RELATIONSHIP OF CONSANGUINITY WITH CONGENITAL HEART DISEASE IN CHILDREN

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ABSTRACT

Objectives: To find the relationship between consanguineous marriage and congenital heart disease in children

Material and Methods: This case-control study was conducted from October 2018 to January 2020 at inpatient and outpatient settings of department of child health, Khyber Teaching Hospital Peshawar. Total 346 children were taken and divided into two equal groups. 173 with congenital heart disease and 173 with no cardiac defect on echocardiography. Consecutive non-probability sampling was employed and echocardiographs of the children were collected and analyzed by SPSS 23.

Results: Out of 346 children from birth to 15 years old, 173 had congenital heart disease and 173 had no cardiac defect. Amongst them, 214(61.8%) were male while 132(38.2%) were female. 274(71.1%) were from 0-1 year age group, 66(19.1%) were from 1-5 years, 20(5.8%) from 5-10 years age group and only 14(4%) were from 10-15 years age group. From the total study population, 119(34.39%) had consanguineous parents and had congenital heart disease with the odds of congenital heart disease 1.68 higher in consanguineous marriages compared to non-consanguineous marriages with a p-value of 0.02.

Conclusion: The odds of having congenital heart disease is 1.68 higher in children born from consanguineous marriages compared to non-consanguineous marriages.

Keywords: Consanguinity, congenital heart disease, children, echocardiography.

This article may be cited as: Shah SIA, Amir S,Younus R, Nazir F, Khaliq A, Rehman Z. Relationship of consanguinity with congenital heart disease in children. J Med Sci 2020 April;28(2):117-120

INTRODUCTION

Congenital heart disease (CHD) refers to the structural heart defect which is present since birth of a child. It is one of the major causes of mortality in the first year of life[1-3]. Congenital heart disease is one of the most frequently occurring birth defects which affects the newborn children and is sometimes picked up by a physician later on[4,5]. Congenital heart diseases (CHD) are common and serious conditions that have significant impact on mortality, morbidity, and healthcare expenses in children and adults[6]. It has a wide variety of clinical presentations ranging from asymptomatic detection of the defects to symptomatic cardiac disease which may lead to death[7].

The worldwide prevalence of CHD among newborns ranges from approximately 3.7 to 17.5 per 1000, accounting for 30-45% of all congenital defects[8]. Variations in birth prevalence of congenital heart disease in different parts of the world have been reported, from 6.9 per 1000 births in Europe to 9.3 per 1000 in Asia[6].

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Date received: 12-05-2020
Date revised: 01-06-2020
Date accepted: 20-06-2020

In Pakistan about 40,000 children are born with a congenital heart defect each year[7]. Incidence was found to be 8.2/1000 live births in a study in China[1], 25/1000 live births in Bangladesh[9] and 8.1/1000 live births in a study in Atlanta[10].

Etiology of Congenital heart disease is not known in majority of cases but numerous environmental and genetic factors have a role in its pathogenesis including tobacco use, maternal diabetes, maternal smoking, consanguinity among parents, infections, maternal age and family history of Congenital heart diseases[11].

Studies have been published in different parts of the world regarding the relationship of consanguinity and CHD in children but not much data is available in this regard in our country and keeping in view the increased ratio of consanguineous marriages, it is imperative to have a data regarding its effect on CHD in children and that is why this study was conducted.

MATERIAL AND METHODS

It was a case-control study conducted both at inpatient and outpatient setting of the department of child health, Khyber teaching hospital, which is one of the largest public sector tertiary care hospital of the Khyber Pakhtunkhwa (KPK) province, located in Peshawar city. This hospital provides health care services to pediatrics

patients most of whom belong to poor community and low socioeconomic class. In addition to local community, many of these patients come from far-flung areas of Khyber Pakhtunkhwa and Federally Administered Tribal Areas (FATA). A total of 346 children from birth to 15 years of age who had done echocardiography due to congenital heart disease or suspicious of congenital heart disease on clinical examination were included in the study and were divided into two equal groups after taking informed consent. Children with acquired heart disease due to any reason were not included.

The case group had 173 children with congenital heart disease and control group also had 173 children but with no congenital heart disease via consecutive non-probability sampling.

Data was collected on pre designed proforma including name, age, sex, congenital heart disease status and consanguinity and was analyzed using SPSS v23. Frequency and percentage was calculated for categorical variables and Odds ratio (OR) was calculated for assessing the risk of consanguinity on congenital heart disease.

RESULTS

Among the 346 children, 214(61.8%) were male and 132(38.2%) were female. Majority of children were infants i.e 0-1yr making about 241(71.1%) of the included children while just 14(4%) were from 10-15yrs of age. From 173 children with congenital heart disease, consanguinity was present in 119(68.73%) and absent only in 54(31.21%) and among children with no congenital heart disease, 98(56.54%) children were born from consanguineous parents while 75(43.35%) parents were not related. Odds ratio was calculated [OR=1.68, 95%CI 1.08-2.61] with P-value of 0.02 which is statistically significant and showed that risk of congenital heart disease in children with consanguineous parents was higher compared to those with non-consanguineous parents.

The common congenital heart diseases that we observed in our study are shown in table. 5. Majority of the children were having complex congenital heart disease i.e 2 or >2 cardiac defects in a child, accounting for 73(42.1%) of all CHD cases and 52 of them were present in children with consanguineous parents compared to 21 cases in non-consanguineous group. The next common defects were ventricular septal defect (VSD) and patent ductus arteriosus (PDA) accounting for 14.4% each but again more cases were found in children with consanguineous parents.

Table 1: Gender distribution of study participants.

Gender	Frequency	Percentage
Male	**214**	**61.8%**
Female	132	38.2%
Total	346	100%

Table 2: Age Groups of study participants.

Age Groups (in Years)	Frequency	Percentage
0-1yr	246	71.1%
1-5yrs	66	19.1%
5-10yrs	20	5.8%
10-15yrs	14	4%
Total	346	100%

Table 3: Frequency of consanguinity in CHD.

Consanguinity	Congenital Heart Disease		Total
	Present	Absent	
Present	119	98	217
Absent	54	75	129
Total	173	173	346

Table 4: Frequency of different congenital heart diseases.

S.No	Type of Congenital heart disease	Consanguinity		Total n (%)
		Present	Absent	
1	Atrial Septal Defect (ASD)	12	4	16 (9.2%)
2	Ventricular Septal Defect (VSD)	14	11	25 (14.4%)
3	Patent Ductal Arteriosus (PDA)	17	8	25 (14.4%)
4	Pulmonary Stenosis (PS)	3	2	5 (2.8%)
5	Transposition of Great Arteries (TGA)	3	2	5 (2.8%)
6	Coarctation of Aorta	2	1	3 (1.7%)
7	Tetralogy of Fallot (TOF)	8	3	11 (6.3%)
8	Atrioventricular Septal Defect (AVSD)	4	0	4 (2.3%)
9	Cor Triatriatum	2	1	3 (1.7%)
10	Total Anomalous Pulmonary Venous Circulation (TAPVC)	1	1	2 (1.1%)
11	Aortic stenosis (AS)	1	0	1 (0.5%)
12	Complex Congenital Heart Disease	52	21	73 (42.1%)
	Total	98	75	173 (100%)

DISCUSSION

In our study Congenital heart diseases were found significantly higher in children born out of consanguineous marriage than in those with non-consanguineous marriage. A study by Deveshwar D also showed that congenital heart disease was significantly higher in children born out of consanguineous marriage than in those with non-consanguineous marriage [OR=4.614][12]. Bassili A in their case-control study in the year 2000 showed that consanguinity was present in 44.1% of Congenital heart

disease cases compared to controls in which it was 23.8% ($p < 0.05$)[13]. Becker et al studied 1013 patients with Congenital heart disease and the data was then compared to rates of consanguinity from a previous study of 3212 Saudi families (El-Hazmi MA), and the comparison indicated a statistically significant association ($p < 0.001$) between first-cousin marriage and Congenital heart disease in the study population[14,15].

In South India, Ramegowda S in his case-control study analyzed 144 cases of congenital heart disease. The parents of 15.5% of the control group were consanguineous compared to 40.3% of the Congenital heart disease families ($p=0.001$)[16]. In another study conducted by El Mouzan MI, it was found that Congenital heart disease was present in 9.1 per 1000 consanguineous families versus 4.3 per 1000 non-consanguineous families, giving an OR of 2.12 (95% CI 1.27–3.57)[17].

Another study by Haq FU demonstrated that amongst the 250 cases of congenital heart disease, 122 patients (49%) were children of consanguineous marriages whereas in controls only 72 patients (29%) showed consanguinity between the parents. On multivariate analysis, consanguinity was found as an independent risk factor for Congenital heart disease in children ($p < 0.001$)[18].

The most common type of congenital heart disease that we found in our study population was complex congenital heart disease both in consanguineous and non-consanguineous groups but was more in consanguineous group. Other common defects observed were ventricular septal defect and patent ductus arteriosus while other defects were very few. In a study by Becker S, atrioventricular septal defect (AVSD) was most likely associated with consanguinity followed by VSD and ASD[14]. Contrary to this Ramegowda S concluded that atrial septal defect (ASD) and patent ductus arteriosus (PDA) were strongly associated with consanguinity, but they found no significant association of consanguinity with VSD or with complex congenital heart disease as found in our study.16 Bassili A reported that VSD and ASD were associated with consanguinity[13]. Same findings were documented by Yunis K in their study[19].

The majority of these studies like ours support the relationship between consanguineous and congenital heart disease in children. The question that how consanguinity causes this increase risk of congenital heart disease in children is not fully understood. Consanguinity could lead to the segregation of autosomal recessive genes, but the contribution of the genes to heritability of cardiac malformations is not well understood. Genetic studies can help to solve this question but it is beyond the scope of this local study. Different populations may be differentially susceptible to genetic and environmental perturbations, and it is important to continue these studies with a global perspective.

After analyzing the result of our study, we recommend that the healthcare professionals and parents should be educated regarding importance of the medical family history and to discuss the potential implications on health based on the family history and clinical assessment with the parents involved in consanguineous marriage. We also suggest to develop parental skills to better manage familial health risks and to prioritize disease prevention and investigation into genetic predispositions to disease and incorporate cultural and social issues such as consanguinity into global health initiatives.

LIMITATIONS

Was performed in a single hospital, we could have had better result if the study was performed on a wider scale with a bigger sample size. Additionally, if genomic study could have been available, a better understanding of the relationship of consanguinity with congenital heart disease could have been made.

CONCLUSION

Congenital heart diseases are common entity in children. Not much has been identified in the area of cause and effect relationship of various prenatal factors causing the congenital heart diseases in children. Consanguinity among parents is an independent risk factor for presence of congenital heart diseases in children and the result of our study and some other studies prove this statement. If we can develop a better understanding of the relationship between consanguinity and congenital heart disease, we can implement more precise genetic counseling and more effective clinical management.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Shah SIA: Principal author and article writing.

Amir S: Statistical analysis and review.

Younas R: Data Collection

Nazir F: Literature searching & Writing References.

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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.