Comparative Efficacy of Labetalol and Methyldopa in the Management of Pregnancy-Induced Hypertension

*Sultana S,[1] Sharmin I,[2] Parvin M,[3] Basak S,[4] Sharmin N,[5] Holy MF[6]

Abstract

Background: Pregnancy-induced hypertension (PIH) is a common obstetric complication marked by elevated blood pressure after 20 weeks of gestation, affecting 5–10% of pregnancies worldwide and contributing significantly to maternal and fetal morbidity and mortality. Effective management is crucial to prevent progression to severe conditions like preeclampsia or eclampsia. Labetalol and methyldopa are two widely used antihypertensives in pregnancy due to their safety and efficacy. Methyldopa offers a long safety record but has a slower onset and more side effects. With quicker action and better tolerability, Labetalol is increasingly preferred, though regional practices and comparative outcomes remain variable.

Aim: This study aims to evaluate the comparative efficacy of these two agents in managing PIH, with a focus on blood pressure control, and maternal side effects.

Methods: This prospective, comparative, cross-sectional study was conducted at the Department of Gynecology and Obstetrics in Dinajpur Medical College Hospital, Dinajpur, Bangladesh to assess the efficacy and safety of Methyldopa and Labetalol in 100 pregnant women with pregnancy-induced hypertension during 2 years , from January 2023 to December 2024. Participants were divided into two groups: Group A received Methyldopa (250 mg TID), and Group B received Labetalol (100 mg BID). Blood pressure, side effects, and treatment responses were monitored closely. Exclusion criteria included chronic hypertension, multiple gestation, and systemic disorders. Data were collected using structured questionnaires and analyzed using SPSS v26. Statistical significance was set at $p<0.05$, with t-tests and Chi-square tests applied for analysis.

Results: The study found Labetalol to be more effective and better tolerated than Methyldopa in managing pregnancy-induced hypertension. Post-treatment systolic and diastolic blood pressures were significantly lower in the Labetalol group (130.4/85.6 mmHg) compared to the Methyldopa group (136.1/89.7 mmHg). Labetalol achieved blood pressure control faster (3.6 ± 1.0 days vs. 4.8 ± 1.2 days, $p = 0.0005$) and required fewer additional antihypertensive agents (10% vs. 20%). Adverse effects were less familiar with Labetalol (16%) than Methyldopa (30%), with more frequent symptoms like headache and edema in the latter group, supporting Labetalol's superior efficacy and tolerability profile.

Conclusion: Labetalol proved more effective and better tolerated than Methyldopa in managing pregnancy-induced hypertension, achieving faster blood pressure control with fewer side effects. While both drugs were effective, Labetalol's superior efficacy and safety profile support its use as a preferred first-line antihypertensive agent by current clinical guidelines.

[Dinajpur Medical College Journal, 2025 Jul; 18 (2):130-137]
[Former M Abdur Rahim Medical College Journal]
DOI: https://www.doi.org/10.69861/djmcj2025v18i2s6

Keywords: Pregnancy-Induced Hypertension, Labetalol, and Methyldopa

1. **Dr. Siddika Sultana, Resident Surgeon (Gynae & Obs), Dinajpur Medical College Hospital, Dinajpur, Bangladesh. drsiddika2017@yahoo.com*
2. *Dr. Ishrat Sharmin, Associate Professor (Gynae & Obs), Dinajpur Medical College Hospital, Dinajpur, Bangladesh.*
3. *Dr. Minara Parvin, Junior Consultant, Dinajpur Medical College Hospital, Dinajpur, Bangladesh.*
4. *Dr. Sima Basak, Registrar (Gynae & Obs), Dinajpur Medical College Hospital, Dinajpur, Bangladesh.*
5. *Dr. Nusrat Sharmin, Resident surgeon (Gynae & obs), Dinajpur Medical College Hospital, Dinajpur, Bangladesh.*
6. *Dr. Mirza Farzana Holy, Junior Consultant, 250 Bedded Hospital, Moulvibazar Sadar, Moulvibazar, Bangladesh*

**For correspondence*

Introduction

Pregnancy-induced hypertension (PIH), also referred to as gestational hypertension, is a significant obstetric complication characterized by the new onset of elevated blood pressure (≥140/90 mmHg) after 20 weeks of gestation in previously normotensive women, without accompanying proteinuria or systemic features of preeclampsia.[1] PIH affects approximately 5–10% of pregnancies globally and is a leading contributor to maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries.[2,3] The condition, if left untreated or poorly managed, can progress to preeclampsia or eclampsia, leading to severe complications such as placental abruption, intrauterine growth restriction, preterm birth, and even maternal or fetal death.[4] Management of PIH requires a delicate balance between optimizing maternal cardiovascular health and minimizing potential adverse effects on the fetus. Antihypertensive therapy is primarily indicated in cases of severe hypertension (≥160/110 mmHg), to prevent cerebrovascular events while avoiding hypotension that could compromise uteroplacental perfusion.[5] Among the various antihypertensive agents used during pregnancy, labetalol and methyldopa are widely recommended due to their safety profiles and relative efficacy.[1,6] Methyldopa, a centrally acting alpha-2 adrenergic agonist, has long been considered a first-line agent for treating hypertension in pregnancy due to its extensive track record of fetal safety.[7] It reduces sympathetic outflow and peripheral vascular resistance, thereby lowering blood pressure. Methyldopa has been shown to have a gradual onset of action. While it is effective in maintaining blood pressure control, its side effects profile, such as sedation, depression, and hepatic dysfunction limits its tolerability in some patients. In contrast, labetalol, a combined alpha- and beta-adrenergic receptor blocker, has gained popularity for its rapid onset and dual mechanism of action. It effectively reduces systemic vascular resistance and heart rate, which is particularly useful in acute hypertensive settings.[8] Clinical trials and meta-analyses have demonstrated labetalol's superior efficacy in achieving blood pressure control compared to methyldopa, with comparable fetal safety outcomes.[9,10] Additionally, labetalol is associated with fewer central nervous system side effects, contributing to better maternal compliance.[11] Despite the widespread use of both drugs, the choice of agent often depends on clinician preference, local guidelines, drug availability, and patient-specific factors. Comparative studies from various regions have yielded mixed results regarding the superiority of one agent over the other.[11,12] In some settings, methyldopa remains the preferred option due to its cost-effectiveness and long-standing usage. In contrast, others advocate for labetalol based on faster blood pressure control and better tolerability.[13] Given the high burden of PIH and its implications for maternal and fetal health, there is a pressing need for context-specific evidence comparing the effectiveness and safety of labetalol and methyldopa. This study aims to evaluate the comparative efficacy of these two agents in the management of PIH, with a focus on blood pressure control, and maternal side effects.

Methods

A prospective, comparative, cross-sectional study was conducted to evaluate the efficacy and safety of Methyldopa and Labetalol in managing pregnancy-induced hypertension (PIH). The study was carried out in the Department of Obstetrics and Gynecology at Dinajpur Medical College Hospital, Dinajpur, Bangladesh, over 2 years form January 2023 to December 2024. The study included 100 pregnant women diagnosed with pregnancy-induced hypertension who attended the

antenatal clinic or were admitted to the obstetrics ward during the study period. A total of 100 patients were selected and divided equally into two groups:

- **Group A:** 50 patients received Methyldopa (initial dose 250 mg TID)
- **Group B:** 50 patients received Labetalol (initial dose 100 mg BID)

Inclusion Criteria

- Pregnant women aged 18–40 years
- Singleton pregnancy beyond 20 weeks of gestation
- Diagnosed with pregnancy-induced hypertension (SBP ≥140 mmHg and/or DBP ≥90 mmHg on two separate readings at least 4 hours apart)
- No prior antihypertensive treatment before hospital visit

Exclusion Criteria

- History of chronic hypertension or secondary hypertension
- Multiple gestations
- Known cardiac, renal, hepatic, or endocrine disorders
- Patients with eclampsia or preeclampsia at presentation
- Hypersensitivity to Methyldopa or Labetalol

Intervention and Monitoring

Following the initial clinical evaluation and laboratory investigations, patients were initiated on either Methyldopa or Labetalol. Blood pressure was monitored twice daily, and the medication dose was adjusted according to the clinical response. Additional antihypertensive agents were introduced if the target blood pressure (<140/90 mmHg) was not achieved. Patients were closely monitored for the time taken to reach the target BP, the need for dose escalation or addition of another drug, and the emergence of any side effects such as headache, edema, palpitations, or drowsiness.

Laboratory investigations included a complete blood picture (CBC) consisting of hemoglobin concentration (Hb%), red blood cell (RBC) count, white blood cell (WBC) count, and platelet count. Renal function was assessed through blood urea, serum creatinine levels, and urine analysis. Liver function was evaluated by measuring serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum albumin, serum bilirubin, serum gamma-glutamyl transferase (GGT), prothrombin time, and international normalized ratio (INR).

As part of the study protocol, each participant's baseline blood pressure was measured using a standard mercury sphygmomanometer after the patient had been seated and resting for 5 to 10 minutes.

Data Collection Tools

A structured questionnaire and clinical data sheet were used to record demographic details, obstetric history, comorbidities, blood pressure readings (pre- and post-treatment), side effects, and treatment outcomes.

Statistical Analysis

Data were analyzed using SPSS version (26.0). Descriptive statistics were used to summarize demographic and clinical data. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the Independent Sample t-test. Categorical variables were expressed as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test as appropriate. A p-value of <0.05 was considered statistically significant.

Results

The comparative study between Methyldopa and Labetalol for managing pregnancy-induced hypertension demonstrated that

Labetalol was more effective and better tolerated than Methyldopa in several clinical parameters. Table III, Labetalol significantly reduced both systolic and diastolic blood pressures. The mean systolic BP post-treatment was significantly lower in the Labetalol group (130.4 ± 5.8 mmHg) compared to the Methyldopa group (136.1 ± 6.2 mmHg, p = 0.001), and similarly, the mean diastolic BP was also lower (85.6 ± 3.7 mmHg vs. 89.7 ± 4.1 mmHg, p = 0.002), as also highlighted in Table IV. Regarding the need for additional antihypertensive agents (Table II), only 10% of patients in the Labetalol group required adjunct therapy compared to 20% in the Methyldopa group (p = 0.14). Side effects were less common in the Labetalol group, with only 16% experiencing adverse effects compared to 30% in the Methyldopa group, indicating better tolerability (Table 2). Specific side effects like headache, leg edema, and palpitations were more frequent in the Methyldopa group (Table V). Additionally, the average time required to control blood pressure was significantly shorter with Labetalol (3.6 ± 1.0 days) compared to Methyldopa (4.8 ± 1.2 days, p = 0.0005), reinforcing Labetalol's faster onset of action (Table V).

Table I: Demographic and Baseline Characteristics

Characteristic	Methyldopa (N=50)		Labetalol (N=50)		P-value
	n	%	n	%	
Age group (in years)					
< 20	5	10.00	4	8.00	
21-30	30	60.00	32	64.00	0.73
31-40	12	24.00	11	22.00	
>40	3	6.00	3	6.00	
Gravida					
<3	32	64.00	33	66.00	
3-5	15	30.00	14	28.00	0.89
>5	3	6.00	3	6.00	
Parity					
<3	40	80.00	38	76.00	
3-5	9	18.00	10	20.00	0.77
>5	1	2.00	2	4.00	
Abortion					
No History	38	76.00	40	80.00	
1-2	10	20.00	8	16.00	0.62
>2	2	4.00	2	4.00	
Comorbidities					
CHD (VSD)	1	2.00	0	0.00	
Diabetes Mellitus	3	6.00	4	8.00	0.56
No comorbidities	46	92.00	46	92.00	

Table II: Treatment Response and Side Effects

Characteristic	Methyldopa (N=50)		Labetalol (N=50)		P-value
	n	%	n	%	
Needed Additional Agent					
No added therapy	40	80.00	45	90.00	0.14
Needed additional anti-HTN	10	20.00	5	10.00	
Change in the Dose					
No change	30	60.00	35	70.00	
Increased x1	15	30.00	13	26.00	0.36
Increased x2	5	10.00	2	4.00	
Side Effect Development					

No side effects developed	35	70.00	42	84.00	0.09
Developed side effect	15	30.00	8	16.00	

Table III: SBP and DBP Comparison (Before and After Treatment)

Variables	Methyldopa (N=50)	Labetalol (N=50)	P-value
	Mean ± SD	Mean ± SD	
SBP pre-treatment	156.2 ± 8.5	158.3 ± 7.9	0.18
SBP post-treatment	136.1 ± 6.2	130.4 ± 5.8	0.001
DBP pre-treatment	102.5 ± 5.2	104.1 ± 6.1	0.14
DBP post-treatment	89.7 ± 4.1	85.6 ± 3.7	0.002

Table IV: Final Blood Pressure Comparison

Variables	Methyldopa (N=50)	Labetalol (N=50)	P-value
	Mean ± SD	Mean ± SD	
SBP post-treatment	136.1 ± 6.2	130.4 ± 5.8	0.001
DBP post-treatment	89.7 ± 4.1	85.6 ± 3.7	0.002

Table V: Side Effect Types and Time to BP Control

Characteristic	Methyldopa (N=50)		Labetalol (N=50)		P-value
	n	%	n	%	
Type of Side Effects					
Headache	5	10.00	2	4.00	0.21
Headache, Leg Edema	4	8.00	2	4.00	
Headache, Edema, Palpitation	3	6.00	1	2.00	
Headache, Edema, Palpitation, Drowsy	3	6.00	3	6.00	
Time to BP control (days)	Mean ± SD		Mean ± SD		
Time (days)	4.8 ± 1.2		3.6 ± 1.0		0.0005

Discussion

Pregnancy-induced hypertension (PIH), including gestational hypertension and preeclampsia, is a significant contributor to maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries like Bangladesh.[14] Antihypertensive treatment is crucial in managing PIH to prevent maternal complications such as eclampsia, placental abruption, and fetal growth restriction.[15] This study aimed to compare the efficacy and tolerability of two commonly used antihypertensive agents, Methyldopa and Labetalol, in managing PIH. Our findings demonstrate that Labetalol is more effective than Methyldopa in achieving timely blood pressure control with fewer side effects. This conclusion aligns with previous studies and supports Labetalol's status as a first-line agent in current clinical guidelines.[16,17] In the present study, both Methyldopa and Labetalol showed significant reductions in systolic and diastolic blood pressures from baseline. However, the mean post-treatment systolic blood pressure was significantly lower in the Labetalol group (130.4 ± 5.8 mmHg) compared to the Methyldopa group (136.1 ± 6.2 mmHg, p = 0.001), as seen in Table III and Table IV. Similarly, the mean diastolic blood pressure was significantly lower with Labetalol (85.6 ± 3.7 mmHg) versus Methyldopa (89.7 ± 4.1 mmHg, p = 0.002). These findings concord with the work of Vigil-De Gracia et al., who reported superior blood pressure-lowering efficacy of Labetalol in hypertensive pregnancies compared to Methyldopa.[18] The time required to achieve BP control is a crucial clinical endpoint, especially in a hospital setting where timely control reduces the risk of maternal and fetal complications. In our study, Labetalol

achieved target blood pressure significantly faster (3.6 ± 1.0 days) than Methyldopa (4.8 ± 1.2 days), p = 0.0005 (Table V). Similar outcomes were observed by Arshad et al., who reported that Labetalol leads to earlier blood pressure normalization and better maternal outcomes in patients with gestational hypertension [19]. The need for additional antihypertensive agents was also lower in the Labetalol group (10%) compared to Methyldopa (20%), although this did not reach statistical significance (p = 0.14). This trend suggests that Labetalol monotherapy is often sufficient, simplifying treatment regimens and improving patient compliance. These results mirror Shekhar et al.'s results, who demonstrated that Labetalol required fewer dose escalations and adjunctive therapies.[20] Tolerability is a significant consideration in choosing antihypertensive therapy during pregnancy, as adverse effects can influence both maternal adherence and fetal safety. In our study, side effects were more frequently reported with Methyldopa (30%) compared to Labetalol (16%), indicating better tolerability of the latter. Common adverse effects in the Methyldopa group included headache, leg edema, palpitations, and drowsiness (Table V), consistent with its known sedative and central alpha-agonist properties.[21] This finding is also supported by Magee et al., who found that women treated with Methyldopa were more likely to report fatigue and depressive symptoms than those on Labetalol.[22] From a pharmacological standpoint, Labetalol's combined alpha- and beta-blocking properties provide rapid vasodilation and decreased cardiac output without significant reflex tachycardia, which may explain its superior efficacy in acute BP control.[23] In contrast, Methyldopa acts centrally to reduce sympathetic outflow, resulting in a slower onset of action, which may not be ideal in moderate-to-severe cases requiring quick blood pressure normalization.

Limitations of the study

This study has some limitations. First, the sample size (n = 100) may not be sufficient to detect minor differences in secondary outcomes like the need for adjunctive therapy. A larger, multicenter randomized controlled trial would offer more generalizable results. Second, fetal and neonatal outcomes were not assessed, which limits our understanding of the drugs' safety profiles on the fetus. Another limitation is the relatively short follow-up period, which did not allow for assessment of long-term outcomes such as progression of preeclampsia or control of postpartum hypertension.

Conclusion

This study demonstrates that Labetalol is more effective and better tolerated than Methyldopa in managing pregnancy-induced hypertension (PIH). Labetalol achieved significantly greater reductions in both systolic and diastolic blood pressures and normalized blood pressure more rapidly, with fewer maternal side effects. While both drugs showed efficacy, the faster onset and lower adverse event profile of Labetalol support its preference as a first-line antihypertensive agent in PIH, consistent with current clinical guidelines. These findings highlight the importance of selecting optimal therapy to ensure better maternal outcomes and reinforce Labetalol’s superiority in controlling hypertension during pregnancy.

Funding: No funding sources
Conflict of interest: None declared

References

1. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 222: gestational hypertension and preeclampsia. Obstet Gynecol. 2020 Jun;135(6):e237-60.
2. Mol BW, Roberts CT, Thangaratinam S,

Magee LA, De Groot CJ, Hofmeyr GJ. Pre-eclampsia. The Lancet. 2016 Mar 5;387(10022):999-1011.

3. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. WB Saunders.
   In Seminars in perinatology 2012 Feb 1;36(1):56-59.
4. Steegers EA, Von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. The lancet. 2010 Aug 21;376(9741):631-44.
5. Magee LA, von Dadelszen P, Singer J, Lee T, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, Gafni A. The CHIPS randomized controlled trial (Control of Hypertension in Pregnancy Study) is severe hypertension just an elevated blood pressure?. Hypertension. 2016 Nov; 68(5):1153-9.
6. Abalos E, Duley L, Steyn DW, Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev. 2018 Oct 1;10(10):CD002252. doi: 10.1002/14651858.CD002252.pub4.
   PMID: 30277556; PMCID: PMC6517078.
7. Podymow T, August P. Antihypertensive drugs in pregnancy. WB Saunders. In Seminars in nephrology 2011 Jan 1;31(1):70-85.
8. Magee LA, Ornstein MP, Von Dadelszen P. Management of hypertension in pregnancy. Bmj. 1999 May 15;318(7194):1332-6.
9. Patel R, Shah R, Lad D, Rana D, Malhotra S. Comparative evaluation of efficacy and safety of methyldopa and labetalol in pregnancy-induced hypertension: A meta-analysis. Tropical Journal of Obstetrics and Gynaecology. 2020 Sep 7;37(1):119-25.
10. Vigil-De Gracia P, Lasso M, Ruiz E, Vega-Malek JC, de Mena FT, López JC. Severe hypertension in pregnancy: hydralazine or labetalol: a randomized clinical trial. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2006 Sep 1;128(1-2):157-62.
11. Qasim A, Siddiqui MH, Salam JU, Nusrat U. Labetalol versus methyldopa: efficacy in pregnancy induced hypertension. Gomal J Med Sci 2014; 12: 233-6.
12. Subhedar V, Inamdar S, Hariharan C, Subhedar S. Comparison of efficacy of labetalol and methyldopa in patients with pregnancy-induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2013 Mar 1;2(1):27-34.
13. Podymow T, August P. Update on the use of antihypertensive drugs in pregnancy. Hypertension. 2008 Apr 1;51(4):960-9.
14. World Health Organization. WHO recommendations on antiplatelet agents for the prevention of pre-eclampsia. World Health Organization; 2021 Dec 7. https://apps.who.int/iris/bitstream/handle/10665/350190/9789240037540-eng.pdf
15. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. The lancet. 2006 Apr 1;367(9516):1066-74.
16. Abalos E, Duley L, Steyn DW, Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev. 2018 Oct 1; 10(10):CD002252. doi: 10.1002/14651858.CD002252.pub4.
   PMID: 30277556; PMCID: PMC6517078.
17. Magee LA, Von Dadelszen P, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, Singer J, Gafni A, Gruslin A. Less-tight versus tight control of hypertension in pregnancy. New England Journal of Medicine. 2015 Jan 29;372(5):407-17.
18. Vigil-De Gracia P, Lasso M, Ruiz E, Vega-Malek JC, de Mena FT, López JC. Severe hypertension in pregnancy:

hydralazine or labetalol: a randomized clinical trial. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2006 Sep 1;128(1-2):157-62.
19. Arshad M, Farooq S, Majeed K, Khalid U, Afsheen A, Artemis P. Labetalol versus Methyldopa for Treatment of Pregnancy Induced Hypertension. Pakistan Armed Forces Medical Journal. 2024 Aug 31;74(4):1024.
20. Shekhar S, Sharma C, Thakur S, Verma S. Oral nifedipine or intravenous labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. Obstetrics & Gynecology. 2013 Nov 1;122(5):1057-63.
21. Sibai BM. Chronic hypertension in pregnancy. Obstetrics & Gynecology. 2002 Aug 1;100(2):369-77.
22. Magee LA, Cham C, Waterman EJ, Ohlsson A, Von Dadelszen P. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. Bmj. 2003 Oct 23;327(7421):955.
23. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, Hall DR, Warren CE, Adoyi G, Ishaku S. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018 Jul;72(1):24-43.