The Incidence and Risk Factors of Congenital Heart Disease in Jos, Nigeria: Rationale and Protocol

Olukemi Omowumi Ige[1]*, Esther Simon Yiltok[1], Christopher Sabo Yilgwan[1], Bose Toma[1], Phyllis Kanki[2], Akinyemi Olugbenga David Ofakunrin[1], Udochukwu Diala[1] and Fidelia Bode- Thomas[1]

[1]Department of Paediatrics, University of Jos/Jos University Teaching Hospital, Nigeria
[2]Department of Immunology and Infectious Diseases, Harvard T. H. Chan School of Public Health, USA

*Corresponding Author: Olukemi Omowumi Ige, Department of Paediatrics, Jos University Teaching Hospital, Jos, Plateau State, Nigeria.

Abstract

Congenital Heart Defect (CHD) is the most common and one of the severe forms of congenital malformations. This contributes significantly to neonatal and infant morbidity and mortality. The incidence of CHD in Nigeria is unknown. The reported incidences since the introduction of echocardiography in are based largely on extrapolations.

This study therefore aims to determine the incidence and pattern of CHD in newborns in Nigeria and to determine their contribution to infant morbidity and mortality.

The study will be carried out at a tertiary health care facility in Jos, Nigeria. Newborn babies delivered or admitted in the hospital will be recruited into the study consecutively after obtaining consent from their parents until 3,000 of them have been studied. A cardiovascular system examination will be performed and babies examined for obvious congenital malformations. All babies recruited will have a screening echocardiography and those with suspicious findings will be booked for confirmatory echocardiography. Babies will be followed up for a year and their morbidities and/or mortalities documented.

Data will be entered into and analyzed using the STATA version 14. Confidence interval for this study will be set at 95% with a p value ≤ 0.05 considered statistically significant.

The study will provide contemporary data on the current incidence and pattern of CHD and other CM in Nigeria as well as its natural or modified history and potential risk factors. The contribution of CHD and other CM to perinatal and neonatal morbidity and mortality will also be determined.

Keywords: Incidence; Congenital Heart Disease; Congenital Malformations; Newborn Babies; Nigeria

Abbreviations

CHD: Congenital Heart Defects; AVSD: Atrioventricular Septal Defects; VSD: Ventricular Septal Defects; TOF: Tetralogy of Fallot; PDA: Patent Ductus Arteriosus; CM: Congenital Malformations; JUTH: Jos University Teaching Hospital; SCBU: Special Care Baby Unit; CVS: Cardiovascular System; ICD: International Statistical Classification of Diseases and Related Health Problems

Introduction

Congenital heart defects (CHD) refers to the presence of a structural abnormality of the heart and/or its great vessels that is present at birth and is of actual or potential functional significance [1]. It is the most common type of birth defect and accounts for nearly one-third

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of all major congenital malformations [2,3]. CHD are also among the most severe and life-threatening birth defects [4]. The world-wide incidence of CHD has until recently, generally been believed to be 6 - 8 per 1000 live births [3]. In fact, the reported incidence rate in developed countries has steadily increased from about 4 - 5 per 1000 live births in the 1950's to as much as 50 - 75 per 1000 more recently [1,5]. This has much to do with the great improvements in the non-invasive diagnosis of CHD in recent years, particularly the refinement of echocardiography equipment, such that machines with much better resolution are now available and some of these are portable. This is in contrast to the earlier studies that were largely based on auscultation, clinical presentation and autopsy findings and has resulted in a dramatic increase in the detection rates of milder lesions such as atrial septal defects (ASD) and small muscular ventricular septal defects (VSD) [1].

A systematic review revealed that approximately 1.35 million infants are born with CHD each year worldwide, but that there could be regional variations [6]. For example, the incidence of congenital heart disease in Taiwan in 2008 was reported to be 35.2 per 1000 live births [7], compared with Columbia in South America with an incidence of 1.2 per 1000 live births [8]. There is however a paucity of data on the incidence or birth prevalence of congenital heart disease in most developing countries, including Nigeria. Estimates of the numbers of children born with CHD in these countries have generally been extrapolated (based on the assumption of similar worldwide incidence) from older studies in developed countries [1,9]. The incidence of CHD in developing countries may actually be much higher than extrapolated figures due to factors such as higher birth rates and higher prevalence of risk factors for CHD. These include the higher proportion of older parents, poverty, which is very often associated with maternal malnutrition and more frequent infections [9]. Other risk factors that have been implicated or suggested include potentially modifiable ones such as smoking, alcohol and folate deficiency (thought to be responsible for up to 30% of some CHDs) [10,11] and inherited ones that are generally not modifiable, which occur in up to 15% of cases of CHD [12,13] (Table 1).

Risk factor	Possible Source	Example
Environmental		
Chemicals and toxins	Work Place	Active/Passive smoking
	Leisure/ recreation	Hair dyes, paints
	Industrial waste pollutants	Auto body parts, pesticides, aromatic solvents
Infections	Viral exanthems	Rubella/ cytomegalovirus
Maternal drug exposure	Recreational	Alcohol, cocaine, tobacco
	Therapeutic	Lithium, thalidomide, steroids (oestrogens, progesterone), warfarin
Radiation	Diagnostic	X- rays
	Therapeutic	Cancer radiotherapy
	Miscellaneous	Nuclear disasters, warheads
Nutritional factors	Poverty	Folate deficiency
Metabolic disorders	Metabolic disorders	Uncontrolled diabetes, maternal Phenylketonuria
Inherited		
Chromosomal abnormalities	Numerical excesses	Trisomies 21, 18
	Numerical deficiencies	Turner's syndrome (XO)
	Structural abnormalities	Del 22q11, DiGeorge syndrome
Genetic complexes	Common associations	Williams syndrome, Noonan's Syndrome

Table 1: Some Risk Factors Implicated in Congenital Heart Disease.

Children with congenital heart defects often have associated extracardiac malformations [14]. The prevalence of these associated malformations was detected to be 20% in the Baltimore-Washington Infant Study [15]. CHD may occur as part of a complex syndrome due to a chromosomal anomaly [16].

Extracardiac malformations were detected in 66% of cases with CHD in a study in Berlin [13]. These malformations involved the central nervous system (31%), the genitourinary system (26%), and the gastrointestinal system (24%). Other organ systems affected were the respiratory and skeletal systems. Associated chromosomal abnormalities were found in 33% of cases with CHD and included trisomy 21 (Down syndrome), trisomy 18 (associated with atrioventricular septal defect - AVSD and VSD), and trisomies 13 and 22. Left ventricular outflow tract obstruction was noted in three cases of X monosomy (45X).

Many of the non- genetic risk factors that have been associated with CHD have also been implicated in other congenital malformations. For example, codeine use by pregnant women in the first trimester has been associated not only with CHD such as septal defects, tetralogy of Fallot (TOF), pulmonary valve stenosis and hypoplastic left heart syndrome (HLHS) but also neural tube defects such as spina bifida [17]. Also, clomiphene use was found not only to increase the incidence of patent ductus arteriosus (PDA), but craniosynostosis, hypospadias, cleft lip and palate and spina bifida [18].

The only study on the incidence of CHD in Nigeria so far is that reported by Gupta and Antia in 1967 [19]. They found the incidence of CHD in Ibadan to be 3.5 per 1000 births – a figure approaching the 4 - 5/1000 live births reported from the western literature of that era [1]. Although that study employed the best available diagnostic tools at the time it was done, its limitations are now obvious in view of recent technical advancements in the echocardiographic diagnosis of CHD. Thus, the true incidence of CHD in the country is likely to be much higher than that reported in that study and even the more recent estimates.

Risk factors that have been associated with CHD in Nigerian children include maternal rubella and the congenital rubella syndrome, perinatal complications (such as prematurity and birth asphyxia) and chromosomal anomalies [20-22]. Congenital heart defects were detected in 73 (72.3%) of 101 patients with congenital anomalies studied in Lagos, Nigeria [23]. Congenital malformations (CM) that were associated with CHD in that study included the congenital rubella and some known genetic syndromes such as Down, Noonan's, Edward, Turner's, and Ellis- Van Creveld syndromes. However, these were clinically diagnosed and no genetic investigations were carried out. Children with musculoskeletal, central nervous and gastrointestinal defects also had CHD. Thus, the role of genetic factors in the causation of CHD and other CM in Nigerian children, have not been fully elucidated. Some of the other suggested risk factors such as rubella, prematurity and birth asphyxia have obvious implications for prevention, while the roles of nutritional deficiencies and environmental teratogens have not been evaluated [24]. The latter is of particular concern in view of the increasing environmental degradation in the country and the lack/poor enforcement of environmental protection laws. Hence, more than 40 years after Gupta and Antia's classic paper, there is much that remains to be known about the true incidence of and the risk factors for CHD and other CM in Nigeria.

Study Rationale

The Federal Republic of Nigeria, currently estimated to have a population of about 180 million people, has some of the worst health statistics in the world (Table 2) [25]. Efforts have been ongoing for many years through various national, international and multilateral agencies to address the major causes of the unacceptably high maternal, neonatal, infant and under-5 mortality rates in Nigeria. However, with its large population and an annual population growth rate of 2.4%, [24] Nigeria is also among the countries estimated to have highest incidences of congenital heart disease in the world (Table 3).

Health index	Annual Number	Ranking from below
Total population	182,202,000	
Annual no. of births	7,133,000	
Neonatal mortality rate	34 per 1,000 live births	
Infant mortality rate	69 per 1,000 live births	
Under-5 mortality rate	109 per 1,000 live births	7
Life expectancy at birth	53 years	

Table 2: Basis Health Indices in Nigeria (State of the World Children 2016).

Country	Estimated affected births per year
Bangladesh	33,843
Brazil	26,568
China	148,843
Dominican Republic	1,587
Ethiopia	22,449
India	198,384
Indonesia	35,076
Nigeria	37,145
Pakistan	42,186

Table 3: Estimated numbers of congenital heart disease live births in selected developing countries.

Adapted from: March of Dimes Global Report on Birth Defects, 2016

Of the 37,145 children estimated to be born with CHD in Nigeria every year, the majority die silently without ever being diagnosed or receiving the necessary care [26]. Studies of the natural history of CHD from other countries have shown that without treatment, 20% of affected children will die in the neonatal period and at least 33% in their 1st year of life; 60% are dead by age 2 years while by adolescence 85 - 90% will be dead [27]. With the high prevalence of infectious diseases in Nigeria and other developing countries, the corresponding mortality data may be higher still. Thus, studies of the prevalence of CHD, for example among school children usually underestimate the burden of CHD – since prevalence depends both on the incidence and mortality or survival rates [28]. Thus an incidence study such as this one is long overdue as it will provide real data and give a truer picture of the incidence, associated risk factors and the problems associated with the management of CHD and other CM in a Nigerian city, and their contributions to child mortality. We envisage that the study will in addition not only provide actual statistics on maternal, perinatal, neonatal and infant morbidity and mortality, but will highlight the need for improved management of CHD and other CM, and the need for preventive measures. It will thus be a concrete step towards reducing the deplorable health statistics of the country and the attainment of the millennium development goals.

Materials and Methods

Setting

The study will be carried out at the Jos University Teaching Hospital (JUTH), located in the city of Jos, the capital of Plateau – a North-Central state in Nigeria. The city is located at an altitude of 1,238 meters above sea level and is known for tin mining. Jos receives 1,400

mm of rainfall every year and the average temperature ranges from 21 - 25°C. JUTH serves as a major referral centre for other hospitals within and outside Plateau State including some north–eastern, north-western and other north-central states.

There an average of about 5 deliveries daily in the labour ward of the hospital, giving an average of 35 deliveries weekly and 1,680 in a year. Also, about two babies are admitted on the average each week at birth or soon after into the Special care baby unit (SCBU) of the hospital.

Study design and study population

This will be a dynamic cohort study. After obtaining consent, babies will be enrolled at delivery or at within the first week of life if delivery did not take place in the hospital until 3,000 babies have been recruited (based on sample size estimation). Those identified to have CHD or any obvious CM will be closely followed up for at least another year and all their therapies and other interventions will be documented.

Study objectives

The specific objectives of the study are:

1. To determine the incidence and pattern of CHD and other obvious CM among babies born to pregnant women in Jos, Nigeria.
2. To describe the natural (or modified) history of CHD occurring among babies born in Jos.
3. To identify some risk factors for CHD and other obvious CM in JUTH, Jos.
4. The contribution of CHD and other obvious CM to neonatal and infant morbidity and mortality in Jos.

Inclusion criteria

1. All babies born at JUTH whose parents freely consent to participate in the study.
2. All babies admitted in JUTH within the first week of life whose parents freely consent to participate in the study.

Exclusion criteria

1. Pregnant women that do not consent to participate in the study.

Data collection

Using a pre-designed proforma, maternal sociodemographic information, relevant medical history and possible risk factors exposure will be recorded. The latter will include: history of heart disease and CM in first degree relatives, maternal drug and hormone ingestion including alcohol and tobacco use, maternal diabetes, febrile illnesses and skin rashes during early pregnancy. Others will cover radiation and other possible exposure to teratogenic substances.

Babies born will be examined at birth for obvious congenital abnormalities such as neural tube defects, cleft lip and/or palate, limb deformities, imperforate anus, abdominal wall defects, hydrocephalus, etc. A cardiovascular system (CVS) clinical examination and pulse oximetry will be performed on all live-born infants within 24 hours of delivery.

The babies will also undergo a screening echocardiogram, to be performed by a trained doctor. This will be done as much as possible before discharge from the hospital or at most scheduled within the 1st week of life. All infants with abnormal CVS examination or screening echo findings will be re-scheduled for a detailed echocardiogram to be performed by an appropriately trained paediatric cardiologist. CHD diagnosis will be made based on the ICD-9 diagnostic codes [29].

Follow- up

All babies recruited will be followed-up for one year.

Infants who were found to be normal at birth will be followed up by telephone calls to their mothers to ascertain the baby's state of health (healthy, sick or dead) at 6 weeks, 6 months and 1 year. Mothers will be encouraged to regularly attend the well-child clinic and to report to the hospital, or contact any of the study physicians if their babies are sick at any time. Sick infants will be asked to report at the emergency paediatric unit for a clinical examination to determine the cause of illness and to render the appropriate treatment.

Infants with congenital malformations will be followed up at the appropriate specialty clinics. The outcome measures to be ascertained at ages 6 weeks 6 months and 1 year will include whether the infant is dead or alive, does not require surgery, is awaiting surgery or has undergone surgery. For those with CHD, other outcome measures to be ascertained include spontaneous closure or a reduction in size of the defect, aneurysmal formation and complications such as congestive cardiac failure, pulmonary hypertension and infective endocarditis [30,31].

Data collected	Enrolment	6 weeks	6 months	1 year
Informed consent	x	-	-	-
Risk factors	x	-	-	-
Baby's medical history	-	x	x	x
Echocardiography	-	x*	x*	x*
Assessment for outcome				
Events	-	x	x	x

Table 4: Schedule of visits and study procedures for children with congenital malformations.

only for those with congenital heart disease

Analysis plan

The pilot phase of the study commenced in November 2016 while the main study commenced in March 2017. Pregnant women will be enrolled over a one to two-year period and their babies followed up for a further one year. It is envisaged that the occurrence of following will be observed over the study period: CHD and other CM, stillbirths, perinatal, neonatal and infant morbidities and mortalities, maternal morbidities and mortalities, and other outcomes from CHD and the other CM detected.

Data will be entered into and analyzed using the STATA version 14. Frequency tables will be used to present qualitative data such age group and socio-economic status of the parents, sex of the babies, presence and pattern of congenital CHD and possible risk factors for CHD. Quantitative data such age of the parents, gestational age of the babies at birth and parents' monthly income will be presented using mean ± standard deviation. Chi square statistical test will be used to determine the relationship between characteristics of the babies/ parents and the presence of CHD as well as the contribution of CHD to mortality and morbidity among the babies. Multivariate logistic regression will also be employed to identify risk factors predicting CHD in this study. Confidence interval for this study will be set at 95% with a p value ≤ 0.05 considered statistically significant.

Ethical considerations

Approval for the study has been obtained from the Jos University Teaching Hospital Ethical Committee. Each mother will receive full information and explanations about the aim and procedures of the study, in the language she best understands. Those who freely consent

to participate will be asked to sign or thumb-print the relevant form to indicate their consent before enrollment. Those who withhold consent will not be denied any necessary care on that account. All procedures related to the study will be done at no cost to the participating women. Babies born with congenital malformations will be commenced on the appropriate medical management (if any) while efforts will be made to assist the families of those who require surgical care. Transportations costs will be provided for women who need to make extra visits to JUTH on account of the study. All study information will be strictly confidential.

Discussion

The CHD study will be the first of its kind to determine the incidence of CHD in Nigeria after the introduction of echo in making a diagnosis. The current pattern of CHD in Nigeria will help to determine the severity of these defects and also their contribution to perinatal and neonatal morbidity and mortality. We will collect information on some potential risk factors for CHD at recruitment.

The babies will be examined and echo performed within the first 24 hours or at most within the first week of life. Babies with congenital anomalies will also be examined at follow- up thus providing us with contemporary data on disease progression and possible outcomes. These possible outcomes will vary depending on the type of CHD the child has. This study will also provide information on associated obvious congenital anomalies in babies with CHD.

The study is however hospital- based and hence, will not be a true reflection of the incidence of CHD in the community. It is however believed that this study will provide information that will guide subsequent larger studies.

Other benefits

The study will also enable us determine the following:

- The pattern of maternal morbidities and the maternal mortality rate among women attending ANC in JUTH.
- The perinatal, neonatal and infant mortality rates among babies born to women attending ANC in JUTH.

Conclusion

The study will provide contemporary data of the current incidence and pattern of CHD and other CM in Nigeria as well as its natural or modified history and potential risk factors. The contribution of CHD and other CM to perinatal and neonatal morbidity and mortality will also be determined.

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Conflict of Interest

No financial or non- financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

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