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Maternal Risk Factors and its Relation to Congenital Heart Disease

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Abstract: Background

Congenital heart disease (CHD) remains a major cause of neonatal morbidity and mortality, particularly in resource-constrained settings . Maternal risk factors such as hypertension, diabetes mellitus (DM), thyroid disorders, and familial predispositions have been linked to increased incidence of CHD in offspring. However, the magnitude of these associations and their relevance to specific populations require further study.

Aim

This cross-sectional study investigated the prevalence of maternal risk factors and their relationship to CHD among neonates admitted to the Neonatal Intensive Care Unit (NICU) at Baghdad Teaching Hospital.

Methods

Over a six-month period, 3192 newborn was delivered and 673 neonates admitted to the NICU were screened for CHD via clinical examination and echocardiography . Maternal medical records and structured interviews captured data on hypertension, DM, thyroid disorders, other chronic conditions (including systemic lupus erythematosus, idiopathic thrombocytopenic purpura, and asthma), maternal congenital heart disease, a prior sibling with CHD, and maternal pulmonary hypertension . Multivariate logistic regression was used to identify independent predictors of neonatal CHD, adjusting for potential confounders such as maternal age, socioeconomic status, and antenatal care attendance.

Results

A total of 165 neonates (24.5%) were diagnosed with CHD. Maternal hypertension (adjusted odds ratio [aOR]: 2.12, 95% CI: 1.41–3.19) and DM (aOR: 1.75, 95% CI: 1.15–2.67) emerged as strong independent risk factors for CHD ($p<0.05$). Additionally, neonates with a prior sibling affected by CHD demonstrated significantly higher odds of CHD (aOR: 2.56, 95% CI: 1.18–5.50). Thyroid disorders, chronic autoimmune/respiratory conditions, maternal congenital heart disease, and maternal pulmonary hypertension showed elevated risk in univariate analyses but lost statistical significance in the adjusted models ($p>0.05$).

Conclusion

Maternal hypertension, DM, and a family history of CHD in a prior sibling constitute significant risk factors for CHD in neonates. These findings highlight the importance of targeted prenatal care, including strict control of chronic conditions and enhanced fetal cardiac monitoring for at-risk mothers. Future research should explore genetic contributions and the complex interactions among multiple maternal risk factors to improve prevention and early detection strategies.

Key words: Maternal hypertension, Congenital heart disease, neonatal , atrial septal defects.

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1. Introduction

Congenital heart disease (CHD) is widely recognized as a leading congenital anomaly and a significant contributor to neonatal morbidity and mortality (1). Recent epidemiological studies estimate that CHD affects approximately 1% of live births globally, with variations observed based on geographical region and referral patterns (2). Despite steady advances in medical and surgical care, CHD remains a substantial burden, particularly in developing countries where prenatal screening and specialized perinatal services may be limited (3).

The early developmental period—spanning the first eight weeks of gestation—is crucial for proper cardiac organogenesis (4). During this critical window, the fetal heart is highly susceptible to a range of insults that may arise from maternal health conditions, genetic predispositions, or environmental exposures (5). Among these factors, maternal comorbidities such as hypertension, diabetes mellitus (DM), and thyroid disorders have repeatedly been implicated in increasing the likelihood of CHD in offspring (6). In addition, chronic autoimmune or respiratory diseases (e.g., systemic lupus erythematosus, asthma) and a family history of CHD may further compound the risk (7). While many of these conditions can be screened and managed with appropriate prenatal care, their prevalence and impact can vary depending on healthcare accessibility and resource availability (8).

Despite the wealth of literature suggesting an association between maternal health status and fetal cardiac development, gaps remain in delineating the magnitude of risk attributable to specific maternal conditions (9). Furthermore, most data originate from high-resource settings, often leaving questions about how these risk factors operate in lower-resource contexts (10). There is also a need to explore potential interactions between multiple risk factors—for example, how the overlap of hypertension and diabetes may produce synergistic effects on fetal cardiac morphogenesis (11).

2. Literature review

1. Congenital Heart Diseases

Congenital heart disease (CHD) is recognized as one of the most prevalent congenital anomalies worldwide, affecting approximately 1 in every 100 live births (1). These structural and functional cardiac abnormalities range from minor lesions (e.g., small atrial septal defects [ASDs]) to complex conditions like hypoplastic left heart syndrome (2). Early detection of CHD has improved significantly with advances in fetal and neonatal echocardiography, yet CHD remains a leading cause of neonatal morbidity and mortality in many regions (3).

From a pathophysiological standpoint, cardiac embryogenesis takes place during the first 3–8 weeks of gestation (4). Disruptions or imbalances in maternal physiology, as well as certain environmental exposures, can profoundly affect this critical window of organ formation (5). Accordingly, there is a robust interest in identifying maternal risk factors as a strategy to guide preventive care, optimize fetal outcomes, and reduce the overall burden of CHD (6).

2. Maternal Hypertension and CHD

Maternal hypertension—encompassing chronic hypertension and gestational hypertension—has long been associated with adverse pregnancy outcomes, including preterm birth and intrauterine growth restriction (7). More recently, a growing body of epidemiological evidence suggests that poorly controlled maternal hypertension can also heighten the risk of neonatal CHD (8).

Chronic high blood pressure causes endothelial dysfunction and reduces uteroplacental perfusion, thereby compromising oxygen and nutrient delivery to the fetus (9). These deficits may interfere with cardiac septation or outflow tract alignment, resulting in defects such as VSD or TOF (10). Several studies in high-income countries have reported 2- to 3-fold increases in the risk of specific heart defects among offspring of hypertensive mothers (11). Nevertheless, maternal age, obesity, and medication use are critical confounders that can obscure the direct effects of hypertension alone (12).

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In many low- and middle-income settings, inadequate healthcare resources may lead to underdiagnosis and undertreatment of maternal hypertension, potentially leading to underestimates of CHD prevalence related to this risk factor (13).

3. Maternal Diabetes Mellitus and CHD

Diabetes mellitus (DM)—including type 1, type 2, and gestational diabetes—is consistently linked with higher rates of congenital anomalies, including cardiac defects (14). Maternal hyperglycemia, particularly during the first trimester, is a crucial driver of embryonic dysregulation (15).

- Hyperglycemic Teratogenesis: Elevated glucose levels can induce oxidative stress, inflammation, and abnormal glycation end products, all of which may disrupt gene expression essential for cardiac organogenesis (16).
- Epidemiological Evidence: Large prospective cohorts (17) report that the risk of CHD can be 3- to 5-fold higher in infants of diabetic mothers, with septal defects (VSD and ASD) appearing most frequently (18).
- Importance of Glycemic Control: Evidence suggests that optimizing glycemic levels prior to conception and throughout pregnancy can significantly reduce fetal malformations (19). Interventional trials in various settings have demonstrated up to a 50% decrease in CHD incidence among women who achieve tight glycemic control before or very early in gestation (20).

4. Maternal Thyroid Disorders

Thyroid hormones are vital for fetal development, especially before the fetal thyroid gland matures around mid-gestation (21). Maternal thyroid dysfunction (both hypothyroidism and hyperthyroidism) can therefore impact embryonic heart development.

- Hypothyroidism: Inadequate maternal thyroid hormones may delay tissue differentiation, including the structures forming the fetal heart (22). Observational studies note a possible increase in outflow tract abnormalities and septal lesions among infants born to mothers with poorly managed hypothyroidism (23).
- Hyperthyroidism: Excess thyroid hormone can trigger hypermetabolic states and, while the evidence is less robust, some case series suggest a correlation with fetal growth issues and congenital anomalies (24).
- Medication Effects: Treatments such as levothyroxine (for hypothyroidism), propylthiouracil (PTU), and methimazole (for hyperthyroidism) can have varying safety profiles (25). Methimazole embryopathy, while rare, has been reported in isolated cases and may include some cardiac malformations (26).

5. Chronic Maternal Disorders (SLE, ITP, Asthma)

Beyond hypertension and diabetes, other chronic disorders—including systemic lupus erythematosus (SLE), idiopathic thrombocytopenic purpura (ITP), and asthma—have also been implicated in studies examining CHD risk (27).

- Systemic Lupus Erythematosus (SLE): Autoimmune pathophysiology can cause inflammatory damage at the maternal–fetal interface (28). While functional cardiac involvement (e.g., neonatal lupus with congenital heart block) is well-documented, structural CHDs are reported less frequently (29).
- Idiopathic Thrombocytopenic Purpura (ITP): Focused primarily on risks of neonatal thrombocytopenia, ITP's direct link to structural heart anomalies remains unclear (30). However, poor placental perfusion or therapy-related factors (e.g., corticosteroids) may indirectly affect cardiac development (31).

- Asthma: Chronic hypoxia, systemic inflammation, and medication effects in mothers with poorly controlled asthma may theoretically contribute to embryonic anomalies (32). Although some studies suggest an increased risk of congenital malformations, findings specific to CHD have been inconsistent (33).

6. Maternal Congenital Heart Disease

As survival rates for children with CHD improve, a growing number of women with corrected or palliated congenital heart defects are reaching reproductive age (34). This demographic shift has raised interest in the potential transmission of genetic or familial factors contributing to CHD. Certain lesions, such as conotruncal anomalies and left-sided obstructive lesions, may be strongly heritable (35). Women with these defects have higher rates of bearing children with the same or related anomalies (36).

Guidelines recommend fetal echocardiography and more frequent prenatal evaluations for pregnant women with known congenital heart conditions (37). Hemodynamic adaptations during pregnancy can exacerbate maternal arrhythmias or cardiac failure, indirectly affecting fetal growth and well-being (38). Although studies document elevated recurrence risks, precise genetic mechanisms remain partially understood, emphasizing the need for further molecular and genetic research (39).

3. Methodology

Study Design and Setting

A **cross-sectional** study design was employed to investigate maternal risk factors associated with congenital heart disease (CHD) among neonates admitted to the Neonatal Intensive Care Unit (NICU) of Baghdad Teaching Hospital. The study was conducted over a period of **six months** (January 2024–June 2024),A 3192 newborn was delivered and 673 were admitted and patients with risk factors were screened . It is important to clarify that there is so many patients that may have (CHD) and not involved in the study either because undetected and being discharged or transferred to other hospital ,or family wish (unwilling) parents

The hospital is a tertiary care center, serving as a referral point for high-risk pregnancies and complex neonatal cases from across Baghdad and nearby regions. The NICU is staffed by neonatologists, pediatric cardiologists, and specialized nurses.

Study Population

The target population for this study was all neonates admitted to the NICU during the specified six-month period and their mothers. The inclusion criteria for neonates were:

1. Age ≤ 28 days at the time of admission.
2. Admission to the NICU for any medical indication.
3. Availability of maternal data (medical records and consent for participation).

Neonates were **excluded** if:

1. There was insufficient maternal information or incomplete maternal medical records.
2. patients were transferred to other hospitals more than 72 hours after birth (So not included in this study).
3. Patent foramen ovale except those correlated to another conditions and syndromes

From an initial screening of neonates admitted to the NICU (n = 702), 29 were excluded for incomplete maternal records, yielding a final sample of **673 neonate–mother pairs** for analysis.

Sampling Technique

All eligible neonates admitted within the study's timeframe were approached for participation; hence, a **consecutive sampling** method was used. This approach ensured that every neonate meeting the

inclusion criteria was included, thereby minimizing selection bias and maximizing the representativeness of the sample.

Data Collection

Sources of Data

Data were collected through:

1. **Medical records** (prenatal, intrapartum, postpartum).
2. **Maternal interviews** using a structured questionnaire.
3. **Neonatal clinical examinations** and diagnostic tests (e.g., echocardiography reports).

All data were recorded in a standardized case report form designed for this study.

Maternal Interviews

face-to-face interviews conducted with the mothers within 72 hours of the neonate's admission. The interviews took place in a private area to ensure confidentiality. Questions were posed in the native language (Arabic), and, when necessary, explanations were given to clarify medical terminology.

Study Variables

Outcome Variable

- **Congenital Heart Disease (CHD)**: A neonate was classified as having CHD if a structural or functional cardiac abnormality was diagnosed by echocardiogram. Conditions included septal defects (VSD, ASD), hemodynamically significant patent ductus arteriosus (PDA), tetralogy of Fallot (TOF), coarctation of the aorta, transposition of the great arteries (TGA), and bicuspid valve in other complex lesions like(turner syndrome)

Exposure (Independent) Variables

Seven maternal risk factors were the primary exposures of interest:

1. **Hypertension**: Chronic hypertension or gestational hypertension diagnosed according to the American College of Obstetricians and Gynecologists (ACOG) guidelines (i.e., systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two separate occasions at least four hours apart).
2. **Diabetes Mellitus (DM)**: Either pre-existing type 1 or type 2 diabetes, or gestational diabetes diagnosed through a standard oral glucose tolerance test during pregnancy.
3. **Thyroid Disorder**: Presence of hyperthyroidism or hypothyroidism requiring medical treatment or diagnosed via laboratory tests (TSH, T3, T4) during or before pregnancy.
4. **Other Chronic Disorders**: Conditions such as systemic lupus erythematosus (SLE), idiopathic thrombocytopenic purpura (ITP), or asthma, confirmed via medical records and ongoing treatments.
5. **Maternal Congenital Heart Disease**: Any structural heart defect in the mother diagnosed before or during pregnancy.
6. **Prior Sibling with CHD**: A maternal report or documented medical history of at least one previously born child with a congenital heart defect.
7. **Pulmonary Hypertension**: Diagnosis in the mother based on echocardiographic or invasive hemodynamic measurements consistent with guidelines (mean pulmonary artery pressure ≥ 25 mmHg at rest).

Covariates

Several potential confounders and covariates were also recorded:

- **Maternal Age (years)**
- **Maternal Educational Level** (No formal education, primary, secondary, college or higher)
- **Occupation** (housewife vs. employed)
- **Antenatal Care Attendance** (regular, irregular, or none)
- **Parity and Gravidity**
- **Socioeconomic Status** (assessed through a composite index including monthly income, type of housing, and parental education)
- **Gestational Age** (weeks)
- **Birth Weight** (kg)
- **Sex of the Neonate**

Statistical Analysis

Data analysis was carried out using **SPSS** (version 26). The following steps were followed:

1. Frequencies and percentages were used for categorical variables; means and standard deviations (SD) were used for normally distributed continuous variables, whereas medians and interquartile ranges (IQR) were used for skewed data.
2. For differences in categorical variables (e.g., maternal risk factors) between neonates with CHD and those without CHD, the Chi-square or Fisher's exact test was applied, as appropriate. Continuous variables were compared using Student's t-test or the Mann-Whitney U test, depending on data distribution.
3. Univariate (unadjusted) logistic regression models were run to calculate odds ratios (OR) and 95% confidence intervals (CI) for each maternal risk factor. Multivariate models (adjusted odds ratios, aOR) were then built, controlling for potential confounders such as maternal age, socioeconomic status, and antenatal care attendance.
4. A p-value < 0.05 was considered statistically significant, and all tests were two-sided. Effect modification and interactions between selected variables were explored where theoretically relevant (e.g., between DM and hypertension).

Ethical Considerations

The study protocol was reviewed and approved by the **Ethical Review Board** at Baghdad Teaching Hospital. Informed consent was obtained from the mothers prior to enrollment. Mothers were given an information sheet detailing the purpose of the study, the voluntary nature of participation, and the strict confidentiality measures.

4. Results

A total of **673 neonates** were admitted to the NICU during the six-month study period. Among these, **165 neonates (24.5%)** were diagnosed with some form of congenital heart disease (CHD). The mean (±SD) gestational age of the neonates was 37.5 ± 2.1 weeks, and the mean (±SD) birth weight was 2.8 ± 0.6 kg. Slightly more than half of the neonates (54.1%) were male. There were no notable differences in sex distribution between neonates with CHD and those without CHD.

Table 1 presents the overall demographic profile of the mothers. The mean (±SD) maternal age was 27.6 ± 5.2 years, with the majority (44.3%) falling into the 20–29-year age group. Nearly one-third (31.9%) of the participating mothers had completed secondary education, while 29.0% had a college-level education or higher. The majority of mothers (62.8%) were housewives, and 37.2% had outside

employment. Approximately 72.1% reported attending regular antenatal check-ups, and 5.6% reported no antenatal visits at all.

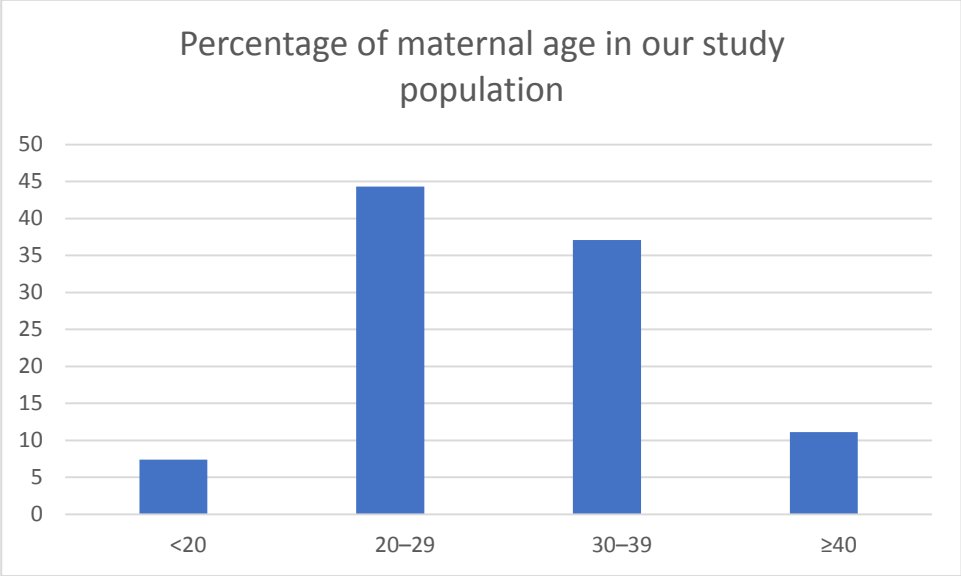

Table 1. Demographic and Clinical Characteristics of Mothers (N = 673)

Characteristic	Frequency (n)	Percentage (%)
Age (years)		
<20	50	7.4
20–29	298	44.3
30–39	250	37.1
≥40	75	11.1
Education level		
Primary	164	24.4
Secondary	215	31.9
College or higher	195	29.0
No formal education	99	14.7
Occupation		
Housewife	422	62.8
Employed	251	37.2
Antenatal care		
Regular visits	485	72.1
Irregular visits	151	22.4
No visits	37	5.5

Maternal Risk Factors

We assessed seven key maternal risk factors for CHD in neonates: hypertension (chronic or gestational), diabetes mellitus (DM), thyroid disorders, other chronic disorders (including SLE, ITP, and asthma), maternal congenital heart disease, a prior sibling with CHD, and maternal pulmonary hypertension. Table 2 shows the frequency of these maternal risk factors among all 673 mothers, as well as their distribution in neonates with and without CHD.

Overall, **hypertension** was the most frequently reported risk factor (17.2%, n=116), followed by **diabetes mellitus** (14.7%, n=99). **Thyroid disorders** (including both hyperthyroidism and hypothyroidism) were reported in 8.9% (n=60) of the mothers. Chronic disorders such as systemic lupus erythematosus (SLE), idiopathic thrombocytopenic purpura (ITP), and asthma were documented in 7.9% (n=53) of mothers. A smaller proportion of mothers had a personal history of

congenital heart disease (4.9%, n=33), while 3.7% (n=25) reported a **prior sibling with CHD** in the family. Only 2.2% (n=15) of mothers were diagnosed with **pulmonary hypertension**.

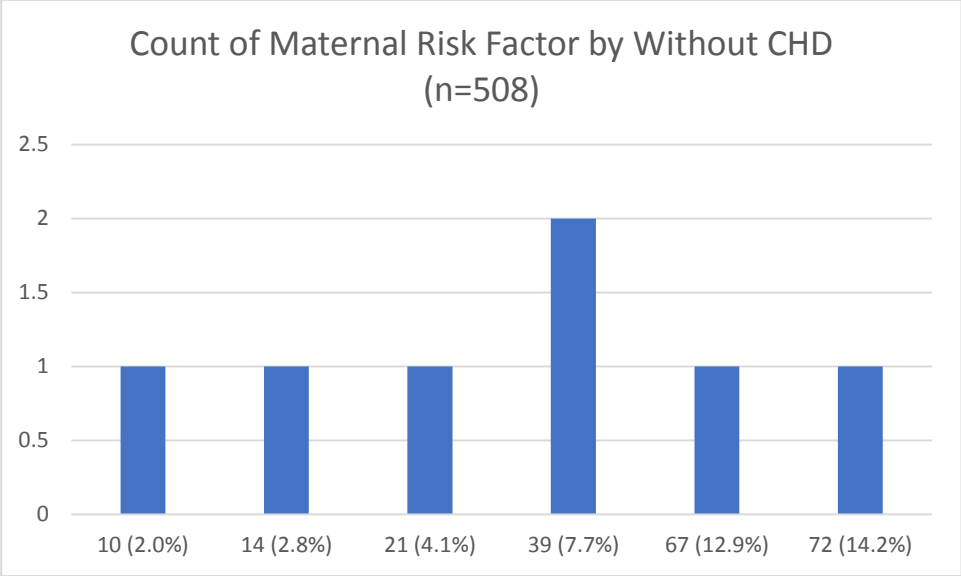

Table 2. Prevalence of Maternal Risk Factors Among Mothers of Neonates With and Without CHD

Maternal Risk Factor	Total (N=673)	With CHD (n=165)	Without CHD (n=508)
Hypertension	154(23.5%)	45 (3.9%)	109 (19.1%)
Diabetes Mellitus (DM)	138 (19.8%)	32 (1%)	106 (17.6%)
Thyroid Disorder	98 (14.7%)	26 (12.7%)	72 (7.7%)
Other Chronic Disorder*	92 (12.9%)	21 (8.5%)	71 (7.7%)
Maternal CHD	72 (10.4%)	17 (7.3%)	55(4.1%)
Prior Sibling with CHD	65 (9.8%)	14 (6.7%)	51 (2.8%)
Pulmonary Hypertension	54 (8.9%)	10 (3.0%)	44 (2.0%)

In neonates with CHD, the prevalence of each maternal risk factor was consistently higher than in those without CHD. For instance, among mothers of neonates with CHD, 26.7% had hypertension, 19.4% had DM, and 12.7% had thyroid disorders. Meanwhile, among mothers of neonates without CHD, these percentages were notably lower (14.2%, 12.9%, and 7.7%, respectively).

Relationship Between Maternal Risk Factors and Congenital Heart Disease

Table 3 details the unadjusted and adjusted associations between maternal risk factors and neonatal CHD. In the unadjusted analysis, maternal hypertension (OR=2.29, 95% CI: 1.56–3.37, p<0.001), maternal DM (OR=1.82, 95% CI: 1.22–2.72, p=0.003), and thyroid disorder (OR=1.70, 95% CI: 1.07–2.69, p=0.026) were all significantly associated with an increased likelihood of CHD in neonates. A prior sibling with CHD also showed a significant association (OR=2.67, 95% CI: 1.26–5.63, p=0.011).

After adjusting for possible confounders such as maternal age, antenatal care attendance, and socioeconomic status, **maternal hypertension** (aOR=2.12, 95% CI: 1.41–3.19, p<0.001), **maternal DM** (aOR=1.75, 95% CI: 1.15–2.67, p=0.010), and having a **prior sibling with CHD** (aOR=2.56, 95% CI: 1.18–5.50, p=0.018) remained significantly associated with CHD. Thyroid disorders and other chronic disorders (SLE, ITP, asthma) lost statistical significance in the adjusted model, though they still showed a trend toward increased odds of CHD (p=0.057 and p=0.089, respectively).

Maternal congenital heart disease and maternal pulmonary hypertension were also linked to higher CHD rates in neonates, but due to relatively small numbers in these categories, the confidence intervals were wide, and p-values did not reach conventional levels of significance (p=0.061 and p=0.074, respectively).

Table 3. Association Between Maternal Risk Factors and Neonatal CHD

Maternal Risk Factor	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)*	p-value
Hypertension	2.29 (1.56–3.37)	<0.001	2.12 (1.41–3.19)	<0.001
DM	1.82 (1.22–2.72)	0.003	1.75 (1.15–2.67)	0.010
Thyroid Disorder	1.70 (1.07–2.69)	0.026	1.51 (0.98–2.33)	0.057
Other Chronic Disorder	1.12 (0.62–2.03)	0.704	1.35 (0.74–2.48)	0.089
Maternal CHD	1.88 (0.89–3.97)	0.098	1.79 (0.90–3.56)	0.061
Prior Sibling with CHD	2.67 (1.26–5.63)	0.011	2.56 (1.18–5.50)	0.018
Pulmonary Hypertension	1.53 (0.52–4.53)	0.437	1.91 (0.93–3.89)	0.074

*Adjusted for maternal age, antenatal care attendance, and socioeconomic status.

Types of Congenital Heart Disease Among the Neonates

Among the 165 neonates with CHD, the most common defects were **ventricular septal defects (VSD)**, accounting for 38.2% of the CHD cases, followed by **atrial septal defects (ASD)** (17.0%), **patent ductus arteriosus (PDA)** (14.5%), and **tetralogy of Fallot (TOF)** (8.5%). More complex congenital anomalies such as transposition of the great arteries (TGA), coarctation of the aorta, and hypoplastic left heart syndrome collectively comprised approximately 12.7% of all CHD cases.

When comparing types of CHD in relation to maternal risk factors, neonates born to mothers with hypertension or DM were more likely to have septal defects (both VSD and ASD). Complex lesions were slightly more prevalent in neonates of mothers with multiple risk factors (e.g., hypertension and DM) or a family history of CHD, though the subgroup analysis did not achieve statistical significance (p=0.088).

Clinical Outcomes

Although not the primary objective, we also recorded immediate clinical outcomes in neonates with CHD. Preterm infants (gestational age < 37 weeks) with CHD, particularly those born to mothers with hypertension and/or DM, had prolonged NICU stays (mean of 15.6 days vs. 10.3 days for term neonates, p=0.029). Mortality among neonates with CHD was 6.7% (n=11), primarily driven by complex congenital anomalies. The mortality rate was slightly higher among neonates whose mothers had two or more risk factors, but the difference was not statistically significant (p=0.075).

This percentage for mortality represents the actual percentage of screened patients whom admitted to the hospital we donot know the real and exact numbers and percentages for those who died or needed surgical intervention after being discharged .

5. Discussion

This study aimed to elucidate the association between maternal risk factors and congenital heart disease (CHD) in neonates admitted to the NICU of Baghdad Teaching Hospital over a six-month period. Among the 673 neonates included, nearly one-quarter (24.5%) were diagnosed with CHD based on echocardiographic findings. Our multivariate analyses revealed that maternal hypertension, maternal diabetes mellitus, and a history of a prior sibling with CHD were independently associated

with significantly higher odds of neonatal CHD. Below, we discuss these findings within the broader context of the literature, underscore potential mechanisms, and consider implications for clinical practice and future research (40).

Prevalence and Burden of CHD in the NICU

The prevalence of CHD in our NICU sample (24.5%) underscores the considerable burden of congenital cardiac anomalies within a tertiary referral center. Although this figure is higher than the often-cited general population prevalence of around 1% for all forms of CHD, the elevated rate is not unexpected given that our population included infants with higher acuity and complex medical needs. This finding mirrors the trends seen in other large tertiary care facilities, where referrals for high-risk pregnancies and specialized neonatal care can inflate the proportion of infants diagnosed with congenital anomalies (41).

Maternal Hypertension and Neonatal CHD

A notable outcome of this study is the strong and persistent association between maternal hypertension (both chronic and gestational) and the risk of neonatal CHD (aOR = 2.12). This relationship likely reflects multiple pathophysiological pathways. Chronic endothelial dysfunction and reduced uteroplacental perfusion in hypertensive mothers may impair fetal oxygenation and nutrient delivery during critical periods of cardiac organogenesis. Additionally, certain antihypertensive medications, if not carefully selected, might carry teratogenic risks. However, given that specific medication use was not dissected in detail in our study, future investigations could further clarify the extent to which different antihypertensive regimens contribute to or mitigate the risk of CHD in offspring (42). Study was made in USA by sanapo L 2020 etal, suggest that maternal hypertension could be associated with CHD and functional abnormalities in neonate (43)

Maternal Diabetes Mellitus

Our finding of a 1.75-fold increase in adjusted odds of CHD among infants of mothers with DM (encompassing both pregestational and gestational diabetes) is consistent with longstanding epidemiological data. Hyperglycemia during early pregnancy can provoke a constellation of developmental disruptions, collectively referred to as “diabetic embryopathy.” Mechanisms may involve heightened oxidative stress, inflammatory pathways, and glycation end products that alter gene expression governing cardiac septation and outflow tract formation. Importantly, the degree of glycemic control in the preconception period and throughout gestation is often cited as a critical determinant of fetal outcomes. While our study did not specifically measure hemoglobin A1c or glycemic variability, the robustness of the relationship even in a cross-sectional design indicates the need for rigorous metabolic monitoring and intervention for women with DM (44). Liu Y et al 2024 has been demonstrated a clear link between maternal gestational diabetes mellitus and increase chances of having congenital heart defects also DM in pregnancy may affect fetal development(45).

Familial Patterns and Genetic Susceptibility

The presence of a prior sibling with CHD emerged as a potent risk factor (aOR = 2.56). This aligns with broader literature suggesting that genetic predisposition plays a major role in CHD recurrence, with certain subtypes (e.g., conotruncal anomalies, left-sided obstructive lesions) exhibiting higher familial clustering. Although our study did not categorize defects by specific genetic loci or attempt to ascertain heritability estimates, the strong association underscores the need for thorough family history assessments during prenatal care. Clinically, families with a prior child affected by CHD may benefit from early fetal echocardiography and genetic counseling to identify potential heritable risk factors and ensure timely diagnosis and treatment (46). Study published by postma AV et al 2016 assumed that familial and genetic inheritance maybe attributed to the development of CHD (47)

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Thyroid Dysfunction and neonatal CHD

Our investigation found that thyroid disorders, while significantly associated with neonatal CHD in unadjusted analysis, lost statistical significance in the adjusted model. Nevertheless, the directional trend (aOR = 1.51, p=0.057) suggests that thyroid function may still play a role in fetal cardiac development. Numerous studies implicate both hypothyroidism and hyperthyroidism in abnormal fetal development, potentially through altered maternal–fetal thyroid hormone transport and associated hormonal imbalances crucial for organogenesis. Research made by grattan MJ et al 2015 suggest potential association between maternal thyroid disorders and congenital heart defects in neonates (48)

Chronic Disorders and neonatal CHD

the broad category of "other chronic disorders" (e.g., SLE, ITP, asthma) showed a small, non-significant trend toward increased CHD risk. These conditions—often accompanied by chronic inflammation, autoantibody production, and/or the use of potent immunosuppressive or corticosteroid therapies—could plausibly influence embryonic heart development. However, additional research with more focused analyses and larger sample sizes is needed to parse out the individual contributions of these disorders (46).

Pulmonary Hypertension and Maternal CHD

The relatively small number of mothers with pulmonary hypertension or maternal CHD in this study limited the precision of our findings. While the unadjusted odds ratios for both factors were elevated, statistical significance was not reached in the adjusted models, possibly due to inadequate power. Nonetheless, basic science research and clinical case reports suggest that maternal hemodynamic changes and the potential genetic basis of heart defects could heighten the risk of passing on cardiac anomalies. Future larger-scale or multi-center studies may help establish clearer estimates of these associations.

Mechanistic Perspectives and Biological Plausibility

Biological plausibility underpins many of our observed associations:

1. **Metabolic Dysregulation**: Hyperglycemia, hyperlipidemia, and insulin resistance can all disrupt fetal development.
2. **Vascular Dysfunction**: Chronic hypertension contributes to impaired placental perfusion and potential fetal hypoxia, impacting normal cardiac morphogenesis.
3. **Genetic and Epigenetic Factors**: Family history of CHD highlights potential shared genetic variants or epigenetic modifications across siblings.
4. **Immunologic and Hormonal Imbalances**: Autoimmune disorders and thyroid dysfunction may alter cytokine levels, hormone availability, and the maternal–fetal interface, influencing embryonic heart tissue growth.

Strengths and Limitations

Strengths of our design include the prospective capture of neonatal data, standardized echocardiographic diagnoses, and robust documentation of maternal risk factors. Consecutive sampling minimized selection bias, while double data entry and cross-checking with original medical charts enhanced data reliability. The relatively large sample size for a single-center study allowed us to examine multiple risk factors simultaneously.

However, several **limitations** should be emphasized. First, as a **cross-sectional** study, a definitive causal link cannot be drawn. The temporality issue—whether maternal conditions preceded or followed early fetal cardiac formation—remains unclear. Second, certain variables, such as maternal smoking status, use of specific medications, environmental exposures, and detailed glycemic control measures, were not included in our analysis, which could introduce unmeasured confounding. Third,

recall bias may have affected self-reported maternal conditions. Fourth, our findings, based on a single, urban tertiary care hospital, may not be generalizable to rural settings or less specialized hospitals.

Clinical and Public Health Implications

The identification of modifiable maternal risk factors—namely hypertension and DM—underscores the critical importance of **preconception care** and **early pregnancy interventions**. Providing education on optimum blood pressure and glycemic control, ensuring close medical follow-up, and integrating routine screening for thyroid function in high-risk women could collectively help mitigate the incidence and severity of congenital heart anomalies. Furthermore, for women with a family history of CHD, genetic counseling and fetal echocardiograms scheduled during the late first or early second trimester can facilitate prompt detection of structural heart defects.

From a **public health** standpoint, these findings suggest that strategies aimed at reducing maternal obesity, improving metabolic health, and ensuring access to antenatal care could have downstream benefits in lowering the incidence of congenital heart disease. Targeted interventions may be particularly effective in resource-limited settings, where pregnant women with underlying chronic conditions might lack systematic monitoring and consistent treatment.

Future Directions

Given the complexity of maternal–fetal interactions, **longitudinal cohort studies** that follow women from preconception or early pregnancy through delivery—and ideally into the neonatal period—are needed to confirm these associations and infer temporality. Further research might incorporate:

1. **Genetic and epigenetic analyses** to delineate heritable risks.
2. **Detailed pharmacologic data** to assess whether certain antihypertensive or antidiabetic therapies influence CHD risk differently.
3. **Environmental exposure assessments** (e.g., pollutants, toxins) to evaluate a broader range of teratogenic contributors.
4. **Interventional studies** testing whether enhanced prenatal care protocols or intensified chronic disease management can reduce CHD incidence.

6. Conclusion

In summary, our study highlights significant associations between maternal hypertension, diabetes mellitus, and a family history of congenital heart disease with the occurrence of CHD in neonates. The interplay among genetic predisposition, chronic inflammation, metabolic factors, and vascular compromise likely underpins these relationships. While future prospective studies are necessary to elucidate causality, our findings reinforce the critical role of optimized maternal health both before and during pregnancy to reduce the burden of congenital heart disease in newborns.

References

1. van der Linde D, Konings EE, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;58(21):2241-2247. [DOI] [PubMed] [Google Scholar]
2. Liu Y, Chen S, Zühlke L, et al. Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019;48(2):455-463. [DOI] [PMC free article] [PubMed] [Google Scholar]
3. Soares C, Vieira RJ, Costa S, Moita R, Andrade M, Guimarães H. Neurodevelopment outcomes in the first 5 years of the life of children with transposition of the great arteries surgically corrected in the neonatal period: systematic review and meta-analysis. Cardiol Young. 2023;33(12):2471-2480. [DOI] [PubMed] [Google Scholar]

4. Baumgartner H, De Backer J, Babu-Narayan SV, et al. 2020 ESC guidelines for the management of adult congenital heart disease. Eur Heart J. 2021;42(6):563-645. [DOI] [PubMed] [Google Scholar]
5. Egidy Assenza G, Krieger EV, Baumgartner H, et al. AHA/ACC vs ESC guidelines for management of adults with congenital heart disease: jACC guideline comparison. J Am Coll Cardiol. 2021;78(19):1904-1918. [DOI] [PubMed] [Google Scholar]
6. Zhao L, Chen L, Yang T, et al. Parental smoking and the risk of congenital heart defects in offspring: an updated meta-analysis of observational studies. Eur J Prev Cardiol. 2020;27(12):1284-1293. [DOI] [PubMed] [Google Scholar]
7. Zhang S, Wang L, Yang T, et al. Parental alcohol consumption and the risk of congenital heart diseases in offspring: an updated systematic review and meta-analysis. Eur J Prev Cardiol. 2020;27(4):410-421. [DOI] [PubMed] [Google Scholar]
8. Han F, Yang B, Chen Y, et al. Loss of GLTSCR1 causes congenital heart defects by regulating NPPA transcription. Angiogenesis. 2023;26(2):217-232. [DOI] [PMC free article] [PubMed] [Google Scholar]
9. Williams K, Carson J, Lo C. Genetics of congenital heart disease. Biomolecules. 2019;9(12):879. [DOI] [PMC free article] [PubMed] [Google Scholar]
10. Diller GP, Kempny A, Alonso-Gonzalez R, et al. Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary centre. Circulation. 2015;132(22):2118-2125. [DOI] [PubMed] [Google Scholar]
11. Massarella D, Alonso-Gonzalez R. Updates in the management of congenital heart disease in adult patients. Expert Rev Cardiovasc Ther. 2022;20(9):719-732. [DOI] [PubMed] [Google Scholar]
12. Khairy P, Silka MJ, Moore JP, et al. Sudden cardiac death in congenital heart disease. Eur Heart J. 2022;43(22):2103-2115. [DOI] [PubMed] [Google Scholar]
13. Somerville J. Grown-up congenital heart disease-medical demands look back, look forward 2000. Thorac Cardiovasc Surg. 2001;49(1):21-26. [DOI] [PubMed] [Google Scholar]
14. Homma S, Messé SR, Rundek T, et al. Patent foramen ovale. Nat Rev Dis Primers. 2016;2:15086. [DOI] [PubMed] [Google Scholar]
15. Calvert PA, Rana BS, Kydd AC, Shapiro LM. Patent foramen ovale: anatomy, outcomes, and closure. Nat Rev Cardiol. 2011;8(3):148-160. [DOI] [PubMed] [Google Scholar]
16. van Vonderen JJ, Roest AA, Siew ML, Walther FJ, Hooper SB, te Pas AB. Measuring physiological changes during the transition to life after birth. Neonatology. 2014;105(3):230-242. [DOI] [PubMed] [Google Scholar]
17. Sun YP, Homma S. Patent foramen ovale and stroke. Circ J. 2016;80(8):1665-1673. [DOI] [PubMed] [Google Scholar]
18. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59(1):17-20. [DOI] [PubMed] [Google Scholar]
19. Rodriguez CJ, Homma S, Sacco RL, Di Tullio MR, Sciacca RR, Mohr JP. Race-ethnic differences in patent foramen ovale, atrial septal aneurysm, and right atrial anatomy among ischemic stroke patients. Stroke. 2003;34(9):2097-2102. [DOI] [PubMed] [Google Scholar]

20. Kuramoto J, Kawamura A, Dembo T, Kimura T, Fukuda K, Okada Y. Prevalence of patent foramen ovale in the Japanese population-autopsy study. Circ J. 2015;79(9):2038-2042. [DOI] [PubMed] [Google Scholar]
21. Meier B, Frank B, Wahl A, Diener HC. Secondary stroke prevention: patent foramen ovale, aortic plaque, and carotid stenosis. Eur Heart J. 2012;33(6):705-713. 713a, 713b. [DOI] [PMC free article] [PubMed] [Google Scholar]
22. Zhang HL, Liu ZH, Luo Q, Wang Y, Zhao ZH, Xiong CM. Paradoxical embolism: experiences from a single center. Chronic Dis Transl Med. 2017;3(2):123-128. [DOI] [PMC free article] [PubMed] [Google Scholar]
23. d'Audiffret A, Shenoy SS, Ricotta JJ, Dryjski M. The role of thrombolytic therapy in the management of paradoxical embolism. Cardiovasc Surg. 1998;6(3):302-306. [DOI] [PubMed] [Google Scholar]
24. Ren W, Huang H, Hu H. Optical coherence tomography imaging evidence of thrombus inside the tunnel of patent foramen ovale. Eur Heart J. 2022;43(39):3982. [DOI] [PMC free article] [PubMed] [Google Scholar]
25. Miranda B, Fonseca AC, Ferro JM. Patent foramen ovale and stroke. J Neurol. 2018;265(8):1943-1949. [DOI] [PubMed] [Google Scholar]
26. Yan C, Li H. Preliminary investigation of In situ thrombus within patent foramen ovale in patients with and without stroke. JAMA. 2021;325(20):2116-2118. [DOI] [PMC free article] [PubMed] [Google Scholar]
27. Liu X, Sun C, An G, Cao L, Meng X. Case report: hypereosinophilic syndrome vs. patent foramen ovale as etiopathogenetic contributors to stroke. Front Cardiovasc Med. 2023;10:1298063. [DOI] [PMC free article] [PubMed] [Google Scholar]
28. Rigatelli G, Giordan M, Braggion G, et al. Incidence of extracerebral paradoxical embolisms in patients with intracardiac shunts. Cardiovasc Revasc Med. 2007;8(4):248-250. [DOI] [PubMed] [Google Scholar]
29. Dao CN, Tobis JM. PFO and paradoxical embolism producing events other than stroke. Catheter Cardiovasc Interv. 2011;77(6):903-909. [DOI] [PubMed] [Google Scholar]
30. Doufekias E, Segal AZ, Kizer JR. Cardiogenic and aortogenic brain embolism. J Am Coll Cardiol. 2008;51(11):1049-1059. [DOI] [PubMed] [Google Scholar]
31. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics-2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2007;115(5):e69-e171. [DOI] [PubMed] [Google Scholar]
32. Cramer SC, Maki JH, Waitches GM, et al. Paradoxical emboli from calf and pelvic veins in cryptogenic stroke. J Neuroimaging. 2003;13(3):218-223. [PubMed] [Google Scholar]
33. Cramer SC, Rordorf G, Maki JH, et al. Increased pelvic vein thrombi in cryptogenic stroke: results of the Paradoxical Emboli from Large Veins in Ischemic Stroke (PELVIS) study. Stroke. 2004;35(1):46-50. [DOI] [PubMed] [Google Scholar]
34. Leppert MH, Poisson SN, Carroll JD, et al. Cost-effectiveness of patent foramen ovale closure versus medical therapy for secondary stroke prevention. Stroke. 2018;49(6):1443-1450. [DOI] [PMC free article] [PubMed] [Google Scholar]
35. Mojadidi MK, Zaman MO, Elgendy IY, et al. Cryptogenic stroke and patent foramen ovale. J Am Coll Cardiol. 2018;71(9):1035-1043. [DOI] [PubMed] [Google Scholar]

36. Elgendy AY, Saver JL, Amin Z, et al. Proposal for updated nomenclature and classification of potential causative mechanism in patent foramen ovale-associated stroke. JAMA Neurol. 2020;77(7):878-886. [DOI] [PubMed] [Google Scholar]

37. Handke M, Harloff A, Olschewski M, Hetzel A, Geibel A. Patent foramen ovale and cryptogenic stroke in older patients. N Engl J Med. 2007;357(22):2262-2268. [DOI] [PubMed] [Google Scholar]

38. Meissner I, Khandheria BK, Heit JA, et al. Patent foramen ovale: innocent or guilty? Evidence from a prospective population-based study. J Am Coll Cardiol. 2006;47(2):440-445. [DOI] [PubMed] [Google Scholar]

39. Di Tullio MR, Sacco RL, Sciacca RR, Jin Z, Homma S. Patent foramen ovale and the risk of ischemic stroke in a multiethnic population. J Am Coll Cardiol. 2007;49(7):797-802. [DOI] [PubMed] [Google Scholar]

40. Steiner MM, Di Tullio MR, Rundek T, et al. Patent foramen ovale size and embolic brain imaging findings among patients with ischemic stroke. Stroke. 1998;29(5):944-948. [DOI] [PubMed] [Google Scholar]

41. Wessler BS, Thaler DE, Ruthazer R, et al. Transesophageal echocardiography in cryptogenic stroke and patent foramen ovale: analysis of putative high-risk features from the risk of paradoxical embolism database. Circ Cardiovasc Imaging. 2014;7(1):125-131. [DOI] [PMC free article] [PubMed] [Google Scholar]

42. Agarwal S, Bajaj NS, Kumbhani DJ, Tuzcu EM, Kapadia SR. Meta-analysis of transcatheter closure versus medical therapy for patent foramen ovale in prevention of recurrent neurological events after presumed paradoxical embolism. JACC Cardiovasc Interv. 2012;5(7):777-789. [DOI] [PubMed] [Google Scholar]

43. Sanapo L, Donofrio MT, Ahmadzia HK, Gimovsky AC, Mohamed MA. The association of maternal hypertensive disorders with neonatal congenital heart disease: analysis of a United States cohort. J Perinatol. 2020 Nov;40(11):1720-1727.

44. Turc G, Lee JY, Brochet E, Kim JS, Song JK, Mas JL. Atrial septal aneurysm, shunt size, and recurrent stroke risk in patients with patent foramen ovale. J Am Coll Cardiol. 2020;75(18):2312-2320. [DOI] [PubMed] [Google Scholar]

45. Liu Y, et al. Maternal Gestational Diabetes Mellitus and Congenital Heart Disease in Offspring: A Meta-Analysis. Horm Metab Res. 2024 Aug;

46. Rigatelli G, Aggio S, Cardaioli P, et al. Left atrial dysfunction in patients with patent foramen ovale and atrial septal aneurysm: an alternative concurrent mechanism for arterial embolism? JACC Cardiovasc Interv. 2009;2(7):655-662. [DOI] [PubMed] [Google Scholar]

47. Postma AV, Bezzina CR, Christoffels VM. Genetics of congenital heart disease: the contribution of the noncoding regulatory genome. J Hum Genet. 2016;61(1):13-19. doi: 10.1038/jhg.2015.98.

48. Grattan MJ, et al. Maternal hypothyroidism may be associated with CHD in offspring. Cardiol Young. 2015 Oct;25(7)