Assessment of Immature Platelet Fraction in Pregnancy-Associated Thrombotic Microangiopathy: (Results)

Assessment of Immature Platelet Fraction in Pregnancy-Associated Thrombotic Microangiopathy

Thesis

Submitted for Partial Fulfillment of Master Degree

in Clinical and Chemical Pathology

By

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Results

Table (3): Characteristics of patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	F/χ^2	DF	p-value
Age (years)	29.5 ± 5.6	25.3 ± 4.5	26.0 ± 4.6	4.086	2, 54	**0.022¶†**
Parity				0.213	1	0.645§
P0	6 (25.0%)	2 (15.4%)	5 925.0%)			
P1	5 (20.8%)	7 (53.8%)	5 (25.0%)			
P2	8 (33.3%)	2 (15.4%)	6 (30.0%)			
P3	2 (8.3%)	1 (7.7%)	3 (15.0%)			
P4	2 (8.3%)	1 (7.7%)	1 (5.0%)			
P5	1 (4.2%)	0 (0.0%)	0 (0.0%)			
Previous abortions				1.319	1	0.251§
Nil	23 (95.8%)	12 (92.3%)	18 (90.0%)			
One	1 (4.2%)	1 (7.7%)	1 (5.0%)			
Three	0 (0.0%)	0 (0.0%)	1 (5.0%)			
Gestational age (weeks)	**30.5 ± 4.0‡**	**29.8 ± 5.4‡**	24.2 ± 3.2	14.597	2, 54	**<0.001¶**

Data are mean ± SD or number (%).
¶One-way analysis of variance (ANOVA).
§Chi-squared test for trend.
†No statistically significant difference among the three groups by the Schéffé post-hoc test.
‡P-value <0.05 versus Control group (Schéffé test).

Table (4): Hemoglobin level, hematocrit, and schistoctyte count in patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	F	DF	P-value
Hemoglobin (g/dl)	10.5 ± 1.6	11.1 ± 1.9	11.4 ± 1.2	1.773	2, 54	0.180¶
Hematocrit (%)	32.3 ± 5.7	33.1 ± 6.5	34.9 ± 3.3	1.457	2, 54	0.242¶
Schistocyte count (%)	**0.5 (0.0 – 1.2)†**	**6.5 (0.8 – 17.6)†‡**	0.0 (0.0 – 0.0)	27.186	2	**<0.0001§**

Data are mean ± SD or median (interquartile range).
¶One-way analysis of variance (ANOVA).
§Kruskal-Wallis test.
†P-value <0.05 versus Control group (Conover test).
‡P-value <0.05 versus SPE/HELLP group (Conover test).

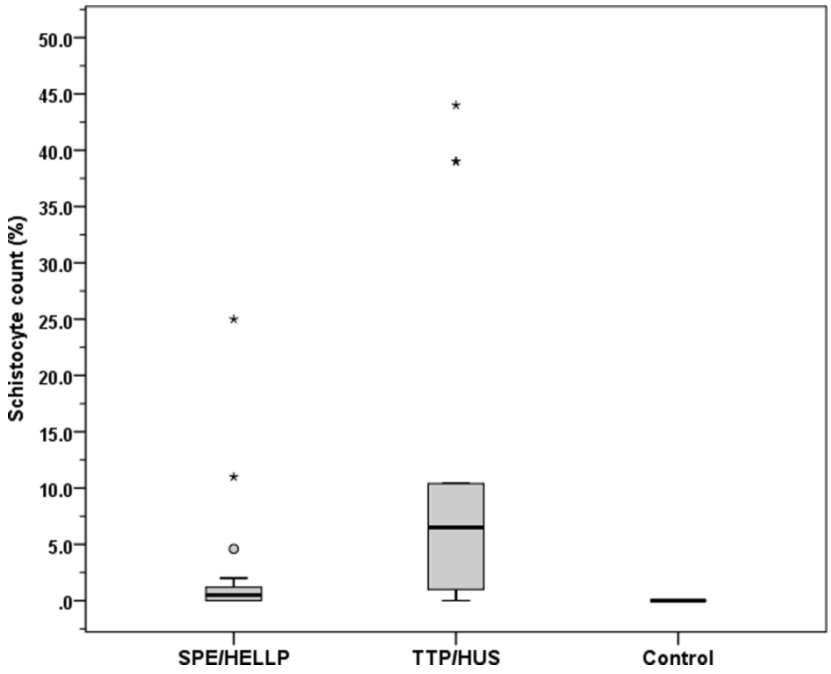

Figure (4): Box plot showing the total platelet count in patients with SPE/HELLP or TTP/HUS and normal controls. Box represents the range from the first to third quartile (interquartile range). Line inside the box represents the median (second quartile). Whiskers represent the range between the minimum and maximum values excluding outliers (rounded markers) and extreme observations (asterisks).

Table (5): Total platelet count, immature platelet count, and immature platelet fraction in patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	χ^2	DF	P-value
Total platelet count (*1,000/mm^3)	**121 (73 – 188.5)†**	**53.0 (37.0 – 81.0)†‡**	269.5 (235.0 – 337.0)	35.333	2	**<0.0001**
Immature platelet count (*1,000/mm^3) A-IPC	**14.875 (11.781 – 22.151)†**	**11.64 (6.410 – 21.238)†**	21.992 (16.945 – 25.431)	10.362	2	**0.006**
Immature platelet fraction (%)IPF-%	**13.0 (9.6 – 22.9)†**	**19.5 (15.1 – 27.7)†‡**	7.2 (6.2 – 11.1)	18.897	2	**<0.0001**

Data are median (interquartile range).

†P-value <0.05 versus Control group (Conover test).

‡P-value <0.05 versus SPE/HELLP group (Conover test).

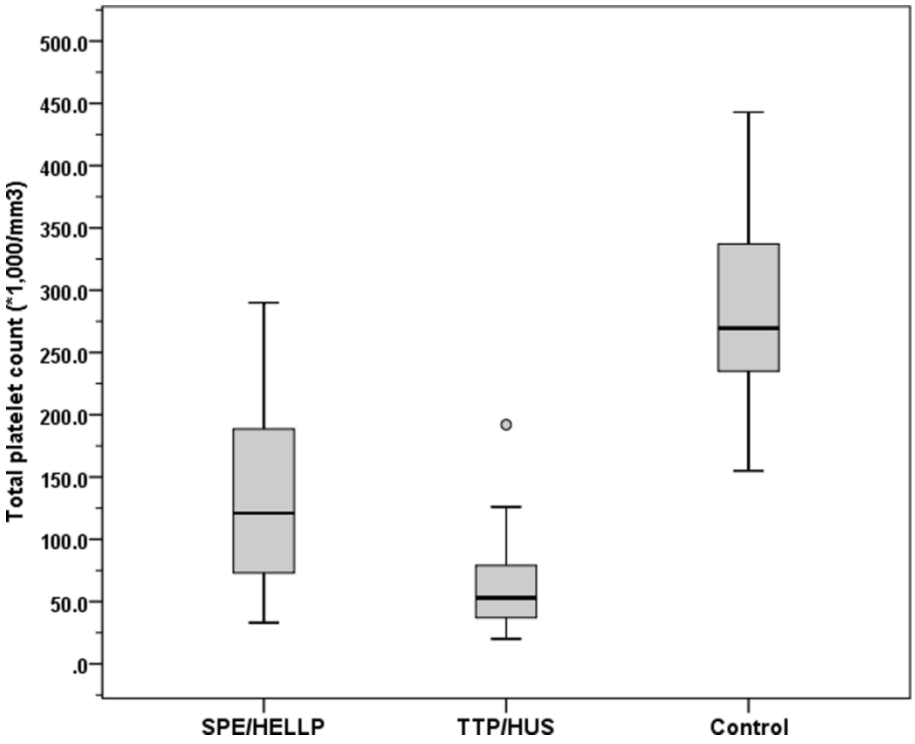

Figure (5): Box plot showing the total platelet count in patients with SPE/HELLP or TTP/HUS and normal controls. Box represents the range from the first to third quartile (interquartile range). Line inside the box represents the median (second quartile). Whiskers represent the range between the minimum and maximum values excluding outliers (rounded markers).

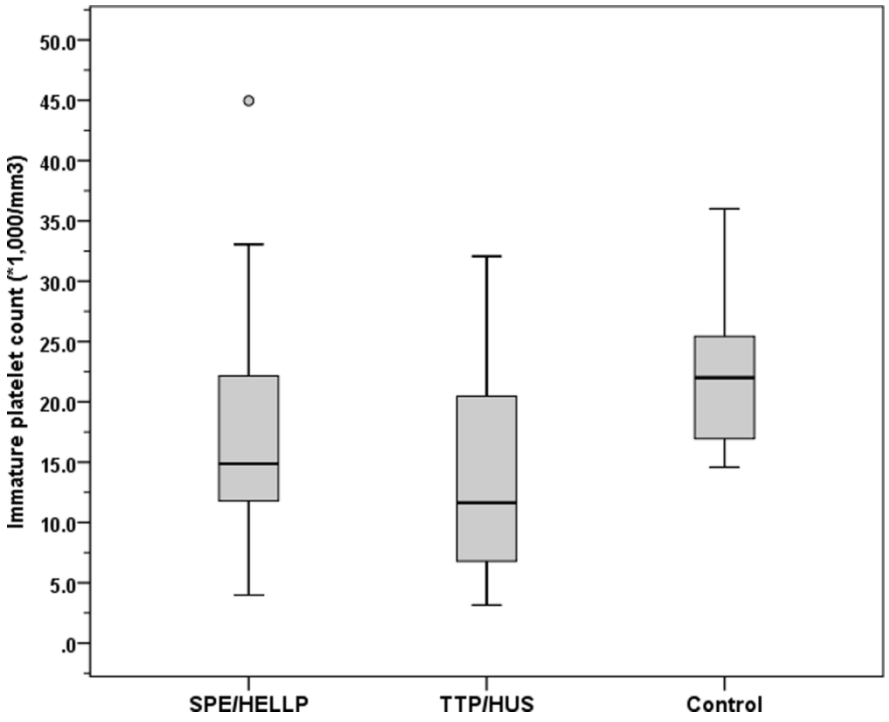

Figure (6): Box plot showing the immature platelet count (IPC) in patients with SPE/HELLP or TTP/HUS and normal controls. Box represents the range from the first to third quartile (interquartile range). Line inside the box represents the median (second quartile). Whiskers represent the range between the minimum and maximum values excluding outliers (rounded markers).

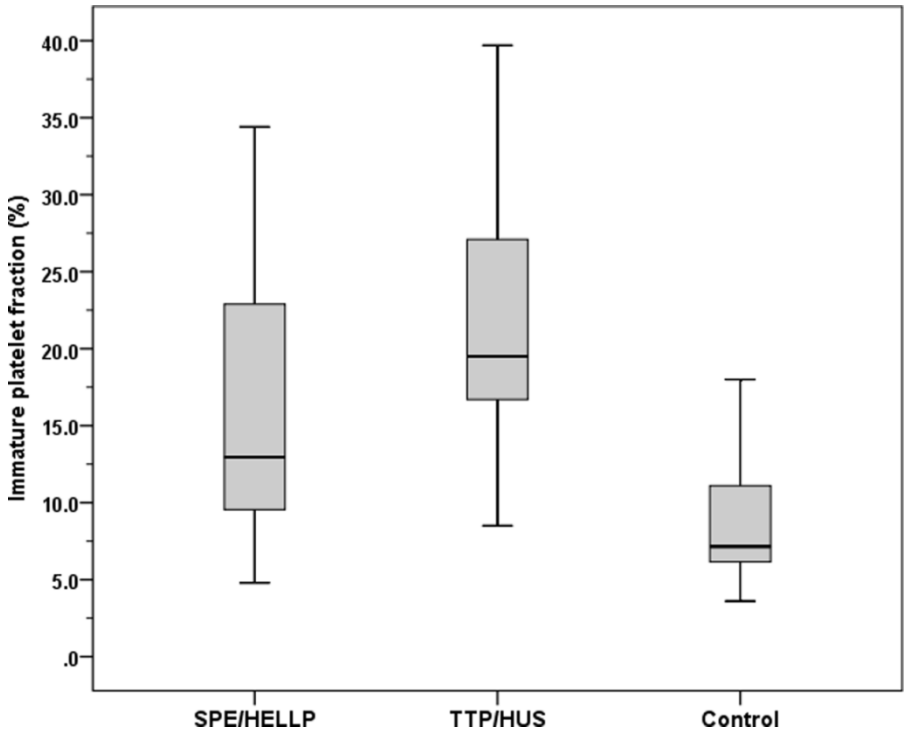

Figure (7): Box plot showing the immature platelet fraction (IPF) in patients with SPE/HELLP or TTP/HUS and normal controls. Box represents the range from the first to third quartile (interquartile range). Line inside the box represents the median (second quartile). Whiskers represent the range between the minimum and maximum values.

Table (6): Prevalence of a low platelet count, high IPF, or high schistocyte count among patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	P-value¶
Low total platelet count (<100,000/mm^3)	9 (37.5%)	11 (84.6%)	0 (0.0%)	**<0.001**
High IPF (>11.2%) **(Machin, 2010)**	14 (58.3%)	10 (76.9%)	5 (25.0%)	**0.008**
High schistocyte count (>0%) **(Gina et al.,2011)**	14 (58.3%)	11 (84.6%)	0 (0.0%)	**<0.001**

Data are number (%).
¶Fisher's exact test.

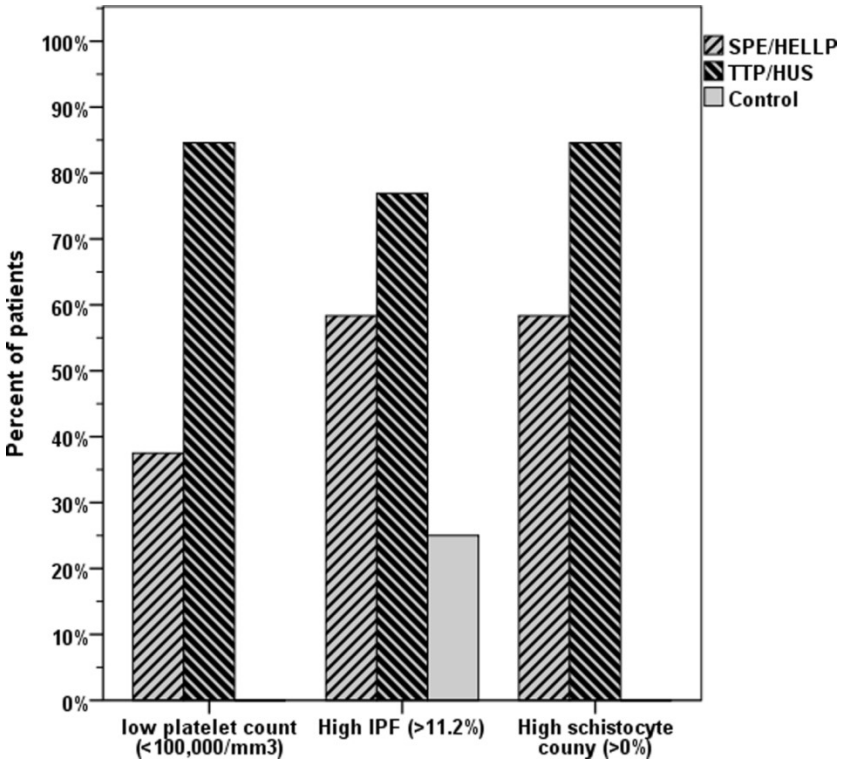

Figure (8): Prevalence of a low platelet count, high IPF, or high schistocyte count among patients with SPE/HELLP or TTP/HUS and normal controls.

Table (7): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF or schistocyte count

	Marker

Assessment of Immature Platelet Fraction in Pregnancy-Associated Thrombotic Microangiopathy: (Results)

Index	IPF	Schistocyte count
Sample size	37	37
Positive group (TTP/HUS)	13 (35.1%)	13 (35.1%)
Negative group (SPE/HELLP)	24 (64.9%)	24 (64.9%)
Area under the ROC curve (AUC)	0.692 (0.519 to 0.833)	0.771 (0.603 to 0.893)
z statistic	2.028	3.022
P-value	**0.043¶**	**0.003¶**
Associated cut-off criterion	>15.9 %	>4.6 %
Sensitivity (%)	76.92 (46.2 - 95.0)	61.54 (31.6 - 86.1)
Specificity (%)	66.67 (44.7 – 84.4)	91.67 (73.0 – 99.0)
Positive predictive value (PPV, %)	55.6 (30.8 - 78.5)	80.0 (44.4 - 97.5)
Negative predictive value NPV, %)	84.2 (60.4 - 96.6)	81.5 (61.9 - 93.7)

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

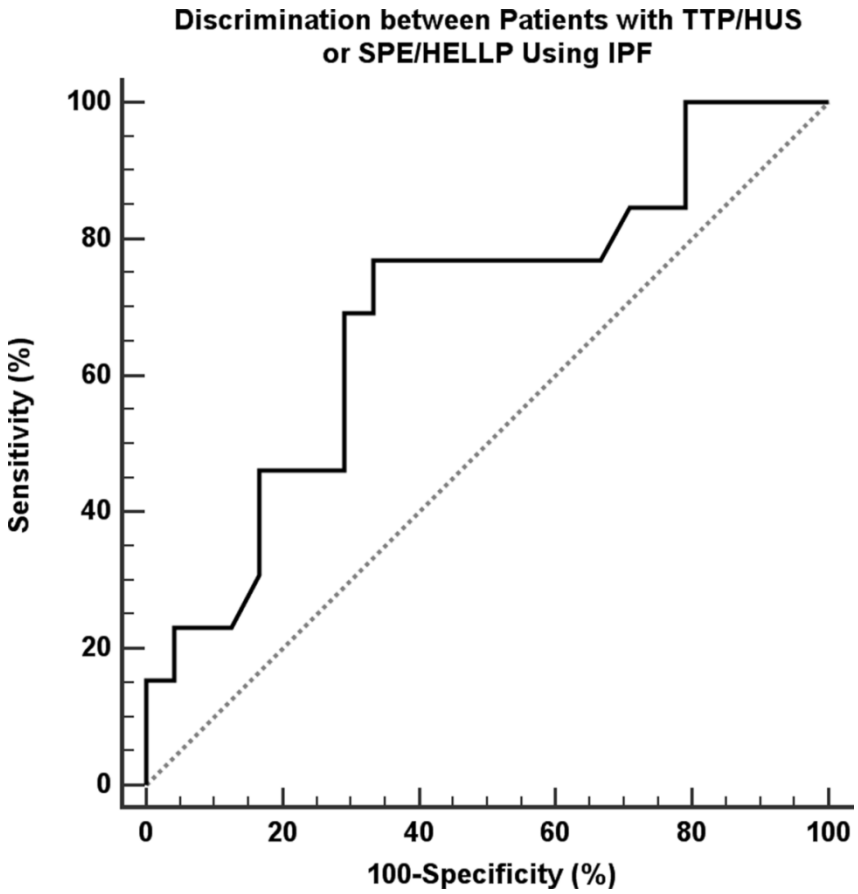

Figure (9): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF.

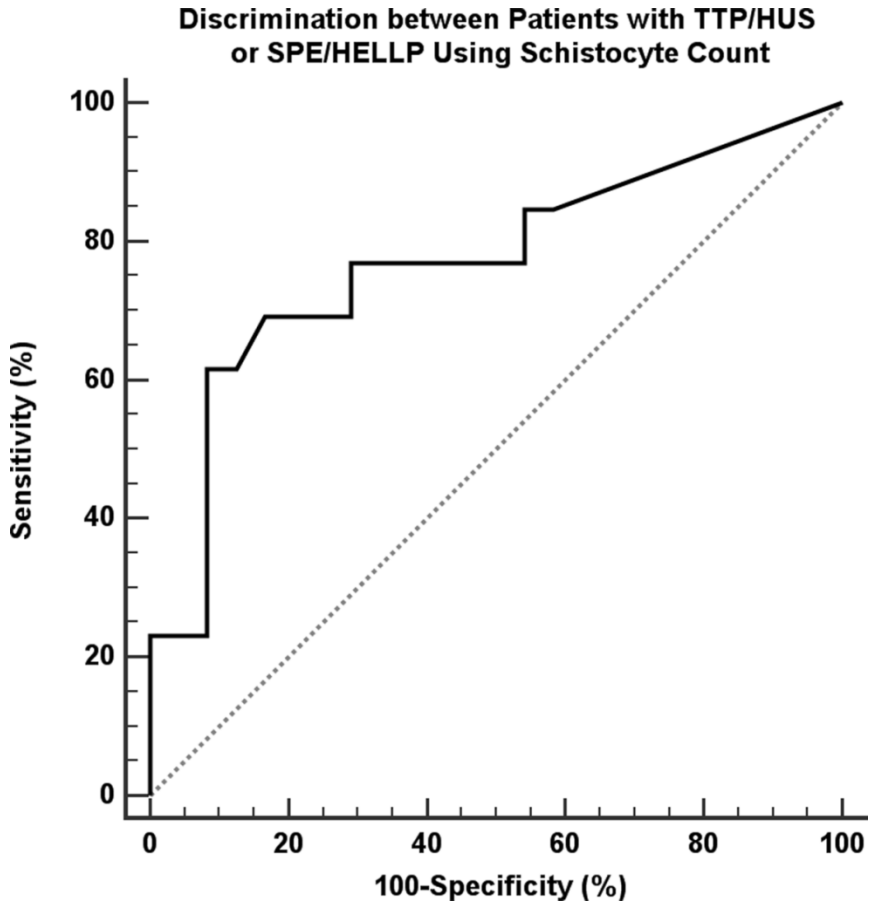

Figure (10): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the schistocyte count.

Table (8): Comparison of the receiver-operating characteristic (ROC) curves for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF-% or schistocyte count

	Marker				
Index	**IPF-%**	**Schistocyte count**	**Difference**	**z**	**P-value¶**
Area under ROC (AUC)	0.692 (0.519 to 0.833)	0.771 (0.603 to 0.893)	0.079 (-0.171 to 0.328)	0.617	0.537

Diagnostic indices are presented as value (95% CI).
¶DeLong method.

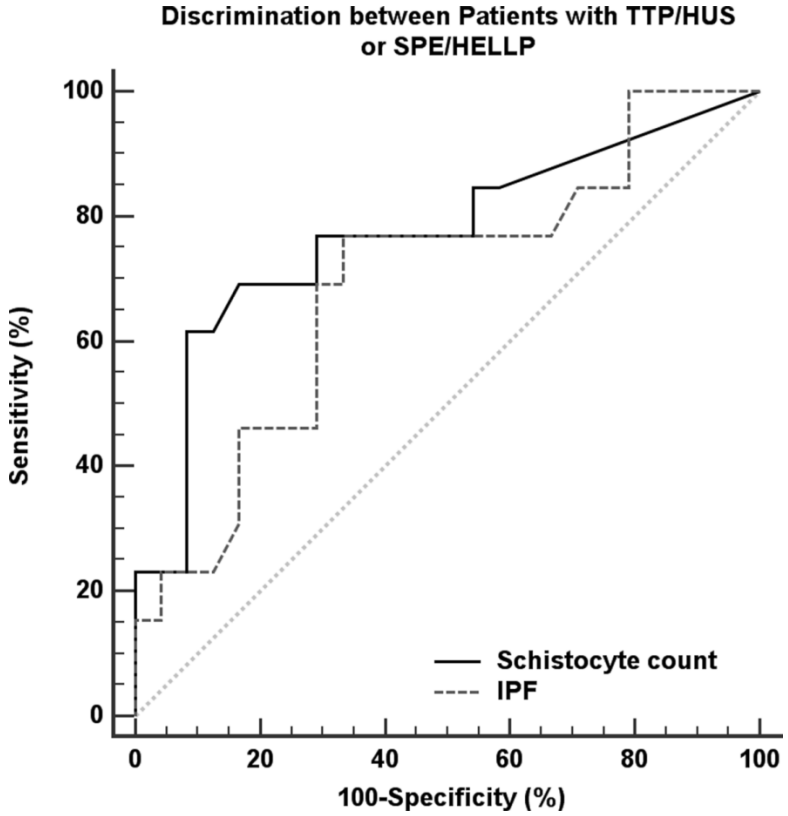

Figure (11): Comparison of the receiver-operating characteristic (ROC) curves for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF or schistocyte count.

Table (9): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TMA and normal controls using the IPF-% or schistocyte count

	Marker

Assessment of Immature Platelet Fraction in Pregnancy-Associated Thrombotic Microangiopathy: (Results)

Index	IPF	Schistocyte count
Sample size	57	57
Positive group (TMA)	37 (64.9%)	37 (64.9%)
Negative group (normal controls)	20 (35.1%)	20 (35.1%)
Area under the ROC curve (AUC)	0.820 (0.695 to 0.909)	0.838 (0.716 to 0.922)
z statistic	5.678	8.660
P-value	**<0.0001¶**	**<0.0001¶**
Associated cut-off criterion	>8.1 %	>0 %
Sensitivity (%)	86.49 (71.2 - 95.5)	67.57 (50.2 - 82.0)
Specificity (%)	65.00 (40.8 - 84.6)	100.00 (83.2 - 100.0)
Positive predictive value (PPV, %)	82.1 (66.5 - 92.5)	100.0 (86.3 - 100.0)
Negative predictive value (NPV, %)	72.2 (46.5 - 90.3)	62.5 (43.7 - 78.9)

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

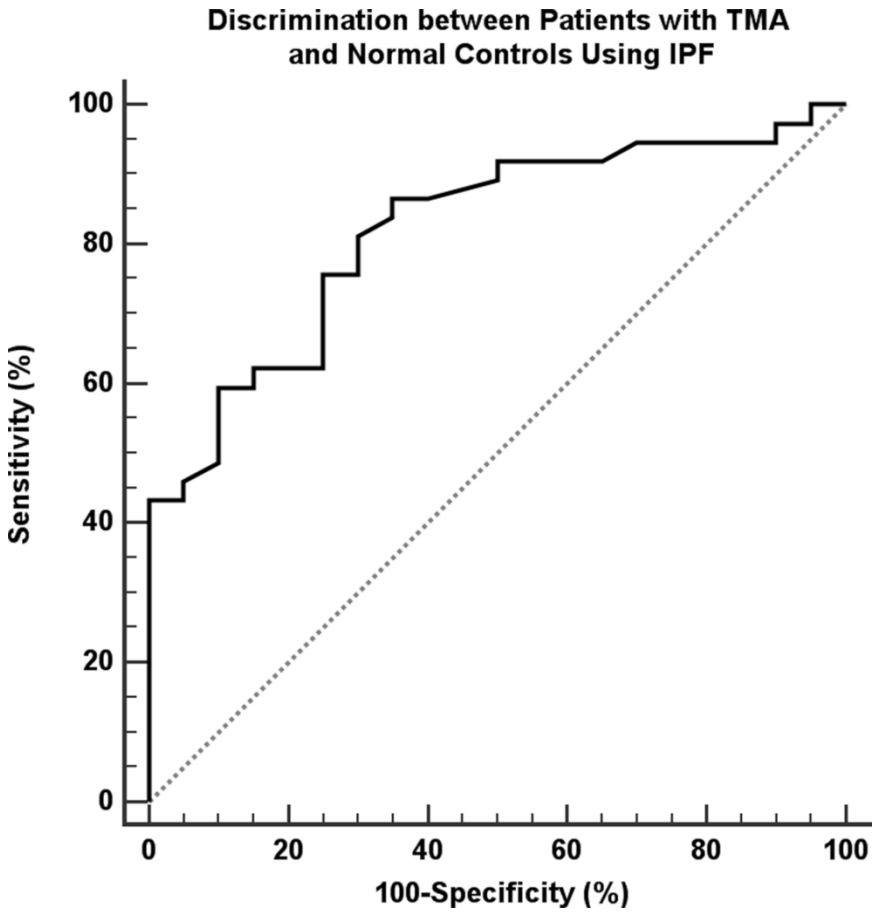

Figure (12): Receiver-operating characteristic (ROC) curve for discrimination between patients with TMA and normal controls using the IPF.

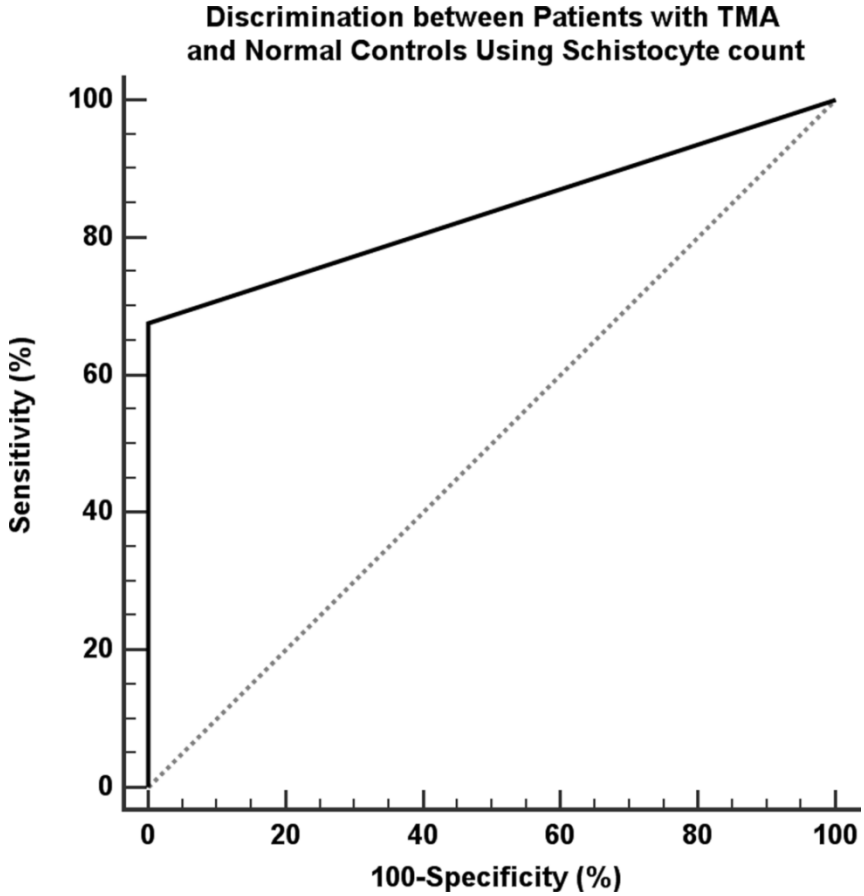

Figure (13): Receiver-operating characteristic (ROC) curve for discrimination between patients with TMA and normal controls using the schistocyte count.

Table (10): Comparison of the receiver-operating characteristic (ROC) curves for discrimination between patients with TMA and normal controls using the IPF or schistocyte count

	Marker				
Index	**IPF**	**Schistocyte count**	**Difference**	**z**	**P-value¶**
Area under ROC (AUC)	0.820 (0.695 to 0.909)	0.838 (0.716 to 0.922)	0.018 (-0.105 to 0.142)	0.290	0.7722

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

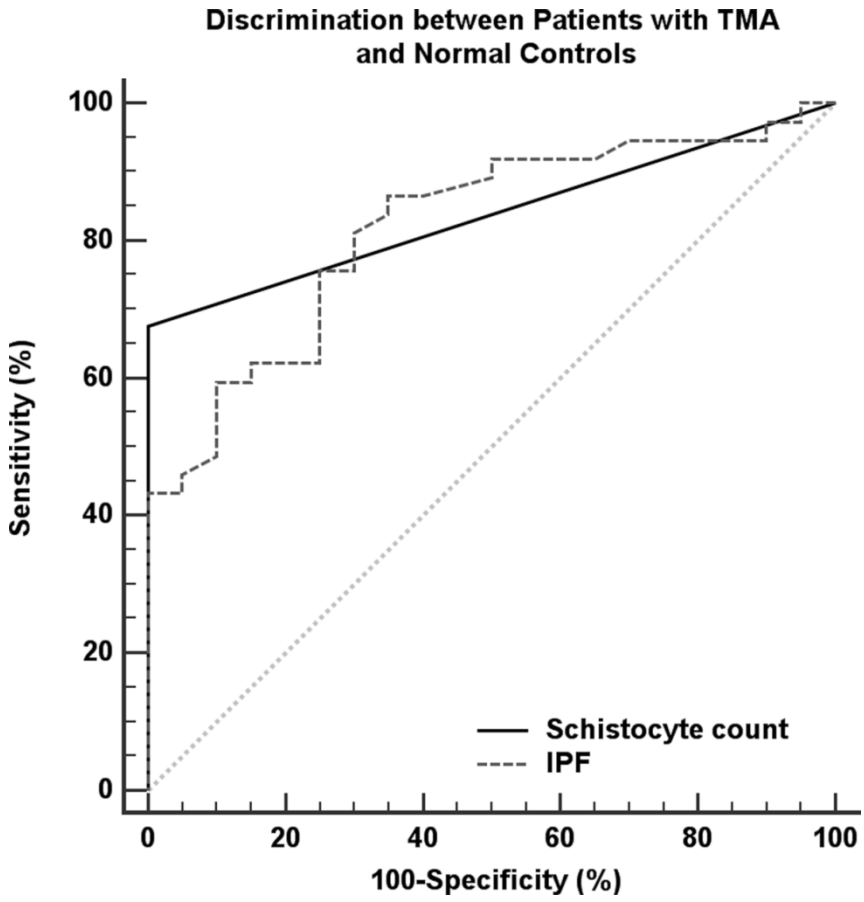

Figure (14): Comparison of the receiver-operating characteristic (ROC) curves for discrimination between patients with TMA and normal controls using the IPF or schistocyte count.

Table (11): Multivariable binary logistic regression analysis for the relation between the IPF-% and TTP/HUS with adjustment for the confounding effect of the gestational age

Variable	Regression coefficient (B)	SE for B	Wald	P-value	Odds ratio (OR)	95% CI for OR
IPF -%	0.084	0.041	4.105	**0.043**	1.088	1.003 to 1.179
Gestational age (weeks)	-0.064	0.087	0.539	0.463	0.939	0.792 to 1.112
Constant	-0.271					

Table (12): Multivariable binary logistic regression analysis for the relation between the schistocyte count and TTP/HUS with adjustment for the confounding effect of the gestational age

Variable	Regression coefficient (B)	SE for B	Wald	P-value	Odds ratio (OR)	95% CI for OR
Scistocyte count (%)	0.101	0.052	3.781	0.052	1.107	0.999 to 1.226
Gestational age (weeks)	-0.052	0.088	0.355	0.551	0.949	0.799 to 1.127
Constant	0.420					

Table (13): Correlation between the IPF and schistocytes count in whole study population, patients with TMA, SPE/HELLP, or TTP/HUS, and normal controls

		Correlation between IPF-% and schistocyte count	
Group	**Number**	**Spearman rho (ρ)**	**P-value**

All study population	57	0.466	**0.0003**
TMA	37	0.231	0.169
SPE/HELLP	24	0.190	0.375
TTP/HUS	13	-0.058	0.851
Control	20	0.000	-

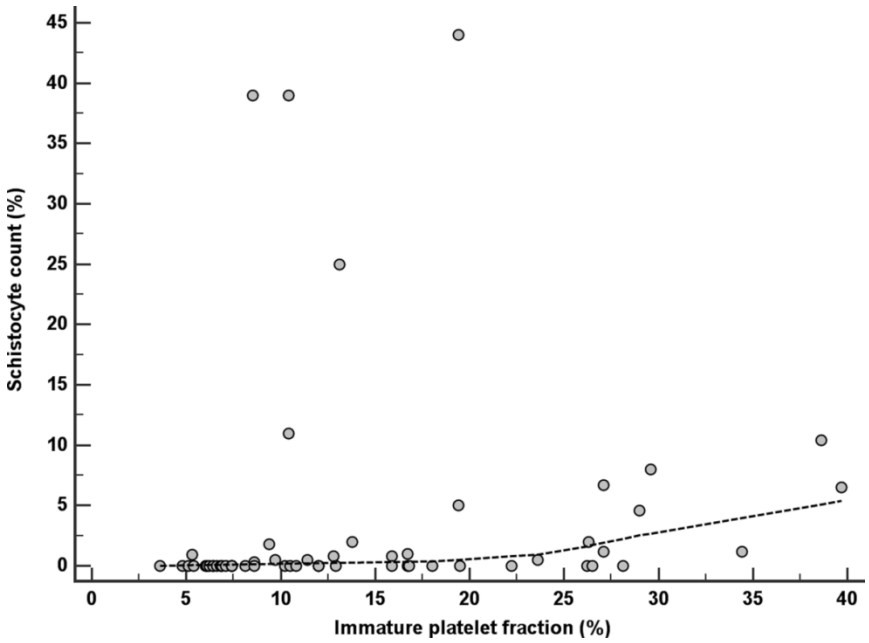

Figure (15): Scatter plot showing the correlation between the IPF and schistocyte count in the whole study population. Fitted lines represent local regression smoothing (LOESS) trend lines.

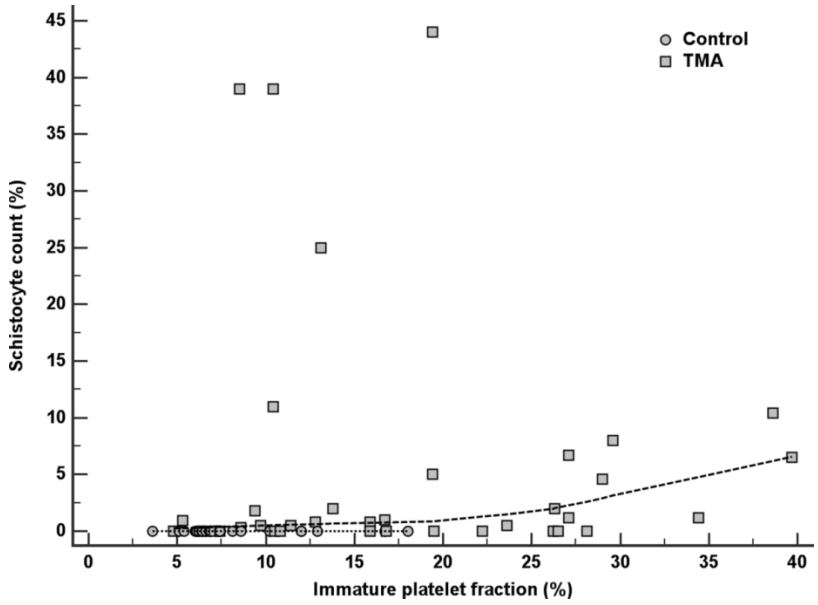

Figure (16): Scatter plot showing the correlation between the IPF and schistocyte count in patients with TMA or normal controls. Fitted lines represent local regression smoothing (LOESS) trend lines.

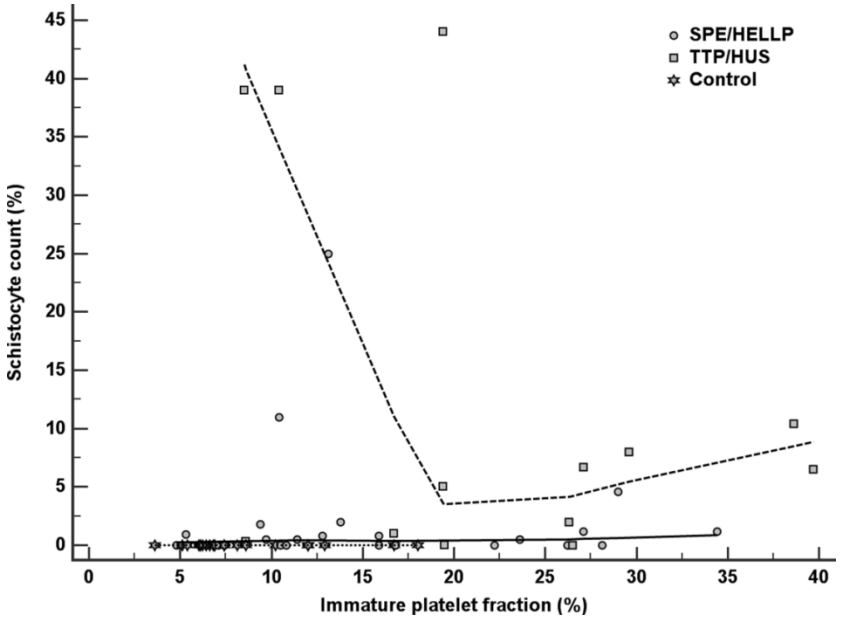

Figure (17): Scatter plot showing the correlation between the IPF and schistocyte count in patients with SPE/HELLP or TTP/HUS and normal controls. Fitted lines represent local regression smoothing (LOESS) trend lines.

The results of the present study are shown in tables (14 -22) and figures (18-29).

Comparison between patients with SPE/HELLP or TTP/HUS and normal controls regarding demographic features:

There was significant difference between the three studied groups regarding maternal age (P <0.05) and high significant difference between the three groups regarding gestational age (P <0.001). However, there was no significant difference between parity and previous abortions (P >0.05). On applying Schéffé post-hoc test revealed no statistically significant difference among the three groups regarding maternal age (P >0.05). However, regarding gestational age, the Schéffé test has revealed a significant difference between either patient group (SPE/HELLP or TTP/HUS) versus control group (P <0.05 for each) **(Table 14)**.

Table (14): Characteristics of patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	F/χ^2	DF	p-value
Age (years)	29.5 ± 5.6	25.3 ± 4.5	26.0 ± 4.6	4.086	2, 54	**0.022¶†**
Parity						
P0	6 (25.0%)	2 (15.4%)	5 (25.0%)	0.213	1	0.645§
P1	5 (20.8%)	7 (53.8%)	5 (25.0%)			
P2	8 (33.3%)	2 (15.4%)	6 (30.0%)			
P3	2 (8.3%)	1 (7.7%)	3 (15.0%)			
P4	2 (8.3%)	1 (7.7%)	1 (5.0%)			
P5	1 (4.2%)	0 (0.0%)	0 (0.0%)			
Previous abortions						
Nil	23 (95.8%)	12 (92.3%)	18 (90.0%)	1.319	1	0.251§
One	1 (4.2%)	1 (7.7%)	1 (5.0%)			
Three	0 (0.0%)	0 (0.0%)	1 (5.0%)			
Gestational age (weeks)	**30.5 ± 4.0‡**	**29.8 ± 5.4‡**	24.2 ± 3.2	14.597	2, 54	**<0.001¶**

Data are mean ± SD or number (%).

¶One-way analysis of variance (ANOVA).

§Chi-squared test for trend.

†No statistically significant difference among the three groups by the Schéffé post-hoc test.

‡P-value <0.05 versus Control group (Schéffé test).

Comparison between patients with SPE/HELLP or TTP/HUS and normal controls regarding to laboratory data:

1) Hemoglobin level: There was no significant difference between the three groups regarding hemoglobin (P >0.05) **(Table 15).**

2) Hematocrit level: There was no significant difference between the three groups regarding hematocrit (P >0.05) **(Table 15).**

3) Schistocytes count: There was high significant difference between the three groups regarding schistocytes count ($p < 0.001$). Applying Conover test reveal; significant difference between SPE/HELLP and control, between TTP/HUS and control and between SPE/HELLP and TTP/HUS **(Table 15), (Figure 18).**

Table (15): Hemoglobin level, hematocrit, and schistocytes count in patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	F	DF	P-value
Hemoglobin (g/dl)	10.5 ± 1.6	11.1 ± 1.9	11.4 ± 1.2	1.773	2, 54	0.180¶
Hematocrit (%)	32.3 ± 5.7	33.1 ± 6.5	34.9 ± 3.3	1.457	2, 54	0.242¶
Schistocyte count (%)	**0.5 (0.0 – 1.2)†**	**6.5 (0.8 –17.6)†‡**	0.01 (0.0 – 0.03)	27.186	2	**<0.0001§**

Data are mean ± SD or median (interquartile range).

¶One-way analysis of variance (ANOVA).

§Kruskal-Wallis test.

†P-value <0.05 versus Control group (Conover test).

‡P-value <0.05 versus SPE/HELLP group (Conover test).

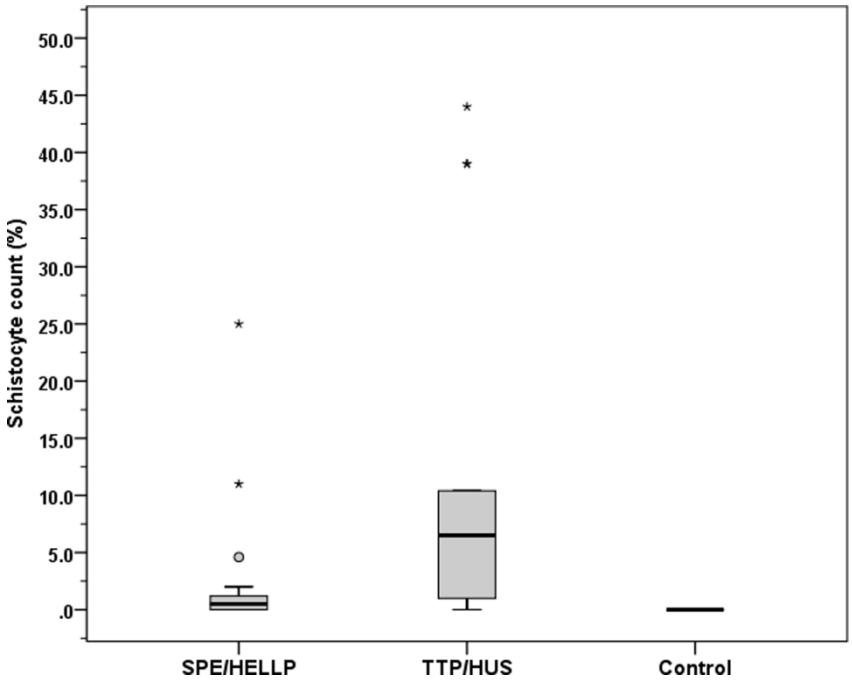

Figure (18): Box plot showing the schistocyte count in patients with SPE/HELLP or TTP/HUS and normal controls.

4) Total platelet count: There was high significant difference between the three groups regarding total platelet count ($p < 0.001$). Applying Conover test reveal; significant difference between SPE/HELLP and control, between TTP/HUS and control and between SPE/HELLP and TTP/HUS **(Table 16), (Figure 19).**

5) Immature platelet count A-IPC : There was significant difference between the three groups regarding immature platelet count ($p < 0.05$). Applying Conover test reveal; significant difference between SPE/HELLP and control, between TTP/HUS and control **(Table 16), (Figure 20).**

6) Immature platelet fraction IPF-%: There was high significant difference between the three groups regarding immature platelet fraction ($p < 0.001$). Applying Conover test reveal; significant difference between SPE/HELLP and control, between TTP/HUS and control and between SPE/HELLP and TTP/HUS **(Table 16), (Figure 21).**

Table (16): Total platelet count, immature platelet count, and immature platelet fraction in patients with SPE/HELLP or TTP/HUS and normal controls

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Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	χ^2	DF	P-value
Total platelet count (*1,000/mm^3)	121 (73 – 188.5)†	53.0 (37.0 – 81.0)†‡	269.5 (235.0 – 337.0)	35.333	2	**<0.0001**
Absolute Immature platelet count (*1,000/mm^3) (A-IPC)	14.875 (11.781 – 22.151)†	11.64 (6.410 – 21.238)†	21.992 (16.945 – 25.431)	10.362	2	**0.006**
Immature platelet fraction (%)(IPF-%)	13.0 (9.6 – 22.9)†	19.5 (15.1 – 27.7)†‡	7.2 (6.2 – 11.1)	18.897	2	**<0.0001**

Data are median (interquartile range).

†P-value <0.05 versus Control group (Conover test).

‡P-value <0.05 versus SPE/HELLP group (Conover test).

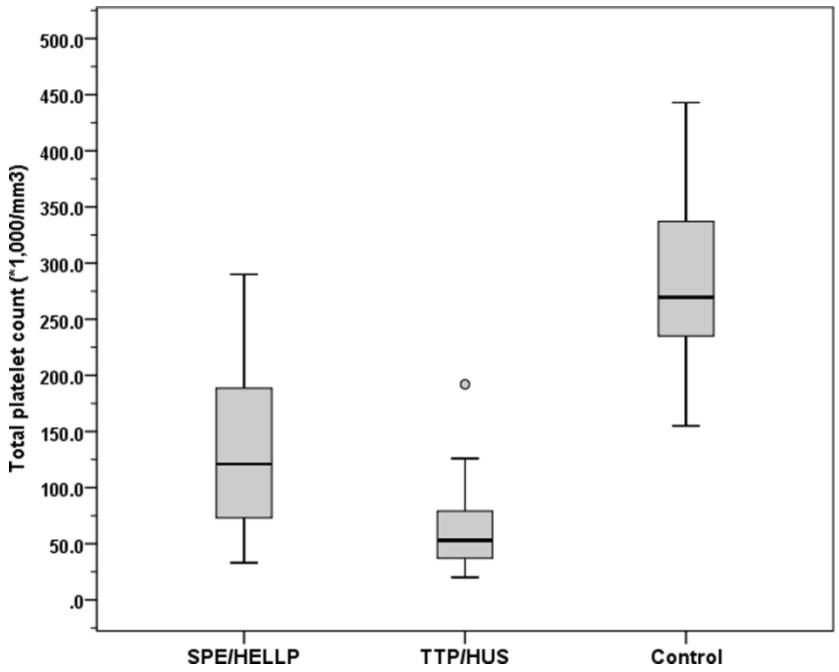

Figure (19): Box plot showing the total platelet count in patients with SPE/HELLP or TTP/HUS and normal controls.

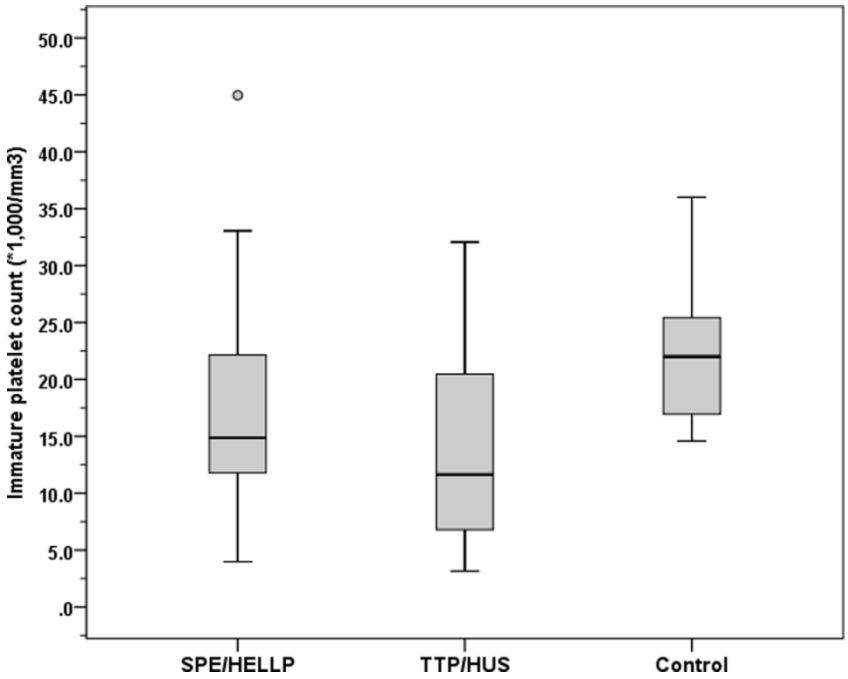

Figure (20): Box plot showing the immature platelet count (IPC) in patients with SPE/HELLP or TTP/HUS and normal controls**.**

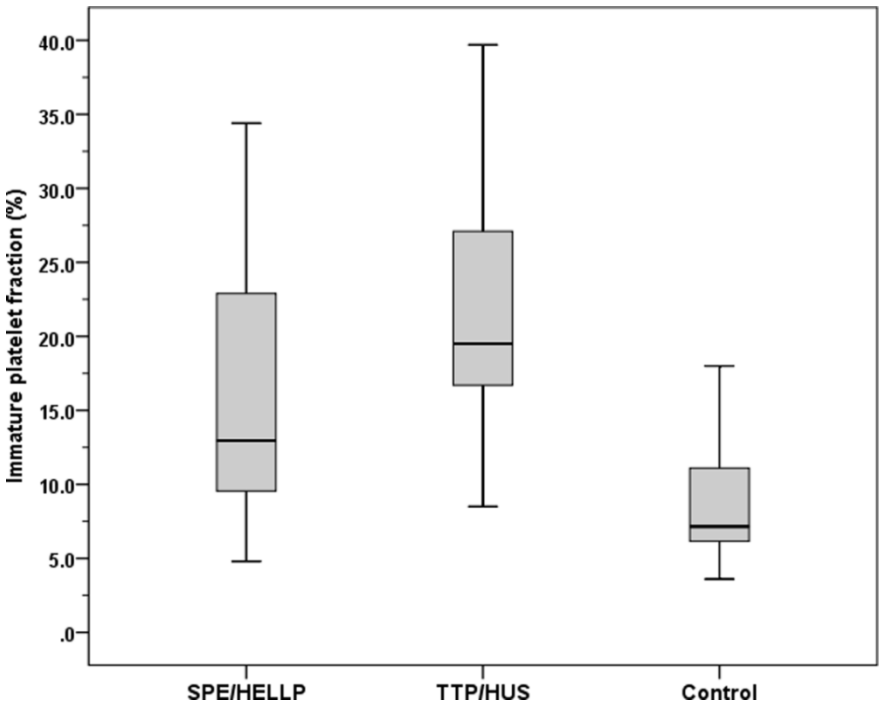

Figure (21): Box plot showing the immature platelet fraction (IPF) in patients with SPE/HELLP or TTP/HUS and normal controls.

- **Prevalence of a low platelet count (A-IPC):** There was high significant difference between the three groups regarding prevalence of a low platelet count (P <0.001) **(Table 17), (Figure 22).**

- **Prevalence of high IPF-%**: There was significant difference between the three groups regarding prevalence of high IPF (P <0.05) **(Table 17), (Figure 22)**.

- **Prevalence of high schistocyte count:** There was high significant difference between the three groups regarding prevalence of high schistocyte count (P <0.001) **(Table 17), (Figure 22)**.

Table (17): Prevalence of a low platelet count, high IPF, or high schistocyte count among patients with SPE/HELLP or TTP/HUS and normal controls

Variable	SPE/HELLP (n=24)	TTP/HUS (n=13)	Control (n=20)	P-value¶
Low total platelet count (<100,000/mm^3)	9 (37.5%)	11 (84.6%)	0 (0.0%)	**<0.001**
High IPF-% (>11.2%) **(Machin, 2010)**	14 (58.3%)	10 (76.9%)	5 (25.0%)	**0.008**
High schistocyte count (>1%) (***Gina et al., 2011***)	14 (58.3%)	11 (84.6%)	0.01 (0.0%)	**<0.001**

Data are number (%).

¶Fisher's exact test.

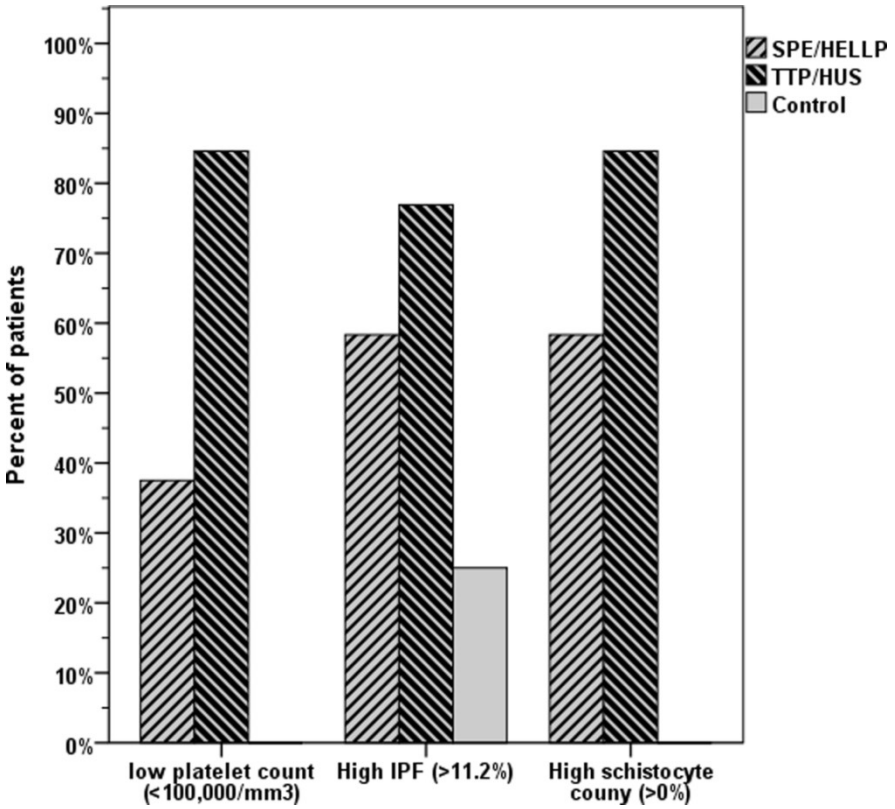

Figure (22): Prevalence of a low platelet count, high IPF, or high schistocyte count among the studied groups.

Receiver-operating characteristic (ROC) curve analysis

Table (18): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF or schistocytes count

Index	Marker

Assessment of Immature Platelet Fraction in Pregnancy-Associated Thrombotic Microangiopathy: (Results)

	IPF	Schistocyte count
Positive group (TTP/HUS)	13 (35.1%)	13 (35.1%)
Negative group (SPE/HELLP)	24 (64.9%)	24 (64.9%)
Area under the ROC curve (AUC)	0.692 (0.519 to 0.833)	0.771 (0.603 to 0.893)
z statistic	2.028	3.022
P-value	**0.043¶**	**0.003¶**
Associated cut-off criterion	>15.9 %	>4.6 %
Sensitivity (%)	76.92 (46.2 - 95.0)	61.54 (31.6 - 86.1)
Specificity (%)	66.67 (44.7 – 84.4)	91.67 (73.0 – 99.0)
Positive predictive value (PPV, %)	55.6 (30.8 - 78.5)	80.0 (44.4 - 97.5)
Negative predictive value (NPV, %)	84.2 (60.4 - 96.6)	81.5 (61.9 - 93.7)

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

- **(ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF-%:** The optimal cutoff values for IPF-% for discrimination between patients with TTP/HUS or SPE/HELLP was >15.9 %. The sensitivity and specificity were 76.92% and 66.7%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 55.6 % and 84.2%, respectively (AUC=0.692) **(Table 18) (Figure 23).**

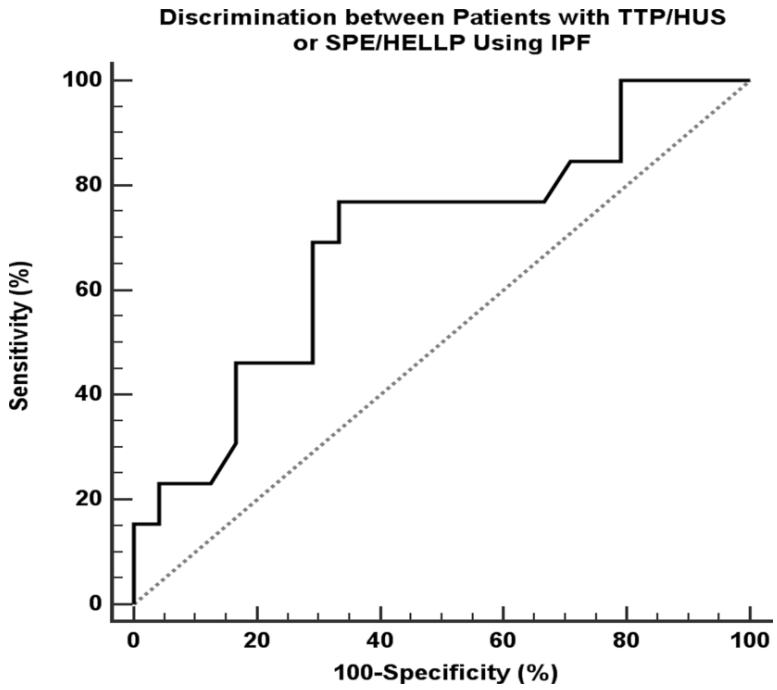

Figure (23): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF.

- **<u>(ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the schistocyte count</u>:** The optimal cutoff values for schistocyte count for discrimination between patients with TTP/HUS or SPE/HELLP was >4.6 %. The sensitivity and specificity were 61.54 % and 91.67%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 80% and 81.5%, respectively (AUC=0.771) **(Table 19), (Figure 24).**

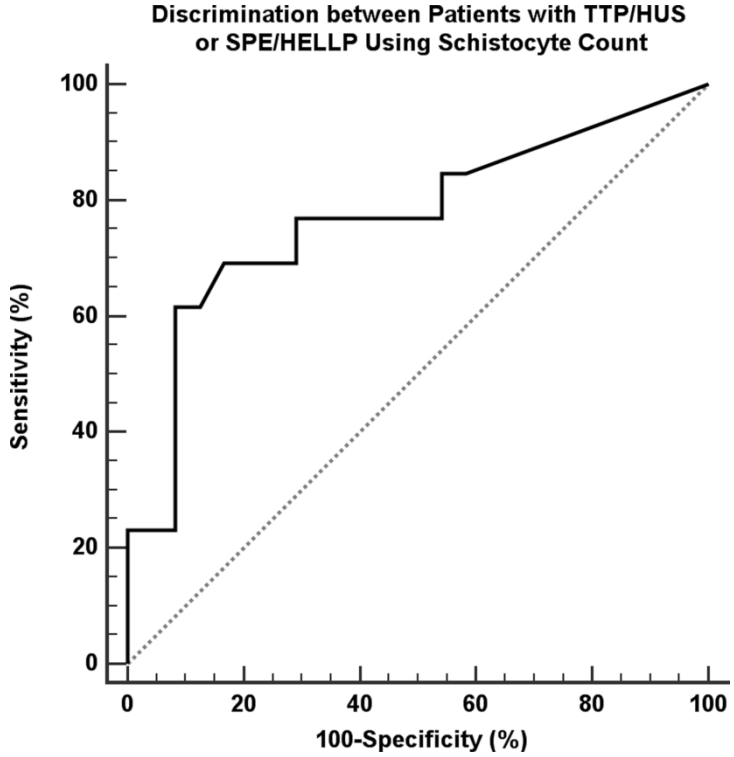

Figure (24): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the schistocyte count.

<u>Comparison of the receiver-operating characteristic (ROC) curves:</u>

Comparison of the receiver-operating characteristic (ROC) curves between IPF-% or schistocyte count revealed no significant difference between IPF-% and schistocyte count regarding discrimination between patients with TTP/HUS or SPE/HELLP (P-value >0.05) **(Table 19), (Figure 25)**.

Table (19): Comparison of ROC curves for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF or schistocyte count

Index	IPF	Schistocyte count	Difference	z	P-value¶
Area under ROC (AUC)	0.692 (0.519 to 0.833)	0.771 (0.603 to 0.893)	0.079 (-0.171 to 0.328)	0.617	0.537

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

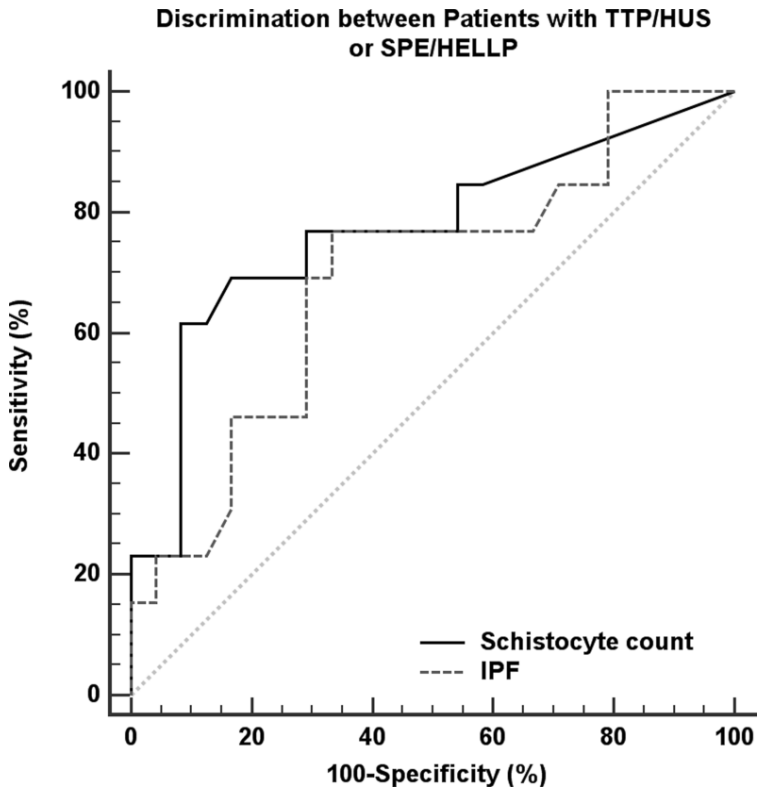

Figure (25): Comparison of ROC curves for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF or schistocyte count.

Table (20): ROC curve analysis for discrimination between patients with TMA and normal controls using the IPF-%s or schistocyte count

Index	**IPF-%**	**Schistocyte count**
Positive group (TMA)	37 (64.9%)	37 (64.9%)
Negative group (normal controls)	20 (35.1%)	20 (35.1%)
Area under the ROC curve (AUC)	0.820 (0.695 to 0.909)	0.838 (0.716 to 0.922)
z statistic	5.678	8.660
P-value	**<0.0001¶**	**<0.0001¶**
Associated cut-off criterion	>8.1 %	>0 %
Sensitivity (%)	86.49 (71.2 - 95.5)	67.57 (50.2 - 82.0)
Specificity (%)	65.00 (40.8 - 84.6)	100.00 (83.2 - 100.0)
Positive predictive value (PPV, %)	82.1 (66.5 - 92.5)	100.0 (86.3 - 100.0)
Negative predictive value (NPV, %)	72.2 (46.5 - 90.3)	62.5 (43.7 - 78.9)

Diagnostic indices are presented as value (95% CI).

¶DeLong method.

- **(ROC) curve analysis for discrimination between patients with TMA or control using the IPF-%:** The optimal cutoff values for IPF-% for discrimination between patients with TMA or control was >8.1%. The sensitivity and specificity were 86.49% and 65%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 82.1 % and 72.2%, respectively **(Table 20), (Figure 26).**

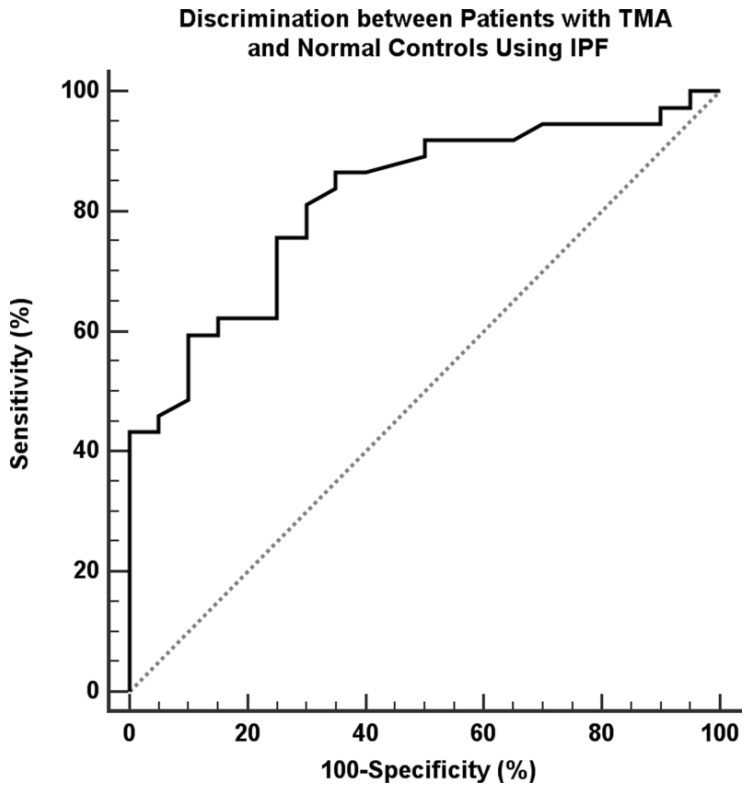

Figure (26): ROC curve for discrimination between patients with TMA and normal controls using the IPF.

- **<u>(ROC) curve analysis for discrimination between patients with TMA or control using schistocyte count:</u>** The optimal cutoff values for schistocyte count for discrimination between patients with TMA and normal controls was >0 %. The sensitivity and specificity were 67.57 % and 100%, respectively. The PPV and NPV were 100 % and 62.5%, respectively **(Table 20)**, (**Figure 27).**

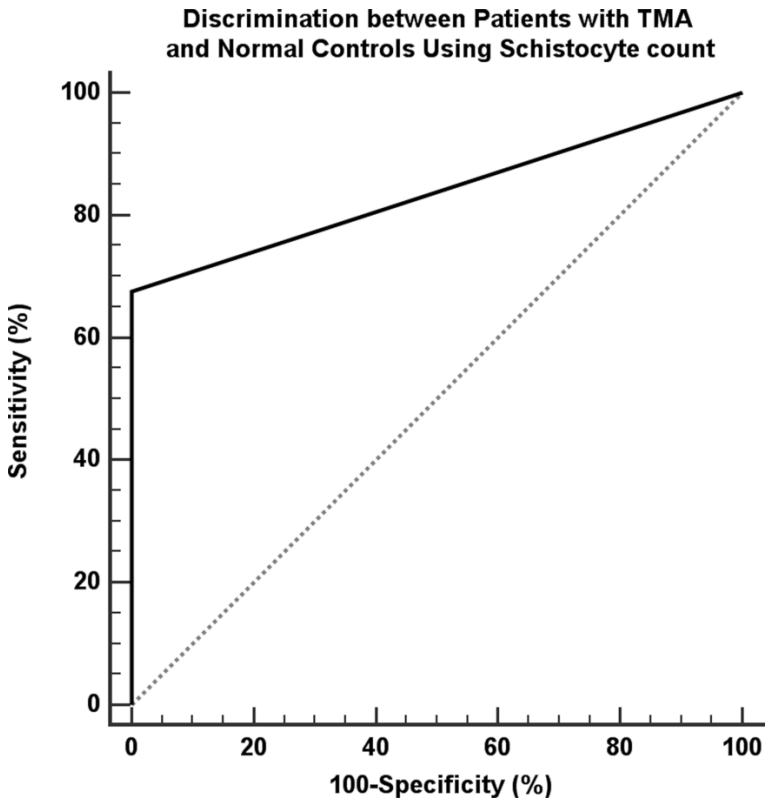

Figure (27): ROC curve for discrimination between patients with TMA and normal controls using the schistocyte count.

- **<u>Comparison of the receiver-operating characteristic (ROC) curves:</u>**

Comparison of the receiver-operating characteristic (ROC) curves between IPF-% or schistocyte count for discrimination between patients with TMA and normal controls revealed no significant difference between IPF and schistocyte count regarding discrimination between patients with TMA and controls (P >0.05) **(Table 21), (Figure 28)**.

Table (21): ROC curves for discrimination between patients with TMA and normal controls using the IPF or schistocyte count

Index	**IPF-%**	**Schistocyte count**	**Difference**	**z**	**P-value¶**
Area under ROC (AUC)	0.820 (0.695 to 0.909)	0.838 (0.716 to 0.922)	0.018 (-0.105 to 0.142)	0.290	0.7722

Diagnostic indices are presented as value (95% CI).

¶DeLong method

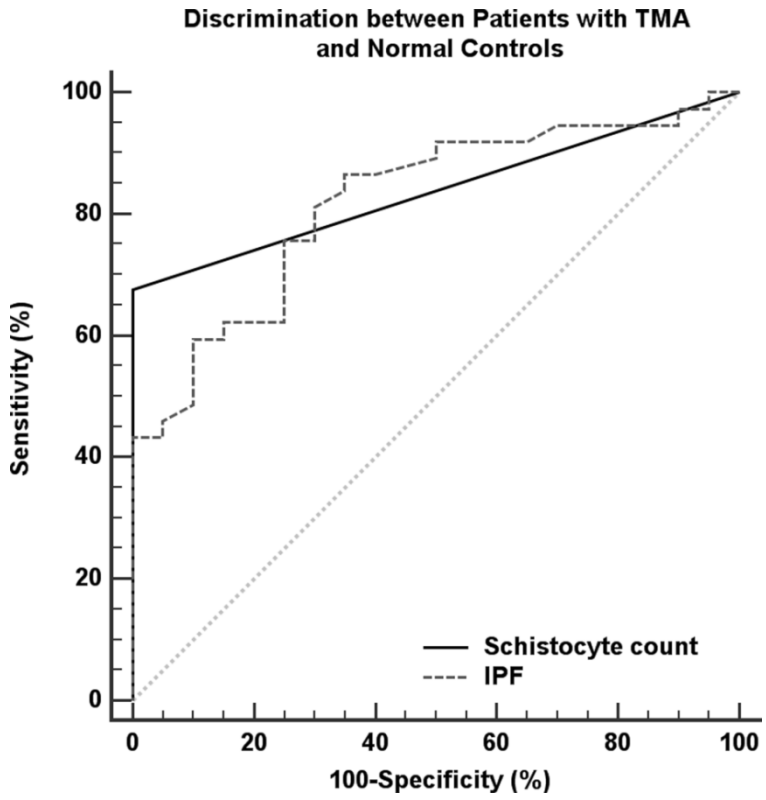

Figure (28): ROC curves for discrimination between patients with TMA and normal controls using the IPF or schistocyte count.

Correlation between IPF and schistocytes count with different parameters

no significant correlation was found between the IPF-% and schistocytes count in patients with SPE/HELLP, or TTP/HUS, as well as the whole TMA study group **(Figure 29), (Table 22)**.

Table (22): Correlation between the IPF-% and schistocytes count in whole study population, patients with TMA, SPE/HELLP, or TTP/HUS, and normal controls

	Correlation between IPF % and schistocyte count		
Group	**Number**	**Spearman rho (ρ)**	**P-value**
TMA	37	0.231	0.169

SPE/HELLP	24	0.190	0.375
TTP/HUS	13	-0.058	0.851

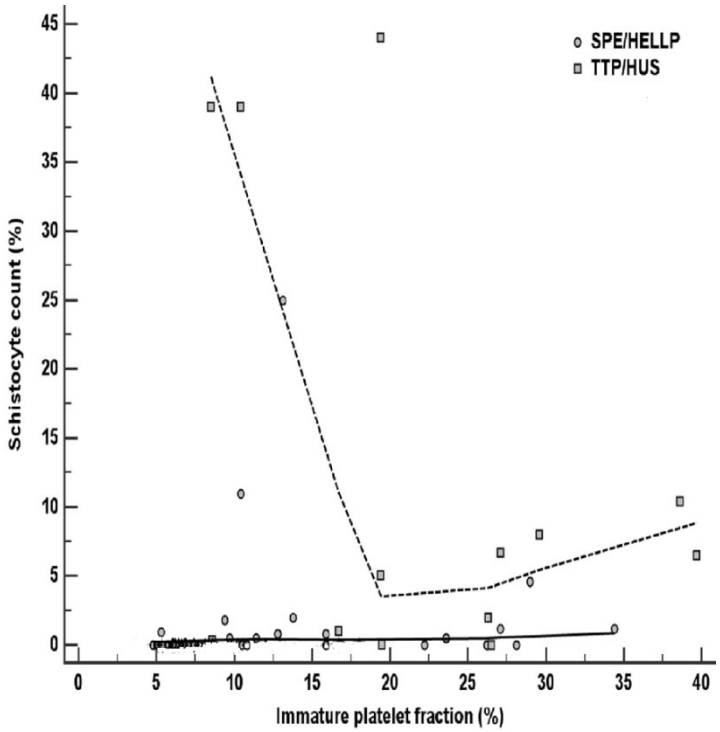

Figure (29): Scatter plot showing the correlation between the IPF and schistocyte count in patients with SPE/HELLP or TTP/HUS.

IPF-% and schistocytes counts in TTP/HUS and SPE/HELLP using multivariate analysis

Multivariable binary logistic regression analysis was used for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF-% and schistocyte count combined. Both IPF-% (odds ratio, 1.11; 95% CI, 1.010 to 1.220; p= 0.031) and schistocyte count (odds ratio, 1.113; 95% CI, 1.016 to 1.219; p= 0.022) were independent predictors for TTP/HUS.

Table (23): Multivariable binary logistic regression analysis for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF and schistocyte count combined

Variable	Regression coefficient (B)	SE for B	Wald	P-value	Odds ratio (OR)	95% CI for OR
IPF (%)	0.104	0.048	4.666	**0.031**	1.110	1.010 to 1.220
Schistocyte count (%)	0.107	0.046	5.283	**0.022**	1.113	1.016 to 1.219
Constant	-3.251					

Table (24): Receiver-operating characteristic (ROC) curve derived from the multivariable binary logistic regression model for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF-% and schistocyte count combined

Sample size	37
Positive group (TTP/HUS)	13 (35.1%)
Negative group (SPE/HELLP)	24 (64.9%)
Disease prevalence (%)	35.1

Index	**Value**
Area under the ROC curve (AUC)	0.827 (0.667 to 0.931)
z statistic	4.385
P-value	**<0.0001**
Sensitivity (%)	92.3 (64.0 - 99.8)
Specificity (%)	62.5 (40.6 - 81.2)
Positive likelihood ratio (+LR)	2.46 (1.4 - 4.2)
Positive likelihood ratio (-LR)	0.12 (0.02 - 0.8)
PPV, %	57.1 (34.0 - 78.2)
NPV, %	93.7 (69.8 - 99.8)

Diagnostic indices are presented as value (95% CI).
¶DeLong method.

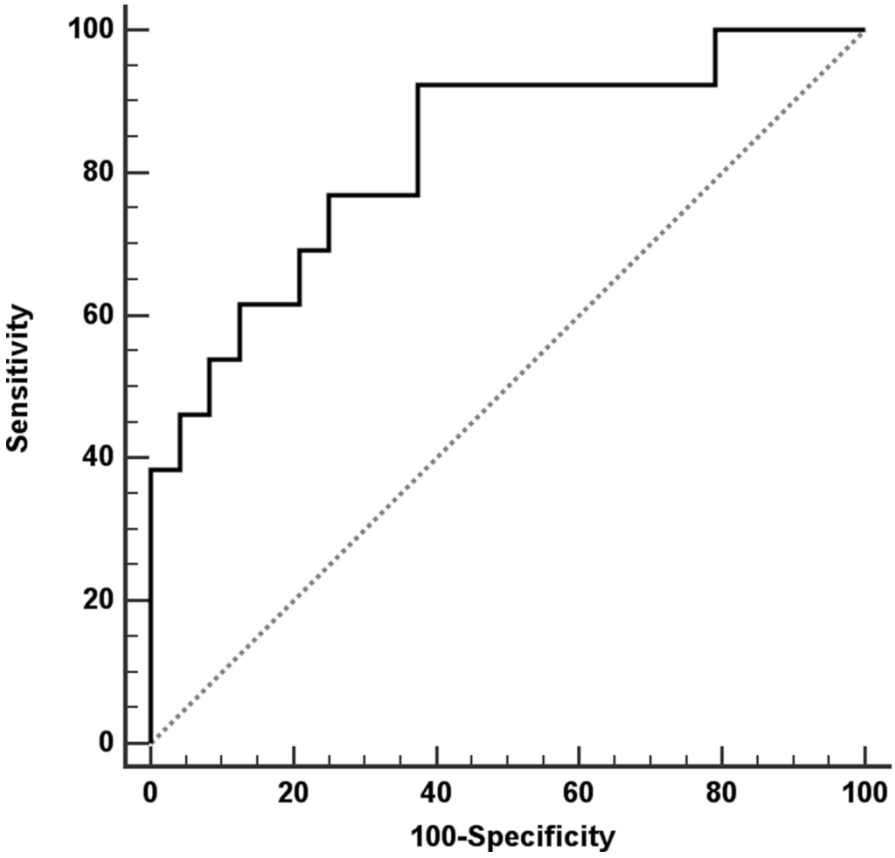

Figure (30): Discrimination between patients with TTP/HUS or SPE/HELLP using IPF-% and schistocyte count combined.

Table 24 and Figure 30 shows the results of ROC curve analysis derived from the predicted probabilities as estimated from the multivariable binary logistic regression model for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF and schistocyte count combined.

Table (25): Comparison of the receiver-operating characteristic (ROC) curves for discrimination between patients with TTP/HUS or SPE/HELLP using the IPF, schistocyte count, or IPF and schistocyte count combined

Marker	AUC	95% CI
IPF-%	0.692	0.519 to 0.833
Schistocyte count	0.771	0.603 to 0.893

IPF-% and schistocyte count combined	0.827	0.667 to 0.931

Marker	Difference between AUCs	95% CI	Z statistic	p-value
IPF-% vs. Schistocyte count	0.079	-0.171 to 0.328	0.617	0.537
IPF-% vs. IPF and Schistocyte count combined	0.135	-0.034 to 0.303	1.569	0.117
Schistocyte count vs. IPF-% and schistocyte count combined	0.056	-0.085 to 0.197	0.780	0.435

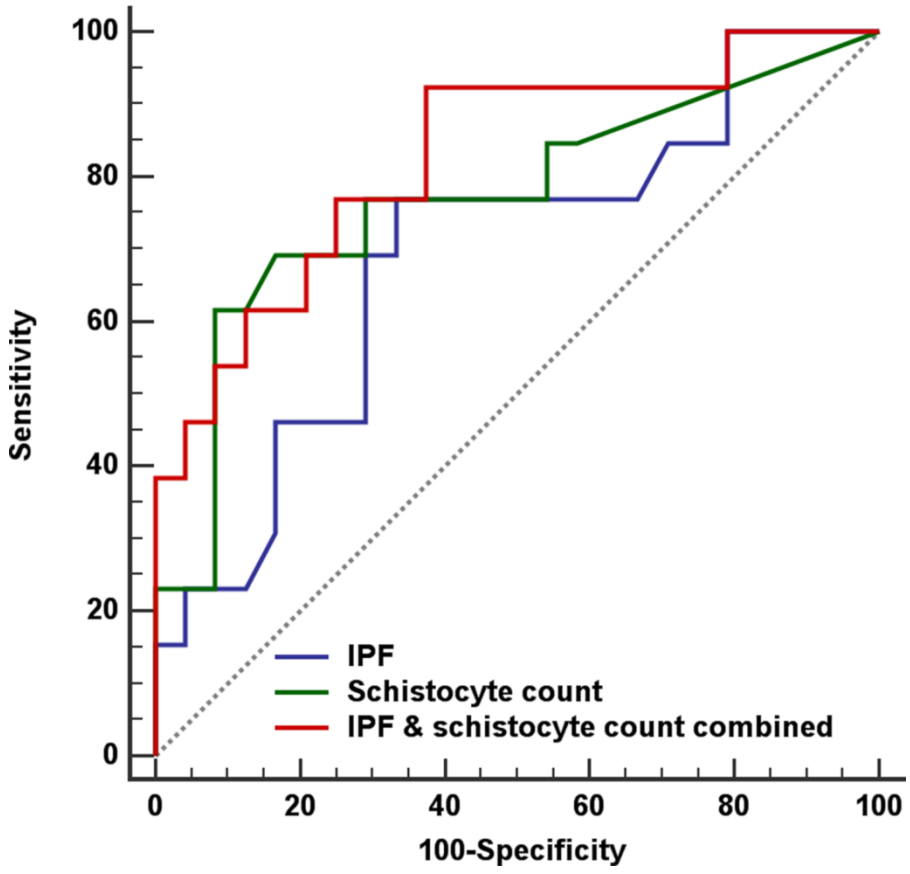

Figure (31): Discrimination between patients with TTP/HUS or SPE/HELLP.

The model had good predictive value as evidenced by increased AUC of 0.827 (95% CI, 0.667 to 0.931). The estimated sensitivity was 92.3% (64.0% - 99.8%), specificity of 62.5% (40.6% - 81.2%), PPV of 57.1%

(34.0% - 78.2%), and NPV of 93.7% (69.8% - 99.8%). However, no statistically significant difference (P >0.05) was revealed on comparing the AUC value of ROC curve of the combined use of IPF-% and schistocyte counts to AUC values of ROC curves of either marker alone for discrimination between patients with TTP/HUS or SPE/HELLP (Table 25, Figure 31).