DOI: 10.14260/jemds/2015/642

ORIGINAL ARTICLE

AN ASSESSMENT OF RISK FACTORS FOR CONGENITAL HEART DISEASES IN CHILDREN OF AGE GROUP 0-10 YEARS: A CASE CONTROL STUDY

Ankit Kumar[1], Rakesh Gupta[2], Prabhat Kumar[3], Mukti Sharma[4]

HOW TO CITE THIS ARTICLE:
Ankit Kumar, Rakesh Gupta, Prabhat Kumar, Mukti Sharma. "An Assessment of Risk Factors for Congenital Heart Diseases in Children of Age Group 0-10 Years: A Case Control Study". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 26, March 30; Page: 4442-4447, DOI: 10.14260/jemds/2015/642

ABSTRACT: BACKGROUND & OBJECTIVES: Congenital heart diseases (CHDs) affect approx 6–8 infants per1000 live births have multifactorial origin. Various studies attribute number of maternal (e.g. family history of congenital heart diseases, consanguinity, febrile illness, co-morbidities like diabetes or hypertension) and fetal factors (prematurity, LBW, chromosomal abnormality) for development of CHDs. There is paucity of data in India; hence this study was conducted to evaluate risk factors in causation of CHDs in children. **METHOD:** It was a case control study conducted from Mar to Aug 2012 among children up to 10 years of age attending tertiary care hospital in Maharashtra, India. A total of 75 cases of CHDs and equal number of matched controls were included in the study. **RESULTS:** The mean age of cases was 19 months and that of controls 18 months. Male to female ratio was 1.5:1 among cases and 1.7:1 among controls. VSD was the commonest cardiac anomaly found in 37(49.33%) cases. In neonatal characteristics, cases had significantly increased number of prematurity and low birth weight as, compared to control(p=0.006), OR-3.25(95% CI 1.35-8.25) and(p<0.001), OR-3.86 (95% CI 1.85- 8.11) respectively. Twenty six (35%) children among cases were born of consanguineous marriage while 8(11%) in controls and association was found statistically significant [p<0.01, OR-4.44 (95% C.I=1.75-12.24)]. Similar associations were seen with family history of congenital heart diseases [OR 4.10(95% C.I=1.34-14.97), co-morbidities [p=0.02, OR- 2.7 (95% CI 1.1-6.93)]. **CONCLUSION:** Our study showed maternal factors like consanguinity, family history of congenital heart diseases, co-morbidities like gestational diabetes, hypertension and drug intake during pregnancy were significant underlying risk factors for development of CHDs in children.

KEYWORDS: Congenital heart disease (CHDs), consanguinity, preterm, low birth weight, chromosomal abnormality.

INTRODUCTION: Congenital heart diseases (CHDs) are the most common birth defects accounting for 30% of all congenital abnormalities affecting 6-8 newborns per thousand live births.[1,2] The prevalence of CHDs ranges from 1 to 50. 89/1000 population in the world including India and the aetiology of majority of CHDs still remains unexplained.[3] A number of studies have shown that CHDs follow multifactorial pattern of inheritance with certain maternal and foetal factors, like parental consanguinity, maternal co-morbidities like diabetes, family history of congenital heart diseases, prematurity and low birth weight.[4-11] However a descriptive study carried out in Pakistan contradicts this theory.[5] Hence this study was undertaken to evaluate the role of various maternal, fetal and environmental risk factors in the development of congenital heart diseases.

METHODS: The present study was a case control study carried out in children up to 10 years of age, having CHD, attending tertiary care hospital in Maharashtra, India, over the period of 5 months from

March to Aug. 2012. Based on the common risk factors like consanguinity and family history of CHDs and review of literature on the similar studies,[3-6] sample size of 75 cases was calculated by assuming an alpha error of 10% with a power of 80% and an anticipated odds ratio of 3 and percentage of exposure approx 20%, among controls. Hence a study population of 75 cases and equal number of matched controls were enrolled in the study. Children having CHD and their parents willing to participate in the study were taken as cases. An equal number of matched patients from pediatric OPD and not suffering from CHDs were taken as controls. Patients above 10 years and having other co-morbidities were excluded from the study.

Diagnosis of cases was established by taking detailed history from parents, clinical examination and confirmed by Echo-cardiography (Echo) by a pediatric cardiologist. The detailed information regarding family history of CHDs, consanguinity, co-morbidities, febrile illness during first trimester, and drug intake during pregnancy and neonatal characteristics like low birth weight and prematurity etc. were extracted from the case records. The data was compiled, tabulated and analysed using SPSS 14.0. For continuous variables Z-test and dichotomous variables, chi-square test was used.

RESULTS: A total of 150 patients (75 cases and 75 controls) were evaluated. The mean age of cases was 19 months and that of controls 18 months. Male to female ratio was 1.5:1 among cases and 1.7:1 among controls. In the neonatal characteristics, the rate of prematurity was higher in study group (33%) as compared to 13% in control and low birth weight prevalence was also higher in study group (60%), as compared to 28% in control and association between the two was statistically significant ($p=0.006$), OR-3.25 (95% CI 1.35 to 8.25) and ($p<0.001$), OR-3.86 (95% CI 1.85 to 8.11) respectively.

Recurrent respiratory tract infections was the commonest presentation in children with CHDs seen in 39 patients (52%), followed by cyanosis (13%) and chest pain (8%). Ventricular septal defect (VSD) was the commonest CHD, constituted 39(52 %) of all cases, followed by cyanotic heart diseases in 21(28%), atrial septal defect (ASD) in 16(21%) and patent ductus arteriosus (PDA) in 12 (16%) cases. 7 children had more than one lesion. Four cases (5%) had associated Down's syndrome and one each with Williams syndrome and congenital oesophageal atresia.

Risk Factors: Mean maternal age was 23.10 years in cases, while 23.25 years among controls. The gestational age of mothers of cases was 37.9 months, lower than that of controls (38.2months). The difference in two groups was not statistically significant.

Twenty six (35%) children with CHDs were born out of consanguineous marriages as compared to 8(10.6%) among controls and association between the two was statistically significant ($p=0.01$), OR- 4.44 (95% CI 1.75 to 12.24). The family history of congenital heart diseases was found more in cases 17 (22.67%), as compared to 5(6.67%) among control group. The prevalence of co-morbidities like hypertension, diabetes, among mothers of cases was observed in 22(29%) while only 10(13%) mothers of controls and association between the two, was found to be statistically significant ($p=0.02$), OR-2.7 (95% CI 1.1 to 6.93).

Among these 22 mothers with co-morbidities, 12 were suffering from hypertension, gestational diabetes in 5, hypothyroidism in 3 and two had seizures on antiepileptic drugs. It was observed during the study, that drug intake during index pregnancy, like antiepileptic, antihyper-

DOI: 10.14260/jemds/2015/642

tensive and over the counter drugs (for fever, joint pain, vomiting) increases the risk of development of CHDs (p=0.001), OR-4.13 (95% CI 1.68 to 10.82). The risk factors for CHDs are shown in table 1 & 2.

SL. No.	Risk Factor	Cases (N=75) (%)	Control (N=75) (%)	p value	OR(ODDS Ratio)	95% CI
1	Consanguineous marriage - Yes - No	 26 (35) 49 (65)	 8 (11) 67 (89)	0.01	4.44	1.75 - 12.24
2	Birth order (1^{st} born)	38 (51)	25 (33)	0.047	2.05	1.01- 4.20
3	Family history of congenital heart diseases - Yes - No	 17 (23) 58 (77)	 5 (7) 70 (93)	0.010	4.10	1.34 - 14.97
4	Febrile illness during pregnancy - Yes - No	 27 (36) 48 (64)	 11 (15) 64 (85)	0.05	3.27	1.39 - 8.01
5	Co-morbidities (Hypertension, diabetes) - Yes - No	 22 (30) 53 (70)	 10 (13) 65 (87)	0.027	2.7	1.1 - 6.93
6	Use of medication during pregnancy - Yes - No	 27 (36) 48 (64)	 9 (12) 66 (88)	< 0.001	4.13	1.68 - 10.82

Table 1: Risk factors of congenital heart diseases in study population

Sl. No.	Risk Factors	Present study (%)	Faheem ul haq et al (%)[6]	Settin A et al (%)[10]
1.	Consanguineous marriage	35	49	-
2.	Family h/o congenital heart diseases	23	14	13
3.	Maternal co morbidities	22	14	6
4.	Extra cardiac manifestation	8	-	6

Table 2: Comparison of risk factors of congenital heart diseases in various studies

DISCUSSION: Congenital heart diseases (CHDs) are the most common of all birth defects and leading cause of morbidity and mortality in the first year of life.(1) The development of the heart involves a

series of collective molecular and morphogenetic events and any deviation from the normal course may result in abnormal structural malformations. About 80% of CHDs are multifactorial and arises through various combinations of genetic and environmental contributors [4]. About 20% of cases can be attributed to chromosomal anomalies, Mendelian syndromes, non-syndromal single gene disorders or teratogens. Down's syndrome and velocardiofacial syndrome are the most commonly seen syndromes in patients with CHD. To date, more than 30 genes have been linked to non-syndromal forms of CHD.[7, 11]

In our study VSD was the most common cardiac anomaly seen in 39(52%) cases, followed by Cyanotic heart diseases, ASD and PDA and results were comparable to previous studies.[4, 6, 9] In the neonatal characteristics, low birth weight was found in 45(60%) cases in our study, which was higher as compared to 23% cases in a study by faheem Ul Haq.[6]

Of the various risk factors observed in our study, 26(35%) children were born of consanguineous marriage, while in a similar study done by Faheem Ul Haq et al found it in 49% cases[6] and Smitha et al 40.28%.[3] There were 4(5.33%) cases of Down's syndrome in our study, similar to observations shown by Settin A in 5.7%.[10] A study done by Meberg et. al. has shown extra cardiac manifestations of CHDs (due to chromosomal abnormality) in up to 20% cases.[12] In our study, 17(23%) cases had family history of congenital heart diseases which was more than the study done by Ahmed Settin et al in (13%)[10] and Faheem UlHaq et al in (14%) children.[6] Our study shows that drug intake during index pregnancy increases the risk of development of CHDs, and comparable to similar studies.[6, 10] Twenty two (29%) mothers of cases had co-morbidities (like diabetes, hypertension, hypothyroidism and seizures), which were higher than studies done by Faheem Ul Haq et al in 14%.[6] and Ahmad settin et al in 5.9%.[10] Study by Mayer et al has shown that diabetes was an independent risk factor for development of congenital heart diseases [13] and a study by Taksande AM et al has shown that diabetes was present in 6.6 % of in mothers of children with CHD as compared to 1.1% in control.[14] The high prevalence of prenatal risk factors for CHD highlights the need for more rigorous screening of genetic and environmental factors including gene-environment interactions for prevention of CHD.[15, 16]

Thus we conclude that consanguinity, positive family history of congenital heart diseases, maternal factors like gestational diabetes, hypertension and drugs intake during pregnancy were significantly associated with development of congenital heart diseases in children. The society should be made aware about adverse effects of these risk factors of CHDs in children and recommend screening by fetal ultrasound / fetal echocardiography should be made part of routine antenatal checkup for high risk pregnancy.

ACKNOWLEDGEMENTS: AK & RG conceived the study and involved in data collection. PK & MS helped in work up of cases and interpretation of data. RG helped in analysis, and drafting the article. PK & MS supervised the study and revised the manuscript.

REFERENCES:

1. Smitha R**,** Nallur B R**.** An understanding the genetic basis of congenital heart disease. Indian Journal of Human Genetics, Vol. 11, No. 1, Jan-Jun, 2005, pp. 14-23.
2. Hoffman JIE, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002; 39:1890–1900.

3. Smitha R, Karat SC, Narayanappa D, Krishnamurthy B et al. Prevalence of congenital heart diseases in Mysore. Indian J Hum genet. 2006; 12: 11-6.
4. Nabulsi MM, Tamim H, Sabbagh M, et al. Parental consanguinity and congenital heart malformations in developing country. Am J Med Genet A. 2003; 116: 342-7.
5. Hassan I, Haleem AA, Bhutta ZA. Profile and risk factors for congenital heart disease. J Pak Med Assoc. 1997 Mar; 47(3):78-81.
6. Faheem UH, Jalil F, Hashmi S, et al. Risk factors predisposing to congenital heart defects. Ann Pediatr Cardiol. 2011; Vol-4:117-21.
7. Blue GM, Kirk EP, Sholler GF, Harvey RP, Winlaw DS. Congenital heart disease: current knowledge about causes and inheritance. Med J Aust. 2012 Aug 6; 197(3):155-9.
8. 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.
9. Ramegowda S, Ramachandra NB. Parental consanguinity increases congenital heart diseases in South India. Ann Hum Biol. 2006; Sep-Dec; 33(5/6):519-28.
10. Settin A, Almarsafawy H, Alhussieny A, Dowaidar M. Dysmorphic features, consanguinity and cytogenetic pattern of Congenital Heart Diseases: a pilot study from Mansoura Locality, Egypt. Int J Health Sci (Qassim). 2008; (2):101-11.
11. Al-Jarallah AS. Down's syndrome and the pattern of congenital heart disease in a community with high parental consanguinity. Med Sci Monit. 2009; 15(8):CR409-12.
12. Meberg A, Otterstad JE, Froland G, Lindberg H, Sorland SJ. Outcome of congenital heart defects-a population based study. Acta Paediatr. 2000; 89:1344-51.
13. Meyer-Wittkopf M, Simpson JM, Sharland GK. Incidence of congenital heart defects in fetuses of diabetic mothers: a retrospective study of 326 cases. Ultrasound Obstet Gynecol. 1996; 8(1):8-10.
14. Taksande AM, Vilhekar K. Study of Risk Factor for Congenital Heart Diseases in Children at Rural Hospital of Central India. J Nepal Paediatr Soc 2013; 33(2):121-124.
15. Fung A, Manlhiot C, Naik S, et al. Impact of prenatal risk factors on congenital heart disease in the current era. J Am Heart Assoc. 2013 May 31; 2 (3):e000064.
16. Tandon A, Sengupta S, Shukla V. Risk Factors for Congenital Heart Disease (CHD) in Vellore, India. Curr. Res. J. Biol. Sci., 2010.2(4): 253-258.

DOI: 10.14260/jemds/2015/642

ORIGINAL ARTICLE

AUTHORS:

1. Ankit Kumar
2. Rakesh Gupta
3. Prabhat Kumar
4. Mukti Sharma

PARTICULARS OF CONTRIBUTORS:

1. Medical Officer, MH, Chennai.
2. Professor and HOD, Department of Pediatrics, Command Hospital (CC) Lucknow.
3. Consultant Paediatrics, Department Pediatrics Cardiology, MH (CTC) Pune.
4. Consultant Paediatrics, Department of Pediatrics Cardiology, Command Hospital (WC). Chandimandir.

FINANCIAL OR OTHER COMPETING INTERESTS: None

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rakesh Gupta,
Professor and HOD,
Department of Pediatrics,
Command Hospital (CC),
Lucknow-226002.
E-mail: colrgupta@gmail.com

Date of Submission: 03/03/2015.
Date of Peer Review: 04/03/2015.
Date of Acceptance: 18/03/2015.
Date of Publishing: 27/03/2015.