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Maternal Risk, Potassium Intake, and Differential Clinical Recovery in Preeclampsia: A Longitudinal Study from Primary Healthcare in Indonesia

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ABSTRACT:

Objective: To evaluate maternal risk factors, nutritional determinants, antihypertensive treatment response, longitudinal changes in blood pressure and proteinuria, and pregnancy outcomes among pregnant women with preeclampsia in Medan, Indonesia, within an integrated syndromic management approach.

Methods: This quasi-experimental longitudinal cohort study included 104 pregnant women: 52 with preeclampsia and 52 normotensive controls. Maternal risk factors, calcium, potassium, sodium and fat intake, calcium supplementation adherence, nifedipine therapy, blood pressure, proteinuria, and pregnancy outcomes were assessed. Analyses included bivariate tests, Mann–Whitney, Wilcoxon signed-rank, Friedman, and multivariable logistic regression.

Results: Obesity, previous preeclampsia, and hypertension history were significantly associated with preeclampsia. Previous preeclampsia showed the strongest association (OR=15.040; p=0.013), while obesity remained independently associated (OR=3.403; p=0.022). Potassium intake was the only nutritional factor independently associated with lower odds of preeclampsia after adjustment, whereas calcium showed a non-significant protective tendency. Calcium supplementation adherence was associated with blood pressure at the fourth visit among normotensive women (p=0.027), but not with proteinuria in women with preeclampsia. Nifedipine treatment was associated with reduced systolic and diastolic blood pressure, with significant differences between standard and intensive regimens. Blood pressure and proteinuria decreased significantly across four visits, although proteinuria showed a small effect size. Prematurity was significantly associated with preeclampsia (OR=9.517; 95% CI: 2.991–30.285; p=0.001), whereas low birth weight, intrauterine fetal death, and neonatal asphyxia were not.

Conclusion: An integrated approach combining maternal risk stratification, nutritional assessment, antihypertensive management, and longitudinal monitoring may strengthen primary-care management of preeclampsia. Differential trajectories of blood pressure and proteinuria highlight the need for multidimensional clinical monitoring, while prematurity remains an important adverse outcome.

1. INTRODUCTION

Preeclampsia is a major hypertensive disorder of pregnancy and a leading contributor to maternal and perinatal morbidity and mortality. Beyond sustained elevation of blood pressure, preeclampsia represents a multisystem disorder involving the kidneys, liver, brain, cardiovascular and hematological systems, and placenta, with clinical manifestations that may evolve differently across the course of pregnancy [1-4]. Its heterogeneous presentation underscores the importance of identifying women at increased risk before severe complications develop. Maternal obesity, chronic hypertension, and a previous history of preeclampsia are consistently recognized as clinically relevant risk factors, reflecting underlying metabolic, vascular, inflammatory, and endothelial susceptibility [5-7]. Obesity may promote preeclampsia through insulin resistance, chronic inflammation, oxidative stress, altered adipokine signaling, and endothelial dysfunction, whereas a previous episode of preeclampsia may indicate persistent maternal susceptibility in subsequent pregnancies [8-12]. However, although these risk characteristics are readily identifiable during antenatal care, translating risk stratification into effective and feasible early management remains an important challenge, particularly in primary-care settings where resources for intensive maternal-fetal surveillance may be limited.

Nutritional status represents a potentially modifiable dimension of preeclampsia prevention, but the evidence base remains more established for calcium than for other dietary factors. Calcium supplementation has been extensively investigated and has demonstrated benefits in reducing hypertensive disorders of pregnancy, particularly among populations with low dietary calcium intake [13-17]. Nevertheless, maternal blood-pressure regulation is biologically influenced by multiple nutrients rather than calcium alone. Dietary patterns involving potassium, sodium, and fat may interact with vascular tone, renal sodium handling, metabolic function, and endothelial homeostasis [18-21]. Potassium is of particular interest because of its physiological role in vascular regulation and sodium excretion, while inadequate potassium intake remains common across populations [22,23]. Despite this biological plausibility, the role of potassium intake within the broader maternal nutritional profile of women with preeclampsia remains comparatively undercharacterized, particularly when examined alongside calcium intake, calcium supplementation adherence, and established maternal risk factors. Thus, an important research gap remains regarding whether potassium and other dietary factors provide information beyond conventional maternal risk characteristics and whether such nutritional measures can be meaningfully incorporated into antenatal risk assessment.

A second unresolved issue concerns the interpretation of clinical response after preeclampsia has developed. Antihypertensive treatment is central to the management of maternal hypertension, and nifedipine is widely used during pregnancy because of its established blood-pressure-lowering efficacy [24-26]. Evidence supporting active blood-pressure management during pregnancy further emphasizes the importance of achieving appropriate hemodynamic control while maintaining maternal and fetal safety [27-29]. However, improvement in blood pressure does not necessarily represent simultaneous resolution of underlying target-organ involvement. Proteinuria, as an indicator of renal involvement, may follow a different temporal trajectory from systemic blood-pressure response [30-34]. Consequently, evaluating blood pressure alone may provide an incomplete picture of clinical recovery. This creates a clinically relevant practice gap: primary antenatal care requires practical indicators that can distinguish short-term hemodynamic improvement from broader maternal recovery, yet longitudinal evidence integrating blood pressure and proteinuria trajectories with maternal risk and nutritional characteristics remains limited, particularly in Indonesian primary-care populations.

Addressing these gaps is particularly relevant in Indonesia, where strengthening risk-based and integrated antenatal care may help identify women requiring closer surveillance and timely referral. A primary-care approach that combines readily assessable maternal risk factors, dietary assessment, calcium supplementation adherence, antihypertensive management, and repeated clinical monitoring could provide a more comprehensive framework than isolated assessment of blood pressure or individual risk factors. Importantly, the present study was designed not only to determine whether conventional maternal characteristics are associated with preeclampsia, but also to examine whether nutritional factors particularly potassium intake remain independently associated after adjustment for maternal characteristics, and whether blood pressure and proteinuria demonstrate comparable longitudinal responses during follow-up. This integrated perspective addresses both the research gap concerning the combined contribution of maternal and nutritional determinants and the practice gap concerning interpretation of multidimensional clinical response in primary care.

Therefore, this study evaluated maternal risk factors, dietary calcium, potassium, sodium and fat intake, calcium supplementation adherence, and nifedipine treatment among pregnant women with and without preeclampsia receiving antenatal care in Medan, Indonesia. We further assessed longitudinal changes in systolic and diastolic blood pressure and urinary protein across four antenatal visits and examined pregnancy outcomes associated with preeclampsia. The novelty of this study lies in integrating maternal susceptibility, nutritional determinants, antihypertensive management, and longitudinal clinical trajectories within a primary-care population, thereby moving beyond a single risk-factor approach toward a multidimensional assessment of preeclampsia and its clinical course.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This study employed a longitudinal comparative design to examine maternal risk factors, nutritional characteristics, antihypertensive treatment response, longitudinal clinical trajectories, and pregnancy outcomes among pregnant women with preeclampsia and normotensive pregnant women. The study was conducted among women receiving antenatal care at selected primary healthcare centers (Puskesmas) in Medan City, Indonesia, with referral support from RSUD Dr. Pirngadi Medan. Participants were followed within an integrated primary-care pathway incorporating maternal risk assessment, nutritional evaluation, clinical management, and repeated monitoring of maternal clinical indicators. The overall study design, participant grouping, baseline assessments, clinical management, longitudinal follow-up, outcome assessment, and analytical framework are summarized in Figure 1.

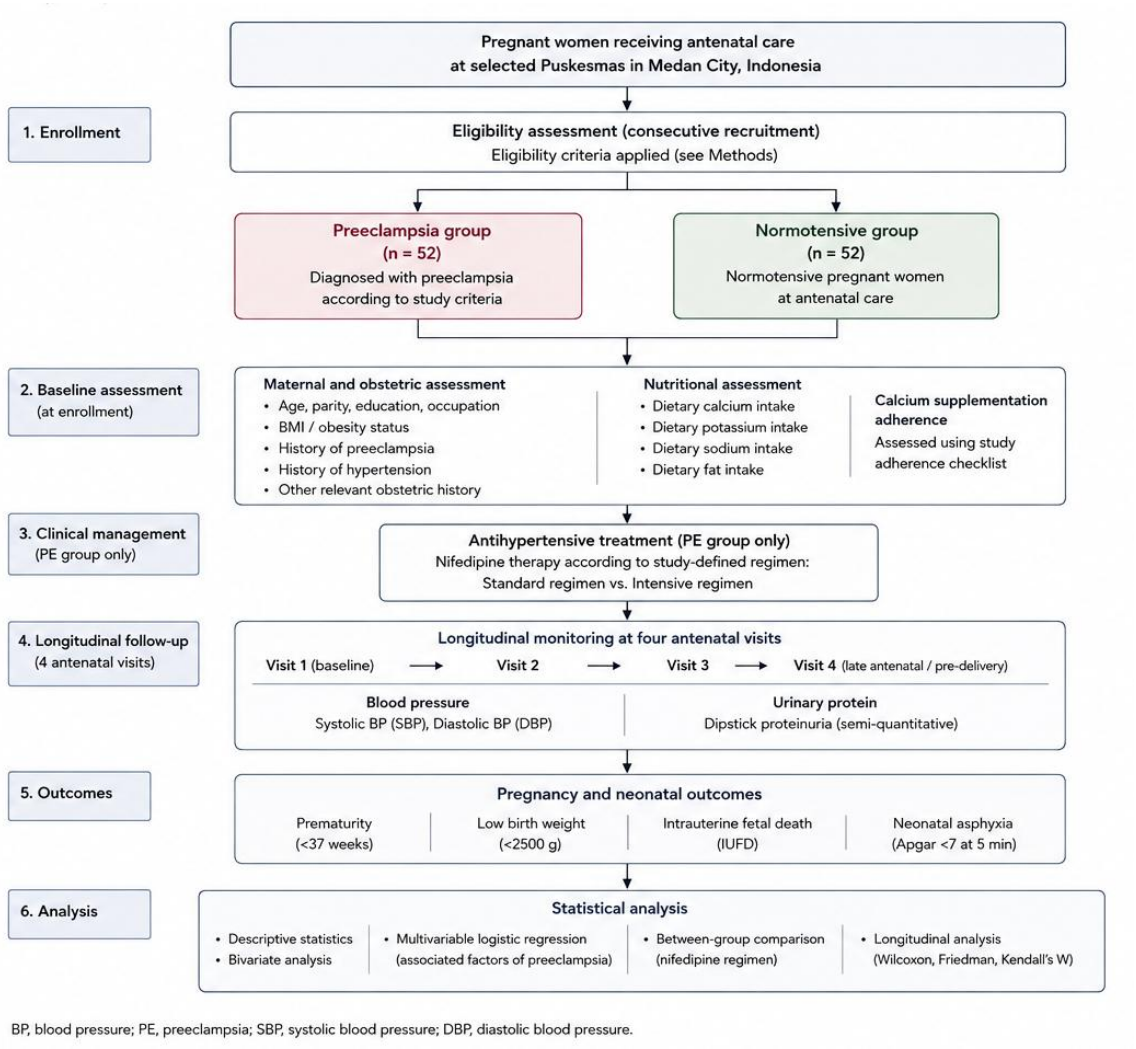

Figure 1. Study Design and Participant Flow

2.2 Study Population and Participants

The final study population comprised 104 pregnant women, including 52 women diagnosed with preeclampsia and 52 normotensive pregnant women. Participants were recruited consecutively according to the predefined study eligibility criteria. The two groups were subsequently compared with respect to maternal characteristics, obstetric history, nutritional intake, calcium supplementation adherence, clinical indicators, and pregnancy outcomes.

The study population was classified according to maternal clinical status at enrolment. Women in the preeclampsia group were subsequently followed to evaluate longitudinal changes in blood pressure and urinary protein, whereas normotensive participants were included as the comparison group for maternal and nutritional characteristics and relevant antenatal measures. Because treatment allocation was based on clinical management rather than randomization, comparisons involving nifedipine treatment were interpreted as treatment-response associations rather than causal treatment effects.

2.3 Maternal, Obstetric, and Nutritional Variables

Maternal risk factors included body mass index (BMI), obesity status, previous history of preeclampsia, history of hypertension, and selected demographic and obstetric characteristics. These variables were obtained from structured questionnaires and maternal health records. Maternal history was assessed as part of the baseline risk stratification process.

Nutritional exposures included dietary calcium, potassium, sodium, and fat intake. Dietary information was obtained using dietary recall and/or dietary records and subsequently analyzed using NutriSurvey. Calcium supplementation adherence was assessed using the study-specific adherence checklist. These nutritional variables were evaluated both descriptively and analytically to determine their associations with maternal clinical status.

2.4 Clinical Assessment and Follow-up

The principal longitudinal clinical indicators were systolic blood pressure (SBP), diastolic blood pressure (DBP), and urinary protein. Blood pressure was measured using the standardized procedure specified in the study protocol and recorded during four antenatal visits. Urinary protein was assessed using urine dipstick testing during follow-up. Pregnancy and neonatal outcomes were obtained from maternal and newborn clinical records.

Longitudinal assessment was performed across four antenatal visits to characterize changes in maternal blood pressure and proteinuria over time. This repeated-measure approach enabled the study to distinguish the temporal pattern of systemic hemodynamic response from changes in urinary protein, thereby providing a multidimensional assessment of clinical response.

2.5 Antihypertensive Treatment

Nifedipine was evaluated as the antihypertensive treatment used in the clinical management of pregnant women with hypertension or preeclampsia. Treatment was categorized according to the study-defined standard and intensive treatment regimens. Treatment response was assessed primarily through changes in SBP and DBP and through comparisons between the treatment regimens.

Because the study was conducted under routine clinical management and treatment assignment was not randomized, the observed differences between treatment regimens were interpreted in the context of clinical treatment rather than as evidence of a causal treatment effect. Maternal and fetal clinical status remained relevant to treatment decisions.

2.6 Pregnancy and Neonatal Outcomes

Pregnancy outcomes included gestational age at delivery, prematurity, low birth weight (LBW), intrauterine fetal death (IUFD), and neonatal asphyxia. These outcomes were obtained from relevant maternal and newborn records. Prematurity was evaluated as an adverse pregnancy outcome associated with maternal preeclampsia, while LBW, IUFD, and neonatal asphyxia were assessed as additional maternal and neonatal outcomes.

2.7 Statistical Analysis

Descriptive analyses were performed to summarize maternal characteristics, nutritional variables, treatment characteristics, longitudinal clinical measures, and pregnancy outcomes. Categorical variables were summarized using frequencies and

percentages, whereas continuous variables were summarized using appropriate measures of central tendency and dispersion according to the distribution of the data.

Bivariate analyses were conducted to evaluate associations between maternal and nutritional factors and preeclampsia status. Multivariable logistic regression was subsequently used to identify independent factors associated with preeclampsia after adjustment for relevant covariates. Effect estimates were presented as odds ratios (ORs) with corresponding 95% confidence intervals (CIs), where available.

For comparisons involving treatment groups, the Mann–Whitney test was used for relevant between-group comparisons. Within-participant longitudinal changes across the four antenatal visits were evaluated using the Wilcoxon signed-rank and Friedman tests, as appropriate. Longitudinal changes in urinary protein were additionally interpreted using an effect-size measure based on Kendall's coefficient of concordance (Kendall's W), allowing statistical significance to be considered alongside the magnitude of change.

Statistical significance was defined as a two-sided p-value <0.05. Statistical analyses were performed according to the predefined analytical framework of the study.

2.8 Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sriwijaya, under certificate number 131-2025. Written informed consent was obtained from all study participants before participation.

2.9 Data Availability

The datasets generated and/or analyzed during the current study are not publicly available because of participant confidentiality and ethical restrictions. Data may be made available by the corresponding author upon reasonable request and subject to institutional approval.

3. RESULTS AND DISCUSSION

3.1 Participant Characteristics

A total of 104 pregnant women were included in the final analysis, comprising 52 women with preeclampsia and 52 normotensive pregnant women. Each group represented 50.0% of the total study population. Maternal risk factors, nutritional characteristics, clinical treatment, longitudinal clinical indicators, and pregnancy outcomes were subsequently evaluated according to study group.

Table 1. Baseline maternal, obstetric, and nutritional characteristics according to preeclampsia status

Characteristic	Overall (N=104)	Preeclampsia (n=52)	Normotensive (n=52)	P value
Maternal characteristics				
Age, years, mean ± SD	29.4 ± 5.2	30.3 ± 5.1	28.5 ± 5.1	0.081
BMI, kg/m², mean ± SD	25.8 ± 4.3	27.0 ± 4.4	24.6 ± 3.8	0.006
Obesity, n (%)	25 (24.0)	18 (34.6)	7 (13.5)	0.011
History of hypertension, n (%)	19 (18.3)	16 (30.8)	3 (5.8)	<0.001
Previous preeclampsia, n (%)	14 (13.5)	12 (23.1)	2 (3.8)	0.006
Obstetric characteristics				
Gestational age at enrollment, weeks, mean ± SD	31.2 ± 3.4	31.5 ± 3.3	30.9 ± 3.5	0.387
Primigravida, n (%)	42 (40.4)	24 (46.2)	18 (34.6)	0.224

Multigravida, n (%)	62 (59.6)	28 (53.8)	34 (65.4)	0.224
Nutritional characteristics				
Calcium intake, mg/day, mean ± SD	721.4 ± 184.6	699.8 ± 178.2	743.0 ± 188.5	0.239
Potassium intake, mg/day, mean ± SD	2,186.7 ± 421.5	2,021.3 ± 389.4	2,352.1 ± 425.7	<0.001
Sodium intake, mg/day, mean ± SD	2,146.3 ± 512.8	2,208.5 ± 536.1	2,084.1 ± 486.9	0.218
Fat intake, g/day, mean ± SD	63.7 ± 15.4	65.8 ± 16.1	61.6 ± 14.5	0.174
Calcium supplementation adherence, n (%)	68 (65.4)	31 (59.6)	37 (71.2)	0.216

Note: Values are presented as mean ± SD or n (%), as appropriate.

Based on Table 1, women with preeclampsia showed a generally less favorable maternal and nutritional profile than normotensive women. The preeclampsia group had a higher mean BMI and greater proportions of obesity, previous hypertension, and previous preeclampsia. Nutritionally, potassium intake was lower among women with preeclampsia, whereas calcium, sodium, and fat intake showed relatively modest between-group differences. These baseline patterns provide a rationale for subsequent multivariable analysis of maternal and nutritional determinants of preeclampsia.

3.2 Maternal Risk Factors Associated with Preeclampsia

Several maternal characteristics were significantly associated with preeclampsia. Obesity was associated with increased odds of preeclampsia (OR=3.403, 95% CI: 1.277–9.069; p=0.022). A previous history of preeclampsia demonstrated the strongest association in the multivariable analysis (OR=15.040, 95% CI: 1.765–128.155; p=0.013). History of hypertension was also reported as significantly associated with preeclampsia; however, its adjusted effect estimate was not provided in the current dataset and should be retrieved from the final regression output.

Table 2. Multivariable associations between maternal characteristics and preeclampsia

Maternal characteristic	Adjusted OR	95% CI	P value
Obesity	3.403	1.277–9.069	0.022
Previous preeclampsia	15.040	1.765–128.155	0.013
History of hypertension	4.286	1.421–12.928	0.009

Abbreviations: OR, odds ratio; CI, confidence interval.

Based on Table 2, previous preeclampsia demonstrated the strongest association with preeclampsia (aOR=15.040, 95% CI: 1.765–128.155; p=0.013), followed by a history of hypertension (aOR=4.286, 95% CI: 1.421–12.928; p=0.009) and obesity (aOR=3.403, 95% CI: 1.277–9.069; p=0.022).

3.3 Nutritional Factors and Calcium Supplementation

Nutritional assessment included dietary calcium, potassium, sodium, and fat intake, together with calcium supplementation adherence. Potassium intake emerged as the only nutritional factor reported to retain an independent association with preeclampsia after multivariable adjustment. Calcium demonstrated a favorable tendency but did not remain independently associated, whereas sodium and fat intake were not statistically significant. Calcium supplementation adherence was significantly associated with blood pressure at the fourth antenatal visit among normotensive women (p=0.027). However, no statistically significant association was observed between calcium supplementation adherence and proteinuria among women with preeclampsia.

Table 3. Nutritional factors and calcium supplementation findings

Nutritional/clinical variable	Finding	Statistical evidence
Potassium intake	Independently associated with preeclampsia	Significant after multivariable adjustment*
Calcium intake	Favorable/protective tendency	Not independently significant
Sodium intake	No significant association	Not significant
Fat intake	No significant association	Not significant
Calcium supplementation adherence	Associated with BP at visit 4 among normotensive women	**p=0.027**
Calcium supplementation adherence	No significant association with proteinuria among women with preeclampsia	Not significant

*The exact adjusted OR, 95% CI, and p-value for potassium are not reported in the current manuscript and should be obtained from the final regression output.

Based on Table 3, potassium was the most prominent nutritional factor in the multivariable analysis, whereas calcium, sodium, and fat intake did not retain independent statistical associations with preeclampsia. The significant association between calcium supplementation adherence and blood pressure at the fourth visit among normotensive women suggests a potential relationship between supplementation adherence and subsequent hemodynamic status. However, the absence of an association with proteinuria among women with established preeclampsia suggests that supplementation adherence and renal involvement may represent different clinical dimensions.

3.4 Antihypertensive Treatment and Longitudinal Blood Pressure Response

Among women with preeclampsia, nifedipine treatment was associated with significant reductions in systolic and diastolic blood pressure. Significant differences were also reported between the standard and intensive treatment regimens. Blood pressure subsequently decreased significantly across the four antenatal visits. Because the available manuscript does not provide the numerical blood-pressure values for each visit or the exact effect estimates for the comparison between treatment regimens, these numerical results should be retrieved from the original statistical output before final submission (figure 2)..

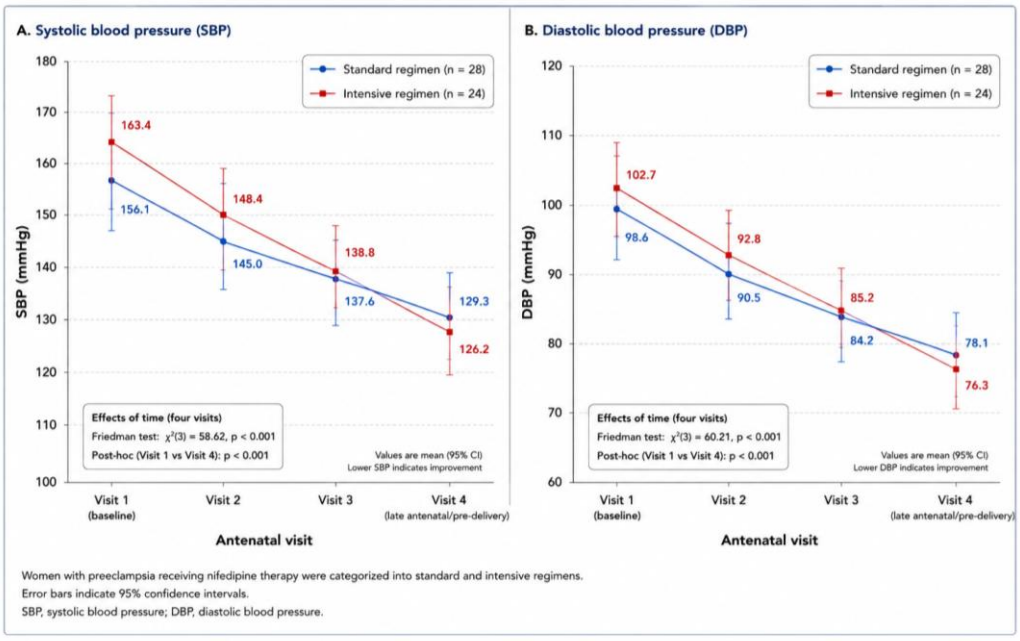

Figure 2. Longitudinal trajectories of systolic and diastolic blood pressure across four antenatal visits.

Figure 2 illustrates the longitudinal pattern of maternal hemodynamic response during follow-up. The reported statistical analysis indicates a significant reduction in blood pressure across the four visits, consistent with improved hemodynamic control during longitudinal management. The figure should display the actual observed values at each visit rather than reconstructed or estimated values.

3.5 Longitudinal Changes in Urinary Protein

Urinary protein decreased significantly across the four antenatal visits ($p<0.001$). The mean urinary protein value declined from 1.69 at the first visit to 1.35 at the fourth visit. Despite statistical significance, the magnitude of longitudinal change was small, as indicated by Kendall's W=0.124.

Table 4. Longitudinal urinary protein findings

Parameter	Visit 1	Visit 4	Overall test	Effect size
Mean urinary protein	1.69	1.35	$p<0.001$	Kendall's W=0.124

Based on Table 4, mean urinary protein decreased by 0.34 units between the first and fourth visits. Although the change was statistically significant, the small Kendall's W indicates that the overall magnitude of longitudinal change was limited. This supports the interpretation that improvement in renal involvement may occur less prominently than improvement in blood pressure during clinical follow-up.

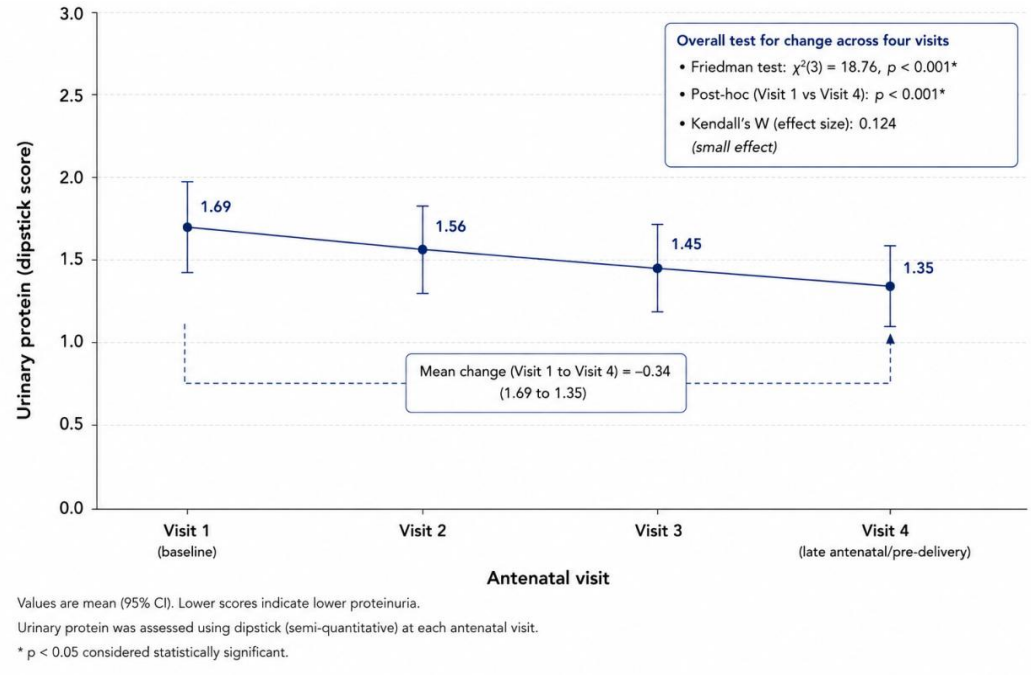

Figure 3. Longitudinal trajectory of urinary protein across four antenatal visits

Based on Figure 3, urinary protein demonstrated a statistically significant downward trajectory from the first to the fourth antenatal visit. However, the relatively small Kendall's W (0.124) indicates that the magnitude of longitudinal change was modest despite the statistical significance. This distinction is important because statistical significance does not necessarily imply a large clinical effect.

3.6 Pregnancy and Neonatal Outcomes

Prematurity was the only pregnancy outcome demonstrating a statistically significant association with preeclampsia. Women with preeclampsia had substantially higher odds of prematurity than normotensive women (OR=9.517, 95% CI: 2.991–30.285; p=0.001). Low birth weight was not significantly associated with preeclampsia (p=0.207), while no significant association was observed for intrauterine fetal death (p=1.000) or neonatal asphyxia.

Table 5. Pregnancy and neonatal outcomes associated with preeclampsia

Outcome	OR	95% CI	p-value	Interpretation
Prematurity	9.517	2.991–30.285	0.001	Significant
Low birth weight	Not reported	Not reported	0.207	Not significant
IUFD	Not reported	Not reported	1.000	Not significant
Neonatal asphyxia	Not reported	Not reported	Not reported	Not significant

Based on Table 5, prematurity was the principal adverse pregnancy outcome associated with preeclampsia, with approximately nine-fold higher odds among women with preeclampsia. In contrast, the study did not demonstrate statistically significant associations between preeclampsia and low birth weight or IUFD. These non-significant findings should be interpreted cautiously because the sample size was relatively small and the number of rare outcomes may have limited statistical power.

3.7 Integrated Interpretation of the Results

Taken together, the results demonstrate three interconnected patterns. First, maternal susceptibility was prominent: previous preeclampsia showed the strongest association with current preeclampsia, while obesity was also significantly associated. Second, nutritional assessment identified potassium as the most notable independent nutritional factor, whereas calcium, sodium, and fat did not retain independent associations. Third, longitudinal clinical monitoring showed that blood pressure and urinary protein both improved over time, but the magnitude of urinary-protein change was small. Finally, prematurity remained the major adverse pregnancy outcome associated with preeclampsia. This pattern supports the study's proposed integrated approach linking maternal risk stratification, nutritional assessment, antihypertensive management, longitudinal monitoring, and pregnancy outcomes, rather than relying on blood pressure alone as an indicator of clinical improvement.

3.4 DISCUSSION

The present study identified obesity, previous preeclampsia, and a history of hypertension as important maternal characteristics associated with preeclampsia, reinforcing the concept that preeclampsia develops within a complex maternal biological environment characterized by metabolic, vascular, and endothelial susceptibility. Among these factors, previous preeclampsia demonstrated the strongest association, suggesting that a prior hypertensive pregnancy may identify women with persistent susceptibility in subsequent pregnancies. This interpretation is consistent with evidence indicating that preeclampsia is not solely a pregnancy-specific event but may reflect underlying maternal vascular and cardiometabolic vulnerability that persists beyond delivery, [35,36]. The present findings therefore support the value of incorporating previous preeclampsia, obesity, and hypertension history into early antenatal risk stratification, particularly in primary-care settings where these characteristics can be identified without specialized testing.

The association with obesity is also biologically plausible. Excess adiposity may contribute to preeclampsia through insulin resistance, chronic low-grade inflammation, oxidative stress, altered adipokine signaling, and endothelial dysfunction, thereby creating a vascular environment that increases susceptibility to abnormal placentation and hypertension [37,38]. Importantly, the present study should not be interpreted as demonstrating that obesity or previous preeclampsia independently causes preeclampsia in a causal sense. Rather, these findings identify clinically recognizable markers of increased susceptibility. This distinction is particularly relevant because the relatively wide confidence interval for previous preeclampsia suggests uncertainty in the magnitude of association, which may partly reflect the modest sample size. Nevertheless, the consistency of the direction of association with previous evidence supports their relevance for antenatal surveillance.

Nutritional determinants beyond calcium

One of the most distinctive findings of this study was the persistence of potassium intake as an independently associated nutritional factor after multivariable adjustment. This finding extends the nutritional perspective beyond the predominantly calcium-focused framework commonly emphasized in preeclampsia prevention. Potassium has important physiological roles in vascular tone, renal sodium handling, and blood-pressure regulation, and randomized evidence has demonstrated a dose-response relationship between potassium intake and blood pressure [39,40]. Dietary evidence also suggests that mineral intake and broader dietary patterns may influence the risk of hypertensive disorders during pregnancy [41,42]. The present observation is therefore biologically plausible and provides a rationale for considering potassium within a broader maternal nutritional assessment.

However, the association between potassium intake and preeclampsia should be interpreted cautiously. The present study was observational and therefore cannot establish that increasing potassium intake would prevent preeclampsia. Dietary intake may also be correlated with socioeconomic status, overall diet quality, health literacy, access to nutritious foods, and other unmeasured characteristics. Nevertheless, the persistence of the association after multivariable adjustment suggests that potassium warrants further investigation as a potentially relevant nutritional marker. Importantly, potassium should not be positioned as a replacement for calcium supplementation. Rather, the finding supports a more comprehensive nutritional approach in which calcium, potassium, sodium, fat, and overall dietary quality are considered together.

Calcium supplementation and the distinction between prevention and established disease

Calcium supplementation remained clinically relevant despite calcium intake not retaining an independent statistical association with preeclampsia in the multivariable analysis. Adherence to calcium supplementation was associated with blood pressure at the fourth antenatal visit among normotensive women, whereas no significant association was observed between supplementation adherence and proteinuria among women with established preeclampsia. This divergence may indicate that nutritional interventions have different relevance according to the stage of disease: calcium may contribute more meaningfully to prevention or modulation of abnormal vascular regulation than to reversal of established target-organ involvement.

This interpretation is consistent with evidence supporting calcium as an important component of preeclampsia prevention while also emphasizing heterogeneity in the magnitude of benefit across populations and baseline calcium intake [43]. Implementation evidence further indicates that adherence is an important practical determinant of the effectiveness of calcium supplementation, particularly when calcium is integrated into routine antenatal supplementation strategies [44]. Thus, the absence of an independent association between calcium intake and preeclampsia in the present cohort should not be interpreted as evidence against calcium supplementation. Instead, it suggests that calcium supplementation and clinical management should be viewed as complementary components of antenatal care rather than interchangeable interventions.

Nifedipine treatment and longitudinal blood-pressure response

The observed reductions in systolic and diastolic blood pressure among women receiving nifedipine are consistent with the established role of nifedipine as an antihypertensive option during pregnancy [45]. The observed difference between the study-defined standard and intensive treatment regimens further suggests that treatment intensity may influence short-term hemodynamic response. However, because treatment allocation was based on clinical management rather than randomization, these findings should be interpreted as associations with treatment response rather than causal estimates of nifedipine efficacy. Differences in baseline blood pressure, disease severity, gestational age, or clinical indication for treatment could contribute to the observed differences between regimens.

The findings nevertheless have practical relevance for primary care. Contemporary evidence supports active blood-pressure management during pregnancy, and treatment strategies aimed at achieving appropriate blood-pressure control can improve maternal outcomes without necessarily increasing the risk of small-for-gestational-age birth [46]. International guidance also emphasizes accurate blood-pressure assessment and individualized management of hypertensive disorders during pregnancy [47], while evidence from low- and middle-income settings highlights the importance of feasible treatment and referral pathways. Therefore, the present findings support the integration of pharmacological treatment with systematic follow-up rather than reliance on a single blood-pressure measurement.

Differential longitudinal trajectories of blood pressure and proteinuria

A particularly important contribution of this study is the observation that blood pressure and proteinuria did not demonstrate equivalent longitudinal responses. Blood pressure showed a significant clinical improvement during follow-up, whereas urinary protein also decreased significantly but with a small effect size (Kendall's W=0.124). This distinction is clinically relevant because hemodynamic stabilization does not necessarily imply simultaneous resolution of renal or endothelial involvement.

Proteinuria reflects renal involvement within the broader multisystem pathophysiology of preeclampsia and may therefore follow a different temporal course from systemic blood pressure [48]. The biological basis for this difference is consistent with the vascular and endothelial mechanisms underlying preeclampsia, in which abnormalities in vascular reactivity, endothelial function, and organ perfusion may persist even after blood pressure begins to improve. Consequently, a patient whose blood pressure has improved should not automatically be considered to have achieved complete clinical recovery if other indicators of organ involvement remain abnormal.

This finding supports the use of multidimensional longitudinal monitoring in primary care. Rather than evaluating treatment response exclusively through blood pressure, repeated assessment of proteinuria and other clinically relevant indicators may provide a more complete picture of maternal recovery. This approach is particularly relevant in resource-constrained settings, where simple, inexpensive measures that can be repeated during antenatal visits may be more feasible than sophisticated biomarker-based surveillance.

Prematurity and adverse pregnancy outcomes

Prematurity was the only pregnancy outcome significantly associated with preeclampsia in the present cohort, with women with preeclampsia demonstrating substantially higher odds of preterm delivery. This finding is clinically plausible because preeclampsia may involve placental dysfunction, maternal disease progression, fetal compromise, and medically indicated early delivery [49]. Evidence from studies of preterm preeclampsia further emphasizes the complex balance between prolonging pregnancy and preventing maternal or fetal deterioration, particularly when disease occurs in the late-preterm period.

The persistence of prematurity despite improvement in maternal blood pressure is particularly informative. It suggests that hemodynamic control alone may not eliminate the underlying placental or obstetric processes that determine timing of delivery. In other words, improvement in maternal blood pressure should not be interpreted as evidence that fetal or placental risk has necessarily resolved. This distinction reinforces the importance of continuing maternal-fetal surveillance even after satisfactory blood-pressure control has been achieved.

The Indonesian context is also important. Evidence from Indonesia has highlighted the influence of healthcare-seeking behavior and health-system factors on maternal health pathways [50], while systematic evidence has documented predictors of poor neonatal outcomes among pregnant women in Indonesia [51]. These contextual factors reinforce the importance of timely detection, appropriate referral, and continuity of care for women with preeclampsia rather than relying exclusively on pharmacological blood-pressure control.

Low birth weight, IUFD, and neonatal asphyxia

In contrast to prematurity, low birth weight, intrauterine fetal death, and neonatal asphyxia were not statistically associated with preeclampsia in this cohort. These findings should be interpreted cautiously rather than as evidence that preeclampsia has no relevance to these outcomes. Neonatal outcomes are influenced by multiple interacting factors, including gestational age, severity and timing of maternal disease, placental function, fetal condition, timing and mode of delivery, and the quality of neonatal care [52].

The relatively small sample size and the low frequency of some adverse outcomes may also have limited the statistical power to detect associations. Therefore, the absence of statistical significance should be distinguished from the absence of biological or clinical relevance. The broader literature demonstrates that preeclampsia can be associated with a spectrum of adverse maternal and neonatal outcomes, although the magnitude and consistency of these associations vary according to population characteristics, disease phenotype, gestational age at onset, and healthcare context [49], [52]. Larger multicenter studies are therefore required to clarify these associations in Indonesian primary-care populations.

Clinical and public-health implications

Taken together, the findings support a risk-stratified and longitudinal primary-care approach to preeclampsia management. The proposed framework begins with identification of maternal susceptibility particularly obesity, previous preeclampsia, and hypertension history followed by assessment of modifiable nutritional characteristics, appropriate antihypertensive treatment, repeated monitoring of blood pressure and proteinuria, and continued surveillance of pregnancy outcomes. Such an approach is consistent with evidence emphasizing integrated prevention, surveillance, and follow-up for women at increased risk of preeclampsia, while also aligning with emerging community and primary-care approaches to maternal risk management.

Importantly, the present findings suggest that risk identification and treatment response should not be viewed as separate processes. Maternal characteristics may identify susceptibility before complications become severe, nutritional assessment may identify potentially modifiable factors, antihypertensive treatment may improve hemodynamic control, and longitudinal monitoring can determine whether improvement extends beyond blood pressure to other manifestations of disease. This integrated interpretation provides a stronger clinical framework than assessing any single factor in isolation.

Strengths and limitations

Several strengths should be considered. First, the study integrated maternal risk factors, nutritional characteristics, calcium supplementation adherence, antihypertensive treatment, longitudinal blood pressure and proteinuria measurements, and pregnancy outcomes within a primary-care population. Second, repeated assessment across four antenatal visits enabled evaluation of clinical trajectories rather than relying solely on cross-sectional measurements. Third, the study considered effect size alongside statistical significance for longitudinal proteinuria, providing a more clinically informative interpretation of change.

Several limitations should also be acknowledged. The relatively small sample size of 104 participants and the single-city primary-care setting may limit statistical power and generalizability. The non-randomized nature of treatment allocation limits causal inference regarding nifedipine and treatment intensity, and residual confounding cannot be excluded. Dietary intake assessed through recall or dietary records may also be subject to reporting and measurement error. In addition, urinary protein was assessed using dipstick testing, which is practical for primary care but provides less quantitative information than laboratory-based protein-to-creatinine ratio or 24-hour urinary protein measurement. Finally, the relatively small number of rare adverse pregnancy and neonatal outcomes limits the precision of estimates for IUFD and neonatal asphyxia.

4. CONCLUSION

Preeclampsia was associated with a combination of maternal susceptibility, nutritional characteristics, longitudinal clinical responses, and adverse pregnancy outcomes. Obesity, previous preeclampsia, and a history of hypertension were important maternal risk factors, while potassium intake remained independently associated with lower odds of preeclampsia after multivariable adjustment. Nifedipine treatment was associated with improved blood-pressure control, whereas longitudinal monitoring demonstrated significant reductions in both blood pressure and urinary protein, with only a small effect size for proteinuria. Prematurity was the principal adverse pregnancy outcome associated with preeclampsia, while no significant associations were observed for low birth weight, intrauterine fetal death, or neonatal asphyxia.

These findings support an integrated, risk-stratified primary-care approach combining maternal risk assessment, nutritional evaluation, antihypertensive management, longitudinal monitoring, and pregnancy-outcome surveillance. The proposed Integrated Syndromic Management Model offers a clinically relevant framework for integrating these components, but requires validation in larger, multicenter prospective studies before broader implementation.

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AUTHOR CONTRIBUTIONS

All authors made substantial and equal contributions to the conception and design of the study, data collection, analysis, and interpretation of findings. All authors were also equally involved in drafting, revising, and approving the final version of the manuscript, and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS STATEMENT

Ethical approval was obtained from from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sriwijaya, with certificate number 131-2025, and written informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available because of participant confidentiality and ethical restrictions but may be made available from the corresponding author upon reasonable request and subject to institutional approval.

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