Review Article

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# Prevalence, Risk Factors and Outcome of Pregnancy-induced Hypertension in Nepal: A Meta-Analysis of Prevalence Studies

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## ABSTRACT

**Background:** Pregnancy induced hypertension is a major cause of global maternal mortality and morbidity. This review was conducted to fulfill the objective of evaluating the status of pregnancy induced hypertension in Nepal.

**Methods:** The protocol for this review was registered in PROSPERO (CRD42020211210). Pubmed, Embase, Google Scholar, Scopus and Pubmed Central were searched using appropriate keywords for relevant studies. Data analysis was performed using Comprehensive Meta-Analysis Software version 3. Forest plot was used to visualize the prevalence and risk factors of Pregnancy induced hypertension. Random effect model was used and the level of heterogeneity was high. Joanna Briggins Institute bias assessment tool was used for the analysis of bias in the included studies.

**Results:** Twenty studies were included in the review. The pooled prevalence of pre-eclampsia and eclampsia were 2.6% (95% CI, 1.2%-5.3%) and 0.5% (95% CI, 0.2%-1.1%) respectively. The majority of cases were young women and had not complete or unbooked antenatal visits. Cesarean delivery was the most common mode of deliveries in 50% of deliveries (proportion, 0.50; 95% CI, 0.40-0.60) among patients with PIH followed by vaginal deliveries in 43.1% (proportion, 0.431; 95% CI, 0.336-0.532); and rest 6.9% were vacuum/forceps assisted deliveries (proportion, 0.069; 95% CI, 0.050-0.093). Common maternal complications were abruption in 6.56% of Pregnancy induced hypertension cases, rest were pulmonary embolism, renal injury.

**Conclusions:** The prevalence of pre-eclampsia and eclampsia in Nepal were 2.6% and 0.5%. Younger woman and women with poor antenatal checkups had increased risk of Pregnancy induced hypertension. Cesarean delivery was the most common route of delivery and common maternal complications were abruption placenta, pulmonary embolism, renal injury etc.

**Keywords:** Eclampsia; hypertension; maternal mortality; Nepal; pre-eclampsia; pregnancy-induced

## INTRODUCTION

Pregnancy induced hypertension is a new onset of hypertension (BP >= 140/90 mm of Hg) that develops as a direct result of the gravid state.[1] It includes gestational hypertension, preeclampsia and eclampsia. PIH is a major cause of maternal morbidity and mortality worldwide that complicates 3-10% of pregnancies.[2,3]The commonest complications of pregnancy are hypertensive disorders of pregnancy with incidence ranging from 5-10%.[4] Different risk factors such as null parity, extreme ages, obesity, family history of hypertension, and inadequate antenatal supervision have been identified.[5] Maternal and neonatal morbidity and mortality are higher in hypertensive disorders of pregnancy as compared to those without the disorders.[6]

Previously published studies on prevalence, risk factors and outcomes of PIH were conducted in different socio-cultural settings and specific parts of the country which is bound to have heterogeneities, and showed different pictures. There has not been a study conducted that pooled the prevalence, risk factors, and outcomes of PIH in Nepal to this date. Hence, there is a need for this meta-analysis to determine the risk factors, prevalence, and outcomes of PIH, in Nepal from 2000 to 2020 based on previously published studies.

## METHODS

Our meta-analysis was based on the MOOSE guideline

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(Meta-analysis of Observational Studies in Epidemiology) and registered in PROSPERO (CRD42020211210).[7,8]

## Study design and search strategy

PubMed, Scopus, PMC, google scholar, and Embase were searched using keywords like "Prevalence", "Risk factors", "Outcome", "Pregnancy induced hypertension", "eclampsia", "gestational hypertension", "Pre-Eclampsia" and "Nepal" with the use of relevant Boolean operators like "AND" or "OR". Detail of electronic search is available in Supplementary file 1. All published studies after 1990 in Nepal were retrieved to be assessed for eligibility of inclusion in this metanalysis.

## Eligibility Criteria

### Inclusion criteria

Published observational studies including cross-sectional, cohort and case-control studies.

Articles in the English language.

Articles that report the prevalence, risk factors, and outcome of PIH in Nepal individually or any combination of the three.

Included the pregnant female population with>=20 weeks of gestation

Studied the prevalence of PIH diagnosed using digital automated, aneroid or mercury sphygmomanometers.

Studies involving one or more risk factors for PIH, such as maternal age, parity, body mass index (BMI), multiple pregnancy, diabetes, and smoking.

studies reporting one or more of the following outcomes on PIH:

Fetal; Neonatal death (NND), preterm, Low Birth Weight (LBW).

Maternal; renal failure, mortality, abruption, Hemolysis Elevated Liver Enzyme and Low Platelets (HELLP).

### Exclusion criteria:

Non-observational studies like intervention studies, case studies, pharmacogenetic studies, case series, qualitative data, comments or letters, audits, narrative reviews, conference proceeding, opinion pieces, methodological, editorials, animal studies, systematic reviews, and meta-analysis

Studies done in other countries except for Nepal

Studies not assessing the prevalence, risk factors, or outcomes on PIH

## Study selection and screening

All articles discovered using the predetermined search terms were kept in Covidence.[9] Duplicate publications were removed. The studies were assessed independently by the first reviewer (KM) and second reviewer (SKJ) for relevance according to the set inclusion and exclusion criteria in two phases: title and abstract in phase I and full article screening in phase II. Agreement between the two searchers on the selection of relevant studies was measured and any discrepancies in including the studies were reviewed and resolved by the third reviewer (SK) before data extraction. The search process is presented in PRISMA flow chart that depicts the studies that were included and excluded (Figure 1).

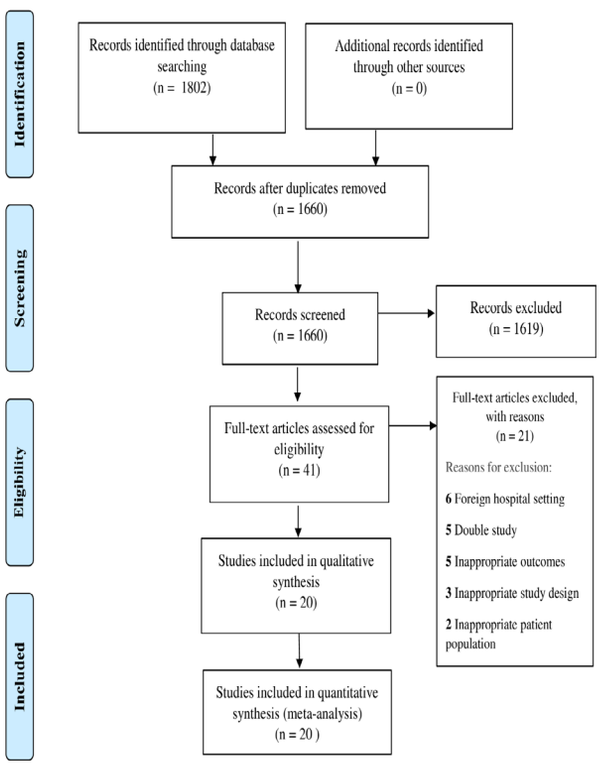


Figure 1. PRISMA flow diagram

## Definition of the outcome of interest

The primary outcome of this study was the prevalence, risk factor, and outcome of Pregnancy Induced Hypertension. Hypertensive disorder of pregnancy includes Pregnancy Induced Hypertension, Pre-eclampsia, Eclampsia, and Preeclampsia superimposed on chronic hypertension.

Hypertension: Elevation of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or both on at least 2 occasions 4 hours apart.

PIH/ Gestational hypertension: BP≥140/90 mmHg at or after 20 weeks' gestation in a woman with previously normal BP in absence of proteinuria.

Preeclampsia: BP≥140/90mmHg and proteinuria at or after 20 weeks of gestation in a woman with previously normal BP.

Eclampsia: Occurrence of seizure on a background of pre-eclampsia

Proteinuria: 24-hour urinary protein excretion of ≥300 mg or ≥1+ on qualitative urine dipstick examination or a urine protein: creatinine ratio ≥30 mg/mmol.

Outcome: Includes both maternal and fetal complications due to hypertensive disorder of pregnancy

### Quality assessment

We assessed the quality of eligible studies by using the Joanna Briggs Institute (JBI) critical appraisal checklist for studies and rate their risk of bias.[10] Quality assessment was performed independently by two authors. Discrepancies in quality assessment were discussed between reviewers and the final assessment was provided following discussions with the third author (Supplementary file **2, Table 1-3**).

### Data extraction process

The data extraction was done using Microsoft Excel creating a customized data collection form. Data extraction included: author's name, study year, study design (cross-sectional, case-control and cohort), sample size, Blood pressure at the time of admission, type of hypertensive disorder in pregnancy, prevalence, fits delivery interval, maternal age, gravidity, parity, week of gestation, twin pregnancy, previous history of hypertensive disorders of pregnancy, family history of hypertension, family history of DM, obtaining nutritional counseling during the antenatal period, religion, antenatal care, BMI, risk factors, maternal complications, and fetal complications were extracted from each article.

### Result synthesis and statistical analysis

Among the selected observational studies, we prepared a qualitative table of study findings. Then we extracted the data depending on our predetermined primary and secondary outcomes. We did a statistical analysis using CMA 3 software.[11] We used proportion for outcome estimation whenever appropriate with 95% Confidence Interval (CI) and used the fixed/random-effects model as per the heterogeneities.

### Heterogeneity and publication bias

We assessed the heterogeneity using the I-squared ($I^2$) test and used the fixed/random-effects model for the pooling of studies. The random effect was used for high heterogeneities and fixed effect model was used for low heterogeneities in our study. We used the Cochrane Handbook for Systematic Reviews of Interventions for interpretation of the I-squared ($I^2$) test.[12] We presented Forest plots to visualize the degree of variation between studies and checked for publication bias by examining the funnel plot and noting for any asymmetry. For sensitivity analysis, we examined the effect of the study based on their weightage and re-running the analysis to see for any differences.

## RESULTS

1802 studies were imported for screening after thorough database searching. After the removal of 142 duplicates, the title and abstracts of 1660 studies were screened. After the exclusion of 1619 studies, full-text eligibility of 41 studies as assessed. 21 studies were excluded for definite reasons and 20 studies were included in the analysis.

### Mode of deliveries

Among eight studies reported deliveries with different PIH spectrum. Pooling of data showed CS was mode of

Table 1. Summary of the study characteristics

| Author/s | Study Period | Study design | Sample size (PIH/total) | Study area | Pre-Eclampsia | Eclampsia | GH |
|---|---|---|---|---|---|---|---|
| Ghimire [13] | June 2014 to June 2015 | Retrospective; CS | 112/8066 | NMC, Biratnagar | - | 112/8066 | - |
| Acharya et al.[14] | June 2011 to December 2013 | Prospective | 145/2305 | COMS-TH, Chitwan | 145/2305 | | - |
| Singh et al.[15] | 2014 | Prospective; CS | 126/3819 | PMWH | - | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Shrestha et al.[16] | February 2014 to March 2016 | Prospective; Observational | 100/- | Kathmandu Medical College, Kathmandu | - | - | 100 |
| Shrestha.[17] | June to December 2018 | Prospective; CS | 93/- | Nepalgunj Medical College, Kohalpur | 33/93 | 17/93 (18%) | 20/93 |
| Joshi et al.[18] | March to august 2011 | CS | 96/3959 | BPKIHS | 35/96 | 51/96 (53.1%) | 10/96 |
| Gautam et al. [9] | April 2011 to March 2012 | Retrospective | 182/4175 | | 178/4175 | 4/4175 (0.09%) | - |
| Rana et al.[20] | July 2011 to June 2016 | CS | 291/16445 | National Medical College, Birgunj | - | 291/16445 | - |
| Pradhan et al.[21] | Feb2012 to Feb 2013 | Prospective | 52/10000 | BPKIHS, Dharan | - | 52/10000 | - |
| Choudhary [22] | Apr 2000 to Apr 2001 | Retrospective | 47/16096 | PMWH | - | 47/16096 | - |
| Pramanik et al.[23] | June 2012 to June 2013 | Case-control | 35/- | NMCTH | 35 | - | - |
| Karki et al.[24] | Feb 2006 to Jan 2007 | Prospective cohort | 153/- | BPKIHS | 110/153 | 43/153 (28.1%) | - |
| Thakur et al.[25] | 2018 | Prospective; CS | 40/- +40 | PMWH | 16/40 | 6/40 | 18/40 |
| Chuni et al.[26] | 2000-2003 | Retrospective | | | | | |
| Das et al.[27] | Sept - Dec 2017 | Case control | 85/4820 | PMWH | 85/4820 | - | - |
| Pant et al.[28] | August 2016-August 2017 | Observational | 44/- +44 | Tribhuvan University, Teaching Hospital | 44 | - | - |
| Pokharel et al.[29] | June 2005- June 2007 | Case-control | 75/- +75 | BPKIHS | - | - | - |
| Jha et al.[30] | 2006 (Aug-Oct) | Prospective | 50/- | Janakpur Zonal Hospital | - | 50 | - |
| Manandhar et al.[31] | 1994 | Case control | 75/- +150 | - | - | - | - |
| Shakya et al.[32] | April 2010- July 2011 | Retrospective | 45/31674 obstetric admissions | PMWH | - | 45 | - |

*BPKIHS= BP Koirala Institute of Health Sciences; CS= Cross-sectional; COMS-TH= College of Medical Sciences Teaching Hospital; NMC= Nobel Medical College; NMCTH= Nepal Medical College Teaching Hospital; PMWH= Paropkar Maternity and Women's Hospital*

## Quantitative analysis

### Pre-eclampsia

Four studies reported the prevalence of preeclampsia in their studies. Pooling of the prevalence showed overall 2.6% of deliveries attended were having pre-eclampsia (Proportion, 0.026; 95% CI, 1.2%-5.3%; $I^2$: 98.2) (**Figure 2**). Sensitivity analysis done by excluding individual studies did not show significant differences (Supplementary file, **Figure 1.**).

### Eclampsia

Seven studies reported the prevalence of eclampsia in their studies. Pooling of the prevalence showed overall 0.5% deliveries attended were having eclampsia (Proportion, 0.005; 95% CI, 0.2%-1.1%; $I^2$: 98.5) (**Figure 3**). Sensitivity analysis done by excluding individual studies did not show significant differences (Supplementary file, **Figure 2.**).

### Age, gravida, parity, ANC, and WOG

Among the deliveries attended with PIH, the majority of females were of below 35 age **(Supplementary file, Table 4).** The majority of PIH cases were primigravida **(Supplementary file, Table 5).** ANC visits were not complete/unbooked in a significant number of PIH cases (Supplementary file, **Table 6).** Term/preterm (Supplementary file, **Table 7).**

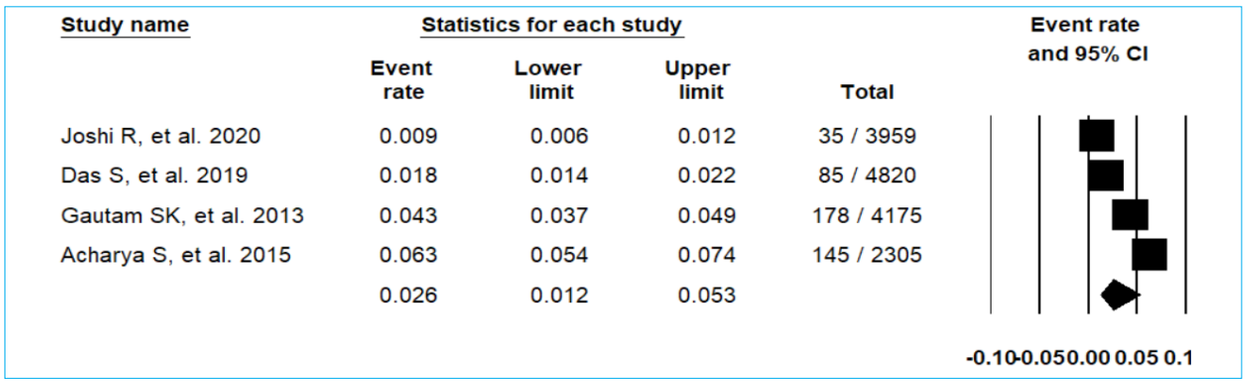


Figure 2. Forest plot showing the prevalence of preeclampsia among deliveries attended

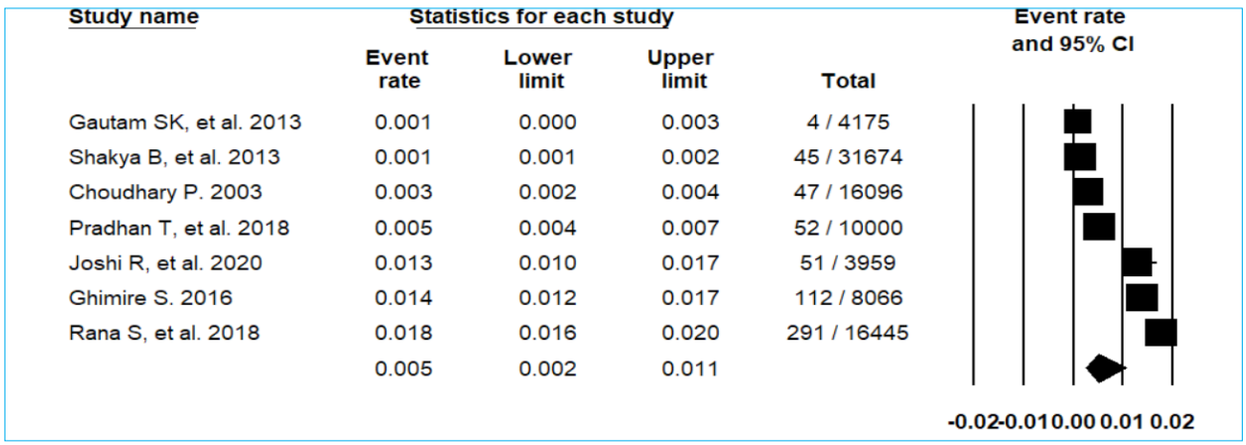


Figure 3. Forest plot showing the prevalence of eclampsia among deliveries attended

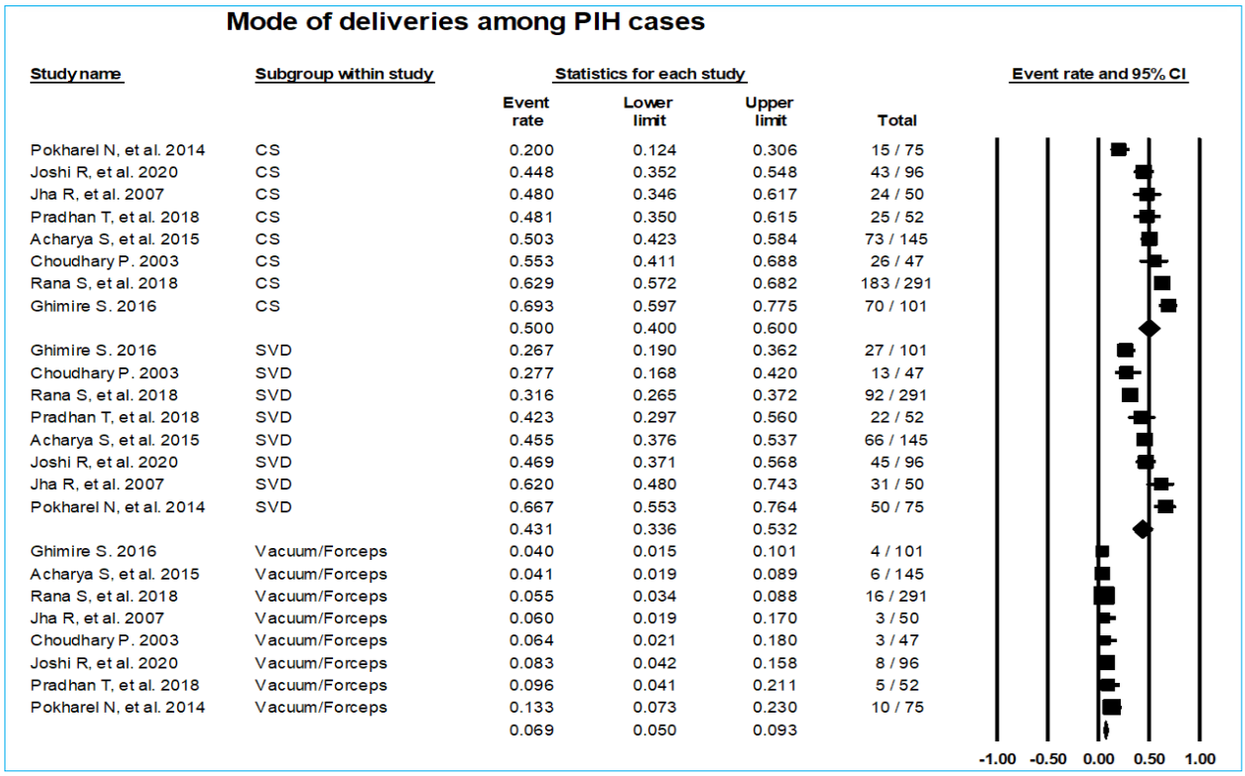


Figure 4. Forest plot showing mode of deliveries among PIH cases

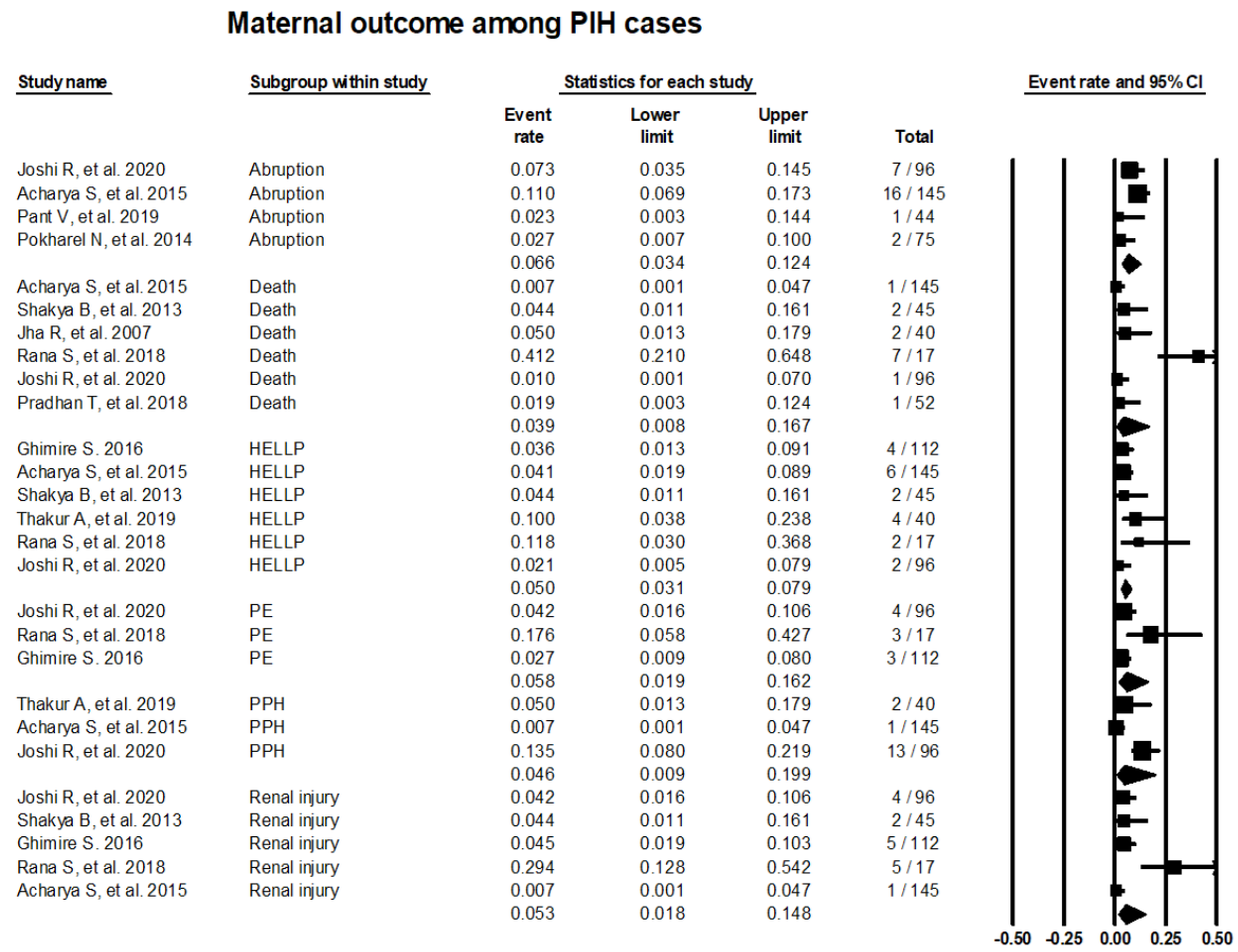


Figure 5. Forest plot showing maternal outcome among PIH cases

deliveries in 50% of deliveries among patients with PIH (proportion, 0.50; 95% CI, 0.40-0.60; $I^2$:86.7); followed by vaginal deliveries in 43.1% (proportion, 0.431; 95% CI, 0.336-0.532; $I^2$: 86.5); and rest 6.9% were vacuum/forceps assisted deliveries (proportion, 0.069; 95% CI, 0.050-0.093; $I^2$: 26.2) (Figure 4).

### Maternal outcome

Placental abruption was reported in four studies. Pooling of their result showed placental abruption in 6.56% of PIH cases (Proportion, 0.066; 95% CI, 0.034-0.124; $I^2$:51). Similarly, maternal mortality was reported in six studies, pooling of their result showed maternal mortality in 3.95% of PIH cases (Proportion, 0.039; 95% CI, 0.008-0.167; $I^2$: 84%). HELLP syndrome was reported in 4.98% (proportion, 0.050; 95% CI, 0.031-0.079; $I^2$: 14). PE was reported in 5.79% (0.058; 95% CI, 0.019-0.162; $I^2$: 67). PPH was reported in 4.57% (Proportion, 0.046; 95% CI, 0.009-0.199; $I^2$:80). Renal injury was reported in 5.28% (Proportion, 0.053; 95% CI, 0.018-0.148; $I^2$: 78) (Figure 5).

### Neonatal outcome

NND, Preterm, and LBW were commonly reported in PIH cases. The pooled analysis was not possible due to heterogeneities (**Supplementary file, Table 8**).

## DISCUSSION

The significant findings of our meta-analysis were the prevalence of preeclampsia (2.6%) and eclampsia (0.5%) among the deliveries. Most of the cases were below 35 years of age and had a poor antenatal checkup. Cesarean section was the commonest mode of delivery in cases of PIH. Common maternal complications found among cases of PIH in Nepal were abruptio placenta followed by pulmonary embolism, renal injury, HELLP, PPH, and maternal mortality.

The prevalence of pre-eclampsia in Nepal was found to be lower than the global prevalence of 4.6%.[33]one of the main causes of maternal deaths, are required at both national and regional levels to inform policies. We conducted a systematic review of the incidence

of hypertensive disorders of pregnancy (HDP It was also lower than other south Asian countries like India (3.2%), Thailand (4.7%), Bangladesh (12%), and Iran (5%).[34] The prevalence of eclampsia was higher than in Iran (0.2%). Our findings align with a prior study has that found that women from the industrial countries have a 0.02% – 0.08% chance of developing eclampsia in comparison to 0.16% – 0.69% for women in less industrialized countries.[35] However, the prevalence of both pre-eclampsia and eclampsia were significantly lower than in Africa. [36] A prior meta-analysis had found the prevalence of pregnancy-induced hypertension (PIH) and preeclampsia/eclampsia alone to be 6.29% and 5.47% respectively.[36] The majority of patients with PIH were below 35 years of age in our study. This finding was similar to prior studies done in other parts of the world like Brazil, Cameroon and Nigeria which showed increased prevalence of pre-eclampsia in younger women compared to older women.[37-39] This could be explained by the fact that younger women are more likely to be nulliparous than older women and nulliparity has been found to be risk factor for PIH.[36] In addition, adolescent pregnancies have found to be increase the risk for pregnancy induced hypertension with early pregnancy being subjected to economic and social inequality as per the systematic review done by Macedo et al.[40] These factors might explain the increased risk of pre-eclampsia in younger women. However, pregnant women who were more than 35 years old were found to have increased risk for PIH in a prior study by Berhe et al. who argued that older women have abnormal lipid profile, increased cholesterol leading to higher risks for vascular damage compared to younger women.[41]

Patients who had poor antenatal checkups were found to be at greater risk for developing PIH as per our study. Many other studies have found an association between lack of antenatal checkups and PIH.[42-44] Absence of regular antenatal visits leads to failure of detection of risk factors and danger signs. Thus, early detection and timely management of preeclampsia/eclampsia to reduce the disease progress and prevention of serious complications to the mother and fetus is not possible. Cesarean deliveries were found to be the most common route of delivery among patients with PIH followed by vaginal deliveries and vacuum-assisted vaginal deliveries. A prior study on patients with chronic hypertension had found a similar finding of increased need for Cesarean section for delivery.[45]

We also found high maternal complications like abruption placenta, renal injury, pulmonary embolism, HELLP, and maternal mortality in Nepal. To address these complications, practices from developed countries like the USA where 'hypertension bundle of care' has reduced the rate of morbidity in women with pre-eclampsia and eclampsia should be introduced in Nepal.[46] The 'hypertension bundle of care' by Illinois Perinatal Quality Collaborative (IPQI) focuses on increasing the proportion of patients that are treated with hypertension, increasing discharge education and follow-up appointments, and doing cases debrief.[47] Pregnant women should be encouraged to regularly visit during antenatal checkups for early diagnosis and management of pre-eclampsia and eclampsia which is possible through massive awareness in the community.

Our meta-analysis is the first meta-analysis to pool the prevalence, risk factors, and outcome of preeclampsia and eclampsia at a national level. A comprehensive search of different databases and quality assessment of the included studies were thoroughly done during the review. However, the study had several limitations. Firstly, The heterogeneities were high owing to the use of different tools and definitions used by the various researchers of the included studies. We were not able to pool the neonatal outcome in our analysis due to the limited and variable data in the included studies. In addition, most of the included studies were hospital-based rather than community-based resulting in a representation of areas around the health centers rather than throughout Nepal.

## CONCLUSIONS

The prevalence of pre-eclampsia and eclampsia in Nepal were 2.6% and 0.5%. Younger women and women with poor antenatal checkups had an increased risk of PIH. Cesarean delivery was the most common route of delivery and common maternal complications were abruption placenta, pulmonary embolism, renal injury and HELLP syndrome in Nepal.

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**Competing interests:** None declared

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