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ORIGINAL ARTICLE

The Burden Of Congenital Heart Disease In Children Born To Consanguineous Parents

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Abstract

Background: Consanguineous marriages have been a longstanding tradition across various global communities for millennia. The prevalence of such marriages fluctuates among nations and is typically linked to various demographic factors including religion, educational attainment, socioeconomic status, geographic location, population density, and whether individuals reside in rural or urban environments. The prevalence of congenital heart disease among cousins' marriages has been a topic of interest due to its potential association with genetic factors. Hence, studying congenital heart disease in offspring of consanguineous couples is crucial for enhancing clinical and public health strategies.
Objective: This study aimed to determine the frequency of congenital heart disease in children born to consanguineous parents.
Material and Methods: In this cross-sectional study, a total of 100 children born to consanguineous parents were included, which was carried out Pediatric Medicine Department, Mardan Medical Complex from 20 November 2021 to 20 May 2022. Echocardiography was done in the cardiology department of all the included children to detect any congenital heart defect. Data was collected for congenital heart disease according to operational definitions.
Results: The mean age of children born to consanguineous parents was 4.25±2.46 years (range:1-15years). Male children constituted 62% and females 38%, with no significant association between CHD prevalence and gender (p=0.963). Congenital heart disease was observed in 15% of children born to parents in cousin marriages. Among CHD cases, arterial septal defects (ASD), ventricular septal defects (VSD), and Tetralogy of Fallot (TOF) were most common. Stratification by age, gender, and parental education revealed a higher prevalence of CHD among children of uneducated parents (28.1%) though this was not statistically significant (p=0.87)
Conclusion: It was found that cousin marriage is a risk factor for congenital heart defects in children.
Keywords: consanguineous marriages, congenital heart disease

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Introduction

Consanguineous marriages have been a longstanding tradition across various global communities for thousands of years. The prevalence of such marriages fluctuates. among nations and is typically linked to various demographic factors including religion, educational attainment, socioeconomic status, geographic location, population density, and whether individuals reside in rural or urban environments1. Blood-related marriages have

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been linked to various complications such as premature births, congenital anomalies and low weight at birth, infant mortality, abortion, cognitive impairment, heart risks, and diverse complex conditions[2]. Communities with high consanguinity rates often prefer cousin marriages due to reasons such as preserving family lineage solidarity, facilitating partner selection, supporting female status and relationship with in-laws, minimizing marriage expenses, enhancing elderly care prospects and, ultimately fostering stronger marital stability[3]. The cultures characterized as protective and semi-protective are prevalent in many Middle Eastern, South Asian, West Asian, and sub-Saharan African countries, where these factors hold greater importance, explaining the high frequency of cousin marriage in these regions4. Congenital heart defects (CHDs) rank as the most prevalent anomalies among children[5]. The global occurrence of Congenital heart defects remains steady at approximately 8 to 10 every 1000 live births. However, this rate increases when parents are cousins or blood-related[6]. Globally, blood-related marriages amplify the likelihood of congenital heart diseases by 2 to 3 times. Research on consanguineous unions reveals an Autosomal Recessive pattern in some CHDs, affirming the potential consanguinity role in its etiology[7]. Research carried out by Fazeriandy A., et al. has shown that the frequency of congenital heart diseases was 14% in children born to consanguineous parents8. Anwar S, et al, in another study, found that the frequency of congenital heart diseases was 45.5% in children of consanguineous marriages[9].

With over 96% population identifying as Muslims, Pakistan maintains a semi-conservative social fabric characterized by strong religious adherence and societal cohesion, which promotes cousin marriages (CM)[10]. However, there is limited data on the prevalence, scale, and clinical ramifications of CM within the nation. Hence, this study intends to ascertain the burden of congenital heart diseases in children born to consanguineous marriages in our society.

Material and Method:

Objective: To find the frequency of congenital heart diseases in children of consanguineous parents

Operational definitions:

Consanguineous marriage: A marriage between two parents who are blood-related to cousins to each other.

Congenital heart disease: It was defined as any structural heart defect present since birth and detected on the Echocardiography.

Study Design: This was a cross-sectional study

Study Setting and Duration: This was conducted at the Pediatric Medicine department, Mardan Medical Complex, Mardan from 20th November 2021 to 20th May 2022.

Sample size: The sample size of 100 children was determined utilizing the WHO sample size software, with a 95% confidence interval, a 7% margin of error, and an anticipated frequency of congenital heart disease at 14% in children born to consanguineous couples 8.

Sampling technique: Nonprobability consecutive sampling

Inclusion criteria:

All children from 1 to 15 years of age of both genders born to consanguineous parents were included.

Exclusion criteria: Children with acquired heart disease, family history of congenital heart disease, and antenatal maternal drug use or commodities like diabetes mellitus, hypertension, and renal diseases, were excluded.

Data Collection Procedure: After explaining the details of the study to them, informed written consent was taken from the parents of enrolled children fulfilling the inclusion criteria and visiting the outdoor and emergency department of the Pediatric Medicine Department. Basic demographics like age, gender, and parent's education level were noted. All patients were sent to the cardiology department for Echocardiography. Data was collected for congenital heart diseases as per operational definition. Data was noted on a pre-designed proforma.

Data Analysis: The statistical analysis program IBM SPSS version 25 was used to analyze the data. Qualitative variables like gender, parent's education level, and congenital heart disease were presented as percentages. Congenital heart disease was stratified according to age, gender, and parent's education level. The Chi-square test was applied after stratification and taking p value ≤0.05 as significant.

Results:

The mean age was 4.250±2.46 years and the age range were 1 to 15 years among children born to blood-related parents. Male children were 62% while female was 38%. However, the analysis showed no statistical significance between Congenital heart disease (CHD) prevalence and the gender of the children (p=0.967). Congenital heart disease was observed in 15% of children born to blood parents of cousin marriages (Table 1).

Table 1: Frequency of CHD in children with Consanguineous Parents(n=100)

Congenital Heart disease	Percentage
Yes	15%
No	85%
Total	100%

The proportion of various congenital heart diseases (CHDs) is shown in Figure No.1

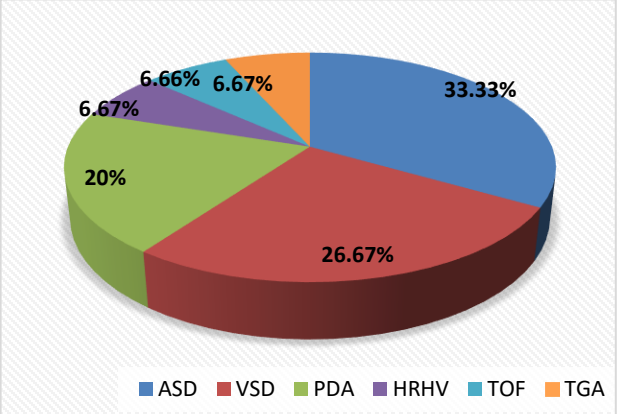

Figure 1. Proportions Of CHDs in Consanguineous Parents

*CHD (congenital heart diseases), ASD (atrial septal defects), VSD (ventricular septal defects), PDA (persistent ductus arteriosus), HRHV (hypoplastic right heart ventricle), TGA (transposition of great arteries), TOF (Tetralogy of Fallot)

Stratification of congenital heart disease concerning age, gender, and parent's education level is shown in Table 2.

Table 2: Frequency of CHD stratified by children's age, gender, and parent's education level

Age group	Congenital Heart Disease		p-value
	Yes	No	
1-7 years	13(14.9%)	74(85.1%)	0.967
8-15 years	2(15.4%)	11(86.6%)	
Gender	**Yes**	**No**	
Male	11(17.7%)	51(82.3%)	0.327
Female	4(10.5%)	34(89.5%)	
Education level	**Yes**	**No**	
Uneducated	9(28.1%)	23(71.9%)	0.087
Primary	4(8.7%)	42(91.3%)	
Secondary	1(6.7%)	14(93.3%)	
Higher	1(14.3%)	6(85.7%)	
Total	**15(15%)**	**85(85%)**	(n=100)

There seems to be a trend of higher CHD prevalence among children of uneducated parents, the difference was not statistically significant (p=0.087).

Discussion:

Although the burden of congenital heart diseases varies among various regions, a notable association emerged between consanguinity and the likelihood of congenital heart disease (CHD) occurrence in the offspring. In a sample of 100 children born of consanguineous marriages, 15 were found to have CHD. This finding mirrors similar observations in various countries Saudi Arabia[11], Iran[13,14], China[15], India[16], Lebanon[17], and Canada[18]. The similarity among these populations lies in shared demographic, religious, and cultural characteristics. Notably, this study did not delve into the degree of relatedness within the consanguineous unions or explore specific genetic factors contributing to the risk of CHD.

Consanguinity emerges as a notable risk factor for CHD occurrence, with the most prevalent types being ventricular septal defects, atrial septal defects, and Tetralogy of Fallot across all populations. Our study revealed that among children born from consanguineous parents, CHDs were predominantly atrial septal defects (33.33%), ventricular septal defects (26.67%), persistent ductus arteriosus (20%), hypoplastic right heart ventricle (6.67%), transposition of great arteries (6.67%%) and Tetralogy of Fallot (6.66%). These proportions closely align with a study conducted in Iraq, with similarly identified atrial septal defect (66%) as the most common CHD type, followed by persistent ductus arteriosus, ventricular septal defect, and transposition of great arteries[10]. Atrial septal defect (49%) was identified as the most common CHD in the United Arab Emirates[11], while similar predominance was observed in research from South India18. However, unlike previous studies in Iraq, Saudi Arabia, and South India, our study did not examine the degree of consanguinity such as first cousin.

A similarity between our study and another local study was the higher prevalence of non-cyanotic CHD compared to cyanotic ones with transposition of great arteries emerging as the most frequent cyanotic CHD in both investigations[12].

An Egyptian study documented Congenital heart defects along with dysmorphic features associated with chromosome disorders such as trisomy 21 and trisomy 2119. Conversely, our study did not observe any dysmorphic features among the study subjects.

Our study found a slightly elevated occurrence of CHD among males, aligning with findings in various studies from Iraq[10], Saudi Arabia[11,] and Pakistan[12]. However, a study from China reported a higher prevalence of CHD in girls[15].

Ethnic relations and cultural customs often shape the prevalence of consanguineous marriages. In our investigation, a significant portion of CHD cases occurred within the Muslim community, likely reflecting the predominantly Muslim population in Pakistan. This trend is consistent with the studies conducted in Iran[13], Lebanon[17,] and Saudi Arabia[11], where Muslim populations are in the majority. However, in a region like India, where Hinduism prevails, the distribution of CHD may differ.

Studies conducted in Pakistan and South India suggest that not all children from consanguineous parents are at risk of CHD[12,18]. These findings align with our study where a small portion (2.5%) of children born to blood-related parents did not develop CHD.

Advancements in genetic technology now enable the detection of genetic mutations linked to congenital heart diseases (CHD), considering the intricate involvement of various genes in cardio genesis. Techniques like single nucleotide polymorphisms (SNPs) offer insights into a person's genetic profile. An Egyptian study indicated the Autosomal Recessive mechanism underlying CHD occurrence in children born from consanguineous parents, except in the case of persistent ductus arteriosus19. In our study, we utilized Echocardiography for CHD diagnosis and conducted interviews to ascertain the parents' consanguinity. However, due to equipment limitations, genetic assessment via SNPs in CHD cases associated with consanguinity was not possible. Therefore, the potential role of Autosomal recessive pattern CHD occurrence among children in this study remains a plausible consideration.

Conclusion:

In summary, consanguineous marriage emerges as a risk factor for congenital heart disease (CHD) among offspring.

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