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Anatomy

NON GENETIC RISK FACTORS AND Nkx2.5 GENE CORRELATION OF CONGENITAL HEART DISEASES IN KANPUR AND PERIPHERY

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ABSTRACT **Introduction:** Congenital Heart Diseases (CHD) are structural anomalies of the heart arising from abnormal development of the heart and major blood vessels. These structural defects are anatomically classified into abnormalities of the septa, the heart valves, and inflow or outflow tract of the heart. These structural defects most often have functional consequences, but of varying degree and significance.

Aim: The aim of study to find out Non Genetic Risk factors and Nkx2.5 Gene correlation of Congenital Heart Diseases (CHD).

Materials And Methods: Total 200 cases of CHD were taken from Rama Hospital, Rama University, and peripheral region of Kanpur, U.P, during the period of 2019 to 2021.The Genetic study was carried out in Central Research Laboratory, Rama Medical College, Rama University, Kanpur, UP. Questionnaire form was prepared and noted the medical history of mother for Non Genetic risk factors.

Results: Total 200 cases of CHDs, VSD-80, ASD-62, TOF-22, PDA-21, PS-06, AS-06, COA-02 and TA-01 are reported. Among all CHDs Nkx2.5 Gene is mostly associated to Atrial Septal Defects, Tetralogy of Fallot and Ventricular Septal Defects. Total 200 cases of CHD patient's mothers medical history was analyzed and noted history of abortions in 65 cases, pregestational diabetes in 60 cases, obesity in 50 cases, family history with CHD in 40 cases, maternal usage of drugs in 15 cases, advanced maternal age in 15 cases and smoking and drinking alcohol in 8 cases.

Conclusion: Both Genetic and Non -genetic risk factors are associated to CHDs. Nkx2.5 gene is the master regulator for process of cardio genesis. Nkx2.5 Gene is mostly associated to Atrial Septal Defects, Tetralogy of Fallot and Ventricular Septal Defects. Community education programs are organized to encourage fertility at certain age, building a healthy life habits, maternal counseling for periconceptional control of blood glucose, adequate weight maintenance, and avoidance of stress is needed to prevent CHD.

KEYWORDS : Congenital Heart Diseases, Non Genetic Risk Factors, Nkx2.5 Gene

INTRODUCTION:

Congenital heart disease (CHD) is defined as a gross structural abnormality of the heart and great vessels that causes significant functional impairment. The estimated birth prevalence of CHD is 9/1000 live births with a significant geographical difference. In India, over 180,000 children are born with CHD every year with state wise variation and contribute to 10% of the present infant mortality. Nearly one thirds of the CHD are critical requiring intervention in the 1st year of life. Most of the CHD are thought to be multifactorial and result from a combination of genetic and environmental insult. According to recent update report of the American Heart Association, atrial septal defect (ASD), ventricular septal defect (VSD), tetralogy of fallot (TOF), patent ductus arteriosus (PDA), pulmonary stenosis, aortic stenosis, coarctation of aorta, and atrioventricular septal defect accounts for 85% of all CHDs.

The congenital heart defects can be life threatening during early childhood, and infants born with this disorder are at much higher risk (~12) of mortality especially in the 1st year of life. The genetic basis for many of these defects remains elusive, mutations in genes encoding core cardiac transcription factors have emerged as major contributors to many forms of congenital heart disease. Many of the genes associated with CHD, including NKX2-5, GATA4, TBX5, NOTCH1, and TBX20, were identified using early genetic techniques.

The non genetic risk factors like rubella during pregnancy, pregestational diabetes, Certain medications taken during pregnancy like(thalidomide, angiotensin-converting enzyme (ACE) inhibitors, statins, the acne medication isotretinoin and lithium),smoking, drinking alcohol during pregnancy, and heredity are commonly associated to CHD. Consequently, we aim to reducing the burden of disease and consolidate our knowledge on multifactorial causes of CHDs and pave a way for further research regarding CHDs.

MATERIALAND METHOD:

Total 200 cases of CHD were taken from Rama Hospital, Rama University, and peripheral region of Kanpur, U.P, during the period of 2019 to 2021.The Genetic study was carried out in Central Research Laboratry , Rama Medical College, Rama Univercity, Kanpur , U.P.

Data Collection

The common parameters like age, sex and stage of heart disease were recorded. All cases were thoroughly examined by chest x-ray, electrocardiogram, and 2D echocardiography. Family history of any heart abnormality, history of multiple abortions, nutrition and drug intake, any other patho-physiological conditions, and parity status of mother were recorded for analysis. Age of below 5 years is included in this study. The normal children of equivalent age group were taken as control.

Inclusion Criteria.

1. Below 5 years of age groups are included in this study.
2. Only Kanpur and peripheral region CHD cases are included in this study.

Exclusion Criteria

1. Age more than 5 years is excluded.
2. If there is no data on history of mother was excluded.

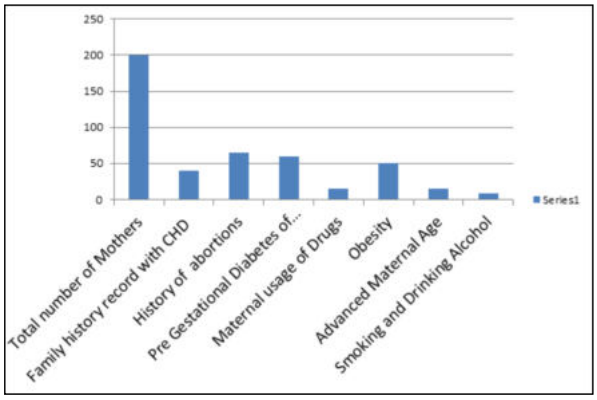
Questionnaire form was prepared and noted the medical history of mother. Parents are also investigated. The molecular analysis of Nkx2.5 Gene was done by using conventional PCR. The Institutional Ethical Committee of Rama Medical College and Hospital approved this study.

RESULTS:

Total 200 cases of CHD patient's mothers medical history was analyzed and noted history of abortions in 65 cases, pregestational diabetes in 60 cases, obesity in 50 cases, family history with CHD in 40 cases, maternal usage of drugs in 15 cases, advanced maternal age in 15 cases and smoking and drinking alcohol in 8 cases.

Total 200 cases of CHDs boys are 106 and girls are 94. The various types of defects are identified. The ventricular septal defect is noted in 80 cases, atrial septal defect in 62 cases, tetralogy of fallot in 22 cases, patent ductus arteriosus in 21cases, pulmonary stenosis in 06 cases, aortic stenosis in 06 cases, coarctation of aorta in 02 cases and tricuspid

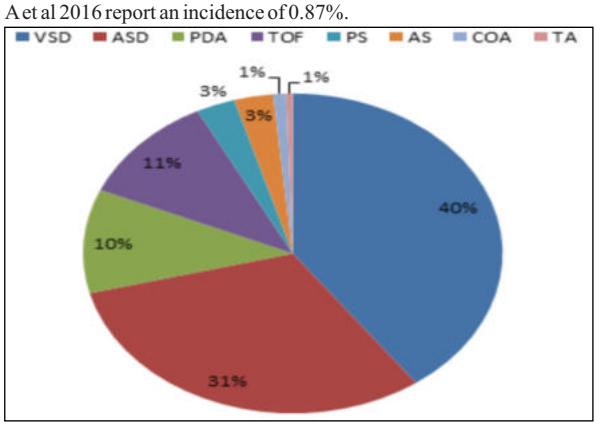
artesia in 01case. Among all CHDs Nkx2.5 Gene is mostly associated to Atrial Septal Defects, Tetralogy of Fallot and Ventricular Septal Defects.



Non Genetic Risk Factors Associated To CHD

DISCUSSION:

Developments in neonatal and pediatric cardiovascular surgery have improved the prognosis of CHD. Current challenges in the primary prevention of CHD are accurate identification of modifiable maternal risk factors. This study aimed to identify possible associations between risk factors and CHD in a Kanpur population. Analyzing the risk factors, we found a high association between diabetes and CHD. Vascular disruption and oxidative stress associated with increased blood sugar levels may lead to increased risk of CHD in diabetes mellitus. Next positive association was abortions, obesity, family history with CHD, increased maternal age, maternal usage of drugs and smoking and drinking alcohol. Ramkumar et al. 2018 states that maternal age, prepregnancy BMI, uncontrolled diabetes, caffeine intake, consanguineous marriages, stress and folic acid deficiency are reliable significant risk factors contributing to CHD in south Indian population. Similar studies done in North Indian population by Saxena A et al 2016 report an incidence of 0.87%.



Types of Congenital Heart Defects

In our study we reported VSD in 40%, ASD in 31%, TOF in 11%, PDA in 10%, PS in 03%, AS in 03%, COA and TA in 01%. Kapoor R and Gupta S 2008 noted CHD in Kanpur with a prevalence of 26.4 per 1000 patients. They reported VSD was the most common heart defect (21.3%), ASD (18.9%), PDA (14.6%), AVSD (10.3%) and TOF (4.6%).

Draus J M 2009 states that Nkx2.5 gene on chromosome 5q34 consists of two exons which encode a 324 amino acid protein. This homeobox transcription factor is expressed during early cardiac morphogenesis and serves as a master regulatory protein. Because of its critical role in cardiogenesis, Nkx2.5 has been a prime candidate in studies to identify the genetic basis of structural Congenital Heart Defects. In our study 200 cases of CHDs Nkx2.5 Gene is mostly associated to Atrial Septal Defects, Tetralogy of Fallot and Ventricular Septal Defects.

CONCLUSION:

Both Genetic and Non -genetic risk factors are associated to CHDs. Nkx2.5 gene is the master regulator for process of cardio genesis. Nkx2.5 Gene is mostly associated to Atrial Septal Defects, Tetralogy of Fallot and Ventricular Septal Defects. Community education programs are organized to encourage fertility at certain age, building a healthy life habits, maternal counseling for periconceptional control of blood glucose, adequate weight maintenance, and avoidance of stress is needed to prevent CHD.

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