Research Square

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Platelet count and AST can reliably predict the onset of plasma leakage in dengue, a low-cost triage tool during epidemics

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Abstract

Background: Dengue is one of the most important mosquito-borne viral infections to affect humans. It is most often a self-limiting febrile illness but in some instances can progress to plasma leakage and in extreme cases culminate in death. Dengue is endemic in Sri Lanka and 2017 saw the largest outbreak on record with over 160,000 cases and over 300 deaths. Health care services reached its' limits coping with this epidemic. The objective of this study was to identify reliable, low-cost, easily-accessible and objective predictors of Dengue hemorrhagic fever (DHF) that can be used as a triage tool in epidemic situations. Methodology/Principal findings: Serologically confirmed 350 serial adult dengue patients were included in the study. 257 (73.4%) were classified as dengue fever (DF, non leakers) and 93 (26.5%) as DHF with plasma leakage. Bedside ultrasonography was used to identify plasma leakage. Bivariate and regression analysis showed platelet count (Pearson r 0.59), and AST (r 0.27) to be significantly correlated with plasma leakage and platelet count to have a moderate predictive association (R2 0.35) with plasma leakage. Platelet count <50,000/mm3 (OR 23.7; 95% CI 12.2-45.9), AST> twice, upper limit of normal (OR 7.5; 95% CI 3.9-14.3) and ALT> twice, upper limit of normal (OR 2.4; 95%CI 1.4-3.6) increased the likelihood of DHF. In the final analysis, logistic regression identified platelet count <50,000/mm3 (OR 17.2; 95% CI 8.6-34.1) and AST>2ULN (OR 5.1, 95% CI 2.1-12.1) at time of plasma leakage as significant independent predictors of DHF. ROC curve performed for Platelet count had an AUC of .89 and at a platelet count of 50,000/mm3 predicted DHF with a sensitivity of 87% and specificity of 79%. AUC for AST was 0.72 and at 93Iu/L predicted DHF with a sensitivity of 85% and specificity of 60%. Conclusion: We have identified 2 laboratory parameters that could be used to identify plasma leakage and might be useful to stratify dengue-infected patients at risk for developing severe dengue.

Background

Dengue fever is endemic in Sri Lanka and a major public health problem. The first serological confirmation of Dengue in Sri Lanka was done in 1962(1) and the first outbreak was recorded in 1965(2).

There is an exponential increase in reported cases annually and it has become the number one killer amongst the mosquito borne infections in Sri Lanka. The Ministry of Health of Sri Lanka confirms that nearly 161,000 suspected dengue cases have been reported to the epidemiology unit during the first nine months of 2017(3). The last major outbreak occurred in 2009 with 35095 reported cases with case fatality rate of 1%. Although the number of new cases increased during the last seven years, the case fatality rate has decreased to less than 0.4%(3).

Death from Dengue is an avoidable cause of mortality(4). At present the case fatality rate due to dengue differs from country to country and can vary from less than 1% to as much as 15%(5, 6). Primary prevention of Dengue has limited success with vector control and other methods of primary prevention such as vaccination. Mortality reduction has therefore focused on better case management in the recent years(7, 8). This strategy of improved clinical case management has proved successful with reduction of case fatality rate from 10-20% to less than 1%(9).

The major cause of death is Dengue Haemorrhagic Fever (DHF)/ Dengue Shock Syndrome (DSS). Ideally the mortality from dengue should be less than 1%(4).

While this may be achieved at times when the case load is low, at times of major outbreaks the over-burdening health infrastructure and service personnel may lead to increase of case fatality rates.

Sri Lanka saw the largest ever outbreak of dengue in 2017 and witnessed over 300 deaths(10). The country and the health services struggled to cope with the current outbreak.

Progression of dengue fever to DHF with attendant plasma leakage can be detected clinically, using the packed cell volume (PCV) and ultrasonography (11, 12). Accurate early identification of plasma leakage is crucial as management, and outcomes of DHF differs significantly from that of DF (11-13). Each method of plasma leakage detection has its advantages and disadvantages. Even minute amounts of plasma leakage can be detected by bedside ultrasonography and is considered the gold standard. Minute amount of plasma leakage into pleural and peritoneal cavities is detected with greater sensitivity with bedside procedure(14, 15). While this mode of testing is feasible at times of low patient turnover, at times of epidemics there is overburdening of health care systems to detect early plasma leakage by ultrasonography. Therefore, if simple laboratory tests such as platelet count can be used as a predictor of plasma leakage, it would be useful in the triage of patients at high-risk of plasma leakage, and may help effective utilization of limited resources.

Low platelet counts have previously been reported with dengue fever and few studies have reported the behavior of platelet counts during progression to severe forms of dengue (16, 17). Declining platelet count is associated with plasma leakage. Previous studies have attempted to find if a satisfactory cut off value for platelets can been be determined which would herald the onset of plasma leakage (17-20). However, none of these studies have taken into account that plasma leakage occurs on different days on different individuals. Therefore using the platelet count of a predetermined (in most cases day 5 of illness) day for the calculation is technically incorrect.

Similarly other laboratory parameters such as Creatine kinase (CK), aspartate aminotransferases (AST) and alanine aminotransferase (ALT) have been used as either individual predictors or used in risk prediction scores with good results (19, 21).

The objective of this study was to see if the platelet-count, hepatic transaminases and rise in baseline hematocrit performed on the day plasma leakage could be used to predict plasma leakage in dengue patients progressing to DHF.

Methods

350 consecutive adult patients with serologically confirmed dengue fever admitted to Teaching Hospital Peradeniya, Sri Lanka from May to August 2017 were included in the study. Ethical clearance to the study

was obtained from the Institutional Ethics Review Committee of the Faculty of Medicine University of Peradeniya.

Sero-positivity for dengue was defined as a positive NS-1 Dengue antigen within 48 hours of fever onset and or a positive Dengue IgM test at day 5 or later after the onset of fever.

The study physician and 2 trained research assistants followed up the patients fulfilling the above criteria during their hospital stay. Data on symptoms, clinical signs and routine laboratory tests and results of bedside tests including ultrasonography and packed cell volume (PCV) on admission were collected. Following this the study team reviewed the patients twice daily and the same parameters were updated and new symptoms, signs and new onset plasma leakage was documented.

Routine laboratory tests included full blood count (FBC), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), C-Reactive Protein (CRP), serum albumin and serum creatinine. In most instances the FBC was performed twice daily 12 hours apart while most other tests were performed once daily during the hospital stay.

Plasma leakage was defined as presence of peri-cholycystic fluid collection or the presence of fluid in the pleural or peritoneal cavities. All patients with at least one warning symptom of postural dizziness, persistent nausea or vomiting, abdominal pain and declining urine output (<0.5ml/Kg/hour) and a rising PCV (>10% of baseline PCV) were subjected to ultrasonography.

Statistical Analysis:

The demographics and clinical characteristics of severe and non-severe dengue cases were described using the mean ± standard deviation (SD) if the data were normally distributed, or by median and range otherwise. Comparisons between the two groups were performed using the Student's *t*-test for continuous variables if the data were normally distributed, otherwise the Mann–Whitney *U* test was used. A chi-square test was used for categorical data. A p value < 0.05 was considered significant.

We conducted univariate and bivariate analysis assessing the relationship between the predictor variables and plasma leakage as defined by the first detection of plasma leakage at anytime during the admission. Correlation analyses to assess strengths of relationships between markers of DHF/plasma leakage were made by computing Pearson *r*. Predictive associations between different biomarkers were analyzed using regression studies. The method yielding the highest R^2 was then reported.

Variables with a p value <0.05 were considered for multivariable analysis using logistic regression built using forward step-wise selection. Variables were then sequentially removed to yield the most parsimonious model (p-value for all <0.05). Variables were retained in the final model if there were statistically significant (p < 0.05).

Using the final equation of the logistic regression model, we attempted to define a threshold for the parameters that were included in order identify the cases with plasma leakage from those without. We selected a threshold for the probability of being a case so that both sensitivity and specificity were maximized. We created an ROC graph to verify the sensitivity and specificity for the selected threshold.

Results

Patient characteristics:

The sample constituted 205 males (58.6%) and 145 females (41.4%). The females were older (mean 37.6, SD 17 years) than the males (mean 30.8, SD 12.8 years). There was no significant difference in age between those with DF and DHF. Of the 350 subjects, 257 (73.4%) were diagnosed as dengue fever (DF, non leakers) and 93 (26.5%) as DHF with plasma leakage.

Most patients with DF and DHF were admitted on day 3 of the illness. Patients with DHF had a longer stay in hospital compared to DF patients (DF: mean 4.1, median 4. DHF: mean 4.76, median 5, $P<0.01$). Most patients with DHF had plasma leakage on day 5 (Mean 5.01 SD 1.3; median 5; range day 2-8) (Table 1).

Twenty-seven (29%) patients with DHF had evidence of plasma leakage at time of admission to hospital on ultrasonography.

Serial platelet, white cell counts and transaminases

The platelet counts done on day 1 and 2 of fever remained above 150,000/mm^3 in both groups and the difference was not significant. The platelet count gradually dropped in both groups from day 3 of fever reaching a lowest mean of 97,000/mm^3 in DF by day 6 and 40,000/ mm^3 in DHF on day 7. The platelet count dropped to less than 50,000/mm^3 on day 5 in DHF patients. The platelet counts remained significantly lower in DHF patients compared to DF patients from day 3 to day 7 ($P=0.000$) (Table-2). The counts gradually started to improve from day 7 in both groups.

The mean percentage drop in absolute platelet count from day prior to leaking to day of leaking was 47.8% (SD 22.9). When serial platelet counts were analyzed against the day of plasma leakage, the platelet count was less than 50,000/mm^3 at time of leaking irrespective of the day of the illness (table 3).

The total white cell count (WCC) dropped in both groups from day 1 to day 4 and then gradually recovered and was significantly higher among leakers compared to non-leakers from day 6 to day 9($P<0.01$, Table 2).

Hepatic transaminases showed progressive elevation from day 1 to day 6 of illness and a gradual decline thereafter in both groups, with AST being higher than ALT. The AST and ALT were significantly higher in

patients with DHF compared to those with DF (P<0.01). The highest mean AST (157.5IU/L) was observed on day 6 and highest mean ALT (112IU/L) was observed on day 5 in patients with DHF (Table 2).

Platelet count <50,000/mm^3 (OR 23.7; 95% CI 12.2-45.9), AST> twice, upper limit of normal (OR 7.5; 95% CI 3.9-14.3) and ALT> twice, upper limit of normal (OR 2.4; 95%CI 1.4-3.6) increased the likelihood of DHF (Table 4).

There was no significant difference between C-Reactive protein (CRP) and rise in haematocrit between the groups.

Correlation and predictive association between markers

Strength of relationships between markers as determined by Pearson *r* and their respective predictive associations as represented by R^2 are shown in table 5.

Plasma leakage had significant correlation with platelet count (*r*- 0.59) and a moderate predictive association (R^2 0.35)at time of leakage. The correlation with AST (*r* 0.271) was less and the association weaker (R^2 0.069). The correlation of leaking with ALT, hematocrit and CRP was much weaker (r< 0.16) and the associations negligible. AST and ALT showed excellent correlation with each other (r 0.89) at time of leaking. There was moderate correlation between platelet count and ALT and AST (table 5).

Logistic regression was performed selecting the laboratory variables with p<.05 in the univariate and bivariate analysis, utilizing the forward step-wise selection method. The platelet count and AST at time of leakage emerged as significant independent predictors of DHF. The Hosmer-Lemeshow goodness of fit test showed a good fit in the 2 independent predictors of DHF/plasma leakage (P=0.85).

Predictive platelet count and AST from ROC

Receiver operated characteristic (ROC) curves for the platelet count and AST at time of plasma leakage were performed separately to obtain a predictive value for DHF. The area under the curve (AUC) for the platelet count was 0.89 (figure 1). We propose a cut-off value of 50,000/$cumm^3$ as reasonable value giving a sensitivity of 87% and specificity of 79% for detecting DHF in adult dengue patients.

AUC for the ROC curve for AST was 0.73 (figure 2). We propose an AST value of 93IU/L with a sensitivity of 85% and a specificity of 60% as a reasonable predictive value for DHF.

Discussion

This study confirmed that platelet counts and hepatic transaminases could be used as reliable markers in dengue fever to detect progression into plasma leakage and DHF. Both DF and DHF patients were admitted to hospital early during the disease, on day 3 and of those progressing to DHF, plasma leakage occurred on day5. This study also found that a sizeable proportion of patients with DHF (29%) had evidence of plasma leakage on admission to hospital, confirmed by ultrasonography.

This emphasizes the need of a routine, low cost, reliable predictor(s) of plasma leakage that can be used as a triage tool.

A multitude of predictors of plasma leakage using individual predictors or more complex scoring systems have been developed in the past (22-24). Most of these predicting systems carry reasonable sensitivity but at times of epidemics in resource poor settings, complex scoring systems are not practicable.

Thrombocytopaenia is commonly seen in both mild and severe forms of dengue infections. However its exact role in the pathogenesis of severe forms of dengue leading to DHF remains controversial. More importantly the platelet count has been established as a marker of progression to severe forms of dengue in many previous studies (25). We observed a mild decline in platelet counts of patients with DF up to day 6 with a gradual recovery thereafter. In contrast those with DHF, the platelet counts rapidly dropped to levels less than 50,000/mm^3 from day 3 to day 6. These findings are in keeping with previous studies. Tee et al reported that thrombocytopenia<35,000/mm^3 was seen more in DHF/DSS than DF patients (26) in Malaysia and Kularatne et al reported very similar counts in Sri Lanka (27). Fernandez et al also concluded platelet counts of <50,000/mm^3 to be associated with DHF (18). Unfortunately most previous studies have not performed serial platelet counts or serial ultrasonography to correlate the onset of plasma leakage and therefore are of limited value. Moreover, we observed that the lowest platelet count was around the time of onset of plasma leakage with a mean reduction of 47.8% of the count compared to the previous day. The aim of this study was to see if this could be used as a sensitive triage tool at times of epidemics in resource poor settings to identify patients with DHF.

A ROC curve to predict the threshold for development of DHF utilizing the platelet count at the onset of plasma leakage, confirmed by ultrasonography has not been reported before. We propose that a count of 50,000/mm^3 or less can predict DHF with a sensitivity of 87% and specificity of 79%. Ralapanawa et al utilized similar methods utilizing the acute phase platelet counts in Sri Lanka and predicted a threshold of 116/cumm for the onset of DHF with a sensitivity of 83% and specificity of 56%(17). Suwarto et al reported an AUC of 0.83 with sensitivity of 72.3% and specificity of 76.1% for predicting DHF at platelet count of 49,500/cumm (19). Lam et al have validated a similar model utilizing daily platelet counts for use among the pediatric patients (20). The implication of our finding necessitates performing daily full blood counts. We believe this method would pick up early -leakers both in and out of hospital and thus prevent patients progressing to complicated dengue.

The total white cell count in both our patient groups showed a gradual decline from day 1 to day 4 and a gradual recovery thereafter. We observed that the WCC was significantly higher in the DHF patients from

day 6-9. Leukopenia defined as total WCC<4,000/mm^3 has been reported in previous studies and has not been a predictor of DHF, in alignment with our findings (16, 27). A similar trend in leucopenia followed by rise in the recovery phase of DHF was earlier reported by Kulratne et al as well (27).

Other haematological parameters such as the absolute neutrophil count and the Haemoglobin has also provided no useful correlation with DHF in previous studies.

In this study the AST and ALT performed at time of plasma leakage was significantly higher in DHF compared to DF. Logistic regression also confirmed AST to be an independent predictor of plasma leakage with an AUC of 0.7. However, ALT was not a significant predictor of plasma leakage when subjected to multivariate analysis.

Hepatic transaminases are elevated in both mild and severe forms of dengue. Dengue virus is hepato-trophic and known to cause hepatitis of varying severity and sometimes result in massive hepatic necrosis(28). Prolonged hypotension and shock in cases of DHF and DSS could be another cause leading hepatic damage. Elevated transaminases levels ranging from 100IU/L to more than 1,000IU/L has been previously reported in patients with DHF (29-32).

Suwarto in Indonesia reported a significant association between AST and plasma leakage while ALT failed to show an association (19). A similar trend of higher AST in DHF patients was also reported in Japan and Brazil previously(16, 33). The reason for persistent greater elevation of AST over ALT in complicated dengue is thought to be due to concomitant release of AST from damage caused to myocytes although this needs to be verified by future research (34). Similar to our study Suwarto et al also attempted a prediction model using AST as a marker of plasma leakage. They reported AUC of 0.77 with a sensitivity of 70.1% and specificity of 74.29% (19). Md Sani et al also demonstrated AST to be a predictor of severe dengue reporting an AUC of 0.7 and also demonstrated that its performance as predictor is at its best when expressed as AST^2/ALT (21). However, AST has not gained prominence as a marker of plasma leakage as evidenced by its absence in the WHO guidelines although its' significance has been proposed by several authors earlier (11, 12).

Our focus in this study was to identify reliable, low-cost and objective markers of plasma leakage that van be used in epidemic situations when health systems struggle deliver optimal care. Previous studies have mostly evaluated clinical and laboratory parameters that are best suited for detection of leaking under optimal care delivery. We believe the identification of platelet count <50,000/mm^3 and AST>93IU/L as reliable predictors of plasma leakage significant findings

Strengths and limitations:

This is the first reported study looking at reliable, low-cost and objective markers of plasma leakage that can be used as triaging tool during dengue epidemics in resource poor settings. We have used an objective marker (ultrasonography) for the detection of plasma leakage and we believe the detection and

timing of plasma leakage to be more accurate in this study. As limitations, we acknowledge that this is a single centre study and that some laboratory investigations like serum albumin, creatinine was not available in all patients and therefore were excluded from the analysis. The absence of data defining patients as primary or secondary dengue infections is also considered a limitation.

Conclusion

We developed a low-cost, reliable and objective triage tool for predicting DHF that can be used at times of epidemics or when health systems are overwhelmed for any reason. These findings need to be validated by a lager multi-center study.

Abbreviations

DF: Dengue fever

DHF: Dengue Hemorrhagic fever

AST: Aspartate aminotransferase

ALT: Alanine aminotransferase

ROC: Receiver operated curve

AUC: Area under the curve

FBC: Full blood count

WCC: White cell count

CRP: C-reactive protein

PCV: Packed cell volume

Declarations

Ethics approval and consent to participate

Ethical clearance to the study was obtained from the Institutional Ethics Review Committee of the Faculty of Medicine University of Peradeniya. A copy of the ethical approval is available for review by the Editor-in-Chief of this journal.

Consent for Publication-

Written informed consent was obtained from the patients and/or relatives for publication. A copies of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material –

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors equally contributed developing the research proposal, collection and analysis of data. All authors read and accepted the final manuscript

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Tables

Table1: Patient Characteristics of DF and DHF

		DF (n=257)		**DHF (n=93)**		**P Value**
1	Gender	Male n (%)	151 (58.7%)	Male n (%)	54 (58.1%)	0.9
		Female n (%)	106 (41.2%)	Female n (%)	39 (41.9%)	
2	Age (Yrs)	Mean (SD)	34 (15.7)	Mean (SD)	32.7 (13.2)	0.70
		Range	26-65	Range	13-75	
3	Admitted on day	Mean (SD)	3.49 (1.51)	Mean (SD)	3.9 (1.2)	0.5
		Range	1-8	Range	1-8	
4	Duration of Stay	Mean (SD)	4.1(1.4)	Mean (SD)	4.76	0.001
		IQR	2	IQR	2	
5	DHF detected on day		Mean (SD)	5.0 (1.3)	-	
			IQR	2		

DF: Dengue fever, DHF: Dengue hemorrhagic fever

Table 2: Selected serial laboratory parameters of DF and DHF patients from day 1 to 10

	Parameter	DF mean (STD)	DHF mean (STD)	P Value
1	AST (IU/L)	113.22 (107.84)	186.30 (149.96)	0.000
2	ALT (IU/L)	93.09 (94.17)	127.83 (103.19)	0.004
3	CRP	18.21 (37.82)	20.79 (27.69)	0.674
4	Day 1 Platelet X1000/mm3	190.64 (48.77)	214.50 (43.29)	0.282
5	Day 2 Platelet X1000/mm3	169.36 (50.51)	150.45 (57.43)	0.090
6	Day 3 Platelet X1000/mm3	137.49 (47.27)	102.89 (51.41)	0.000
7	Day 4 Platelet X1000/mm3	123.58 (53.49)	72.97 (51.81)	0.000
8	Day 5 Platelet X1000/mm3	114.03 (50.43)	49.09 (35.12)	0.000
9	Day 6 Platelet X1000/mm3	97.36 (47.10)	42.77 (30.21)	0.000
10	Day 7 Platelet X1000/mm3	97.30 (49.80)	40.45 (27.16)	0.000
11	Day 8 Platelet X1000/mm3	95.58 (54.00)	60.35 (42.62)	0.002
12	Day 9 Platelet X1000/mm3	107.07 (53.05)	86.44 (41.26)	0.189
13	Day 10 Platelet X1000/mm3	135.14 (96.96)	165.29 (79.10)	0.536
14	Day 1 WCC X X1000/mm3	5.52 (2.13)	6.50 (1.51)	0.299
15	Day 2 WCC X1000/mm3	4.75 (1.71)	5.31 (2.17)	0.153
16	Day 3 WCC X1000/mm3	3.55 (1.95)	3.82 (1.83)	0.387
17	Day 4 WCC X1000/mm3	3.26 (1.58)	3.35 (1.25)	0.667
18	Day 5 WCC X1000/mm3	3.53 (4.28)	4.23 (2.96)	0.189
19	Day 6 WCC X1000/mm3	3.58 (1.85)	5.21 (3.76)	0.000
20	Day 7 WCC X1000/mm3	4.01 (1.93)	5.61 (2.85)	0.000
21	Day 8 WCC X1000/mm3	4.56 (1.81)	6.23 (2.57)	0.001
22	Day 9 WCC X1000/mm3	4.51 (1.39)	6.27 (2.08)	0.003
23	Day 10 WCC X1000/mm3	5.03 (1.25)	7.05 (3.54)	0.180

WCC: White Cell Count, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, CRP: C-Reactive Protein, HCT: Hematocrit.

Table 3: Mean serial platelet counts of patients with DHF according to day of plasma leakage

Day of plasma Leakage		Mean platelet count							
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
3 (n=6)	Mean (STD)	170.00	139.20 (70.7)	42.40 (24.6)	33.50 (23.9)	44.83 (50.1)	27.75 (14.2)	38.00	94.00
4 (n=24)	Mean (STD)	182.00 (12.7)	138.80 (52.9)	74.71 (42.2)	39.83 (22.3)	28.71 (14.4)	32.66 (18.3)	54.80 (35.3)	-
5 (n=30)	Mean (STD)	259.50 (26.2)	156.12 (55.8)	122.71 (41.1)	81.11 (34.0)	43.40 (26.4)	43.28 (37.6)	43.08 (31.1)	61.42 (54.5)
6 (n=12)	Mean (STD)	234.00	139.50 (46.0)	100.67 (21.3)	87.75 (47.6)	63.88 (29.6)	42.08 (15.5)	31.25 (14.5)	61.67 (52.9)
7 (n=12)	Mean (STD)	-	214.33 (38.7)	173.80 (43.3)	154.44 (60.1)	99.78 (39.2)	57.33 (34.9)	30.58 (13.7)	47.60 (15.4)

Table 4: Odds ratios with 95% Confidence intervals of selected laboratory parameters with plasma leakage

		DF (n) 257	DHF (n) 93	P	OR (95% CI)
1	AST X2 ULN	107	79	0.000	7.5(3.9-14.3)
2	ALT X2 ULN	78	49	0.000	2.4(1.4-3.6)
3	Platelet<100,000/mm	149	90	0.000	30.5(7.3-126.6)
4	Platelet <50,000/mm	51	79	0.000	23.7(12.2-45.9)
5	HCT> 10% baseline	29	19	0.24	2.0(1.1-3.9)
6	WCC<4,000/mm	201	74	0.99	1.0(0.54-1.8)
7	WCC<2,000/mm	64	23	0.91	0.9(0.55-1.6)
8	CRP>10md/dl	34	25	0.13	1.7(0.8-3.4)

WCC: White Cell Count, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, CRP: C-Reactive Protein, HCT: Hematocrit, ULN: Upper Limit of Normal.

Table 5: Correlation and correlation coefficients of selected laboratory parameters with plasma leakage

	Parameter	n	Pearson r	95% Confidence intervals	P	R2
1	Platelet count at leaking	342	- 0.541**	-0.59 –0.44	0.000	0.27
2	WCC at leaking	342	- 0.011	-0.10 - 0.96	0.840	0.000
3	AST at leaking	332	0.271**	0.16 - 0.40	0.001	0.069
4	ALT at leaking	332	0.169*	-0.11 - 0.33	0.048	0.025
5	CRP	139	0.046	-0.09 - 0.26	0.596	0.001
6	Platelets less than 100 at leaking	342	0.354**	0.25 - 0.45	0.000	0.137
7	Platelets less than 50 at leaking	342	0.59**	0.46 - 0.72	0.000	0.35
8	AST >2 upper limit	332	0.347**	0.21 - 0.48	0.000	0.139
9	ALT>2 upper limit	332	0.148	0.016 - 0.31	0.085	0.037
10	>10% rise of baseline HCT	335	0.103	-0.07 - 0.03	0.23	0.015
11	WCC<2000/mm	342	0.11	-0.15 - 0.19	0.9	0.001
12	WCC<4000/mm	342	0.039	-0.12 - 0.21	0.65	0.000
13	ALT- AST (at leaking)	332	0.88	0.80-0.92	0.000	0.77
14	AST> 2ULN-platelet (at leaking)	332	0.37	-0.58 to -0.35	0.000	0.24

WCC: White Cell Count, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, CRP: C-Reactive Protein, HCT: Hematocrit, ULN: upper limit of Normal.

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

Figures

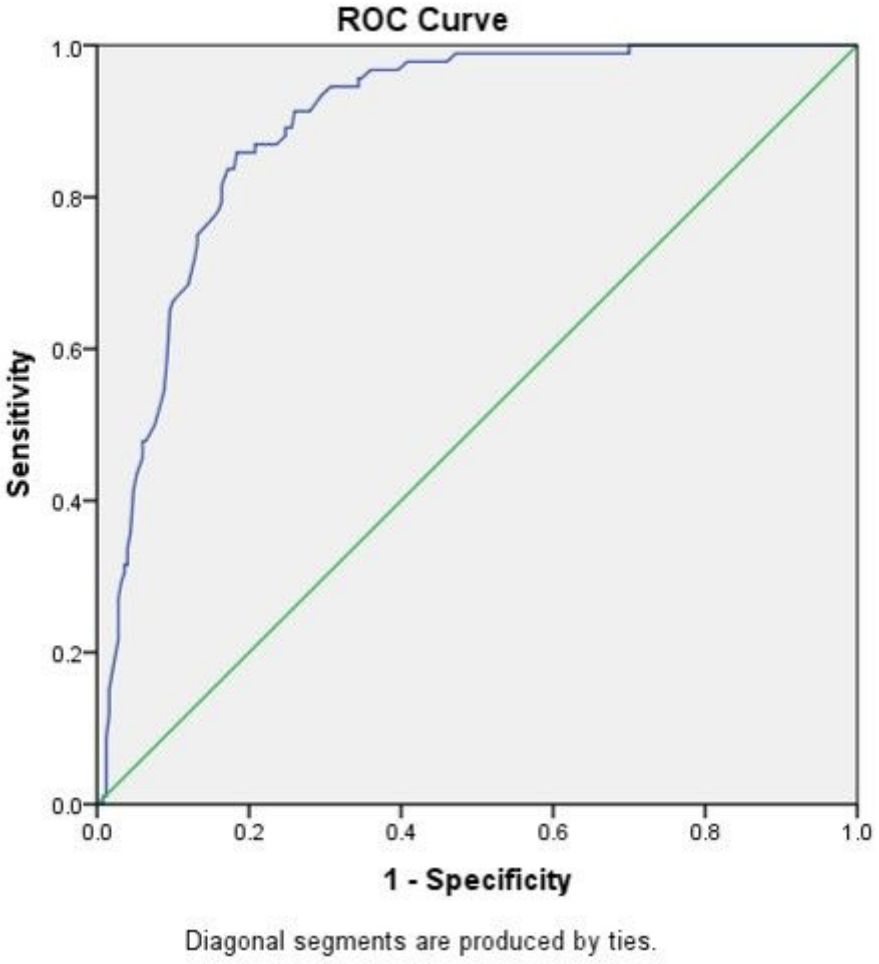

Figure 1

ROC for platelet count at plasma leakage. AUC: 0.89

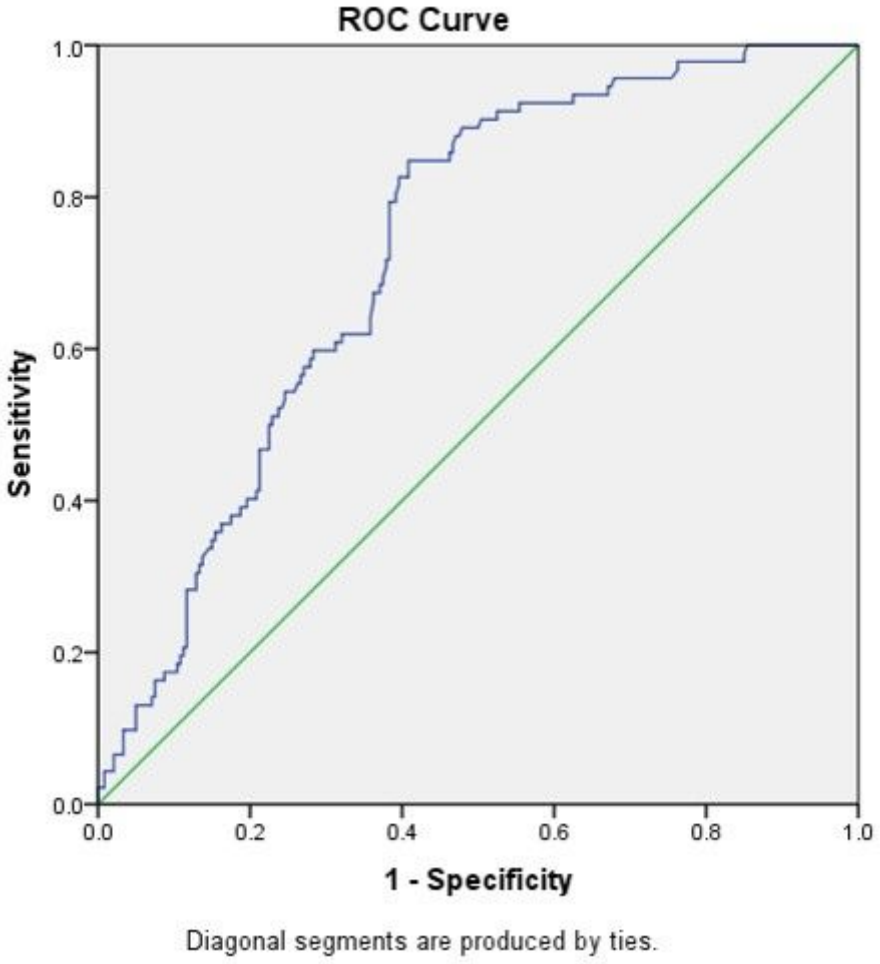

Figure 2

ROC Curve for AST. AUC: 0.72