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ORIGINAL RESEARCH

Independent Predictors of Major Adverse Cardiac and Hepatic Outcomes Following Acute Liver Complications of Pregnancy; A Retrospective Cohort Study

Ellada Sariyeva[1], Gubakhanım Hajızada[2], Nurana Hamidova[1], Ilaha Guliyeva[3], Lamiya Aghakishiyeva[1], Farida Gurbanova[1], Parvana Javanshir[1], Elnur Imanov[4], Sahib Bilalzade[5], Ilaha Shahverdiyeva[6], Aida Bandalieva[7], Zumrud Abaszade[8]*

1. Department of Obstetrics and Gynecology II, Azerbaijan Medical University, Baku, Azerbaijan
2. Director, Obstetrics and Gynecology, Azerbaijan Medical University, Baku, Azerbaijan
3. Department of Obstetrics and Gynecology, A. Aliyev Azerbaijan State Advanced Training Institute for Doctors, Baku, Azerbaijan
4. Department of Pediatrics II, Azerbaijan Medical University, Baku, Azerbaijan
5. Department of Oral and Maxillofacial Surgery, Azerbaijan Medical University, Baku, Azerbaijan
6. Scientific Research Laboratory, Department of Biochemistry, Azerbaijan Medical University, Baku, Azerbaijan
7. Department of Pharmaceutical Technology and Management, Azerbaijan Medical University, Baku, Azerbaijan
8. Department of Normal Physiology, Azerbaijan Medical University, Baku, Azerbaijan

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Abstract: **Introduction:** Acute liver complications of pregnancy (ALCP) remain major contributors to maternal morbidity. This study aimed to characterize cardio-hepatic crosstalk and identify independent predictors of hepatic failure and major cardiovascular events in patients with ALCP. **Methods:** This retrospective cohort study was conducted to investigate cardio-hepatic crosstalk, endothelial dysfunction, and cardiovascular risk stratification among pregnant women with ALCP (4 diagnostic categories: HELLP syndrome, pre-eclampsia with hepatic involvement, acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy). Independent predictors of cardiac and hepatic outcomes following ALCP, among endothelial, cardiac, inflammatory, coagulation, and renal biomarkers, were detected using correlation, multivariable regression, and receiver operating characteristic (ROC) analyses. **Results:** 400 patients with ALCP were studied. All 22 studied biomarkers differed significantly across diagnostic categories. The ratio of soluble fms-like tyrosine kinase-1 to placental growth factor (sFlt-1/PlGF ratio) correlated most strongly with N-terminal pro-B-type natriuretic peptide (NT-proBNP) ($r = 0.57$, $p < 0.001$) and independently predicted major cardiovascular events (adjusted odds ratio (OR) = 1.38, 95**Conclusion:** Hepatic and cardiovascular derangement in ALCP constitute an interconnected, biomarker-detectable syndrome, supporting integrated biomarker-guided risk stratification for emergency management and delivery-timing decisions.

Keywords: Biomarkers; Cardiovascular diseases; Risk assessment; HELLP syndrome; Liver diseases; Pregnancy complications; pre-eclampsia

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1. Introduction

Acute liver complications of pregnancy (ALCP) continue to be among the most significant causes of maternal morbidity and mortality globally, particularly in emergency obstetric care (1, 2). Hemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome), pre-eclampsia with hepatic involvement, acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy are among the most important ALCP. All these conditions are associated with an increased risk of adverse outcomes for pregnant women and their fetuses (3). Due to clinical heterogeneity, biochemical overlap, and narrow therapeutic window for intervention, ALCP remain a challenge for emergency and critical care teams worldwide, and early recognition of the conditions allows for risk-adjusted triage and prompt intervention (4, 5). Knowledge about these disorders has progressed significantly. HELLP syndrome and severe pre-eclampsia have been identified as two conditions caused by the same anti-angiogenic and endothelial pathway, and acute fatty liver of pregnancy (AFLP) is associated with impaired mitochon-

***Corresponding Author:** Zumrud Abaszade; Department of Normal Physiology, Azerbaijan Medical University, Baku, Azerbaijan. Email: abaszade@yandex.com, Tel: +99455 889 43 59, ORCID: https://orcid.org/0009-0000-6790-0466.

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drial fatty acid oxidation, causing hepatocyte lipid accumulation and synthetic hepatic dysfunction (6, 7). Management strategies focus on stabilizing the mother, controlling blood pressure, administering magnesium sulfate prophylaxis, correcting coagulopathy, and delivering the baby as soon as possible, usually by a multidisciplinary critical care team (8). Notwithstanding these improvements, the role of isolated hepatic parameters in clinical decision-making remains prominent, while cardiovascular involvement is comparatively under-assessed in routine emergency protocols (9). The interplay between liver injury and cardiovascular dysfunction during pregnancy is now recognized to be more complex than independent liver injury (10). All three conditions can trigger or worsen each other and have overlapping microcirculatory and inflammatory pathways, which lead to hepatic hypoperfusion, systemic inflammation, and impaired maternal hemodynamic adaptation (11, 12). This cardio-hepatic crosstalk is clinically relevant (13): a cardiovascular strain in a woman presenting with primarily hepatic derangements may be missed, and appropriate escalation of care may be delayed; conversely, cardiovascular monitoring alone, without hepatic correlation, may fail to detect progressive organ dysfunction (14, 15). Endothelial dysfunction is one of the key mechanistic bridges in this crosstalk. Angiogenic imbalance, defined as an increased ratio of soluble fms-like tyrosine kinase-1 (sFlt-1) to placental growth factor (PlGF), is associated with reduced nitric oxide bioavailability, increased vascular leakage and vasoconstriction, placental dysfunction, and vascular injury in the systemic circulation (16). This endothelial insult is further exacerbated by inflammatory mediators, which are also relevant outside the placental bed in the maternal myocardium and hepatic sinusoids and could be a potential link between hepatic and cardiovascular emergency presentations (17, 18). In pregnancy-related liver disease, the potential for diagnosis and predicting the prognosis of the disease has been established in the hepatic (transaminase, bilirubin, albumin, and bile acid), cardiac (troponin and natriuretic peptides), inflammatory (C-reactive protein (CRP), interleukin-6 (IL-6)), endothelial, and coagulation domains using biomarkers (19, 20). Most of the available evidence evaluates these markers in single-organ or single-diagnosis settings; however, their relative and additive predictive values in various acute liver complications and multiple hepatic and cardiovascular endpoints are poorly understood (21).

Most recognized risk stratification strategies use blood pressure cut-off values in isolation and do not reflect the overall hemodynamic, electrocardiographic (ECG), or echocardiographic assessments, which are useful for emergency triage and allocation of critical care resources (22). In the studies that exclusively focus on the hepatic complications of pregnancy, cardiovascular assessment is not always present, and comparative evidence is provided in few studies (23). This can limit the establishment of integrated pathway-based emergency management approaches using biomarkers (24). This gap needs to be addressed in a design that can simultaneously assess hepatic, endothelial, cardiac, inflammatory, coagulation, and hemodynamic parameters, with the aim of directly assessing the cardio-hepatic relationship and its role in adverse outcomes (25). This comprehensive strategy can help in the early detection of women who are likely to develop hepatic failure or major cardiovascular events and aid in making more personalized choices about the management of emergencies and timing of delivery (26). Therefore, this study aimed to identify the independent predictors of major adverse cardiac and hepatic outcomes of ALCP from a comprehensive metabolic panel of 22 hepatic, endothelial, cardiac, inflammatory, coagulation, and renal biomarkers.

2. Methods

2.1. Study design and setting

This retrospective cohort study was conducted to investigate cardio-hepatic crosstalk, endothelial dysfunction, and cardiovascular risk stratification among pregnant women with ALCP. The study was carried out at the Educational-Surgical Clinic of Azerbaijan Medical University, in collaboration with the Departments of Obstetrics and Gynecology, Hepatology, and Cardiology, Baku, Azerbaijan, between January 2025 and December 2025 (12-month enrollment period). The hospital is a 650-bed tertiary referral hospital with a 24-hour obstetric emergency triage unit, a dedicated maternal high-dependency unit with eight beds and a 12-bed obstetric intensive care unit with maternal-fetal medicine specialists, hepatologists, cardiologists, and critical care physicians. The institution has its own clinical biochemistry laboratory, cardiac catheterization-capable cardiology unit, and specially designed obstetric ultrasonography and echocardiographic rooms, which allow for consultation with other specialties within the same shift for liver and heart emergencies. The primary goal was to identify the independent predictors of major adverse cardiac and hepatic outcomes of ALCP from a comprehensive metabolic panel of 22 hepatic, endothelial, cardiac, inflammatory, coagulation, and renal biomarkers. The secondary goals were to compare baseline hemodynamic and biomarker measurements between the four diagnostic groups, quantify the correlation between hepatic and cardiac biomarker measurements, assess the discriminative ability of endothelial and cardiac markers for hepatic failure and major cardiovascular events, and characterize the determinants of a composite cardiovascular risk score based on electrocardiographic, echocardiographic, and hemodynamic parameters. The study was approved by the Ethics Committee of Azerbaijan Medical University (Approval No. AMU/EC-2022-051/9) in accordance with the Declaration of Helsinki. Written informed consent, anonymized coding, and confidentiality were ensured, and participants had the right to withdraw at any point.

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2.2. Participants

The target population was pregnant women aged 18-45 years in the 2nd or 3rd trimester of pregnancy with clinically and/or biochemically confirmed ALCP (pre-eclampsia with hepatic involvement, HELLP syndrome, acute fatty liver of pregnancy, or intrahepatic cholestasis with hepatic dysfunction). The eligibility criteria included singleton pregnancies (20 weeks) and provision of written informed consent. The exclusion criteria were pre-existing chronic liver disease, pre-existing structural cardiac disease, known coagulopathy (not pregnancy-related), multifetal gestation, and refusal to participate. Since the exposures and outcomes under study are specific to pregnancy, the cohort was restricted by biological sex to women; sex was self-reported and confirmed against obstetric records.

2.3. Sample size determination

The sample size was calculated as 367 patients, with the assumption that hepatic-cardiovascular co-involvement would be 15

2.4. Sampling technique

Consecutive sampling was used. Women who presented to the emergency obstetric unit were screened chronologically, and eligibility was confirmed by the attending obstetrician and reviewing hepatologist. Enrollment continued until a total of 400 eligible cases was achieved. A centralized log of women screened but not enrolled (due to ineligibility or non-consent) was not maintained separately from the clinical record; consequently, exact screening-to-enrollment ratios cannot be reported. This is acknowledged as a limitation in the discussion.

2.5. Data gathering

All participants were subjected to a standardized emergency assessment at admission, including maternal history, obstetric examination, and monitoring of vital signs (blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen saturation (O2SAT), and temperature). The cardiovascular assessment included 12-lead ECG and bedside echocardiography performed by a cardiologist within 2 hours of admission. Hepatic examinations included abdominal ultrasonography and clinical examination for hepatomegaly, tenderness, and jaundice. A single venous blood sample was collected at admission (before intervention) for the entire set of biomarkers. All findings were documented on a pretested structured proforma based on a predefined set of variables on admission, and the clinical course was followed up from admission to discharge, using recorded maternal, hepatic, cardiovascular, and neonatal outcomes. Admission biomarker levels, blood pressure, and gestational age were independent variables. Maternal, hepatic, and cardiovascular outcomes were included as dependent variables. Confounding variables included maternal age, parity, and body mass index (BMI), while covariates included gestational age at presentation and baseline hemodynamic status.

2.6. Biomarker assessment

Blood samples collected at admission were used to measure liver function markers (alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, albumin, total bile acids, and lactate dehydrogenase (LDH)), endothelial dysfunction biomarkers (soluble fms-like tyrosine kinase-1 (sFlt-1), placental growth factor (PlGF), and endothelin-1 (ET-1)), cardiac biomarkers (high-sensitivity troponin I (hs-TnI) and N-terminal proBNP (NT-proBNP)), inflammatory markers (C-reactive protein (CRP) and interleukin-6 (IL-6)), coagulation profile (platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen (Fg)), and renal profile (creatinine and urea). Samples were centrifuged within 30 min, aliquoted, and frozen at 80°C until batch analysis using calibrated automated immunoassay and chemistry analyzers, performed daily according to the manufacturers' specifications, with daily internal quality control. Cardiovascular risk was determined using 12-lead electrocardiogram (ECG) parameters, transthoracic echocardiography (TTE) (ejection fraction and diastolic function), a single admission blood pressure measurement, and a validated modified maternal cardiovascular risk score based on the above parameters at admission. The initiation of stabilization was based on standardized protocols that involved evaluation of airway-breathing-circulation, antihypertensive treatment, and administration of magnesium sulfate as needed. Hepatic dysfunction and cardiac compromise were managed by a multidisciplinary team that included obstetricians, hepatologists, and cardiologists. Antihypertensive therapy, magnesium sulfate, blood product transfusion, and admission to the intensive care unit (ICU) were measured as binary management indicators for each participant.

2.7. Outcome measures

The primary outcomes were maternal mortality, hepatic failure, and major cardiovascular events. Hepatic failure and major cardiovascular events were adjudicated by the treating multidisciplinary team (obstetrician, hepatologist, and cardiologist) based on the overall clinical, biochemical, and echocardiographic picture at the time of the event, rather than a single pre-specified numerical threshold. Other outcomes included ICU admission, hospital stay, type of delivery, neonatal outcome (live birth at term, preterm live birth admitted to the neonatal intensive care unit (NICU) or stillbirth), birth weight, and 5-minute Apgar score for live births.

2.8. Data quality assurance

The research staff were trained and pilot tested on the standardized proforma before the enrollment process. All clinical and laboratory measurements were performed according to standard operating procedures, using instruments such as ECG and echocardiography devices, and laboratory analyz-

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ers were routinely calibrated. Range and internal consistency checks were run to identify implausible or contradictory values before the analytic dataset was locked. The structural non-applicability of neonatal birth weight and Apgar score was used for stillbirths and was coded as such, not imputed.

2.9. Statistical analysis

Python software version 3.10 was used to analyze the data. Data were presented as categorical variables (frequency and percentage) or continuous variables (mean ± standard deviation (SD) or median and interquartile range (IQR)) after Shapiro-Wilk normality testing. Independent t-tests, Mann–Whitney U tests, chi-square tests, and one-way ANOVA were used for group comparisons across the diagnostic groups. Adverse outcome predictors were identified using multivariate logistic and multiple regression models adjusted for maternal age, parity, and BMI. ROC curve analysis was used to assess the discriminative value of endothelial and cardiac biomarkers for hepatic and cardiovascular outcomes, and correlation analysis was used to assess the correlation between cardiac and hepatic biomarkers. Optimal cutoff values for ROC curve analysis were determined using the Youden index, and 95

3. Results

3.1. Baseline characteristics of studied patients

The final analytic cohort comprised 400 pregnant women across four diagnostic categories: HELLP syndrome (n = 139, 34.8Most baseline characteristics were comparable across the four diagnostic categories. Maternal age (29.0 (25.0–32.0) years, H = 2.83, p = 0.419), body mass index (27.7 (24.6–30.3) kg/m², H = 1.56, p = 0.668), respiratory rate (H = 1.00, p = 0.802), and nulliparity (24.8Gestational age at presentation, however, did diverge significantly (H = 59.81, p < 0.001, ² = 0.147): women with acute fatty liver of pregnancy presented latest (35.0 (33.2–38.0) weeks), while those with pre-eclampsia presented earliest (31.0 (30.0–33.0) weeks). Hemodynamic parameters showed the sharpest between-group divergence of any baseline measure. Systolic and diastolic blood pressure carried the two largest effect sizes in the entire baseline panel (² = 0.618 and ² = 0.656, both p < 0.001), ranging from 163.0/106.0 mmHg in pre-eclampsia down to 117.0/74.0 mmHg in cholestasis. Heart rate was highest in acute fatty liver of pregnancy (106.0 (101.0–110.0) beats/min; F = 71.65, p < 0.001, ² = 0.352). Three categorical measures also varied significantly by diagnosis: third-trimester presentation (95.5Maternal mortality occurred in 2 of the 400 women (0.5

3.2. Biomarker profile across diagnostic categories

All 22 biomarkers spanning the hepatic, endothelial, cardiac, inflammatory, coagulation, and renal domains differed significantly across the four diagnoses (Table 2, all p < 0.001). The largest effect sizes were seen for platelet count (² = 0.750), the sFlt-1/PlGF ratio (² = 0.747), and lactate dehydrogenase (² = 0.738). Acute fatty liver of pregnancy showed the most severe hepatocellular and synthetic derangement of any group: ALT = 229.5 (183.0–266.8) U/L, AST = 234.0 (187.2–295.8) U/L, total bilirubin = 7.4 (4.4–8.9) mg/dL, and albumin = 2.6 (2.4–2.8) g/dL. This group also had the most prolonged coagulation profile of any diagnosis (prothrombin time = 17.6 (15.6–19.2) s; activated partial thromboplastin time = 40.8 (35.9–44.6) s; fibrinogen = 178.0 (145.8–213.8) mg/dL, the lowest of any group). The sFlt-1/PlGF ratio followed a different pattern, peaking in pre-eclampsia (460.3 (324.4–613.9)) and falling to its lowest in cholestasis (11.5 (8.3–14.2)); an almost inverse mirror of total bile acids, which were markedly elevated only in cholestasis (37.4 (25.1–50.9) mol/L, versus 5.4–8.9 mol/L in the other three groups). Cardiac biomarkers peaked in different groups depending on the marker: troponin I was highest in acute fatty liver of pregnancy (22.9 (15.0–28.5) ng/L), while NT-proBNP was highest in pre-eclampsia (482.0 (371.0–617.0) pg/mL). Cholestasis, by contrast, consistently showed the most favorable cardiovascular profile, with the highest ejection fraction (63.0

3.3. Determinants of major adverse maternal outcomes

Table 3 compares biomarker and clinical profiles by outcome status. Women who developed a major cardiovascular event (n = 39) had higher total bilirubin (1.8 (1.1–2.5) vs. 1.3 (0.9–2.0) mg/dL, p = 0.031), troponin I (17.0 (11.8–24.2) vs. 12.9 (7.3–21.1) ng/L, p = 0.013), C-reactive protein (25.6 (20.0–32.9) vs. 21.3 (13.1–29.0) mg/L, p = 0.008), and interleukin-6 (48.7 (31.9–56.9) vs. 33.5 (18.9–44.2) pg/mL, p < 0.001), along with lower platelet counts (85.0 (62.5–161.0) vs. 120.0 (72.0–197.0) ×10/L, p = 0.027). ALT approached but did not reach significance (p = 0.050); the sFlt-1/PlGF ratio, endothelin-1, NT-proBNP, ejection fraction, and cardiovascular risk score did not differ meaningfully between groups (p = 0.068–0.370). The biomarker signature of major cardiovascular event was thus comparatively narrow and driven mainly by inflammatory and hepatic markers, in contrast to the broader derangement seen with hepatic failure below. Hepatic failure (n = 28) showed a broader and more pronounced biomarker signature. ALT was more than double that of women without hepatic failure (207.5 vs. 94.5 U/L), total bilirubin was nearly fourfold higher (4.5 vs. 1.2 mg/dL), and albumin was reduced with a large effect size (2.8 vs. 3.1 g/dL, Cohen's d = -0.88). C-reactive protein, interleukin-6, platelet count, and cardiovascular risk score all differed significantly as well (p < 0.001 to p = 0.012). Notably, the sFlt-1/PlGF ratio (p = 0.111) and NT-proBNP (p = 0.302) did not track with hepatic failure status — a pattern that becomes relevant when interpreting the multivariable models below.

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3.4. Multivariable predictors of adverse outcomes and cardiovascular risk

After adjusting for maternal age, parity, body mass index, gestational age, systolic blood pressure, and the relevant biomarker panel (Table 4), the sFlt-1/PlGF ratio remained the only independent predictor of major cardiovascular event (adjusted per-SD OR = 1.38, 95The hepatic failure model was considerably more robust. C-reactive protein (adjusted OR = 1.08, 95In the multiple linear regression for cardiovascular risk score, six of eleven covariates were independently significant: systolic blood pressure (B = 0.02, p = 0.001), diastolic blood pressure (B = 0.04, p < 0.001), troponin I (B = 0.028, p = 0.013), NT-proBNP (B = 0.001, p = 0.026), total bilirubin (B = 0.119, p = 0.026), and albumin (B = -0.623, p = 0.016). Parity remained non-significant (B = -0.046, p = 0.521). The full model explained 45.9

3.5. Cardio-hepatic correlation structure and biomarker discriminative performance

Spearman correlation analysis (Table 5 and Figure 2) showed statistically significant associations between every hepatic and cardiac biomarker pair examined (p 0.040). The strongest relationship in the entire matrix was between the sFlt-1/PlGF ratio and NT-proBNP (r = 0.57, 95ROC analysis (Table 5, Figure 3) told a different story for the two outcomes. For major cardiovascular event, discrimination was modest across all five biomarkers tested: C-reactive protein performed best (AUC = 0.63, 95For hepatic failure, discrimination was appreciably stronger for the same inflammatory and cardiac markers. C-reactive protein achieved the highest AUC recorded in the study (0.79, 95

4. Discussion

This observational study included 400 pregnant women with acute liver complications who presented to our hospital. The study showed that hepatic and cardiovascular derangements are not discrete organ events but form a single syndrome detectable by markers of the liver and cardiovascular system. The biochemical signatures of the four diagnostic groups, namely HELLP syndrome, pre-eclampsia with hepatic involvement, acute fatty liver of pregnancy, and intrahepatic cholestasis, were unique but internally coherent, and all biomarkers in each of the hepatic, endothelial, cardiac, inflammatory, coagulation, and renal biochemical domains were significantly different between diagnoses (27). The central hypothesis of this study was that there is measurable and clinically stratifiable crosstalk between the heart and liver in pregnancy-associated liver disease, with direct implications for emergency triage and risk-adjusted management, which is supported by our findings. Each diagnostic group showed a distinct pattern of organ derangement, and this distribution was biologically coherent rather than arbitrary. Hepatocellular injury, synthetic dysfunction, and coagulopathy associated with AFLP are the most severe complications of this condition. As expected from its underlying mechanism, impaired mitochondrial fatty acid oxidation and hepatocyte lipid accumulation are responsible for both metabolic and synthetic liver impairment (2, 28). The prominent decrease in sFlt-1/PlGF in cholestasis and the marked increase in the pre-eclampsia phenotype confirm that the pre-eclamptic hepatic-cardiovascular phenotype is most likely not directly driven by hepatocellular injury but by antiangiogenic placental signaling. This consistently positive cardiovascular profile in cholestasis (both higher ejection fraction and lower composite risk scores) is biologically plausible because cholestasis is mostly due to dysfunction of bile acid transporters and is not the result of a general compromise of endothelial or placental function (29-31). Mechanistically, the observed cardiohepatic linkage is most likely attributable to the presence of a common pathway involving placental ischemia, anti-angiogenic imbalance, and systemic endothelial dysfunction. Increased sFlt-1/PlGF levels decrease the bioavailability of vascular endothelial growth factor (VEGF) and PlGF, leading to reduced endothelial nitric oxide synthesis, vasoconstriction, leakiness, and microvascular injury in various organs, such as the myocardium and hepatic sinusoids (32, 33). This endothelial injury, along with the systemic inflammatory status (higher levels of CRP and IL-6) and oxidative stress, may account for the association between the sFlt-1/PlGF ratio and NT-proBNP, which was the strongest correlation in the overall correlation matrix (34, 35), indicating that anti-angiogenic placental factors may contribute to subclinical cardiac strain before overt cardiovascular events occur. The degree of hepatocellular injury, as reflected by the level of hepatic transaminases and bilirubin, was moderately correlated with the level of troponin I but inversely correlated with that of the ejection fraction, suggesting that hepatocellular injury and myocardial microvascular compromise share common inflammatory and hemodynamic triggers and do not occur independently (36, 37). The results are consistent with the existing literature, which shows that angiogenic imbalance is associated with both hepatic and cardiovascular disease in pre-eclampsia and HELLP syndrome, and they extend this connection by quantifying the relationship between the biomarkers in a comparative four-group study that included all acute liver complications of pregnancy (ALCP) groups, not just pre-eclampsia (38). While the discriminatory value of angiogenic and cardiac biomarkers for major cardiovascular events is modest, the value of CRP and troponin I for hepatic failure was significantly higher, which differs somewhat from the studies emphasizing sFlt-1/PlGF as a dominant biomarker, possibly due to differences in outcome definition (39). The absolute event rate in this cohort was relatively low for major cardiovascular events, and the cardiovascular event was a composite event compared to the more biochemically proximal hepatic failure (40). Clinically, these findings suggest that a biomarker-based approach for emergency risk stratification may be more useful when using both CRP and creatinine rather than only angiogenic markers to

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identify women at risk of hepatic failure, and that cardiovascular risk stratification should continue to be based on integrated hemodynamic and biochemical parameters instead of any single biomarker (41). This stratification may suggest earlier multidisciplinary engagement, more informed decisions in the ICU regarding the timing of delivery, and more appropriate triage in acute presentations (42, 43). The main advantages of this study are as follows: the sample size was sufficient, the panel of biomarkers was comprehensive, multiple domains were covered, and cardiology and hepatology evaluations were performed on the same shift; also, the statistical analyses were prespecified and protocol concordance was verified (44). However, this study had some limitations. Future studies should focus on larger, prospective, multicenter studies to confirm these biomarker-outcome associations in different populations and longitudinal studies that account for the recovery of cardiovascular function after pregnancy. Mechanistic studies directly connecting angiogenic imbalance with myocardial microvascular function (45, 46) could lead to more effective risk discrimination than individual markers, and integrated predictive models combining hepatic, cardiac, and inflammatory biomarkers using machine learning approaches could improve risk discrimination (47). This study illustrates that during pregnancy, there is a measurable diagnosis-specific cardio-hepatic biomarker signature and that endothelial and inflammatory pathways are potential mechanistic links between hepatic and cardiovascular injury, which suggests that integrated biomarker-guided risk stratification can be implemented in emergency obstetric care.

5. Limitations

This study has limitations regarding causal inferences and generalizability to other settings that differ in referral patterns and/or resource availability. Although selection bias was lowered by using consecutive sampling rather than convenience sampling, referral-related selection effects are inherent to tertiary centers and cannot be avoided. A formal record of screened-but-excluded patients was not retained, precluding the calculation of a Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)-style enrollment flow diagram; future prospective studies should log this information. Conclusions can only be drawn regarding the acute presentation period due to residual confounding by unmeasured factors and the lack of follow-up after pregnancy (48, 49). The low absolute number of maternal deaths and cardiovascular events reduced the statistical power to study these specific outcomes. For the major cardiovascular event model, the events-per-variable ratio was approximately 3.5 (39 events across 11 predictors) (50), and 2.5 for the hepatic failure model (28 events across 11 predictors). Additionally, hepatic failure and major cardiovascular events were defined by multidisciplinary clinical adjudication rather than a single pre-specified numerical threshold; while this reflects real-world emergency decision-making, it may introduce some inter-observer variability that a prospectively fixed diagnostic algorithm would avoid (51). Results from the Firth penalized logistic regression sensitivity analysis (ST S5) yielded the same independent predictors (sFlt-1/PlGF ratio for major cardiovascular events and C-reactive protein and serum creatinine for hepatic failure) with similar effect sizes and significance, confirming the robustness of the findings, despite the relatively low event-per-variable ratio (52).

6. Conclusions

Biomarkers of hepatic and cardiac function were significantly correlated across the cohort, suggesting a link between the two and that the derangement of these organs is a common process. The sFlt-1/PlGF ratio was the most important correlate of cardiovascular strain, while inflammatory and renal markers (C-reactive protein and creatinine) could more accurately predict hepatic failure, as confirmed by the sensitivity analysis. These data suggest a biomarker-driven strategy for emergency risk stratification based on the combination of hepatic, endothelial, cardiac, and renal variables rather than on just one single variable, which could result in earlier multidisciplinary engagement and influence the timing of delivery decisions.

7. Declarations

7.1. Acknowledgments

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7.2. Authors contributions

Ellada Sariyeva: Conceptualization, Methodology, Formal analysis, Writing – original draft. Gubakhanım Hajızada, Nurana Hamidova, Ilaha Guliyeva, Lamiya Aghakishiyeva, Farida Gurbanova, Parvana Javanshir, Elnur Imanov, Sahib Bilalzade, and Ilaha Shahverdiyeva: Investigation, Data curation, Writing – review & editing. Aida Bandalieva: Supervision, Validation. Zumrud Abaszade: Conceptualization, Supervision, Writing – review & editing. All authors read and approved the final version of the manuscript.

7.3. Conflict of interest

The authors declare no conflict of interest.

7.4. Data availability

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

7.5. Funding and support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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7.6. Ethical considerations

The study was approved by the Ethics Committee of Azerbaijan Medical University (Approval No. AMU/EC-2022-051/9) in accordance with the Declaration of Helsinki. Written informed consent, anonymized coding, and confidentiality were ensured, and participants had the right to withdraw at any point.

7.7. Using artificial intelligence chatbots

During the preparation of this manuscript, the authors used an AI-based tool for grammar correction and proofreading purposes only. The authors reviewed and edited the content as necessary and take full responsibility for the content of this publication.

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Table 1: Comparing the baseline demographic, clinical. and obstetric characteristics of the studied cases between different acute liver complications of pregnancy (N = 400)

Variable	Overall	HELLP	Pre-eclampsia	AFLP	ICP	Test (p)
Age						
Maternal (years)	29.0 (25.0–32.0)	29.0 (25.0–32.0)	29.0 (26.0–33.0)	28.0 (24.2–31.8)	29.0 (25.0–31.0)	0.419
Gestational (weeks)	33.0 (31.0–36.0)	33.0 (31.0–36.0)	31.0 (30.0–33.0)	35.0 (33.2–38.0)	34.0 (32.0–36.0)	< 0.001
BMI (kg/m^2)						
Median (IQR)	27.7 (24.6–30.3)	27.7 (24.7–30.1)	27.8 (24.6–30.7)	28.4 (24.9–30.1)	27.1 (24.6–29.1)	0.668
Vital signs						
SBP (mmHg)	152 (136–164)	158 (148–166)	163 (154–173)	142 (134–146)	117 (112–127)	< 0.001
DBP (mmHg)	97 (84–105)	100 (95–106)	106 (100–110)	87.0 (81.2–91.0)	74.0 (69.2–78.0)	< 0.001
HR (/min)	92.5 ± 12.1	97 (89.0–102.5)	91 (85.0–98.0)	106 (101–110)	80.5 (75.0–86.0)	< 0.001
RR (/min)	19 (17.0–21.0)	19 (17.0–21.0)	19 (17.0–21.0)	19 (17.0–21.0)	19 (17.0–22.0)	0.802
O_2 saturation (%)	96 (95.0–98.0)	96.0 (95.0–98.0)	97 (95.0–98.0)	97 (96.0–98.0)	97 (95.0–98.0)	0.220
Trimester at presentation						
Third	382 (95.5)	136 (97.8)	108 (89.3)	52 (96.3)	86 (100.0)	0.001
Parity						
0	99 (24.8)	38 (27.3)	29 (24.0)	14 (25.9)	18 (20.9)	0.740
Delivery type						
Cesarean	271 (67.8)	103 (74.1)	85 (70.2)	45 (83.3)	38 (44.2)	0.001
ICU admission						
Yes	120 (30.0)	46 (33.1)	38 (31.4)	29 (53.7)	7 (8.1)	0.001

Data are presented as median (interquartile range; IQR) or frequency (%) or mean ± standard deviation. HELLP: HELLP syndrome; AFLP: acute fatty liver of pregnancy; ICP: intrahepatic cholestasis of pregnancy; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; RR: Respiratory rate; BMI: Body mass index; ICU: intensive care unit. Continuous variables were compared using one-way ANOVA (normally distributed) or the Kruskal–Wallis H test (non-normally distributed); categorical variables were compared using the chi-square test of independence. Effect sizes (^{2}, ^{2}, Cramér's V) are provided in the underlying data files. Two-tailed $p < 0.05$ denotes statistical significance.

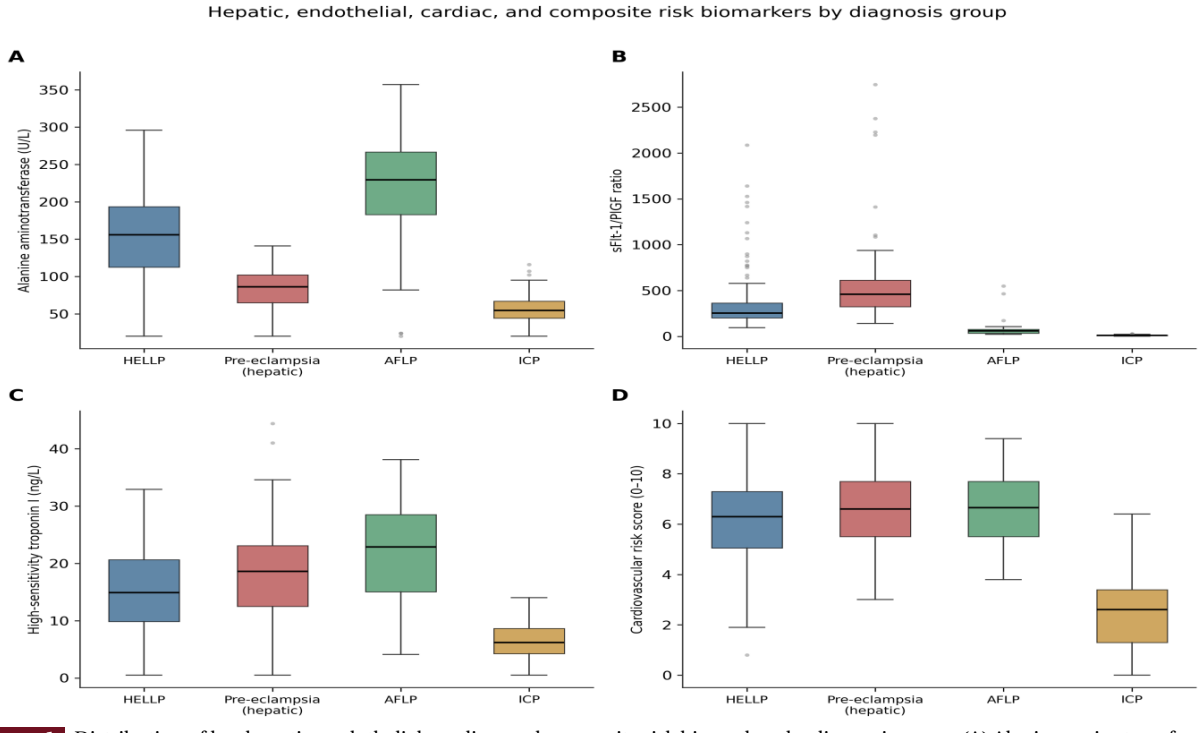

Figure 1: Distribution of key hepatic, endothelial, cardiac, and composite risk biomarkers by diagnosis group. (A) Alanine aminotransferase. (B) sFlt-1/PlGF ratio. (C) High-sensitivity troponin I. (D) Cardiovascular risk score. HELLP: HELLP syndrome; AFLP: acute fatty liver of pregnancy; ICP: intrahepatic cholestasis of pregnancy; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor.

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Table 2: Comparing the hepatic, endothelial, cardiac, inflammatory, coagulation, and renal biomarker profile between different acute liver complications of pregnancy (N = 400)

Domain	Biomarker	HELLP	Pre-eclampsia	AFLP	ICP	P
Hepatic						
	ALT (U/L)	156.0 (112.5–193.5)	86.0 (65.0–102.0)	229.5 (183.0–266.8)	54.5 (44.2–67.0)	< 0.001
	AST (U/L)	176.0 (141.0–212.0)	85.0 (64.0–105.0)	234.0 (187.2–295.8)	51.0 (38.0–63.0)	< 0.001
	Total bilirubin (mg/dL)	1.9 (1.4–2.3)	1.0 (0.8–1.2)	7.4 (4.4–8.9)	0.9 (0.6–1.2)	< 0.001
	Serum albumin (g/dL)	2.9 (2.7–3.1)	3.2 (3.0–3.4)	2.6 (2.4–2.8)	3.5 (3.3–3.7)	0.001
	Total bile acids (μmol/L)	7.0 (5.5–8.6)	5.4 (4.0–6.7)	8.9 (6.1–11.9)	37.4 (25.1–50.9)	< 0.001
	LDH (U/L)	716.0 (635.0–798.0)	393.0 (295.0–468.0)	587.5 (533.2–673.8)	231.0 (158.2–329.2)	< 0.001
Endothelial						
	sFlt-1 (pg/mL)	8669 (7541–9875)	10147 (8745–12035)	5068 (3774–6358)	2046 (1626–2493)	< 0.001
	PlGF (pg/mL)	34.0 (24.5–43.0)	23.0 (17.0–29.0)	90.5 (73.5–108.0)	184.5 (156.0–208.8)	< 0.001
	sFlt-1/PlGF ratio	254.7 (201.8–364.6)	460.3 (324.4–613.9)	60.6 (34.4–75.8)	11.5 (8.3–14.2)	< 0.001
	Endothelin-1 (pg/mL)	9.1 (7.7–10.2)	9.4 (7.9–10.7)	5.8 (4.8–7.5)	3.0 (2.0–3.9)	0.001
Cardiac						
	Troponin I* (ng/L)	14.9 (9.9–20.6)	18.6 (12.5–23.1)	22.9 (15.0–28.5)	6.2 (4.2–8.6)	0.001
	NT-proBNP (pg/mL)	422.0 (287.5–512.5)	482.0 (371.0–617.0)	352.5 (285.0–407.0)	101.0 (73.2–137.2)	0.001
Inflammatory						
	C-reactive protein (mg/L)	26.2 (20.9–31.5)	19.6 (14.0–24.5)	36.0 (30.2–38.5)	7.4 (3.1–13.6)	0.001
	Interleukin-6 (pg/mL)	41.4 (33.2–51.1)	29.2 (19.3–37.5)	56.9 (45.7–68.4)	11.5 (3.9–23.2)	0.001
Coagulation						
	Platelet count ($\times 10^9$/L)	67.0 (53.0–83.5)	170.0 (143.0–197.0)	75.0 (60.2–88.0)	225.5 (198.5–254.8)	0.001
	Prothrombin time (s)	13.2 (12.2–14.4)	12.4 (11.9–13.0)	17.6 (15.6–19.2)	11.8 (11.4–12.2)	0.001
	Activated PTT (s)	33.6 (30.6–36.7)	29.1 (26.9–31.8)	40.8 (35.9–44.6)	27.6 (25.7–29.2)	0.001
	Fibrinogen (mg/dL)	322.0 (277.5–382.5)	419.0 (373.0–464.0)	178.0 (145.8–213.8)	450.5 (409.0–496.0)	0.001
Renal	Serum creatinine (mg/dL)	1.0 (0.8–1.1)	1.0 (0.8–1.2)	1.4 (1.3–1.7)	0.6 (0.5–0.6)	0.001
	Serum uric acid (mg/dL)	7.0 (6.5–7.7)	7.5 (6.9–8.2)	6.2 (5.5–7.0)	4.0 (3.2–4.8)	0.001
Cardiac function	LVEF, %	58.0 (54.0–61.0)	59.0 (55.0–62.0)	57.0 (54.2–59.0)	63.0 (60.0–68.0)	0.001
Composite risk	CRS, 0–10	6.3 (5.0–7.3)	6.6 (5.5–7.7)	6.7 (5.5–7.7)	2.6 (1.3–3.4)	0.001

Values are presented as median (interquartile range). Groups compared using one-way ANOVA or the Kruskal–Wallis H test according to Shapiro–Wilk normality results. HELLP: HELLP syndrome; AFLP: acute fatty liver of pregnancy; ICP: intrahepatic cholestasis of pregnancy; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; PTT: partial thromboplastin time; LVEF: Left ventricular ejection fraction, CRS: Cardiovascular risk score. All 22 measured biomarkers are reported; none were excluded from analysis. * High-sensitivity troponin I

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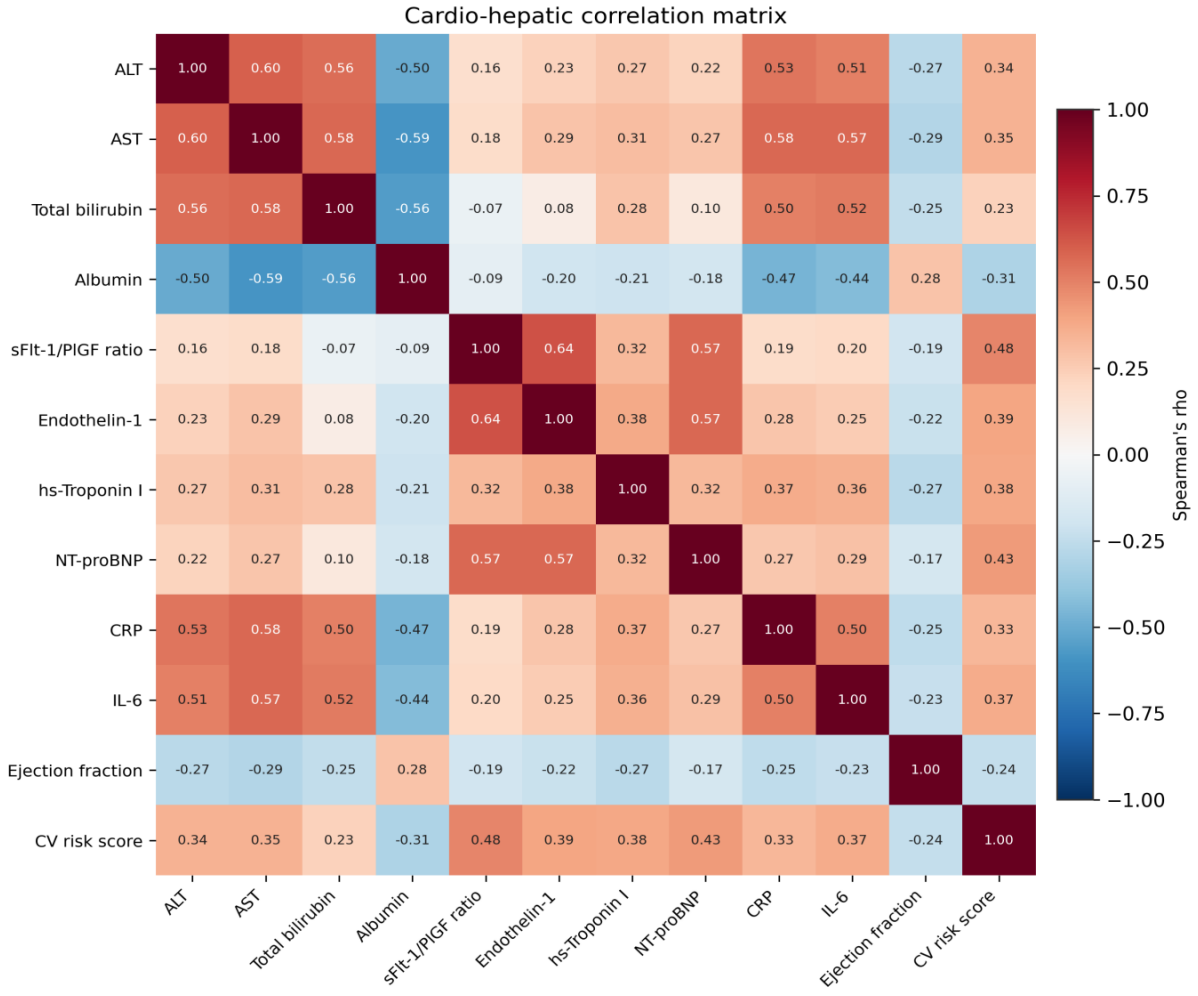

Figure 2: Cardio-hepatic correlation matrix (Spearman's rho) across hepatic, endothelial, cardiac, and inflammatory biomarkers. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide; hs: high-sensitivity; CRP: c-reactive protein; IL: interleukin; CV: cardiovascular.

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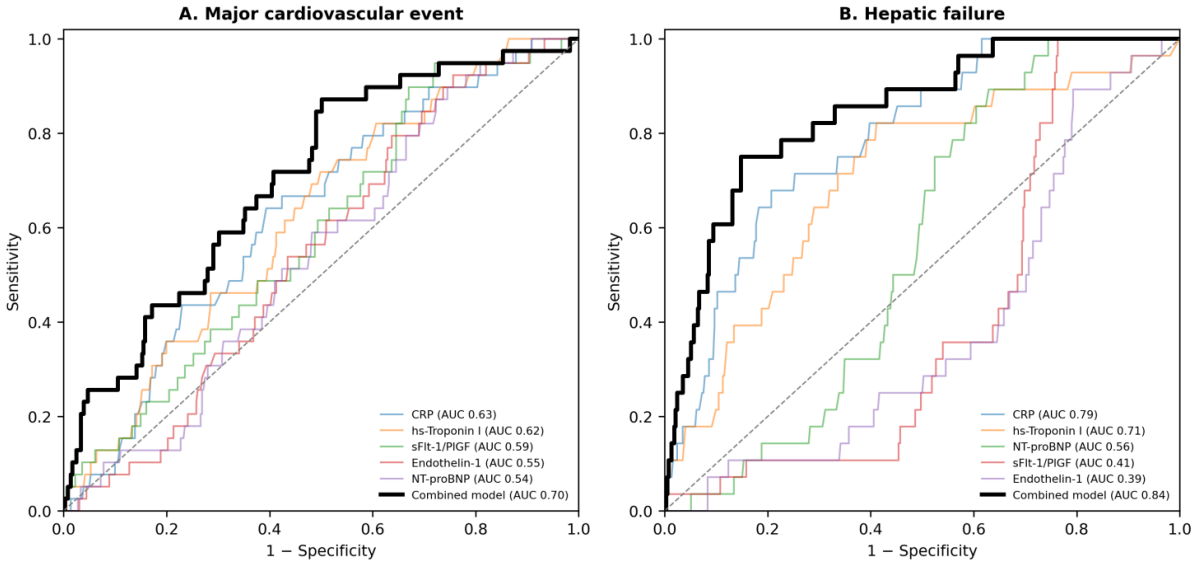

Figure 3: Receiver operating characteristic curves for individual biomarkers and the combined multivariable model. (A) Major cardiovascular event. (B) Hepatic failure. Bold black line denotes the combined logistic regression model (Table 4); colored lines denote individual biomarkers. sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide; hs: high-sensitivity; CRP: c-reactive protein; AUC: area under the curve.

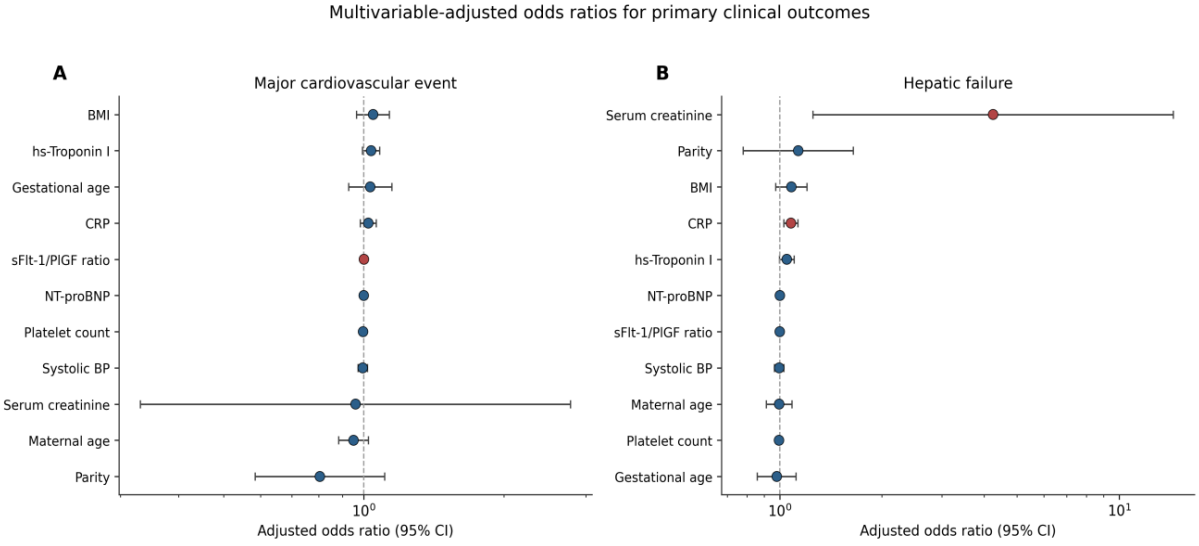

Figure 4: Multivariable-adjusted odds ratios (95% CI) for primary clinical outcomes. (A) Major cardiovascular event. (B) Hepatic failure. Red markers denote predictors significant at $p < 0.05$. BMI: Body mass index; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide; hs: high-sensitivity; CRP: c-reactive protein; BP: blood pressure.

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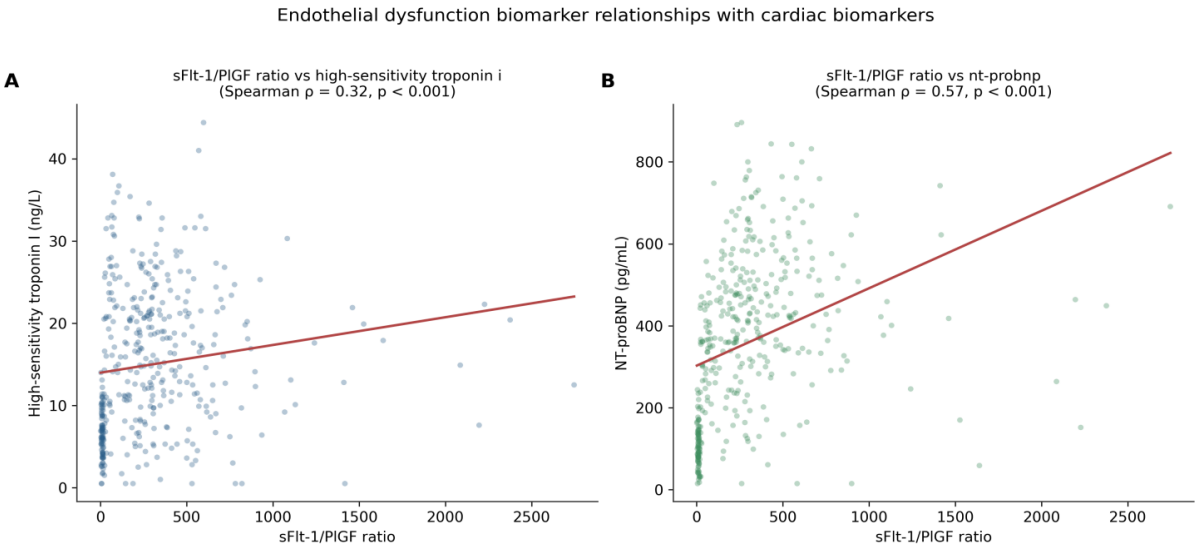

Figure 5: Endothelial dysfunction biomarker relationships with cardiac biomarkers. (A) sFlt-1/PlGF ratio versus high-sensitivity troponin I. (B) sFlt-1/PlGF ratio versus NT-proBNP. sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Table 3: Comparative biomarker and clinical profile by major adverse cardiovascular and hepatic outcomes

Biomarker	**Major adverse cardiovascular outcome**		**Test**	**P/effect size**
	Yes (n = 39)	**No (n = 361)**		
Alanine aminotransferase, U/L	128.0 (74.0–211.5)	96.0 (63.0–163.0)	Mann–Whitney U	0.050; $r = -0.19$
Aspartate aminotransferase, U/L	149.0 (82.5–212.0)	102.0 (61.0–178.0)	Mann–Whitney U	0.071; $r = -0.18$
Total bilirubin, mg/dL	1.8 (1.1–2.5)	1.3 (0.9–2.0)	Mann–Whitney U	0.031; $r = -0.21$
Serum albumin, g/dL	3.1 (2.7–3.3)	3.1 (2.8–3.4)	Welch t-test	0.447; $d = -0.13$
sFlt-1/PlGF ratio	264.0 (106.3–454.9)	227.9 (28.5–406.0)	Mann–Whitney U	0.068; $r = -0.18$
Endothelin-1, pg/mL	8.3 (6.4–9.6)	7.9 (4.7–9.7)	Mann–Whitney U	0.323; $r = -0.10$
High-sensitivity troponin I, ng/L	17.0 (11.8–24.2)	12.9 (7.3–21.1)	Mann–Whitney U	0.013; $r = -0.24$
NT-proBNP, pg/mL	409.0 (260.0–481.5)	362.0 (163.0–503.0)	Mann–Whitney U	0.370; $r = -0.09$
C-reactive protein, mg/L	25.6 (20.0–32.9)	21.3 (13.1–29.0)	Mann–Whitney U	0.008; $r = -0.26$
Interleukin-6, pg/mL	48.7 (31.9–56.9)	33.5 (18.9–44.2)	Mann–Whitney U	< 0.001; $r = -0.36$
Platelet count, $\times 10^9$/L	85.0 (62.5–161.0)	120.0 (72.0–197.0)	Mann–Whitney U	0.027; $r = 0.22$
Left ventricular ejection fraction, %	57.0 (54.0–60.5)	59.0 (56.0–63.0)	Mann–Whitney U	0.099; $r = 0.16$
Cardiovascular risk score, 0–10	6.4 (5.2–7.2)	5.8 (4.0–7.3)	Mann–Whitney U	0.146; $r = -0.14$
Biomarker	**Hepatic Failure**		**Test**	**P/effect size**
	Yes (n = 28)	**No (n = 372)**		
Alanine aminotransferase, U/L	207.5 (145.0–254.8)	94.5 (62.0–159.0)	Mann–Whitney U	< 0.001; $r = -0.58$
Aspartate aminotransferase, U/L	195.0 (135.5–253.8)	101.5 (59.8–176.0)	Mann–Whitney U	< 0.001; $r = -0.46$
Total bilirubin, mg/dL	4.5 (2.1–7.4)	1.2 (0.8–2.0)	Mann–Whitney U	< 0.001; $r = -0.65$
Serum albumin, g/dL	2.8 (2.5–2.9)	3.1 (2.8–3.4)	Welch t-test	< 0.001; $d = -0.88$
sFlt-1/PlGF ratio	81.2 (58.9–232.5)	235.8 (34.2–430.0)	Mann–Whitney U	0.111; $r = 0.18$
Endothelin-1, pg/mL	5.8 (4.6–8.2)	8.0 (5.0–9.7)	Mann–Whitney U	0.045; $r = 0.23$
High-sensitivity troponin I, ng/L	21.1 (17.2–26.2)	12.9 (7.3–20.8)	Mann–Whitney U	< 0.001; $r = -0.41$
NT-proBNP, pg/mL	382.5 (349.5–450.8)	363.0 (160.0–503.8)	Mann–Whitney U	0.302; $r = -0.12$
C-reactive protein, mg/L	33.3 (25.3–37.3)	20.9 (13.1–28.5)	Mann–Whitney U	< 0.001; $r = -0.58$
Interleukin-6, pg/mL	49.4 (37.0–59.3)	33.2 (18.8–45.1)	Mann–Whitney U	< 0.001; $r = -0.51$
Platelet count, $\times 10^9$/L	76.0 (68.8–90.2)	122.5 (72.0–197.2)	Mann–Whitney U	0.001; $r = 0.37$
Left ventricular ejection fraction, %	57.5 (50.8–60.2)	59.0 (55.8–63.0)	Mann–Whitney U	0.048; $r = 0.22$
Cardiovascular risk score, 0–10	6.8 (5.6–7.9)	5.8 (4.1–7.2)	Mann–Whitney U	0.012; $r = -0.28$

Two-group comparisons used the independent-samples (Welch) t-test with Cohen's d for normally distributed variables, or the Mann–Whitney U test with rank-biserial correlation (r) for non-normally distributed variables, per Shapiro–Wilk testing. Two-tailed $p < 0.05$ denotes statistical significance. sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

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Table 4: Multivariate regression models for major cardiovascular outcomes, hepatic failure, and cardiovascular risk score

Predictor	Adjusted OR	95% CI	P
Major cardiovascular event (n = 400; **McFadden pseudo-**R^2 = 0.074; **model** p = 0.063)			
Maternal age	0.95	0.88–1.02	0.175
Parity	0.80	0.58–1.11	0.184
Body mass index	1.05	0.97–1.14	0.264
Gestational age	1.03	0.93–1.15	0.557
Systolic blood pressure	0.99	0.97–1.02	0.671
sFlt-1/PlGF ratio	1.00	1.00–1.00	0.031
High-sensitivity troponin I	1.04	0.99–1.08	0.095
NT-proBNP	1.00	1.00–1.00	0.934
C-reactive protein	1.02	0.98–1.06	0.260
Platelet count	1.00	0.99–1.00	0.303
Serum creatinine	0.96	0.33–2.78	0.940
Hepatic failure (n = 400; **McFadden pseudo-**R^2 = 0.226; **model** $p < 0.001$)			
Maternal age	1.00	0.91–1.09	0.930
Parity	1.13	0.78–1.65	0.511
Body mass index	1.08	0.97–1.20	0.143
Gestational age	0.98	0.86–1.12	0.764
Systolic blood pressure	1.00	0.97–1.03	0.817
sFlt-1/PlGF ratio	1.00	1.00–1.00	0.946
High-sensitivity troponin I	1.05	1.00–1.10	0.062
NT-proBNP	1.00	1.00–1.00	0.572
C-reactive protein	1.08	1.03–1.13	0.002
Platelet count	0.99	0.99–1.00	0.312
Serum creatinine	4.25	1.25–14.42	0.020
Cardiovascular risk score, 0–10 (n = 400; R^2 = 0.459; **adjusted** R^2 = 0.444; $F(11,388) = 29.96$, $p < 0.001$)			
Maternal age	-0.001	-0.036–0.033	0.942
Parity	-0.046	-0.188–0.095	0.521
Body mass index	0.002	-0.038–0.042	0.926
Systolic blood pressure	0.020	0.008–0.032	0.001
Diastolic blood pressure	0.040	0.022–0.058	< 0.001
sFlt-1/PlGF ratio	0.001	-0.000–0.001	0.054
High-sensitivity troponin I	0.028	0.006–0.050	0.013
NT-proBNP	0.001	0.000–0.002	0.026
C-reactive protein	0.016	-0.002–0.035	0.087
Total bilirubin	0.119	0.015–0.224	0.026
Serum albumin	-0.623	-1.131–(-0.115)	0.016

sFlt-1/PlGF ratio row → change "1" to "1" in the Adjusted OR column.

Reported per-unit on native scale; given the wide range of the ratio, the per-SD OR (1.38, 95% CI: 1.03–1.85) is the interpretable effect size (see Results, "Multivariable predictors"). All three models were adjusted for the same core covariate set (maternal age, body mass index, gestational age/blood pressure, and key hepatic, endothelial, cardiac and inflammatory biomarkers). Adjusted OR: adjusted odds ratio; B: unstandardized regression coefficient; CI: confidence interval; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

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Table 5: Cardio-hepatic correlation and receiver operating characteristic (ROC) discriminative analysis for primary outcomes

Biomarker	Cardiac marker	Method	*r* (95% CI)	P
A. Cardio-hepatic crosstalk correlations				
Alanine aminotransferase	hs-Troponin I	Spearman	0.27 (0.18–0.36)	< 0.001
	NT-proBNP	Spearman	0.22 (0.13–0.32)	< 0.001
	Ejection fraction	Spearman	-0.27 (-0.36—0.17)	< 0.001
	CV risk score	Spearman	0.34 (0.26–0.43)	< 0.001
Aspartate aminotransferase	hs-Troponin I	Spearman	0.31 (0.22–0.40)	< 0.001
	NT-proBNP	Spearman	0.27 (0.18–0.36)	< 0.001
	Ejection fraction	Spearman	-0.29 (-0.38—0.20)	< 0.001
	CV risk score	Spearman	0.35 (0.26–0.43)	< 0.001
Total bilirubin	hs-Troponin I	Spearman	0.28 (0.19–0.37)	< 0.001
	NT-proBNP	Spearman	0.10 (0.00–0.20)	0.040
	Ejection fraction	Spearman	-0.25 (-0.34—0.16)	< 0.001
	CV risk score	Spearman	0.23 (0.14–0.32)	< 0.001
sFlt-1/PlGF ratio	hs-Troponin I	Spearman	0.32 (0.23–0.41)	< 0.001
	NT-proBNP	Spearman	0.57 (0.50–0.64)	< 0.001
	Ejection fraction	Spearman	-0.19 (-0.28—0.09)	< 0.001
	CV risk score	Spearman	0.48 (0.41–0.56)	< 0.001
Total bile acids	hs-Troponin I	Spearman	-0.30 (-0.38—0.21)	< 0.001
	NT-proBNP	Spearman	-0.45 (-0.52—0.36)	< 0.001
	Ejection fraction	Spearman	0.11 (0.02–0.21)	0.022
	CV risk score	Spearman	-0.36 (-0.44—0.27)	< 0.001
B. ROC analysis – major cardiovascular event				
Biomarker	**AUC (95% CI)**	**Optimal cutoff**	**Sensitivity**	**Specificity**
C-Reactive Protein	0.63 (0.53–0.73)	24.5	0.64	0.61
High-sensitivity cardiac troponin I	0.62 (0.52–0.72)	13.1	0.72	0.50
sFlt-1/PlGF ratio	0.59 (0.49–0.69)	49.5	0.95	0.28
Endothelin-1	0.55 (0.45–0.65)	4.6	0.92	0.24
Combined multivariable model	0.70 (0.61–0.78)	0.079	0.87	0.50
C. ROC analysis – hepatic failure				
Biomarker	**AUC (95% CI)**	**Optimal cutoff**	**Sensitivity**	**Specificity**
C-Reactive Protein	0.79 (0.69–0.89)	30	0.68	0.79
High-sensitivity cardiac troponin I	0.71 (0.60–0.82)	16	0.82	0.59
NT-proBNP	0.56 (0.44–0.67)	283	0.89	0.37
sFlt-1/PlGF ratio	0.41 (0.31–0.51)	24.4	1.00	0.24
Endothelin-1	0.39 (0.29–0.49)	4.3	0.89	0.21
Combined multivariable model	0.84 (0.77–0.91)	0.109	0.75	0.85

Data are presented with 95% confidence interval (CI). NT-proBNP: N-terminal prohormone of brain natriuretic peptide; sFlt-1: soluble fms-like tyrosine kinase-1; PlGF: placental growth factor; AUC: area under the curve; hs: high-sensitivity; CV: cardiovascular.

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