

# Assessment the risk factors of congenital heart disease among children below 5 years age in Babylon province

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## Abstract

**Background:** Congenital heart diseases (CHDs) account for 25% of all congenital malformations. CHDs are an important cause of morbidity and mortality in children. Prevention of CHDs can be achieved by preventing exposure to modifiable risk factors that affect the cardiac development during pregnancy. **Objectives:** To assess the sociodemographic and medical risk factors of congenital heart diseases among children below five years in Babylon city, Iraq. **Materials and Methods:** A retrospective case control study conducted from 1<sup>st</sup> of February to 1<sup>st</sup> of May, 2022, at Shaheed Al-Mehrab center, Babylon Maternity/Pediatric Hospital and Al-Imam Al-Sadik General Teaching Hospital, consisted of 100 participants classified to 50 CHDs cases and 50 controls by Echocardiogram, the mother/caregiver of each child was interviewed using a pre-tested questionnaire. **Results:** The age of the participants ranged from one day to 4.5 years, with a mean age (10.4 ± 13.2) months. (52%) of CHDs cases were females, (68%) of them were below one year age and (54%) of them reside in urban area, 28% of CHDs was VSD and 42% of the cases present with chest infection. BMI percentile was significantly lower in cases of CHDs ( $P = 0.008$ ) and there was a significant relationship between CHDs and family history of CHDs ( $P = 0.013$ ). **Conclusion:** Majority of the cases were females, below one year age and reside in urban area, presented with VSD and chest infection. BMI percentile was lower in cases of CHDs and there was a significant relationship between CHDs and family history of CHDs.

**Keywords:** Children, congenital heart diseases, risk factors

## INTRODUCTION

Congenital heart diseases (CHDs) are the abnormalities of the heart's structure, function or position present from birth and affect the heart or the adjacent blood vessels that are detected in infancy or thereafter.<sup>[1]</sup> CHDs prevalence is approximately 8/1000 live births, but only 2–3 of them are going to show symptoms within the first year of life. The incidence is higher in stillbirth (3–4%), spontaneous abortions (10–25%), and premature infants (2%), excluding; MVP, PDA in preterm babies, and bicuspid aortic valve (normally presents in 1%–2% of adults).<sup>[2]</sup> Most CHDs still have unknown causes and many types of CHDs are complex and originate from a mix of genetic predisposition and environmental stimulation, CHDs present in >90% of individuals with trisomy 18, 50% of individuals with trisomy 21, and 40% of individuals with Turner syndrome.<sup>[3]</sup> It was hypothesized that environmental agents act on the individual's genetic

predisposition to the malformation, and the exposure must occur at the period of cardiac development, which is during the first 8 weeks of gestation.<sup>[4]</sup> Multiple risk factors are associated with CHDs, including; The teratogenic effects of drugs during pregnancy; for example; many of the anticonvulsant drugs alter the folate metabolism in early pregnancy that lead to neural tube defects and congenital heart diseases.<sup>[5]</sup> First trimester fever in general, especially if by viral infection carries an increased risk of offspring CHDs, mainly coarctation of aorta, tricuspid atresia, d-TGA, VSD,<sup>[6]</sup> especially maternal infection

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with Rubella (congenital rubella syndrome) that cause pulmonic stenosis, patent ductus arteriosus, and, less frequently, tetralogy of Fallot.<sup>[7]</sup> Parental consanguinity.<sup>[8]</sup> Family history of congenital heart defects,<sup>[9]</sup> especially if first-degree relative (parent or sibling) is affected.<sup>[3]</sup> Low birth weight.<sup>[9]</sup> Age related maternal factors.<sup>[10]</sup> Maternal Diabetes mellitus is associated with arterio-ventricular septal defects.<sup>[11]</sup> Environmental and behavioral factors, such as cigarette smoking have also been associated with risk of CHDs, especially septal defects.<sup>[12]</sup> Some studies show that periconceptional intake of folic acid may reduce the risk of CHDs in offspring, and folic acid consumption during pregnancy may result in a 50% reduction in the risk of CHDs, which similar to the risk reduction for neural tube defects.<sup>[13,14]</sup>

### Objective of the study

To assess the sociodemographic and medical risk factors of congenital heart diseases among children below five years in Babylon city, Iraq.

## MATERIALS AND METHODS

This is a retrospective case control study, carried out from the 1<sup>st</sup> of February to the 1<sup>st</sup> of May 2022, at Shaheed Al-Mehrab center for cardiac catheterization and surgery, Babylon Maternity and Pediatric Hospital and Al-Imam Al-Sadik General Teaching Hospital in Babylon city, Iraq. The mother or the caregiver of each child was interviewed using a pre-tested questionnaire, including socio-demographic information of the child and the mother, clinical presentation and the possible risk factors of CHDs, including: parental consanguinity, rubella and COVID-19 infections during pregnancy, maternal history of hypertension, diabetes and abortion, intake of folic acid, hormonal medications, aspirin and tetanus vaccine during pregnancy and family history of congenital heart diseases. BMI of the children was calculated by measuring the weight of each child (in kilograms) by beam balance or electronic scale and measuring the height/length of each child (in centimeters) using length board with full extension for any child below two years age and by fixed board on the wall in standing position for any child above two years age.

### The inclusion criteria

The mother or the caregiver of children below five years age, who attended or were admitted to the general wards, the intensive care unit, respiratory care unit and the emergency unit of the mentioned hospitals and who are living in Babylon governorate.

### The exclusion criteria

The mother or the caregiver who refused to participate in the study, whose children are above five years age, whose children with syndromes and who are living in other governorate.

### The limitations of the study

Short duration of the study, relative small sample size and this study is retrospective case control study so it is inefficient for rare exposures, the temporal relationship between the exposure and the disease may be difficult to established and it is prone to the selection and recall bias.

### Data analysis

The data were analyzed using the SPSS IBM, version 27. Data entered and managed using descriptive statistics (frequency distribution and percentage) and inferential statistic (the Chi-square test was used to test association between categorical variables, while t student test was used to compare the means of quantitative continuous variables). P-value of <0.05 considered statistically significant and Odd's ratio was calculated.

### Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 52 (including the number and the date in 11/4/2022) to get this approval. Verbal consent was obtained from the participants, after explaining to them the purpose of the study.

### Results

This study included (100) children under 5 years: (50) CHDs cases and (50) controls. [Table 1] is comparison between the cases and controls regarding socio-demographic characteristics showed that no significant differences were observed between them regarding age, gender, residence, maternal education and occupation (P-value >0.05). [Table 2]: Chest infection alone was the commonest presentation, accounting for (42.0%) of the cases, and the commonest type of congenital heart disease was VSD (28.0%) as detailed in [Table 3]. [Table 4]: BMI percentile was found to be significantly lower in cases with CHDs ( $23.65 \pm 29.95$ ) compared to controls ( $41.88 \pm 37.34$ ), with (P-value of 0.008). [Table 5]: Relationship between CHDs and family history of CHDs was found to be significant, with (P-value of 0.013), Odds ratio was calculated to be 3.22, which means that children with family history of CHDs were 3 times more likely to have CHDs compared to those with no family history of CHDs. [Table 6]: summarize the possible risk factors; including: consanguinity, rubella infection (fever, headache, myalgia and rash) and COVID-19 infection during pregnancy, maternal previous history (hypertension, diabetes and abortion) and history of medications and vaccinations during pregnancy (folic acid, hormonal medications, aspirin, and tetanus vaccine), no significant relationship

**Table 1: Socio-Demographic characteristics of study participants(n=100)**

| Variable            |                  | Group      |            | Total     | P-value |
|---------------------|------------------|------------|------------|-----------|---------|
|                     |                  | CHD        | Control    |           |         |
| Age Group           | < 1              | 34 (48.6%) | 36 (51.4%) | 70 (100%) | 0.107   |
|                     | 1                | 7 (38.9%)  | 11 (61.1%) | 18 (100%) |         |
|                     | 2                | 5 (100%)   | -          | 5 (100%)  |         |
|                     | 3                | 4 (66.7%)  | 2 (33.3%)  | 6 (100%)  |         |
|                     | 4                | -          | 1 (100%)   | 1 (100%)  |         |
| Gender              | Male             | 24 (42.9%) | 32 (57.1%) | 56 (100%) | 0.107   |
|                     | Female           | 26 (59.1%) | 18 (40.9%) | 44 (100%) |         |
| Residence           | Urban            | 27 (46.6%) | 31 (53.4%) | 58 (100%) | 0.418   |
|                     | Rural            | 23 (54.8%) | 19 (45.2%) | 42 (100%) |         |
| Maternal Education  | Illiterate       | 10 (52.6%) | 9 (47.4%)  | 19 (100%) | 0.346   |
|                     | Primary          | 19 (41.3%) | 27 (58.7%) | 46 (100%) |         |
|                     | Secondary        | 13 (65.0%) | 7 (35.0%)  | 20 (100%) |         |
|                     | Higher education | 8 (53.3%)  | 7 (46.7%)  | 15 (100%) |         |
| Maternal Occupation | Housewife        | 43 (48.9%) | 45 (51.1%) | 88 (100%) | 0.538   |
|                     | Working          | 7 (58.3%)  | 5 (41.7%)  | 12 (100%) |         |

**Table 2: Presentation of congenital heart disease (n=50)**

| Presentation of CHD               | Frequency | Percentage (%) |
|-----------------------------------|-----------|----------------|
| Chest infection                   | 21        | 42.0%          |
| Accidental                        | 13        | 26.0%          |
| Cyanosis                          | 11        | 22.0%          |
| Both chest infection and cyanosis | 5         | 10.0%          |

**Table 3: Types of congenital heart disease (n=50)**

| Type of CHD | Frequency | Percentage (%) |
|-------------|-----------|----------------|
| VSD         | 14        | 28.0%          |
| PDA         | 10        | 20.0%          |
| ASD         | 9         | 18.0%          |
| TOF         | 3         | 6.0%           |
| PS          | 2         | 4.0%           |
| CoA         | 1         | 2.0%           |
| Complex     | 11        | 22.0%          |

was observed between congenital heart disease and any of these risk factors.

## DISCUSSION

This study compared between CHDs cases and controls regarding socio-demographic characteristics and showed that females were more than males (52%, 48%, respectively), another study conducted in Karbala/Babylon, Iraq, also showed female predominance (56.6% of the cases),<sup>[15]</sup> but in this study, there was no significant difference between cases and controls regarding their gender, this is consistent with<sup>[16]</sup> study, (68%) of the cases were below 1 year age, another study was done in in Ramadi city, Iraq, reported that (71.76%) of the cases were below 1 year age,<sup>[17]</sup> however, there was no significant

difference regarding the age of participants of the current study, which agrees with another study in Mosul city, Iraq,<sup>[18]</sup> 54% of the cases reside in urban area, a study was done in china found that (69.7%) of the cases were living in urban area,<sup>[19]</sup> anyway, there was no significant difference regarding the residence of the participants of this study, which goes in line with<sup>[20]</sup> study, also there was no significant differences between the cases and controls regarding maternal education and occupation, which is similar to another study.<sup>[19]</sup> The commonest type of CHDs in this study was VSD (28% of the cases), this is consistent with a study conducted in Karbala/Babylon, Iraq, which found that VSD was the commonest type (38.3% of the cases).<sup>[15]</sup> This study found that chest infection was the commonest presentation, accounts for (42% of the cases presentation), which is similar to the finding of a study in Al-Diwanyia city, Iraq,<sup>[21]</sup> in which chest infection accounts for (36% of the cases presentation), as many subtypes of CHDs cause pulmonary over circulation and pulmonary edema, which is a good nidus for the infection for the lower respiratory tract.<sup>[22]</sup> BMI percentile in CHDs cases was found to be significantly lower than controls, this is similar to the result of another study,<sup>[23]</sup> as impaired hemodynamic status in children with CHDs lead to impair growth and lower BMI,<sup>[24]</sup> while another study reported that decrease energy intake, malabsorption and increase energy requirements lead to underweight in children with CHDs.<sup>[25]</sup> The current study had observed that the relationship between CHDs and family history of CHDs was found to be significant and odds ratio was calculated to be (3.22), this is consistent with the result of another study, which found that there was significant relationship between CHDs and family history of CHDs with odd's ratio of (3.4),<sup>[26]</sup> the result of both studies means that parents with family history of CHDs were 3 times more likely to have offspring with CHDs compared to those with

**Table 4: Comparison between cases and controls regarding BMI percentile**

| Group                    | N   | BMI percentile (%) |       |              | P-value       |
|--------------------------|-----|--------------------|-------|--------------|---------------|
|                          |     | Mean               | SD    | Range        |               |
| Congenital Heart Disease | 50  | 23.65              | 29.95 | 0.10 – 94.37 | <b>0.008*</b> |
| Control                  | 50  | 41.88              | 37.34 | 0.10 – 99.82 |               |
| Total                    | 100 | 32.77              | 34.90 | 0.10 – 99.82 |               |

\* Significant at  $P \leq 0.05$

**Table 5: Family history of congenital heart diseases**

| Family history of CHD | Group      |            | Total      | P-value       |
|-----------------------|------------|------------|------------|---------------|
|                       | CHD        | Control    |            |               |
| Present               | 19 (70.4%) | 8 (29.6%)  | 27 (100%)  | <b>0.013*</b> |
| Not present           | 31 (42.5%) | 42 (57.5%) | 73 (100%)  |               |
| Total                 | 50 (50.0%) | 50 (50.0%) | 100 (100%) |               |

Odds ratio: 3.22 (95% C.I. 1.25 – 8.30)

\* Significant at  $P < 0.05$

**Table 6: Risk factors of CHD**

| Variables                         |             | Groups     |            | Total     | P-value |
|-----------------------------------|-------------|------------|------------|-----------|---------|
|                                   |             | CHD        | Control    |           |         |
| Consanguinity                     | Present     | 34 (56.7%) | 26(43.3%)  | 60(100%)  | 0.102   |
|                                   | Not present | 16 (40.0%) | 24(60.0%)  | 24(60.0%) |         |
| Fever, Headache, Myalgia, or Rash | Present     | 9 (39.1%)  | 14 (60.9%) | 23(100%)  | 0.235   |
|                                   | Not present | 41 (53.2%) | 36 (46.8%) | 77 (100%) |         |
| COVID-19                          | Present     | 2 (25.0%)  | 6 (75.0%)  | 8 (100%)  | 0.140   |
|                                   | Not present | 48 (52.2%) | 44 (47.8%) | 92 (100%) |         |
| HT                                | Present     | 3 (75.0%)  | 1 (25.0%)  | 4 (100%)  | 0.307   |
|                                   | Not present | 47 (49.0%) | 49 (51.0%) | 96 (100%) |         |
| DM                                | Present     | 1 (33.3%)  | 2 (66.7%)  | 3 (100%)  | 0.558   |
|                                   | Not present | 49 (50.5%) | 48 (49.5%) | 97 (100%) |         |
| Abortion                          | Present     | 16 (59.3%) | 11 (40.7%) | 27 (100%) | 0.260   |
|                                   | Not present | 34 (46.6%) | 39 (53.4%) | 73 (100%) |         |
| Folic acid                        | Yes         | 37 (50.7%) | 36(49.3%)  | 73(100%)  | 0.822   |
|                                   | No          | 13 (48.1%) | 14(51.9%)  | 27(100%)  |         |
| Hormonal medications              | Yes         | 20 (45.5%) | 24(54.5%)  | 44(100%)  | 0.420   |
|                                   | No          | 30 (53.6%) | 26(46.4%)  | 56(100%)  |         |
| Aspirin                           | Yes         | 8 (61.5%)  | 5 (38.5%)  | 13(100%)  | 0.372   |
|                                   | No          | 42 (48.3%) | 45(51.7%)  | 87(100%)  |         |
| Tetanus vaccine                   | Yes         | 28(50.0%)  | 28(50.0%)  | 56(100%)  | 1.000   |
|                                   | No          | 22 (50.0%) | 22(50.0%)  | 44(100%)  |         |

no family history. This study reported that there was no significant relationship between CHDs and consanguinity, this is similar to the result of another study conducted in India,<sup>[27]</sup> both studies found that the consanguineous marriage was the common pattern of marriage between the parents of cases and controls, which lead to this non-significant result. This study discussed the effect of rubella infection (fever, headache, myalgia and rash) and COVID-19 (positive PCR/chest CT scan) as a risk of CHDs, and showed that there was no significant relationship between

CHDs and infection with rubella/COVID-19 during pregnancy, another study conducted in Mosel city, Iraq, found that there was no significant relationship between CHDs and rubella infection.<sup>[26]</sup> Cardiac malformations are the most common congenital anomaly in diabetic pregnant woman,<sup>[28]</sup> but this study found that there was no significant difference between CHD and maternal diabetes, this result agrees with another study conducted in Saudi Arabia,<sup>[29]</sup> in both studies, just few cases reported diagnosed maternal diabetes, so we need to screen for

chronic diabetes through the preconception counselling and to screen for gestational diabetes in pregnant woman with risk factors by glucose tolerance test at 24–28 weeks of gestation through antenatal care. The current study reported no significant difference between CHDs and maternal hypertension, this is consistent with the finding of another study.<sup>[18]</sup> Complex CHDs may cause spontaneous abortion or stillbirth.<sup>[30]</sup> This study found that 32% of the cases' mother and 22% of the controls' mother reported history of abortion, so there was no significant difference between CHDs and maternal history of abortion, which agrees with the result of a study conducted in China, in which history of abortion in the cases' and controls' mother was 28%, 25% respectively, so there was no significant difference between CHDs and maternal history of abortion.<sup>[31]</sup> This study found that 74% of CHDs cases' mother and 72% of controls' mother reported use of folic acid supplements during pregnancy, so there was no significant relationship between CHD and folic acid intake as these percentages are convergent, another study demonstrated that folic acid intake among the mothers of CHDs children was significantly lower in corresponding to mothers of children without CHDs, so there was a significant relationship between CHDs and lack of folic acid intake during pregnancy.<sup>[26]</sup> Intake of progesterone in the early pregnancy increases the risk (5 times) of CHDs in the offspring, especially VSD.<sup>[32]</sup> This study reported that 40% of the cases and 48% of the controls confirmed the maternal hormone use during pregnancy, thus there was no significant relationship between CHDs and hormonal treatment, while another study was done in Gaza Strip identified 37% of the mothers of children with CHDs and 18% of the controls' mothers were exposed to hormonal treatment during pregnancy, so there was a positive association between hormonal treatment and CHDs in the offspring,<sup>[33]</sup> thus it is mandatory to improve the knowledge of the healthcare providers and pregnant women about the risks of progesterone for and limit its usage during first trimester unless where a clear indication existed. The use of NSAIDs during pregnancy especially in the third trimester poses a potential threat to the myocardium and cause persistent pulmonary hypertension and premature closure of the ductus arteriosus.<sup>[34]</sup> The current study reported no significant relationship between CHDs and aspirin intake, this result is similar to the result of a study conducted in Basra city, Iraq,<sup>[35]</sup> both studies found that just few cases reported the use of aspirin during pregnancy. Several studies have pointed to Tdap vaccine safety in pregnancy to both maternal and newborn health,<sup>[37,38]</sup> and the risk of birth defects in general is minimal.<sup>[36]</sup> The current study found that no significant relationship was observed between CHDs and tetanus toxoid vaccine, while another study conducted in Boston, USA; discussed the Tdap vaccine in pregnancy and risk of major birth defects in the offspring also reported that

there was no significant relationship between CHDs and tetanus vaccine.<sup>[39]</sup> However, other studies also discussed vaccine in pregnancy and its relation to the risk of major birth defects.<sup>[40,41]</sup>

## CONCLUSION

CHDs are one of the most important causes of fetal deaths, thus to prevent CHDs, it is mandatory to understand CHDs' risk factors. This study had observed that majority of the cases were females, below one year age, reside in urban area, presented with VSD and chest infection and there was a significant relationship between CHDs and family history of CHDs, also BMI percentile was found to be lower in cases of CHDs compared to controls.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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