosomal Cases			
	No of LB	No of FD	No of TOPFA	Total Cases	No of LB	No of FD	No of TOPFA	Total non-chromosomal cases
Other anomalies/syndromes								
Skeletal dysplasias								
Craniosynostosis								
Congenital constriction bands/amniotic band								
Situs inversus								
Conjoined twins								
Congenital skin disorders								
VATER/VACTERL								
Vascular disruption anomalies								
Laterality anomalies								
Teratogenic syndromes with malformations								
Fetal alcohol syndrome								
Valproate syndrome								
Maternal infections resulting in malformations								
Genetic syndromes + microdeletions								
Chromosomal								
Down syndrome								
Patau syndrome/trisomy 13								
Edwards syndrome/trisomy 18								
Turner syndrome								
Klinefelter syndrome								

LB= Live births
FD= Fetal deaths / Still births from 20 weeks gestation
TOPFA = Termination of pregnancy for fetal anomaly following prenatal diagnosis

* All Anomalies = ALL cases of congenital anomaly, excluding cases with only minor anomalies as defined in Chapter 3.2. Cases with more than one anomaly are only counted once in the "All Anomalies" subgroup.

Source: Boyle B, Addor MC, Arriola L, Barisic I, Bianchi F, Csáky-Szunyogh M, et al. Estimating Global Burden of Disease due to congenital anomaly: An analysis of European data. Arch Dis Child Fetal Neonatal Ed [Internet] 2018

Appendix 6: Ethics clearance certificate – Cape Coast Teaching Hospital

In case of reply the reference number and the date of this Letter should be quoted

Our Ref.: CCTH

Your Ref.:

P. O. Box CT.1363
Cape Coast
CC-071-9967
Tel: 03321-34010-14
Fax: 03321-34016
Website: www.ccthghana.org
email: info@ccthghana.com

1st October, 2020

Dr. Betty Anane-Fenin
Cape Coast Teaching Hospital
Cape Coast

Dear Madam,

ETHICAL CLEARANCE – REF: CCTHERC/EC/2020/081

The Cape Coast Teaching Hospital Ethical Review Committee (CCTHERC) has reviewed your research protocol titled, "***A Ten-Year Review of Congenital Abnormalities at A Tertiary Hospital in Ghana***" which was submitted for Ethical Clearance. The ERC is glad to inform you that you have been granted provisional approval for implementation of your research protocol.

The CCTHERC requires that you submit periodic review of the protocol and a final full review to the ERC on completion of the research. The CCTHERC may observe or cause to be observed procedures and records of the research during and after implementation.

Please note that any modification of the project must be submitted to the CCTHERC for review and approval before its implementation.

You are required to report all serious adverse events related to this study to the CCTHERC within ten (10) days in writing. Also note that you are to submit a copy of your final report to the CCTHERC Office.

Always quote the protocol identification number in all future correspondence with us in relation to this protocol.

Yours sincerely

Dr. Stephen Laryea
Medical Director
For: Prof. Ganiyu Rahman, Chairman ERC

Appendix 7: Ethics clearance certificate – University of the Witwatersrand

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Postgraduate Affairs)

TO:	Dr. B Anane-Fenin School of Clinical Medicine Department of Obstetrics and Gynaecology Medical School University E-mail: oparebea81@gmail.com
CC:	Supervisor: Professor L Chauke <Lawrence.Chauke@wits.ac.za> and <HREC-Medical Research Office@wits.ac.za>
FROM:	Mr Iain Burns Human Research Ethics Committee (Medical) Tel: 011 717 1252 E-mail: Iain.Burns@wits.ac.za
DATE:	2021/04/12
REF:	R14/49
PROTOCOL NO:	**M2011122** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)
PROJECT TITLE:	*A ten-year review of neonatal congenital abnormalities and parental perceptions at a tertiary hospital in Ghana*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps