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Pregnancy-induced Hypertension Complicated by Acute Liver Disease and Disseminated Intravascular Coagulation: A Cross-sectional Study

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ABSTRACT

Background: Pregnancy-induced hypertension (PIH) is a major obstetric complication with significant maternal and fetal morbidity, particularly when associated with acute liver dysfunction and disseminated intravascular coagulation (DIC). These conditions present unique challenges, requiring timely recognition and management. This study aimed to evaluate the clinical and biochemical profiles of women with PIH complicated by liver dysfunction and DIC and assess their maternal and perinatal outcomes.

Methods: A cross-sectional study was conducted at Women Medical and Dental College Abbottabad from January 2023 to January 2024. A total of 102 participants diagnosed with PIH, liver dysfunction, and DIC were included through non-probability consecutive sampling. Clinical data, laboratory investigations, and maternal-fetal outcomes were analyzed. Statistical significance was determined with a p-value <0.05.

Results: The mean age of participants was 28.6 ± 5.1 years, and the average gestational age was 32.4 ± 3.2 weeks. Elevated systolic (158.7 ± 12.4 mmHg) and diastolic (102.3 ± 9.6 mmHg) blood pressures were significantly associated with adverse outcomes ($p < 0.01$). Proteinuria (368.2 ± 75.3 mg/dL) and liver dysfunction, including elevated ALT (85.2 ± 32.7 U/L) and AST (94.8 ± 40.6 U/L), were notable findings. Coagulation abnormalities, such as prolonged PT (15.8 ± 2.3 seconds) and aPTT (38.7 ± 6.2 seconds), low fibrinogen (182.4 ± 58.3 mg/dL), and elevated D-dimer levels (2375 ± 624 ng/mL), were strongly indicative of DIC ($p < 0.01$). Maternal outcomes included ICU admissions (41.2%), blood transfusions (34.3%), and a mortality rate of 7.8%. Fetal complications included stillbirth (11.8%), low Apgar scores (<7 at 5 minutes in 27.4%), and fetal growth restriction (35.3%).

Conclusion: PIH complicated by liver dysfunction and DIC significantly impacts maternal and fetal health, leading to severe complications. Early recognition, multidisciplinary management, and timely interventions are essential to improve outcomes. Further research is recommended to develop predictive markers and optimize care for high-risk pregnancies.

Keywords: Pregnancy-induced hypertension, liver dysfunction, disseminated intravascular coagulation, maternal outcomes, fetal outcomes, high-risk pregnancies.

INTRODUCTION

Pregnancy-induced hypertension (PIH) is a significant obstetric complication characterized by elevated blood pressure that emerges after 20 weeks of gestation in women who were previously normotensive [1]. This condition can lead to severe maternal and fetal morbidity and mortality, particularly when complicated by acute liver dysfunction and disseminated intravascular coagulation (DIC). PIH encompasses a spectrum of hypertensive disorders, including preeclampsia and eclampsia, which are often associated with multi-organ involvement and systemic complications [2].

Acute liver disease in the context of PIH may present as elevated liver enzymes, hepatic rupture, or liver failure, further exacerbating the clinical scenario[3]. Similarly, DIC—a condition marked by widespread activation of the coagulation cascade—can lead to thrombotic events, severe bleeding, and consumptive coagulopathy. These complications create a critical situation requiring immediate intervention [4, 5].

The dual complications of liver dysfunction and DIC in PIH pose unique challenges in diagnosis and management due to overlapping clinical and laboratory findings. Early identification of these complications is crucial to mitigate adverse outcomes and improve survival rates for both the mother and the fetus. This study aims to assess the clinical and biochemical profiles of women with PIH complicated by acute liver dysfunction and DIC and evaluate their maternal and perinatal outcomes. This study underscores the importance of prompt recognition and multidisciplinary management of these high-risk pregnancies by identifying significant markers and patterns.

METHODOLOGY

The study was a cross-sectional analysis conducted at Women Medical and Dental College Abbottabad, over one year from January 2023 to January 2024. The research aimed to evaluate the clinical, biochemical, and maternal-fetal outcomes in pregnant women diagnosed with pregnancy-induced hypertension (PIH) complicated by acute liver dysfunction and disseminated intravascular coagulation (DIC). The study included one hundred-two participants selected through non-probability consecutive sampling. The inclusion criteria required pregnant women with a confirmed diagnosis of PIH after 20 weeks of gestation, accompanied by evidence of liver dysfunction (elevated liver enzymes, jaundice, or hypoalbuminemia) and laboratory findings indicative of DIC (prolonged PT, aPTT, elevated INR, low fibrinogen, or elevated D-dimer levels). Patients with pre-existing liver diseases, coagulation disorders unrelated to pregnancy, chronic hypertension, or incomplete medical records were excluded from the study.

Ethical approval was obtained from the Institutional Review Board of Women Medical and Dental College Abbottabad, and written informed consent was obtained from all participants involved in prospective data collection. Anonymity and confidentiality were maintained throughout the study, ensuring adherence to ethical standards in clinical research. This methodology provided a robust framework for assessing the interplay between PIH, acute liver dysfunction, and DIC and its impact on maternal and fetal health outcomes.

Data were collected both retrospectively and prospectively using a standardized data collection form. Retrospective data were extracted from patient records, while prospective cases were followed throughout their hospital stay. The collected information included demographic details such as age, gestational age, parity, BMI, and socioeconomic status. Clinical parameters were recorded, including blood pressure readings, symptoms like headache and epigastric pain, and proteinuria levels. Laboratory investigations encompassed liver function tests (ALT, AST, bilirubin, and albumin levels), coagulation markers (PT, aPTT, INR, fibrinogen, and D-dimer), and hematological parameters from a complete blood count (CBC), including hemoglobin, hematocrit, WBC count, neutrophil and lymphocyte percentages, and red cell indices (MCV, MCH, MCHC, RDW). Maternal outcomes, such as ICU

admissions, blood transfusions, mode of delivery, and mortality, were recorded, along with fetal outcomes, including Apgar scores, fetal growth restriction, stillbirth, and neonatal death.

Diagnostic criteria were strictly adhered to, with PIH defined as blood pressure readings of ≥140/90 mmHg measured on two occasions at least four hours apart after 20 weeks of gestation. Liver dysfunction was identified based on elevated liver enzymes (ALT or AST ≥2 times the upper limit of normal) or total bilirubin >2 mg/dL. DIC was diagnosed using a combination of prolonged PT or aPTT, elevated INR (>1.2), decreased platelet counts (<100 ×10⁹/L), low fibrinogen (<200 mg/dL), and elevated D-dimer levels (>500 ng/mL).

The data were analyzed using SPSS version 25.0. Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. Associations between categorical variables were evaluated using the chi-square test, and comparisons of continuous variables were made using the student's t-test, depending on the data distribution. A p-value of <0.05 was considered statistically significant.

RESULTS

The study analyzed 102 participants to evaluate the impact of pregnancy-induced hypertension (PIH) complicated by acute liver disease and disseminated intravascular coagulation (DIC). Demographic and clinical characteristics revealed a mean age of 28.6 years and an average gestational age of 32.4 weeks, showing significant associations with outcomes (p = 0.045 and p = 0.021, respectively). Blood pressure readings, including a mean systolic pressure of 158.7 mmHg and diastolic pressure of 102.3 mmHg, were highly significant (p < 0.01), emphasizing their critical role in PIH. Additionally, elevated proteinuria levels (368.2 mg/dL) were associated with adverse outcomes (p = 0.018).

Table 1: Demographic and Clinical Characteristics of the Participants (n = 102)

Variable	Mean ± SD / N (%)	P-value
Age (years)	28.6 ± 5.1	0.045*
Gestational age (weeks)	32.4 ± 3.2	0.021*
Parity (Primigravida)	58 (56.9%)	0.067
BMI (kg/m²)	29.3 ± 4.6	0.053
Socioeconomic status (Low)	45 (44.1%)	0.039*
Blood pressure (Systolic, mmHg)	158.7 ± 12.4	0.001**
Blood pressure (Diastolic, mmHg)	102.3 ± 9.6	0.002**
Proteinuria (mg/dL)	368.2 ± 75.3	0.018*

*Statistically significant (P < 0.05), **highly significant (P < 0.01).

The liver function test results highlighted systemic liver involvement. Elevated ALT (85.2 U/L) and AST (94.8 U/L) were enormously significant (p = 0.005 and p = 0.002), alongside increased total bilirubin (3.1 mg/dL) and direct bilirubin (1.4 mg/dL), which were also significant (p = 0.014 and p = 0.046). Low albumin levels (2.8 g/dL) were notable (p = 0.003), reflecting impaired liver synthetic function.

Table 2: Liver Function Test Results

Variable	Mean ± SD / Median (IQR)	P-value
ALT (U/L)	85.2 ± 32.7	0.005**
AST (U/L)	94.8 ± 40.6	0.002**
Total bilirubin (mg/dL)	3.1 ± 1.5	0.014*
Direct bilirubin (mg/dL)	1.4 ± 0.8	0.046*
Albumin (g/dL)	2.8 ± 0.6	0.003**

The coagulation and hematological markers, including CBC, showed pronounced abnormalities. Prolonged prothrombin time (15.8 seconds), aPTT (38.7 seconds), and elevated INR (1.4) were highly significant ($p < 0.01$), indicating coagulation dysfunction consistent with DIC. Severe thrombocytopenia (platelet count: 78.2 $\times 10^9$/L) was substantial ($p = 0.001$), along with low fibrinogen (182.4 mg/dL) and elevated D-dimer (2375 ng/mL), confirming the presence of consumptive coagulopathy. CBC abnormalities included reduced hemoglobin (9.6 g/dL) and hematocrit (29.4%), mild anemia, and elevated WBC count (14.2 $\times 10^9$/L), with a neutrophilic predominance (78.5%).

Table 3: Coagulation and Hematological Markers

Variable	Mean ± SD / Median (IQR)	P-value
Prothrombin time (PT, seconds)	15.8 ± 2.3	0.001**
Activated partial thromboplastin time (aPTT, seconds)	38.7 ± 6.2	0.012*
INR	1.4 ± 0.2	0.004**
Platelet count ($\times 10^9$/L)	78.2 ± 32.6	0.001**
Fibrinogen (mg/dL)	182.4 ± 58.3	0.007**
D-dimer (ng/mL)	2,375 ± 624	0.001**
Hemoglobin (g/dL)	9.6 ± 1.5	0.041*
Hematocrit (%)	29.4 ± 4.8	0.039*
WBC count ($\times 10^9$/L)	14.2 ± 3.7	0.031*
Neutrophil count (%)	78.5 ± 8.4	0.018*
Lymphocyte count (%)	15.3 ± 3.2	0.044*
RBC count ($\times 10^{12}$/L)	3.2 ± 0.4	0.052
Mean corpuscular volume (MCV, fL)	84.7 ± 7.3	0.061
Mean corpuscular hemoglobin (MCH, pg)	28.3 ± 2.1	0.056
Mean corpuscular hemoglobin concentration (MCHC, g/dL)	33.2 ± 1.4	0.049*
Red cell distribution width (RDW, %)	16.8 ± 2.3	0.038*

Maternal and obstetric outcomes underscored the severity of the complications. Cesarean deliveries were prevalent (66.7%, $p = 0.003$), and adverse fetal outcomes, including stillbirth (11.8%, $p = 0.001$) and low Apgar scores (<7 at 5 minutes: 27.4%, $p = 0.021$), were significant. Fetal growth restriction (35.3%, $p = 0.015$) and placental abruption (13.7%, $p = 0.012$) were also notable. Maternal complications included ICU admissions (41.2%, $p = 0.004$), blood transfusion requirements (34.3%, $p = 0.003$), and maternal mortality (7.8%, $p = 0.001$), highlighting the life-threatening nature of the condition.

Table 4: Maternal and Obstetric Outcomes

Variable	N (%)	P-value
Mode of delivery (C-section)	68 (66.7%)	0.003**
Fetal outcome (Stillbirth)	12 (11.8%)	0.001**
Apgar score < 7 at 5 minutes	28 (27.4%)	0.021*
Fetal growth restriction	36 (35.3%)	0.015*
Placental abruption	14 (13.7%)	0.012*
ICU admission	42 (41.2%)	0.004**
Blood product transfusion	35 (34.3%)	0.003**
Maternal mortality	8 (7.8%)	0.001**

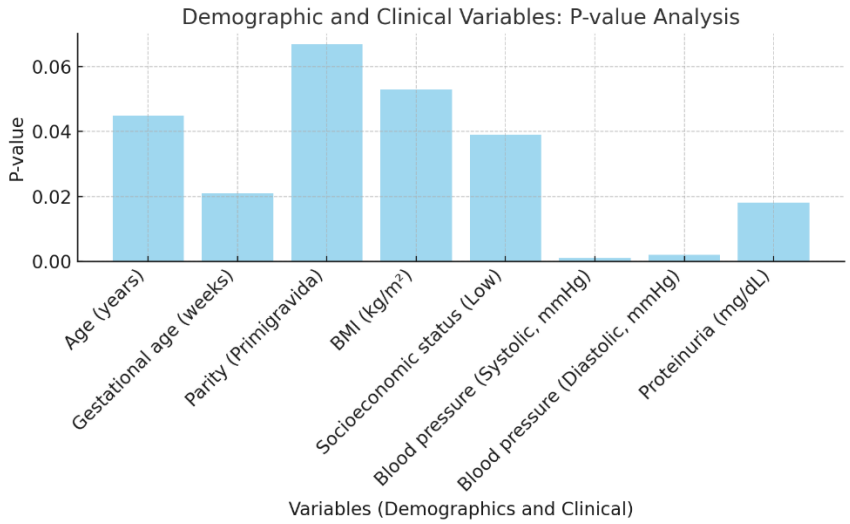

Figure 1 illustrates the significance of demographic and clinical variables, with systolic and diastolic blood pressures and proteinuria showing the strongest associations. Overall, the study findings emphasize the systemic impact of PIH complicated by liver dysfunction and DIC, demonstrating significant associations across liver function tests, coagulation parameters, and maternal-fetal outcomes. These findings underscore the importance of early diagnosis and aggressive management to improve outcomes for both mother and fetus.

DISCUSSION

This study highlights the significant clinical and biochemical abnormalities associated with pregnancy-induced hypertension (PIH) complicated by acute liver dysfunction and disseminated intravascular coagulation (DIC). The findings align with existing literature, emphasizing these conditions' severe maternal and fetal risks.

The mean age of participants in this study (28.6 years) and the predominance of PIH in women at 32 weeks of gestation are consistent with previous studies that reported similar demographic patterns in hypertensive pregnancies. Research demonstrated that PIH often manifests in the late second or third trimester, particularly in women with certain risk factors, such as obesity, and primigravida, which were observed in this study [6, 7]. Elevated BMI (mean 29.3 kg/m²) was a common finding, corroborating evidence that obesity exacerbates the risk of hypertensive disorders in pregnancy.

The significantly elevated systolic and diastolic blood pressure readings observed in this study mirror findings in the studies that identified elevated blood pressure as a key determinant of adverse maternal and fetal outcomes [8, 9]. Proteinuria, noted in all participants, has been widely recognized as a hallmark of preeclampsia and a predictor of disease severity. Its association with adverse outcomes in this study aligns with previous findings that[10-12] reported that higher levels of proteinuria indicate renal and endothelial dysfunction in preeclampsia.

Liver dysfunction, as evidenced by elevated liver enzymes (ALT and AST) and hyperbilirubinemia in this study, was consistent with patterns described in studies on HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome [13]. Studies noted similar biochemical derangements in patients with hypertensive disorders complicated by liver dysfunction, highlighting the systemic nature of preeclampsia [14, 15]. Low albumin levels observed in this study further reflect the impaired synthetic function of the liver and ongoing systemic inflammation, which aligns with studies [16, 17].

The coagulation abnormalities observed in this study—prolonged PT, aPTT, elevated INR, thrombocytopenia, and hypofibrinogenemia—are hallmark features of DIC. These findings were consistent with the studies, which reported that DIC frequently accompanies severe hypertensive

disorders, often exacerbated by placental abruption or intrauterine fetal death[18, 19]. Elevated D-dimer levels indicative of fibrinolysis were significantly associated with adverse outcomes in this study, aligning with prior research highlighting D-dimer as a marker of disease severity in DIC[20].

The maternal and fetal outcomes in this study underscore the life-threatening nature of PIH with liver dysfunction and DIC. A cesarean delivery rate of 66.7% reflects the clinical decision-making aimed at optimizing maternal and fetal survival, similar to findings in the study[21]. The high rates of ICU admissions (41.2%) and blood transfusion requirements (34.3%) highlight the critical care needs of these patients, findings consistent with those of studies on severe preeclampsia and its complications [22].

Adverse fetal outcomes, including a stillbirth rate of 11.8% and low Apgar scores in 27.4% of cases, align with findings that demonstrated that PIH with systemic involvement significantly increases the risk of fetal morbidity and mortality [23]. Fetal growth restriction, observed in 35.3% of cases, is a well-documented consequence of impaired placental perfusion in hypertensive disorders, further supported by studies [24].

This study emphasizes the need for early diagnosis and multidisciplinary management to reduce complications. Timely interventions, including blood pressure control, coagulation support, and delivery planning, are critical in mitigating maternal and fetal risks. Future research should focus on early predictive markers and tailored management strategies to improve outcomes for this high-risk population.

CONCLUSION

This study underscores the severe impact of pregnancy-induced hypertension complicated by liver dysfunction and disseminated intravascular coagulation on maternal and fetal health. Significant findings included elevated blood pressure, proteinuria, liver dysfunction, and coagulation abnormalities, all strongly associated with adverse outcomes. High rates of ICU admissions, maternal mortality, and poor fetal outcomes highlight the critical nature of these conditions.

Early diagnosis, multidisciplinary care, and timely interventions are vital to improving outcomes. Identifying key clinical and biochemical markers can aid in better management strategies for high-risk pregnancies. Further research is essential to enhance predictive and preventive approaches in these cases.

REFERENCES

1. Thorat, M., S. Kadam, and H. Mohite, *Comparison of Maternal Characteristics and Fetal Changes in Pregnant Women with Mild and Severe Pregnancy-Induced Hypertension (PIH) and Pregnant Women with Normotension.* Journal of Coastal Life Medicine, 2023. **11**: p. 2747-2754.
2. Preet, A. and T. Palve, *A study on pregnancy-induced hypertension complications.* Global Journal of Medical Research: E Gynecology and Obstetrics, 2020. **20**(2): p. 21-26.
3. Terrault, N.A. and C. Williamson, *Pregnancy-associated liver diseases.* Gastroenterology, 2022. **163**(1): p. 97-117. e1.
4. Verduzco, J.C.R., *Acute Fatty Liver of Pregnancy, a Diagnostic Challenge Compared to Other Causes of Disseminated Intravascular Coagulation. Case Report and Literature Review.* EC Gynaecology, 2024. **13**: p. 01-14.
5. Ang, S.X., et al., *Comparison of maternal and neonatal outcomes between acute fatty liver of pregnancy and hemolysis, elevated liver enzymes and low platelets syndrome: a retrospective cohort study.* BMC Pregnancy and Childbirth, 2021. **21**: p. 1-11.

6. Kay, V.R., N. Wedel, and G.N. Smith, *Family history of hypertension, cardiovascular disease, or diabetes and risk of developing preeclampsia: a systematic review.* Journal of Obstetrics and Gynaecology Canada, 2021. **43**(2): p. 227-236. e19.
7. Staff, A.C., J.G. Umans, and A. Jeyabalan, *Prediction, and Prevention of Preeclampsia*, in *Chesley's Hypertensive Disorders in Pregnancy*. 2022, Elsevier. p. 405-417.
8. Lai, J., et al., *Impact of new definitions of preeclampsia at term on identification of adverse maternal and perinatal outcomes.* American journal of obstetrics and gynecology, 2021. **224**(5): p. 518. e1-518. e11.
9. Greenberg, V.R., et al., *Perinatal outcomes in women with elevated blood pressure and stage 1 hypertension.* American Journal of Obstetrics and Gynecology, 2021. **224**(5): p. 521. e1-521. e11.
10. Bartal, M.F., M.D. Lindheimer, and B.M. Sibai, *Proteinuria during pregnancy: definition, pathophysiology, methodology, and clinical significance.* American journal of obstetrics and gynecology, 2022. **226**(2): p. S819-S834.
11. Lei, T. et al., *Proteinuria may be an indicator of adverse pregnancy outcomes in patients with preeclampsia: a retrospective study.* Reproductive Biology and Endocrinology, 2021. **19**(1): p. 71.
12. Ren, J., et al., *The interval between the onset of increased blood pressure and proteinuria in preeclampsia and the contributing factors.* Archives of Gynecology and Obstetrics, 2024. **310**(2): p. 757-767.
13. Lisonkova, S., et al., *Incidence and risk factors for severe preeclampsia, hemolysis, elevated liver enzymes, low platelet count syndrome, and eclampsia at preterm and term gestation: a population-based study.* American Journal of Obstetrics and Gynecology, 2021. **225**(5): p. 538. e1-538. e19.
14. Ali, M., et al., *Preeclampsia: A comprehensive review.* Clinica Chimica Acta, 2024: p. 119922.
15. Ives, C.W., et al., *Preeclampsia—pathophysiology and clinical presentations: JACC state-of-the-art review.* Journal of the American College of Cardiology, 2020. **76**(14): p. 1690-1702.
16. Ren, H., et al., *Fibrinogen to albumin ratio, a novel serum indicator for evaluating the severity of preeclampsia: a single-center retrospective study.* Medicine, 2023. **102**(13): p. e33419.
17. Afrose, D., et al., *The diagnostic potential of oxidative stress biomarkers for preeclampsia: Systematic review and meta-analysis.* Biology of Sex Differences, 2022. **13**(1): p. 26.
18. Gomez-Tolub, R., et al., *Placental abruption as a trigger of DIC in women with HELLP syndrome: a population-based study.* The Journal of Maternal-Fetal & Neonatal Medicine, 2022. **35**(17): p. 3259-3269.
19. Erez, O., et al., *DIC in pregnancy–pathophysiology, clinical characteristics, diagnostic scores, and treatments.* Journal of Blood Medicine, 2022: p. 21-44.
20. Zhang, Y., et al., *Predictive value of coagulation function and D-dimer for pregnancy outcome in pregnancy-induced hypertension.* American Journal of Translational Research, 2023. **15**(2): p. 1150.
21. Adu-Bonsaffoh, K., *Respectful Maternity Care: Optimizing the quality of care for women with hypertensive disorders of pregnancy in Ghana*. 2023, Utrecht University.
22. Sundrani, O., et al., *Interventions required and outcome in pregnancy induced hypertension patients in Intensive Care Unit: An observational study.* Indian Journal of Clinical Anaesthesia, 2023. **10**(1): p. 32-36.
23. Wu, R., et al., *Hypertensive disorders of pregnancy and risk of cardiovascular disease-related morbidity and mortality: a systematic review and meta-analysis.* Cardiology, 2020. **145**(10): p. 633-647.

24. Getaneh, T., et al., *The impact of pregnancy-induced hypertension on low birth weight in Ethiopia: systematic review and meta-analysis.* Italian journal of pediatrics, 2020. **46**: p. 1-11.