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Risk factors of Congenital Heart Disease: A study in a Tertiary care Hospital

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ABSTRACT

INTRODUCTION

The most common congenital condition contributing to infant mortality is congenital heart disease with 1.5 million new cases worldwide. The lack of studies in this field in our part of the world, and the lack of knowledge about the true determinants of CHD in the pediatric population in our setup has prompted us to take such an initiative.

METHODOLOGY

We devised a case control study among pediatric patients who attend the ECHO examination. 125 cases and 200 controls were selected and were interviewed using a structured questionnaire. Data was analyzed statistically using Chi square test for significance. The strength of association was measured using Odd's ratio and its 95% confidence limits. Binary Logistic Regression analysis was done following a forward step wise method to eliminate confounders.

RESULT

Further analysis using binary logistic regression showed the significant risk factors for congenital heart disease to be:Low Birth Weight (<2.5kg at birth) babies; Corrected Odd's – 3.38; p value< 0.001,Gestational Diabetes; Odd's – 3.41; p value <0.001,Gestational Phenytoin Intake – Odd's 10.9; p value < 0.05. These 3 factors contributed to 15.3% of total risk factors according to Cox & Snell R Square value.

CONCLUSION

In our setting the major risk factors of congenital heart disease were LBW, GDM & Gestational Phenytoin consumption.

KEYWORDS : Congenital heart defects, Risk factors, Children

Introduction

Congenital Heart diseases (CHD) are defined as the structural, functional or positional abnormality of the heart, in isolation or in combination present from birth, but may manifest any time after birth or may not manifest at all[1]. Some of these may be discovered later. These are primarily seen in neonates, infants and children, although, in our country, it is not uncommon to see adults with uncorrected CHD. The burden of congenital heart diseases in India is likely to be enormous, due to a very high birth rate. This heavy burden emphasizes the importance of this group of heart diseases and understanding the etiology behind it.

In spite of this, steps need to be taken to reduce this IMR to even lower values. When the IMR is high the major cause of it is infectious diseases and other communicable diseases, which are relatively easy to control. When the IMR is low, the cause of infant death in more due to non communicable diseases and congenital anomalies, the incidence of which is difficult to bring down and constitutes the main challenge that faces us today when we try to control IMR. The most common congenital condition contributing to infant mortality is congenital heart disease[2].

The incidence of congenital heart disease in full term live born infants is between 6 and 8 per 1000 and each year there are about 1.5 million new cases worldwide[3]. Even though a lot of the risk factors associated with CHD are preventable, not much initiative are taken in this context. The lack of studies in this field in our part of the world, and the lack of knowledge about the true determinants of CHD in the pediatric population in our setup has prompted us to study the risk factors of the same.

Approximately about six to eight infants per 1000 live births have cardiovascular malformations[4]. Various studies have shown the etiology of congenital heart disease (CHD) and its pattern of inheritance to be of multifactorial origin[5]. A review of the literature showed that consanguinity, [5-7] and a variety of maternal ailments e.g., infections, maternal smoking, and gestational diabetes mellitus play a major role in the development of CHD. In addition, there are several fetal factors such as prematurity, low birth weight and stillbirth which are found to be associated with CHD[8].

Methodology

A case control study was carried out in a tertiary care hospital from April 2013 to April 2014

Study population – Children in the pediatric age group undergoing echocardiographic evaluation during the study period.

CASE Definition – All Children less than 12 yrs diagnosed with Congenital Heart Disease (CHD) by echocardiogram during the study period.

CONTROL– All Children less than 12 yrs without CHD as confirmed by echocardiogram during the study period.

Exclusion Criteria - Children who were terminally ill or whose parents were non co-operative / unwilling.

Sample size – Case – 125

Control – 200

Study variables– Gender, Birth Weight of Subject, Socio Demographic characteristics of parents, Drug intake during pregnancy, Diseases during Pregnancy, Previous History of Abortions and Family History of Congenital Diseases.

Study tool – Interviewer administered structured questionnaire.

Method of analysis - Data was analyzed statistically using Chi square test for significance. The strength of association was measured using Odd's ratio and its 95% confidence limits. Binary Logistic Regression analysis was done following a forward step wise method to eliminate confounders.

Ethical consideration – Informed consent were obtained from all participants. All information provided by them was kept confidential and used only for research purposes

Results and discussion

Among the cases in our study population 84% of cases were diagnosed at an **age** less than 5yrs and only 16% were diagnosed at an age greater than 5 yrs.

The **Gender** distribution of cases showed a slight female preponderance with 51.2% of cases being females and only 48.8% of cases being males but this gender difference does not have a significant association with CHD with 95% confidence interval ranging from 0.903 – 2.47.

On analyzing the **pattern** of various congenital heart diseases in our study population, ASD forms the greater proportion, followed by VSD. This might not tally with the accepted literature about the proportion of various congenital heart diseases in our community[9] or worldwide[10]. We believe this is due to the inclusion of all, whether clinically apparent or inapparent, self healing or non-self-healing, cases of congenital heart disease confirmed by echo cardiogram, in our study.

On analyzing, the factors which came up with a significant ODD's ratio were: -

Table 1: Univariate analysis

Factor	Odd's Ratio	Significance	95% CI for Odd's Lower	Upper
Family H/o Congenital Diseases	1.84	0.048	1.39	4.78
Maternal PKU	2.65	0.04	2.31	4.05
Maternal Gestational C/c Respiratory D/s	3.02	0.042	1.99	9.25
GDM	3.41	<0.001	1.67	6.96
Gest. Phenytoin	10.9	0.031	2.21	74.32
Birth weight < 2.5kg	3.38	<0.001	1.96	5.78

On performing the binary logistic regression following a forward step wise method to eliminate confounders, the following factors were obtained as significant risk factors:

Table 2: Binary logistic regression

	Corrected Odd's	Significance	95% CI for Exp (B) Lower	Upper
GDM	3.41	<0.001	1.67	6.96
Birth weight < 2.5kg	3.38	<0.001	1.96	5.78
Gest. Phenytoin	10.9	0.031	2.21	74.32

Low Birth Weight or LBW in babies ie weight <2.5kg at birth is not a disease by itself but just a manifestation of many diseases. Thus *an association with congenital heart disease* is the correct terminology which might be used to denote the relationship between LBW and Congenital Heart Disease. In this association a cause effect relationship cannot be determined from our study i.e. whether CHD causes LBW or vice versa cannot be determined. There is a moderate association of congenital heart disease with **low birth weight** according to studies conducted by the American Heart association[11]. The increased prevalence of low birth weight infants in our community makes it an important and significant association in our setup.

Phenytoin has well known and documented teratogenic effects the manifestations of which in the infant are summarized as Fetal Hydantoin Syndrome. This includes anomalies like hypoplastic phalanges, cleft palate, hare lip, microcephaly and congenital heart disease, all of these probably caused by its arenoxide metabolite[12]. With well knownteratogenic effects the chances of it being intentionally prescribed as an anti epileptic in pregnancy, in a state like Kerala, is low. Thus the probable cause of appearance of cases with gestational Phenytoin intake is the periconceptional intake of Phenytoin and its continued administration by the mother, without the knowledge that she is pregnant, at least for some period of gestation.

Gestational Diabetes Mellitus was found to be an important risk factor for developing congenital heart disease. The finding correlated with studies done in developed countries[13] where GDM was an established risk factor but studies done in under developed countries[14]showed no association of CHD with GDM. This is probably due to the less no. of cases of GDM in under developed countries than in developed countries and also signifies the increasing case load of GDM in our setup.

On further evaluation, the severity of GDM, as graded by women on insulin for GDM control, against those on diet controlled GDM was found to have a say in the occurrence of Congenital Heart Disease in the infant.

We can see that the corrected ODD's ratio for GDM on Insulin (4.33) is higher than that of Total GDM (3.41) and GDM on Diet control (0.53). Obviously it does not mean that the time tested insulin is a risk factor for CHD. What it probably conveys is that, the severity of GDM and uncontrolled GDM requiring insulin has more of a say in the occurrence of CHD. However, since the no. of cases in our study with GDM on diet control is very small, the ***power***of such a statement from our study will be low and hence we cannot commit to such a statement from the results of our study. Thus further studies need to be done in depth with the association of severity of GDM and uncontrolled GDM, with the occurrence of congenital heart disease.

Family History of Congenital Heart Disease is a risk factor in some studies undertaken on this subject[7] while it is insignificant in others[15]. There is no significant Correlation of Family History of CHD in our study and this may be due to the large no. of undiagnosed and asymptomatic congenital heart diseases among the family members of the affected.

No Correlation was found between Congenital Heart Disease and **consanguinity of marriage** between parents of the cases. This finding co related with findings of other studies conducted in similar setup.[15]

No cases were elicited of **Maternal Rubella, or Diagnosed Fetal Syndromes or Chromosomal Abnormalities** among the cases in the study population. These are established risk factors for Congenital Heart Disease[16] and the absence of cases with these risk factors are probably due to the low incidence of maternal rubella in our study population, late and inadequate diagnosis of Chromosomal Abnormalities and named Syndromes in our setup and also due to the short time period of our study

Conclusion:

Thus from our study the prevalent and significant risk factors/ Associations of CHD in our setup are

Gestational Phenytoin Intake

Low Birth Weight among babies

Gestational Diabetes Mellitus

The best strategy for **prevention of Phenytoin** exposure to fetus is a periconceptional shift to safer anti epileptic drugs before getting pregnant and while planning pregnancy. The so called *Safe* Anti epileptics during pregnancy are the new generation anti epileptics like Gabapentine, Lamotrigine or old age anti epileptics in low dose like Carbamazepine. Caution should be maintained by the practitioners on the need to substitute Phenytoin to a safer anti epileptic, if patient plans to get pregnant during the course of the drug regime. Phenytoin exposure, if suspected, should be checked for fetal malformations as early as possible by ultrasound and termination considered if period of gestation is below 20 weeks.

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