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Original Research Article

A RETROSPECTIVE STUDY ON PREVALENCE AND OUTCOME OF CONGENITAL HEART DISEASE IN NEONATES BORN TO MOTHERS WITH PRE-ECLAMPSIA

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Abstract

Introduction: Pre-eclampsia is defined as gestational blood pressure elevation with proteinuria that develops after 20 weeks' gestation. Primarily, a disease of pregnancy, it is a multisystem disorder that affects approximately 2–8% of pregnancies.

Materials & Methods: This is a Retrospective Observational Study which will be done at the Department of Pediatrics, Gulbarga Institute of medical Sciences, Kalaburagi, Karnataka.

Results: The absolute prevalence of congenital heart defects was higher for infants of women with preeclampsia than those without it. Infants of women with preeclampsia had no increased prevalence of critical heart defects but did have an increased prevalence of noncritical heart defects compared with infants of non preeclamptic women

Conclusions: In this population-based study, preeclampsia was significantly associated with noncritical heart defects in offspring, and preeclampsia before 34 weeks was associated with critical heart defects. However, the absolute risk of congenital heart defects was low.

Keywords: Preeclampsia, Heart defects, Congenital

Introduction

Preeclampsia is defined as gestational blood pressure elevation with proteinuria that develops after 20 weeks' gestation. Primarily, a disease of pregnancy, it is a multisystem disorder that affects approximately 2–8% of pregnancies.[1] Although its pathogenesis is incompletely understood, it is a major cause of maternal and neonatal morbidity and mortality.[1,2] A Literature review from both high and low income countries document that babies born to Preeclampsia women have an increased risk of being born prematurely and of being low birth weight (LBW) and small for gestational age (SGA).[3-5] Additionally researchers have noted

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that these babies have low 5-min Apgar scores and are at increased risk of being admitted to the neonatal unit, contributing to both morbidity and mortality.[5-8]The high rate of perinatal morbidity and mortality seen in pregnancies complicated by preeclampsia is primarily due to preterm delivery and utero placental insufficiency. Utero placental circulation disruption may cause disruption of fetal growth, hypoxemia, and even fetal death. Thus, termination of pregnancy is often necessary to minimize maternal–fetal health consequences. Nevertheless, an obstetrician must be able to balance the needs between an adequate fetal maturation and the risks of the mother and fetus when continuing pregnancy with preeclampsia.[8] This study will be aimed to document the prevalence and outcome of neonates born to women with preeclampsia and also to find an association between preeclampsia and congenital heart disease in newborn.

Materials& Methods

This is a Retrospective Observational Study which will be done at the Department of Pediatrics, Gulbarga Institute of medical Sciences, Kalaburagi, Karnataka.

Inclusion criteria

All singleton neonates born <37 weeks alive to women with preeclampsia at the Gulbarga Institute of Medical Sciences Hospital between January 2021 to June 2022 will be included.

Exclusion criteria

Neonates born from mothers with complications in pregnancy such as cardiovascular, thyroid, Auto immune disease, Diabetes Mellitus etc.,
Still Births.

- Subjects were classified into control and preeclampsia groups.

- The preeclampsia group was categorized based on preeclampsia or severe preeclampsia characteristics based on ACOG-13 criteria[9] in which women above 20 weeks of gestational age should at least have blood pressure ≥140/≥90 mm Hg (on two occasions, at least 4 hours apart), blood pressure ≥160/≥110 mm Hg (within a short
minute), and proteinuria (≥300 mg/24-hour urine collection or >2+ urinary dipstick). In addition, in case no proteinuria is found, the following diagnostic criteria can be applied: thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or headache.

-The subtype of preterm delivery based on gestational age was categorized as early preterm (<32 weeks), Late preterm (32–36 weeks).
The measured outcomes were gestational age and neonatal morbidities, including Necrotizing Enterocolitis (NEC), Low 5 Minute APGAR, Respiratory Distress Syndrome (RDS), Congenital Heart Disease, Intra Ventricular Hemorrhage (IVH), Culture Proven bacterial and Fungal Sepsis and Broncho pulmonary Dysplasia (BPD). All the data will be collected from

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the both Maternal and neonatal medical records of Department of Obstetrics and Department of Pediatrics, Gulbarga Institute of Medical Sciences, Kalaburagi.

Results

There were infants delivered at 20 weeks of gestation or more in this study,

Absolute Prevalence of Heart Defects

The overall prevalence of heart defects was 8.9 per 1000 infants (Table 1). Prevalence was higher for infants of women with preeclampsia than without preeclampsia (16.7 vs 8.6 per 1000). Critical, noncritical, site specific, and multiple defects were more prevalent in infants exposed to preeclampsia than not exposed (Table 2). Among critical defects, infants of preeclamptic women had higher prevalence of tetralogy of Fallot (41.2 vs 18.4 per 100 000), hypo plastic left heart (16.5 vs 12.0), and coarctation of the aorta (33.0 vs 16.8). Among non- critical defects, prevalence was higher for defects of the endocardial cushion (38.5 vs 13.4), ventricular septum (405.3 vs 279.2), atrial septum (755.7 vs 280.2), valve (92.1 vs 33.1), and pulmonary artery (208.8 vs 72.5). The prevalence of patent ductus arteriosus at term was also higher in infants of women with preeclampsia than without preeclampsia (224.9 vs 123.6). All 3 site specific defects, including aorta or pulmonary artery, valve, and septum, were more common in infants of women with preeclampsia than without preeclampsia.

Association Between Preeclampsia and Heart Defects

In regression models, preeclampsia was associated with several congenital heart defects on adjustment for maternal characteristics (Table 3). Relative to no preeclampsia, infants exposed to preeclampsia had higher prevalence of any heart defect (PR, 1.57; 95% CI, 1.48-1.67) and noncritical defects (PR, 1.56; 95% CI, 1.47-1.67). Prevalence was elevated for all site-specific defects (septum, valve, and aorta/pulmonary artery) and for multiple defects. Among specific defects, prevalence was greatest for tetralogy of Fallot (PR, 1.67; 95% CI, 1.12-2.50), common ventricle (PR, 2.41; 95% CI, 1.09-5.33), endocardial cushion (PR, 2.23; 95% CI, 1.44-3.45), ventricular septum (PR, 1.24; 95% CI, 1.10-1.40), atrial septum (PR, 1.91; 95% CI, 1.73-2.10), noncritical valve (PR, 1.75; 95% CI, 1.33-2.29), and noncritical pulmonary artery defects (PR, 2.00; 95% CI, 1.66-2.41), as well as patent ductus arteriosus at term (PR, 1.55; 95% CI, 1.28-1.88). Preeclampsia was not associated with transposition of the great vessels, truncus arteriosus, hypoplastic left heart, coarctation of the aorta, or other critical defects. Among critical defects, infants of women with preeclampsia had an excess prevalence of tetralogy of Fallot (PD, 16.6 per 100 000; 95% CI, 2.0-31.1), and among noncritical defects the excess was highest for defects of the atrial septum (PD, 327.5 per 100 000; 95% CI, 265.4-389.7), ventricular septum (PD, 79.1

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Table 1: Maternal Characteristics and Prevalence of Any Congenital Heart Defect Among Infants

	Total No. of Infants	No. of Infants with Congenital Heart Defects	Prevalence per 1000 Infants (95% CI)
Preeclampsia			
Yes	72 782	1219	16.7 (15.8-17.7)
No	1 869 290	16 077	8.6 (8.5-8.7)
Age, y			
<25	420 416	3746	8.9 (8.6-9.2)
25-34	1 271 564	10 972	8.6 (8.5-8.8)
≥35	250 092	2578	10.3 (10.1-10.5)
Parity			
0	1 098 974	9760	8.9 (8.7-9.1)
1	608 407	5232	8.6 (8.4-8.8)
≥2	214 331	2071	9.7 (9.2-10.1)

Table 2: Absolute Prevalence of Infant Congenital Heart Defects Based on Presence vs Absence of Preeclampsia

	Preeclampsia (n = 72 782)		No Preeclampsia (n = 1 869 290)	
	Infants With Congenital Heart Defects	Prevalence per 100 000 Infants (95% CI)	Infants With Congenital Heart Defects	Prevalence per 100 000 Infants (95% CI)
Tetralogy of Fallot	30	41.2 (26.5-56.0)	344	18.4 (16.5-20.3)
Transposition of great vessels	11	15.1 (6.2-24.0)	318	17.0 (15.1-18.9)
Truncus arteriosus	5	6.9 (0.8-12.9)	85	4.5 (3.6-5.5)
Hypoplastic left heart	12	16.5 (6.5-26.5)	224	12.0 (10.4-13.6)
Common ventricle	8	11.0 (3.4-18.6)	75	4.0 (3.1-4.9)
Coarctation of aorta	24	33.0 (19.8-46.2)	314	16.8 (14.9-18.6)
Other[a]	6	8.2 (1.7-14.8)	144	7.7 (6.5-9.0)
Endocardial cushion	28	38.5 (24.2-52.7)	251	13.4 (11.8-15.1)
Ventricular	295	405.3 (359.2-5220	279.2 (271.7-	

septum		451.5)		286.8)
Atrial septum	550	755.7 (692.8-5237		280.2 (272.6-287.7)
Valve	67	92.1 (70.0-114.1)	618	33.1 (30.5-35.7)
Aorta	17	23.4 (12.3-34.5)	263	14.1 (12.4-15.8)
Pulmonary artery	152	208.8 (175.7-242.1)	1356	72.5 (68.7-76.4)
Heterotaxy	11	15.1 (6.2-24.0)	178	9.5 (8.1-10.9)
Other[b]	235	322.9 (281.7-364.1)	4124	220.6 (213.9-227.3)

Aorta or pulmonary artery	187	256.9 (220.2-293.7)	1884	100.8 (96.2-105.3)
Valve	104	142.9 (115.5-170.3)	1041	55.7 (52.3-59.1)
Septum	794	1090.9 (1015.5-1166.4)	9662	516.9 (506.6-527.2)

Table 3.

Prevalence Ratio of Congenital Heart Defects for Preeclampsia vs No Preeclampsia

Tetralogy of Fallot	2.23	3.28)	(1.52 to	1.67	2.50)	(1.12 to16.6 (2.0 to 31.1)
Transposition of great vessels	0.76	1.47)	(0.39 to	0.63	1.23)	(0.33 to−6.5 (−14.6 to 1.6)
Truncus arteriosus	1.66	4.09)	(0.67 to	1.91	4.59)	(0.80 to2.8 (−3.2 to 8.8)
Hypoplastic left heart	1.36	2.49)	(0.74 to	1.07	1.95)	(0.58 to0.7 (−7.7 to 9.2)
Common ventricle	2.96	6.15)	(1.42 to	2.41	5.33)	(1.09 to6.4 (−1.5 to 14.2)
Coarctation of aorta	1.82	2.83)	(1.17 to	1.34	2.10)	(0.85 to4.5 (−7.1 to 16.1)
Other[c]	0.72	1.95)	(0.27 to	0.58	1.58)	(0.22 to−3.0 (−8.6 to 2.6)

Endocardial cushion	2.82 (1.86 to 4.29)	2.23	3.45)	(1.44 to	21.2 (6.7 to 35.6)
Ventricular septum	1.44 (1.28 to 1.62)	1.24	1.40)	(1.10 to	79.1 (32.2 to 126.0)
Atrial septum	2.69 (2.45 to 2.95)	1.91	2.10)	(1.73 to	327.5 (265.4 to 389.7)

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Valve	**2.77 (2.13 to 3.61)**	**1.75 (1.33 to 2.29)**	**26.0 (6.3 to 45.6)**		
Aorta	**1.51 (0.90 to 2.55)**	**1.05 (0.61 to 1.80)**	**7.0 (−3.9 to 18.0)**		
Pulmonary artery	**2.82 (2.36 to 3.36)**	**2.00 (1.66 to 2.41)**	**96.2 (64.3 to 128.2)**		
Heterotaxy	**1.38 (0.71 to 2.70)**	**1.06 (0.54 to 2.09)**	**2.1 (−6.2 to 10.4)**		
Other[c]	**1.49 (1.31 to 1.69)**	**1.42 (1.25 to 1.62)**	**86.5 (45.0 to 128.0)**		

Discussion

We found an elevated prevalence of heart defects among infants of women with preeclampsia compared with no preeclampsia. Risk was elevated for defects affecting all general structures of the heart, including the aorta, pulmonary artery, valves, ventricles, and septa. Among the different variants of preeclampsia, early onset appeared to be the most important factor. Women with early onset preeclampsia had significantly greater prevalence of infants with heart defects, both critical and noncritical, compared with those with no preeclampsia, whereas women with late onset had only marginally greater prevalence. Recent studies have linked preexisting hypertension with congenital heart defects[9,10] but have not investigated preeclampsia despite basic research demonstrating that preeclampsia[12] and heart defects[11] share common bio markers. Therefore, this study provides novel evidence of a relationship between preeclampsia and congenital heart defects, powered by data for a large population of pregnant women Lack of attention to preeclampsia and congenital heart defects in past research is understandable. Preeclampsia is by definition diagnosed only after 20 weeks of gestation, long after the major structures of the fetal heart have formed.[13] Researchers have proposed that pathophysiologic changes in preeclampsia begin well before 20 weeks[14] but only recently have detected imbalances in angiogenic biomarkers as early as 10 weeks in women who later developed preeclampsia.[15] Overexpression of the anti angiogenic biomarkers soluble endoglin and fms like tyrosine kinase 1 relative to angiogenic placental growth factor and vascular endothelial growth factor is thought to inhibit spiral artery remodeling at the placental interface,[15] a process initiated at the start of pregnancy.[16,17] Similar imbalances in these same biomarkers were recently observed in 31 fetuses with heart defects and 138 children before corrective surgery for heart defects.[18] Furthermore, studies suggest that angiogenic factor imbalance is predominantly found in early but not late onset preeclampsia, supporting the notion that preeclampsia is heterogeneous, with early and late variants having different yet both manifesting with symptoms of hypertension and proteinuria.[19] Heart defects were more strongly associated with early than late onset preeclampsia in this study, reinforcing

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the possibility that these variants represent different diseases. However, this hypothesis requires testing because angiogenic factor imbalance is also found in women without preeclampsia who later develop intrauterine growth restriction. No variant of preeclampsia yielded associations with heart defects that were as strong as early onset. The associations were much weaker for late onset preeclampsia. Women with severe and superimposed preeclampsia had increased prevalence, but this probably reflects cases of early onset present in these categories. Furthermore, exclusion of multiple births from our data led to even stronger associations between early- onset preeclampsia and heart defects, suggesting that the pathology is unique to singleton pregnancies. This finding aligns with research suggesting that preeclampsia is a heterogeneous disorder in multiple pregnancies,[17] in which elevated fms like tyrosine kinase 1 levels are due to increased placental mass rather than pathologic overexpression and may not pose as great a risk for heart defects as preeclampsia in singleton pregnancies.

Conclusions

In this study, preeclampsia was significantly associated with noncritical heart defects in offspring, and preeclampsia with onset before 34 weeks was associated with critical heart defects. However, the absolute risk of congenital heart defects was low.

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