Congenital Heart Disease In Preterm Infants

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Abstract

Background: Congenital heart defects and preterm birth are two important causes of neonatal and infant mortality. However, the relationship between them has not yet been fully clarified.

Objective: To find the association of congenital heart disease with premature delivery.

Patients and Methods: The study is an observational cross sectional study, done in Al-Batool teaching hospital for maternity and children from July 2022 to January 2023. A self-prepared questionnaire was used to gather data. Gestational age was calculated mainly on postnatal gestational assessment by Dubowitz/Ballard method by a pediatrician. Echocardiography was done by Echocardiography specialist doctor to identify the presence and types of congenital heart defects. SPSS version 25 was used for statistical analysis.

Results: Total number of births (term and preterm) was 1616, congenital heart diseases were detected in 60(3.71%) of them, most of them were isolated heart defect. In preterm babies, the congenital heart diseases were detected in 8% (p value was <0.001), they were of different types as followings: patent ductus arteriosus (n=10,26%), atrial septal defect (n=8,21%), ventricular septal defect (n=7,18%), transposition of the great arteries (n=4,10%), tetralogy of Fallot (n=2,5%), and complex of congenital heart disease (n=7,18%), while in full term babies, the rate of congenital heart diseases was only 1.9%.

Conclusion: The incidence of congenital heart disease was higher in preterm than full term delivered babies, mostly in the group of transposition of the great arteries, ventricular septal defect, complex heart defects, followed by atrial septal defect.

Keywords: Preterm, delivery, congenital heart disease.

Introduction

Preterm birth is defined as a birth before 37 weeks gestational weeks. It is about 15 million infants were born premature, with resulting complications and it is the primary cause of about one million neonatal deaths annually and a substantial contributor to childhood morbidities. Low and middle income countries carry a higher burden of disease attributed to preterm birth [1]. Although most preterm babies survive, they are at increased risk of neurodevelopmental impairments and respiratory and gastrointestinal complications [2].

Congenital heart defects (CHD) include structural malformations of the heart and/or major vessels present at birth or persisting...
abnormally after birth; it is the most frequent group of major congenital anomalies with a live prevalence that varies between 4.05 and 10.4 per 1000 live births [3,4,5].

Preterm birth (PTB) and congenital heart defects (CHD) are two major causes of mortality, morbidity and disability of perinatal origin [6]. Reported infant mortality rates for preterm newborns with CHD was range from 20% to 65% and most of the deaths occurring within the first 28 days of life [7, 8].

The relationship between them remains unclear. However, there are few specific data regarding the relationship of prematurity and CHD and the association between specific categories of CHD and preterm birth. The etiology of most non-syndromic CHD and preterm birth is uncertain. Probably it involves complex interactions between multiple environmental exposures and genetic susceptibilities. It is conceivable that both may occur independently but share common risk factors [9,8,11]. Alternatively, preterm birth in neonates with CHD may be caused by abnormal fetal hemodynamic profiles [11].

The objective of this study is to determine the prevalence of congenital heart diseases in the preterm infants in Diyala province and to study some of risk factors for CHD in this population group.

Patients and Methods
The study is an observational cross sectional study on the preterm babies in Al-Batool Teaching Hospital for Maternity and Children in the period from July 2022 to January 2023.

A self-prepared questionnaire was used for data collection. It included the neonatal and maternal and family data. Neonatal data included: gender, birth weight, gestational age, the existence of CHD, other fetal anomalies, and mode of delivery. Maternal and family data included: maternal age, history of CHD in the family, maternal chronic diseases, history of maternal smoking and any diseases during pregnancy (gestational diabetes, gestational hypertension).

Regarding birth weight and maturity, infant electronic scale was used for measurement (gram) and gestational age was calculated depending on postnatal gestational assessment by Dubowitz/Ballard method, supported by method depend on LMP (last menstrual period) provided by mothers and/or ultrasound gestational age assessment.

Inclusion/Exclusion Criteria
All newly delivered live infant (preterm and full term) during the period of the study were included, while dead infants were excluded.

Type of CHD
Echocardiography was done by Echocardiography specialist doctor for term and preterm babies after full clinical examination by a pediatrician to identify the presence and types of congenital heart disease. If there was more than one type of heart defect, it was considered as a complex congenital heart disease.

Statistical Analysis
Analysis of data were done by using Statistical Package for Social Science (SPSS) version 25 to look for the association of premature delivery and congenital heart disease. Pearson Chi square was calculated, p value was significant at level less than (0.05).
Results

Total birth number during the study period was 1616, out of them, CHDs were detected in 60 (3.71%) of them. In Preterm babies, CHDs were 38 (8%) of different types and this comprise 80 / 1000 a live birth, while in full term babies it was only 22 (1.9%, 19/1000 live birth). Table (1) shows distribution of CHD to the maturity, the rate of CHD was more in preterm delivery, p value (0.000).

Table (1): Distribution of CHD to preterm and full term delivered babies

<table>
<thead>
<tr>
<th>Maturity</th>
<th>Newborn</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With CHD no. (%)</td>
<td>Without CHD no. (%)</td>
<td>Total no. (%)</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Preterm</td>
<td>38 (8)</td>
<td>439 (92)</td>
<td>477 (100)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Full term</td>
<td>22 (1.9)</td>
<td>1113 (98.1)</td>
<td>1135 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>60 (3.7)</td>
<td>1552 (96.3)</td>
<td>1612 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CHD: Congenital heart disease.

Table (2) shows distribution of the study sample of newborn with CHD to the gender and maturity, it indicates a fair distribution of preterm and full term delivery to the gender.

Table (2): Association of the congenital heart diseases with the gender and birth weight

<table>
<thead>
<tr>
<th>Newborn criteria</th>
<th>Preterm newborn no.(%)</th>
<th>Full term newborn no.(%)</th>
<th>Total no.(%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23 (62)</td>
<td>14 (38)</td>
<td>37 (100)</td>
<td>0.811</td>
</tr>
<tr>
<td>Female</td>
<td>15 (65.2)</td>
<td>8 (34.8)</td>
<td>23 (100)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38 (63.3)</td>
<td>22 (36.7)</td>
<td>60 (100)</td>
<td></td>
</tr>
<tr>
<td>Birth weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2500 gm</td>
<td>37 (67.3)</td>
<td>18 (32.7)</td>
<td>55 (100)</td>
<td>0.036</td>
</tr>
<tr>
<td>&gt;2500 gm</td>
<td>1 (20)</td>
<td>4 (80)</td>
<td>5 (100)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38 (63.3)</td>
<td>22 (36.7)</td>
<td>60 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Table (3) shows the subtypes CHD distributed to the maturity, 87% were acyanotic and 13% cyanotic heart disease. Although more cases are detected in many subtypes of CHD in preterm babies, including VSD, ASD, and complex CHD, no significant statistical differences was present between preterm and full term newborn.

Table (3): Types of congenital heart defects in 60 children

<table>
<thead>
<tr>
<th>CHD</th>
<th>Newborn with CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preterm no. (%)</td>
</tr>
<tr>
<td>VSD</td>
<td>7 (70)</td>
</tr>
<tr>
<td>ASD</td>
<td>8 (62)</td>
</tr>
<tr>
<td>PDA</td>
<td>10 (50)</td>
</tr>
<tr>
<td>TGA</td>
<td>4 (100)</td>
</tr>
<tr>
<td>TOF</td>
<td>2 (67)</td>
</tr>
<tr>
<td>Complex CHD</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Total</td>
<td>38 (63.3)</td>
</tr>
</tbody>
</table>

Table (4) shows no effect of the mentioned maternal criteria (age, gravidity and mode of delivery) on incidence of CHD in both preterm and full term.

<table>
<thead>
<tr>
<th>Maternal criteria</th>
<th>Newborn with CHD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preterm no. (%)</td>
<td>Full term no. (%)</td>
</tr>
<tr>
<td><strong>Maternal age (yrs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>20 (57)</td>
<td>15 (43)</td>
</tr>
<tr>
<td>&gt;30-40</td>
<td>16 (72.7)</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>2 (66.6)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>38 (63.3)</td>
<td>22 (36.7)</td>
</tr>
<tr>
<td><strong>Mode of delivery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VD</td>
<td>4 (57)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>C/S</td>
<td>34 (64)</td>
<td>19 (36)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>38 (63.3)</td>
<td>22 (36.7)</td>
</tr>
<tr>
<td><strong>Gravidity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primigravida</td>
<td>11 (84.6)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Multigravida</td>
<td>27 (57.4)</td>
<td>20 (42.6)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>38 (63.3)</td>
<td>22 (36.7)</td>
</tr>
</tbody>
</table>

* VD: Vaginal delivery. C/S: Caesarean section. CHD: Congenital heart disease

Discussion

This study investigates the incidence of CHD in preterm born infants. Importantly, the combination of prematurity and CHD results in a further increased risk of mortality and significant morbidity.

Detection of CHD in preterm born neonates prenatally will help in management and even guide perioperative management [12].

We found in the current study that the incidence of CHD among preterm infants was 7.9% it was about four folded than that found in term infants, (p value <0.001 ), these results were rather similar to that found by Chu et al and Mustafa et al, while patricia et al was found more incidence of CHD in preterm born infants (116/1000) and lesser for term newborns (6-10/ 1000), this may be due to the design of the last study which was retrospective because still we have many deliveries occur at home and not reported in the study and this is mostly for term newborns. Anyhow there was more incidence of CHD in preterm delivered babies than term one, this might be explained by early initiation of delivery mechanism due to CHD due to hypoxia or other pathophysiology like intrauterine tachycardia or overactive or compromised cardiac muscles [13-15].

Generally, high prevalence of congenital heart diseases in premature infants is partially due to high prevalence of atrial septal defects which are undoubtedly more frequently diagnosed in premature infants due to neonatal care admission of these infant in
comparison to term infants (who are usually asymptomatic) and the increased probability of detection by an echocardiogram. Nevertheless, rate of ASD in preterm newborn was 8 (21% in preterm infants) and this alone will not affect the overall incidence globally if we ignore this disparity [16-20].

There was no difference between term and preterm newborns regarding gender, this is concurrent with the general equality of male and female gender in CHD incidence [21] most of the preterms with CHD delivered in this institution were having low birth weight (less than 2500 g), (p value 0.036), this LBW was explained in many studies due to the CHD itself, where they found LBW is associated more with certain CHD like ASD, PDA, VSD, pulmonary stenosis, and TOF, and this is corresponding with that detected in the current study, this may support the suggested theory of intrauterine hypoxia or compromised cardiac muscles affecting birth weight [22].

Regarding the association between the prevalence of CHD in Diyala province and maternal age, the findings suggest that the total prevalence preterms was more common among mothers 20-30 years of age as it is the most productive age group in the society, while in association with prematurity, CHD were more in preterms of older age group mothers compared to the reference category, but this difference was statistically not significant (p value0.490), this finding agree with previous studies conducted in USA, Hawaii and Saudi arabia, which reported an increased possibility of congenital heart disease incidence with advanced maternal age (35–44 years of age), while Best et al found no association of risk of CHD with advanced maternal age (>35)[23,24,25,26].

As a part of arrangement for management of babies with cardiac defect at delivery room, we searched for association of preterm babies with CHD with mode of delivery, but there was no difference between preterm and full term born infants with CHD in rate of cesarean delivery in the current study and this was consistent with that found by Keren et al, this may be due to high demand of cesarean section delivery in the society, even for term healthy babies, although they found that operative assisted vaginal delivery was more in non-reassuring fetal heart rate in pregnancies complicated by a prenatal diagnosis of CHD than other pregnancies have non-anomalous fetuses [27].

On other hand, several maternal co-morbidities such as diabetes and smoking, could partially describe the relationship between CHD subtypes and advanced maternal age. For example, the infant study, Baltimore-Washington, stated that women of advanced maternal age who smoked more than 1 pack of cigarettes per day, were more possibly to have a newborn with CHD compared to younger nonsmoking mothers, these maternal risk factors were less reported in the current study to support or disregard this association [28].

The main limitations to our study were the size of the sample which cannot be subgrouped to the type of defect and study each one separately, and to study many coexistent factor with CHD and preterm delivery.

**Conclusions**

The incidence of congenital heart disease was higher in preterm than full term
delivered babies, mostly in the group of TGA, VSD, complex heart defects, followed by ASD, so we can conclude for a strong association between preterm delivery and incidence of CHD.

**Recommendations**

Routine echocardiography should be considered for early recognition of CHD before and after preterm delivery to arrange for management in the delivery room and thereafter.

**Source of funding:** The current study was funded by our charges with no any other funding sources elsewhere.

**Ethical clearance:** Ethical approval was obtained from the College of Medicine / University of Diyala ethical committee for this study.

**Conflict of interest:** Nil

**References**


الملخص

خلفية الدراسة: عيوب القلب الخلقية والولادة المبكرة هما من أهم أسباب الوفيات عند الأطفال الخدج حديثي الولادة. إلا أن العلاقة بينهما لم توضح بشكل كامل بعد.

أهداف الدراسة: تتضمن العوامل المرتبطة بتطور ارتفاع ضغط الدم الشرياني الرئوي في مرضى الداء الكلوي بمرحلة الأخيرة الذين يتلقون علاجا بالغسيل الكلوي.

المرضى والطريقة: الدراسة هي عبارة عن دراسة مقطعية رصدية أجريت في مستشفى البطل التعليمي للأطفال والولادات في الفترة من يوليو 2022 إلى يناير 2023. وتم استخدام استبيانات معدة ذاتياً من قبل الباحثين لجمع البيانات. تم تقييم عمر فترة الحمل بالدرجة الأساسية على طريقة دوبيتز/الارد من قبل أخصائي الأطفال، تم إجراء تخطيط صدى القلب من قبل أخصائي الايكو لتحديد وجوء أو عيوب عيوب القلب الخلقية. ثم تحليل البيانات إحصائيا.

النتائج: بلغ إجمالي عدد الولادات (المكتملة و حديثي الولادة) 1616، تم الكشف عن أمراض القلب الخلقية في 60 (3.71%) منها، معظمها كانت عيبًا قلبيًا متفرقاً، أي بدون عيوب خلقية أخرى عند الأطفال الخدج، تم الكشف عن أمراض القلب الخلقية في 8٪ (قيمة الإحصائية الإحصائية أقل من 0.01)، وكانت من أنواع مختلفة على النحو التالي: القناة الشريانية السالقة (العدد = 10)، عيب الحاجز الأذيني (العدد = 8)، عيب الحاجز البطيني (العدد = 7), تبديل الشرايين الكبيرة (العدد = 4)، عيب الحاجز الأذيني (العدد = 2), عيب الحاجز البطيني (العدد = 1). بينما كان معدل أمراض القلب الخلقية عند الأطفال الذين ولدوا في فترة الحمل الكاملة (11.9%) فقط.

الاستنتاجات: نتتضح من ذلك معدل الإصابة بأمراض القلب الخلقية أعلى عند الأطفال الخدج حديثي الولادة مقارنة بالأطفال الذين ولدوا فترة حمل كاملة، ومعظمهم في مجموع تبديل الشرايين الكبيرة، عيب الحاجز البطيني، عيب الحاجز الأذيني، عيب الحاجز البطيني.

الكلمات المفتاحية: الخدج، الولادة، أمراض القلب الخلقية

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2 مستشفى البطل التعليمي - دائرة صحة ديالى - ديالى - العراق
3 كلية الطب - جامعة ديالى - ديالى - العراق