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Article

Assessment of Maternal Hematological parameters, Kidney and Liver Injury Markers across Adverse Pregnancy Outcomes: A Cross Sectional study

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Abstract

Background and Aim: Adverse pregnancy outcomes (APOs) such as prematurity, low birth weight, stillbirth, and birth defects remain significant global health challenges. While many risk factors are known, APOs encompass a wide range of outcomes with diverse, sometimes poorly understood etiologies. Pregnancy-related acute kidney injury (PR-AKI) and liver injury are particularly associated with increased maternal and fetal mortality. This study investigated the association between hematological parameters, kidney and liver injury markers and adverse pregnancy outcomes. **Materials and Methods:** This cross-sectional study involved 714 pregnant women aged 18-40 years, conducted between August 2021 and August 2022. Maternal blood samples were collected before and after delivery to compare hematological parameters. Kidney and liver injury markers were measured using standard methods. The study analysed the association of these parameters with adverse pregnancy outcomes. **Results:** The median age of participants was 24 years (Q1, Q3: 21, 26). Women with adverse pregnancy outcomes had statistically significant serum creatinine levels [0.52 mg/dL (0.45, 0.58)] compared to those without [0.50 mg/dL (0.44, 0.56)], although the difference was not clinically significant. Elevated AST levels (>90th percentile) were statistically associated with adverse pregnancy outcomes. Pairwise comparisons with Bonferroni corrections revealed significant differences in Hb, WBC, RBC, platelet, and PCV levels before and after delivery ($p < 0.05$) in both groups. **Conclusions:** The study revealed a statistically significant yet clinically negligible difference in creatinine levels between women with and without adverse pregnancy outcomes. Elevated AST levels showed an association with APOs, whereas other biochemical markers showed no association.

Keywords: pregnancy; adverse pregnancy outcomes; liver markers; kidney markers

1. Introduction

Adverse pregnancy outcomes (APOs), including prematurity, low birth weight, stillbirth, and birth defects, remain significant global health challenges [1]. Over 15 million babies are born prematurely each year worldwide, representing more than 10% of all birth [2]. APOs are influenced by various factors, including maternal characteristics, medical conditions, and obstetric complications [3].

Pregnancy induces physiological changes in multiple organ systems, which can exacerbate pre-existing conditions and lead to kidney and liver complications [4][5]. Studies have shown that impaired kidney and liver functions are associated with poor obstetric outcomes, particularly preterm birth, preeclampsia, and fetal growth restriction [6][7]. Liver transaminases (AST, ALT) and kidney markers (creatinine, urea) serve as important indicators of organ function during pregnancy. [5][8] Notably, pregnancy-related acute kidney injury (PR-AKI) is associated with increased maternal and fetal mortality [9]. Hematological parameters also undergo significant changes during pregnancy, known as the physiologic anemia of pregnancy [10]. These alterations affect various blood components and are believed to facilitate utero-placental perfusion [11].

While previous research has analyzed hematological parameters at specific pregnancy stages, there is a need to monitor these profiles before delivery and during the postpartum period. Moreover, the relationship between hematological parameters, liver and kidney injury markers, and adverse pregnancy outcomes remains unclear. This study aimed to assess the association of kidney and liver injury markers and hematological parameters with adverse pregnancy outcomes, focusing on measurements before delivery and during the postpartum period. By investigating these relationships, we seek to contribute to a better understanding of the complex interplay between maternal physiological changes and pregnancy outcomes.

2. Results

2.1 Demographic and Clinical Characteristics

A total of 714 pregnant women were included in the study; demographic and clinical variables of the study population are presented in Table 1. The median age of the women in this study was 24 (Q1, Q3:21,26) years. Within the composite adverse pregnancy outcome, the proportion of LBW was higher [17.23 % (95%CI: 17.15,23.15)] when compared to PTB and stillbirth [6.89% (95%CI: 5.14,9.01) and 0.84% (95%CI: 0.31,1.82) respectively]. Maternal BMI was found to be associated with APOs. However, there was no clinical difference observed between other maternal characteristics and adverse pregnancy outcomes.

Table 1. Maternal Characteristics and Adverse pregnancy outcomes.

Maternal characteristics	Adverse pregnancy outcomes		Mann-Whitney U statistic	p-value	
	Yes [(median,(Q ₁ ,Q ₃)] ⁿ	No [(median(Q ₁ ,Q ₃)] ⁿ			
Maternal age (years)	23(21, 26)	143	24(22, 26)	568 38689.50	0.379
BMI(Body mass index) (kg/m ²)	23.1(21.4, 26.2)	142	24.6(22.3, 26.9)	571 33541.50	0.001*
Gestational age at delivery (weeks)	37(36, 38)	143	39(38,40)	568 16791.50	<0.001*
Systolic Blood Pressure (SBP)(mmHg)	120(112,120)	143	120(110,120)	571 37744.50	0.138
Diastolic Blood Pressure (DBP)(mmHg)	80(70,80)	143	80(70,80)	571 39095.50	0.396
Maternal weight (Kg)	54(49,60)	143	58(52,64)	571 31200.00	<0.001*
Maternal height (mm)	152(150,154)	143	152(150,155)	571 32593.50	<0.001*

*statistically significant

2.2. Association Between Kidney Injury Markers and Adverse Pregnancy Outcomes

Man-Whitney U test was used to compare the average kidney injury and liver injury markers across groups with adverse and normal pregnancy outcomes. The average levels of creatinine were moderately elevated in adverse pregnancy outcomes group 0.52 (0.45,0.58) when compared to the group without adverse pregnancy events 0.50 (0.44,0.56). None of the other kidney injury markers were found to be statistically significant.

Table 2. Association between average kidney injury markers and adverse pregnancy outcomes.

Parameters	Adverse pregnancy outcome				Mann Whitney U statistic	p-value
	Yes		No			
	Median (Q ₁ ,Q ₃)	n	Median (Q ₁ ,Q ₃)	n		
Urea (mg/dL)	12(10,15)	141	12(10,14)	562	36754.5	0.17
Creatinine (mg/dL)	0.52((0.45,0.58)	141	0.50(0.44,0.56)	562	34356.5	0.015*
Sodium (mEq/L)	136(134,138)	141	136(134,138)	562	39139	0.82
Potassium (mEq/L)	4.15(3.78, 4.80)	141	4.11(3.79,4.54)	562	37679.5	0.36
Chloride (mEq/L)	100.0 (98,102)	141	100.0 (98.0,102.0)	562	38352.5	0.55
Bicarbonate (mmol/L)	18.0 (16.0,20.0)	141	18.0 (16.0,19.0)	562	38332.5	0.54

*statistically significant

2.3. Association Between Liver Injury Markers and Adverse Pregnancy Outcomes

Chi-Square tests were used to assess the association between liver injury markers and adverse pregnancy outcomes. For AST levels, 16.4% of women with adverse pregnancy outcomes had elevated AST (>90th percentile) compared to 7.1% of women without adverse outcomes. The odds of experiencing an adverse pregnancy outcome were 2.57 times higher among mothers with AST >90th percentile compared to those with AST ≤90th percentile [OR: 2.57 (95% CI: 1.48, 4.45)]. Regarding ALT levels, 13.6% of women with adverse pregnancy outcomes had elevated ALT (>90th percentile) compared to 9.1% of women without adverse outcomes. The odds of experiencing an adverse pregnancy outcome were 1.57 times higher among mothers with ALT >90th percentile compared to those with ALT ≤90th percentile [OR: 1.57 (95% CI: 0.90, 2.76)]. However, no statistically significant association was observed between ALT levels and adverse pregnancy outcomes.

Table 3. Association of Serum Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) Levels across adverse pregnancy outcomes.

Parameters	Adverse pregnancy outcomes		Chi-Square test statistic	OR (95% CI)	p-value
	Yes	No			
	n (%)	n (%)			
ALT (U/L) (≤90 th percentile)	121 (86.4)	511 (90.9)		ref	
ALT (U/L) (>90 th percentile)	19 (13.6)	51 (9.1)	2.524	1.57(0.90,2.76)	0.112
AST (U/L) (≤90 th percentile)	117 (83.6)	522 (92.9)		ref	
AST (U/L) (>90 th percentile)	23 (16.4)	40 (7.1)	11.895	2.57(1.48,4.45)	0.001*

*Statistically significant OR - Odds Ratios CI- confidence intervals

2.4. Hematological Parameters and Adverse Pregnancy Outcomes

Two-way Repeated Measures Analysis of Variance (RM-ANOVA) was used to compare trends in hematological parameters over time (before and after delivery) across groups, as presented in Table 4. A statistically significant interaction between time points and adverse pregnancy outcomes was observed for Hb, PCV, and RBCs ($p < 0.05$). Other parameters did not show statistically significant interactions. After conducting pairwise comparisons within each group and implementing Bonferroni corrections, we found that Hb, WBC, RBC, platelet, and PCV levels were significantly different before and after delivery ($p < 0.05$). Specifically, average platelet levels decreased after delivery compared to before delivery, while average WBC levels increased after delivery compared to before delivery. No significant differences were observed in the average levels of MCV, MCH, MCHC, and RDW before and after delivery.

Table 4. Comparison of hematological parameters before and after delivery among normal and adverse pregnancy outcomes.

Hematological parameters	Adverse pregnancy outcome	Sample size (n)	Time period		Mean Difference (95% CI)	Interaction F-value (p-value)
			Before delivery	After delivery		
Hb (gms %)	Yes	141	11.7(1.45)	10.8(1.41)	0.89 (0.702, 1.07)	5.52(0.019*)
	No	564	11.6(1.41)	10.5(1.39)	1.14 (1.04, 1.23)	
Total (WBC) count ($10^3/\mu\text{L}$)	Yes	141	16.0(4.48)	17.9(4.56)	-1.89(-2.60, -1.18)	0.19(0.65)
	No	564	15.6(4.24)	17.7(4.66)	-2.07(-2.43, -1.72)	
Platelets count ($10^3/\mu\text{L}$)	Yes	141	228.8(59.91)	216.9(52.35)	11.92 (6.60, 17.24)	1.12(0.29)
	No	564	225.0(66.91)	216.3(60.89)	8.71 (6.05, 11.37)	
RBC count ($10^6/\mu\text{L}$)	Yes	141	4.20(0.53)	3.86(0.54)	0.33 (0.26, 0.40)	4.54(0.03*)
	No	564	4.23(0.47)	3.81(0.50)	0.41 (0.384, 0.45)	
PCV (%)	Yes	141	36.2(4.05)	33.2(4.14)	3.04 (2.45, 3.63)	4.42(0.036*)
	No	564	36.1(3.93)	32.4(4.08)	3.75 (3.45, 4.04)	
MCV (fL)	Yes	141	86.7(7.98)	86.3(7.68)	0.37 (0.03, 0.72)	0.21(0.64)
	No	564	86.7(7.55)	85.2(7.67)	0.46 (0.29, 0.63)	
MCH (pg)	Yes	141	28.1(3.13)	28.2(3.08)	-0.14 (-0.25, -0.04)	3.2(0.08)
	No	564	27.7(3.04)	27.7(3.03)	-0.03 (-0.09, 0.01)	
MCHC (g/dL)	Yes	141	32.3(1.02)	32.6(1.07)	-0.31 (-0.44, -0.18)	1.35(0.24)
	No	564	32.2(1.12)	32.5(1.03)	-0.22 (-0.29, -0.16)	
RDW (%)	Yes	141	15.9(3.52)	15.8(3.55)	0.13 (-0.08, 0.36)	0.62(0.43)
	No	564	16.1(3.38)	16.1(3.65)	0.03 (-0.07, 0.14)	

*Statistically significant

3. Discussion

3.1. Main Findings

This study investigated the associations between maternal hematological parameters, kidney and liver injury markers, and adverse pregnancy outcomes among women presenting for delivery. Serum creatinine was statistically higher in women with APOs, though the absolute difference was

clinically negligible; and elevated AST levels were significantly associated with APOs, while ALT and other biochemical markers showed no meaningful associations; also hematological parameters, particularly Hb, RBC and PCV, exhibited significant variations across time points, with modest differences between outcome groups.

3.2. Kidney Function Markers and APOs

Serum creatinine was marginally elevated in women experiencing APOs compared to those without, though the absolute increase (0.02 mg/dL) was within the physiological range. This aligns with findings from Yalamati et al. and Deng et al., who reported that higher serum creatinine (≥ 0.8 mg/dL) was associated with adverse outcomes, particularly preterm birth [13,14]. Similarly, Harel et al. demonstrated that pre-pregnancy kidney dysfunction increased the risk of preterm birth [15]. However, Champion et al. observed no association between creatinine levels and APOs in pregnancies complicated by diabetes when creatinine remained below 1.2 mg/dL [16].

Physiologically, pregnancy lowers serum creatinine through increased renal plasma flow and glomerular filtration, with nadirs reached in the first and second trimesters and gradual rises toward term. Thus, even small differences may signal impaired renal adaptation. While our observed difference was statistically significant, it is unlikely to hold clinical utility in isolation, particularly in the absence of overt pregnancy-related acute kidney injury (PR-AKI), which is well known to worsen maternal and neonatal prognosis [17,18]. In contrast, urea and electrolytes showed no significant associations with APOs. Our findings mirror those of Ambad et al., who found that serum urea and creatinine did not significantly differ between preeclamptic and normal pregnancies, though both were higher in eclampsia [19]. Discrepancies with other reports linking electrolyte imbalances to preeclampsia may reflect population heterogeneity and differences in study design [20].

3.3. Liver Function Markers and APOs

Among liver markers, elevated AST levels (>90th percentile) were significantly associated with APOs, conferring a 2.57-fold increased risk. ALT elevation showed a weaker, non-significant association. These results agree with prior evidence suggesting that abnormal liver enzymes may signal higher risk of maternal and fetal complications. For instance, Thangaratnam et al. reported that elevated liver function tests in preeclampsia predicted adverse maternal and fetal outcomes [21]. Conversely, Losy et al. and Kozic et al. found no independent association between elevated transaminases and adverse outcomes [22,23]. Physiologically, AST elevations likely reflect hepatocellular stress secondary to placental ischemia, systemic inflammation, or hypertensive disorders of pregnancy. These mechanisms have been implicated in the pathogenesis of APOs such as preterm birth and intrauterine growth restriction. Our findings reinforce the utility of AST as a low-cost, accessible marker of heightened risk in resource-limited settings, though specificity remains limited.

3.4. Hematological Parameters and APOs

Pregnancy induces haemodilution, producing physiologic anemia due to disproportionate expansion of plasma volume relative to red cell mass [24]. In our cohort, Hb, PCV, and RBC counts demonstrated significant time–outcome interactions, with women experiencing APOs showing more pronounced declines. Platelet counts decreased and WBC counts increased postpartum across both groups, consistent with normal delivery-associated changes.

These findings are consistent with observations by Hana et al., who described trimester-specific alterations in RBC indices and platelet counts, and by Dahlstrom et al., who reported postpartum platelet reductions. In contrast, Mensah et al. observed no meaningful relationship between hematological indices and birth outcomes, while Shigemi et al. similarly found that white blood cell counts lacked predictive value for maternal complications, underscoring variability across populations and study designs [25–29]. The inconsistencies across studies likely reflect

methodological heterogeneity and population differences. Taken together, our data suggest that while Hb, RBC, and PCV shifts reflect maternal adaptation to pregnancy and delivery, they are not robust standalone predictors of APOs. Rather, these parameters provide physiological context and may complement biochemical markers in risk assessment.

The identification of simple, cost-effective biomarkers is particularly important in resource-limited settings. Advanced biomarker assays may not be feasible in such contexts, but readily available parameters such as creatinine, AST, and routine hematological indices could serve as early warning tools for heightened risk of APOs. Their clinical applicability, however, requires validation through prospective, multicentre studies and integration with other maternal risk factors.

3.5. Strength and Limitations

A notable strength of this study is its relatively large sample size, which enhances the statistical reliability of the findings. The simultaneous evaluation of hematological, kidney and liver markers at two time points (before and after delivery) provides a more comprehensive understanding of maternal physiological changes than studies restricted to a single measurement. The use of standardized laboratory protocols ensured consistency and accuracy of biochemical and hematological assessments. The cross-sectional design restricts causal inference, while the absence of pre-pregnancy baseline values limits the ability to distinguish between pre-existing abnormalities and pregnancy induced changes. Additionally, as the study was conducted at a single centre, the generalizability of findings to broader populations may be limited.

4. Materials and Methods

This cross-sectional study was part of the larger "Limiting Adverse Birth Outcomes in Resource-Limited Settings" (LABOR) Study, a multi-country, prospective, observational cohort study [12]. It was conducted from August 2021 to August 2022 at KLE's Dr. Prabhakar Kore Hospital, Belagavi, Karnataka, India, and approved by the Institutional Ethics Committee KAHER, (KAHER/EC/21-22/002), Belagavi.

This site analysis included 714 women aged 18-40 years with intrauterine singleton pregnancies who provided written informed consent. Its sample size was preset by the parent, multi-country protocol. Women were screened upon presenting for delivery at the hospital. We recorded composite adverse events for mothers (death, hemorrhage, hypertensive disorders, or infection) and fetuses/newborns (intrapartum stillbirth, neonatal death, encephalopathy, or sepsis) attributable to the intrapartum period.

"Adverse pregnancy outcomes" (APOs) were defined as low birth weight, preterm birth, or stillbirth. Normal births without these complications were categorized as "no APOs." Maternal characteristics recorded included age, gestational age, height, weight, systolic and diastolic blood pressure (SBP, DBP). Body mass index (BMI) was calculated using pre-pregnancy weight (kg) divided by height squared (m²).

The study excluded women with multiple pregnancies, those admitted for elective caesarean without comorbidities, those unable to provide informed consent, and any participants with social or medical conditions deemed unsafe or unfeasible for participation by study staff.

4.1. Sample Collection and Biochemical Analysis

Blood samples were collected from women under aseptic conditions from a large peripheral vein at hospital admission and after delivery, following approved standard operating procedures. Sample collection, processing, and result reporting adhered to good clinical laboratory practice standards.

Pre-delivery, 5 ml of blood was collected: 2 ml in EDTA for complete blood count (CBC) and 3 ml in a Serum Separation Tube (SST). The SST sample was allowed to clot for one hour, then centrifuged at 3000 rpm for 10 minutes at room temperature to separate serum. This serum was used

to measure electrolytes, kidney, and liver injury markers. Post-delivery, an additional 2 ml of blood was collected in EDTA for CBC.

Biochemical assays were performed using a Cobas 6000 analyzer. The following methods were employed: Aspartate and alanine aminotransferases were measured by enzymatic method (UV with P5P); sodium, potassium, chloride, and bicarbonate by ion selective electrode indirect method; creatinine by enzymatic IFCC-IDMS method; and urea by urease UV enzymatic method. Complete Blood Count was measured by using hematology analyser (Beckman coulter LH 780 hematology analyser).

4.2. Statistical Analysis

Continuous variables (e.g., age, Hb, SBP, DBP) were summarized using Mean(SD) or Median (Q1, Q3), depending on data normality assessed by the Kolmogorov-Smirnov test. Categorical variables (e.g., stillbirth, preterm birth, low birth weight) were summarized using frequencies and percentages. Comparisons of maternal characteristics and kidney injury markers between groups with and without adverse pregnancy outcomes were conducted using the Mann-Whitney U test. Chi-Square tests were used to assess associations between liver injury markers and adverse pregnancy outcomes. Odds Ratios (OR) with 95% confidence intervals were reported. Two-way Repeated Measures Analysis of Variance (RM-ANOVA) was employed to compare trends in hematological parameters over time (before and after delivery) across groups. All statistical analyses were performed using SPSS version 29.0, with a P-value less than 0.05 considered statistically significant.

5. Conclusions

Our findings indicate that creatinine levels differ significantly between women with and without adverse pregnancy outcomes; however, the variation is clinically negligible. Elevated AST levels were significantly associated with adverse outcomes, whereas other kidney and liver markers showed no associations. Hematological parameters such as Hb, RBC, and PCV demonstrated significant temporal variations, reflecting normal physiological adaptations rather than reliable predictors of risk. These findings highlight the potential role of simple, low-cost biomarkers particularly creatinine and AST in early risk stratification, especially in resource-limited settings where advanced diagnostics are less feasible. Larger, multicenter longitudinal studies are needed to validate these associations and strengthen predictive strategies for maternal and neonatal outcomes.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the KLE Academy of Higher Education and Research, Belagavi (approval number: KAH/EC/21-22/002; date of approval: 2021-07-29).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The original contributions presented in this study are included in this article/the Supplementary Material. Further inquiries can be directed to the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest

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