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Association of Plasma Fibrinogen Levels with Severity of Postpartum Hemorrhage: A Cross-Sectional Study

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ABSTRACT

Postpartum hemorrhage (PPH) significantly contributes to maternal morbidity and mortality worldwide. Identifying women at risk for severe PPH early is essential for timely intervention. **Objective:** To compare the mean plasma fibrinogen level between women with severe and non-severe postpartum hemorrhage (PPH). **Methods:** This comparative cross-sectional study was performed after its approval from the ethical committee with approval number Admin/PF/722A dated 2nd July 2025 in the Department of Obstetrics and Gynecology at Cantt General Hospital, Rawalpindi, from July 3, 2025, to December 30, 2025. A total of 60 women with postpartum hemorrhage were enrolled using a consecutive sampling technique and categorized into non-severe PPH (n=30) and severe PPH (n=30) based on predefined clinical criteria. Plasma fibrinogen levels were assessed at the time of postpartum hemorrhage diagnosis with IBM SPSS version 25.0. A p-value of less than 0.05 was considered statistically significant. **Results:** Women experiencing severe PPH exhibited significantly lower fibrinogen levels in comparison to those with non-severe hemorrhage. The mean fibrinogen level in the non-severe postpartum hemorrhage group was 4.55±1.06 g/L, but in the severe PPH group it was 3.53±0.66 g/L, indicating a statistically significant difference (p=0.001). The findings demonstrate an inverse association between fibrinogen concentration and the severity of PPH, showing that lower fibrinogen levels are associated with an increased likelihood of severe bleeding. **Conclusions:** Reduced fibrinogen levels were significantly associated with severe PPH. Early measurement of fibrinogen may assist in identifying patients at increased risk of severe hemorrhage and ensure prompt management.

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most common causes of maternal morbidity and mortality worldwide, especially in low- and middle-income countries. Defined as a blood loss of 500mL or more after vaginal delivery or 1000mL or more after cesarean section, PPH is responsible for a considerable number of preventable maternal deaths [1]. Statistics show that 99% of all maternal deaths occurred in developing countries, and of them, 27.1% are caused by postpartum hemorrhage [2]. Early recognition and prompt management are vital for counteracting the negative effects that this condition can lead to. Amid the slew of determinants that affect the severity of PPH, fibrinogen status has become a hugely important determinant in recent years [3]. Fibrinogen is a glycoprotein predominantly produced in the liver and is integral to the hemostatic mechanism. It serves as the substrate for thrombin, facilitates platelet aggregation, and generates fibrin clots crucial for hemostasis. During pregnancy, the fibrinogen levels usually increase to compensate for the hypercoagulable state needed to prevent hemorrhage during delivery [4]. However, in cases of severe PPH, hypofibrinogenemia is an early marker of coagulopathy that is associated with increased bleeding severity and poor clinical outcome. Despite this known

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relationship between fibrinogen and PPH, consensus exists only to a limited extent on exactly how low fibrinogen levels are predictive of critical PPH and the extent to which they should shape the clinical decision process [5]. Fibrinogen plasma levels can predict the likelihood of significant bleeding in patients with postpartum hemorrhage; nevertheless, it remains uncertain whether the association between fibrinogen and PPH is causal or associative [6]. A retrospective cohort study of 103 patients indicated that early fibrinogen replacement based on shock index and lactate levels improves hemostatic control and reduces intensive care unit admissions in major postpartum hemorrhage [7]. This study was designed to assess the mean fibrinogen level and severity of PPH, focusing on the identification of possible thresholds for intervention and the prognostic implications of hypofibrinogenemia. By clarifying this relationship, we hope to yield insights that will lead to improved risk stratification and lead to evidence-based management protocols for PPH, which ultimately lead to improved maternal outcomes.

Despite growing evidence that fibrinogen is an early indicator of hemorrhage severity, low- and middle-income countries (LMICs), such as Pakistan, where PPH is a prominent cause of maternal mortality, have inadequate data, highlighting a critical gap in context-specific evidence. Early laboratory predictors that assist doctors in quickly identifying women at risk of severe bleeding are especially useful in resource-limited settings, where delayed recognition contributes to poor maternal outcomes. Therefore, this study compared plasma fibrinogen levels in women with severe and non-severe PPH to assess their therapeutic relevance in early risk stratification, especially in Pakistani healthcare.

METHODS

After receiving approval from the Ethical Review Committee (Ref. No. Admin/PF/722A; dated 2nd July, 2025), a comparative cross-sectional study was undertaken in the Department of Obstetrics and Gynecology of Cantt General Hospital, Rawalpindi, for 6 months from 3rd July 2025 to 30th December 2025. A total of 60 women were included in the study, with 30 patients in each group. The sample size was calculated using the World Health Organization sample size calculator version 2.0 for comparison of two means, assuming a power of 80% and a significance level of 5%. The calculation was based on previously reported mean fibrinogen levels of 4.2±1.2 g/L in non-severe postpartum hemorrhage and 3.4±0.9 g/L in severe postpartum hemorrhage [8]. Study participants were recruited using consecutive sampling from all eligible women presented with PPH during the study duration. Women aged between 18 and 45 years with postpartum hemorrhage (PPH) as per the operational definition presented for the study. PPH was defined as blood loss of ≥500 mL after vaginal delivery or cesarean delivery within 24 hours after childbirth. Non-severe PPH was considered when bleeding would only necessitate medical handling without hemodynamic instability (i.e., hemodynamic instability defined as systolic blood pressure <90 mmHg or heart rate >100 beats/min) or operative treatment. Severe PPH was defined as hemorrhage that was characterized by hemodynamic instability, blood transfusion of two or more units, or surgery, such as uterine artery embolization or hysterectomy. Women with pre-existing coagulopathies, liver dysfunction or incomplete medical records were excluded from the study. After informed consent, eligible patients were included. The patients were predominantly divided into two groups, namely, non-severe and severe PPH, based on predefined operational definitions. Fibrinogen levels were checked at the time of diagnosis for the PPH with standard laboratory methods. The mode of delivery (spontaneous vaginal delivery, assisted delivery, or cesarean section) was recorded. Data was collected on a structured questionnaire, and it contained patient identification information (serial number, registration number, name, and age), obstetric history (gestational age and parity), physical parameters (BMI), classification of PPH (severe or non-severe), and clinical outcomes (mean fibrinogen levels). To minimize potential confounding, stratification was conducted based on age, gestational age, body mass index (BMI), parity, and mode of delivery. Post-stratification statistical comparisons were then conducted to assess whether these variables affected the association between fibrinogen levels and the severity of PPH. Normality of continuous variables was evaluated using the Shapiro-Wilk test before applying parametric statistical tests.

Data were analyzed using IBM SPSS version 25.0. Continuous variables were presented as Mean ± SD, while categorical variables were expressed as frequencies and percentages. An independent sample t-test was applied to compare mean fibrinogen levels between severe and non-severe postpartum hemorrhage groups. Furthermore, binary logistic regression analysis was conducted to evaluate the association between fibrinogen levels and the severity of postpartum hemorrhage while controlling for potential confounders. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The demographic and obstetric characteristics of women with non-severe (Group A) and severe (Group B) postpartum hemorrhage. The mean age was 30.60 ± 8.04 years for Group A and 31.20 ± 7.04 years for Group B. Gestational ages ≤39 weeks were found in 70.0% of Group A and 73.3% of

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Group B, with mean gestational ages of 38.97 ± 1.47 weeks. Group A had a mean BMI of 25.90 ± 3.81 kg/m2. Most study participants (56.7% Group A, 63.3% Group B) had normal BMIs. Multiparous women were the largest subgroup (43.3% in Group A, 46.7% in Group B), and vaginal deliveries were most common (Table 1).

Table 1: Baseline Demographic and Obstetric Characteristics of Study Participants

Variables	Group A (Non-severe PPH) n=30	Group B (Severe PPH) n=30	p-value
Age Groups			
≤30 years	17 (56.7%	16 (53.3%)	0.790
>30 years	13 (43.3%	14 (46.7%)	
Mean Age (Years)	30.60 ± 8.04	31.20 ± 7.04	0.760
Gestational Age			
≤ 39 weeks	21 (70.0%)	22 (73.3%)	0.770
>39 weeks	9 (30.0%)	8 (26.7%)	
Mean Gestational age (weeks)	38.97 ± 1.47	38.50 ± 1.58	0.230
BMI Category			
Normal	17 (56.7%)	19 (63.3%)	0.740
Overweight	8 (26.7%)	8 (26.7%)	
Obese	5 (16.6%)	3 (10.0%)	
Mean BMI (kg/m^2)	25.90 ± 3.81	25.47 ± 3.42	0.640
Parity			
Nulliparous	5 (16.7%)	3 (10.0%)	0.810
Primiparous	12 (40.0%)	13 (43.3%)	
Multiparous	13 (43.3%)	14 (46.7%)	
Mode of Delivery			
Vaginal	14 (46.7%)	15 (50.0%)	0.850
Assisted Vaginal	7 (23.3%)	8 (26.7%)	
Cesarean section	9 (30.0%)	7 (23.3%)	

The comparison of mean fibrinogen levels between women with non-severe and severe postpartum hemorrhage. The mean fibrinogen level in Group A (non-severe PPH) was 4.55 ± 1.06 g/L, whereas it was significantly lower in Group B (severe PPH) at 3.53 ± 0.88 g/L. The mean difference of 1.03 g/L reveals that non-severe PPH patients had much higher fibrinogen levels. The true difference in fibrinogen levels between groups is probably within the 95% confidence interval (CI) (0.52-1.52). The difference between the two groups was statistically significant (p = 0.001). These findings showed a significant difference in mean fibrinogen levels between severe and non-severe PPH groups (Table 2).

Table 2: Comparison of Mean Plasma Fibrinogen Levels Between Study Groups

Variables	Group A (Non-severe PPH) n=30	Group B (Severe PPH) n=30	Mean difference	95% CI	p-value
Fibrinogen Level (g/L)	4.55 ± 1.06	3.53 ± 0.88	1.02	0.52-1.52	0.001

In the stratified study, significant postpartum hemorrhage was associated with decreased fibrinogen levels across most categories. In women aged ≤30, fibrinogen levels were higher in the non-severe group (4.46 ± 0.97 g/L) than in the severe group (3.39 ± 0.64 g/L) (p=0.001). Similar patterns were seen for gestational age ≤39 weeks (4.57 ± 1.16 versus 3.60 ± 0.89; p-value = 0.004) and normal BMI (4.54 ± 1.11 versus 3.54 ± 0.95; p-value = 0.008). Assisted deliveries showed a significant difference (p=0.005), but vaginal deliveries did not (p=0.083) (Table 3).

Table 3: Stratification of Mean Fibrinogen Levels Between Groups with Respect to Different Variables

Variables	Groups		p-value
	Group A (Non-severe PPH), Mean Difference	Group B (Severe PPH), Mean Difference	
Age Groups			
≤30 years	4.46 ± 0.97	3.39 ± 0.64	0.001
>30 years	4.67 ± 1.19	3.69 ± 1.10	0.035
Gestational Age			
≤ 39 weeks	4.57 ± 1.16	3.60 ± 0.89	0.004
>39 weeks	4.52 ± 0.81	3.34 ± 0.89	0.012
BMI			
Normal	4.54 ± 1.11	3.54 ± 0.95	0.006
Overweight	4.92 ± 1.07	3.64 ± 0.73	0.015
Obese	4.01 ± 0.73	3.15 ± 1.00	0.039
Parity			
Nulliparous	4.94 ± 0.78	2.92 ± 0.54	0.008
Primiparous	4.27 ± 1.01	3.50 ± 0.63	0.031
Multiparous	4.67 ± 1.19	3.69 ± 1.10	0.035
Mode of Delivery			
Vaginal	4.48 ± 1.18	3.83 ± 0.70	0.083
Assisted Vaginal	4.80 ± 0.90	3.23 ± 0.90	0.005
Cesarean section	4.47 ± 1.05	3.23 ± 1.09	0.037

DISCUSSION

This study proved a significant relationship between low fibrinogen levels and the severity of PPH. The average fibrinogen level in women with severe PPH (3.53 ± 0.88 g/L) was significantly lower than the fibrinogen level in women with non-severe PPH (4.55 ± 1.06 g/L). These findings add to the literature, which has previously suggested that fibrinogen concentration is a strong predictor of hemorrhage severity and the need for aggressive management interventions. Cui *et al.* performed a multicenter study addressing fibrinogen dynamics in obstetrical disseminated intravascular coagulation (DIC), which showed that women with severe PPH had a high incidence of fibrinogen deficiency (less than 3g/L) and marked the importance of fibrinogen as an important biomarker in assessing risk of maternal bleeding, with low fibrinogen being associated with adverse maternal outcome [9]. Obaro and Heazell also attach importance to fibrinogen as a crucial biomarker in maternal bleeding risk assessment, showing that low fibrinogen is associated with poor outcomes [10]. A recent analysis by Kobayashi *et*

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al. concluded that fibrinogen levels tend to be rapidly depleted in severe obstetric bleeding owing to consumption coagulopathy, in which mean values of 3.2 ± 0.6g/L were reported, corresponding to our result [11]. Similar to our work, Tardy-Poncet *et al.* concluded that maintaining fibrinogen concentrations of more than 3.5g/L optimized transfusion requirements and improved clinical outcomes [12]. The association between fibrinogen depletion and hemorrhage severity was also backed up by Daikuara *et al.* who showed that fibrinogen below 3g/L after it was associated with a three times higher risk of uncontrolled bleeding at delivery [13]. Ren *et al.* also highlighted the importance of fibrinogen measurement as part of coagulation screening; it provides important prognostic information for early intervention [14]. The average fibrinogen value in severe PPH in our study (3.53 g/L) is slightly higher than those reported by Cui *et al.* (3 g/L) and Daikuara *et al.* (2.9 g/L) [9, 13]. This difference could potentially be due to differences in patient selection, timing of measurement, and management protocols. In our study setting, samples were taken immediately upon diagnosis of PPH, possibly before total consumption of clotting factors, whereas in other studies, levels were measured later during active hemorrhage. Moreover, our population was made up of women without pre-existing coagulopathies, which may explain the rather higher baseline fibrinogen levels. Kiani *et al.* both reaffirmed that fibrinogen rises physiologically throughout pregnancy to reach levels of 4-6 g/L by the third trimester of pregnancy, and a rapid decrease below 3g/L during delivery is suggestive of pathological bleeding. These physiological considerations are consistent with our findings in which non-severe cases of PPH maintained mean levels within the expected range for late pregnancy (4.55 g/L) [15]. In comparison, another study conducted by Kaur *et al.* showed that the mean fibrinogen levels in patients needing surgical interventions for PPH were 2.95 ± 0.97 g/L (almost at the same level as in our severe PPH group). Another study conducted by Hofer *et al.* reinforced that women with persistent hemodynamic instability after PPH had significantly low fibrinogen and platelet count, further supporting fibrinogen's hemostatic role in the management of maternal recovery [2, 16]. A study by Park et al. supported the importance of early guiding laboratory management and fibrinogen as a rapid response indicator in massive transfusion protocols [17]. After postpartum hemorrhage, decreased fibrinogen is the earliest hemostatic sign of coagulopathy [18]. Significant PPH is predicted by lower fibrinogen levels before delivery and upon postpartum hemorrhage onset. In severe conditions, early goal-directed fibrinogen concentrate treatment [19]. Among reviewed studies, the mean fibrinogen levels in severe cases of PPH were 2.8 to 3.6 g/L, and in non-severe cases were 4.2 to 4.8 g/L. Our results (3.53 g/L and 4.55 g/L, respectively) are well within these ranges, implying external validity and concomitance with international findings. This strengthens the validity of our study results and may help the increasing consensus that fibrinogen concentration provides an early biomarker that predicts the severity of PPH and can guide clinical modalities. A comparative cross-sectional study of 60 patients found that severe postpartum hemorrhage has much lower mean fibrinogen levels, 200 mg/dL, than mild PPH (more than 250 mg/dL) [20].

The findings suggest the potential use of fibrinogen level estimation as a quick, cheap, and effective predictor that can be used at bedside to identify patients at risk of developing severe PPH. Inclusion of routine fibrinogen testing as a component of protocols around obstetric hemorrhage can facilitate early targeted therapy and include early use of fibrinogen concentrate or cryoprecipitate. Larger multicentric trials are needed to provide optimal cut-off levels for fibrinogen, dependent on the population and the healthcare setting. This study was limited in its single-center design with a relatively small sample size (n = 60), which may limit the study's generalizability. Fibrinogen was only measured (single measurement) at the time of diagnosis, and not serially over time to examine dynamic trends. In addition, the effects of factors that influence the production of fibrinogen (liver synthetic function, nutrition, and genetic variation) were not investigated. Longitudinal sampling is needed; consideration should be given to the kinetics of fibrinogen to bleeding ratio, and the use of POC technologies would enable quick decision-making in low-resource settings. Limited sample sizes in some stratified subgroups may reduce statistical power and/or violate assumptions of parametric tests.

CONCLUSIONS

Low levels of fibrinogen were significantly associated with severe PPH. Estimating the levels of fibrinogen at an early stage could be a valuable indicator of patients who are likely to present with serious haemorrhage and enable prompt intervention with management strategies.

Authors' Contribution

Conceptualization: AZ, MKN
Methodology: AZ, EF
Formal analysis: RF, SSQH
Writing and Drafting: HO, SSQH
Review and Editing: AZ, MKN, EF, RF, HO, SSQH

All authors approved the final manuscript and take responsibility for the integrity of the work

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Conflicts of Interest

All the authors declare no conflict of interest.

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