Risk Factors for Congenital Heart Disease Among Infants In Mosul City

Qusay Ahmed Attia\(^{(1)}\) \quad Riyadh Abdulatif Al-Obeidi\(^{(2)}\)

Abstract:

**Background:** Congenital Heart Disease (CHD) is a problem of the heart's structure with its function at birth and it is the most common congenital anomaly. Etiology of congenital heart diseases are often unknown. However, many cases of CHD may result from genetic factors, environmental stimuli as well as chromosomal abnormalities. Our study aimed to assess the degree of association of suggestive risk factors with the occurrence of congenital heart disease in infants at pediatric teaching hospitals in Mosul.

**Materials and Methods:** A case-control prospective study was carried out at pediatric teaching hospitals in Mosul city (Ibn Al Atheer and Al Khansaa Hospitals) on infants \(\leq 12\) month of age with congenital heart diseases, who attended the pediatric cardiology units during 3 months from November 2019 to February 2020. To collect the data, a questionnaire was performed through interviews with parents of enrolled infants \(n=557\) (cases \(n=272\), controls \(n=285\)).

**Results:** Residence of rural area, poverty, housewife mothers, parental low level of education, parental consanguinity, use of contraceptive measures, gestational diabetes, prematurity, low birth weight, twins and caesarean section have significant associations with the occurrence of CHD.

**Conclusions:** Significant association were found between prematurity, low birth weight, twins, caesarian section, positive family history for CHD, low parental education and poverty, and the development of CHD.

**Key words:** Congenital heart disease, risk factors, infants, parents.

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heart defect, it may ultimately correlated with the increase in morbidity and mortality rates in early life or long term complications in adolescents or even adulthood (Spector et al, 2018). Because of the adverse impact of CHD upon population level, a public health nearly is required to title the challenges of these common, critical and costly circumstances (Jenkins and Honein, 2018). To present an accurate picture the load of congenital heart disease, we classified CHD as a major or minor. The major defects when the total structural complexity was of functional indication, e.g. atrioventricular septal defect (AVSD), hypoplastic left heart syndrome (HLHS), coarctation of the aorta (CoA), large atrial septal defect (ASD) and large ventricular septal defect (VSD), and surgical repair or catheter intervention may be required (Pei et al, 2017). Prevention can be achieved through many ways like a reduction in the occurrence of congenital infections, modification of risk factors through lifestyle changes, (Garcia et al, 2018). Also preventing and promotion of cardiac health can be achieved by: first: to recognize the economic and social risk factors as well as educational health services, second: implementation of a screening program for the social factors associated with CHD (Kuo et al, 2016). Treatment may include: surgery, catheterization or medical conservative measures (lewis, 2018).

In our study, we aimed to evaluate the strength of associations of suggestive risk factors with the development of congenital heart diseases in infants of Mosul city.

**Materials and Methods:**

This case–control cohort study was conducted in Ibn Al-Atheer Pediatric Hospital and Al-Khansaa Teaching Hospitals, in Mosul, Iraq, from November 2019 to February 2020, and was approved by the local ethical medical research committee. Infants under the age of 12 months who visited the cardiology units and Echo units as well as those neonates

### 1.1. Introduction

Congenital heart disease (CHD) is a problem of the heart’s structure with its function at birth, affect the heart and or adjacent blood vessels, detected at birth or later in life (Chelo et al, 2016). It is considered as the most common congenital anomaly (Garcia et al, 2018) which can be resulted from fetal event that occurs during the first 8 weeks of gestation (Balat and Sahu, 2018) and it accounts for 28% of congenital anomalies in general (Quartermain et al, 2015). It is also considered as one of the most common causes of death during the first year of life compared with other birth defects. It is an important cause of morbidity and mortality in infancy (Wong et al, 2018). Mostly, the causes of congenital heart diseases are unknown. However, many cases of CHD may result from a contribution of genetic factor environmental stimuli as well as chromosomal abnormalities (Kliegman et al, 2016). The genetic and environmental factors may affect the growth during pregnancy, that influence the blood flow and oxygenation abnormalities (Steurer et al, 2018). Multiple risk factors may contribute to CHD; including the teratogenic effects of drugs during pregnancy such as the effect of warfarin (Kliegman et al, 2020), maternal infection such as Rubella, diabetes (Karen, 2019), and chromosomal abnormalities as well as familial predisposition (Kliegman et al, 2020). Other risk factors includes; low birth weight, maternal morbidity, family history of congenital heart defect, first born child, prolonged exposure to environmental pollution (Nicoll, 2018), and age related maternal factors (Schulkey et al, 2015). Lack of orientation about the risk factors, mostly modifiable environmental and behavioral factors add adverse effects on fetus cardiac development (Chou et al, 2016); such as maternal lifestyle factors including; drinking strong tea or coffee cigarette smoker, smokeless tobacco and alcohol consumption have also been associated with risk of CHD (Zhu et al, 2016). As the problem of congenital
12 months, were attending the hospital but without congenital heart diseases, were considered as controls. To measure the statistical significance for the possible risk factors associated with the CHD, Odd ratio(OR), was calculated in a case-control analysis using fourfold (2x2) tables. The test of significance of OR was provided by Chi-square test with one degree of freedom, and 95% Confidence Interval. P value is considered significant when <0.05. Statistical analysis was performed through the use of statistical package for social science (SPSS) version 23.

Results:

Table 1. Demographic Variables of the infants and the Parents of cases vs. controls:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Cases; n(272) (%)</th>
<th>Controls; n(285) (%)</th>
<th>Odds Ratio (OR)</th>
<th>95% CI</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (baby)</td>
<td>1mon. &lt;</td>
<td>128 (47.1%)</td>
<td>127 (44.6%)</td>
<td>1.105</td>
<td>0.792-1.543</td>
<td>0.554</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>142 (52%)</td>
<td>140 (49%)</td>
<td>1.131</td>
<td>0.811-1.577</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>231 (84.9%)</td>
<td>132 (46.3%)</td>
<td>6.530</td>
<td>4.352-9.797</td>
<td>0.000</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother’s age</td>
<td>23 – 28</td>
<td>123 (45.2%)</td>
<td>114 (40%)</td>
<td>1.238</td>
<td>0.884-1.733</td>
<td>0.213</td>
</tr>
<tr>
<td>Family income</td>
<td>150 – 300</td>
<td>164 (60%)</td>
<td>114 (40%)</td>
<td>2.277</td>
<td>1.622-3.198</td>
<td>0.000</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother occupation</td>
<td>Housewife</td>
<td>252 (93%)</td>
<td>191 (67%)</td>
<td>6.201</td>
<td>3.164-10.409</td>
<td>0.000</td>
</tr>
<tr>
<td>Mother education level</td>
<td>Primary</td>
<td>214 (79%)</td>
<td>190 (67%)</td>
<td>1.844</td>
<td>1.260-2.699</td>
<td>0.001</td>
</tr>
<tr>
<td>Father education level</td>
<td>Primary</td>
<td>183 (67.3%)</td>
<td>149 (52.3%)</td>
<td>1.876</td>
<td>1.330-2.646</td>
<td>0.000</td>
</tr>
<tr>
<td>The parents consanguinity</td>
<td></td>
<td>213 (78.3%)</td>
<td>123 (43.2%)</td>
<td>4.754</td>
<td>3.279-6.894</td>
<td>0.000</td>
</tr>
</tbody>
</table>

The table (1) shows that CHD is found more among families from low socioeconomic status, low educational levels, unemployed mothers, familial consanguinity, and rural residence.
Table 2. *Cases versus controls in the infants risk factors for CHD*:

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Cases; n(%)</th>
<th>Controls; n(%)</th>
<th>(OR)</th>
<th>95% CI</th>
<th>P .value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight Premature</td>
<td>91(33.5%)</td>
<td>47(16.5%)</td>
<td>2.545</td>
<td>1.703-3.804</td>
<td>0.000</td>
</tr>
<tr>
<td>Premature developmental abnormalities with CHD</td>
<td>186(68.4%)</td>
<td>29(10.2%)</td>
<td>19.092</td>
<td>12.036-30.282</td>
<td>0.000</td>
</tr>
<tr>
<td>Twins</td>
<td>22.1(8%)</td>
<td>3(1.1%)</td>
<td>8.272</td>
<td>2.446-27.969</td>
<td>0.000</td>
</tr>
<tr>
<td>Family history with CHD</td>
<td>39(14.3%)</td>
<td>16(5.6%)</td>
<td>2.814</td>
<td>1.532-5.167</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 2 reveals that prematurity, low birth weight, developmental abnormalities, twins, and familial predisposition for congenital heart diseases.

Table 3. *Cases versus controls in the parents risk factors for CHD*:

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Cases n (%)</th>
<th>Controls; f(%)</th>
<th>(OR)</th>
<th>95% CI</th>
<th>P .value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used the mother contraceptive</td>
<td>72(26.5%)</td>
<td>27(9.5%)</td>
<td>3.440</td>
<td>2.130-5.555</td>
<td>0.000</td>
</tr>
<tr>
<td>Smoker (mother)</td>
<td>6(2.2%)</td>
<td>2(0.7%)</td>
<td>3.191</td>
<td>0.638-15.952</td>
<td>0.157</td>
</tr>
<tr>
<td>Smoker (father)</td>
<td>124(45.6%)</td>
<td>130(45.6%)</td>
<td>0.999</td>
<td>0.715-1.394</td>
<td>0.995</td>
</tr>
<tr>
<td>First child</td>
<td>48(17%)</td>
<td>23(8%)</td>
<td>0.726</td>
<td>1.547-4.722</td>
<td>0.000</td>
</tr>
<tr>
<td>Mother cumbersome homework</td>
<td>152(55.9%)</td>
<td>125(43.9%)</td>
<td>1.621</td>
<td>1.160-2.260</td>
<td>0.004</td>
</tr>
<tr>
<td>previous miscarriages</td>
<td>45(16.5%)</td>
<td>21(7.4%)</td>
<td>2.492</td>
<td>1.441-4.308</td>
<td>0.001</td>
</tr>
<tr>
<td>Mother problems (Epilepsy, Migraine, Asthma, Anemia)</td>
<td>36(13.2%)</td>
<td>2(0.7%)</td>
<td>21.584</td>
<td>5.143-90.589</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetes Mellitus gestational</td>
<td>23(8.5%)</td>
<td>12(4.2%)</td>
<td>2.10</td>
<td>1.02-4.13</td>
<td>0.042</td>
</tr>
<tr>
<td>Hypertension of pregnancy use of drugs during pregnancy</td>
<td>16.1</td>
<td>46</td>
<td>0.89</td>
<td>0.56-1.41</td>
<td>0.639</td>
</tr>
<tr>
<td></td>
<td>198(72.8%)</td>
<td>48(16.8%)</td>
<td>8.773-19.893</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.211</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caesarean birth</td>
<td>70(25.7%)</td>
<td>26(9.1%)</td>
<td>3.452</td>
<td>2.122-5.614</td>
<td>0.000</td>
</tr>
</tbody>
</table>

The table 3. use of contraceptives, first baby, gestational diabetes, drug intake during pregnancy, caesarian section, and genetic diseases, having a significant association with CHD.
Discussion:

1. Demographic Variables of the infants cases vs. controls

1.1. Age:
In our study, we did not find any significant role for age of the baby in the development of CHD, while Mecklin et al., (2017) reported more cases among infants younger than 2 months.

1.2. Gender:
In this study, the gender was not found to be of significance. This result was consistent with the study conducted by Mecklin et al., (2017) who found that no significant association between cases and controls. In addition, Zhang et al., (2019) also showed the same outcome.

1.3. Residence:
The CHD appeared significantly more in infants from rural regions. This finding was in agreement with Liu and Yan, (2016) who stated that in the rural residence there was a significant difference between cases and controls. In addition, Yang et al., (2019) also noted a similar finding.

2. Demographic Variables of the Parents of cases vs. controls:

2.1. Mother age (years):
The study showed that there was no significant role for certain mother age. These result agreed with the study of Zhang et al., (2019) who indicated that the mothers age had no significant role. But Peng et al., (2019) in his study found that most of his CHD cases were from mothers of ages 25-29.

2.2. Family income:
In our study, we found a significant role for the family income with the occurrence of CHD. These result agreed with that of Liu and Yan, (2016).

2.3. Mother occupation:
We found a significant role for others housewives in the occurrence of CHD. This finding was in agreement with Liu and Yan, (2016).

2.4. Parents educational level:
The study appeared that the frequency of CHD increased in families of parents of primary school educational level with a significant association with the development of CHD. These result are consistent with other study that was conducted by Arjmandnia et al., (2018) and by (Liu and Yan, 2016).

2.5. The parents consanguinity:
The rate of infants with CHD was more among families of consanguineous parents than those from non-relative couples. This result was same with another study that was conducted by Shoukri et al., (2017).

3. Cases versus controls, in the infants risk factors for CHD:
3.1. Low infants weight at birth:
In this study, low infants weight (< 2500gm) shows a significant association with the development of CHD. This finding is in agreement with the study conducted by Zhang et al., (2019).

3.2. Premature baby:
The study noted a significant role for prematurity in the occurrence of CHD. This result was approximately in consistent with the study conducted by Mecklin et al., (2017). In addition, Zhang et al., (2019), showed the same outcome.

3.3. Developmental abnormality with CHD:
In the study, infants with Developmental abnormality showed CHD in 8.1% of cases compared with control group of 1.1%. This finding showed a significant association.

3.4. Twins:
Our study found that twin babies have a significant association with the development of CHD. Study of Yang et al., (2019), similarly, reported that twins may play a role in CHD.

3.5. Family history and CHD:
The study clarified that the family history of CHD may play a role in the increment of CHD incidence. Similarly, a study in Hunan province by Li et al., (2017) found that the family history with CHD showed a significant role.

4. Cases versus controls, in the parents risk factors for CHD:

4.1. Contraceptives:
We noticed that the frequency of CHD was increased among mothers who used contraception before the pregnancy of the affected gestation. Zaqout et al., (2017) noticed the same outcome with the use of contraceptives.

4.2. Parents smoking:
In our study, we did not find any significant role for parental smoking in the development of CHD. This finding is similar to that reported by Liu and Yan, (2016).

4.3. Previous miscarriages:
We found that the frequency of CHD increased among mothers known to have frequent previous abortions. The result is in contrast to the study done by Zhang et al., (2019) who found that the percentages of case and control groups of previous miscarriages were (28.1%, 25.2%), and they concluded no significant role.
4.4. Health problems during pregnancy:

The study showed that the mothers with health problems during pregnancy like gestational diabetes, Epilepsy, Migraine, Asthma, and Anemia may have a noted role in the increase of the frequency of CHD.

4.5. Mother with drugs:

The results appeared that the frequency of CHD increased among mothers who received drugs during pregnancy, these results have a significant association with the development of CHD. This finding is similar to that reported by other study that was conducted by Liu and Yan , (2016). In addition, Yang et al., (2019), showed the same outcome.

4.6. Birth methods:

The study has noted a significant role for the caesarean section in the occurrence of CHD. This result is consistent with the finding of Behzad et al., (2013) who reported that the caesarean delivery may have a significant association with CHD.

Conclusions and Recommendations:

Conclusions:

Most of the cases with CHD were seen among infants less than 1 months of age. Majority of these cases were from rural areas. Significant association between poverty, low parental education, consanguineous marriage and the development of CHD were noted. Also that prematurity, low birth weight babies, first born babies in the family, baby of twin, and positive family history, are likely risk factors. Related to parents of infant with CHD, use of contraceptives, maternal smoking, heavy mother home work, familial diseases, pensive abortions, gestational diabetes, anemia, use of drugs during pregnancy like; antiepileptic, anti-migraine, and delivery by caesarian section are probable risk for the occurrence of CHD.

Recommendations:

Based upon the findings and conclusions of the study, we encourage mother's good nutrition during pregnancy with light work, education of parents about anomalies and the risk factors that contributes to congenital heart disease, encourage education and schooling, avoid intake of drugs during pregnancy without the prescription order of doctor. Also avoidance as much as possible the marriage between the relatives, especially for these who have a history of congenital heart disease.

References:


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