Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and Prognosis of Patient Initially Diagnosed as HELLP Syndrome

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Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and Prognosis of Patient Initially Diagnosed as HELLP Syndrome (Study results)

Results

The current study was conducted at Ain Shams University Maternity Hospital during the period between January2015 and December 2015. A total of 100 women with an initial diagnosis of HELLP syndrome were recruited in the study. Blood sample taken within 12hrs peripartum and patients followed up 48hrs after delivery and subdivided in to 2 groups according to improvement or deterioration after 48hrs after delivery . All results were collected, tabulated and statistically analyzed.

Table-4 and figures 8-10 show the initial characteristics of included women.

Table-4 Initial Characteristics of Included Women .

Age (years)	
Range	18 – 38
Mean ± SD	27.51 ± 4.98
Parity	
Range	0 – 5
Median (IQR)	1 (1 – 2)
Gestational Age (weeks)	
Range	27 – 38
Mean ± SD	34.3 ± 2.91

SD standard deviation

IQR interquartile range [central 50% of ascendingly-ordered set of data]

Data presented as range, mean ± SD; or range, median (IQR)

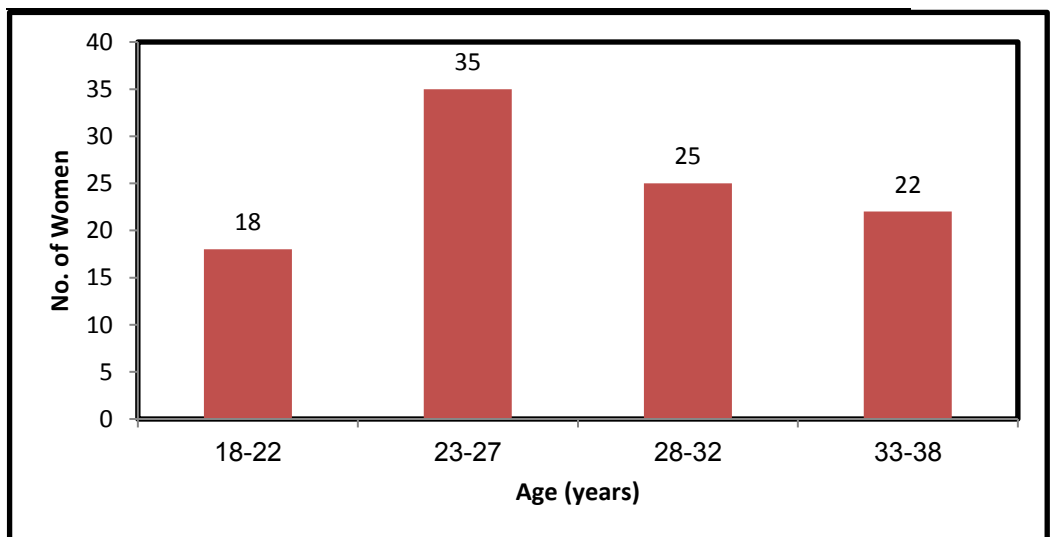**Figure-8** Bar-Chart showing Maternal Age Distribution in Included Women .

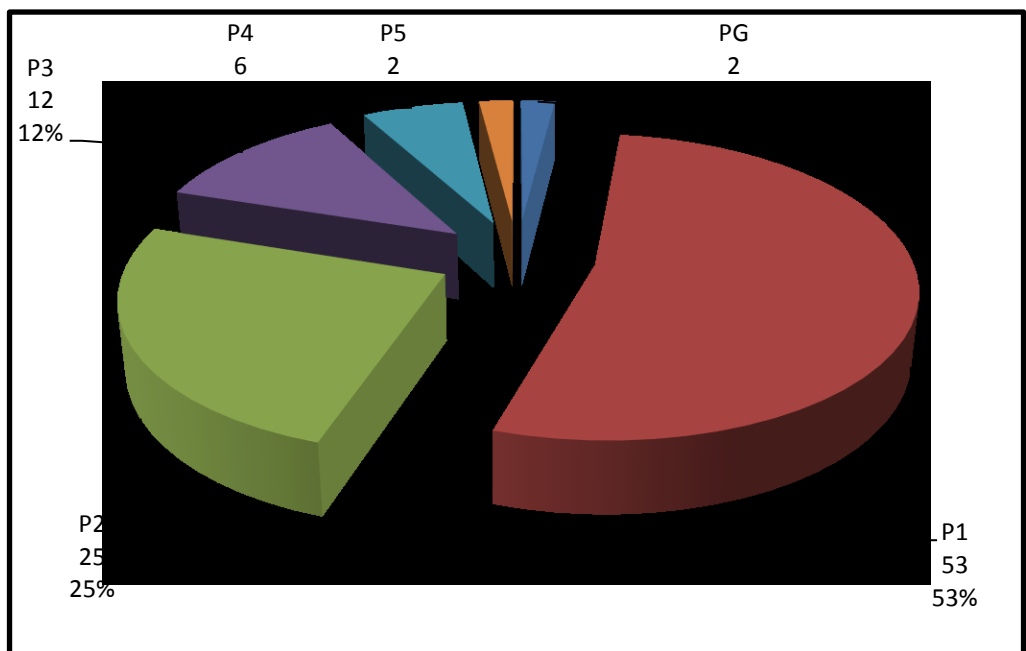**Figure-9** Pie-Chart showing Parity Distribution in Included Women .

Figure-10 Bar-Chart showing Gestational Age Distribution in Included Women .
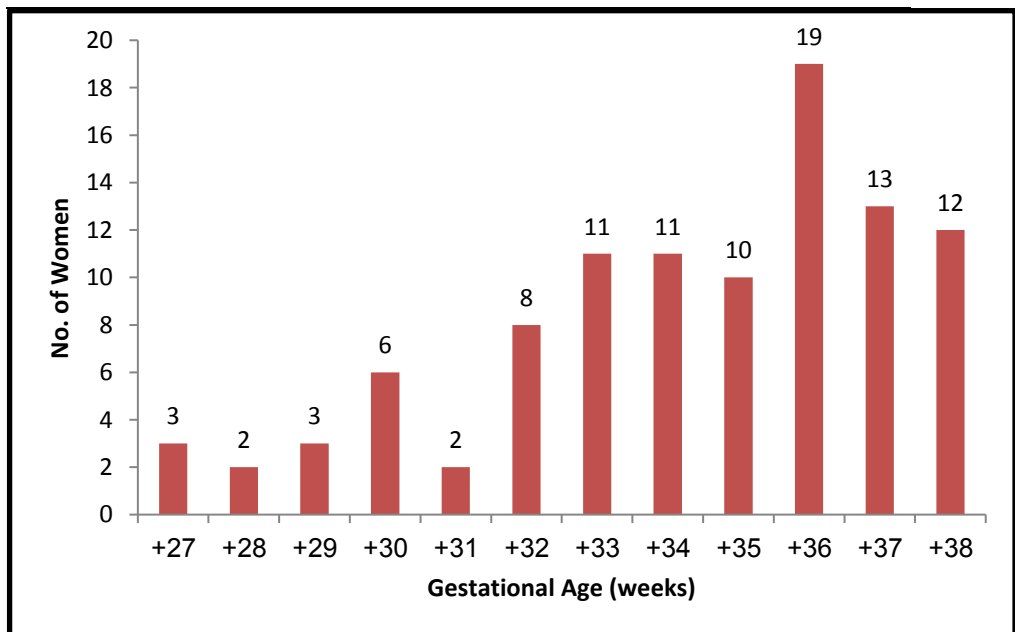
Table-5 and figures 11-18 show the initial clinical and laboratory data of included women.

Table-5 Initial Clinical and Laboratory Data in Included Women .

Initial Data	
Systolic Blood Pressure (mm Hg) **Range** **Median (IQR)**	170 – 240 180 (170 – 190)
Diastolic Blood Pressure (mm Hg) **Range** **Median (IQR)**	90 – 150 100 (100 – 120)
Albuminuria **3+** **4+** **5+**	41 (41%) 32 (32%) 27 (27%)
Hb Concentration (g/dl) **Range** **Median (IQR)**	6.5 – 9.8 8.7 (8 – 9)
Platelet Count (x 10,000 per mm^3) **Range** **Median (IQR)**	28 – 97 77 (67 – 85)
Serum ALT (u/l) **Range** **Median (IQR)**	91 – 895 200 (149 – 278)
Serum AST (u/l) **Range** **Median (IQR)**	79 – 779 179 (135 – 250)
Serum Total Bilirubin (mg/dl) **Range** **Median (IQR)**	1.2 – 7.9 2.3 (1.6 – 3.3)
Serum Creatinine (mg/dl) **Range** **Median (IQR)**	1.4 – 6.3 1.9 (1.8 – 2.1)

IQR interquartile range [central 50% of ascendingly-ordered set of data]
Data presented as range, median (IQR); or number (percentage)
Hb hemoglobin
ALT alanine transaminase
AST aspartate transaminase

Figure-11 Box-Plot Chart showing Initial Systolic and Diastolic Blood Pressure in Included Women .
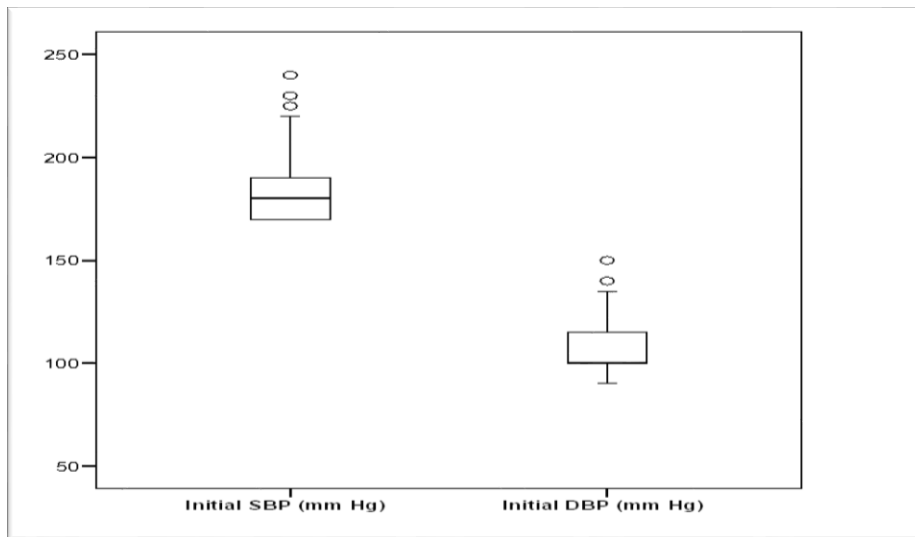

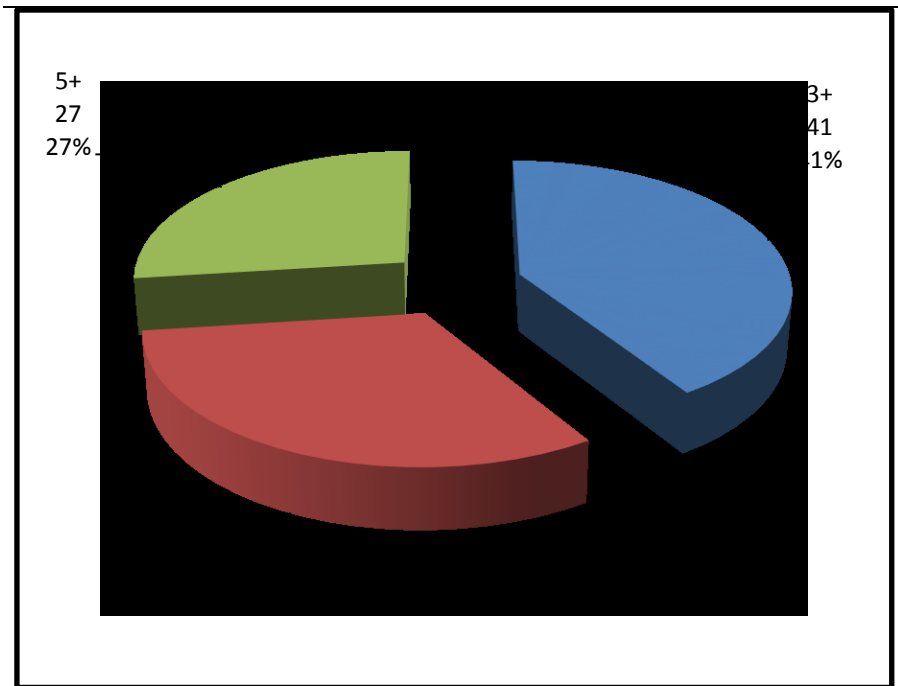**Figure-12** Pie-Chart showing Albuminuria in Included Women .

5+
27
27%

3+
41
41%

Figure-13 Box-Plot Chart showing Initial Hb Concentration
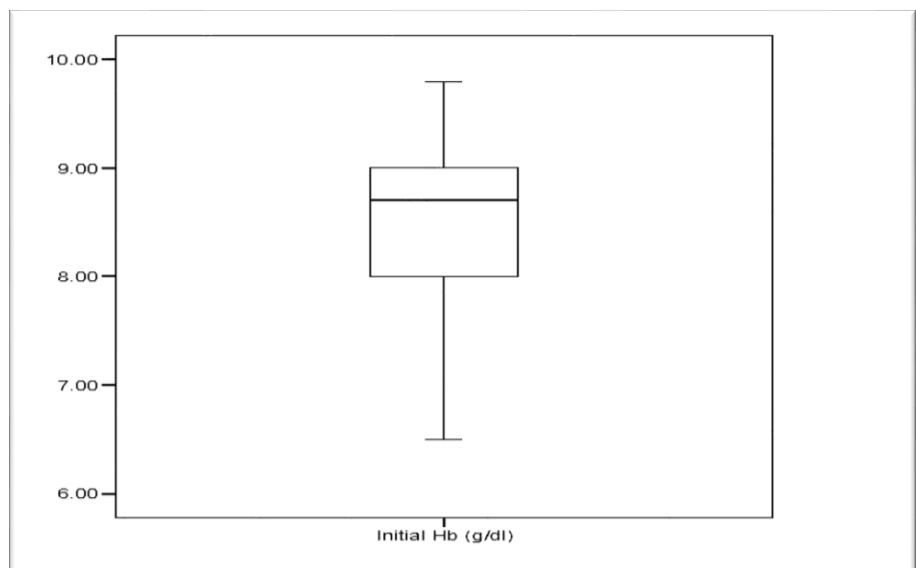in Included Women .

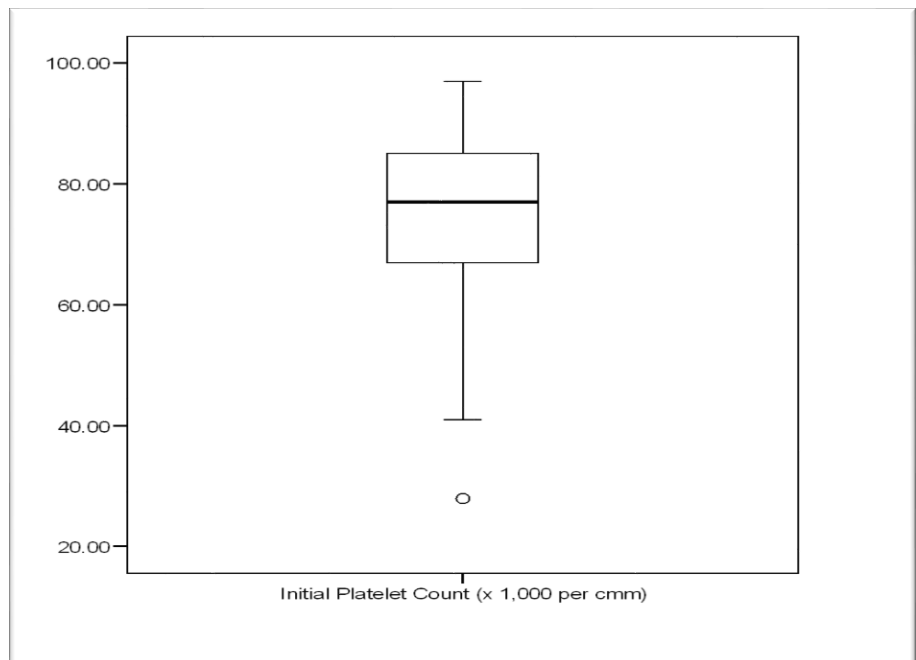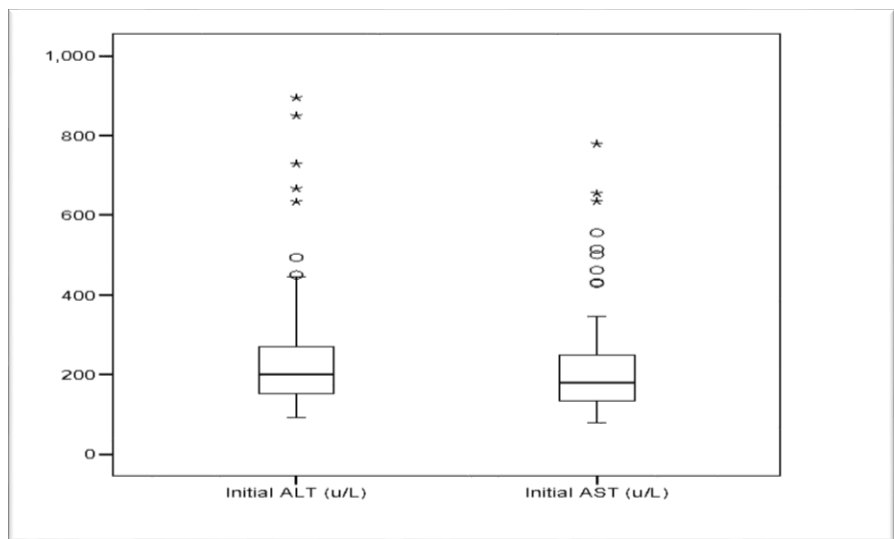**Figure-14** Box-Plot Chart showing Initial Platelet Count in Included Women .

Figure-15 Box-Plot Chart showing Initial Liver

Transaminases in Included Women .

Figure-16 Box-Plot Chart showing Initial Serum Bilirubin and Creatinine in Included Women .
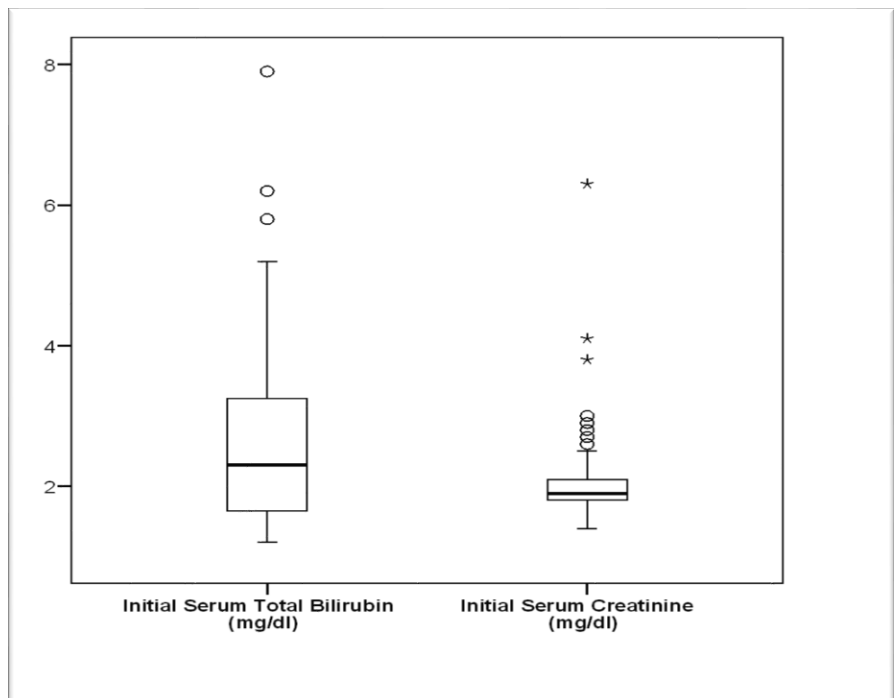

Table-6 and figures 17-21 show the clinical and laboratory data 48 hours postpartum in included women.

Table-6 Clinical and Laboratory Data 48 hours Postpartum in Included Women .

Data 48 hours Postpartum	
Systolic Blood Pressure (mm Hg) **Range** **Median (IQR)**	110 – 230 135 (120 – 185)
Diastolic Blood Pressure (mm Hg) **Range** **Median (IQR)**	60 – 130 90 (70 – 100)
Hb Concentration (g/dl) **Range** **Median (IQR)**	5 – 13.3 9.7 (7.12 – 11)
Platelet Count (x 10,000 per mm^3) **Range** **Median (IQR)**	20 – 303 115 (65 – 135)
Serum ALT (u/l) **Range** **Median (IQR)**	7 – 2165 55 (25 – 281.5)
Serum AST (u/l) **Range** **Median (IQR)**	7 – 2143 36 (15 – 250)
Serum Total Bilirubin (mg/dl) **Range** **Median (IQR)**	0.1 – 10 1.3 (1.1 – 1.8)
Serum Creatinine (mg/dl) **Range** **Median (IQR)**	0.5 – 14.5 0.75 (0.6 – 2.75)

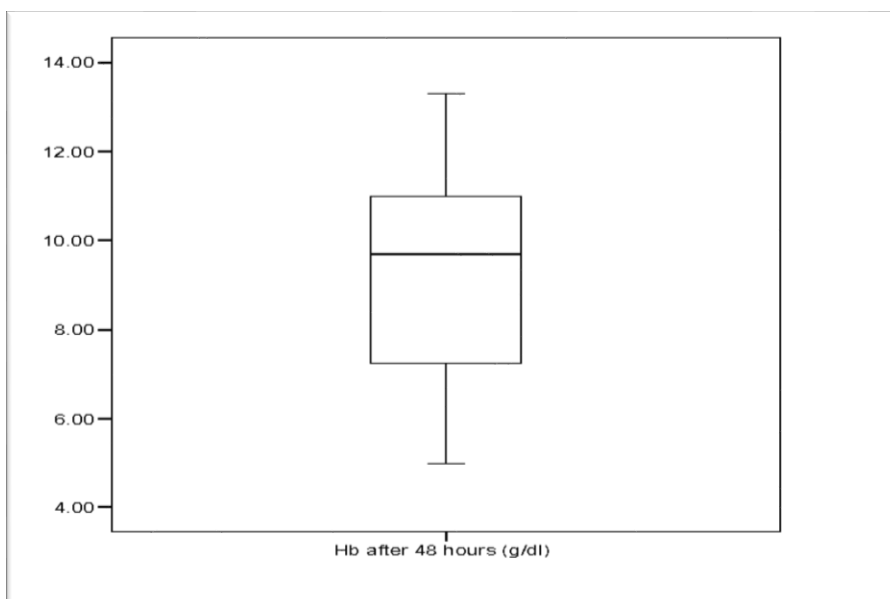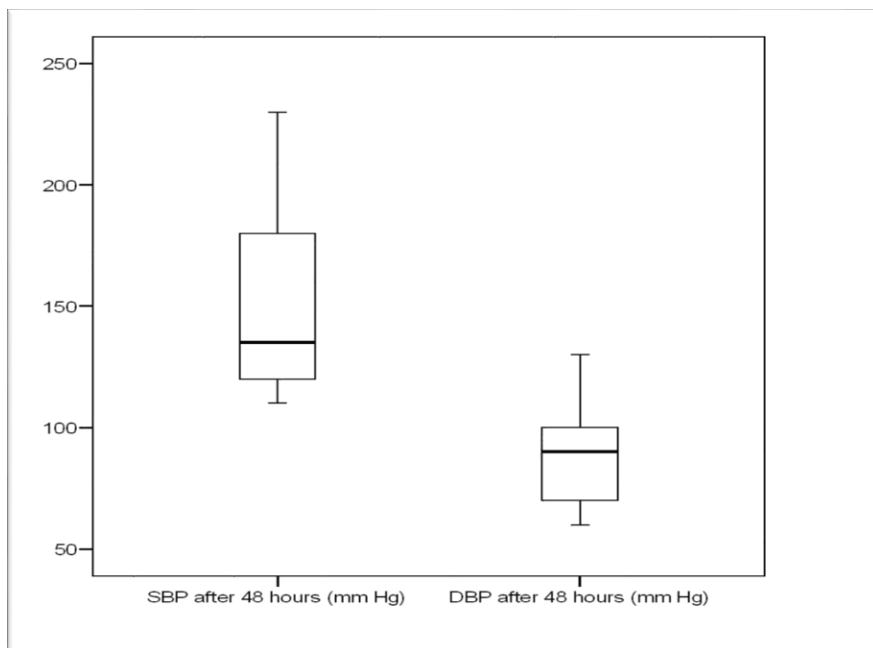IQR interquartile range [central 50% of ascendingly-ordered set of data]

Data presented as range, median (IQR)

Hb hemoglobin

ALT alanine transaminase
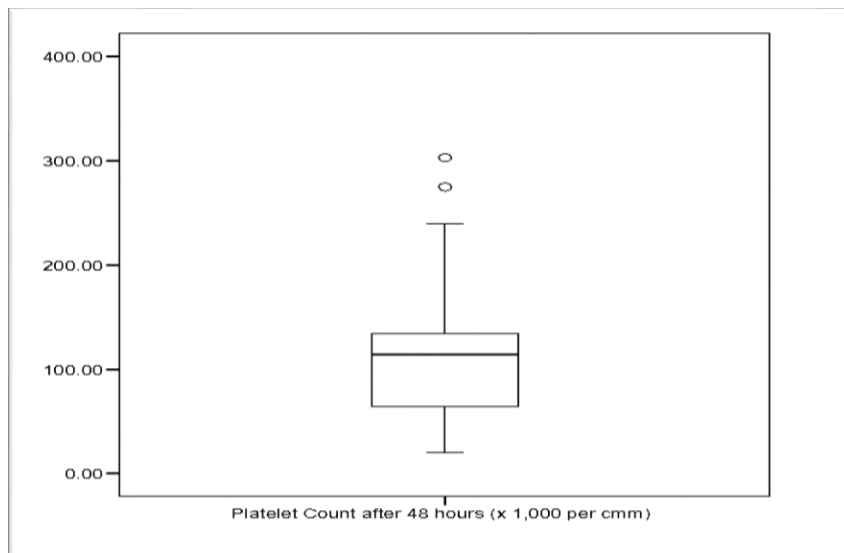
AST aspartate transaminase

Figure-17 Box-Plot Chart showing Systolic and Diastolic

Blood Pressure 48 hours Postpartum in Included Women.
Figure-18 Box-Plot Chart showing Hb Concentration 48 hours Postpartum in Included Women .

Figure-19 Box-Plot Chart showing Platelet Count 48 hours

Postpartum in Included Women .

Figure-20 Box-Plot Chart showing Liver Transaminases 48 hours Postpartum in Included Women .

Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and Prognosis of Patient Initially Diagnosed as HELLP Syndrome (Study results)
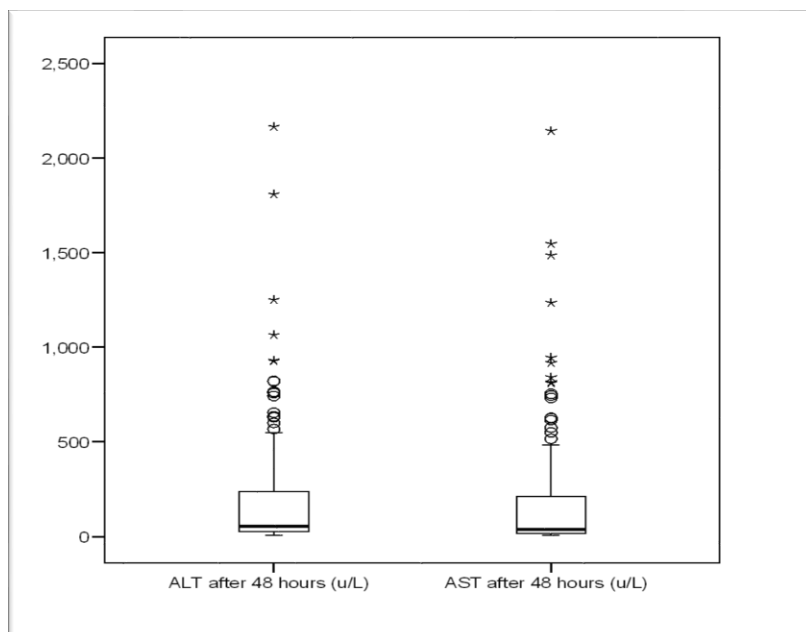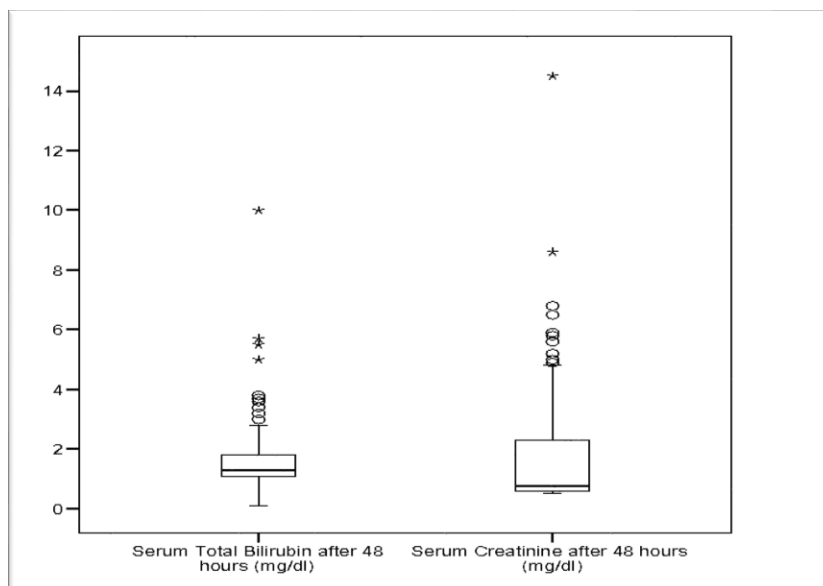
Figure-21 Box-Plot Chart showing Serum Bilirubin and

Creatinine 48 hours Postpartum in Included Women .
Of the included 100 women, 25 (25%) women showed clinical and laboratory deterioration 48 hours postpartum. All women who deteriorated postpartum received plasma exchange. Of the included 100 women, 3 (3%) died (table-7, figures 22-23).

Table-7 Postpartum Deterioration and Mortality in Included Women .

Postpartum Deterioration	
Yes	25 (25%)
No	75 (75%)
Received Plasma Exchange-steroids	
Yes	25 (25%)
No	75 (75%)
Maternal Mortality	
Yes	3 (3%)

No	97 (100%)

Data presented as number (percentage)

Figure-22 Pie-Chart showing Postpartum Deterioration in Included Women .
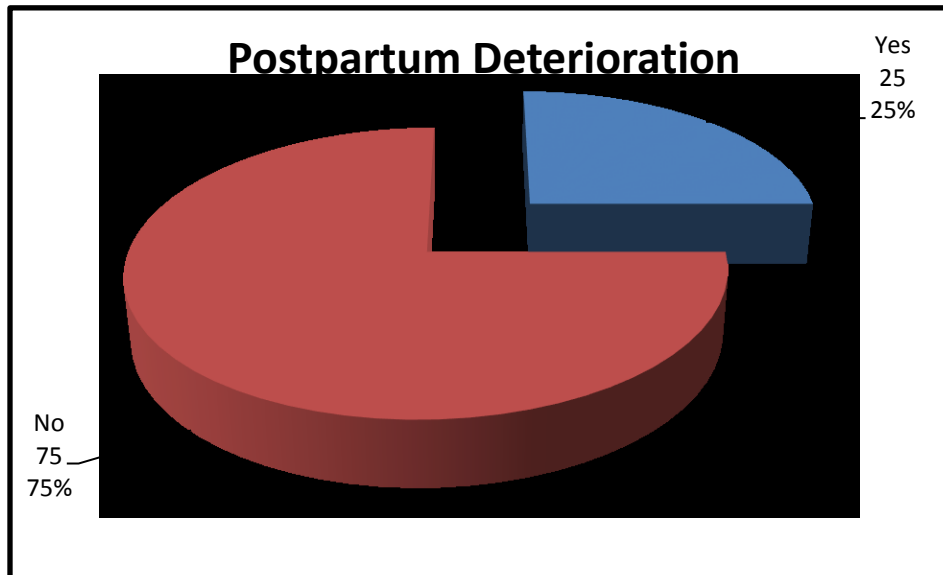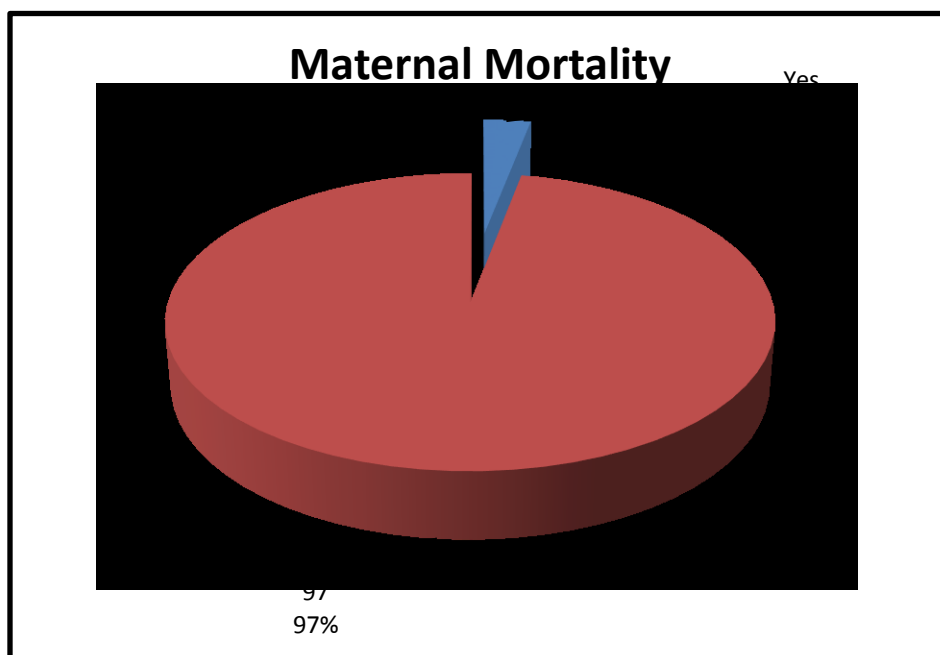

Figure-23 Pie-Chart showing Maternal Mortality in Included Wome .

There were no significant differences between women who deteriorated postpartum and women who did not regarding age, parity or gestational age (table-8, figures 24-26).

Table-8 Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial Characteristics .

	Women who Deteriorated Postpartum (n=25)	Women who Did not Deteriorate Postpartum (n=75)	*P*
Age (years) **Range** **Mean ± SD**	18 – 35 27.08 ± 4.58	18 – 38 27.65 ± 5.13	0.621* NS
Parity **Range** **Median (IQR)**	1 – 4 1 (1 – 2)	0 – 5 1 (1 – 2)	0.972** NS
Gestational Age (weeks) **Range** **Mean ± SD**	27 – 38 33.88 ± 3.14	27 – 38 34.44 ± 2.83	0.407* NS

SD standard deviation

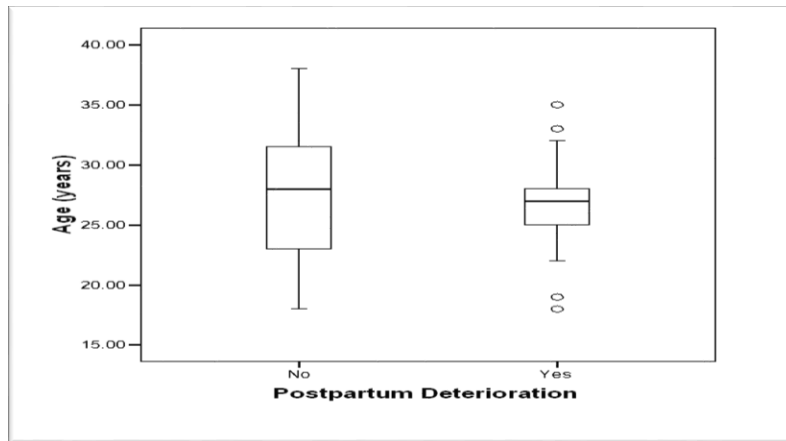IQR interquartile range [central 50% of ascendingly-ordered set of data]

Data presented as range, mean ± SD; or range, median (IQR)
* Analysis using Independent Student's t-test
** Analysis using Mann-Whitney's U-Test
NS non-significant

Figure-24 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Maternal Age .

Figure-25 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did not regarding Parity .

Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and Prognosis of Patient Initially Diagnosed as HELLP Syndrome (Study results)
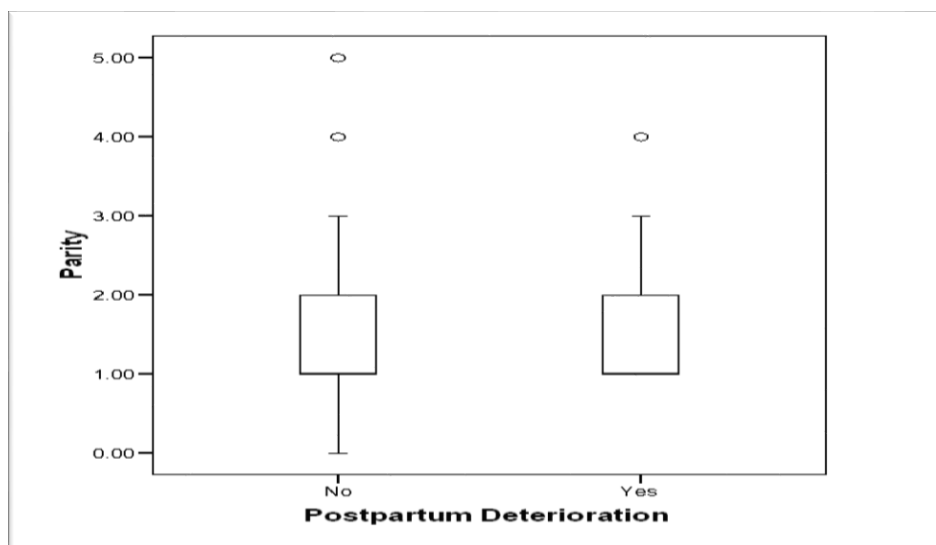
Figure-26 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Gestational Age .

There were no significant differences between women who deteriorated postpartum and women who did not regarding the initial values of systolic blood pressure, diastolic blood pressure, albuminuria, hemoglobin concentration, platelet count or serum creatinine. The initial levels of serum ALT, AST and total bilirubin were, however, significantly, higher in women who deteriorated postpartum (table-9, figures 27-34).

Table-9 Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial Clinical and Laboratory Data .

Initial Data	Women who Deteriorated Postpartum (n=25)	Women who Did not Deteriorate Postpartum (n=75)	*P*
Systolic Blood Pressure (mm Hg) **Range**	170 – 190	170 – 240	0.366*

Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and
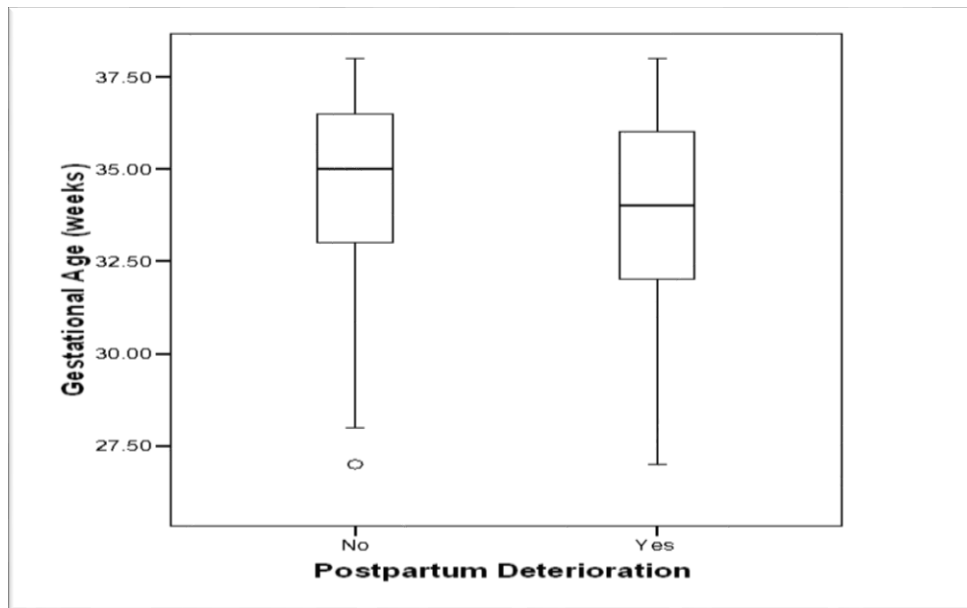*Prognosis of Patient Initially Diagnosed as HELLP Syndrome (Study results)*

Median (IQR)	180 (170 – 190)	180 (170 – 190)	NS
Diastolic Blood Pressure (mm Hg)			
Range	100 – 130	90 – 150	0.123*
Median (IQR)	100 (100 – 110)	110 (100 – 120)	NS
Albuminuria			
3+	13 (52%)	28 (37.7%)	
4+	5 (20%)	27 (36%)	0.287**
5+	7 (28%)	20 (26.7%)	NS
Hb Concentration (g/dl)			
Range	6.6 – 9.5	6.5 – 9.8	0.747*
Median (IQR)	8.6 (7.5 – 9.05)	8.7 (8 – 9)	NS
Platelet Count (x 10,000 per mm³)			
Range	41 – 90	28 – 97	0.285*
Median (IQR)	70 (58 – 85)	78 (67 – 85)	NS
Serum ALT (u/l)			
Range	91 – 895	95 – 494	0.043*
Median (IQR)	287 (145 – 448)	196 (155 – 233)	S
Serum AST (u/l)			
Range	87 – 779	79 – 515	0.004*
Median (IQR)	256 (155 – 430)	170 (125 – 224)	S
Serum Total Bilirubin (mg/dl)			
Range	1.4 – 7.9	1.2 – 5.2	<0.001*
Median (IQR)	3.4 (2.4 – 4.2)	1.9 (1.6 – 2.7)	HS
Serum Creatinine (mg/dl)			
Range	1.5 – 6.3	1.4 – 3.8	0.105*
Median (IQR)	2 (1.8 – 2.3)	1.9 (1.8 – 2)	NS

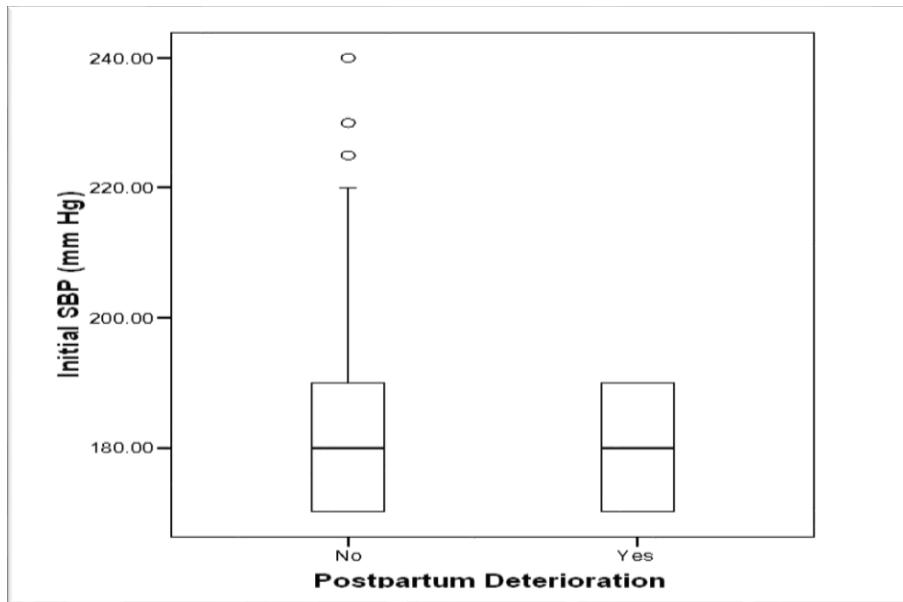IQR interquartile range [central 50% of ascendingly-ordered set of data]
Data presented as range, median (IQR); or number (percentage)
* Analysis using Mann-Whitney's U-Test
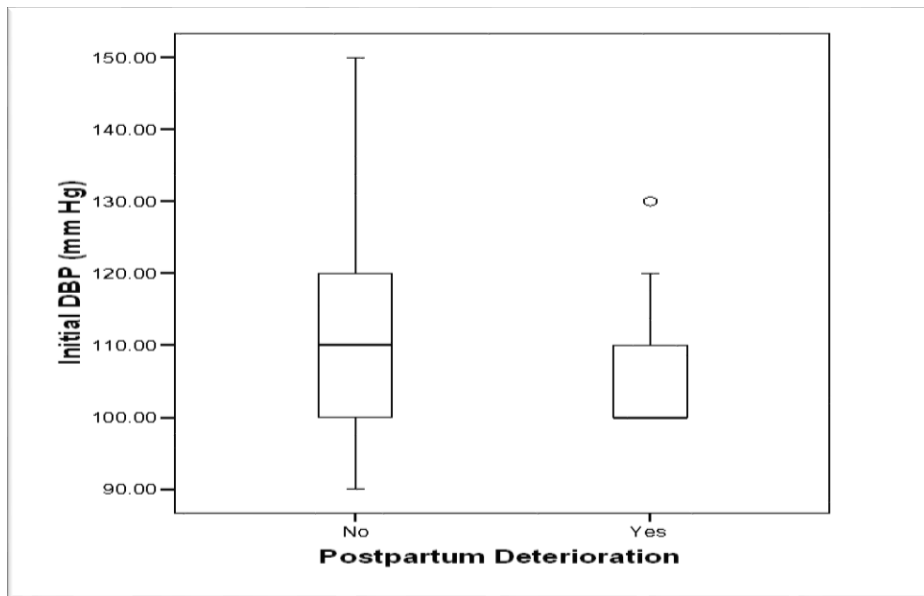** Analysis using Chi-squared Test
NS non-significant – S significant – HS highly significant

Figure-27 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Initial Systolic Blood Pressure .

Figure-28 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Initial Diastolic Blood Pressure .

Figure-29 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial Hemoglobin Concentration .
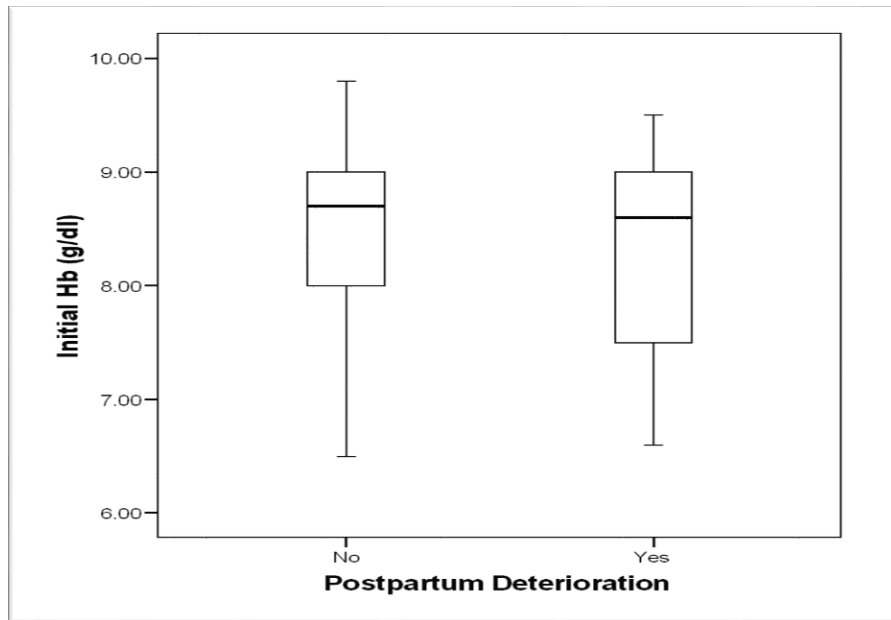

Figure-30 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial Platelet Count .
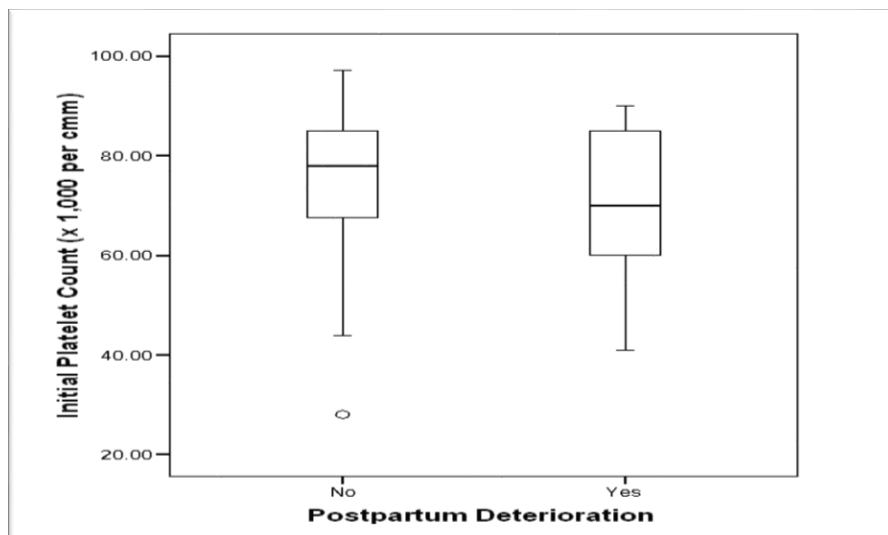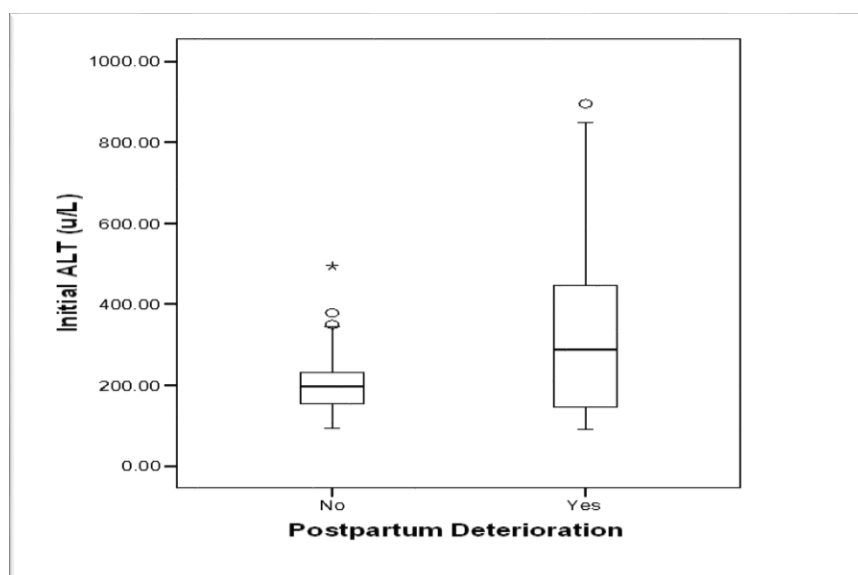
Figure-31 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Initial ALT .

Figure-32 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial AST .
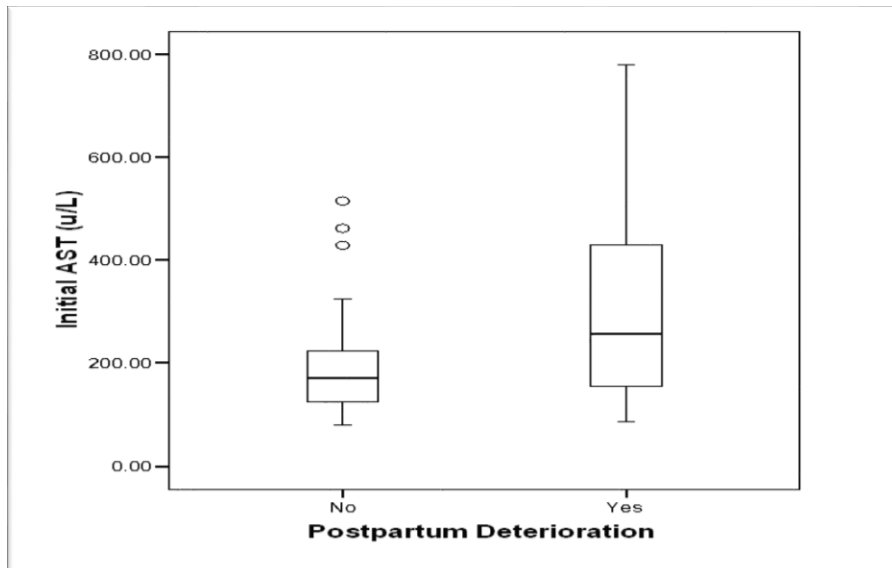

Figure-33 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did not regarding Initial Serum Total Bilirubin .
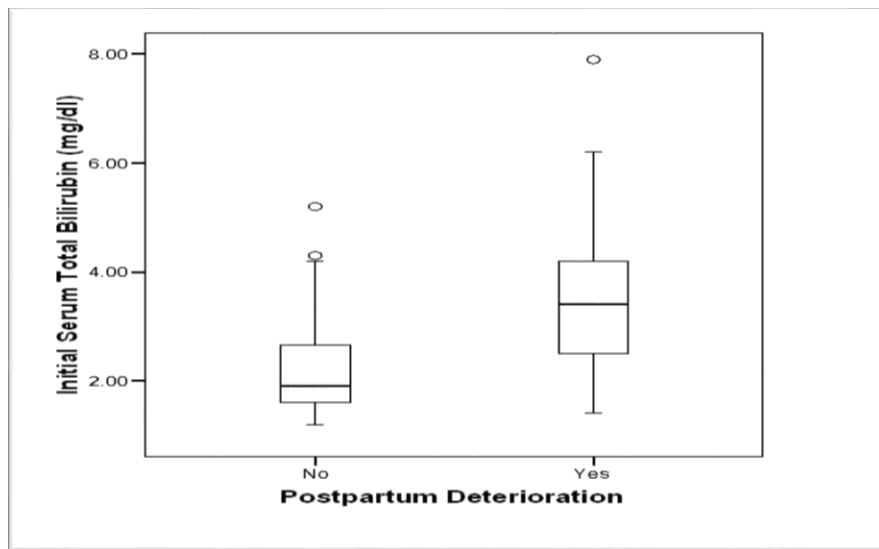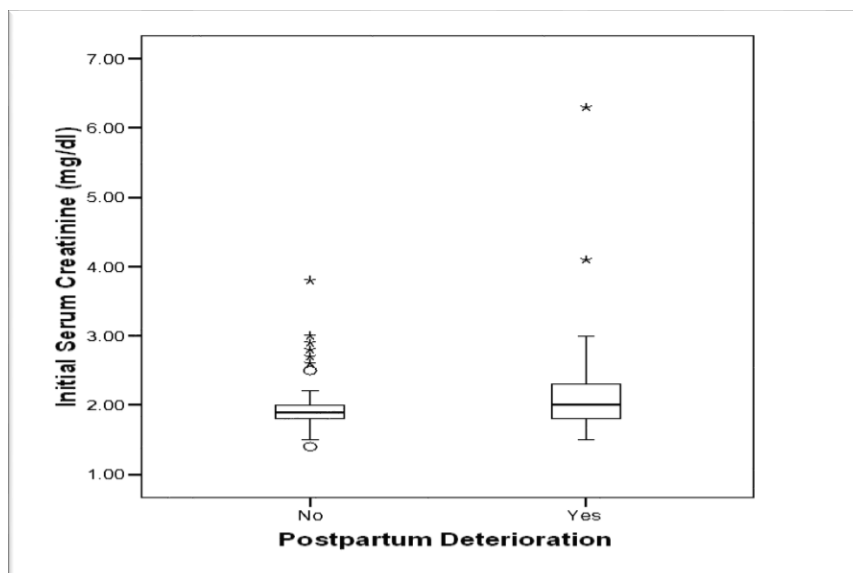
Figure-34 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Initial Serum Creatinine .

The median schistocytes percentage was significantly higher in women who showed postpartum deterioration, when compared to women who did not deteriorate (table-10, figure-35).

Table-10 Difference between Women who Deteriorated Postpartum and Women who did not regarding Schistocytes Percentage .

	Women who Deteriorated Postpartum (n=25)	Women who Did not Deteriorate Postpartum (n=75)	*P*
Schistocytes (%) **Range** **Median (IQR)**	0 – 44 5.5 (2 – 8.4)	0 – 6 0.5 (0.05 – 0.7)	<0.001* HS

IQR interquartile range [central 50% of ascendingly-ordered set of data]
Data presented as range, median (IQR)
* Analysis using Mann-Whitney's U-Test
HS highly significant

Figure-35 Box-Plot Chart showing Difference between Women who Deteriorated Postpartum and Women who did

not regarding Schistocytes Percentage .

The median schistocytes percentage was significantly higher in women who died when compared to women who survived (table-11, figure-36).

Table-11 Difference between Women who Died and Women who Survived regarding Schistocytes Percentage .

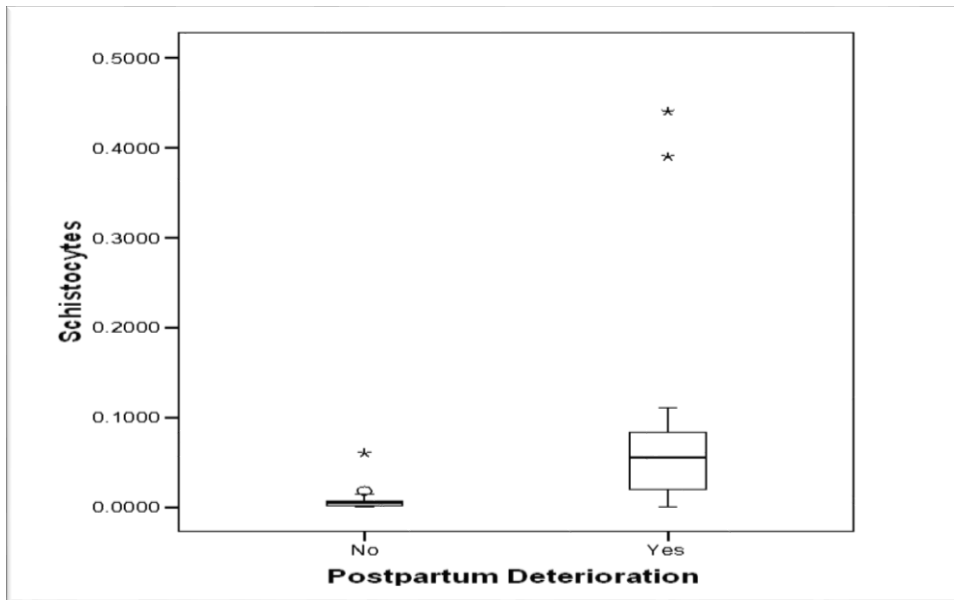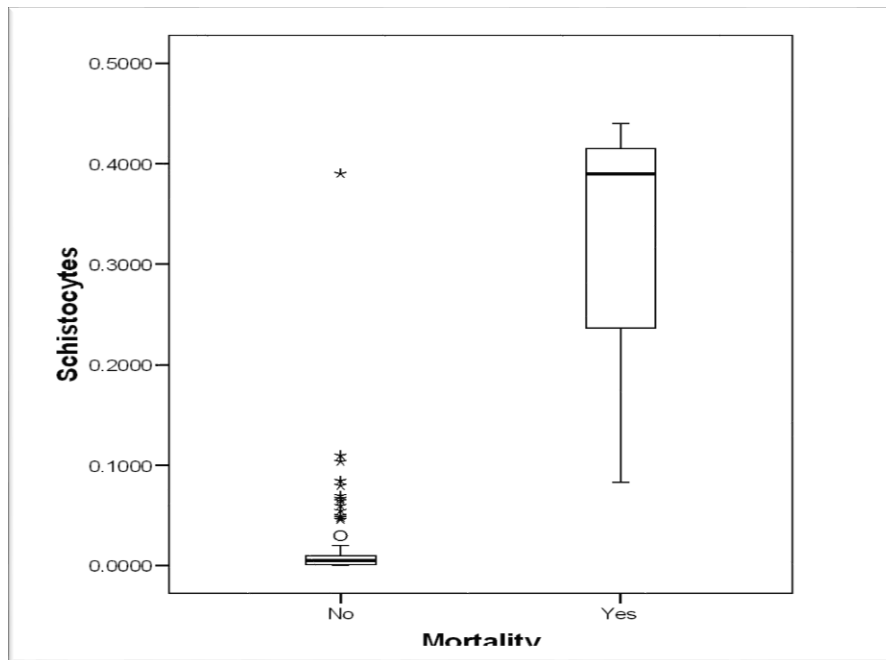|	Women who Died (n=3)	Women who Survived (n=97)	*P*
Schistocytes (%) **Range** **Median (IQR)**	8.3 – 44 39 (8.3 – 44)	0 – 39 0.5 (0.1 – 1.1)	<0.001* HS

IQR interquartile range [central 50% of ascendingly-ordered set of data]

Data presented as range, median (IQR)

* Analysis using Mann-Whitney's U-Test

HS highly significant

Figure-36 Box-Plot Chart showing Difference between Women who Died and Women who Survived regarding Schistocytes Percentage .

Receiver operator characteristic (ROC) curve was constructed for schistocytes percentage as a predictor of postpartum deterioration in included women. The curve showed a significant predictability as denoted by the significantly large area under the curve (AUC) (figure-37).

Figure-37 ROC Curve for Schistocytes Percentage as Predictor of Postpartum Deterioration in Included Women .

AUC = 0.883, 95% CI (0.770 to 0.996), p<0.001

Table-15 shows the validity of schistocytes at different cutoff values as predictor of postpartum deterioration.

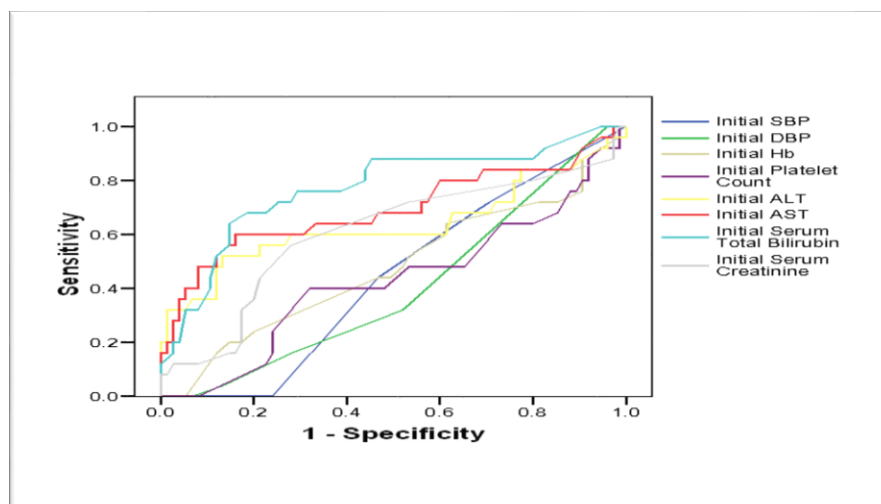**Table-12** Validity of Schistocytes as Predictor of Postpartum Deterioration in Included Women .

Schistocytes	Sensitivity	Specificity	PPV	NPV	FP	FN	LR+
≥ 0.95%	88%	85.3%	66.7 %	95.5 %	14.7 %	12 %	6
≥ 1.4%	84%	96%	87.5 %	94.7 %	4%	16 %	21
≥ 1.9%	80%	98.7%	95.2 %	93.7 %	1.3%	20 %	60

PPV positive predictive value -NPV negative predictive value
FP false positive -FN false negative-LR+ positive likelihood ratio

ROC curves were constructed for initial clinical and laboratory data as predictors of postpartum deterioration. Among all measured variables, only initial ALT, initial AST and initial total bilirubin were significant predictors of postpartum deterioration. Their AUCs, though being significantly large, were smaller than the AUC for

schistocytes; indicating that the latter is a more significant and better predictor for postpartum deterioration (figure-38).

Figure-38 ROC Curves for Initial Clinical and Laboratory Data as Predictors of Postpartum Deterioration in Included Women .

Initial SBP: AUC = 0.441, 95% CI (0.324 to 0.559), p=0.381
Initial DBP: AUC = 0.404, 95% CI (0.283 to 0.525), p=0.152
Initial Hb Concentration: AUC = 0.479, 95% CI (0.341 to 0.616), p=0.750
Initial Platelet Count: AUC = 0.429, 95% CI (0.293 to 0.564), p=0.286
Initial ALT: AUC = 0.636, 95% CI (0.484 to 0.787), p=0.043
Initial AST: AUC = 0.694, 95% CI (0.553 to 0.834), p=0.004
Initial Serum Total Bilirubin: AUC = 0.772, 95% CI (0.656 to 0.887), p=<0.001
Initial Serum Creatinine: AUC = 0.607, 95% CI (0.468 to 0.746), p=0.110

Table-13 shows the validity of initial values of ALT, AST, and total bilirubin as predictors of postpartum deterioration. Again, the validity parameters were remarkably lower than the corresponding parameters of schistocytes.

Table-13 The validity of initial values of ALT, AST, and total bilirubin as predictors of postpartum deterioration.

	Sensitivity	Specificity	PPV	NPV	FP	FN	LR +
Initial ALT ≥ 230 u/L	60%	72%	41.7 %	84.4 %	28%	40%	2.1
Initial AST ≥ 240 u/L	60%	84%	55.6 %	86.3 %	16%	40%	3.8
Initial Total Bilirubin ≥ 2.95 mg/dl	68%	81.3%	54.8 %	88.4 %	18.7 %	32%	3.6

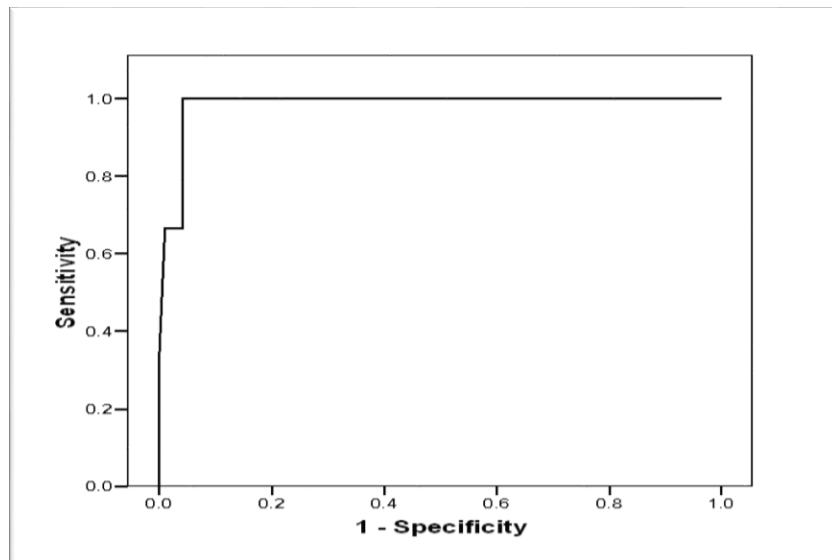ALT alanine transaminase - AST aspartate transaminase
PPV positive predictive value -NPV negative predictive value
FP false positive -FN false negative
LR+ positive likelihood ratio

ROC curve was constructed for schistocytes percentage as a predictor of maternal mortality in included women. The curve showed a significant predictability as denoted by the significantly large area under the curve (AUC) (figure-39).

Figure-39 ROC Curve for Schistocytes Percentage as Predictor of Maternal Mortality in Included Women .

AUC = 0.985, 95% CI (0.956 to 1.103), p=0.004

Table-14 shows the validity of schistocytes as predictor of maternal mortality in included women.

Table-14 Validity of Schistocytes as Predictor of Maternal Mortality in Included Women .

Schistocytes	Sensitivity	Specificity	PPV	NPV	FP	FN	LR+
≥ 8.2%	100%	95.9%	42.9%	100%	4.1%	0%	24.3

PPV positive predictive value
NPV negative predictive value
FP false positive
FN false negative
LR+ positive likelihood ratio

There were significant positive correlations between schistocytes percentage and each of systolic and diastolic blood pressures, serum ALT, serum AST, serum total bilirubin and serum creatinine 48 hours postpartum. There were significant negative correlations between schistocytes and each of hemoglobin concentration and platelet count 48 hours postpartum (table-15, figures 40-43).

Table-15 Correlation between Schistocytes and Both Clinical and Laboratory Data 48 hours Postpartum in Included Women .

Data 48 hours Postpartum		Schistocytes
Systolic Blood Pressure	r_s	0.479
	P	<0.001
		HS
Diastolic Blood Pressure	r_s	0.439
	P	<0.001
		HS
Hb Concentration	r_s	-0.527
	P	<0.001
		HS
Platelet Count	r_s	-0.406
	P	<0.001
		HS

Serum ALT	r_s	0.373
	P	<0.001
		HS
Serum AST	r_s	0.353
	P	<0.001
		HS
Serum Total Bilirubin	r_s	0.313
	P	0.002
		S
Serum Creatinine	r_s	0.411
	P	<0.001
		HS

Hb hemoglobin ,ALT alanine transaminase

AST aspartate transaminase

r_s Spearman's rank correlation coefficient

HS highly significant - S significant

Figure-40 Scatter-Plot Chart showing Correlation between Schistocytes and Platelet Count 48 hours Postpartum in Included Women .
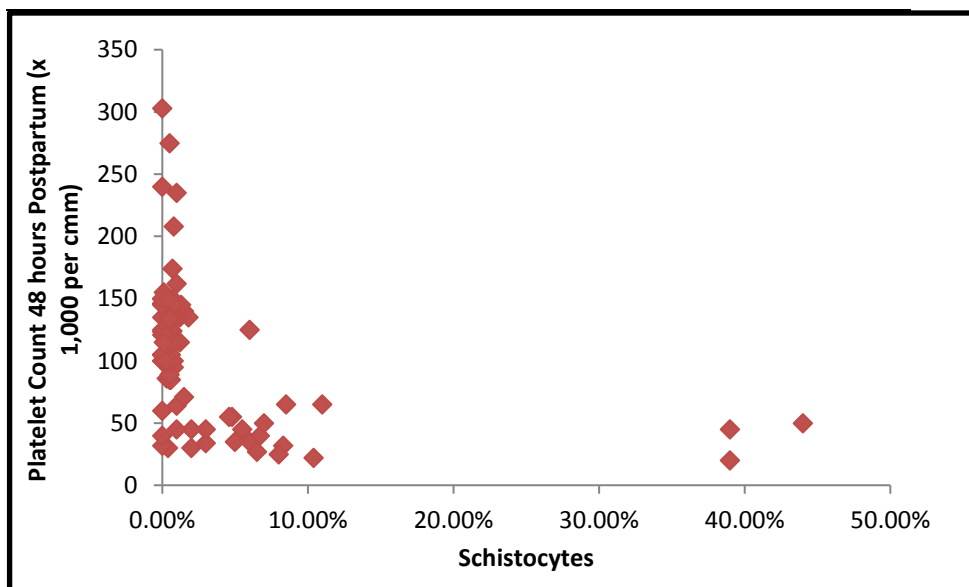

Figure-41 Scatter-Plot Chart showing Correlation between Schistocytes and ALT 48 hours Postpartum in Included Women .
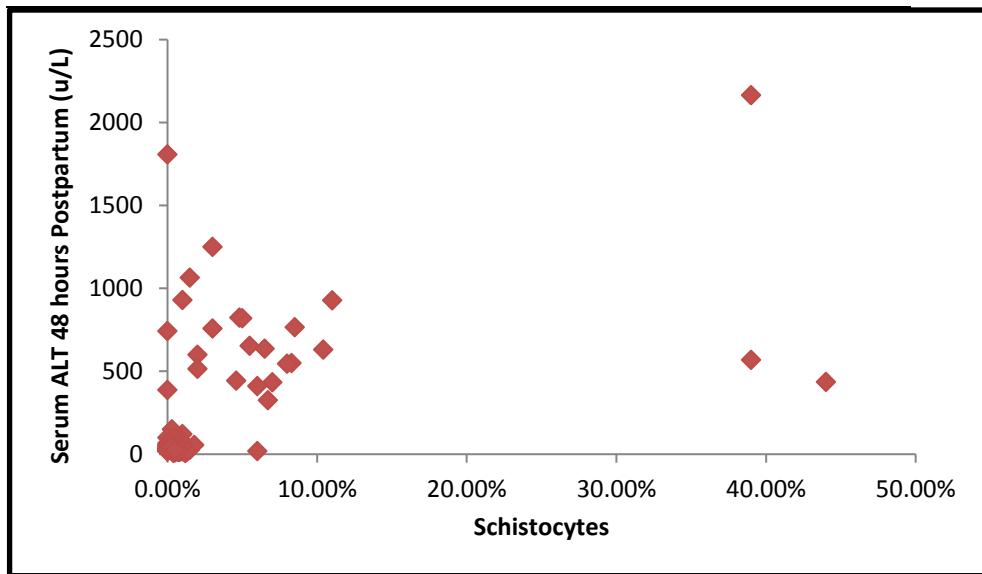
Figure-42 Scatter-Plot Chart showing Correlation between Schistocytes and Total Bilirubin 48 hours Postpartum in Included Women .
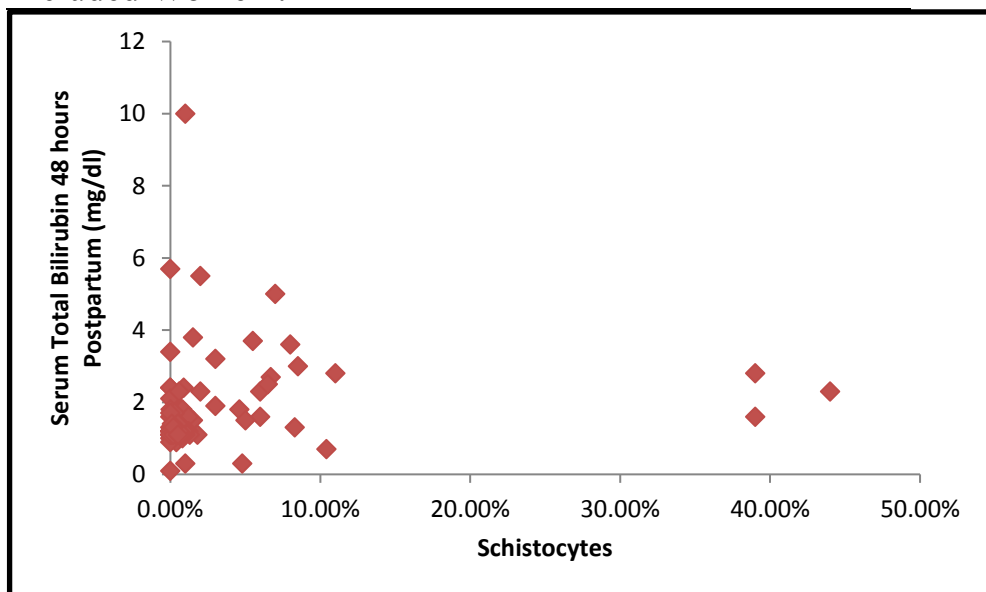

Figure-43 Scatter-Plot Chart showing Correlation between Schistocytes and Serum Creatinine 48 hours Postpartum in Included Women .

Association between the Quantitative Assessment of Schistocytes in Peripheral Blood Smear and Prognosis of Patient Initially Diagnosed as HELLP Syndrome (Study results)