Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2024, 14, 923-937
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

D-Dimer: Predictor of Postpartum Hemorrhage among Pre-Eclampsia at Kilimanjaro Christian Medical Centre

Husna Silim Ally[1*], Nyasatu G. Chamba[1,2], Raziya Gaffur[1], Nasra Batchu[1], Glory Mangi[1], Pendo S. Mlay[1,2], Bariki Mchome[1,2], Mtoro J. Mtoro[1], Thomas J. Kakumbi[1], Rafiki N. Mjema[1], Doris Rwenyagila[1], Eusebius Maro[1,2], Fredrick Mbise[1], Gilleard Masenga[1,2], Patricia S. Swai[1,2]

[1]Department of Obstetrics and Gynaecology, KCMC Hospital, Moshi, Tanzania
[2]Department of Obstetrics and Gynaecology, Kilimanjaro Christian Medical University College (KCMUCo), Moshi, Tanzania
Email: *husnaally931001@gmail.com, nyasatuchamba@yahoo.com, rfgaffur@gmail.com, batchunasra@gmail.com, glorymangi@gmail.com, pendo.mlay@kcmuco.ac.tz, barikimchome@gmail.com, mtorojabar@gmail.com, tom.kakumbi@kcmc.ac.tz, rafikimjema123@gmail.com, rwenyagiladoris@gmail.com, sebiwilly@gmail.com, bahatifreddy8@gmail.com, drgmasenga@yahoo.com, patriciaswai@yahoo.com

How to cite this paper: Ally, H.S., Chamba, N.G., Gaffur, R., Batchu, N., Mangi, G., Mlay, P.S., Mchome, B., Mtoro, M.J., Kakumbi, T.J., Mjema, R.N., Rwenyagila, D., Maro, E., Mbise, F., Masenga, G. and Swai, P.S. (2024) D-Dimer: Predictor of Postpartum Hemorrhage among Pre-Eclampsia at Kilimanjaro Christian Medical Centre. *Open Journal of Obstetrics and Gynecology*, **14**, 923-937.
https://doi.org/10.4236/ojog.2024.146074

Received: May 11, 2024
Accepted: June 22, 2024
Published: June 25, 2024

Abstract

Background: Postpartum hemorrhage (PPH) is the major contributor to maternal mortality and morbidity worldwide as well as in Tanzania. Studies have shown Pre-eclampsia as a risk indicator for Postpartum hemorrhage and D-dimer tends to rise in women with pre-eclampsia. Few studies that have shown the association between D-dimer and PPH have been controversial and differ according to ethnicity and lifestyle. Hence there is no suitable reference interval for D-dimer in predicting Postpartum hemorrhage among women with pre-eclampsia. **Broad Objective:** This study aimed to assess the association, sensitivity, and specificity of D-dimer as a laboratory predictor of postpartum hemorrhage among women with pre-eclampsia at KCMC hospital. **Methodology:** This was a hospital-based analytical cross-sectional study conducted at KCMC Hospital in Northern Tanzania from September 2022 to March 2023. A total of 195 women with pre-eclampsia were included in this study. Plasma D-dimer levels were taken from women with pre-eclampsia pre-delivery. Haematocrit was compared before and after delivery, and a fall of 10% was considered as Postpartum hemorrhage together with clinical assessment of the patient. Participants were divided among those who had severe features and those who did not have severe features and were further categorized into those who had PPH and those who did not have PPH. Logistic regression was used to determine the association between D-dimer and PPH adjusting for other factors. The Receiver Operating Curve (ROC) was used to evaluate the predictive value. **Results:** Higher median D-dimer levels were

seen among women who had PPH compared to those who had no PPH. D-dimer was seen to be associated with PPH, thus for every unit increase of μg/ml of D-dimer among women who had pre-eclampsia without severe features there was a 14% significant increase in the odds of having postpartum hemorrhage and a 45% significant increase of having postpartum hemorrhage among those who had pre-eclampsia with severe features. Furthermore, the cut-off point of a D-dimer level of 0.66 μg/ml significantly predicts postpartum hemorrhage with a sensitivity of 75% and specificity of 55%. For those who had no severe features the cut-off point was 0.53 μg/ml with a sensitivity of 95% and specificity of 53%, and for those who had severe features the cut-off point was 3.58 μg/ml with a sensitivity of 50% and specificity of 96%. **Conclusion:** D-dimer can be used to predict postpartum hemorrhage among pre-eclampsia, especially among those who have severe features. This shows that D-dimer has specificity in predicting PPH in women with pre-eclampsia and can be applied in clinical services to save women from maternal morbidity and mortality. Blood products such as fresh frozen plasma, platelets, and whole blood together with tranexamic acid should be readily available in women with pre-eclampsia especially those with severe features with a D-dimer level of 3.58 μg/ml and above during delivery as they are at high risk of developing PPH.

Keywords

D-Dimer, Preeclampsia, Postpartum Hemorrhage, Tanzania

1. Introduction

Postpartum hemorrhage is responsible for around 25% of maternal deaths worldwide, reaching 60% in developing countries [1], and is the major leading cause of maternal deaths in Tanzania [2]. Pre-eclampsia is seen to be a second major contributor to maternal mortality reaching 14% worldwide, 12.9% in developed regions, and 16% in sub-Saharan Africa [3]. Women with pre-eclampsia are more likely to suffer postpartum hemorrhage compared to non-pre-eclamptic women. A study done in Australia showed 7.4% of women with pre-eclampsia developed postpartum hemorrhage [4] while that in Pakistan was 27.6% [5], 22% in Kenya [6], and 24% in Songea Tanzania [7].

Postpartum hemorrhage was found to be associated with pregnancy complications due to coagulation defects caused by Pre-eclampsia, such complications are ICU admissions, Shock, Acute kidney injury, and loss of fertility due to hysterectomy [8]. D-dimer tends to rise in women with pre-eclampsia [9], this is due to exacerbation of the hypercoagulable state in pre-eclampsia, platelet activation, and overproduction of thrombin [10]. D-dimer is the ultimate degradation product of a fibrin clot cross-linked by factor XIII [11].

Few studies that have shown the association between D-dimer and Postpartum hemorrhage reported its value is controversial and differs according to eth-

nicity and lifestyle [11] [12]. Studies have shown higher odds of association between D-dimer and PPH, with an elevated D-dimer level of (≥2.02-μg/ml) among women with pre-eclampsia with severe features in developing postpartum hemorrhage [11]. The cut-off D-dimer value of 1.555 μg/ml has shown a sensitivity of 94.1% and a specificity of 58.6% in predicting PPH among women with pre-eclampsia with severe features [11].

Several studies have used fibrinogen as a marker for a coagulable state in predicting postpartum hemorrhage, which is not available in our setting [13] [14] [15]. From this study, we assessed the association, sensitivity, and specificity of D-dimer as a laboratory predictor of postpartum hemorrhage among women with pre-eclampsia at KCMC hospital.

2. Methods

2.1. Study Design and Area

This was a hospital-based analytical cross-sectional study conducted at Kilimanjaro Christian Medical Center (KCMC) from September 2022 to March 2023. KCMC is a tertiary referral hospital located in the Kilimanjaro region in the Northern part of Tanzania, serving patients from the Kilimanjaro region and its neighboring regions in the Northern zone such as Arusha, Manyara, Tanga, and even other parts of the United Republic of Tanzania and sometimes serves people from neighboring countries like Kenya. Kilimanjaro is one of the regions in the Northern part of Tanzania comprised of seven districts, covering 13250 Km^2. The region was projected by the year 2020 to have an estimated population of 1,951,252 people and an annual growth rate of 2.3% [16].

2.2. Study Population

This study included pre-eclamptic women who were in their third trimester, either in the latent phase of labor or those who were prepared for cesarean section and consented to participate in the study, and women with deep venous thrombosis and pulmonary embolism were excluded. A sample size of 195 participants was enrolled in the study by using the Keshlies formula with a prevalence of 10% proportion of PPH attributed to pre-eclampsia [17].

2.3. Study Settings

Identification of women with pre-eclampsia was performed in the obstetrics and gynecology ward. Consent from the patients was obtained and blood samples for plasma D-dimer were taken during the latent phase of labor or when prepared for cesarean section. Clinical data such as Age, Area of residency, Marital status, Gravidity, Gestation age, Body mass index, the severity of pre-eclampsia, number of fetuses, number of previous scars, blood pressure before and after delivery, hemoglobin, platelet levels before delivery, Hematocrit levels before delivery, birth weight, the score of the baby, estimated blood loss, and other causes of PPH, if occurred such as retained placenta, perineal and cervical tear, abrup-

tion placenta and placenta previa, was extracted from the patient's file in the Electronic file system. Furthermore, 12 - 18 hours post vaginal delivery or Cesarean section (C/S), blood for hematocrit was taken again. Hematocrit results were compared pre and post-vaginal delivery or C/S. A fall of hematocrit by 10% was considered as post-partum hemorrhage (PPH) together with clinical assessment of the patient [18].

2.4. Statistical Methods

Descriptive statistics were summarized using medians (Inter quartile range) for continuous variables, and categorical variables were summarized by frequency and proportions and presented by table and narrations. A proportion of post-partum hemorrhage was computed as a 10% change in hematocrit before and after delivery. Normality for continuous variables was checked by plotting histograms and assessing skewness. The Mann-Whitney U-test compared the median d-dimer level between post-partum categories.

Classical logistic regression was used to determine the association between d-dimer level and post-partum hemorrhage adjusting for other factors. Crude and Adjusted Odds Ratio (OR) with their respective 95% confidence interval were reported to estimate the magnitude of the association. Furthermore, the receiver operating characteristic curve (ROC) was taken to evaluate their predictive values in pre-eclampsia complicated with postpartum hemorrhage. A statistical significance was considered for a p-value of less than 0.05.

Cleaned datasets were analyzed using Stata version 15.0 (Stata Corp, College Station, TX).

2.5. Ethical Consideration

Ethical approval to conduct the study was obtained from KCMU College and Research Ethics Review Committee with clearance no; PG 148/2022. Permission was also obtained from the department's Head of Obstetrics and gynecology. Written and informed consent was obtained from study participants, with prior information about the study procedure before they decided to participate in the study. Participants were provided with identity numbers to preserve anonymity as one of the methods of maintaining confidentiality. Women who sustained postpartum hemorrhage were managed according to postpartum hemorrhage protocol.

3. Results

3.1. The Enrolment of Study Participants

195 women with pre-eclampsia in their third trimester who signed the consent form were enrolled in the study. Participants were divided among pre-eclampsia with severe features and pre-eclampsia without severe features. Among those two groups were further divided into those who had PPH and those who did not have PPH (**Figure 1**).

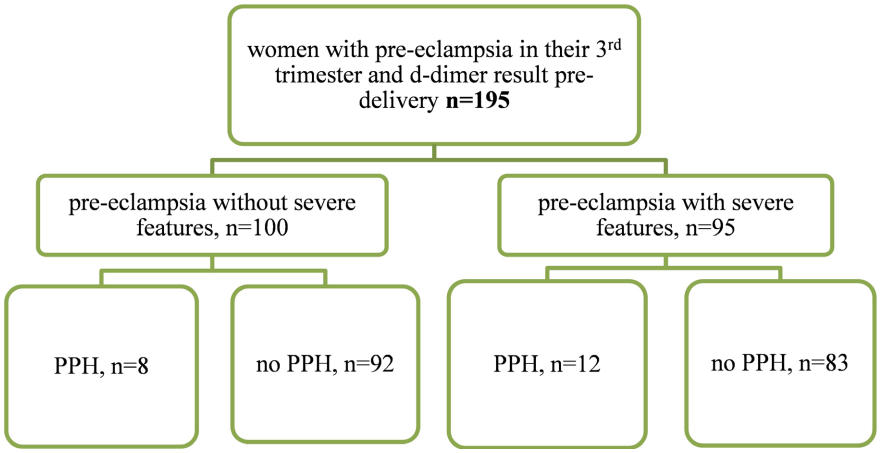

Figure 1. The enrollment of participants and distribution of cases among pre-eclampsia at KCMC.

3.2. Social Demographic and Obstetrics Characteristics

A total of 195 women were enrolled in this study. More than half of the participants 134 (68.7%) were aged between 20 - 34 years and 22.1% between the age of 35 - 39 years, with a mean age of 29.9 (±6.07). The majority of women 149 (76.4%) were either married or cohabiting and only 5 (2.6%) were either separated or divorced. Most of the participants 128 (65.6%) delivered by Cesarean section and more than half were referrals 114 (58.5%). On the other hand, there was almost an equal distribution between women who had Pre-eclampsia without severe feature 100 (51.3%) and Pre-eclampsia with severe feature 95 (48.7%) (**Table 1**).

3.3. The Median D-Dimer Level among Women with/without Severe Features of Pre-Eclampsia at KCMC

The median D-dimer level among all pre-eclamptic women was 0.623 µg/ml with an interquartile range of 0.85 µg/ml to 1.35 µg/ml. The median D-dimer level in pre-eclamptic women with severe features was 0.75 µg/ml which was higher compared to that in pre-eclamptic women without severe features which was 0.5505 µg/ml with a significant p-value of 0.011 (**Figure 2**).

3.4. The Median D-Dimer Level in Postpartum Hemorrhage among Pre-Eclampsia at KCMC

There was a high median D-dimer level of 1.13 µg/ml in women who had PPH compared to the median D-dimer level in women without PPH 0.591 µg/ml, among pre-eclampsia with a significant p-value of 0.001 (**Figure 3**).

3.5. The Association of D-Dimer and Postpartum Hemorrhage among Women with Pre-Eclampsia at KCMC

3.5.1. Association of D-Dimer among Participants Who Had Pre-Eclampsia with Severe Features against PPH

For every unit increase of µg/ml in the d-dimer level, there is a 47% significant

Table 1. Sociodemographic and obstetric characteristics of women who delivered at KCMC with pre-eclapsia (n = 195).

Characteristics	N	%
Age group (years)		
15 - 19	9	4.6
20 - 34	134	68.7
35 - 39	43	22.1
40+	9	4.6
Mean (SD)	29.9 ± 6.07	
Residence		
Arusha	9	4.7
Manyara	2	1.0
Moshi	182	93.3
Tanga	1	0.5
Mwanza	1	0.5
Referrals		
Referrals	114	58.5
Not referrals	81	41.5
Marital Status		
Married/Cohabiting	149	76.4
Separated/Divorced	5	2.6
Single	41	21
Mode of delivery		
SVD	67	34.4
CS	128	65.5
Gestation age at delivery (weeks + days)		
Early pre-term (28 - 32)	27	13.9
Late pre-term (32 + 6 - 36 + 6)	81	41.5
Early term (37- 38 + 6)	54	44.6
Late term (39 - 41 + 6)	33	16.9
Gravidity		
1	59	30.3
2 - 4	109	55.9
5+	27	13.8
Parity		
1	67	34.4
2 - 4	111	56.9
5+	17	8.7
Pre-eclampsia		
Pre-eclampsia without severe features	100	51.3
Pre-eclampsia with severe features	95	48.7

Continued

Number of fetuses		
Single	186	95.4
Twin	9	4.6
Number of previous scars		
None	138	70.8
One	32	16.4
Two or more	25	12.8
Birth weight (grams)		
<2500	93	47.7
2500 - 3999	100	51.3
>4000	2	1.03
Median (IQR)	2500 (1800 - 3000)	

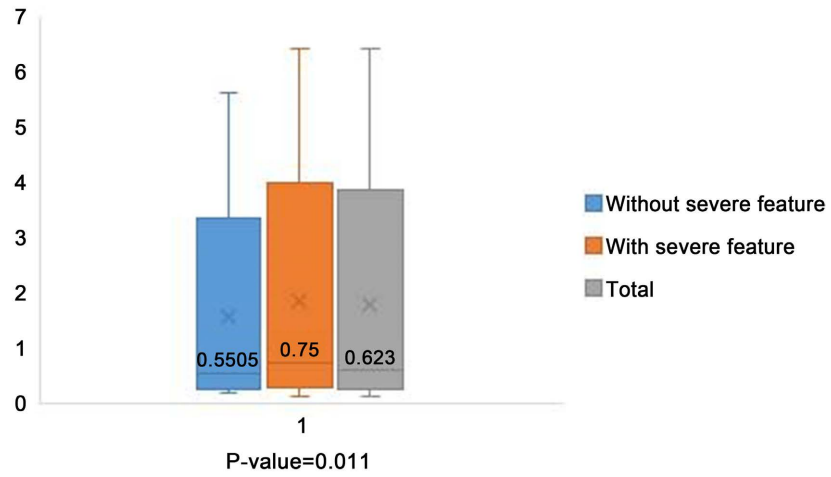

Figure 2. The Median D-dimer level among women with/without severe features of pre-eclampsia at KCMC.

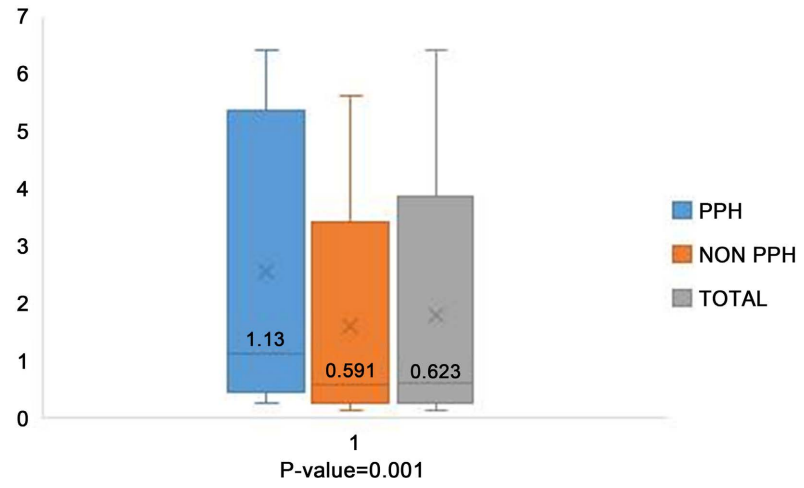

Figure 3. The median D-dimer level in PPH among pre-eclampsia at KCMC.

increase in the odds of having postpartum hemorrhage among women with pre-eclampsia with severe features (cOR: 1.47; 95% CI: 1.19 - 1.83). After controlling for confounders there was a 45% significant increase in the odds of having postpartum hemorrhage. (aOR: 1.43; 95% CI: 1.11 - 1.84) (Table 2).

Table 2. Bivariate and Multivariable logistic regression showing an association between D-dimer and PPH among pre-eclampsia at KCMC.

Characteristics	COR (95% CI)	p-Value	AOR (95% CI)	p-Value
With severe features (n = 95)				
D-dimer level	**1.47 (1.19 - 1.83)**	**<0.001**	**1.45 (1.09 - 1.92)**	**0.011**
Gestation age (in weeks)	0.80 (0.64 - 1.00)	0.055	0.79 (0.59 - 1.05)	0.112
Maternal Age (in years)	1.04 (0.96 - 1.14)	0.322	1.10 (0.94 - 1.29)	0.224
Parity	1.19 (0.78 - 1.81)	0.415	0.81 (0.36 - 1.79)	0.601
Number of fetuses				
Singleton	1.00			
Twin	3.68(0.30 - 14.62)	0.306	31.89 (1.27 - 798)	0.035
Previous scars	0.53 (0.11 - 2.50)	0.426	0.84 (0.15 - 4.69)	0.842
Mode of delivery				
SVD	1.00		1.00	
CS	1.63 (0.32 - 8.29)	0.558	3.83 (0.57 - 25.71)	0.168
Other factors contributing to PPH (previa, abruption, tears, retained products)				
No	1.00		1.00	
Yes	27.3 (2.53 - 294.76)	0.006	25.73 (3.16 - 209.33)	0.002
Without severe features (n = 100)				
D-dimer lever	**1.13 (0.91 - 1.41)**	**0.277**	**1.14 (0.68 - 1.92)**	**0.612**
Gestation age (in weeks)	0.95 (0.84 - 1.07)	0.412	0.92 (0.74 - 1.14)	0.426
Maternal Age (in years)	0.96 (0.88 - 1.05)	0.403	1.04 (0.89 - 1.23)	0.562
Parity	0.65 (0.40 - 1.06)	0.084	0.35 (0.14 - 0.89)	0.028
Number of fetuses				
Singleton	1.00			
Twin	11.73 (1.57 - 87.88)	0.017	27.36 (1.26 - 592.08)	0.035
Previous scars	0.70 (0.29 - 1.68)	0.425	1.02 (0.92 - 1.14)	0.671
Mode of delivery				
SVD	1.00		1.00	
CS	1.67 (0.30 - 9.14)	0.556	0.80 (0.12 - 5.59)	0.826
Other factors contributing to PPH (previa, abruption, tears, retained products)				
No	1.00		1.00	
Yes	30.33 (2.37 - 389.0)	0.009	41.97 (4.41 - 753.53)	0.005

Key: OR: Odds ratio, CI: Confidence Interval, SVD: Spontaneous Vaginal delivery. AOR was adjusted for age, parity, number of fetuses, previous scar, and mode of delivery.

3.5.2. Association of D-Dimer among Participants Who Had Pre-Eclampsia without Severe Features against PPH

On average, for every unit increase of μg/ml in the d-dimer level, there is 13% increase in odds of having postpartum hemorrhage among women who had pre-eclampsia without severe features (cOR: 1.13; 95% CI: 0.91 - 1.41) and after controlling for confounders there was a 14% significant increase in the odds of having postpartum hemorrhage among women who had pre-eclampsia without severe features (aOR: 1.14; 95% CI: 0.68 - 1.92) (Table 2).

3.6. D-Dimer Cut-Off Point in Predicting Postpartum Hemorrhage among Pre-Eclampsia at KCMC

The cutoff point of the D-dimer level in predicting PPH among women with pre-eclampsia was 0.66 μg/ml with sensitivity of 75% and specificity of 55%.

Pre-eclamptic women with severe features: Cuttoff point was 3.58 μg/ml, sensitivity 50% and specificity of 96%, AUC 0.73, 95% CI: 0.51 - 0.89.

For women who had pre-eclampsia without severe features, the cutoff point was 0.53 μg/ml with a sensitivity of 95% and specificity of 53%, AUC 0.77, 95% CI: 0.61 - 0.87 (Table 3), (Figure 4).

Table 3. ROC curve of D-dimer for evaluation with PPH.

Variable	Cutoff point	Sensitivity	Specificity	AUC	95% CI	
					Lower	Upper
D-dimer	0.66	75.0%	55.0%	0.72	0.60	0.84

Key: AUC: Area under the curve. CI: Confidence Interval.

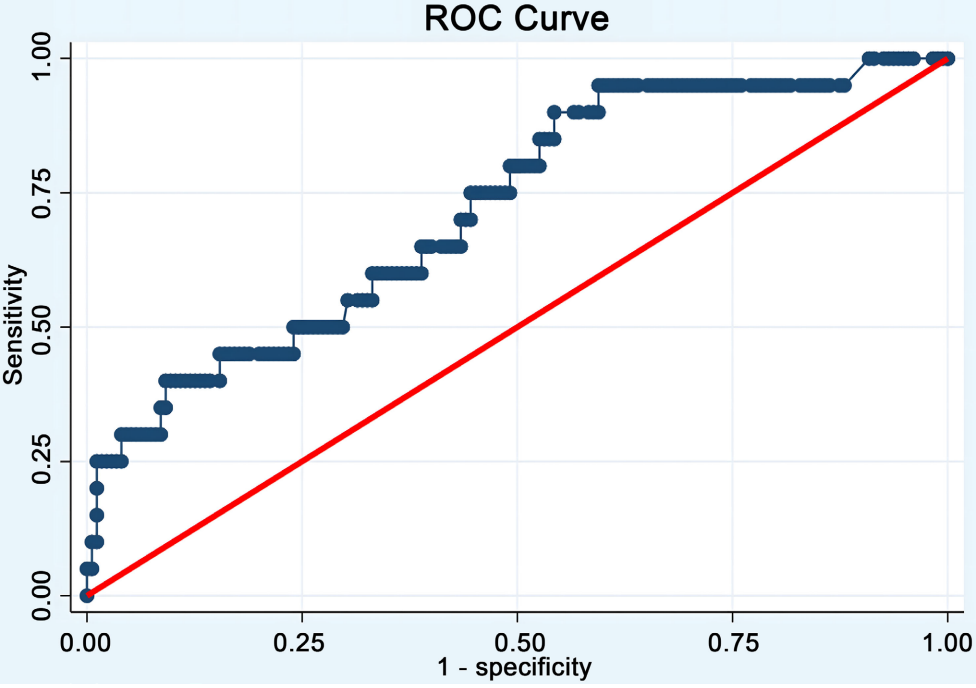

Figure 4. ROC curve for the sensitivity and specificity of the cut-off point of the d-dimer level.

4. Discussion

Findings from this study there was a higher D-dimer level of 0.75 μg/ml among pre-eclampsia with severe features than pre-eclampsia without severe features 0.55 μg/ml. Also, there was a highly significant median D-dimer level of 1.13 μg/ml in women with PPH compared to the median D-dimer level in those who had no PPH of 0.591 μg/ml. A true association was seen after adjusting for other factors between D-dimer and PPH. That is for every unit increase of μg/ml of D-dimer level among pre-eclamptic women with severe features, there was a significant increase of 45% in the odds of having PPH, and a significant increase of 14% among pre-eclampsia without severe features. Furthermore, the cut-off point of a D-dimer level of 0.66 μg/ml significantly predicts PPH with a sensitivity of 75% and specificity of 55% and for those who had severe features cutoff point was 3.58 μg/ml predicts PPH with sensitivity of 50% and specificity of 96%. For those without severe features, the cutoff point was 0.53 μg/ml, sensitivity of 95%, and specificity of 53%.

Median D-dimer levels that were seen in women who had PPH were higher at 1.13 μg/ml compared to the median D-dimer level in those who had no PPH at 0.591 μg/ml among pre-eclamptic women with/without severe features (**Figure 3**). Shao reported that D-dimer levels were elevated in the PPH group with severe features of pre-eclampsia (2.02 μg/ml) compared to those who had no PPH (1.37 μg/ml) [11]. High values of D-dimer levels in our study seen in the PPH group compared to the non-PPH group correlated significantly to Shao's study, but the values of D-dimer levels in our study were seen to be lower than Shao's. This may be due to the selected group in Shao's study being more sick/severe cases only while the selected group in our study were both with and without severe features of pre-eclampsia. This was supported also by **Figure 2** which showed a higher D-dimer level of 0.75 μg/ml among pre-eclampsia with severe features than pre-eclampsia without severe features 0.55 μg/ml due to aggressiveness in the severe form of pre-eclampsia. This high value of D-dimer above 1 explains the hypercoagulable state in pre-eclampsia and more aggressive hyperconsumption of fibrin hence high D-dimer is expected to be seen in severe form. Thus these women are more prone to bleeding. This indicates that D-dimer might be associated with postpartum hemorrhage among pre-eclamptic women. A range above 1 should be used as a value for diagnosis, as few studies showed this value in pre-eclampsia as a predictor for PPH.

After adjusting for other factors there was an association seen between D-dimer and postpartum hemorrhage among pregnant women with pre-eclampsia in both groups, i.e.; those who had severe features and those who had no severe features. These factors are maternal age, gestational age, parity, number of fetuses, previous scar, mode of delivery, and other factors contributing to postpartum hemorrhage such as abruption placenta, placenta previa, retained products and cervical tear. Thus for every unit increase of μg/ml in the d-dimer level, there was a 14% significant increase in the odds of having postpartum hemorrhage among women who had pre-eclampsia without severe features (aOR: 1.14; 95%

CI: 0.68 - 1.92), and for every unit increase of μg/ml in the d-dimer level, there was a 45% significant increase in the odds of having postpartum hemorrhage among women with pre-eclampsia with severe features (aOR: 1.45; 95% CI: 1.09 - 1.92) (**Table 2**). These findings support Shao's study as D-dimer significantly associated with PPH among women who had pre-eclampsia with severe features [11]. This indicated that in pre-eclampsia, there is hyper-coagulopathy thus the formation of fibrin clots and hence D-dimer formation. This shows that D-dimer can be used as a predictive tool, as there is an association seen between D-dimer and Postpartum hemorrhage among pre-eclampsia. Higher odds of 1.45 of D-dimer in sustaining PPH among those who have severe features and 1.14 higher odds of D-dimer in sustaining PPH among those with pre-eclampsia without severe features.

The cut-off point of D-dimer in predicting postpartum hemorrhage was 0.66 μg/ml which had a sensitivity of 75% and specificity of 55% with a narrow confidence interval (**Table 3**). The area under the curve (AUC) of 0.72 shows a good prediction ability to discriminate between individuals with and those without postpartum hemorrhage (**Figure 4**). This means D-dimer has 72% predictability against postpartum hemorrhage. Hence patients who are at risk of developing postpartum hemorrhage can be predicted early. A good prediction was also seen among pre-eclamptic women without severe features with a D-dimer cut-off point of 0.53 μg/ml together with a sensitivity of 95% and specificity of 53%. The area under the curve was 0.77, which showed a 77% good prediction ability of D-dimer against postpartum hemorrhage among pre-eclamptic women without severe features. Those who had Pre-eclampsia with severe features had a higher cut-off point of 3.58 μg/ml with a sensitivity of 50% and specificity of 96%. This shows that for those who had severe features the cutoff point is more specific with 73% predictability against postpartum hemorrhage. Shao *et al.* reported that the cut-off D-dimer value was 1.555 μg/ml in predicting PPH with a sensitivity of 94.1% and a specificity of 58.6% among women with pre-eclampsia with severe features [11]. The difference might be due to disparities in testing methods, sample size and differences in race. This shows that D-dimer is more sensitive and more specific in predicting PPH in women with pre-eclampsia especially those with severe features and can be applied in clinical services to save maternal morbidity and mortality. The cut-off point of above 1 can be used as a predictive value as is sensitive in picking women who are at risk in sustaining postpartum hemorrhage as the value is supported by our study and other studies as well. Thus D-dimer can be used as a screening value in women who have pre-eclampsia with severe features.

5. Strength

This study used Receiver operating characteristics (ROC) in predicting the cut-off point which provided us with a precise and valid estimate that can be used for clinical implementation.

Also, this study specifically looked into high-risk groups, and an association of

factors was done to get the true value. Thirdly, this is one of the first few studies that tried to predict the association between d-dimer level and postpartum hemorrhage in Africa. Lastly, the Estimation of PPH was by checking hematocrit thus, it did not affect those who delivered by c/s as they received fluid post-delivery.

6. Limitation

This study did not check for the D-dimer levels in the first and second trimesters. Also, this study design did not allow checking for the D-dimer levels post-delivery for follow-up. Lastly, there are limited studies that could be used to compare with our study in the discussion part.

7. Conclusion

D-dimer can be used to predict postpartum hemorrhage among pre-eclampsia, especially for those who have severe features. This shows that D-dimer has high specificity in predicting PPH among women who have pre-eclmpsia with severe features and can be applied in clinical services to save women's maternal morbidity and mortality. Blood products such as fresh frozen plasma, platelets, and whole blood together with tranexamic acid should be readily available for women with pre-eclampsia especially those with severe features with a D-dimer level of 3.58 μg/ml and above during delivery. We wish to generalize the results as it is one hospital with one pathological disease ie pre-eclampsia, disease physiology and laboratory maker seem to apply to other patients.

8. Recommendations

More studies with a longer follow-up period and larger sample size should be considered to explain or confirm our findings.

Women with pre-eclampsia should be checked for D-dimer levels antenatally, those who tend to have a rise in D-dimer values should be prepared early as they approach term, as D-dimer increases with gestation age [19] [20] [21] hence they are at high risk of developing postpartum hemorrhage.

Blood products such as fresh frozen plasma, platelets, and whole blood together with tranexamic acid should be readily available for women with pre-eclampsia with a raised D-dimer level especially those who had pre-eclampsia with severe features having 3.58 μg/ml and above during delivery.

Consent for Publication

Not applicable.

Authors' Contributions

All authors contributed to the discussion, conclusion, and review of this work. However, PSS and MJM advised on the analysis and statistic part. All authors contributed to this study's design, drafting, and manuscript preparation.

Acknowledgements

We would like to thank our Almighty God, families, friends, and all study participants who participated and contributed to the accomplishment of this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Fahmy, N.G., Eskandar, F.S.L., Khalil, W.A.M.A., Sobhy, M.I.I. and Amin, A.M.A.A. (2021) Assessment the Role of Tranexamic Acid in Prevention of Postpartum Hemorrhage. *Ain-Shams Journal of Anesthesiology*, **13**, Article No. 35. https://doi.org/10.1186/s42077-021-00154-6

[2] Moshi, F.V. and Tungaraza, M. (2021) Factors Associated with Blood Pressure Check-up during Pregnancy among Women of Reproductive Age in Tanzania: An Analysis of Data from 2015—16 Tanzania Demographic and Health Survey and Malaria Indicators Survey. *BMC Pregnancy and Childbirth*, **21**, Article No. 465. https://doi.org/10.1186/s12884-021-03963-7

[3] Say, L., Chou, D., Gemmill, A., Tunçalp, Ö., Moller, A., Daniels, J., *et al.* (2014) Global Causes of Maternal Death: A WHO Systematic Analysis. *The Lancet Global Health*, **2**, e323-e333. https://doi.org/10.1016/s2214-109x(14)70227-x

[4] von Schmidt auf Altenstadt, J.F., Hukkelhoven, C.W.P.M., van Roosmalen, J. and Bloemenkamp, K.W.M. (2013) Pre-Eclampsia Increases the Risk of Postpartum Haemorrhage: A Nationwide Cohort Study in the Netherlands. *PLOS ONE*, **8**, e81959. https://doi.org/10.1371/journal.pone.0081959

[5] Un Nisa, S.U., Shaikh, A.A. and Kumar, R. (2019) Maternal and Fetal Outcomes of Pregnancy-Related Hypertensive Disorders in a Tertiary Care Hospital in Sukkur, Pakistan. *Cureus*, **11**, e5507. https://doi.org/10.7759/cureus.5507

[6] Muasya, E. and Makumi, M. (2021) Incidence of Postpartum Hemorrhage among Women with Hypertensive Disorders in Pregnancy at Kenyatta National Hospital in 2019: A Prospective Cohort Study. University of Nairobi Research Archive.

[7] Mvandal, S.P. and Coletha, K. (2021) Prevalence, Causes and Associated Factors for Postpartum Haemorrhage (PPH) at St. Joseph Referral Hospital Peramiho-Songea, Tanzania; A Hospital-Based Retrospective Cross-Sectional Study. Preprint. https://doi.org/10.21203/rs.3.rs-926839/v1

[8] Kebede, B.A., Abdo, R.A., Anshebo, A.A. and Gebremariam, B.M. (2019) Prevalence and Predictors of Primary Postpartum Hemorrhage: An Implication for Designing Effective Intervention at Selected Hospitals, Southern Ethiopia. *PLOS ONE*, **14**, e0224579. https://doi.org/10.1371/journal.pone.0224579

[9] Shams, N., Taimoor, A., Nazir, A., Zaman, U., Shams, H. and Javed, S. (2022) Original of D-Dimer Levels in Preeclampsia and Nosheen Pregnancy. *Pakistan Journal of Physiology*, **18**, 20-22.

[10] Macey, M.G., Bevan, S., Alam, S., Verghese, L., Agrawal, S., Beski, S., *et al.* (2010) Platelet Activation and Endogenous Thrombin Potential in Pre-Eclampsia. *Thrombosis Research*, **125**, e76-e81. https://doi.org/10.1016/j.thromres.2009.09.013

[11] Shao, H., Gao, S., Dai, D., Zhao, X., Hua, Y. and Yu, H. (2021) The Association of Antenatal D-Dimer and Fibrinogen with Postpartum Hemorrhage and Intrauterine

Growth Restriction in Preeclampsia. *BMC Pregnancy and Childbirth*, **21**, Article No. 605. https://doi.org/10.1186/s12884-021-04082-z

[12] Endo-Kawamura, N., Obata-Yasuoka, M., Yagi, H., Ohara, R., Nagai, Y., Mayumi, M., *et al.* (2016) Higher D-Dimer Level in the Early Third Trimester Predicts the Occurrence of Postpartum Hemorrhage. *Journal of Perinatal Medicine*, **44**, 551-556. https://doi.org/10.1515/jpm-2015-0287

[13] McNamara, H. and Mallaiah, S. (2019) Managing Coagulopathy Following PPH. *Best Practice & Research Clinical Obstetrics & Gynaecology*, **61**, 106-120. https://doi.org/10.1016/j.bpobgyn.2019.04.002

[14] Roberts, I., Shakur, H., Fawole, B., Kuti, M., Olayemi, O., Bello, A., *et al.* (2018) Haematological and Fibrinolytic Status of Nigerian Women with Post-Partum Haemorrhage. *BMC Pregnancy and Childbirth*, **18**, Article No. 143. https://doi.org/10.1186/s12884-018-1794-1

[15] Butwick, A.J. and Goodnough, L.T. (2015) Transfusion and Coagulation Management in Major Obstetric Hemorrhage. *Current Opinion in Anaesthesiology*, **28**, 275-284. https://doi.org/10.1097/aco.0000000000000180

[16] NBS (2019) 2019 Tanzania in Figures.

[17] Bourjeily, G. (2014) D-Dimer Use in Venous Thromboembolic Disease in Pregnancy. *BJOG*: *An International Journal of Obstetrics & Gynaecology*, **122**, 401. https://doi.org/10.1111/1471-0528.12858

[18] Sneha, K., Girish Babu, M. and Manjunath, M.L. (2020) Haematocrit as Diagnostic Tool for Assessing Primary Postpartum Haemorrhage. *Indian Journal of Clinical Anatomy and Physiology*, **5**, 210-213. https://doi.org/10.18231/2394-2126.2018.0048

[19] de Barros Pinheiro, M., Junqueira, D.R.G., Coelho, F.F., Freitas, L.G., Carvalho, M.G., Gomes, K.B., *et al.* (2012) D-Dimer in Preeclampsia: Systematic Review and Meta-Analysis. *Clinica Chimica Acta*, **414**, 166-170. https://doi.org/10.1016/j.cca.2012.08.003

[20] Murphy, N., Broadhurst, D., Khashan, A., Gilligan, O., Kenny, L. and O'Donoghue, K. (2014) Gestation-Specific D-Dimer Reference Ranges: A Cross-Sectional Study. *BJOG*: *An International Journal of Obstetrics & Gynaecology*, **122**, 395-400. https://doi.org/10.1111/1471-0528.12855

[21] Izquierdo, G., Pérez, M.A.J. and de Guadiana Romualdo, L.G. (2018) D-Dimer during Pregnancy: Establishing Trimester-Specific Reference Intervals. *Scandinavian Journal of Clinical and Laboratory Investigation*, **78**, 439-442. https://doi.org/10.1080/00365513.2018.1488177

Abbreviations

C/S	Cesarean Section
DIC	Disseminated Intravascular Coagulopathy
GA	Gestation Age
ICU	Intensive Care Unit
KCMC	Kilimanjaro Christian Medical Center
OBGYN	Obstetrics and Gynecology
PPH	Postpartum Hemorrhage
SVD	Spontaneous Vaginal Delivery
WHO	World Health Organization