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Comparison of Environmental and Parental Risk factors on Children with Congenital Heart Defects.

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Abstract: Heart defects are structural birth defects, which is the number one cause of infants morbidity and mortality in the world. The rationale of the study was to compare the demographic characteristics that were in distribution between those parental health conditions and environmental exposures of children with CHDs and controls that matched their age. A cross-sectional study has recruited 100 children aged ≤12 months in which 50 had congenital heart defects (CHDs) and another 50 children were controls. Parental age, maternal comorbidities (diabetes mellitus and hypertension), and environmental exposures (air pollution, chemical exposure, contaminated drinking water and smoking) were determined. Relative analysis was aimed at determining possible correlations between these factors and the occurrence of CHD. Results showed that **c**hildren with CHDs were more accompanied by the environmental exposures which included air pollution (22% vs. 18%), chemical exposure (24% vs. 20%), and drinking water contamination (27% vs. 20%). There was higher rate of smoking in the control group (42% vs. 27%). There was a relative similarity in the distributions of maternal comorbidities and parental age. It was concluded that the incidence of CHDs in this cohort may be more influenced by environmental factors than by maternal health conditions or parental age. These findings demonstrate the complex etiology of congenital cardiac defects and emphasize the significance of public health initiatives and environmental health interventions to lower avoidable exposures during crucial stages of cardiac development. To further clarify these associations, larger studies with thorough exposure assessment are necessary.

Keywords: Heart failure, congenital heart defects, Periconceptual

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Introduction

Congenital heart defects (CHDs) account for nearly one-third of all major congenital anomalies, and birth defects affect about 3–4% of live births globally [1]. CHDs are the most common type of congenital malformation, with an estimated prevalence of 6 to 9 per 1,000 live births [2]. CHDs continue to be a major cause of infant morbidity and mortality related to birth defects, despite significant advancements in prenatal diagnosis, medical management, and surgical

interventions [3]. The long-term health consequences of CHDs emphasize how crucial it is to comprehend their underlying causes and preventative measures [4].

Despite the fact that genetic and chromosomal diseases explain a percentage of CHDs, emerging evidence suggests that environmental, metabolic, infectious and behavioral determinants are influencing cardiac malpractices [5]. Notably, most of these risk factors can be altered, which offer good prevention possibilities by the use of population health measures and prenatal consultation services [6]. The development of cardiac morphogenesis is mainly during gestational weeks 2 to 7 which is a critical period when the developing fetal heart is extremely vulnerable to teratogenic factors [7]. As a result, the health state of parents and various environmental exposures during periconceptional period that is three months before conceiving up to the first trimester of pregnancy are especially pertinent to the risk of developing CHD [8].

The individual traits of parents and health-related issues are well-researched concerning the risk of CHD. Both high and early maternal age were found to be related to a higher risk of CHDs [9]. Maternal age has been identified as advanced (linking it with such defects as atrial septal defects, ventricular septal defects, coarctation of the aorta and transposition of the great arteries) and young maternal age with defects such as tricuspid atresia and total anomalous pulmonary venous return [10]. In the same manner, there is a correlation between advanced paternal age with a greater risk of septal defects possibly due to age related de novo genetic mutation or epigenetic changes in sperm. One of the most consistently identified and the strongest risk factors of CHDs is maternal pre-gestational diabetes mellitus [11]. Various studies have shown that there are two to five times higher chances of congenital heart defects in infants born of mothers with diabetes and mostly conotruncal defects, atrioventricular septal defects, hypoplastic left heart syndrome, and transposition of the great arteries [12]. It is believed that hyperglycemia in the early embryos development alters the migration of the neural crest cells and cardiac looping. Good glycemic levels during preconception have been established to have a substantial impact on the prevention of CHDs, and therefore, management of diabetes is considered as one of the prevention strategies [13].

Maternal hypertension that could be either chronic or pregnancy-induced has also been linked with the enhanced risk of CHDs [14]. Even though the exact mechanisms of the issue are not fully understood, the following factors may potentially contribute to it: placental insufficiency, vascular dysfunction, and the impact of antihypertensive medications taken at the earliest pregnancy stages [15]. The study needs to be further refined to isolate the effect of the underlying condition and the effect of pharmacological treatment. Although passive smoking exposure has also been indicated to be risky. Sperm DNA damage and epigenetic changes have been implicated in paternal smoking, and these changes could be of significance in abnormal cardiac development [16]. A large number of studies have linked alcohol intake in early pregnancy with the risk of septal defects and conotruncal defects, and illicit drugs, especially cocaine and marijuana especially paternal exposure with vascular disruption and epigenetic pathways. Another critical field of research in CHD is the environmental and occupational exposures. It has been shown that exposure to air contaminants like carbon monoxide, nitrogen dioxide, and particle matter increases the risk of CHD. Other environmental risks are organic solvents, pesticides, heavy metals, endocrine-disrupting toxins like phthalates, and polluted drinking water containing such chemicals as trichloroethylene. Parental occupational exposure especially that of fathers has increasingly been identified as a cause of CHD [17].

The etiologic heterogeneity of CHD is supported by evidence that phenotypes of the condition are linked to particular exposure profiles. Mothers more aged, who are obese or use selective serotonin reuptake inhibitors have been implicated in atrial septal defects, and maternal diabetes, smoking and infertility treatment in tetralogy of Fallout. An effective percentage of CHDs can be avoided using specific public health measures such as preconception diabetes and weight control,

smoking and alcohol quitting, regular folic acid supplementation, prevention and vaccination of infections, and environmental and occupational exposures reduction. Possible solutions to alleviating the global burden of congenital heart defects are to strengthen the policy of public health and conduct specific preconception and prenatal counseling [18].

Methods

Study Design and Setting

This cross-sectional study was carried out at Pakistan's Baqai Medical University as a comparative observational study. The objective was to assess the relationship between environmental, maternal, and parental risk factors and congenital heart defects (CHDs) in children between the ages of 0 and 12 months. All participants' parents or legal guardians provided written informed consent, and the study was approved by Baqai Medical University's Institutional Review Board (IREB).

Study Population

Fifty (50) children with structural CHDs (CHD group) and 50 age-matched children without CHDs (control group) made up the total of 100 children enrolled. Children with confirmed structural heart defects diagnosed either prenatally or postnatally were included in the CHD group, while children without any known cardiac abnormalities who visited the hospital for routine pediatric care or minor illnesses were included in the control group.

The Declaration of Helsinki's tenets were followed in this study. The Institutional Review Board of Baqai Medical University granted ethical approval, and prior to enrollment, all participants' parents or guardians gave their informed consent. To ensure confidentiality, all data was anonymized [19].

This approach made it possible to thoroughly evaluate environmental and parental risk factors during the crucial periconceptional phase [20]. The small sample size, reliance on self-reported exposure data, and lack of formal statistical testing are among the limitations that could limit causal inferences and introduce recall bias.

Inclusion and Exclusion Criteria

Inclusion criteria: Children of 0-12 months old, who are diagnosed with structural CHDs in the CHD group, and age controls who are not diagnosed with CHDs. Informed consent was obtained by parents.

Exclusion: Those children with chromosomal abnormalities, syndromic heart defects, metabolic disorders, or significant system illness. The cases that had not been fully exposed to parental or environmental effects were also filtered out.

Data Collection

Data were collected using a structured questionnaire administered to parents, which included:

1. **Demographic information:** Age, Sex & Birth history of child.
2. **Parental factors:** Maternal and paternal age, maternal comorbidities diabetes mellitus, hypertension and the use of medication during pregnancy.
3. **Exposure to the environment:** Preconceptual maternal and paternal smoking, chemical exposure, air pollution, and periconceptual maternal and paternal exposure of maternal and paternal drinking water three months before conception until the first trimester.

Additional clinical information on CHD type and diagnosis was obtained from medical records.

Exposure Assessment

Parents self-reported environmental exposures, which were compared to local environmental data where they had these data. Maternal comorbidities were confirmed by the use of antenatal

records and in-hospital reports. The periconceptional period was highlighted because it was important in the cardiac morphogenesis (gestational weeks 2–7).

Data Analysis

The demographic factors, parental health factors, and environmental exposures were summarized using descriptive statistics. Categorical variables were calculated using frequencies and percentages. The comparison between the CHD and the control groups was presented in tabular and graphical forms. The sample size was small and exposures were heterogeneous, so no statistical significance testing was done, but trends and relative distributions were presented.

Results

Fifty (50) children with congenital heart defects (CHD group) and 50 children without congenital heart defects (control group) made up the study's total of 100 participants. Males made up slightly more of the control group (60%) than the CHD group (50%), while females made up 40% of the control group and 50% of the CHD group. In terms of age distribution, 60% of controls and 64% of CHD cases in both groups were between the ages of 6 and 12 months. The age distribution of the two groups was similar, with 40% of the control group and 36% of the CHD group being infants between the ages of 0 and 6 months (Table 1).

Compared to controls, children with CHDs reported environmental risk factors more frequently. Compared to 18% of the control group, 22% of the CHD group reported being exposed to air pollution. 24% of CHD cases had chemical exposures, which is marginally higher than the 20% of controls. Among environmental factors, drinking water contamination was reported in 27% of the CHD group and 20% of the control group. On the other hand, the control group reported smoking exposure more frequently (42%) than the CHD group (27%) (Table 1).

The distribution of risk factors related to maternal and parental health was comparable between the two groups. While advanced paternal age was noted in 23% of the CHD group and 25% of the control group, advanced maternal age was reported in 20% of CHD cases and 22% of controls. 27% of CHD cases and 26% of controls had maternal diabetes mellitus. Parents of children with CHDs had a slightly higher prevalence of hypertension (30%) than controls (27%) (Table 1).

The distribution of parental risk factors, environmental exposures, and demographic traits between the CHD and control groups is shown in Figures 1, 2, and 3, respectively. Overall, children with congenital heart defects were more likely to be exposed to environmental factors, such as air pollution, chemical exposure, and contaminated drinking water, while the distributions of parental age and maternal comorbidities were comparable between the two groups.

Table 1: Comparison of Characteristics & Risk Factors

Characteristics	**Control (n=50)**	**CHD (n=50)**
Male %	60%	50%
Female%	40%	50%
Age		
0-6 Months	40%	36%
6-12 Months	60%	64%
Environmental Risk Factors		
Air Pollution	18%	22%
Chemical Exposures	20%	24%
Drinking water Contamination	20%	27%
Smoking	42%	27%
Others		
Advance Maternal Age	22%	20%
Advance Paternal Age	25%	23%

Diabetes Mellitus	26%	27%
Hypertension	27%	30%

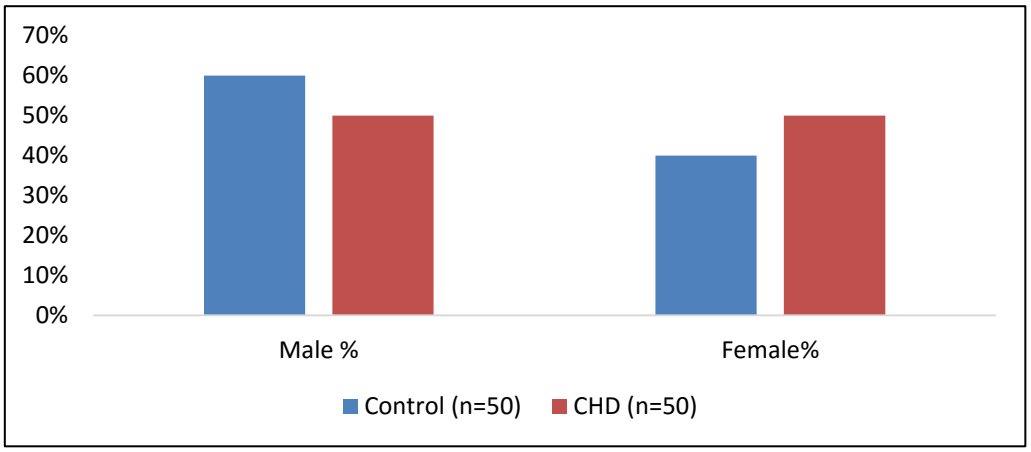

Figure: 1 Comparison of Gender.

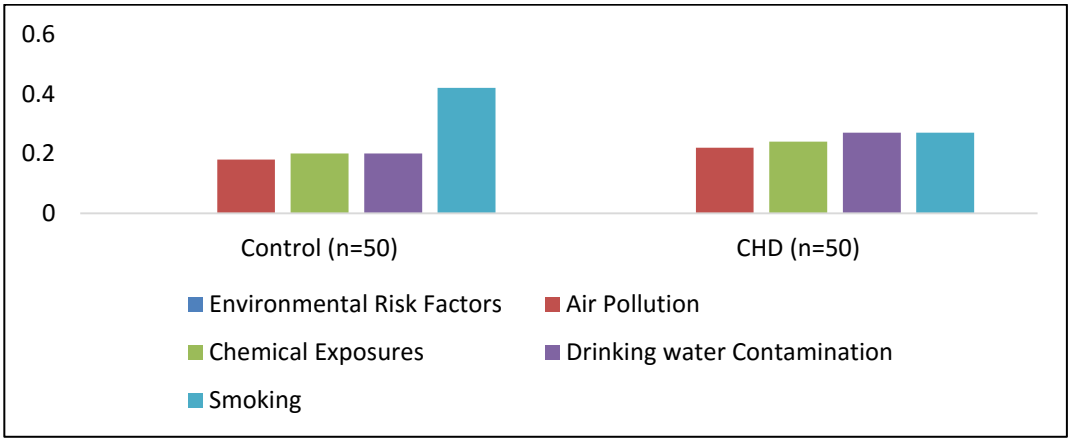

Figure 2: Comparison of Environmental Risk Factors

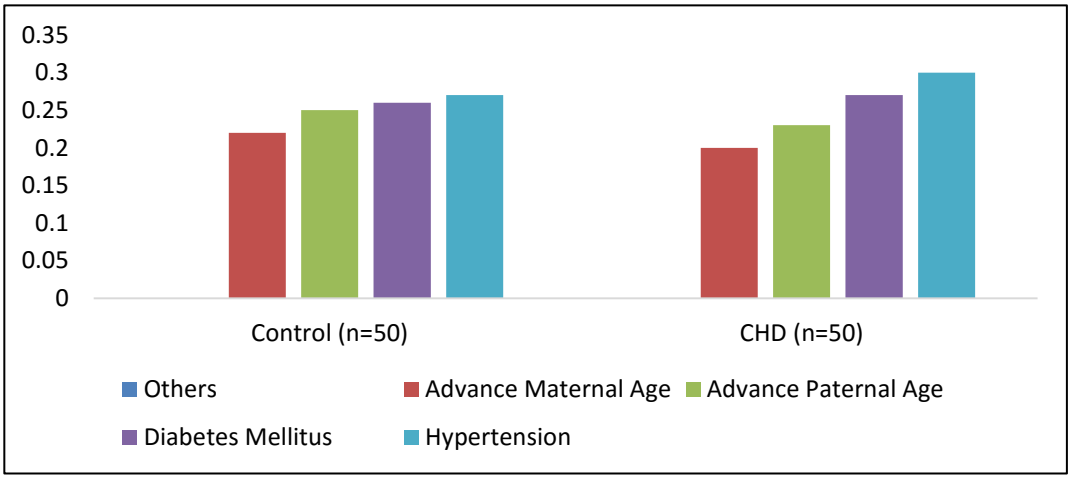

Figure 3: Comparison of Advance Age, Diabetes Mellitus & Hypertension Risk Factors

Discussion

The current study involved the comparison of demographic factors, environmental exposures, and

parental health-related risk factors between the children with the congenital heart defects and the controls of the same age [21]. The results help to understand that there may be some correlations between chosen environmental and parental variables and the prevalence of CHDs and also identify those areas where the risk distributions did not differ significantly between the groups. The sex distribution of the current study had a slight imbalance of males in the control group than the CHD group but females were equally distributed among the CHD cases [22]. Though it has been observed that male dominance has been observed in some forms of congenital heart defects, the comparatively equal sex distribution of this study shows that sex might not be a key determinant of CHD occurrence in this group of people. The age distribution was also comparable between groups, with the majority of participants in both the CHD and control groups falling within the 6–12 month age range, thereby minimizing age-related bias in exposure reporting [23].
The prevalence of environmental risk factors was higher among children with CHDs as compared to controls. Air pollution, chemical substances and drinking water contamination were all significantly greater in CHD group [24]. These data are consistent with emerging data that environmental pollutants can be associated with abnormal cardiac development due to the effects of oxidative stress, endocrine, and interference of embryonic signaling pathways. The largest difference between groups was found with drinking water contamination, which supports prior reports that industrial solvents and other contaminants exposures have the potential to elevate the risk of structural heart defects. Conversely, the control group was more exposed to smoking than children with CHDs [25]. This is contrary to the observation made by other epidemiological studies which reveal that maternal smoking is a risk factor in certain congenital heart defects. The given discrepancy can be explained by underreporting, variations in the exposure timing, passive and active smoking, or the rather limited size of the research [26]. It can also indicate fluctuation in smoking habits or the existence of other confounding variables in the study group which cannot be measured. The parental ages and maternal health cases were relatively the same in both groups. More mature and paternal age were a bit higher in the controls compared to CHD cases indicating that age factor of parents by itself may not be a very high risk factors in this cohort [27]. Equally, maternal diabetes mellitus and maternal hypertension prevalence were similar between groups though hypertension was slightly higher in CHD cases. Although diabetes and high blood pressure cases are already known as risk factors of congenital heart defects in bigger population-based studies, the absence of significant differences in the current study could be due to the effective disease management or a small sample size or the lack of stratification according to the severity of the disease and the level of glycemic or blood pressure management [28]. This research has highlighted the complexity of the etiology of congenital heart defects as well as its multifactorial character and indicated that environmental exposures can be more significant than parental demographic or medical factors in this group population [29]. Nevertheless, there is no statistically significant testing which restricts the possibility to make unambiguous conclusions in terms of causality. Also, dependence on reported exposures can lead to bias on recall especially on environmental and lifestyle related factors [30]. Notwithstanding these limitations, the research provides substantial preliminary evidence of the possible role played by environmental risk factors including air pollution, chemical exposure and drinking water and contamination in causing congenital heart defects [31]. These findings illustrate the need to do larger better designed studies with objective exposure measurement, finer exposure timing and genetic disposition in order to provide a better explanation of the complexity of the interactions in CHD etiology. The age of parents and maternal comorbidity were both evenly distributed between CHDs and controls but environmental exposures to CHDs appeared to be higher [32]. The data also contribute to the further recognition of the environmental influence on the formation of the congenital heart and contribute to the reestablishment of the worth of environmental health interventions and the policies in the sphere of public health aimed to reduce the influence of risk

factors that may be avoided at the crucial state of preconceptual development [33].

Conclusion

The current research paper outlines the possibility of related environmental exposures to the incidence of congenital heart defects in children. Although the demographic factors such as sex and age distribution were similar in children with CHDs and controls, some of the environmental risk factors such as air pollution, exposure to chemical substances, and drinking water were more common among children with congenital heart defects. Parental age and maternal medical history including diabetes mellitus and hypertension, on the contrary, did not vary in distribution between the two groups. These results highlight the multifactorial etiology of congenital heart defects and postulate that environmental influences can be added to the roles of parental and maternal characteristics. Even though the study was not able to show that there were strong differences in parental age or maternal comorbidities, the trends in environmental exposures observed support the value of targeting the modifiable environmental risks in the periconceptional period. Since the sample is small, and no statistical significance test was conducted, the results are to be taken with a grain of salt. However, the present study presents some initial signs of the necessity of raising awareness, environmental health interventions and conducting larger scale studies to better understand the intricate interactions between the environmental exposures and the development of the heart during conception. Empowering policies and preventive mechanisms of the population in combating harmful exposures can be useful in minimizing the number of affected populations with congenital heart defects.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approved by IREB of Baqai Medical University; Consent was achieved from each participants before inclusion in the study.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The study on humans was conducted in accordance with the ethical rules of the Helsinki Declaration and Good Clinical Practice.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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None

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