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Original Research Article

Atherogenic index of plasma as a marker of severity in pre-eclampsia

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ABSTRACT

Background: Pre-eclampsia is a major hypertensive disorder of pregnancy associated with endothelial dysfunction, metabolic disturbance and adverse maternal-perinatal outcomes. The atherogenic index of plasma (AIP), derived from fasting triglyceride and high-density lipoprotein cholesterol values, may provide an integrated measure of atherogenic burden.

Methods: This hospital-based comparative cross-sectional study included 312 third-trimester pregnant women: 156 with pre-eclampsia and 156 normotensive pregnant women. Clinical parameters, biochemical markers, fasting lipid profile, AIP and fetomaternal outcomes were compared. AIP was categorized as low (<0.10), intermediate (0.10-0.24) and high risk (>0.24), and its associations with severity and delivery/neonatal outcomes were evaluated among women with pre-eclampsia.

Results: Women with pre-eclampsia had significantly higher BMI, blood pressure, random blood sugar, serum creatinine, LDH, total cholesterol, triglycerides and LDL-C, with lower HDL-C (all $p<0.001$, except gestational age). Mean AIP was higher in pre-eclampsia (0.39±0.13 versus 0.15±0.14; $p<0.001$), with high-risk AIP in 84.0% versus 23.7% of controls. High-risk AIP occurred in 98.2% of severe and 76.2% of mild pre-eclampsia ($p=0.001$). AIP correlated inversely with birth weight ($\rho=-0.759$) and 5-minute Apgar score ($\rho=-0.699$), while adverse outcomes were concentrated in the high-risk category.

Conclusions: Third-trimester pre-eclampsia was associated with higher AIP, greater disease severity and less favourable fetomaternal outcomes. AIP may serve as a low-cost adjunct marker for severity and short-term risk stratification, although prospective multivariable validation is required.

Keywords: Atherogenic index of plasma, Dyslipidemia, Fetomaternal outcomes, Hypertensive disorders of pregnancy, Pre-eclampsia, Severity marker

INTRODUCTION

Pre-eclampsia remains one of the most important hypertensive disorders of pregnancy and contributes substantially to maternal and perinatal morbidity and mortality, particularly in low- and middle-income settings. It is classically characterized by new-onset hypertension after mid-pregnancy with proteinuria or evidence of systemic involvement, and its burden is disproportionately greater in developing countries where early recognition and specialist obstetric care may be delayed.[1,2]

The pathophysiology of pre-eclampsia is multifactorial. Abnormal placental implantation and impaired spiral-artery remodelling initiate placental hypoperfusion, followed by release of anti-angiogenic and inflammatory mediators that promote systemic endothelial dysfunction. Endothelial injury, vasoconstriction, oxidative stress and increased vascular permeability account for the clinical

expression of hypertension, proteinuria and multi-organ involvement.[3,4]

Pregnancy is accompanied by physiological changes in lipid metabolism that support fetal growth, especially during the third trimester. However, in pre-eclampsia this adaptive lipid response may become exaggerated, with higher triglycerides, total cholesterol and low-density lipoprotein cholesterol (LDL-C), along with lower or dysfunctional high-density lipoprotein cholesterol (HDL-C). Such dyslipidemia may intensify oxidative stress, endothelial activation and placental vascular compromise.[5-9]

The Atherogenic Index of Plasma (AIP), calculated as log10 of the molar triglyceride/HDL-C ratio, was introduced as a marker reflecting the balance between atherogenic triglyceride-rich particles and protective HDL-C. It has been associated with small dense LDL particles and cardiovascular risk. In hypertensive pregnancy disorders, AIP may be clinically attractive because it is derived from routinely available lipid parameters and may summarize the atherogenic milieu more effectively than isolated lipid fractions.[9-12]

Recent studies have reported higher atherogenic indices in pre-eclampsia and have suggested potential relationships with blood-pressure burden and disease severity.[11-13] Nevertheless, Indian data, particularly from Central India, remain limited. Evidence is also insufficient regarding whether AIP can help stratify women with pre-eclampsia according to severity and fetomaternal risk in resource-constrained antenatal and obstetric settings. This study was undertaken to compare fasting lipid profile and AIP between third-trimester women with pre-eclampsia and normotensive pregnant women, and to evaluate the association of AIP with disease severity, blood-pressure burden and fetomaternal outcomes among women with pre-eclampsia.

METHODS

Study design and setting

This was a hospital-based comparative cross-sectional study conducted over one year in the department of obstetrics and gynecology at a tertiary care institute of Central India. Participants were recruited from the outpatient department and labour room after approval from the institutional ethics committee.

Participants and sampling

Eligible third-trimester pregnant women were enrolled consecutively into two groups: women diagnosed with pre-eclampsia and normotensive pregnant women without co-morbidities. Consecutive sampling was used to minimize selection bias in the hospital-based setting.

Eligibility criteria

Women with gestational age of at least 28 weeks were eligible. Cases had pre-eclampsia, defined by hypertension with proteinuria documented on two occasions. Normotensive pregnant women without co-morbidities were enrolled as controls. Women with gestational age below 28 weeks, pre-existing chronic hypertension, co-morbid conditions in the normotensive group or unwillingness to participate were excluded.

Sample size

The sample size was estimated for detecting a mean difference in AIP between groups using 95% confidence and 80% power, assuming a standard deviation of 0.23 and expected inter-group mean difference of 0.083, yielding 156 participants per group and a total sample of 312 women.

Clinical definitions and study variables

Pre-eclampsia severity was categorized among cases as mild or severe according to blood-pressure severity and evidence of end-organ involvement. Mild disease included systolic blood pressure 140-159 mmHg or diastolic blood pressure 90-109 mmHg. Severe disease included systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg and/or end-organ involvement.

AIP was calculated as the logarithmically transformed ratio of molar concentrations of triglycerides to HDL-C: AIP = $\log_{10}$(TG/HDL-C). For descriptive analysis, AIP was categorized as low risk (<0.10), intermediate risk (0.10-0.24) and high risk (>0.24).[10]

Data collection and measurements

After eligibility confirmation and written informed consent, socio-demographic details, obstetric history, parity, gestational age and co-morbidities were recorded using a structured case record form. General examination included weight, height and blood-pressure recording. Body mass index (BMI) was calculated from measured weight and height. Laboratory investigations included random blood sugar, serum creatinine, serum lactate dehydrogenase (LDH) and fasting lipid profile comprising total cholesterol, triglycerides, LDL-C and HDL-C. AIP was computed from fasting triglyceride and HDL-C values. Participant-level delivery and neonatal variables recorded for analysis included mode of delivery, birth weight, 5-minute Apgar score, neonatal location (ward or NICU) and final fetal/neonatal outcome.

Outcomes

The primary outcome was the difference in AIP between women with pre-eclampsia and normotensive pregnant women. Secondary outcomes included inter-group differences in lipid profile and biochemical parameters,

distribution of AIP risk categories, association of AIP with pre-eclampsia severity and blood-pressure burden, comparison of fetomaternal outcomes between groups, and participant-level association of AIP with delivery and neonatal outcomes among women with pre-eclampsia.

Statistical analysis

Categorical variables were summarized as frequency and percentage. Continuous variables were summarized as mean±standard deviation. Between-group comparisons for continuous variables were performed using Student's unpaired t-test; the Mann-Whitney U test was applied where required for non-normally distributed variables. Categorical variables were compared using the chi-square test, and Fisher's exact test was used where appropriate. For the AIP-fetomaternal outcome analysis among women with pre-eclampsia, continuous outcomes across the three AIP risk categories were compared using the Kruskal-Wallis test, while categorical outcomes were assessed using the Fisher-Freeman-Halton exact test because of sparse cells. Continuous AIP values were compared between binary outcome groups using the Mann-Whitney U test, and Spearman's rank correlation was used to evaluate the relationship of AIP with birth weight and 5-minute Apgar score. A two-sided p value <0.05 was considered statistically significant.

Ethical considerations

The study was initiated after approval from the institutional ethics committee (IEC/RDGMC/2024/50/2024; dated 09 May 2024). Written informed consent was obtained from all participants. Confidentiality was maintained throughout, and participation did not alter routine clinical care.

RESULTS

A total of 312 third-trimester pregnant women were analysed, including 156 women with pre-eclampsia and 156 normotensive pregnant women. The results are presented as continuous clinical-biochemical profile, lipid parameters, AIP-related severity findings and participant-level associations between AIP and fetomaternal outcomes among women with pre-eclampsia.

Table 1: Continuous clinical, biochemical and lipid parameters.

Measure	Pre-eclampsia Mean±SD (n=156)	Normotensive Mean±SD (n=156)	P value
Maternal age (years)	26.12±4.18	24.56±3.45	<0.001
Gestational age (weeks)	35.63±3.29	36.18±3.09	0.133
Body mass index (kg/m^2)	27.30±4.13	24.64±3.33	<0.001
Systolic blood pressure (mmHg)	156.05±12.83	113.58±7.10	<0.001
Diastolic blood pressure (mmHg)	101.71±8.82	71.44±6.10	<0.001
Random blood sugar (mg/dl)	108.26±18.34	95.35±15.91	<0.001
Serum creatinine (mg/dl)	0.93±0.23	0.70±0.12	<0.001
Serum LDH (U/l)	456.14±109.18	299.66±55.56	<0.001
Total cholesterol (mg/dl)	237.37±26.40	207.69±23.16	<0.001
Triglycerides (mg/dl)	244.76±59.67	172.15±42.50	<0.001
LDL-C (mg/dl)	152.15±22.09	120.24±20.77	<0.001
HDL-C (mg/dl)	42.38±6.08	51.67±6.99	<0.001

Unpaired t-test was used for between-group comparisons; gestational age was assessed using the Mann-Whitney U test where applicable. LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Table 2: Distribution of atherogenic index of plasma risk categories by study group.

AIP risk category	Pre-eclampsia N (%) (n=156)	Normotensive N (%) (n=156)	Total N (%) (n=312)	P value
Low risk (<0.10)	4 (2.6)	46 (29.5)	50 (16.0)	<0.001
Intermediate risk (0.10-0.24)	21 (13.5)	73 (46.8)	94 (30.1)	
High risk (>0.24)	131 (84.0)	37 (23.7)	168 (53.8)	

AIP categories were compared using the chi-square test. AIP- atherogenic index of plasma.

Mean maternal age and BMI were significantly higher among women with pre-eclampsia. Both systolic and diastolic blood pressures were markedly higher in the pre-eclampsia group. Random blood sugar, serum creatinine and serum LDH were also significantly elevated among women with pre-eclampsia. The lipid profile showed a consistent atherogenic pattern, with significantly higher total cholesterol, triglycerides and LDL-C, and significantly lower HDL-C among women with pre-eclampsia (Table 1).

Mean AIP was significantly higher in women with pre-eclampsia than in normotensive pregnant women (0.39±0.13 versus 0.15±0.14; p<0.001) (Figure 1).

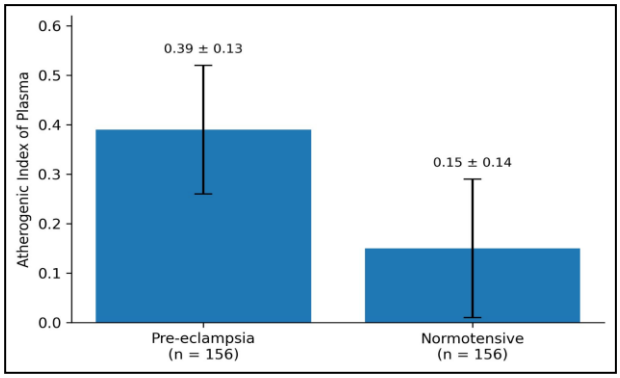

Figure 1: Mean atherogenic index of plasma by study group.

The distribution of AIP risk categories differed significantly between groups (p<0.001). High-risk AIP (>0.24) was present in 131/156 (84.0%) women with pre-eclampsia compared with 37/156 (23.7%) normotensive women. Low-risk AIP was uncommon in the pre-eclampsia group (4/156, 2.6%) but was observed in 46/156 (29.5%) normotensive women (Table 2).

Among women with pre-eclampsia, adverse fetomaternal outcomes showed a marked AIP gradient (Table 3). Cesarean delivery occurred in 0/4 (0.0%) low-risk, 4/21 (19.0%) intermediate-risk and 69/131 (52.7%) high-risk participants (p=0.001). Mean birth weight decreased from 2.75±0.13 kg in the low-risk group to 2.52±0.09 kg in the intermediate-risk group and 1.99±0.27 kg in the high-risk group (p<0.001); low birth weight was present in 131/131 (100.0%) high-risk participants. Low 5-minute Apgar score and NICU admission each occurred in 59/131 (45.0%) high-risk participants and in none of the low- or intermediate-risk participants (both p<0.001). All eight fetal/neonatal deaths occurred in the high-risk group, although the categorical association was not statistically significant because of the small number of events (p=0.677). As continuous measures, AIP correlated inversely with birth weight (Spearman ρ=-0.759, p<0.001) and 5-minute Apgar score (ρ=-0.699, p<0.001). Mean AIP was higher among women who underwent cesarean delivery, whose neonates had low birth weight or low Apgar scores, required NICU admission, or died (all p<0.001).

Table 3: Association of atherogenic index of plasma risk categories with fetomaternal outcomes among women with pre-eclampsia (n=156).

Variable	Low-risk AIP (<0.10) (n=4)	Intermediate-risk AIP (0.10-0.24) (n=21)	High-risk AIP (>0.24) (n=131)	P value
Mode of delivery, N (%)				0.001
Vaginal delivery	4 (100.0)	17 (81.0)	62 (47.3)	
Caesarean section (LSCS)	0 (0.0)	4 (19.0)	69 (52.7)	
Birth weight (kg), mean±SD	2.75±0.13	2.52±0.09	1.99±0.27	<0.001
Low birth weight (<2.5 kg), N (%)	0 (0.0)	5 (23.8)	131 (100.0)	<0.001
Apgar score at 5 minutes, mean±SD	8.50±0.58	8.00±0.00	6.44±1.14	<0.001
Low 5-minute Apgar score (<7), N (%)	0 (0.0)	0 (0.0)	59 (45.0)	<0.001
Neonatal location, N (%)				
Ward	4 (100.0)	21 (100.0)	72 (55.0)	<0.001
NICU admission	0 (0.0)	0 (0.0)	59 (45.0)	
Final fetal/neonatal outcome, N (%)				
Survived	4 (100.0)	21 (100.0)	123 (93.9)	0.677
Expired	0 (0.0)	0 (0.0)	8 (6.1)	

Continuous variables were compared using the Kruskal-Wallis test; categorical variables were compared using the Fisher-Freeman-Halton exact test. AIP, Atherogenic Index of Plasma; LSCS, lower-segment caesarean section; NICU, neonatal intensive care unit.

Among the 156 women with pre-eclampsia, 101 (64.7%) had mild disease and 55 (35.3%) had severe disease. High-risk AIP showed a clear severity gradient: 77/101 (76.2%) women with mild pre-eclampsia and 54/55 (98.2%) women with severe pre-eclampsia were in the high-risk AIP category (Fisher exact test, p=0.001) (Figure 2). Within the pre-eclampsia group, blood pressure differed significantly across AIP risk categories. Mean systolic blood pressure was 150.00±5.89 mmHg in the low-risk AIP group, 147.52±8.22 mmHg in the intermediate-risk group and 157.60±13.02 mmHg in the high-risk group (p=0.001). Mean diastolic blood pressure was 93.00±3.46 mmHg, 97.62±5.08 mmHg and 102.63±9.09 mmHg across the same categories, respectively (p=0.007) (Figure 3).

Overall, third-trimester pre-eclampsia was characterized by higher maternal adiposity, greater blood-pressure burden, systemic biochemical derangement, a more atherogenic lipid profile and less favourable fetomaternal

outcomes. AIP was substantially elevated in cases, was concentrated in the high-risk category, and showed significant associations with disease severity, blood-pressure burden, birth weight, 5-minute Apgar score, cesarean delivery and NICU admission.

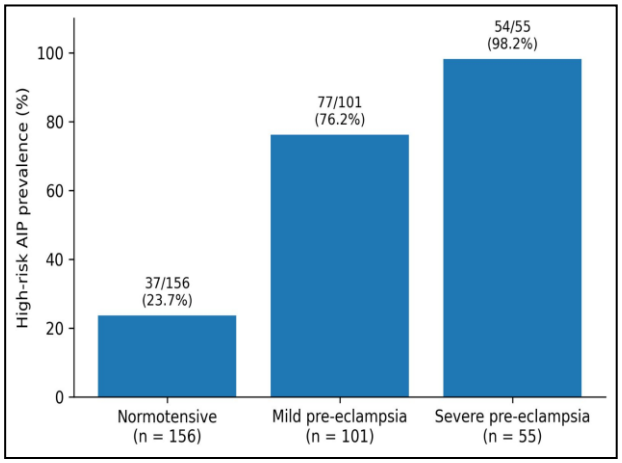

Figure 2: High-risk AIP prevalence across clinical strata.

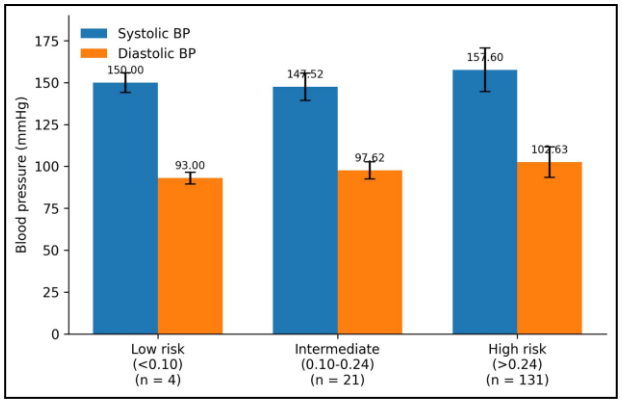

Figure 3. Systolic and diastolic blood pressure across AIP risk categories among women with pre-eclampsia.

DISCUSSION

This study evaluated AIP, fasting lipid profile and fetomaternal outcomes among third-trimester women with pre-eclampsia and normotensive pregnant women at a tertiary care centre in Central India. Women with pre-eclampsia had a significantly more adverse clinical, biochemical and lipid profile, markedly higher AIP and less favourable delivery and neonatal outcomes. Within the pre-eclampsia cohort, high-risk AIP clustered with severe disease and greater blood-pressure burden, while increasing AIP was associated with cesarean delivery, lower birth weight, lower 5-minute Apgar score and NICU admission. These convergent findings support AIP as an integrated marker of atherogenic and endothelial-metabolic disturbance with potential value for obstetric risk stratification.

The baseline profile showed that women with pre-eclampsia were older and had higher BMI than normotensive women. Similar observations have been reported by Sun et al., who found that advanced maternal age and pre-pregnancy overweight or obesity increased the risk of pre-eclampsia, and by Dantas et al, who reported greater maternal body weight among women with pre-eclampsia.[14,15] Ambad and Dhok also observed higher BMI and blood pressure among pre-eclamptic women than among normotensive controls.[16] The biological plausibility is strong: excess adiposity promotes insulin resistance, chronic low-grade inflammation, oxidative stress and endothelial dysfunction, all of which overlap with the pathophysiological pathways of pre-eclampsia.

The lipid findings were consistent and clinically meaningful. Women with pre-eclampsia had higher total cholesterol, triglycerides and LDL-C, and lower HDL-C, indicating a distinctly atherogenic lipid pattern. Salma et al., reported similar lipid alterations in pre-eclampsia, with higher total cholesterol, triglycerides and LDL-C and lower HDL-C than in normotensive pregnancy.[17] Oyeniran et al also reported abnormal serum lipid levels in pre-eclamptic women.[18] Indian data from Kumari et al and Patar and Acharjee have similarly shown higher third-trimester triglycerides, total cholesterol and LDL-C with lower HDL-C in women with pre-eclampsia.[19,20] These observations are further supported by the meta-analysis of Tesfa et al., which found increased TG, TC, LDL-C and VLDL-C in pre-eclamptic pregnancies compared with normotensive pregnancies.[8]

The pattern of lipid abnormality observed in this study is pathophysiologically relevant. Triglyceride-rich lipoproteins and elevated LDL-C can undergo oxidative modification and contribute to vascular inflammation, while reduced HDL-C diminishes reverse cholesterol transport and antioxidant protection. In pre-eclampsia, this atherogenic milieu may amplify placental hypoxia, oxidative stress and systemic endothelial dysfunction. Stadler et al. emphasized that pre-eclampsia affects lipid metabolism and HDL function in both mothers and offspring, supporting the relevance of lipid quality and function, not merely lipid quantity.[7]

The most important finding of this study was the marked elevation of AIP in pre-eclampsia. AIP integrates two central lipid changes seen in pre-eclampsia: increased triglycerides and reduced HDL-C. This makes it a more compact and biologically coherent summary of atherogenic risk than either parameter alone. The present mean AIP was 0.39 in women with pre-eclampsia compared with 0.15 in normotensive women, and 84.0% of cases fell into the high-risk category. This aligns with Singh et al, who demonstrated significantly increased atherogenic indices in pregnancy-induced hypertension, and with Abdulkadir et al, who found elevated atherogenic indices among preeclamptic and eclamptic patients.[10,11] Agu et al reported significantly elevated AIP and related atherogenic indices in pre-eclampsia, while Aragon-

Charris et al also documented higher AIP in patients with pre-eclampsia than in healthy pregnant women.[12,13]

The association between AIP and disease severity is particularly relevant for clinical translation. High-risk AIP was present in almost all women with severe pre-eclampsia and was significantly more frequent in severe than mild disease. Blood pressure also differed across AIP categories, with the highest diastolic and systolic values in the high-risk AIP group. Singh et al reported a positive relationship between systolic blood pressure and AIP in hypertensive pregnancy, and Agu et al found a positive correlation between mean arterial pressure and AIP in pre-eclampsia.[10,12] These comparable findings suggest that AIP may reflect not only the presence of pre-eclampsia but also the intensity of maternal vascular disease.

Serum creatinine and LDH were significantly higher in women with pre-eclampsia in this cohort. These findings are consistent with the systemic nature of pre-eclampsia, where renal endothelial injury and tissue hypoxia contribute to biochemical derangement. Eleti et al reported higher serum LDH in preeclamptic-eclamptic women and demonstrated correlation with fetomaternal outcome.[21] Nasir et al further showed that LDH correlated with disease severity and maternal-perinatal outcomes, while Teklemariam et al supported the diagnostic utility of LDH as a potential biomarker in pre-eclampsia.[22,23] Together with the AIP findings, these biochemical changes reinforce the interpretation of pre-eclampsia as a systemic endothelial-metabolic disorder rather than an isolated hypertensive state.

Kumari et al reported the relevance of lipid abnormalities to fetomaternal outcome in pre-eclampsia.[19,21,22] The combined maternal and neonatal pattern in the present cohort reinforces the clinical importance of early severity and outcome-risk stratification.

The participant-level AIP-outcome analysis adds an important dimension to the present findings. AIP showed strong inverse correlations with birth weight and 5-minute Apgar score, and higher AIP was associated with cesarean delivery, low birth weight, low Apgar score, NICU admission and fetal/neonatal death. Adverse outcomes were concentrated in the high-risk AIP category; however, the categorical association with mortality did not reach statistical significance because only eight deaths occurred among cases. Previous studies have predominantly examined AIP in relation to the presence or severity of hypertensive pregnancy disorders, whereas Kumari et al linked conventional lipid abnormalities with fetomaternal outcomes.[10,13,19] The present results therefore suggest that AIP may capture both maternal vascular severity and short-term fetal-neonatal compromise. Nevertheless, these are unadjusted associations and may be partly mediated by disease severity, gestational age and other clinical determinants; independent prognostic value cannot be inferred from this design.

The findings also have longer-term implications. Hypertensive disorders of pregnancy are associated with increased future cardiovascular risk, and pre-eclampsia may reveal a woman's underlying predisposition to endothelial and metabolic disease.[24,25] AIP may therefore have relevance beyond immediate obstetric stratification by identifying women who may benefit from postpartum cardiometabolic counselling and follow-up. However, this application also requires longitudinal validation.

The study has several strengths. It included an adequately powered comparative sample with equal numbers of pre-eclamptic and normotensive third-trimester women. It evaluated individual lipid fractions as well as continuous AIP and clinically interpretable AIP risk categories. Participant-level linkage of AIP with disease severity, blood-pressure burden and delivery-neonatal outcomes enabled direct assessment of its clinical relevance, while exact tests and rank-based correlations were used for sparse or non-normally distributed outcome data.

The limitations should be acknowledged. The cross-sectional, single-centre design precludes causal inference and definitive prognostic claims. Lipid profile and AIP were measured only in the third trimester, and the interval between sampling and delivery was not modelled. The AIP-outcome analyses were unadjusted for potential confounders such as gestational age, maternal BMI, pre-eclampsia severity, treatment and obstetric indication for delivery. The low-risk AIP subgroup was small, and the limited number of fetal/neonatal deaths reduced power for categorical mortality analysis. Larger prospective multicentre studies with prespecified sampling, multivariable adjustment and formal discrimination and calibration analyses are required before AIP can be adopted as an independent prognostic marker.

CONCLUSION

Third-trimester pre-eclampsia was associated with a distinctly adverse metabolic, atherogenic and fetomaternal profile. Women with pre-eclampsia had higher BMI, blood pressure, serum creatinine, LDH, total cholesterol, triglycerides and LDL-C, with lower HDL-C than normotensive pregnant women. They also had more cesarean deliveries, lower neonatal birth weight, more frequent low 5-minute Apgar scores, greater NICU admission and higher fetal/neonatal mortality. AIP was markedly higher in pre-eclampsia, and high-risk AIP was substantially more frequent among cases than controls.

Within women with pre-eclampsia, higher AIP was associated with severe disease, greater systolic and diastolic blood-pressure burden, cesarean delivery, lower birth weight, lower 5-minute Apgar score and NICU admission. AIP was also higher among fetal/neonatal deaths, although the categorical mortality analysis was underpowered. These findings support AIP as a simple, low-cost adjunct marker for maternal severity and short-term fetomaternal risk stratification. Its use as an

independent prognostic marker requires prospective validation with appropriate adjustment for clinical confounders and formal assessment of predictive performance.

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