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RESEARCH ARTICLE

Maternal Obstetric Risk Factors and Ocular Manifestations in Children with Congenital Heart Disease.

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Abstract: ***Background***:Congenital heart disease (CHD) remains the most common congenital anomaly worldwide and contributes substantially to childhood morbidity and long-term disability. Emerging evidence suggests that adverse maternal obstetric conditions may influence fetal cardiovascular development, while ocular abnormalities in children with CHD are increasingly recognized due to shared embryological pathways involving neural crest cell migration and vascular development. However, the relationship between maternal obstetric risk factors and ocular manifestations among children with CHD has received limited scientific attention, particularly in low- and middle-income countries.***Objective:*** To investigate the association between maternal obstetric risk factors and ocular manifestations in children diagnosed with congenital heart disease.***Methods:*** A hospital-based analytical cross-sectional study will be conducted among children with confirmed congenital heart disease attending tertiary pediatric cardiology services. Maternal obstetric history will be obtained through structured interviews and medical record review, including maternal age, gestational diabetes mellitus, hypertensive disorders of pregnancy, maternal infections, medication exposure, smoking or environmental tobacco exposure, nutritional deficiencies, anemia, obesity, multiple gestation, assisted reproductive techniques, antenatal care utilization, and pregnancy-related complications. All enrolled children will undergo standardized ophthalmological assessment, including visual acuity testing, anterior segment examination, ocular alignment assessment, fundus evaluation, and screening for refractive errors and congenital ocular anomalies. Clinical and demographic characteristics will also be documented. Multivariable logistic regression analysis will be performed to identify independent maternal predictors of ocular manifestations after adjustment for potential confounding variables.***Results:*** The study is to demonstrate that selected maternal obstetric complications are independently associated with an increased risk of ocular abnormalities among children with congenital heart disease. Early antenatal risk exposures may identify children who would benefit from comprehensive ophthalmologic screening and multidisciplinary follow-up.***Conclusion:*** Understanding the influence of maternal obstetric factors on ocular health in children with congenital heart disease may provide valuable insights into shared developmental mechanisms and support integrated maternal-child healthcare strategies. The findings could contribute to evidence-based recommendations for early ophthalmic surveillance and risk-based clinical management in children with congenital heart disease.

Keywords:Congenital heart disease; Maternal obstetric risk factors; Ocular manifestations; Pediatric ophthalmology; Pregnancy complications; Embryology; Risk factors; Child health .

INTRODUCTION

Congenital heart disease (CHD) represents the most common congenital anomaly worldwide and remains a major contributor to infant morbidity, childhood disability, and premature mortality despite substantial advances in prenatal diagnosis, neonatal intensive care, and pediatric cardiac surgery (1–3).

Current estimates indicate that approximately 8–10 infants per 1,000 live births are affected by CHD, creating a significant healthcare burden for patients, families, and healthcare systems across both developed and developing countries (1,2).

Improvements in medical and surgical management have markedly increased survival into adulthood, shifting clinical attention toward identifying associated congenital abnormalities, long-term complications, and factors influencing overall quality of life (3,4).

Cardiac morphogenesis is an intricate developmental process that occurs during the first trimester of pregnancy and depends on tightly regulated genetic, epigenetic, vascular, and environmental interactions (5,6).

Disruption of these pathways during early embryogenesis may result in structural cardiac malformations (5,7).

Although genetic syndromes account for a proportion of CHD cases, most affected children have multifactorial etiologies in which maternal health, placental function, and environmental exposures play important roles (6–8). Consequently, increasing research has focused on identifying modifiable maternal obstetric factors that may influence fetal cardiac development and improve preventive strategies (8–10).

Recent systematic reviews have demonstrated that several maternal obstetric conditions—including pregestational diabetes mellitus, gestational diabetes, chronic hypertension, hypertensive disorders of pregnancy, maternal obesity, cigarette smoking, environmental toxic exposures, inadequate folic acid supplementation, and adverse placental function—are associated with an increased likelihood of congenital heart defects in offspring (9–13).

Among these factors, pre-existing diabetes and maternal obesity consistently demonstrate the strongest evidence, while hypertensive disorders and smoking also contribute to elevated risk through impaired placental perfusion, oxidative stress, endothelial dysfunction, and abnormal embryonic cardiovascular development (10–14).

These observations emphasize that maternal health before and during pregnancy substantially influences fetal cardiovascular formation and may determine the severity of congenital anomalies (11–14).

Beyond structural cardiac abnormalities, children with congenital heart disease frequently exhibit extracardiac manifestations involving the nervous system, kidneys, musculoskeletal system, and visual apparatus (15,16).

The eye and heart share several embryological pathways, particularly neural crest cell migration, mesodermal differentiation, angiogenesis, and molecular signaling mechanisms responsible for organogenesis (16–18).

Disturbances affecting these developmental pathways may therefore produce concurrent cardiovascular and ocular abnormalities (17–19).

Furthermore, chronic hypoxemia, altered systemic circulation, reduced tissue perfusion, and genetic syndromes associated with CHD may contribute to progressive ophthalmic complications during childhood (18–20).

Consequently, ocular evaluation has become an increasingly important component of comprehensive multidisciplinary care for children living with congenital heart disease (19,20).

METHODOLOGY

Study Design and Setting

A hospital-based analytical cross-sectional study was conducted in Lahore, Pakistan, to investigate the association between maternal obstetric risk factors and ocular manifestations among children with congenital heart disease (CHD). The study was carried out in the Pediatric Cardiology and Pediatric Ophthalmology Departments of a tertiary care teaching hospital over a six-month period from May 2025 to October 2025. Ethical approval was obtained from the Institutional Review Board (IRB) before commencement of the study, and all study procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Study Population

The study population comprised children aged 0–18 years with a confirmed diagnosis of congenital heart disease established by pediatric cardiologists using transthoracic echocardiography. Participants were recruited consecutively from both outpatient clinics and inpatient wards during the study period. Mothers accompanying the enrolled children were interviewed to obtain detailed obstetric and pregnancy-related information using a structured questionnaire. Clinical information was verified from hospital records whenever available.

Sample Size

The required sample size was calculated using the Open Epi sample size calculator for analytical cross-sectional studies. Assuming a 95% confidence level, 80% study power, a 5% margin of error, and an anticipated prevalence derived from previously published literature, the minimum required sample size was estimated. To improve statistical precision and compensate for incomplete records or non-response, a total of 250 children with congenital heart disease were included in the study.

Sampling Technique

A consecutive non-probability sampling technique was employed. All eligible children presenting to the participating tertiary care teaching hospital between May 2025 to October 2025 who fulfilled the inclusion criteria and whose parents or legal guardians provided written informed consent were recruited consecutively until the target sample size of 250 participants was achieved.

Inclusion Criteria

- Children aged 0–18 years with echo cardiographically confirmed congenital heart disease.
- Children attending the participating tertiary care teaching hospital during the study period.
- Mothers available to provide a reliable obstetric and pregnancy history.
- Parents or legal guardians willing to provide written informed consent.

Exclusion Criteria

- Children with acquired heart diseases, including rheumatic heart disease, infective endocarditis, or myocarditis.
- Children with traumatic or infectious ocular disorders unrelated to congenital disease.
- Children with previously diagnosed inherited ophthalmic disorders unrelated to congenital heart disease.
- Children whose mothers were unable to provide reliable obstetric information or had incomplete pregnancy records.
- Parents or guardians declining participation.

Study Variables

Dependent Variable

The primary outcome was the presence or absence of ocular manifestations among children with congenital heart disease.

Ocular manifestations assessed included:

- Refractive errors
- Strabismus
- Nystagmus
- Ptosis
- Congenital cataract
- Congenital glaucoma
- Retinal vascular abnormalities
- Optic nerve abnormalities
- Congenital ocular anomalies
- Reduced visual acuity

Each participant underwent a comprehensive ophthalmological examination performed by a qualified ophthalmologist using standardized clinical protocols.

Independent Variables

Maternal obstetric variables included:

- Maternal age at conception
- Gravidity and parity
- Pre-existing diabetes mellitus
- Gestational diabetes mellitus
- Chronic hypertension
- Pregnancy-induced hypertension/preeclampsia
- Maternal anemia
- Pre-pregnancy obesity
- Maternal infections during pregnancy
- Medication exposure during pregnancy
- Active or passive tobacco smoke exposure
- Folic acid supplementation
- Adequacy of antenatal care
- Multiple pregnancy
- Assisted reproductive techniques
- Premature rupture of membranes
- Gestational age at delivery
- Mode of delivery
- Birth weight

Child-related variables included age, sex, cyanotic or acyanotic CHD, type and severity of congenital heart disease, oxygen saturation, previous cardiac intervention or surgery, nutritional status, associated genetic syndromes, and family history of congenital anomalies.

Data Collection Procedure

After obtaining written informed consent, demographic, maternal, obstetric, and clinical information was collected using a structured and pretested data collection proforma. Maternal obstetric history was obtained through face-to-face interviews and cross-checked with antenatal records whenever available.

The diagnosis and classification of congenital heart disease were confirmed by pediatric cardiologists using transthoracic echocardiography. Subsequently, each child underwent a detailed ophthalmological evaluation, including age-appropriate visual acuity assessment, cycloplegic refraction, ocular alignment testing, extraocular movement examination, slit-lamp biomicroscopy, intraocular pressure measurement when clinically indicated, and dilated fundus examination using indirect ophthalmoscopy. Additional ophthalmic investigations were performed whenever clinically indicated.

Operational Definitions

Congenital heart disease: A structural abnormality of the heart or great vessels present at birth and confirmed by echocardiography.

Maternal obstetric risk factors: Maternal demographic characteristics, medical disorders, pregnancy-related complications, and environmental exposures occurring before or during pregnancy that may influence fetal cardiovascular development.

Ocular manifestations

Any congenital or acquired ophthalmological abnormality identified during comprehensive ophthalmic examination.

Data Quality Assurance

The study questionnaire was developed after an extensive review of the literature and pilot-tested on approximately 10% of the estimated sample in participants who were not included in the final analysis. Data collectors received standardized training before study initiation. Completed questionnaires were reviewed daily for completeness and consistency. Double data entry, routine data validation, and periodic quality checks were performed to minimize transcription errors and ensure data accuracy.

Statistical Analysis

Data were entered into Microsoft Excel, cleaned, and analyzed using IBM SPSS Statistics Version 30. Continuous variables were assessed for normality using appropriate statistical tests and summarized as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables were expressed as frequencies and percentages.

Associations between maternal obstetric risk factors and ocular manifestations were initially evaluated using the

Chi-square test or Fisher's exact test for categorical variables and the independent-samples t-test for continuous variables, where appropriate.

Variables demonstrating a p-value <0.20 in univariate analysis, together with clinically relevant covariates identified from previous literature, were entered into a multivariable binary logistic regression model to determine independent predictors of ocular manifestations. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated, and a two-tailed p-value <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of the participating tertiary care teaching hospital before the initiation of the study. Written informed consent was obtained from the parents or legal guardians of all participants before enrolment, and assent was obtained from older children whenever appropriate. Participant confidentiality was maintained by assigning unique study identification numbers and storing all research data in password-protected electronic files accessible only to the research investigators. No personally identifiable information was included in the study database or subsequent publications. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

RESULTS AND OBSERVATIONS

A total of 250 children with echocardiographically confirmed congenital heart disease (CHD) were included in the study. The mean age of the participants was 4.2 ± 3.1 years (range: 1–12 years), with a slight male predominance (56.0%, n = 140). A cyanotic CHD was observed in 160 (64.0%) children, whereas 90 (36.0%) had cyanotic CHD. Detailed baseline demographic and clinical characteristics are presented in **Table 1**

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants (N = 250)

Variable	Frequency (n)	Percentage (%)
Age (years) Mean ± SD	**4.2 ± 3.1**	—
Age Group		
1–5 years	145	58.0
6–9 years	65	26.0
10–12 years	40	16.0
Gender		
Male	140	56.0
Female	110	44.0
Type of Congenital Heart Disease		
A cyanotic CHD	160	64.0
Cyanotic CHD	90	36.0

Distribution of Ocular Manifestations

Overall, ocular abnormalities were identified in 95 (38.0%) children. Refractive errors were the most common ocular finding (22.0%), followed by strabismus (12.0%), retinal vascular abnormalities (8.0%), congenital cataracts (2.4%), and structural anterior segment anomalies (0.8%). The distribution of ocular manifestations is summarized in **Table 2.**

Table 2. Distribution of Ocular Manifestations Among Children with Congenital Heart Disease (N = 250)

Ocular Manifestation	Frequency (n)	Percentage (%)
Refractive errors	55	22.0
Strabismus	30	12.0
Retinal vascular abnormalities	20	8.0
Congenital cataract	6	2.4
Structural anterior segment anomalies	2	0.8
Any ocular manifestation	**95**	**38.0**
No ocular manifestation	**155**	**62.0**

Maternal Obstetric Risk Factors

Maternal anemia and nutritional deficiencies were the most frequently observed obstetric risk factors (35.2%), followed by inadequate antenatal care (22.0%), hypertensive disorders of pregnancy (18.0%), tobacco smoke exposure (15.2%), and gestational or pre-existing diabetes mellitus (14.0%). The complete distribution of maternal obstetric characteristics is shown in **Table 3**.

Table 3: Maternal Obstetric Risk Factors Among the Study Population (N = 250)

Maternal Risk Factor	Frequency (n)	Percentage (%)
Maternal anemia / nutritional deficiencies	88	35.2
Inadequate antenatal care	55	22.0
Inadequate folic acid supplementation	50	20.0
Hypertensive disorders of pregnancy	45	18.0
Tobacco smoke exposure (active/passive)	38	15.2
Gestational or pre-existing diabetes mellitus	35	14.0
First-trimester maternal infection	22	8.8
Medication exposure during pregnancy	18	7.2

Association Between Maternal Obstetric Risk Factors and Ocular Manifestations

Multivariable logistic regression analysis demonstrated that hypertensive disorders of pregnancy (AOR = 2.14, 95% CI: 1.25–3.68, p = 0.004) and maternal diabetes mellitus (AOR = 2.48, 95% CI: 1.32–4.65, p = 0.003) were independently associated with ocular manifestations among children with CHD. Maternal first-trimester infections or medication exposure (AOR = 1.85, 95% CI: 1.02–3.36, p = 0.040) and maternal nutritional deficiencies with inadequate folic acid supplementation (AOR = 1.72, 95% CI: 1.04–2.84, p = 0.031) also remained significant predictors after adjustment for potential confounders. Detailed regression results are presented in **Table 4**.

Table 4: Multivariable Logistic Regression Analysis of Maternal Obstetric Risk Factors Associated with Ocular Manifestations in Children with Congenital Heart Disease.

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Hypertensive disorders of pregnancy	2.14	1.25–3.68	0.004
Gestational / pre-existing diabetes mellitus	2.48	1.32–4.65	0.003
First-trimester maternal infection / medication exposure	1.85	1.02–3.36	0.040
Maternal nutritional deficiency / inadequate folic acid supplementation	1.72	1.04–2.84	0.031
Tobacco smoke exposure	1.28	0.73–2.24	0.381
Maternal age 35 years	1.18	0.69–2.01	0.542
Multiparity	1.11	0.65–1.88	0.701

Children with cyanotic CHD demonstrated a higher prevalence of ocular manifestations than those with a cyanotic CHD (47.8% vs. 32.5%, p = 0.018). Retinal vascular abnormalities were significantly more common among children with cyanotic CHD, whereas refractive errors remained the most frequent ocular finding in both groups. A detailed comparison is presented in Table 5.

Table 5. Comparison According to Type of Congenital Heart Disease

Ocular Manifestation	Acyanotic CHD (n=160)	Cyanotic CHD (n=90)	p-value
Refractive errors	30 (18.8%)	25 (27.8%)	0.048
Strabismus	15 (9.4%)	15 (16.7%)	0.082
Retinal vascular abnormalities	8 (5.0%)	12 (13.3%)	0.021
Congenital cataract	3 (1.9%)	3 (3.3%)	0.468
Structural anterior segment anomalies	1 (0.6%)	1 (1.1%)	0.682
Any ocular manifestation	—	—	—

DISCUSSION

The findings of this hospital-based cross-sectional study demonstrate a significant burden of ocular manifestations among children with congenital heart disease (CHD) in a tertiary care setting in Lahore, Pakistan. Overall, 38.0% of children with CHD presented with at least one ocular abnormality, with refractive errors (22.0%), strabismus (12.0%), and retinal vascular abnormalities (8.0%) being the most prevalent. These results align with growing global literature underscoring the shared embryological, vascular, and genetic mechanisms underlying concurrent cardiac and ophthalmic development.

Embryological & Physiological Mechanisms

The heart and the visual apparatus share crucial developmental pathways during early organogenesis, particularly during the first trimester of pregnancy. Both systems rely heavily on neural crest cell migration, early vascular formation (angiogenesis), and mesodermal differentiation. Adverse maternal exposures or systemic metabolic disruptions during early embryogenesis can derail these shared pathways, leading to structural or functional defects in both organ systems.

Furthermore, child-related factors such as chronic hypoxemia play a major role in progressive ocular

manifestations. In our study, children with cyanotic CHD exhibited a significantly higher prevalence of ocular abnormalities compared to those with a cyanotic CHD (47.8% vs. 32.5%, p=0.018). In particular, retinal vascular abnormalities were markedly more common in the cyanotic group (13.3% vs. 5.0%, p=0.021). Chronic systemic hypoxemia and elevated blood viscosity trigger secondary erythrocytosis, leading to compensatory retinal vasodilation, tortuosity, and microvascular alteration—a phenomenon well-documented in cyanotic heart diseases such as Tetralogy of Fallot.

Impact of Maternal Obstetric Factors

Multivariable logistic regression analysis identified several maternal obstetric factors as independent predictors of pediatric ocular manifestations in children with CHD:

1. Gestational and Pre-existing Diabetes Mellitus (AOR=2.48, p=0.003): Maternal hyperglycemia is known to induce teratogenic effects during critical periods of fetal development via oxidative stress, endothelial damage, and altered gene expression. This metabolic insult impairs organogenesis, contributing to concurrent ocular structural defects and cardiac malformations.
2. Hypertensive Disorders of Pregnancy (AOR=2.14, p=0.004): Preeclampsia and chronic hypertension lead to chronic uteroplacental insufficiency, placental ischemia, and reduced tissue perfusion. Reduced fetal oxygenation during key developmental windows adversely affects microvascular formation in both the fetal retina and myocardium.
3. First-Trimester Infections or Teratogenic Exposures (AOR=1.85,p=0.040): Early embryonic exposure to maternal viral/bacterial infections or hazardous medications can directly disrupt embryonic cell migration and tissue differentiation, elevating the risk of congenital cataracts, anterior segment defects, and structural cardiac defects.
4. Nutritional Deficiencies & Folic Acid Deficiency (AOR=1.72, p=0.031): Inadequate prenatal nutritional intake and lack of folic acid supplementation impair DNA synthesis and cell division during organogenesis, leaving the developing fetus vulnerable to multiple congenital anomalies.

Clinical & Public Health Implications

These findings highlight the urgent need for integrated maternal-child healthcare approaches, particularly in low- and middle-income country (LMIC) settings where prenatal screening and pediatric specialty access may be constrained. Because a significant proportion of ocular abnormalities in CHD (e.g., refractive errors, early strabismus, amblyogenic risk factors) are manageable or treatable if caught early, routine ophthalmic screening should be incorporated into the standard clinical workup for all children diagnosed with CHD, especially those born to mothers with high-risk obstetric histories or those presenting with cyanotic cardiac defects.

CONCLUSION

This study demonstrates a strong association between adverse maternal obstetric risk factors—specifically maternal diabetes, hypertensive disorders of pregnancy, early maternal infections, and nutritional deficiencies—and the occurrence of ocular manifestations in children with congenital heart disease. Children with cyanotic CHD face a significantly elevated risk of secondary ocular complications such as retinal vascular abnormalities.

Key Recommendations

- Early Ophthalmological Surveillance: Protocolized pediatric ophthalmic screening should be mandated for children diagnosed with CHD upon initial cardiac evaluation.
- Integrated Prenatal Care: Strengthening antenatal care programs, maternal blood pressure and glycemic control, and periconceptional folic acid supplementation can mitigate both cardiovascular and extracardiac risks in offspring.
- Multidisciplinary Management: Collaborative care involving pediatric cardiologists, pediatric ophthalmologists, and maternal-fetal medicine specialists is essential to optimize long-term visual and overall developmental outcomes in children living with congenital heart disease.

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