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Risk Factors for Congenital Heart Defects among Neonates in Port Harcourt, Rivers State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Congenital Heart Defects (CHDs) are the most common congenital anomalies in the world but there is a paucity of data regarding possible causes or risk factors. Babies born with severe forms of these defects are likely to die in the neonatal period.
Objectives: The aim of this study was to determine the risk factors for CHDs among neonates delivered in Port Harcourt, Rivers State, Nigeria.
Methods: Using a case control study design, 150 neonates were included in the study. Fifty of the neonates with CHD and 100 controls were selected from the University of Port Harcourt Teaching Hospital, Obio Cottage Hospital and Primary Health Centre Rumuigbo between November 2019 to March 2020. The biodata of the parents and socio-demographic information were obtained through an interviewer-administered questionnaire to the mothers. Physical examination and echocardiograghy were performed on all the neonates. The data obtained were analyzed using the T-test, Spearman correlation coefficient and multi-variable logistic regression.
Results: Based on the results of multivariate logistic regression, the risk factors identified in this study were proximity to oil/gas flaring station, history of diabetes in pregnancy, high birth order and use of pregnacare during pregnancy ($p<0.05$).

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The study observed no significant difference in gender of neonates, gestational age status, birth weight, socioeconomic status, family history of CHD, advanced maternal age, fever in pregnancy, mode of conception, ingestion of alcohol during pregnancy, and gestational plurality.
Conclusion: Risk factors for CHD in Port Harcourt include diabetes mellitus in pregnancy, use of supplements such as pregnacare in pregnancy, high birth order and proximity to oil/gas station.

Keywords: Congenital heart defects; neonates; congenital anomalies; cardiology.

1. INTRODUCTION

"Congenital heart defects are the most common forms of major birth defects and account for a third of all major congenital abnormalities in the world" [1,2]. "Babies born with severe forms of these defects are twelve times more likely to die in the first year of life especially if the defect is missed in the neonatal period" [3,4].

Risk factors associated with CHD could be genetic or environmental [5,6]. About 30% of children with chromosomal abnormalities have congenital heart defects [7]. Congenital heart defects have been found to be due to single gene defects and chromosomal aneuploidy [7]. Nearly a hundred percent of children with Edward syndrome and fifty percent of those with Down syndrome have CHDs [7]. Other genetic syndromes known to be associated with CHD include Noonan, Holt-Oram, Di Georges, Alagille, William-Beuren syndrome etc [6,8]. Non genetic risk factors include advanced maternal age, infections, diabetes Mellitus, phenylketonuria, alcohol ingestion, parental smoking, consanguinity, teratogenic drugs, organic solvents, pesticides, carbon monoxide exposure, particulate matter, ionizing radiation and socio-demographic factors [9,10].

"The city of Port Harcourt, situated in the Niger Delta region is known for its oil exploration activities. Due to weak environmental laws, it is highly polluted" [11]. "Gas flaring poses a potential threat to inhabitants of Port Harcourt as maternal exposure to these chemicals (hydrocarbons, organic solvents, air pollutants) especially in the first trimester is a potential risk factor for CHD" [10]. This study was structured to identify the risk factors for CHD in Port Harcourt.

2. METHODS

This cross-sectional study was carried out among neonates delivered in Port Harcourt, Rivers State. It was done over a five-month period in the University of Port Harcourt Teaching Hospital, Obio Cottage Hospital and Primary Health Centre Rumuigbo from November 1st 2019 to March 30th 2020. Port Harcourt is the capital and largest city of Rivers State Nigeria. It is located in the Niger Delta region and is a major oil-producing city [12]. It is home to the first oil refinery in Nigeria [12]. The study population consisted of neonates ≥28 weeks of gestation aged 0-7 days delivered in selected hospitals in Port Harcourt. Preterm neonates with solitary Patent Ductus Arteriosus and all neonates with an isolated Patent Foramen Ovale were excluded. The study was carried out in the neonatal and immunization units of the Hospitals [13].

2.1 Data Collection

Data was collected using pretested interviewer-administered questionnaires. All the babies recruited into the study had a physical examination and echocardiodiograph done. A portable SONOSITE MICRO MAXX transthoracic echocardiograph machine with an 8-4MHz transducer was used and echocardiography was done by the researcher according to the American Society of Echocardiography Guidelines for performance of paediatric echocardiography [14]. Neonates with CHD were referred to the Paediatric Cardiologist at UPTH for follow up. The data collected were entered and analyzed using the Statistical Package for Social Sciences (SPSS) software version 25 and p-value of <0.05 was considered statistically significant [13].

3. RESULTS

There were 150 neonates included in the study, 50 neonates with CHD and 100 controls. Table 1 presents the biodata of neonates and parents. The study observed no significant difference in gender of neonates, socioeconomic status and family history of CHD ($p>0.05$). Birth order and maternal age showed a statistically significant association with CHD status of neonates. Forty-two percent (42.55%) of neonates with birth order third child or more had CHD compared to those who are either a first or second child

(*p=0.043*). Also, mothers 35 years and older (≥35 years) had more children with CHD compared to those less than 35 years (<35 years) (50.0% vs. 29.51%, *p=0.039*). The distribution of CHD among neonates was thus significantly associated with the mother's age (*p-value* <0.05).

Table 2 presents the neonatal characteristics. The study showed no statistically significant difference in gestational age status, gestational weight classification, and CHD status (p>0.05). Gestational plurality and low birth weight showed a statistically significant association with CHD status. Seventy-one percent (71.43%) of mothers with multiple births (*p=0.041*) and 54.55% of neonates with low birth weight (*p=0.041*) had CHD compared to mothers that gave birth to singleton babies (31.47%).

Table 3 presents the maternal risk factors of CHD. The study showed no statistically significant difference with fever and CHD status (p>0.05). Mode of conception, proximity to oil/gas flaring station, history of diabetes in pregnancy and use of Pregnacare during pregnancy showed a statistically significant association with CHD status.

Table 1. Biodata of neonates and parents

Variables	CHD Status		Total	χ2	p-value
	Present (n=50)	Absent (n=100)			
	n(%)	n(%)			
Gender					
Male	26 (31.33)	57 (68.67)	83 (100.0)	0.17	0.684
Female	24 (35.82)	43 (64.18)	67 (100.0)		
Birth Order					
First Child	22 (36.67)	38 (63.33)	60 (100)		
Second Child	8 (18.60)	35 (81.40)	43 (100)	6.30	**0.043***
Third child or more	20 (42.55)	27 (57.45)	47 (100)		
Maternal Age					
≥35 years	14 (50.0)	14 (50.0)	28 (100.0)	4.27	**0.039***
<35 years	36 (29.51)	86 (70.49)	122 (100)		
Socio-economic status					
Lower	33 (35.87)	59 (64.13)	92 (100.0)		
Middle	13 (27.66)	34 (72.34)	47 (100.0)		0.609$^{\gamma}$
Upper	4 (36.36)	7 (63.64)	11 (100.0)		
Family History of CHD					
Yes	2 (28.57)	5 (71.43)	7 (100.0)		1.000$^{\gamma}$
No	48 (33.57)	95 (66.43)	143 (100.0)		

**Statistically significant (p<0.05); χ2=Chi-Square; μ=Student t-test, γ=Fisher's Exact p*

Table 2. Neonatal characteristics

Variables	CHD Status		Total	χ2	p-value
	Present (n=50)	Absent (n=100)			
	n(%)	n(%)			
Gestational Plurality					
Multiple	5 (71.43)	2 (28.57)	7 (100.0)		**0.041*$^{\gamma}$**
Singleton	45 (31.47)	98 (68.53)	143 (100.0)		
Gestational age status					
Preterm	8 (42.11)	11 (57.89)	19 (100.0)	0.37	0.543
Term	42 (32.06)	89 (67.94)	131 (100.0)		
Low Birth Weight					
Yes	12 (54.55)	10 (45.45)	22 (100.0)	4.16	**0.041***
No	38 (29.69)	90 (70.31)	128 (100.0)		

**Statistically significant (p<0.05); χ2=Chi-Square; γ=Fisher's Exact p*

Table 3. Maternal risk factors of CHD

Variables	CHD Status		Total	χ2	p-value
	Present (n=50)	Absent (n=100)			
	n(%)	n(%)			
Conception mode					
Assisted Reproductive Technology (ART)	7 (70.0)	3 (30.0)	10 (100.0)		**0.016*ᵞ**
Natural conception	43 (30.71)	97 (69.29)	140 (100.0)		
Proximity to Oil /Gas Flaring Station					
Yes	35 (42.17)	48 (57.83)	83 (100.0)	5.67	**0.017***
No	15 (22.39)	52 (77.61)	67 (100.0)		
History of Diabetes in Pregnancy					
Yes	5 (83.33)	1 (16.67)	6 (100.0)		**0.016*ᵞ**
No	45 (31.25)	99 (68.75)	144 (100.0)		
Fever in Pregnancy					
Yes	13 (39.39)	20 (60.61)	33 (100.0)	0.39	0.531
No	37 (31.62)	80 (68.38)	117 (100.0)		
Use of Pregnacare during Pregnancy					
Yes	8 (61.54)	5 (38.46)	13 (100.0)	3.80	**0.051***
No	42 (30.66)	95 (69.34)	137 (100.0)		
Ingestion of Alcohol during Pregnancy					
Yes	5 (35.71)	9 (64.29)	14 (100.0)	**0.00**	**1.000**
No	45 (33.09)	91 (66.91)	136 (100.0)		

**Statistically significant (p<0.05); χ2=Chi-Square; γ=Fisher's Exact p*

Table 4 presents a logistic regression model of the risk factors of CHD in the study population. The regression analysis after adjusting for confounding variables showed that neonates with birth order third child or more (AOR=2.72; *p=0.048*; 95%CI: 1.0-7.31) were at risk for CHD. Other factors observed with increased risk for CHD were residential proximity to or an oil/gas flaring station (AOR=2.34; *p=0.023*; 95%CI: 1.12-4.85), maternal diabetes (AOR=13.71; *p=0.019*; 95%CI: 1.54-122.02), and use of pregnacare in the index pregnancy (AOR=3.60; *p=0.035*; 95%CI: 1.09-11.86).

4. DISCUSSION

The exact aetiology of CHDs are unknown in most cases but the risk factors could be genetic or environmental [6,15]. The risk factors for CHD identified in this study include proximity to oil and gas flaring locations, maternal diabetes, high birth order and use of antenatal supplements like pregnacare.

Oil spillage and gas flaring which are off shoots of oil exploration have been documented to probably have adverse effects on the inhabitants of Port Harcourt [16,17]. Ordinioha and Brisibe [11] in 2013 estimated that an average of 240,000 barrels of crude oil are spilled on a yearly basis in the Niger Delta and these oils contaminate the ground water, surface water, air and crops with hydrocarbons [18]. These toxic chemicals may cause a genetic mutation in foetuses during the period of organogenesis and lead to various congenital anomalies [19].

There was a significant relationship between diabetes mellitus in pregnancy and CHD and this was in keeping with other studies [20-23]. The exact mechanism through which diabetes in pregnancy causes CHD is not known but it has been postulated that maternal hyperglycaemia will lead to foetal hyperglycaemia creating an abnormal biochemical environment that could dysregulate genes responsible for normal fetal development [9,24].

The finding that CHDs occurs in siblings of higher birth order has been demonstrated in other studies [9,25]. A study carried out by Lei et al. [26] in China on the birth prevalence and risk

Table 4. Multivariable results for associated risk factors of CHD in the neonates

Variables	Model I		Model II	
	cOR [95% CI]	P-value	aOR [95% CI]	P-value
Birth Order				
First Child [R]	-	-	-	
Second Child	0.78 [0.36-1.71]	0.536	1.04 [0.46-2.39]	
Third or more	0.31 [0.12-0.81]	**0.017***	2.72 [1.0-7.31]	**0.048***
Maternal Age				
<35 years [R]	-	-	-	
≥35 years	2.39 [1.04-5.52]	**0.041***	2.15 [0.88-5.24]	0.093
Gestational Plurality				
Singleton [R]	-	-	-	
Multiple	5.44 [1.02-29.14]	**0.048***	4.22 [0.76-23.57]	0.101
Low Birth Weight				
No [R]	-	-	-	
Yes	2.84 [1.13-7.14]	**0.026***	2.34 [0.89-6.13]	0.083
Conception mode				
Natural conception [R]	-	-	-	
Assisted Reproductive Technology (ART)	5.26 [1.29-21.33]	**0.020***	4.07 [0.96-17.34]	0.058
Proximity to Gas Flaring Station				
No [R]	-	-	-	
Yes	2.53 [1.23-5.19]	**0.012***	2.34 [1.12-4.85]	**0.023***
History of Diabetes in Pregnancy				
No [R]	-	-	-	-
Yes	11.0 [1.25-96.89]	**0.031***	13.71 [1.54-122.02]	**0.019***
Use of Pregnacare during Pregnancy				
No [R]				
Yes	3.62 [1.12-11.72]	**0.032***	3.60 [1.09-11.86]	**0.035***

Notes: R=reference, cOR=crude Odds Ratio, aOR=Adjusted Odds Ratio

factors of CHD noted that a high maternal parity was associated with increased risk of CHD [26]. The reason for this is not known but it has been suggested that an excessive number of parturitions may lead to reproductive errors [27].

Maternal ingestion of Pregnacare during pregnancy was found to be associated with CHD and this was similar to findings in Port Harcourt where the possible teratogenic effect of Pregnacare was mentioned [16]. This claim needs to be further investigated as only 23 of the mothers took Pregnacare. Pregnacare contains betacarotene (a precursor of vitamin A) and several other vitamins. Some precursors of vitamin A can be teratogenic when taken in the first trimester of pregnancy [20,28,29] but the effects of beta carotene on the foetus is not well documented [30].

Low birth weight babies were more likely to have CHD when compared to normal weight and macrosomic babies but this finding was not statistically significant.

Congenital heart defect was found more among neonates of mothers who conceived via assisted reproductive technology (ART) but his difference was however not statistically significant. The mode of conception was not an independent predictor of CHD probably because most of the mothers that conceived through ART had other issues like advanced maternal age and diabetes melitus. This finding has to be investigated further as only 10 of the mothers conceived via ART. A case-control study done in Port Harcourt in 2014 by Orazulike et al. [31] showed that CHD was significantly higher among neonates whose mothers conceived via ART when compared to those that conceived naturally.

In this study, CHD status was not dependent of gestational age and this is in contrast to other studies that have found CHD to be commoner in

preterms [32,22]. A possible explanation for this is that not enough preterms were sampled as only about 7% of the study population was delivered prematurely.

Congenital heart defect was found more among neonates delivered in multiples when compared with babies born singleton this difference was not statistically significant. This is in contrast to other studies that have found CHD to be commoner in multiple gestation pregnancies. This could be because of the small population of neonates of multiple gestation in this study.

It should be noted that the role of herbal concoction was not assessed as a possible contributory factor to CHD. Also maternal smoking did not feature in this study as non of the mothers used tobacco products.

5. CONCLUSION

Risk factors for CHD in Port Harcourt include advanced maternal age, diabetes mellitus in pregnancy, use of supplements such as pregnacare in pregnancy and proximity to oil/gas station.

ETHICAL APPROVAL AND CONSENT

Ethical clearance for the study was obtained from the Research and Ethics Committee of the University of Port Harcourt Teaching Hospital (UPTH) before the commencement of the study. Permission was gotten from the Rivers State Health Management Board and the Management of Obio Cottage Hospital. A written informed consent was obtained from the parents of the neonates selected for this study and the information retrieved in this study was kept confidential. All neonates with congenital heart defects were referred for management and long term follow up in the Paediatric Cardiology Unit of the University of Port Harcourt Teaching Hospital. The cost of the echocardiograghy was borne by the researcher.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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