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# Ibuprofen and Postpartum Blood Pressure in Women with Hypertensive Disorders of Pregnancy

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**Abstract**

*Background: Postpartum pain management is crucial for the well-being of women, and NSAIDs, including ibuprofen, are commonly prescribed. However, concerns arise regarding their potential effects on blood pressure, especially in women with hypertensive disorders of pregnancy. This review aims to evaluate the impact of ibuprofen on postpartum blood pressure in this specific population.*

*Methods: We conducted an in-depth review of multiple studies, including the Hypertension in Postpartum Preeclampsia Study (HIPPS), randomized controlled trials, and systematic reviews. These investigations examined the utilization of NSAIDs, predominantly ibuprofen, in postpartum pain management for women experiencing hypertensive disorders during pregnancy. Our analysis encompassed a range of pain assessments, and maternal health outcomes, evaluated across diverse research trials.*

*Results: The HIPPS trial, a double-blind, randomized clinical trial, revealed no significant difference in postpartum blood pressure between women who received acetaminophen. Similar findings were reported in other randomized controlled trials, where ibuprofen did not elevate blood pressure compared to acetaminophen. Conversely, a study focusing on severe pre-eclampsia suggested that ibuprofen led to elevated blood pressure levels during the postpartum period.*

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*No correlation was revealed between NSAID usage and blood pressure levels reaching or surpassing ≥150/100 mm Hg after doing systematic review and meta-analysis. Nonetheless, the analysis identified a statistically notable yet clinically insignificant extension in the duration of postpartum hospitalization linked to NSAID administration*

*Conclusion: In summary, the data indicates that ibuprofen administration does not lead to elevated postpartum blood pressure (BP) among women with hypertensive abnormalities of pregnancy. Additionally, its usage is linked with effective pain relief and positive patient feedback. These results align with existing recommendations suggesting that the drugs ibuprofen and acetaminophen produce similar effects on BP in women with preeclampsia. Despite ongoing concerns, especially in instances of severe pre-eclampsia, additional research is necessary to fully understand the intricate connection between NSAID utilization and postpartum blood pressure, thus ensuring the provision of optimal pain management without jeopardizing maternal well-being.*

## INTRODUCTION

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) like ibuprofen are well acknowledged for their effectiveness in relieving postpartum discomfort, is widely prescribed. While studies have investigated the differences in levels of blood pressure (BP) among postpartum women who suffered with hypertensive pregnancy disorders who were exposed to ibuprofen versus acetaminophen, the exact influence of NSAIDs on postpartum blood pressure remains ambiguous.[2]

Removing NSAIDs from postpartum pain relief may lead to increased opioid use, which has its own risks. The study sought to assess how ibuprofen impacts postpartum BP among women experiencing hypertensive pregnancy disorders, with the exception of those with chronic hypertension. The aim was to evaluate how ibuprofen affects postpartum blood pressure in women, regardless of whether they had severe hypertension. The combined data revealed fluctuations in mean blood pressure ranging from 3 to 6 mm Hg, varying based on the method of measurement.

This review focuses on comparing ibuprofen's effect on hypertensive pregnancy disorders in postpartum women. The Hypertension in Postpartum Preeclampsia Study (HIPPS), conducted over a span from January 17, 2017, to February 24, 2018, stands out as a meticulously designed double-blind, randomized clinical trial. Its main objective was to delve into the realm of postpartum BP dynamics, particularly among women navigating the challenges of pregnancy-related hypertension.. Participants were pregnant women aged 18 or older, diagnosed with a hypertensive pregnancy condition, and beyond 24 weeks pregnant

Following childbirth, participants were randomly allocated to receive one of two postpartum pain relief treatments: Participants were administered either 600 mg of NSAID, ibuprofen by mouth every 6 hours (referred to as the “ibuprofen group") or 650 mg of acetaminophen by mouth every 6 hours (referred to as the "acetaminophen group"). Pain levels were meticulously assessed and recorded at intervals of no more than 12 hours, utilizing either visual cues (such as the Wong-Baker facial grimace scale) or verbal descriptors (numeric analog scales). The main focus of the study was on the average mean arterial blood pressure measurements documented throughout each participant's postpartum hospitalization.

Measurements were conducted from the initiation of the study medication until the patients were discharged. A total of 61 participants completed the trial, with 31 in the ibuprofen group and 30 in the control group. Participants in the ibuprofen group received medication approximately 3.0 hours after delivery, while those in the control group received it after 3.4 hours, on average. Notably, there was no noteworthy difference in the number of women meeting diuresis criteria before being discharged between the two groups. Moreover, the findings did not indicate any elevation in postpartum blood pressure with ibuprofen administration compared to individuals not receiving NSAIDs. Both ibuprofen and acetaminophen provided effective pain relief, high patient contentment, and similar clinical results. These findings imply that Non-Steroidal Anti-Inflammatory Drugs, generally, do not worsen BP in postpartum women with hypertensive pregnancy disorders, unless severe hypertension is recorded. On average, each patient underwent 17 blood pressure checks from the beginning of medication administration to discharge. While a randomized controlled trial couldn't decisively determine the impact of NSAIDs on postpartum blood pressure in women, an open-label trial hinted at a heightened probability of postpartum hypertension among women who took ibuprofen.

Without features that were equated to be severe in the patients, as determined by ACOG before childbirth, were eligible for inclusion. Ibuprofen or acetaminophen was provided to eligible participants in a 1:1 ratio for managing postpartum pain. Participants received the assigned medication every 6 hours for the initial 24 hours following randomization, followed by the alternate drug for the subsequent 24 hours. The primary focus of the study was to measure the adjusted mean difference in systolic blood pressure (SBP) after 24 hours of medication administration compared to the baseline. Out of the initial pool of 126 eligible women, 74 consented to participate, and eventually, 43 were randomly selected for the study. The intention-to-treat analysis included 37 women, with 19 initially receiving ibuprofen and 18 receiving acetaminophen. There was no significant change in systolic blood pressure from baseline after exposure to either ibuprofen ($p = 0.11$) or acetaminophen. However, there was a statistically notable decrease in diastolic blood pressure from baseline following ibuprofen administration. The incidence of severe BP readings did not differ between the two treatment groups, and no intravenous antihypertensive therapy was required during the study period. Pain scores recorded during the study revealed no significant differences between ibuprofen and acetaminophen.

In conclusion, ibuprofen and acetaminophen exhibited similar effects, or lack thereof, on postpartum systolic blood pressure after 24 hours of drug exposure in this randomized controlled trial. No notable difference was observed in the occurrence of severe blood pressure readings between the two groups, and neither study arm required intravenous antihypertensive medication.

The subsequent study[3] aimed to investigate whether individuals with severe postpartum preeclampsia who were administered ibuprofen differed in blood pressure levels compared to those given acetaminophen. Participants were randomly assigned to receive either 400 mg of ibuprofen every 8 hours until discharge or 1g of acetaminophen every 6 hours for 2-3 days. The primary variable examined was the presence of systolic blood pressure ≥ 150 mmHg and/or diastolic blood pressure ≥ 100 mmHg within the first 24 hours postpartum (24 to 96 hours postpartum). Secondary variables included arterial blood pressure readings taken at 24 hours, 48 hours, 72 hours, and 96 hours postpartum, as well as postpartum maternal complications such as bleeding, upset stomach, postpartum eclampsia, and encephalopathy. A total of 113 patients participated in the study: 56 in the acetaminophen group and 57 in the ibuprofen group.

Severe hypertension, defined as blood pressure levels of ≥ 160/110 mmHg between 24 and 96 hours postpartum, results did not reveal significant differences between the groups, with rates of 14.5% versus 24.5%; however, the ibuprofen group had twice as many cases. SBP showed a notable increase in the ibuprofen (NSAID) group at intervals of 24, 48, and 96 hours, while DBP was significantly elevated in the ibuprofen group at 72 and 96 hours. Additionally, mean blood pressure was notably increased in the ibuprofen group at the 24, 72, and 96 hours mark. In conclusion, this study suggests that administering ibuprofen raises the BP in women with severe pre-eclampsia during their postpartum period.

In a separate investigation[4], individuals diagnosed with severe preeclampsia were randomly distributed to receive continual oral administration of either 600 mg of ibuprofen or 650 mg of acetaminophen every 6 hours. The primary parameter of interest was the length of time (measured in hours) from childbirth until the last recorded blood pressure reading reached or surpassed the threshold of ≥160/110 mm Hg, defining severe-range hypertension. Secondary assessments encompassed the interval from delivery to the last blood pressure measurement meeting or surpassing ≥150/100 mm Hg, alongside the evaluation of mean arterial pressure and the necessity for antihypertensive drugs upon discharge. A cohort of one hundred subjects was randomly allocated to receive either ibuprofen or acetaminophen postpartum as an initial intervention for pain management. No significant variances in baseline characteristics were observed between the two groups, and there were no discrepancies detected in the duration of severe-range hypertension between those administered ibuprofen versus acetaminophen. Consequently, the preliminary application of ibuprofen, a nonsteroidal anti-inflammatory drug (NSAID), for alleviating postpartum discomfort did not extend the duration of severe-range hypertension in individuals with severe preeclampsia.

Additionally, a comprehensive systematic review and meta-analysis[5] sought to thoroughly examine the correlation between postpartum NSAID utilization among women diagnosed with hypertensive disorders during pregnancy (HDP) and the incidence of adverse postpartum consequences. The primary aim was to explore maternal blood pressure levels, particularly those meeting or surpassing 150 mm Hg SBP and/or 100 mm Hg DBP.

Secondary endpoints comprised sustained elevation in blood pressure beyond the thresholds of 160 mm Hg SBP and/or 110 mm Hg DBP, MAP, initiation or escalation of antihypertensive medication, duration of hospital stay, readmission due to blood pressure management concerns, and consumption of postpartum opioids. The review encompassed 7 studies, including 4 randomized trials and 3 cohort studies, with a collective sample size of 777 patients. While cohort investigations exhibited modest levels of bias, evaluation of two randomized controlled trials unveiled significant risks of bias associated with blinding and inclusion criteria.

No significant correlation was detected between NSAID usage and blood pressure levels equal to or surpassing 150 mm Hg SBP and/or 100 mm Hg DBP, as indicated by a risk ratio (RR) of 1.21 with a 95% confidence interval (CI) ranging from 0.89 to 1.64. However, the administration of NSAIDs led to a statistically significant but clinically insignificant increase in the length of postpartum hospitalization (0.21 days, 95% CI: 0.05-0.38). Nevertheless, there were no significant differences in other secondary outcomes between the 2 groups.

In the context of the review article[6], the documented rise in postpartum hypertension among women who received ibuprofen in an open-label study prompts inquiries into the potential impact of NSAIDs on blood pressure regulation following childbirth. Nevertheless, contrasting results from other studies hint at a complex interplay between NSAID usage and the continuity of hypertension in women grappling with severe HDP. This disparity highlights the necessity for additional investigations to unravel the underlying mechanisms behind these observations and to discern the practical implications for postpartum care strategies.

The primary outcomes assessed, including systolic and diastolic blood pressure, provide essential insights into the physiological effects of NSAIDs on cardiovascular health in the postpartum period. Additionally, secondary measures such as mean arterial pressure, occurrence of severe-range blood pressure, and severe hypertension offer a comprehensive evaluation of the impact of NSAID use on overall blood pressure control.

Comparative analysis between ibuprofen and acetaminophen revealed similar outcomes for mean arterial pressure, occurrence of severe-range blood pressure, and incidence of severe hypertension, suggesting comparable efficacy and safety profiles between the two medications. However, the discrepancy observed in the incidence of elevated blood pressure readings among women with severe preeclampsia features highlights the importance of considering individual patient characteristics and clinical context when selecting postpartum pain management strategies.

Overall, these findings underscore the complexity of managing HDP in the postpartum period and emphasize the need for personalized treatment approaches tailored to individual patient needs and risk profiles. Further research is warranted to clarify the potential implications of NSAID use on blood pressure regulation and to optimize postpartum care protocols for women with HDP.

Based on limited evidence, the American College of Obstetricians and Gynecologists (ACOG) suggests avoiding postpartum Non-Steroidal Anti-Inflammatory Drugs (such as ibuprofen and acetaminophen) use in women with preeclampsia who develop postpartum hypertension. In conclusion, it can be extrapolated that the use of ibuprofen and acetaminophen may not affect the blood pressure of women with preeclampsia significantly

## METHODOLOGY

Literature Search:

A systematic literature search was conducted on reputable databases, including Google Scholar and PubMed, to identify relevant studies published between 2016 and 2021. The search strategy utilized keywords such as "postpartum pain management," "NSAIDs," "ibuprofen," and "hypertensive disorders of pregnancy." The inclusion criteria were limited to papers written in English to ensure consistency in language comprehension.

Study Selection:

The initial search yielded a pool of potential articles. After screening titles and abstracts, studies that focused on the impact of NSAIDs, particularly ibuprofen, on postpartum blood pressure in women with hypertensive disorders of pregnancy were selected. The criteria included randomized controlled trials, systematic reviews, meta-analyses, and observational studies that provided relevant insights into the topic.

Inclusion Criteria:

1. Articles written in the English language.
2. Studies published between 2016 and 2021.
3. Papers available on reputable databases such as Google Scholar and PubMed.
4. Focus on postpartum pain management using NSAIDs, specifically ibuprofen.
5. Relevance to the topic of blood pressure outcomes in women with hypertensive disorders of pregnancy.

Exclusion Criteria:

1. Studies not written in the English language.
2. Studies published before 2016 or after 2021.
3. Irrelevant to the topic of postpartum pain management with NSAIDs.
4. Lack of focus on blood pressure outcomes in women with hypertensive disorders of pregnancy.
5. Poor methodological quality, as assessed during full-text review.

**Data Extraction:**

Data extraction included details on study design, participant characteristics, interventions (ibuprofen or acetaminophen), outcome measures (blood pressure readings, pain scores, and maternal complications), and key findings. The collected data facilitated a comprehensive analysis of the impact of NSAIDs on postpartum blood pressure in the specified population.

Quality Assessment:

The methodological quality of selected studies was assessed to ensure the reliability of the evidence. This assessment considered factors such as study design, participant selection, blinding, and outcome measurement. Studies with methodological flaws were carefully scrutinized during the interpretation of results and discussion.

Data Synthesis:

The synthesized data from selected studies were organized and presented according to key themes, including blood pressure outcomes, pain control, and patient satisfaction. Any discrepancies or variations in study results were discussed, providing a nuanced understanding of the impact of NSAIDs on postpartum blood pressure in women with hypertensive disorders of pregnancy.

## RESULTS

HIPPS Trial: HIPPS[1], a rigorous double-blind, randomized clinical trial, revealed no discernible disparity in postpartum blood pressure readings between women administered ibuprofen and those given acetaminophen. This outcome resonated with findings from other randomized controlled trials (RCTs), including investigations into postpartum blood pressure outcomes among women with pregnancy-related hypertension.[2]

Examining Severe Pre-eclampsia:

A dedicated study on severe pre-eclampsia[3] unveiled a statistically notable rise in systolic, diastolic, and mean blood pressure (MBP) levels in the ibuprofen-treated group in comparison to those receiving acetaminophen. Nonetheless, the clinical significance of these fluctuations remains uncertain, underlining the imperative for further scrutiny in this specific subgroup.

Insights from Systematic Review and Meta-analysis:

An exhaustive systematic review and meta-analysis[5], incorporating findings from seven studies, found no conclusive link between NSAID utilization and blood pressure levels reaching or exceeding ≥150/100 mm Hg. However, the analysis did reveal a statistically significant, albeit modest, increase in the duration of postpartum hospital stays associated with NSAID intake.

Perspective from Review Article:

The comprehensive review article[6] shed light on the heightened occurrence of postpartum hypertension among women who had a history of ibuprofen intake in an open-label study. However, a divergent narrative emerged from other studies, suggesting a lack of a straightforward association between NSAID use and the persistence of postpartum hypertension in women dealing with severe hypertensive disorders of pregnancy. The primary metrics under scrutiny included SBP and DBP, providing crucial insights into the hemodynamic effects of NSAIDs during the postpartum period. Additionally, secondary endpoints, such as MAP, the incidence of severe-range blood pressure, and the prevalence of severe hypertension (>160/110 mmHg), were evaluated, alongside satisfaction levels, offering a comprehensive assessment of the impact of NSAID administration on blood pressure dynamics and patient experience postpartum.

Synthesizing the Evidence:

To summarize, the collective evidence indicates that administering ibuprofen for postpartum pain management does not notably impact blood pressure outcomes in women with hypertensive disorders of pregnancy. Nonetheless, prudence is warranted in severe pre- eclampsia scenarios, where potential elevations in blood pressure were noted.[3] Additionally, the meta-analysis indicates a marginal uptick in postpartum hospital stays linked to NSAID usage.[5]

Clinical Implications:

Despite concerns raised in specific subgroups, the overall findings indicate comparable efficacy between ibuprofen and acetaminophen in pain control and patient satisfaction. This supports their use in postpartum analgesia for women with hypertensive disorders of pregnancy ([1], [2], [5]). Clinicians should weigh the risk-benefit profile, especially in severe pre-eclampsia cases, where the evidence is less conclusive ([3], [6]).

## DISCUSSION

Consistency of Findings:

The consistent findings across various studies underscore the reassuring safety profile of ibuprofen in postpartum pain management for women with HDP. Both the HIPPS trial and other randomized controlled trials (RCTs) ([1] , [2]) revealed comparable postpartum blood pressure levels between individuals administered ibuprofen and those given acetaminophen. This convergence of evidence provides robust support for the notion that ibuprofen usage does not significantly affect blood pressure in this population.

Caution in Severe Pre-eclampsia:

However, a note of caution is warranted, particularly in severe pre-eclampsia cases. The article by Vigil-De Gracia et al.[3] reported a significant increase in BP in the ibuprofen group compared to the acetaminophen group, emphasizing the need for careful consideration in this specific subgroup. These findings suggest that the impact of ibuprofen on blood pressure might vary depending on the severity of the hypertensive disorder.

Inconsistencies in Severe Pre-eclampsia Studies:

It's noteworthy that other studies, such as the trial conducted by Blue et al.[4], did not observe a significant difference in blood pressure outcomes between ibuprofen and acetaminophen groups in severe pre-eclampsia. This discrepancy in findings underscores the complexity of the relationship between NSAIDs and blood pressure in specific clinical scenarios, warranting further exploration.

Systematic Review Insights:

Premkumar et al.'s systematic review and meta-analysis[5] offered a comprehensive overview by synthesizing evidence from multiple studies. While reaffirming the absence of a link between NSAID usage and blood pressure levels ≥150/100 mm Hg, it did identify a statistically significant, albeit clinically inconsequential, extension in postpartum hospital stays linked to NSAID administration. This underscores the importance of conducting a balanced risk-benefit evaluation when contemplating NSAID usage for postpartum pain relief

Limitations and Heterogeneity:

The interpretation of these findings is subject to several limitations. Heterogeneity in study designs, participant characteristics, and measurement methods introduces potential sources of bias. The variability in defining and categorizing hypertensive disorders of pregnancy further contributes to the complexity of synthesizing results. Additionally, the limited number of studies specifically addressing severe pre-eclampsia underscores the necessity for more targeted research in this high-risk population.

Clinical Implications and Future Research:

The overall findings support the administration of ibuprofen and acetaminophen interchangeably for postpartum pain management in women suffering from hypertensive disorders of pregnancy, excluding those with severe pre-eclampsia. The potential elevation in blood pressure observed in severe cases necessitates careful consideration and individualized decision-making. Future research should focus on elucidating the specific factors contributing to the observed discrepancies in blood pressure outcomes, with an emphasis on refining guidelines for NSAID use in the postpartum period.

## CONCLUSION

There was no indication that ibuprofen led to elevated postpartum blood pressure when compared to women who did not receive NSAIDs. Moreover, both ibuprofen and acetaminophen demonstrated effective pain management, high patient satisfaction levels, and similar clinical outcomes.[1] Evidence suggests that neither ibuprofen nor acetaminophen significantly affect blood pressure in cases of preeclampsia.[2] After 24 hours of drug exposure, ibuprofen (an NSAID) and acetaminophen showed comparable effects on SBP postpartum.[2] However, NSAID usage was linked to a statistically significant, yet clinically inconsequential, prolongation of postpartum hospital stays. No significant disparities were observed in other secondary outcomes between the two groups.

# DECLARATION

## Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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The authors affirm the absence of conflicts of interest related to this research. No financial or non financial competing interests exist.

## Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

## Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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## REFERENCES

(1).Penfield CA, McNulty JA, Oakes MC, Nageotte MP. Ibuprofen and Postpartum Blood Pressure in Women with Hypertensive Disorders of Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2019 Dec;134(6):1219-1226. doi: 10.1097/AOG.0000000000003553. PMID: 31764732. https://pubmed.ncbi.nlm.nih.gov/31764732/

(2). Triebwasser JE, Hesson A, Langen ES. A randomized-controlled trial to assess the effect of ibuprofen on postpartum blood pressure in women with hypertensive disorders of pregnancy. Pregnancy Hypertens. 2019 Oct; 18:117-121. doi: 10.1016/j.preghy.2019.09.012. Epub 2019 Oct 3. PMID: 31586784. https://pubmed.ncbi.nlm.nih.gov/31586784/

(3). Vigil-De Gracia P, Solis V, Ortega N. Ibuprofen versus acetaminophen as a post- partum analgesic for women with severe pre-eclampsia: randomized clinical study. J Matern Fetal Neonatal Med. 2017 Jun;30(11):1279-1282. doi: 10.1080/14767058.2016.1210599. Epub 2016 Aug 2. PMID: 27384376. https://pubmed.ncbi.nlm.nih.gov/27384376/

(4). Blue NR, Murray-Krezan C, Drake-Lavelle S, Weinberg D, Holbrook BD, Katukuri VR, Leeman L, Mozurkewich EL. Effect of ibuprofen vs acetaminophen on postpartum hypertension in preeclampsia with severe features: a double-masked, randomized controlled trial. Am J Obstet Gynecol. 2018 Jun;218(6): 616.e1-616.e8. doi: 10.1016/j.ajog.2018.02.016. Epub 2018 Mar 2. PMID: 29505772. https://pubmed.ncbi.nlm.nih.gov/29505772/

(5). Premkumar A, Ayala NK, Miller CH, Grobman WA, Miller ES. Postpartum NSAID Use and Adverse Outcomes among Women with Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-analysis. Am J Perinatol. 2021 Jan;38(1):1-9. doi: 10.1055/s-0040-1713180. Epub 2020 Jul 18. PMID: 32682329. https://pubmed.ncbi.nlm.nih.gov/32682329/

(6). Wang B, Yang X, Yu H, Man X. The comparison of ibuprofen versus acetaminophen for blood pressure in preeclampsia: a meta-analysis of randomized controlled studies. J Matern Fetal Neonatal Med. 2020 Jun 7:1-6. doi: 10.1080/14767058.2020.1720641. Epub ahead of print. PMID: 32508173. https://pubmed.ncbi.nlm.nih.gov/32508173/