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Original Research Article

Epidemiology, risk factors and prevalence of maternal and neonatal outcomes with critical care requirements in hypertensive disorders of pregnancy: a prospective observational study

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ABSTRACT

Background: Hypertensive disorders of pregnancy (HDP) remain a leading cause of maternal and neonatal morbidity and mortality worldwide. This study examined maternal and neonatal outcomes across the different HDP subtypes and identified factors linked to ICU and NICU admission.

Methods: In this prospective observational analytical study, 144 pregnant women diagnosed with gestational hypertension, non-severe pre-eclampsia, severe pre-eclampsia, eclampsia, chronic hypertension, or superimposed pre-eclampsia (as defined by FOGSI guidelines) were enrolled. Maternal characteristics, maternal complications, ICU admission, neonatal complications, NICU admission, and mortality were recorded from hospital records. Data were analyzed using the Chi-square test, Fisher's Exact test, multivariate logistic regression, odds ratio estimation, and ROC curve analysis.

Results: Severe pre-eclampsia and superimposed pre-eclampsia emerged as independent predictors of maternal ICU admission, while eclampsia and superimposed pre-eclampsia independently predicted NICU admission. Maternal ICU admission was strongly linked to neonatal NICU admission ($\chi^2=13.09$, $p<0.001$). The predictive model performed well, with an AUC of 0.8789, sensitivity of 83.6%, and specificity of 85.7%.

Conclusions: Severe HDP subtypes carry a substantially higher risk of adverse maternal and neonatal outcomes. Early recognition, close monitoring, and timely intervention remain central to improving prognosis in hypertensive pregnancies.

Keywords: Hypertensive disorders of pregnancy, ICU and NICU admission, Maternal complications, Neonatal outcomes, Pre-eclampsia

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) rank among the leading causes of maternal and neonatal morbidity and mortality worldwide. The term covers gestational hypertension, pre-eclampsia, eclampsia, chronic hypertension, and superimposed pre-eclampsia-conditions that range from mild blood pressure elevation to severe, multisystem disease affecting both mother and

fetus.¹ On the maternal side, complications can involve the kidneys, liver, nervous system, heart, and blood; on the fetal and neonatal side, they include growth restriction, preterm birth, low birth weight, fetal distress, NICU admission, and neonatal death.² A 2025 systematic review and meta-analysis placed the global prevalence of pre-eclampsia at 4.43%, eclampsia at 0.43%, and HELLP syndrome at 0.39%, with wide variation by region.³

HDP arises through abnormal placentation, endothelial dysfunction, oxidative stress, inflammation, and impaired blood flow to the uterus and placenta.⁴ Reduced placental perfusion can limit oxygen and nutrient delivery to the fetus, contributing to growth restriction and preterm birth. Severe maternal disease often calls for closer monitoring, ICU admission, and early delivery, each of which raises the risk of neonatal complications.⁵ Other work points to placental dysfunction and maternal vascular abnormalities as central to how pre-eclampsia develops and progresses, with growing interest in biomarkers that could flag at-risk women before adverse maternal or perinatal outcomes occur.⁶

The burden of HDP is especially heavy in developing countries, including India, where late diagnosis, thin antenatal coverage, delayed referral, and limited access to specialist maternal and neonatal care all contribute to worse outcomes.⁷ Current guidelines call for early recognition of severe hypertension, prompt treatment, close maternal-fetal monitoring, and timely intervention.⁸ A prospective cohort of 1,650 pregnant women in rural Central India found an HDP incidence of 7.15%; affected women had higher rates of preterm delivery, caesarean delivery, anaemia, thrombocytopenia, and placental abruption, and their infants were more often born small-for-gestational-age, preterm, or with low birth weight, with higher perinatal mortality.⁹

Maternal age, obesity, and chronic hypertension are recognised risk factors for HDP, but once hypertension has set in, the subtype and severity of disease may matter more for determining whether a woman needs critical care. Maternal and neonatal outcomes are also closely linked: severe maternal disease is often accompanied by placental dysfunction, fetal growth restriction, prematurity, and NICU need.¹⁰ Work from India and Tanzania shows that both the severity and timing of HDP shape perinatal outcomes- severe pre-eclampsia carried the highest risk of perinatal death, and early-onset HDP was associated with markedly higher risks of perinatal death, stillbirth, preterm birth, and low birth weight compared with disease appearing later in pregnancy.¹¹

This study set out to describe the epidemiology, subtypes, and severity of HDP in a tertiary-care hospital, along with the associated maternal complications, ICU admission, neonatal complications, and NICU admission.¹² It also examined independent predictors of maternal ICU and neonatal NICU admission through multivariate analysis, and assessed how well the resulting ICU model discriminated between patients using ROC curve analysis.¹³ A recent systematic review and meta-analysis of 110 studies covering 506,178 women with HDP underlines why this matters: prediction models and biomarkers are playing a growing role in identifying at-risk women, though the review also stressed that such models need validation in the populations where they will actually be used.¹¹

Research gap

Much of the existing literature on HDP looks at prevalence and epidemiological risk factors in isolation from maternal and fetal outcomes, or the reverse. Few studies have examined, within a single hospital-based cohort, how the different HDP subtypes relate to maternal risk factors, ICU and NICU admission, and adverse neonatal outcomes together.

Many of the studies that do exist rely on retrospective reviews or meta-analyses that compare disease severity only loosely across categories such as gestational hypertension, severe pre-eclampsia, eclampsia, chronic hypertension, and superimposed pre-eclampsia. There is also limited evidence on how well severe maternal complications predict neonatal morbidity and mortality in high-risk pregnancies.

Few Indian hospital-based studies have combined multivariate logistic regression, odds ratio analysis, and ROC curve analysis to identify independent predictors of ICU and NICU admission in HDP. This study aims to address that gap through a detailed statistical evaluation of epidemiological factors, HDP severity, maternal complications, and neonatal outcomes in one cohort.

METHODS

Study type

It was a prospective observational analytical study.

Study place

GMERS Medical college and Hospital, Sola, Ahmedabad, Gujarat, India.

Study period

The study took place from October 2025 to April 2026.

Subject selection criteria

All singleton pregnant women with hypertension were involved in study.

Procedure

Data were collected from hospital medical records and patient interview included maternal demographic details, blood pressure measurements, BMI, gestational age at delivery, maternal complications, ICU admission, neonatal complications, NICU admission, and neonatal mortality. Statistical analysis was performed using descriptive and inferential methods. Chi-square and Fisher's Exact tests were used to assess associations between HDP types and categorical outcomes, while odds ratios with 95% confidence intervals were calculated to estimate risk. Multivariate logistic regression analysis was performed to

identify independent predictors of ICU and NICU admission. ROC curve analysis was used to evaluate the predictive performance of the statistical model. A p value less than 0.05 was considered statistically significant.

Ethical approval

The study was approved by research and ethics committee of GMERS Medical College and Civil Hospital, Sola, Ahmedabad, 380060, Gujarat, India (GMERSMCS/IEC/114/2025).

RESULTS

Baseline characteristics

A total of 144 pregnant women diagnosed with hypertensive disorders of pregnancy (HDP) were included in the study.

Table 1: Baseline characteristics.

Variable	Value
Sample size	144
Maternal age (years)	26.26±5.27
Body mass index (kg/m ²)	26.58±5.88
Systolic blood pressure (mmHg)	162.00±15.57
Diastolic blood pressure (mmHg)	101.92±10.68
Gravida	2.11±1.20
Parity	1.01±1.13
Abortion	0.15±0.43

This cohort of 144 women with HDP had a mean age of 26.26 years and a BMI in the overweight range on average. Blood pressure readings were markedly elevated, consistent with a high proportion of severe hypertension in the sample. Most participants were multigravida with a low rate of prior abortion, reflecting a high-risk obstetric population overall.

Distribution of HDP

Gestational hypertension (27.1%) and severe pre-eclampsia (26.4%) accounted for roughly half the cohort between them. A sizeable share of patients had severe or complicated disease- eclampsia and superimposed pre-eclampsia together made up over a fifth of cases- pointing to a high-risk population with substantial disease severity.

Table 2: Distribution of HDP types.

Type of HDP	Frequency (%)
Gestational hypertension	39 (27.1)
Severe pre-eclampsia	38 (26.4)
Non-severe pre-eclampsia	19 (13.2)
Chronic hypertension	17 (11.8)
Superimposed pre-eclampsia	16 (11.1)
Eclampsia	15 (10.4)

Factors associated with ICU admission

Type of HDP and severe hypertension were both significantly associated with ICU admission, while maternal age and BMI were not. This points to disease severity, rather than baseline demographic characteristics, as the main driver of critical-care need in this cohort, and argues for early identification and aggressive management of the higher-risk HDP subtypes.

Table 3: Bivariate analysis for ICU admission.

Variable	P value	Interpretation
Type of hypertensive disorders of pregnancy	<0.001	Strong association
Severe hypertension	<0.001	Significant
Maternal age	0.29	Not significant
Body mass index	0.14	Not significant

Neonatal outcomes (NICU admission)

Multivariate logistic regression singled out eclampsia and superimposed pre-eclampsia as independent predictors of NICU admission.

Table 4: NICU admission model.

Variable	Adjusted OR	95% CI	P value
Eclampsia	12.74	2.09-115.68	0.01
Superimposed pre-eclampsia	6.74	1.13-58.19	0.049
Birth weight	0.83	NS	0.54
Severe hypertension	NS		0.46

Neonates of mothers with eclampsia had roughly 12.7 times higher odds of NICU admission (OR=12.74, 95% CI: 2.09-115.68, p=0.01), pointing to a strong link between severe maternal neurological involvement and adverse neonatal outcomes. Superimposed pre-eclampsia raised the odds by a smaller but still significant margin, increasing them roughly 7-fold; birth weight and severe hypertension were not independently significant in this model.

Maternal mortality

No statistically significant independent predictors of maternal mortality emerged from this analysis. Maternal deaths did occur in the cohort, but too few to support a stable regression model- the resulting confidence intervals were wide and statistical power limited. These findings on mortality should therefore be read with caution; larger studies are needed to identify reliable predictors of maternal death in pregnancies complicated by hypertensive disorders.

Graphical analysis

Figure 1 plots neonatal birth weight against maternal ICU admission and neonatal NICU admission (0- no; 1- yes). Neonates in the group with neither maternal ICU nor NICU admission (0.0) had the highest median birth weight and the narrowest spread, consistent with better overall neonatal condition. The ICU-only group (1.0) showed the widest spread, ranging from very low to near-normal birth weight.

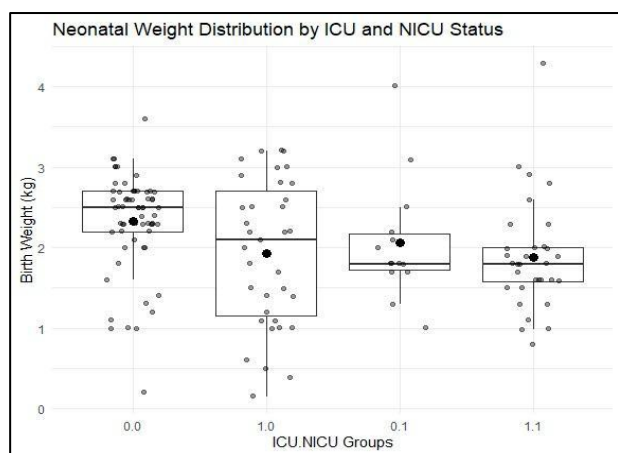


Figure 1: Box plot of neonatal weight distribution based on ICU and NICU admission.

The NICU-only group (0.1) had moderately lower birth weights on average, suggesting that neonatal complications can arise independently of maternal ICU admission- for instance through fetal or placental factors. Several low-weight outliers (<1.5 kg) appeared in the ICU-associated groups, pointing to a higher risk of adverse neonatal outcomes when maternal disease is severe.

The combined ICU-and-NICU group (1.1) had the lowest median birth weight and the tightest clustering around low values, with a comparatively high share of low-birth-weight babies.

Taken together, these patterns identify combined maternal ICU and neonatal NICU admission as the highest-risk scenario in this cohort.

ROC curve analysis

ROC curve analysis assessed how well the model predicted maternal ICU admission. It performed well, with an Area Under the Curve (AUC) of 0.8789- a high level of discrimination between women who required ICU admission and those who did not.

At the optimal cut-off, the model reached a sensitivity of 83.6% and a specificity of 85.7%, correctly identifying both true positive and true negative cases in most instances. The curve sat well above the line of chance throughout.

These results suggest the model could serve as a useful clinical tool for early risk assessment, targeted monitoring, and timely intervention in pregnancies complicated by hypertensive disorders.

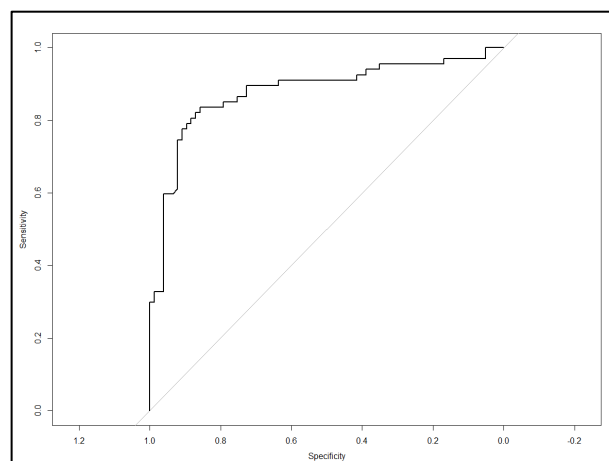


Figure 2: ROC curve.

Table 5: Association between maternal ICU admission and neonatal NICU admission.

ICU Admission	NICU admission (no)	NICU admission (yes)	Total
No	63	14	77
Yes	35	32	67
Total	98	46	144

Maternal ICU admission was significantly associated with neonatal NICU admission ($\chi^2=13.09$, $p<0.001$). Among women admitted to the ICU, 47.8% of their neonates needed NICU care. The odds of NICU admission were about 4.1 times higher for neonates born to ICU-admitted mothers, underlining how closely maternal disease severity and neonatal outcomes track together in this cohort.

DISCUSSION

This study examined the epidemiology, risk factors, and maternal and neonatal outcomes of hypertensive disorders of pregnancy (HDP) in a tertiary-care setting, with particular attention to critical-care needs- maternal ICU admission and neonatal NICU admission.¹⁴ Disease severity emerged as the central factor behind adverse outcomes on both sides: severe pre-eclampsia, eclampsia, and superimposed pre-eclampsia carried the highest risk of complications.

Gestational hypertension and severe pre-eclampsia made up the largest share of HDP cases in this cohort, a pattern also reported by Mathew et al, who found hypertensive disorders common among pregnant women and reported a substantial burden of severe disease in a comparable high-risk population.¹⁵ A similar picture emerged from a systematic review and meta-analysis from India by

Schaefer et al, which pointed to a significant HDP prevalence and its contribution to maternal and perinatal morbidity.¹⁶

Severe hypertension and HDP subtype were significantly associated with ICU admission here, while maternal age and BMI were not- a pattern also seen by Kole et al, and is also consistent with the observations of Sitharam, who found that disease severity, more than demographic factors alone, drives adverse pregnancy outcomes.^{17,18} Obesity and maternal age are recognised risk factors for developing HDP in the first place, but findings from Dhinva et al suggest that once the disorder is established, progression to severe disease becomes the main determinant of whether critical care is needed.¹⁹

Severe pre-eclampsia and superimposed pre-eclampsia were independent predictors of maternal ICU admission on multivariate analysis here, matching report by Lakhute et al showing higher maternal morbidity among women with severe hypertensive disorders.²⁰ Similarly, Shrestha et al found that severe pregnancy-induced hypertension carried a higher burden of maternal complications and poor outcomes.²¹ Together with the present results, this points to advanced disease phenotype- not simply elevated blood pressure in isolation- as the driver of maternal critical-care utilisation.

On the neonatal side, eclampsia and superimposed pre-eclampsia were the significant independent predictors of NICU admission, echoing a report of higher neonatal complications and NICU admission among pregnancies with chronic hypertension and severe hypertensive disorders.²² Similarly, Das et al found that maternal hypertension raised neonatal morbidity and the need for specialised neonatal care. The strength of the association seen here reflects how severe maternal disease affects fetal wellbeing and the newborn's adaptation after birth.

Maternal ICU admission was also significantly associated with NICU admission in this cohort: neonates of mothers needing intensive care were considerably more likely to need it themselves, reinforcing how closely maternal and neonatal outcomes are tied together. A similar pattern of higher neonatal complication rates in pregnancies with severe maternal disease was reported by Umesava et al, and the present findings suggest that a worsening maternal clinical picture can itself signal neonatal risk.²⁴

The birth-weight analysis told a consistent story: neonates who needed NICU care, particularly those whose mothers were admitted to the ICU, had lower birth weights than other groups- in keeping account of placental dysfunction and impaired fetal growth as a consequence of hypertensive disorders in pregnancy.²⁴ Reduced blood flow to the uterus and placenta in severe HDP likely contributes to growth restriction and low birth weight, raising the burden of neonatal morbidity and intensive-care need.

The ROC analysis showed the statistical model discriminated well between women who went on to need ICU admission and those who did not, suggesting that routine clinical and disease-related variables can meaningfully support risk stratification in hypertensive pregnancy. Predictive modelling of this kind remains relatively uncommon in the HDP literature, which has focused mainly on prevalence and outcomes; this study adds evidence for the value of such models in flagging high-risk cases that need closer monitoring.²²

Overall, these results align with observations of Shamsi et al that severe forms of HDP carry significantly worse maternal and neonatal outcomes, while extending it by bringing HDP subtype, maternal critical-care need, neonatal intensive-care need, and predictive modelling together within one analytical framework.²⁵

Above all, the findings point to the value of early diagnosis, accurate classification of disease severity, continuous maternal-fetal surveillance, and timely intervention in reducing the burden of maternal and neonatal complications from hypertensive disorders of pregnancy.

CONCLUSION

Severe forms of hypertensive disorders of pregnancy (HDP)- particularly severe pre-eclampsia, eclampsia, and superimposed pre-eclampsia- were closely tied to poor maternal and neonatal outcomes in this cohort. As disease severity increased, so did rates of maternal ICU admission, NICU admission, neonatal complications, and neonatal mortality. Severe pre-eclampsia and superimposed pre-eclampsia independently predicted maternal ICU admission, while eclampsia stood out as the key determinant of NICU admission.

Maternal ICU admission was also significantly linked to NICU admission, showing that a worsening maternal clinical picture tends to go hand in hand with poorer neonatal outcomes. The predictive model built from these data discriminated well between high- and low-risk cases, suggesting it could have a place in clinical risk assessment and decision-making.

Taken together, these findings point to the need for prompt detection, careful risk assessment, multidisciplinary care, and timely obstetric intervention to improve maternal and neonatal outcomes in pregnancies complicated by hypertensive disorders.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of GMERS Medical College and Civil Hospital, Sola, Ahmedabad, Gujarat, India (GMERSMCS/IEC/114/2025)

REFERENCES

- Bączkowska M, Kosinska-Kaczynska K, Zgliczynska M, Brawura-Biskupski-Samaha R. Epidemiology, risk factors, and perinatal outcomes of placental abruption- detailed annual data and clinical perspectives from Polish tertiary center. *Int J Environ Res Public Health.* 2022;19(9):5148.
- Mohanty S, Pradhan M, Champatiray JR, Ganguly S. Neonatal outcome in hypertensive disorders of pregnancy in a tertiary care centre. *Panacea J Med Sci.* 2022;12(1):23-8.
- Vera-Ponce VJ, Loayza-Castro JA, Ballena-Cacedo J, Valladolid-Sandoval LA, Zuzunaga-Montoya FE, Gutierrez De Carrillo CI. Global prevalence of preeclampsia, eclampsia, and HELLP syndrome: a systematic review and meta-analysis. *Front Reprod Health.* 2025;7:1706009.
- Panda S, Das R, Sharma N, Das A, Deb P, Singh K. Maternal and perinatal outcomes in hypertensive disorders of pregnancy and factors influencing it: A prospective hospital-based study in Northeast India. *Cureus.* 2021;13(3):e13982.
- Poon LC, Kametas NA, Chelemen T, Leal A, Nicolaides KH. Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. *J Hum Hypertens.* 2010;24(2):104-10.
- Bucher V, Roddy Mitchell A, Gudmundsson P, Atkinson J, Wallin N, Asp J, et al. Prediction of adverse maternal and perinatal outcomes associated with pre-eclampsia and hypertensive disorders of pregnancy: a systematic review and meta-analysis. *eClinMed.* 2024;76:102861.
- Rocha FR, Gonçalves TN, Xavier-Ferreira MI, Laranjeira F, Magalhães GM, Lopes MI, et al. Obstetric intensive care admissions and neonatal outcomes: 15 years of experience from a single center. *Medicina.* 2024;60(12):1937.
- Subki AH, Algethami MR, Baabdullah WM, Alnefaie M, Alzanbagi MA, Alsolami RM, et al. (2018). Prevalence, risk factors, and fetal and maternal outcomes of hypertensive disorders of pregnancy: A retrospective study in Western Saudi Arabia. *Oman Med J.* 2018;33(5):409-15.
- Jain S, Mor S, Jain M, Shivkumar PV, Mittal G. Feto-maternal outcomes in hypertensive disorders of pregnancy: A prospective community-based cohort study in rural central India. *Pregnancy Hypertens.* 2026;44:101481.
- Wang W, Xie X, Yuan T, Wang Y, Zhao F, Zhou Z, et al. Epidemiological trends of maternal hypertensive disorders of pregnancy at the global, regional, and national levels: a population-based study. *BMC Pregnancy Childbirth.* 2021;21(1):364.
- Pembe AB, Dwarkanath P, Kikula A, Raj JM, Perumal N, Paulo HA, et al. Hypertensive disorders of pregnancy and perinatal outcomes: two prospective cohort studies of nulliparous women in India and Tanzania. *BMJ Glob Health.* 2025;10(7):e016339.
- Yousofzai BS, Walizada K, Mehmood R, Latoui RB, Subhan M, Espiegle E, et al. Maternal and neonatal outcomes in pregnant women with chronic hypertension: a retrospective study of 50 cases. *Cureus.* 2024;16(9).
- Chen W. (2026). A prospective study on maternal and neonatal outcomes and influencing factors in pregnant women with borderline hypertension. *J Matern Fet Neonat Med.* 2026;39(1),
- Traub A, Sharma A, Gongora MC. (2024). Hypertensive disorders of pregnancy: A literature review- pathophysiology, current management, future perspectives, and healthcare disparities. *US Cardiol Rev.* 2024;18:e03.
- Mathew R, Devanesan BP, Srijana, Sreedevi NS. Prevalence of hypertensive disorders of pregnancy, associated factors and pregnancy complications in a primigravida population. *Gynecol Obstet Clin Med.* 2023;3(2):119-23.
- Schaefer V, Hilfiker-Kleiner D, Keil C. Hypertension in pregnancy. *Cardiovasc Med.* 2023;26(3):80.
- Kole U, Raddi SA, Dalal A. (2022). Maternal and neonatal outcomes in hypertensive disorders during pregnancy: A hospital-based study. *Indian J Phys Ther Res.* 2022;4(2):127-32.
- Sitharam S. (2022). Maternal and perinatal outcome in hypertensive disorders of pregnancy in a tertiary care rural hospital. *Southeast Asian J Case Rep Rev.* 2022;8(1):21-5.
- Dhinwa M, Gawande K, Jha N, Anjali M, Bhadoria AS, Sinha S. Prevalence of hypertensive disorders of pregnancy in India: a systematic review and meta-analysis. *J Med Evid* 2021;2(2):105-12.
- Lakhute SV, Kendre V, Dixit J. A study of epidemiological factors in antenatal mothers with pregnancy-induced hypertension at the tertiary care hospital. *Med J Dr. D. Y. Patil Vidyapeeth.* 2021;14(1):52-6.
- Shrestha DB, Budhathoki P, Malbul K, Katwal S, Jha SK, Prajapati R, et al. Prevalence, risk factors and outcome of pregnancy induced hypertension in Nepal: a meta-analysis of prevalence studies. *J Nepal Health Res Council.* 2021;19(2):221-9.
- Sengodan SS, Sreepathi N. Prevalence of hypertensive disorders of pregnancy and its maternal outcome in a tertiary care hospital, Salem, Tamil Nadu, India. *Int J Reprod Contracept Obstet Gynecol.* 2019;9(1):236-40.
- Das S, Sahu M, Mohapatra S, Padmavati VM, Panigrahi PK. Pregnancy induced hypertension and feto-maternal outcome in a tertiary care hospital in eastern India: A Prospective Study. *J Clin Diagn Res.* 2018;12(11).

24. Umesawa M, Kobashi G. Epidemiology of hypertensive disorders in pregnancy: Prevalence, risk factors, predictors and prognosis. *Hypertens Res*. 2017;40(3):213-20.
25. Shamsi U, Saleem S, Nishter N, Ameen A. Epidemiology and risk factors of preeclampsia; an overview of observational studies. *Al Ameen J Med Sci*. 2013;6(4):292-300.

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