International Journal of Contemporary Pediatrics
Dev D et al. Int J Contemp Pediatr. 2016 Aug;3(3):868-871
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20162356

Research Article

Evaluation of consanguinity as a risk factor for congenital heart diseases

Deveshwar Dev[1]*, Rambabu Sharma[2], Meenakshi Sharma[3], Kamlesh Agrawal[4], Manisha Garg[5]

[1]Medical Officer, Rajasthan Government, Jaipur, Rajasthan, India
[2]Department of Pediatrics Cardiology, SPMCHI, Jaipur, Rajasthan, India
[3]Department of Physiology, SMS Medical College, Jaipur, Rajasthan, India
[4]Department of Pediatrics, SPMCHI, Jaipur, Rajasthan, India
[5]Department of Pediatrics, SMS Hospital, Jaipur, Rajasthan, India

Received: 14 March 2016
Accepted: 11 April 2016

***Correspondence:**
Dr. Deveshwar Dev,
E-mail: ashnhlmci@gmail.com

ABSTRACT

Background: Congenital heart disease (CHD) is the most common malformation in children. It is an important cause of infant mortality, long term morbidity and disability. There are multiple risk factors associated with CHDs, but in most of them cause and effect relationship has not been established till recently. Consanguinity as a risk factor has been studied by some workers with a small number of subjects hence requires to be evaluated through a study with a significant size of cohort. The objective of the study was to find out the association between parental consanguinity and the risk of CHDs among their off springs.
Methods: This is a hospital based, comparative, cross sectional, observational study. 518 children with CHDs, confirmed by echocardiography were included as cases and 240 children without any obvious congenital anomaly matched for age and sex were taken as control. The following clinical observations were collected through questionnaires in a predesigned performa: maternal and paternal age at conception; parental consanguinity; maternal medical, gestational and obstetric history; and other birth defects.
Results: Children from case and control groups were comparable with respect to age and sex at the inclusion in the study. Out of the total 758 study participants, 41 patients (5.41%) had parents who had a consanguineous marriage. Of these, 34 patients (6.56%) were cases and 7 (2.92%) were controls (P value was highly significant).
Conclusions: Consanguinity in parental marriages confer an increased risk of CHDs in their off springs (p value <0.005).

Keywords: Congenital heart disease, Consanguinity, Echocardiography

INTRODUCTION

The reported incidence of CHDs is 6-8/1000 live births according to various series from different parts of the world.[1,2] With a believed incidence rate of 8/1000 live birth, nearly 180,000 children are born with CHDs each year in India. Of these nearly 60,000 to 90,000 suffer from critical CHDs per year, requiring early intervention.[3]

CHDs are thought to result from the combined effects of a number of factors, presumably both genetic and environmental. Despite this complexity, consanguinity could increase the likelihood of disease, particularly if the disease has a recessive or multifactorial inheritance pattern. This possibility has been explored by a number of groups, who have attempted to quantify the potential degree of increased risk. However, these studies have varied in their scope, design and analysis, and as a result the conclusions drawn have been varied. For this state we planned to study correlation between parental consanguineous marriages with CHDs in a representative sample of pediatric population.[4]

METHODS

The present study has been conducted in Sir Padampat Mother and Child Health Institute, Department of Paediatric Medicine, Tertiary health care, Medical College. It was a hospital based, comparative, cross sectional, observational study. Children below 5 years attending outdoor, indoor and cardiac clinics who were suspected for CHDs on the basis of sign and symptoms were subjected to various investigations e.g. Chest X ray, ECG, and 2D Echocardiography. After applying inclusion and exclusion criteria, the confirmed cases of CHDs were enrolled for study. Written consent was obtained by parent(s) of all enrolled children. A predesigned performa was used to collect following informations: age and sex of children, religion, parental educational status, parental consanguinity,

Inclusion criteria

Children aged between 0-5 years, confirmed cases of CHDs diagnosed by clinical examination plus echocardiography with or without cardiac catheterization (study group)**,** and children without any CHDs matched for age but not for gender, ethnicity or social class (control group).

Exclusion criteria

Unwilling guardians and patients whose data regarding parental consanguinity are not available.

Statistical analysis

Data was entered on excel sheet and analyzed statistically using XL- stat software. Quantitative data was summarized in form of Mean±sd. Qualitative data was summarized in the form of percentage and proportion and difference were analyzed using Chi-Square test. The Confidence interval for all the analysis was kept 95% and α-error of 5 %.

RESULTS

A total of 780 patients were enrolled in the study, out of which 12 patients did not fulfill the inclusion criteria, in 8 patients parents refused to participate in the study and in 2 patients history was either doubtful or incomplete. So, total 22 subjects were excluded. 758 patients were finally included in the study (Table 1). Total included subjects were further divided into study group which included 518 patients with CHDs and control group comprised of 240 patients without CHDs which served as control.

Table 1: Distribution of study subjects according to age and sex.

Age group (in Yrs)	Subjects with CHD (Study group)			Subjects without CHD (Control group)		
	Male No. (%)	Female No. (%)	Total No. (%)	Male No. (%)	Female No. (%)	Total No. (%)
0-1 yr.	300 (57.92)	133 (25.66)	433 (83.59)	61 (25.42)	81 (33.75)	142 (59.17)
>1-2 yr.	23 (4.44)	11 (2.12)	34 (6.56)	11 (4.58)	4 (1.67)	15 (6.25)
>2-3 yr.	8 (1.54)	5 (0.96)	13 (2.51)	19 (7.92)	9 (3.75)	28 (11.67)
>3-4 yr.	8 (1.54)	1 (0.19)	9 (1.74)	12 (5.00)	12 (5.00)	24 (10.00)
>4-5 yr.	21 (4.05)	8 (1.54)	29 (5.60)	23 (9.58)	8 (3.33)	31 (12.92)
Total	360 (69.50)	158 (30.50)	518 (100.00)	126 (52.50)	114 (47.50)	240 (100.00)

Table 2: Distribution of study subjects according to Consanguinity in parental marriage.

Consanguinity status	Study group No. (%)	Control group No. (%)	Total No. (%)
Present	34 (6.56)	7 (2.92)	41 (5.41)
Absent	484 (93.44)	233 (97.08)	717 (94.59)
Total	518 (100.00)	240 (100.00)	758 (100.00)

χ^2= 4.260; d.f =1; Odd ratio=0.428; 95 % CI = 0.187 – 0.979; P < 0.05; Significant.

Maximum numbers of children with CHDs were observed in 0-1 year age group (Table 1) which contributes to more than 4/5th (83.59%) of study group. Out of the total 758 subjects, 41 patients (5.41%) had parents who had a consanguineous marriage (Table 2). Of these, 34 patients (6.56%) were from study group and only 7 (2.92%) were controls (Odd's ratio=0.428, 95 % CI = 0.187 – 0.979, P <0.05).

Table 3: Distribution of muslim subjects according to consanguinity status.

CHDs	Consanguinity status		Total
	Present No. (%)	Absent No. (%)	
Present	34 (83)	20 (51)	54 (67.5)
Absent	7 (17)	19 (49)	26 (32.5)
Total	41 (100)	39 (100)	80 (100)

χ^2= 7.738; Odd ratio=4.614; 95 % CI = 1.651 – 12.89; P <0.005; Significant.

Consanguinity was observed only in parents of Muslim subjects. Amongst 80 Muslim subjects the percentage of consanguinity in parents of children having CHDs was

83%, while it was observed in 20% of parents in children without CHDs (Table 3).

DISCUSSION

In present study CHDs were found significantly higher in children born out of consanguineous marriage than in those with non-consanguineous marriage (p <0.005). In Indian population the consanguineous marriages are prohibited in Hindu religion so it was observed among Muslim parents only.

Badaruddoza et al in 1994 found that 4.41% of the children of consanguineous parents versus 1.22% of non-consanguineous parents had CHDs (p <0.001).[5] Bassili et al in their case-control study in 2000 found that consanguinity was present in 44.1% of CHD cases versus 23.8% of controls (p <0.05).[6]

Becker et al examined 1013 patients with CHDs and the data were then compared to rates of consanguinity from an earlier structured study of 3212 Saudi families (El-Hazmi et al), and the comparison indicated a statistically significant association (p <0.001) between first-cousin marriage and CHDs in the study population.[7,8]

Nabulsi et al investigated the consanguinity profile of the 759 CHDs patients and observed that 20.2% of CHD patients were born to first cousins, whereas first cousin marriage in the control group was maximally 13.2%.[9] The difference in cases and controls may suggest an association between CHDs and consanguinity (p <0.0001).

In South India, Ramegowda and Ramachandra in their cases-controls study (Ramegowda et al) analyzed 144 cases of CHDs.[10] The parents of 15.5% of the control group were consanguineous versus 40.3% of the CHD families (p=0.001).

Yunis et al reported that consanguinity was present in 17.9% of cases of CHDs versus 9% of controls and the results attain statistical significance at p <0.001.[10]

Chehab et al found that consanguinity was present in a higher proportion of CHD cases versus controls when the analysis was performed on first-cousins (consanguinity in 19.4% of cases versus 14.4% in controls) parental relationships (p <0.0001).[12]

The study by El Mouzan et al found that CHDs 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, p <0.003).[13]

Haq F et al showed that amongst the 250 cases of CHDs, 122 patients (49%) were children of consanguineous marriages while in controls only 72 patients (29%) showed consanguinity amongst parents.[1] On multivariate analysis, consanguinity was found as an independent risk factor for CHDs in children (p <0.001).

A relatively higher incidence of CHDs was observed in consanguineous marriages by various workers. Quite high incidence (>20%) was observed by Bassili et al, Becker et al, Nabulsi et al, Ramegowda et al and Haq F et al. High incidence (10-20%) was observed by Chehab et al and Yunis et al. Almost similar incidence (<10%) to our study was observed by Badaruddoza et al and El Mouzan et al.

The majority of studies are in support of a significant association between consanguineous parentage and presence of CHDs in their children.

CONCLUSION

CHDs in children are not an uncommon entity. Not much is known in the area of cause and effect relationship of various antenatal factors causing CHDs in children. Consanguinity in parental marriages is an independent risk factor for presence of CHDs in children (p <0.005). Pre-marriage counseling and avoidance of consanguineous marriages should be propagated with the help of health education by various means including media messages and henceforth cause a decline in the rates of CHDs in our population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Haq F, Jalil F, Hashmi S, Jumani MI, Imdad A, Jabeen M, et al. Risk factors predisposing to congenital heart defects. APC. 2011;4(2):117-21.
2. Chadha SL, Singh N, Shukla DK. Epidemiological study of congenital heart disease. Indian Journal of Pediatrics. 2001;68:507-10.
3. Saxena A. CHD in India: A status report. Indian J Pediatr. 2005;72:595-8.
4. Shieh. Consanguinity and the Risk of Congenital Heart Disease. Am J Med Genet A. 2012;158A(5):1236-41.
5. Badaruddoza, Afzal M, Akhtaruzzaman. Inbreeding and congenital heart diseases in a north Indian population. Clin Genet. 1994;45:288-91.
6. Bassili A, Mokhtar SA, Dabous NI, Zaher SR, Mokhtar MM, Zaki A. Risk factors for congenital heart diseases in Alexandria, Egypt. Eur J Epidemiol. 2000;16(9):805-14.
7. Becker SM, Al Halees Z, Molina C, Paterson RM. Consanguinity and congenital heart disease in Saudi Arabia. Am J Med Genet. 2001;99:8-13.
8. El-Hazmi MA, Warsy AS, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Consanguinity among the Saudi Arabian population. J Med Genet. 1995;32:623-6.

9. Nabulsi MM, Tamim H, Sabbaqh M, Obeid MY, Yunis KA, Bitar FF. Parental consanguinity and congenital heart malformations in a developing country. Am J Med Genet A. 2003;116A(4):342-7.
10. Ramegowda S, Ramachandra NB. Parental consanguinity increases congenital heart diseases in South India. Ann Hum Biol. 2006;33:519-28.
11. Yunis K, Mumtaz G, Bitar F, Chamseddine F, Kassar M, Rashkidi J, et al. Consanguineous marriage and congenital heart defects: a case-control study in the neonatal period. Am J Med Genet A. 2006;140:1524-30.
12. Chéhab G. Congenital heart disease, maternal age and parental consanguinity in children with Down's syndrome. J Med Liban. 2007;55(3):133-7.
13. El Mouzan MI, Al Salloum AA, Al Herbish AS, Qurachi MM, Al Omar AA. Consanguinity and major genetic disorders in Saudi children: a community-based cross-sectional study. Ann Saudi Med. 2008; 28:169-73.

Cite this article as: Dev D, Sharma R, Sharma M, Agrawal K, Garg M. Evaluation of consanguinity as a risk factor for congenital heart diseases. Int J Contemp Pediatr 2016;3:868-71.