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## THE ASSOCIATION BETWEEN SMOKING DURING PREGNANCY AND HYPERTENSIVE DISORDERS OF PREGNANCY : A SYSTEMATIC REVIEW

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### ABSTRACT

**Background:** Smoking is known to have an adverse effect on various health prognosis, and affects obstetric outcomes, such as stillbirth, preterm birth, and low birth weight during pregnancy. Conversely, the effect of smoking on hypertension during pregnancy is still unclear, with recent studies suggesting the effect differs by ethnicity.

**The aim:** This study aims to show the association between smoking during pregnancy and hypertensive disorders of pregnancy.

**Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Result:** In the PubMed database, the results of our search brought up 101 articles, whereas the results of our search on SagePub brought up 117 articles. The results of the search conducted for the last year of 2013 yielded a total 53 articles for PubMed and 70 articles for SagePub. The result from title screening, a total 11 articles for PubMed and 17 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

**Conclusion:** The association of maternal smoking during pregnancy with blood pressure and hypertension suggests that maternal smoking during pregnancy may have a long-term effect on children's BP. This information should be transmitted to pregnant women and healthcare workers to decrease the risk of adverse cardio-metabolic outcomes.

**Keyword:** Smoking, pregnancy, hypertensive disorder.

## INTRODUCTION

Smoking is worldwide the most common preventable cause of morbidity and mortality. Every year, it is responsible for nearly 6 million deaths, of which more than 5 million result directly from smoking and over 600 000 occur in nonsmokers due to passive exposure. Despite a global decrease in prevalence, one billion adults are smokers. Most are aged 20–40 years, the child-bearing age, and when more time is expected to be spent by parents with children. This contributes to expose approximately 700 million children worldwide to secondhand smoke (SHS), mostly at home. However, smoking influences the life course since intrauterine life. Research into maternal smoking during pregnancy suggests that alterations in fetal programming, in response to an adverse fetal environment, might be involved in the origins of chronic conditions later in life, apart from increasing the risk of preterm birth, intrauterine growth restriction, and perinatal death. Later, during the pediatric period, it increases the risk of respiratory illnesses, neurobehavioral problems, and poor school performance.<sup>1</sup>

Hypertensive disorders of pregnancy (HDP) is usually classified as four categories: 1) gestational hypertension, 2) preeclampsia-eclampsia (PE-E), 3) chronic hypertension with superimposed preeclampsia, and 4) chronic hypertension (of any cause). Gestational hypertension and preeclampsia are the two most familiar types. Today, obstetricians note that proper prenatal care, close monitor of blood pressure, rational use of anti-hypertensive drugs, detection of preeclampsia symptoms before delivery and timely termination of pregnancy have reduced the incidence of pregnancy-induced hypertension. However, it is undeniable that hypertensive disorders of pregnancy still exist and significantly influence the maternal pregnancy status and fetal survival rate. Statistics showed that pregnancy related hypertension affects 3-10% of pregnancies. In the United States, the morbidity of preeclampsia increased by 25% between 1987 and 2004, while pregnancy-induced hypertension increased by 184% . The incidence of hypertension was on the rise partially because of some changes in maternal basic demographics, like earlier maternal age and weight gain before pregnancy. In addition, there are also several other factors that may elevate the incidence of hypertensive disorders of pregnancy, such as lower education, diabetes mellitus and certain elements deficiency, including vitamin D, magnesium and calcium. It is an urgent task to find the possible influencing factors of hypertensive disorders of pregnancy, so that a reasonable prevention and treatment process can be planned for pregnant women.<sup>2</sup>

In the past twenty years the incidence of hypertensive disorders of pregnancy (HDP) have increased by 25%, and about 5% to 10% of pregnant women are diagnosed with at least one HDP. This increase in HDP has been attributed to the rise of mothers of an advanced maternal age, obesity, and comorbidities such as diabetes mellitus and nutrient deficiencies. The two most common HDP are gestational hypertension (GH) and pre-eclampsia (PE) with 25 to 50% of those with GH developing PE. GH can only be diagnosed after 20-weeks of gestation. 10 HDP are associated with maternal morbidity and mortality, largely due to maternal strokes. PE can progress to eclampsia which can be lethal and has an estimated 1.8% mortality rate in developed countries.<sup>3</sup>

## METHODS

### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

### Criteria for Eligibility

For the purpose of this literature review, we compare and contrast of the association between smoking during pregnancy and hypertensive disorders of pregnancy. It is possible to accomplish this by researching or investigating the association between smoking during pregnancy and hypertensive disorders of pregnancy. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about the association between smoking during pregnancy and hypertensive disorders of pregnancy. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

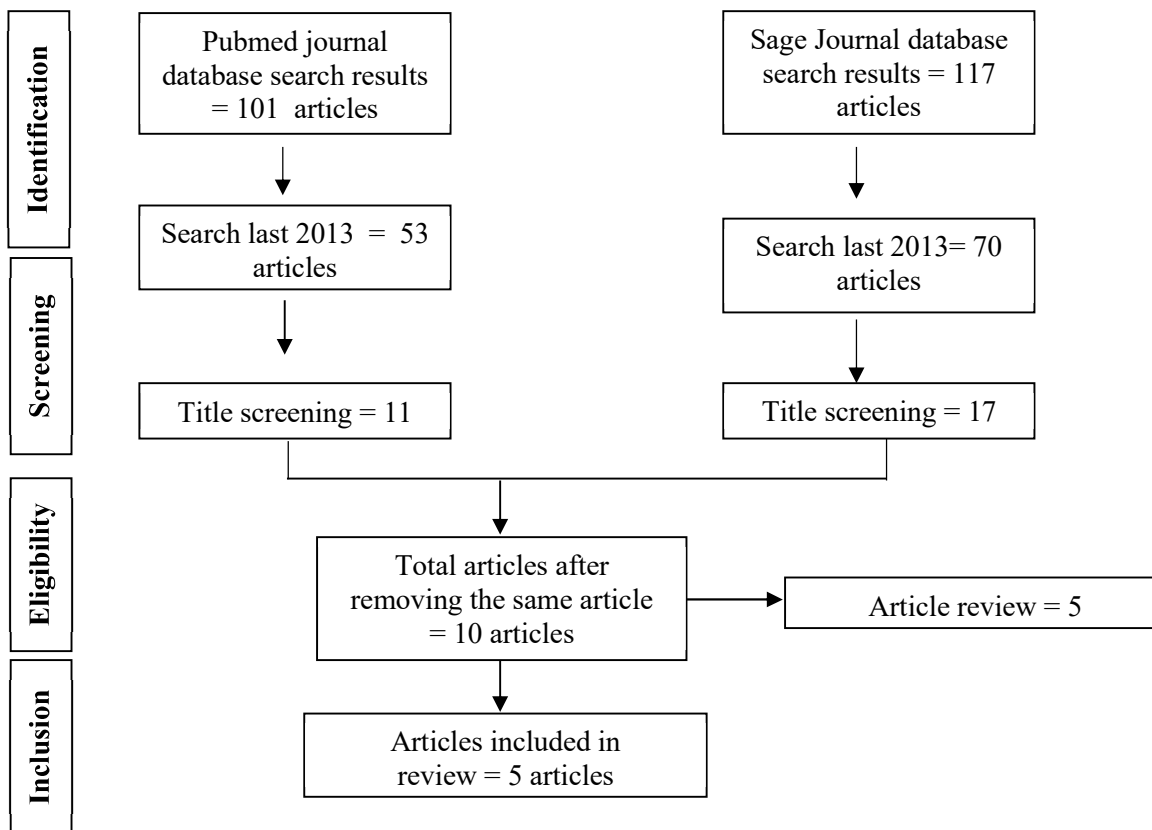
### Search Strategy

We used "The association between smoking during pregnancy"; "Hypertensive disorders of pregnancy" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: (("Smoking during pregnancy"[MeSH Subheading] OR "Hypertensive disorders of pregnancy"[All Fields] OR "The impact of smoking in pregnancy"[All Fields]) AND ("Association smoking and hypertensive"[All Fields] OR "Outcome of smoking during pregnancy"[All Fields]) AND ("Hypertensive in

pregnancy"[MeSH Terms] OR ("smoking and hypertensive during pregnancy"[All Fields]) OR ("Complication of smoking during pregnancy [All Fields])) used in searching the literature.

**Data retrieval**

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.



**Figure 1. Article search flowchart**

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

**Quality Assessment and Data Synthesis**

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. In order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

**RESULT**

In the PubMed database, the results of our search brought up 101 articles, whereas the results of our search on SagePub brought up 117 articles. The results of the search conducted for the last year of 2013 yielded a total 53 articles for PubMed and 70 articles for SagePub. The result from title screening, a total 11 articles for PubMed and 17 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

Tanaka, K *et al* (2022)<sup>4</sup> showed that the relative risk for SHS exposure and HDP risk changed as a result of adjusting for possible confounding factors. In the multivariate analyses regarding the impact of SHS exposure frequency on HDP risk, after adjusting for maternal confounding factors (model 1), a previous history of GDM and HDP (model 2), and partner factors (model 3), pregnant women with SHS exposure of 4–7 days/week had a higher risk of developing HDP (aRR: 1.20, 95% CI: 1.03–1.39; aRR: 1.19, 95% CI: 1.03–1.38; aRR: 1.18, 95% CI: 1.02–1.36, respectively) than the reference group. A linear trend was observed between SHS exposure frequency and HDP risk after adjustment for all models ( $p < 0.05$ ). In the multivariate analyses regarding the impact of SHS exposure duration on HDP risk, with adjustment as per Models 1, 2, and 3, the estimated risk of HDP development among pregnant women with SHS exposure of  $\geq 2$  h/day was ~1.3 times higher than that of the reference group (aRR: 1.30, 95% CI: 0.99–1.71; aRR: 1.28, 95% CI: 0.97–1.68; aRR: 1.27, 95% CI: 0.96–1.67, respectively); this effect was not statistically significant. A linear trend was also observed between the duration of SHS exposure per day and the risk of developing HDP after adjustment for all models ( $p < 0.05$ ).

Morisaki, N *et al* (2022)<sup>5</sup> showed the association of smoking only during early pregnancy and beyond early pregnancy with risk of HDP compared to no smoking during pregnancy. The associations within each individual cohort were insignificant in all cohorts and showed heterogeneity for effect of smoking only during early pregnancy (I-squared = 52%) but not for continuous smoking beyond early pregnancy (I-squared = 0%). Meta-analysis pooling of ORs using the common-effect inverse-variance model produced non-significant ORs of 1.01 (95% CI, 0.86–1.20) for the effect of smoking only during early pregnancy and 1.24 (95% CI, 0.88–1.87) for the effect of smoking beyond early pregnancy.

**Table 1. The literature include in this study**

Author	Origin	Method	Sample Size	Result
Tanaka, K <i>et al.</i> , 2022 <sup>4</sup>	Japan	Cohort study	2433 participants	the univariate analyses on HDP risk in nonsmokers and all participants, respectively. Compared to women with rare SHS exposure, pregnant women with SHS exposure of 1–3 and 4–7 days/ week showed a higher risk of developing HDP (RR: 1.15, 95% confidence interval [CI]: 1.01–1.31 and RR: 1.35, 95% CI: 1.17–1.55, respectively). Additionally, pregnant women with SHS exposure of 1–2 or $\geq 2$ h/day had a significantly higher risk of developing HDP (RR: 1.49, 95% CI: 1.21–1.83 and RR: 1.48, 95% CI: 1.13–1.95, respectively) than those with SHS exposure of
Morisaki, N <i>et al.</i> , 2022 <sup>5</sup>	Japan	Cohort study	28219 participants	Meta-analysis of four cohort studies including 28,219 participants produced an odds ratio (OR) of 1.24 (95% confidence interval [CI], 0.88–1.87) for the effect of smoking beyond early pregnancy compared to women who did not smoke during pregnancy. These results combined with those from the Japan Environment and Children’s Study (JECS) yielded an OR of 1.19 (95% CI, 1.00–1.43, P = 0.056). Meta-analysis results for categories of smoking volume were insignificant, but when combined with JECS yielded an OR of 0.86 (95% CI, 0.65–1.12) for smoking 1–4 cigarettes, 1.25 (95% CI, 0.98–1.60) for smoking 5–9

				cigarettes, and 1.27 (95% CI, 1.04–1.54) for smoking 10 or more cigarettes per day. All effects were insignificant for preeclampsia.
<b>Gudnadottir, TA et al., 2016<sup>6</sup></b>	Denmark	Case-control study	1445 participants	The odds of being diagnosed with a hypertensive disorder during pregnancy were lower for smokers than non-smokers (13.9% vs. 21.2%); with a crude odds ratio of 0.60 (95% CI 0.44–0.82). Adjusting for parity, multiple gestation, maternal age or any other available covariate did not affect the effect estimate (OR <sub>adjusted</sub> = 0.60, 95% CI 0.44–0.82). We found a reverse association of smoking with each separate hypertensive outcome but the OR magnitude differed; preeclampsia (OR <sub>adjusted</sub> = 0.68, 95% CI 0.47–0.96), gestational hypertension (OR <sub>adjusted</sub> = 0.31, 95% CI 0.13–0.75) and pre-existing hypertension (OR <sub>adjusted</sub> = 0.53, 95% CI 0.26–0.97). The point estimates of the reverse associations diminished in magnitude with increasing BMI, for any hypertensive disorder and for preeclampsia
<b>Bromfield, SG et al., 2023<sup>7</sup></b>		Propensity-matched retrospective cohort study	140425 expectant mothers	We observed the highest risk of cesarean delivery (odds ratio [OR]:1.61 and 1.99) in mothers and preterm delivery (OR:2.22 and 5.37), respiratory distress syndrome (OR:2.39 and 4.19), and low birthweight (OR:3.64 and 9.61) in babies born to mothers with preeclampsia or superimposed preeclampsia compared to no hypertension, respectively (p< 0.05 for all outcomes). These outcomes were slightly higher among chronic or gestational hypertension compared to no hypertension, however, most were not statistically significant. Risk of neonatal intensive care unit utilization was higher among more severe hypertensive disorders (OR:2.41 for preeclampsia, OR:4.87 for superimposed preeclampsia). Obesity/overweight and having a history of preeclampsia during a prior pregnancy were most likely to predict progression from

				gestational/chronic hypertension to preeclampsia/superimposed preeclampsia.
Zaitu, M <i>et al.</i> , 2021 <sup>8</sup>	Japan	Cross-sectional study.	923 responses	The prevalence of ever and current HTP use were 11.7% and 2.7% in postdelivery women and 12.6% and 1.1% in currently pregnant women, respectively. Among currently pregnant women who were former combustible cigarette smokers, 4.4% (4/91) were current HTP smokers. Among postdelivery women, ever HTP smokers had a higher HDP incidence (13.8% vs 6.5%, p=0.03; age-adjusted OR=2.48, 95%CI 1.11 to 5.53) and higher LBW incidence (18.5% vs 8.9%,

Gudnadottir, TA *et al* (2016)<sup>6</sup> showed the odds ratio for any hypertensive disorder was 3.91 (95% CI 1.78–8.59) among smokers and 2.98 (95% CI 2.07–4.31) among non-smokers, when comparing obese with normal weight women. The effect estimates stratified by smoking status were of similar magnitude for preeclampsia, but we lacked statistical power to meaningfully evaluate the association of BMI with gestational hypertension and pre-existing hypertension. Neither additive nor multiplicative interactions of maternal smoking and overweight/obesity were significant. We found a significant joint effect in a multiplicative scale for maternal smoking and obesity for any hypertension (p-value = 0.025), preexisting hypertension (p-value <0.001) but not for preeclampsia (p-value = 0.077).

Bromfield, SG *et al* (2023)<sup>7</sup> showed mothers and neonates born to mothers with preeclampsia or superimposed preeclampsia experienced more adverse outcomes compared to those without hypertension. Mothers and neonates born to mothers with gestational hypertension had outcomes similar to those without hypertension. Outcomes for those with chronic hypertension fell in between gestational hypertension and preeclampsia. Obesity/overweight and having a history of preeclampsia during a prior pregnancy were strong risk factors for hypertension progression.

Zaitu, M *et al* (2021)<sup>8</sup> showed the incidence of HTP use seems to exceed 10% among pregnant women, and HTP smoking may be associated with increased maternal and neonatal risks in Japan. Undoubtedly, smoking in reproductive age women can cause unfavourable perinatal outcomes. Hence, efforts should be made to investigate the risk of HTP use in reproductive age women, to prevent lifethreatening perinatal complications and deaths.

**DISCUSSION**

Eclampsia, preeclampsia, and gestational hypertension are the most common hypertensive disorders of pregnancy (HDP) and result in adverse pregnancy outcomes. It is the leading cause of maternal and perinatal morbidity and mortality. Furthermore, placental abruption, maternal bleeding, premature birth, low birth weight, and neonatal or maternal death are some of the common risks associated with hypertension during pregnancy. HDP is also associated with an increased risk of cardiovascular disorders and related complications in women during the later stage of life compared to those who had normotensive pregnancies. Further, children whose mothers had preeclampsia during their pregnancy have higher chances of experiencing hypertension, insulin resistance, diabetes mellitus, neurological and mental health disorders.<sup>9</sup>

Maternal smoking during pregnancy (MSDP) is known to be associated with adverse birth outcomes (stillbirth, neonatal death, and perinatal death) as well as low birth weight. Several studies have linked MSDP to long-term consequences on children’s health especially on increasing obesity risk. There is also growing evidence that MSDP may increase the risk of diabetes and metabolic syndrome as well as contribute to the development of hypertension. These effects are suggested to be associated with differential methylation of cytosine–phosphate–guanine base pairs in the newborn that can be persistent up to the adolescence when exposed early to tobacco.<sup>10</sup>

While obesity is a known risk factor for preeclampsia and other hypertensive disorders, smoking during pregnancy has been shown to be inversely associated with the development of preeclampsia. Data are scarce on the potential interaction of these two lifestyle-related factors on these common pregnancy conditions. To what extent maternal smoking and body mass index (BMI) interact in the development of preeclampsia and gestational hypertension is not well established. We therefore aimed to examine the association between BMI and hypertensive disorders during pregnancy, accounting for demographic and pregnancy related factors, as well as to assess the combined effect of BMI and smoking on hypertensive disorders among pregnant women.<sup>6</sup>



## CONCLUSION

The association of maternal smoking during pregnancy with blood pressure and hypertension suggests that maternal smoking during pregnancy may have a long-term effect on children's BP. This information should be transmitted to pregnant women and healthcare workers to decrease the risk of adverse cardio-metabolic outcomes.

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