International Journal of Contemporary Pediatrics
Subramanian AC et al. Int J Contemp Pediatr. 2023 Jun;10(6):920-924
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20231501

Systematic Review

Outcome of neonates born to mothers with pregnancy induced hypertension/preeclampsia - a systematic review

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Received: 16 April 2023
Revised: 12 May 2023
Accepted: 15 May 2023

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ABSTRACT

Preeclampsia affects 3-10% of pregnancies worldwide. It has significant adverse effect on both the fetus and the neonate. Hence there is a need to study the impact of pregnancy induced hypertension (PIH) on the fetus and the neonate. Databases like PubMed and Cochrane are searched independently by two authors to identify relevant studies. Data were collected for outcomes like birth weight, gestational age, fetal death/stillbirth and intrauterine growth retardation (IUGR). Preeclampsia is associated with significant increase in the incidence of low birth weight (LBW), IUGR and prematurity compared to normotensive women. Also, there is an increased rate of fetal death/ stillbirths in preeclampsia. In addition, there is an increased need for neonatal intensive care unit (NICU) admission in neonates born to PIH mothers. Maternal preeclampsia results in significant adverse effect on the fetus and neonate. There is an increased incidence of stillbirth, LBW, IUGR and preterm deliveries in neonates born to preeclamptic mothers. There is an overall increase in the composite outcomes of neonates of PIH mothers. The objective of the study is to compare the neonatal outcomes of preeclamptic or women with gestational hypertension with that of normotensive women.

Keywords: Preeclampsia, IUGR, Stillbirth, LBW, Stillbirth, NICU

INTRODUCTION

Preeclampsia (PE) is associated with several short term and long-term complications in the baby. This is due to alterations in the maternal and fetal vasculature as well as the placenta. Placental morphological changes include decidual arteriopathy, infarcts and abruption.[1] Fetal testing is required to identify fetuses at risk of death and other short term and long-term complications.

Preeclampsia is a disorder exclusive of pregnant women and affects 3-5% of all pregnancies. It is defined as new-onset hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) and proteinuria of recent onset after 20 weeks of gestation in a previously normotensive patient.[2] Early onset preeclampsia has poor prognosis for neonatal outcomes than late onset preeclampsia.[3] Intrauterine death is an important outcome which is more common in severe preeclampsia than mild preeclampsia. Also, the rate of intrauterine fetal death is higher in low-income countries than high income countries. Rates of premature deliveries is increased due to maternal and fetal risks incurred during continuation of pregnancy.

METHODS

The protocol was registered in the international prospective register of systematic reviews (PROSPERO) database. The review was conducted as per preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines.

Inclusion criteria

Studies which compared women with gestational or pregnancy induced hypertension or preeclampsia with normotensive control women and studies which compared preeclamptic women with eclamptic women were included in the study.

Exclusion criteria

Pregnant women with essential hypertension, chronic renal disease, chronic heart disease and gestational diabetes mellitus were excluded from the study.

Search eligibility and search strategy

In this systematic review, articles are searched in PubMed, Cochrane and google scholar databases. The electronic search strategy used a combination of keywords along with their related medical subjects' headings (MeSH) terms. The results of the study were reported as per PRISMA guidelines. Data regarding outcome measures like birth weight, gestational age, small for gestational age (SGA), IUGR, NICU admission and fetal death/stillbirth are obtained from eligible studies.

Data extraction

Two authors independently searched databases like Pubmed, Cochrane and google scholar for related articles. Study details including year of study, place of study, study and control groups and outcomes reported were represented in Table 1.

Statistical analysis

Statistical analysis was performed using statistical package for the social sciences (SPSS) software. For continuous data, mean and standard deviation are calculated. Unpaired t-test is used to test the significance of difference between the groups. For categorical data, Chi-squared test was used to find the statistical significance. A p value of <0.05 is considered statistically significant.

RESULTS

The search revealed 852 studies, which were screened for eligibility. Of these 10 studies were found eligible. Six studies are case control studies whereas others are retrospective studies. Five studies used normotensive women as controls. There is a significant increase in the rate of low birthweight in babies born to preeclamptic mothers compared to normotensive women (216 [477] versus 66 [771]; p<0.001) (Table 2).

The mean birth weight of babies born to preeclamptic mothers is significantly less compared to normotensive women (Table 3). The rates of premature deliveries are high in babies born to preeclamptic women compared to normotensive women (203 [477] versus 55 [771] p<0.001) (Table 4). The average gestational age was low in infants of preeclamptic mothers than those born to normotensive women (Table 5).

There is also a significant increase in the incidence of stillbirth and IUGR (132 [432] versus 63 [726]; p<0.001) in neonates of PIH mothers compared to normotensive women (Tables 8 and 9). NICU admission rates (157 [419] versus 46 [671]; p<0.001) and composite of adverse outcome scores (233 [363] versus 162 [667]; p<0.001) are high in babies born to preeclamptic mothers. In two of the studies, there is a significant increase in the risk of birth asphyxia.[4,5]

One study compared preeclamptic women with eclampsia.[6] In the study which compared preeclamptic women with eclamptic women, there is no significant difference in birth weight between the two groups.

However, there is a significant increase in premature deliveries in eclamptic mothers. In another study, PIH was compared with gestational hypertension.[7] In this study it was shown that there is a significant decrease in birth weight and increase in prematurity rates and IUGR in infants born to preeclamptic women than infants born to mothers with gestational hypertension.

Table 1: Characteristics of included studies.

Author	Study design	Period of study	Place of study	Study group	Control group	Outcomes
Abadi et al[4]	Cohort study	Feb 2018 - Feb 2019	Ethiopia	Preeclampsia - 260	Normotensive - 522	Low birth weight, prematurity, fetal deaths/stillbirth, APGAR scoring, NICU admission, birth asphyxia, composite of adverse outcomes
Kerri et al[8]	Case control study	Jan 2010 - Aug 2011	Jamaica	Preeclampsia - 114 (52%)	Normotensive - 104 (48%)	Low birth weight, prematurity, fetal deaths/stillbirth, NICU admission
Yilgwan et al[5]	Case control study	Apr 2017 - May 2018	Nigeria	Preeclampsia - 45	Normal pregnancy - 45	Low birth weight, prematurity, fetal deaths/stillbirth, NICU admission, birth asphyxia, composite of adverse outcomes

Continued.

Author	Study design	Period of study	Place of study	Study group	Control group	Outcomes
Katarzyna et al[7]	Case control study	April 2015 to July 2017	Poland	Preeclampsia - 44	Gestational hypertension (n=44)	Low birth weight, prematurity, SGA/IUGR
Lawrence et al[6]	Case control study	Oct 2018 to Nov 2020	Ghana	Eclampsia (121)	Preeclampsia (1097)	Low birth weight, prematurity, SGA/IUGR, composite of adverse outcomes
Ramya et al[9]	Case control study	2020	India	58 (GH, PE, eclampsia)	100 (normotensive women)	Low birth weight, prematurity, SGA/IUGR, composite of adverse outcomes

Table 2: Incidence of low birth weight in preeclampsia versus normotensive women.

Study	Preeclampsia; total number of women (n)	Normotensive women; total number of women (n)	P value
Abadi et al[4]	98 (37.7%); n=260	32 (6.1%); n=522	<0.001
Kerri et al[8]	66 (58%); n=114	6 (6%); n=104	< 0.001
Yilgwan et al[5]	19 (42.2%); n=45	5 (11.1%); n=45	<0.001
Ramya et al[9]	33 (57%); n=58	18 (18%); n=100	<0.001
Total	216 (45%); n=477	61 (8%); n=771	<0.001

Table 3: Average birth weight in preeclampsia versus normotensive women.

Study	Preeclampsia	Normotensive women	P value
Kerri et al[8]	2.2±0.9; n=114	3.2±0.4; n=104	<0.001
Yilgwan et al[5]	2. 508±0.819; n=45	3.015±0.559; n=45	0.004

Table 4: Incidence of prematurity in preeclampsia versus normotensive women.

Study	Preeclampsia; total number of women (n)	Normotensive women; total number of women (n)	P value
Abadi et al[4]	106 (40.8%); n=260	29 (5.6%); n=522	<0.001
Kerri et al[8]	54 (47%); n=114	4(4%); n=104	<0.001
Yilgwan et al[5]	18(40%) ; n=45	5 (11.1%); n=45	0.02
Ramya et al[9]	25 (43%); n=58	17 (17%); n=100	<0.001
Total	203 (49.6%); n=477	55 (7.1%); n=771	<0.001

Table 5: Average gestational age in preeclampsia versus normotensive women.

Study	Preeclampsia	Normotensive women	P value
Kerri et al[8]	35.3±3.7 ; n=114	38.6±1.4; n=104	<0.001
Yilgwan et al[5]	36.8±3.3; n=45	38.6±1.5; n=45	0.004

Table 6: NICU admission rates in preeclampsia versus normotensive women.

Study	Preeclampsia	Normotensive women	P value
Abadi et al[4]	75 (28.8%); n=260	28 (5.4%); n=522	<0.001
Kerri et al[8]	67(59%) ; n=114	13 (13%); n=104	<0.001
Yilgwan et al[5]	15 (33.3%); n=45	5 (11.1%); n=45	0.01
Total	157 (37.4%); n=419	46 (6.8%); n=671	<0.001

Table 7: Composite of adverse outcomes in neonates.

Study	Preeclampsia	Normotensive women	P value
Abadi et al[4]	172 (66.4 %); n=260	115 (22.2%); n=522	<0.001
Yilgwan et al[5]	28 (48.9%); n=45	12 (26.7%); n=45	0.01

Continued.

Study	Preeclampsia	Normotensive women	P value
Ramya et al[9]	33 (57%) ; n=58	35 (35%); n=100	0.007
Total	233 (64.1%); n=363	162 (24.2%); n=667	<0.001

Table 8: Fetal death/stillbirth and neonatal rates in preeclampsia vs normotensive women.

Study	Preeclampsia	Normotensive women	P value
Abadi et al[4]	39 (15%); n= 260	14 (2.7%); n=522	<0.001
Kerri et al[8]	NND 18(28%) prematurity-12, sepsis-3, IVH-1, pneumonia-1, non-immune hydrops-1; n=114	0 (0%); n=104	0.023
Yilgwan et al[5]	NND 6 (13.3%); n=45	0; n=45	<0.001
Total	63; n=419	14; n=671	

Table 9: Small for gestational age/ IUGR rates in preeclampsia versus normotensive women.

Study	Preeclampsia	Normotensive women	P value
Abadi et al[4]	95 (36.7%); n=260	56 (10.7%); n=522	<0.001
Kerri et al[8]	27 (31%); n=114	2 (2%); n=104	<0.001
Ramya et al[9]	10 (18.9%); n=58	5 (5%); n=100	0.01
Total	132 (30.5%); n=432	63 (8.7%); n=726	<0.001

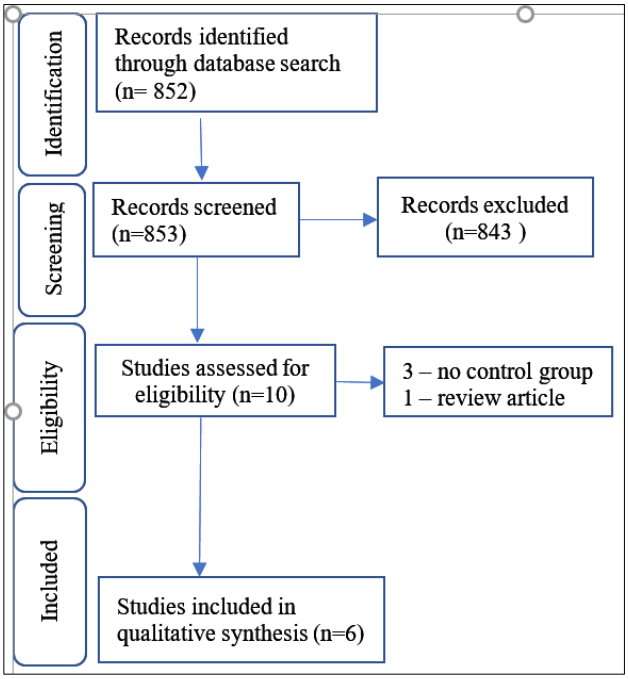

Figure 1: PRISMA flow diagram.

DISCUSSION

The study highlighted that preeclampsia is associated with significant increase in adverse neonatal outcomes than normotensive women. In a cohort study by Verena et al, premature babies born to PE mothers to premature deliveries due to other reasons were compared.[10] It was found that premature babies born to PE mothers had better outcomes than premature deliveries due to other reasons. They found that very low birth weight (VLBW) infants born to PE mothers have lower risk of intracranial hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, and death than those born VLBW due to other reasons.

In a review done by Temitope et al, it was found that preeclampsia is a major cause of neonatal morbidity and mortality, and it poses threat to the fetus at any stage.[11] Moawad et al found that fetal doppler parameters are associated with late onset (>34 weeks) preeclampsia and determined poor neonatal outcomes.[12] Piotr et al studied the link between angiogenesis markers in maternal blood including anti-angiogenic factor soluble fms-like tyrosine kinase-1 (sFlt-1) and pro-angiogenic factor, placental growth factor (PlGF) and its impact on neonatal outcomes.[13-15] It was found that a high sFlt-1/PlGF before 32 weeks GA was associated with significant increase in adverse neonatal outcomes including respiratory distress syndrome, patent ductus arteriosus, sepsis, intreventricular hemorrhage, retinopathy of prematurity and bronchopulmonary dysplasia.[13]

Delivery is required in all mothers with preeclampsia at 37 weeks. This is because the risk to the baby outweighs the benefits of continuation of pregnancy.[16] Also, preeclampsia has been associated with an increased incidence of late preterm infants and its attendant complications including RDS, transient tachypnea of newborn (TTN) and persistent pulmonary hypertension of the newborn.

Neonatal and infant mortality are higher in the late preterm infants. Other complications occurring in preterm infants born to preeclamptic women include IUGR, thrombocytopenia, neutropenia and BPD.[17,18] However, recent evidence suggests that there is no increase in adverse neurodevelopmental outcomes in infants born to

preeclamptic mothers. A large population-based study revealed that infants exposed to preeclampsia showed an increase in the risk of endocrine, nutritional and metabolic changes during adolescence and adulthood.[19]

CONCLUSION

Preeclampsia is associated with significant adverse effects on the fetus and neonate including low birth weight, prematurity, IUGR, fetal death and stillbirth. Other morbidities are due to prematurity including respiratory distress syndrome and other complications like neutropenia and thrombocytopenia. More controlled studies are needed to elucidate rare and important complications in the neonate due to maternal preeclampsia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Arulparithi CS, Manjani S, Prakash P. Outcome of neonates born to mothers with pregnancy induced hypertension/preeclampsia - a systematic review. Int J Contemp Pediatr 2023;10:920-4.