BNS University
Critical Care Department
The Egyptian Journal Of Intensive Care And Emergency Medicine (JICEM)

Prognostic Value of Estimated versus Measured Plasma Fibrinogen Level in Traumatized Critically Ill Patients

Mervat Mohamed Khalaf[1], Walaa Mohamed Zaki Mohamed[2], Emad Eldein Omar Abd Al Aziz[3], Enas Abd Alatif Ahmed[4]

[1]*Associated professor of critical care medicine, Faculty of Medicine, Cairo University*

[2]*Master degree of critical care medicine, Cairo University*

[3]*Professor of Critical care, Faculty of medicine, Cairo University*

[4]*Professor of Clinical Pathology, faculty of medicine, Cairo University*

Abstract:

Background: This prospective observational study aimed to evaluate the prognostic value of both measured and estimated plasma fibrinogen levels in predicting mortality and morbidity in critically ill trauma patients. **Methods:** A total of 80 severely injured trauma patients (Injury Severity Score [ISS] 3-5) were enrolled, along with 20 healthy controls for comparison. Fibrinogen levels were measured and estimated, and their correlation with clinical outcomes, including mortality, length of stay (LOS), and ICU duration, was analyzed.

Results:

- A significant inverse correlation was observed between plasma fibrinogen levels and APACHE II scores (p = 0.0001).
- Fibrinogen levels were significantly inversely correlated with ICU length of stay (p = 0.037).
- A fibrinogen threshold of **222.5 mg/dl** was found to predict survival with:
    - Sensitivity: 67%
    - Specificity: 78%
    - p-value: 0.007
- A higher fibrinogen cutoff of **332 mg/dl** was predictive of severe trauma (ISS 4 or 5), with an **area under the curve (AUC)** of **0.98**, sensitivity of **100%**, and specificity of **98%**.
- A lower cutoff value of **247 mg/dl** demonstrated:

  - Sensitivity: 100%
  - Specificity: 75%

- Base excess, hemoglobin, and Injury Severity Score (ISS) were incorporated into a statistical model for estimating log-transformed fibrinogen levels, yielding an R^2 of 79% and a correlation coefficient of 75% between estimated and measured log fibrinogen levels.
- Lower fibrinogen levels were significantly associated with worse outcomes, including longer hospital stays. The estimation of fibrinogen levels in severe trauma cases is crucial for predicting survival and identifying patients who may benefit from targeted transfusion of coagulation factors.

Keyword: FIB, TIC, ISS, APACHE II, BE

1. Introduction:

Fibrinogen (FIB) is a key coagulation factor that plays a crucial role in both primary and secondary hemostasis [1].Trauma-induced coagulopathy (TIC) is a major cause of bleeding and the need for massive blood transfusions (MT) in severely traumatized patients [2]. TIC is associated with increased mortality, prolonged length of stay (LOS) in the intensive care unit (ICU), and poor patient outcomes [3].

FIB is mostly the coagulation factor to be consumed at first in poly-trauma patients with TIC [4]. Consequently, early estimation of FIB levels in such patients is essential for urgent management of severe bleeding. Notably, coagulation factors do not uniformly decrease in severe trauma patients, and specifically fibrinogen (FIB) decreases to critical level before other coagulation factors [5]. FIB is the primary coagulation factor that decreases with severe bleeding, as observed with both TIC [6] and postpartum hemorrhage (PPH) [7].

To maintain the integrity of coagulation function, it is recommended to replace fibrinogen when its levels fall below 150 to 200 mg/dL [8]. Early recognition and replacement of FIB deficiency can rapidly reverse TIC, arrest hemorrhage, and improve patient outcomes [8].

- **Type of the Study:** This study is a prospective observational controlled study.

Objectives:

A. To investigate the predictive ability of laboratory parameters, including hemoglobin (Hb) and base excess (BE), and the addition of the injury severity score (ISS) to estimate fibrinogen (FIB) levels in major trauma patients upon admission to the emergency room (ER) and intensive care unit (ICU). This will be done using an equation model based on readily available, inexpensive results to save time.

B. To assess the predictive ability of fibrinogen and other factors regarding morbidity and mortality in trauma patients.

2. Patients and Methods:

Patient Selection:

Eighty critically ill poly-trauma patients admitted to the ER or ICU of El-Bank El-Ahly Complimentary Hospital were consecutively enrolled in this study. Additionally, 20 healthy individuals were enrolled as a control group. The study was conducted between December 2015 and March 2016.

Methodology:

Inclusion Criteria:

- Patients aged between 16 and 70 years.
- Poly-trauma patients with trauma severity classified according to the Injury Severity Score (ISS) as serious, severe, or critical, who presented to the emergency room and were admitted to the ICU.

Exclusion Criteria:

- Co-morbidities or medications affecting the coagulation profile (e.g., liver disease, warfarin) prior to admission.
- Refusal of the patient or designated surrogate decision-maker to provide written informed consent, or inability to obtain consent within 48 hours of diagnosis.
- Congenital coagulopathies.
- Direct hepatic trauma.
- Pregnancy.

Clinical Evaluation:

- **Past Medical History:** Including conditions such as diabetes mellitus (DM), hypertension (HTN), renal disease, liver disease, cardiac or chest diseases, and drug history.
- **Mechanism of Injury:** Information from Emergency Medical Services, family members, or bystanders was collected to understand the mechanism and circumstances of the injury. This helped in assessing the energy or speed involved and the potential severity of trauma.

Clinical Examination:

- **Hemodynamic Parameters:** Blood pressure, heart rate, respiratory rate, and temperature.
- **Full Clinical Examination:** Comprehensive physical examination.
- **Glasgow Coma Scale (GCS):** To assess the neurological status of the patient.
- **Injury Severity Score (ISS):** Cases were categorized as serious (16-24), severe (25-49), or critical (50-74).
- **APACHE II Score:** To assess the severity of illness.

Investigations:

Routine Laboratories:

- Complete Blood Count (CBC)
- Coagulation Profile: Prothrombin Time (PT), Platelet Count (PC), International Normalized Ratio (INR), and Partial Thromboplastin Time (PTT)
- Arterial Blood Gases (ABGs)
- Liver Function Tests (LFTs)
- Kidney Function Tests
- Creatine Phosphokinase (CPK)
- Disseminated Intravascular Coagulation (DIC) Score
- Random Blood Sugar (RBS)
- Troponin I

Study-Specific Laboratory Parameters:

- Hemoglobin (Hb) (g/dL)
- Base Excess (BE) (mmol/L)
- Fibrinogen (FIB) (mg/dL, measured using the Clauss method)

Sample Collection:

- Samples were collected upon admission to the ER department via peripheral vein.
- Specimens were collected in 3.2% sodium citrate tubes, with a collection ratio of 9:1 (blood to anticoagulant).

Statistical Analysis:

Data were collected, revised, coded, and entered the Statistical Package for Social Sciences (SPSS) version 17 for analysis. The following statistical methods were employed:

1. **Qualitative Data:**
   - Presented as numbers and percentages.
   - Comparison between two groups with qualitative data was conducted using the Chi-square test.
2. **Quantitative Data:**
   - Presented as means, standard deviations, and ranges.
   - Comparison between two groups with quantitative data was carried out using the independent t-test.
3. **Correlation Analysis:**
   - Pearson correlation coefficients were used to assess the relationship between two quantitative parameters.

4. **Receiver Operating Characteristic (ROC) Curve:**
   - ROC analysis was used to determine a cutoff value for a quantitative test variable to predict a nominal outcome. The area under the curve (AUC), sensitivity, and specificity were estimated.
5. **Multivariate Analysis:**
   - A multivariate analysis was conducted to examine the ability of hemoglobin (Hb), base excess (BE), and injury severity score (ISS) to predict fibrinogen (FIB) levels.
6. **Linear Regression:**
   - Linear regression was used to explore the relationship between Hb, BE, ISS, and FIB. Due to slight positive skewness and homoscedasticity issues in the data, the regression analyses were performed with FIB on the log scale.
   - Initially, the effect of each predictor variable on FIB was examined separately, and the relationship between each predictor and the outcome was assessed.
   - If a nonlinear relationship was identified, squared terms for each predictor were introduced into the model.
   - Subsequently, the effect of the predictor variables was evaluated in combination, using predetermined combinations of variables.
   - The predictive ability of the models was assessed by R^2 and adjusted R^2 values.

3. Results:

This study included 100 participants, divided into two groups:

- **Case Group:** 80 patients who were admitted to the ICU following trauma.
- **Control Group:** 20 healthy individuals.

Descriptive Analysis:

1. **Age:** There was no statistically significant difference in age between the two groups.
2. **Gender and Comorbid Conditions:** Gender distribution and other comorbid conditions did not show significant differences between the case and control groups.
3. **Hemodynamic Parameters:**
   - **Systolic Blood Pressure (SBP):** The case group had significantly lower SBP compared to the control group.
   - **Heart Rate (HR) and Respiratory Rate (RR):** Both HR and RR were significantly higher in the case group compared to the control group.
   - **Temperature:** No significant difference in temperature was observed between the two groups (Table 1).

Table (1): showing comparison of hemodynamics data between 2 study groups:

Parameter	***Group 1 (n=80)*** ***Mean ± SD***	***Group 2 (n=20)*** ***Mean ± SD***	***ρ_value***
SBP	*89.22±23*	*109.95± 11.8*	***0.0001***
HR	*100.34±15*	*87.3 ±4.4*	***0.0001***
RR	*25 ± 8*	*13±2*	***0.0001***
TEMP	*36.8±0.37*	*37.2± 0.4*	*0.171*

Measured Fibrinogen and Hemoglobin (Hb):

The measured fibrinogen levels and Hb% were statistically lower in the case group compared to the control group, as shown in Table (2).

Table (2): Comparison of Measured Fibrinogen and Hb% between Case and Control Groups

parameter	***Group 1 (n=80)*** ***Mean ± SD***	***Group 2 (n=20)*** ***Mean ± SD***	***ρ_value***
Fibrinogen level	231.8 ± 114.5	385.9 ± 46.9	0.0001
Hemoglobin %	8.8 ± 2.7	12.9± 1.9	0.0001

II. Descriptive data of case group:

Epidemiological Characteristics and Co-morbid Conditions:

- Males comprised 75% of the case group.
- Diabetic patients represented 5%, hypertensive patients were 10%, and smokers accounted for 38% of the case group.

Type of Trauma:

- 90% of the admitted cases had blunt trauma, while 10% had penetrating trauma.

Site of Trauma:

- The sites of trauma are illustrated in Figure (1), with the highest frequency observed for head and extremity trauma.

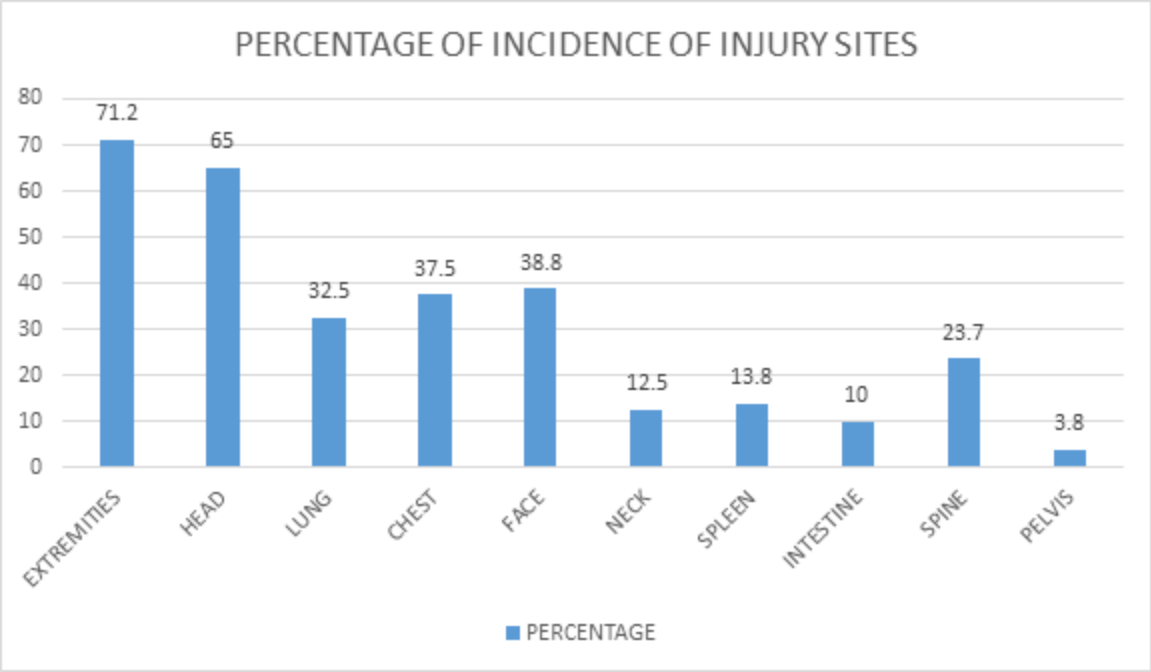

Fig (1): percentage of trauma site incidence

Need for Surgery:

- 33.8% of the cases required surgery in the operating room (OR).

Mechanical Ventilation (MV) and Inotropic Support:

- 60% of trauma patients required mechanical ventilation (MV).
- 33% of patients needed inotropic support.

Injury Severity Score (ISS):

- Trauma severity was categorized as follows:
  - 21 patients (26.2%) had serious trauma (ISS 3).
  - 19 patients (23.8%) had severe trauma (ISS 4).
  - 40 patients (50%) had critical trauma (ISS 5).

Troponin Level:

- Positive troponin was detected in 30% of cases.

Mortality:

- 31 patients (38.8%) died during the hospital stay.

Complications:

- 45 patients (56.25%) developed hospital-acquired pneumonia (HAP).
- 16 patients (20%) developed acute respiratory distress syndrome (ARDS).
- 12 patients (15%) experienced acute kidney injury (AKI).
- 9 patients (11.25%) developed disseminated intravascular coagulation (DIC).

These findings are summarized in Figure (2).

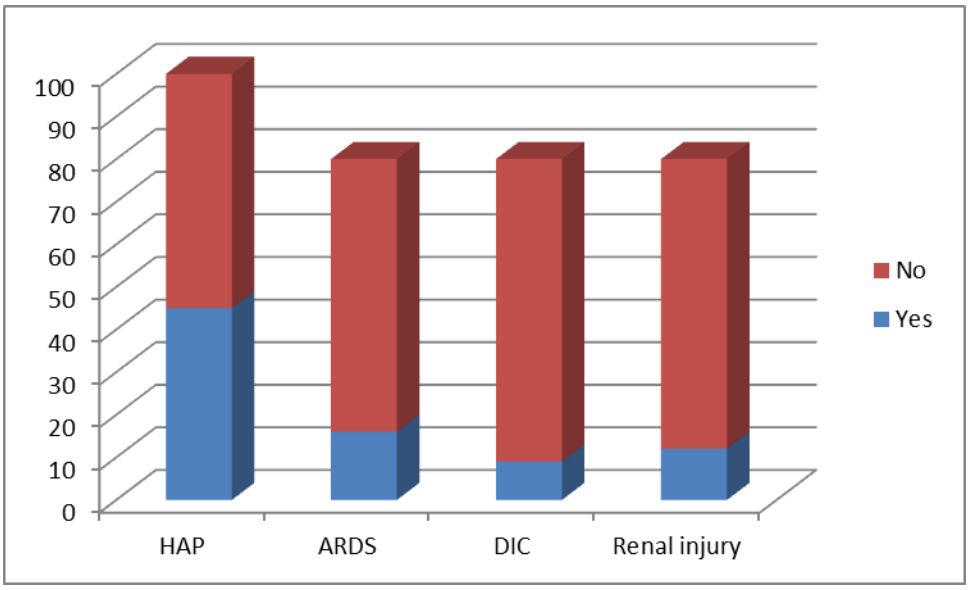

Figure (2): The incidence of complications in case groups

III. Comparative Data between Survivors and Non-Survivors

Regarding age, hemodynamic parameters, and routine laboratory profile of the non-survival group, significant differences were observed. The non-survival group demonstrated significantly lower systolic blood pressure (SBP) and hemoglobin (Hb%), along with higher heart rate (HR), respiratory rate (RR), and base excess (BE). Additionally, this group had a longer length of stay (LOS), as shown in Tables (3) and (4).

Table (3): comparison of age and hemodynamic parameters between survivals Vs non-survivals:

	Survivals group (n= 49)	**Non-survivals group (n= 31)**	***ρ_value***
Age (yrs)	32 ± 12	29 ± 11	0.28
SBP (mm Hg)	94 ± 24	81 ±18	0.01
HR (b/min)	97.6 ± 15.7	104.6 ± 12.6	0.03
RR	22.5± 5.7	28.5± 9.2	0.001
TEMP	36.8 ±0.4	36.2±0.3	0.09

Table (4): comparison of laboratory investigations and LOS between survivals Vs non-survivals:

Parameter	Survivals group (n= 49)	Non-survivals group (n= 31)	ρ_value
PH	7.31 ± 0.07	7.32 ± 0.04	0.4
BE	-6.7±3.5	-8.8 ±4.0	**0.01**
WBC	13.5 ±2.7	14.3 ± 1.7	0.2
HB	9.6 ± 2.7	7.8 ± 2.2	**0.003**
PLT	242 ± 121	218 ± 89	0.32
ALT	165.5 ± 222	125.5 ± 191.6	0.42
AST	172.12± 219.9	124.6 ± 160.6	0.26
UREA	51.6 ± 15.8	49 ± 8.9	0.34
CREAT	1.37±0.34	1.31 ± 0.22	0.45
Na	136 ± 2.7	137 ± 2.1	0.8
K	3.7 ±0.3	3.6 ±0.4	0.6
INR	1.57±0.55	1.56 ± 0.26	0.9
RBS	126.9 ± 65	124.5 ± 52	0.82
LOS	5.8 ± 2.2	8.6 ± 3.4	**0.0001**

Fibrinogen Parameters:

The non-survivor group exhibited significantly lower levels of measured fibrinogen, as well as significantly lower log-transformed fibrinogen values (Log FIB), whether estimated based on measured fibrinogen (Log fib) or calculated using statistical equations (estimated log fibrinogen). These findings are summarized in Table (5).

Table (5): Comparison between measured & estimated and calculated fibrinogen:

Parameter	Survivals group (n= 49)	Non-survivals group (n= 31)	ρ_value
Fib (measured)	265.8 ± 119	178.8 ± 84.5	**0.0001**
Fib (log fib)	2.4 ± 0.25	2.2± 0.18	**0.003**
Fib (Est log)	2.2 ± 0.32	2.0 ± 0.29	**0.002**

Clinical Scores:

The mortality group showed statistically significant lower Glasgow Coma Scale (GCS) scores and higher Injury Severity Score (ISS) and APACHE II scores compared to the survival group. These differences are presented in Table (6).

Table (6): GCS& ISS and APACHE II comparison between survivals and non-survivals:

Parameter	Survivals group (n= 49)	Non-survivals group (n= 31)	*ρ*_value
GCS	11 ± 3.9	9 ± 3.1	**0.019**
ISS	36.6 ± 16.2	50.4 ± 14	**0.0001**
APACHE II	21.8 ± 15	28 ± 7.7	**0.018**

There was no significant gender difference between both groups. Additionally, there was no significant difference between the two groups regarding co-morbid conditions or the need for inotropes. However, a statistically significant difference was observed between the 2 groups in terms of the need for mechanical ventilation (MV) and surgical procedures, with the non-survival group showing a higher requirement. These findings are summarized in Table (7).

Table (7): comparisons of incidence of comorbid conditions and need for MV & inotropic support and surgery:

Parameter	Survivals group (n= 49)	Non-survivals group (n= 31)	*ρ*_value
DM	**3/49**	**1/31**	**0.49**
HTN	**6/49**	**2/31**	**0.47**
Need of inotropic support	**20/31**	**13/31**	**0.5**
Need for MV	**23/49**	**25/31**	**0.005**
Need for surgery	**8/49**	**19/31**	**0.001**
High troponin	**13/49**	**11/31**	**0.45**

Outcome and Severity of Injury (ISS Score):

A statistically significant difference was observed in the Injury Severity Score (ISS) between the non-survival and survival groups, with 22 out of 31 non-survivors having an ISS of 5, compared to 18 out of 49 survivors. The p-value for this difference was 0.002.

Outcome and Site of Injury:

- **Intestinal Trauma:** The incidence of intestinal trauma was significantly higher in the non-survival group (7/31) compared to the survival group (1/49), with a p-value of 0.005.
- **Pelvic Trauma:** Pelvic trauma was also significantly more common in the non-survival group (13/31) compared to the survival group (10/49), with a p-value of 0.04.
- **Splenic Trauma:** Although a higher rate of splenic trauma was observed in the non-survival group, the difference was not statistically significant, with a p-value of 0.07.
- **Other Trauma Sites:** No significant differences in the incidence of injuries at other trauma sites were found between the survival and non-survival groups.

Division of Case Group by ISS Score:

The case group was categorized into three groups based on ISS score:

- **ISS 3 Group:** 21 patients with serious injuries.
- **ISS 4 Group:** 19 patients with severe injuries.
- **ISS 5 Group:** 40 patients with critical injuries.

When comparing the three ISS groups in terms of age, hemodynamic parameters, laboratory variables, and clinical scoring systems, the **ISS 5 (Critical) Group** showed significantly lower systolic blood pressure (SBP), pH, hemoglobin (Hb), and Glasgow Coma Scale (GCS) scores, along with higher heart rate (HR), respiratory rate (RR), base excess (BE), international normalized ratio (INR), APACHE II scores, and length of stay (LOS). However, other parameters did not show significant differences. These findings are summarized in **Table 8** and **Figure 3**

Table (8): comparing the three ISS groups for hemodynamic, laboratory variables and scoring systems:

Parameter	ISS 3 (n=21)	ISS 4 (n= 19)	ISS 5 (n= 40)	ρ–*value*
SBP	108.3± 13.3	103.3 ± 17.7	72.5± 16.3	**0.0001**
HR	87.6 ± 5.2	93 ± 11.4	110.5 ±12.7	**0.0001**
RR	21.1± 7.2	21.3± 7.0	28.3± 8.2	**0.0001**
Ph	7.34 ± 0.017	7.35 ± 0.035	7.29 ± 0.067	**0.0001**
BE	4.0 ± 1.9	6.1 ±2.0	10.1±3.8	**0.0001**
Hb% (g/dl)	11.7 ± 1.1	10.3 ± 1.8	6.7 ± 1.5	**0.0001**
INR	1.26± 0.33	1.5± 0.49	1.75±0.4	**0.0001**
GCS	13 ± 1.7	12 ± 3	7.8 ± 3	**0.0001**
APACHE	12.4 ± 3.5	17.8 ± 11.3	33.5 ± 9.6	**0.0001**
LOS	6.1 ± 1.5	5.7 ± 1.7	7.8 ± 3.9	**0.018**
FIB M	377.8 ±28.7	270.4 ±74.5	136.9 ± 46.7	**0.0001**
FIB Log	2.6 ± 0.03	2.4 ±0.16	2.1 ± 0.13	**0.0001**
FIB Est Log	2.5 ± 0.21	2.3 ± 0.15	1.9 ± 0.16	**0.0001**

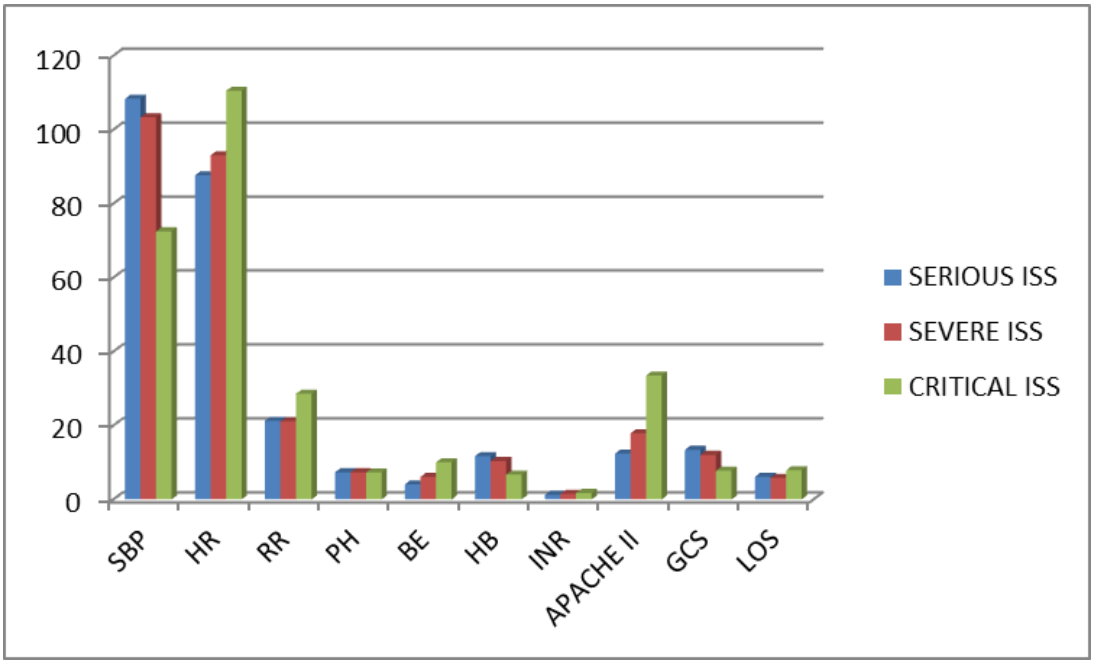

Figure (3): Comparing the three ISS groups for hemodynamic, laboratory variables and scoring systems.

Measured and Estimated Fibrinogen Levels:

The measured and estimated fibrinogen levels were significantly lower in the ISS 5 group, with a p-value of 0.0001, as shown in **Table 8** and **Figure 4**.

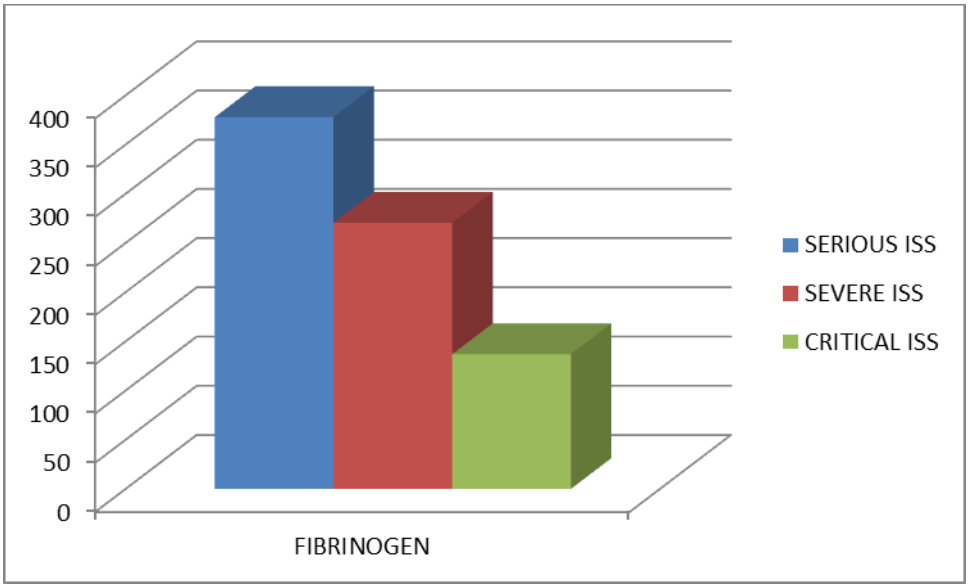

Figure (4): The measured and estimated fibrinogen levels in ISS groups 3, 4 and 5.

Complications:

The ISS 5 group showed a significantly higher frequency of all types of complications, as shown in **Table 9**.

Table (9): correlative results between different complications and the 3 groups of injury severity score (ISS)

Parameter	ISS 3 (n=21)	ISS 4 (n= 19)	ISS 5 (n= 40)	$\rho-value$
HAP (n=45)	6/45	9/45	30/45	**0.0001**
ARDS (n=16)	1/16	3/16	12/16	**0.001**
AKI (n=12)	1/12	3/12	8/ 12	**0.002**
DIC (n=9)	1/9	2/9	6/9	**0.045**

Correlative Analysis of Results:

- **Base Excess (BE)** was significantly inversely correlated to **Hemoglobin (Hb)** with **R = -0.74** and **p-value = 0.0001**.
- **BE** was significantly inversely correlated to **Fibrinogen** with **R = -0.66** and **p-value = 0.0001**.
- **BE** was significantly directly correlated to **Injury Severity Score (ISS)** with **R = 0.75** and **p-value = 0.0001**.
- **ISS** was significantly inversely correlated to **Hb** with **R = -0.87** and **p-value = 0.0001**.
- **ISS** was significantly inversely correlated to **Fibrinogen** with **R = -0.895** and **p-value = 0.0001**.
- **Hemoglobin (Hb)** was significantly directly correlated to **Fibrinogen** with **R = 0.88** and **p-value = 0.0001**.
- **Systolic Blood Pressure (SBP)** was significantly directly correlated to **Fibrinogen** with **R = 0.83** and **p-value = 0.0001**.
- **Glasgow Coma Scale (GCS)** was significantly directly correlated to **Fibrinogen** with **R = 0.79** and **p-value = 0.0001**.
- **International Normalized Ratio (INR)** was significantly inversely correlated to **Fibrinogen** with **R = -0.589** and **p-value = 0.0001**.
- **APACHE II** was significantly inversely correlated to **Fibrinogen** with **R = -0.86** and **p-value = 0.0001**.
- **Length of Stay (LOS)**, including **ICU stay**, was significantly inversely correlated to **Fibrinogen** with **R = -0.234** and **p-value = 0.037**.

Linear Regression Analysis:
Linear regression analysis of significant variables correlating with fibrinogen levels revealed that **Base Excess (BE)**, **Hemoglobin (Hb)**, and **Injury Severity Score (ISS)** were the only independent variables capable of predicting fibrinogen levels, as shown in **Table (10)**.

Table (10): Variables that predicted fibrinogen level:

		Unstandardized Coefficients		Standardized Coefficients	P-Value
		B	**Std. Error**	**Beta**	
	(Constant)	2.018	0.147		0.0001
	BE	-0.005	0.005	-0.21	**0.024**
	HB	0.053	0.010	0.60	**0.0001**
	ISS	-0.006	0.002	-0.38	**0.001**

Cutoff Value of Fibrinogen to Predict Survival:

A fibrinogen level of 222.5 mg/dL was identified as a predictive cutoff for survival, with an Area Under the Curve (AUC), sensitivity of 67.3%, and specificity of 78%. The p-value for this cutoff was 0.0001, as shown in Table (11) and Figure (5)**.**

Table (11): Cut off value for fibrinogen to predict survival:

Test Result Variable(s): FIBRINOGENM				
Area	**Cut off value**	**P-value**	**Sensitivity**	**Specificity**
0.678	**222.5**	0.007	67.3%	78%

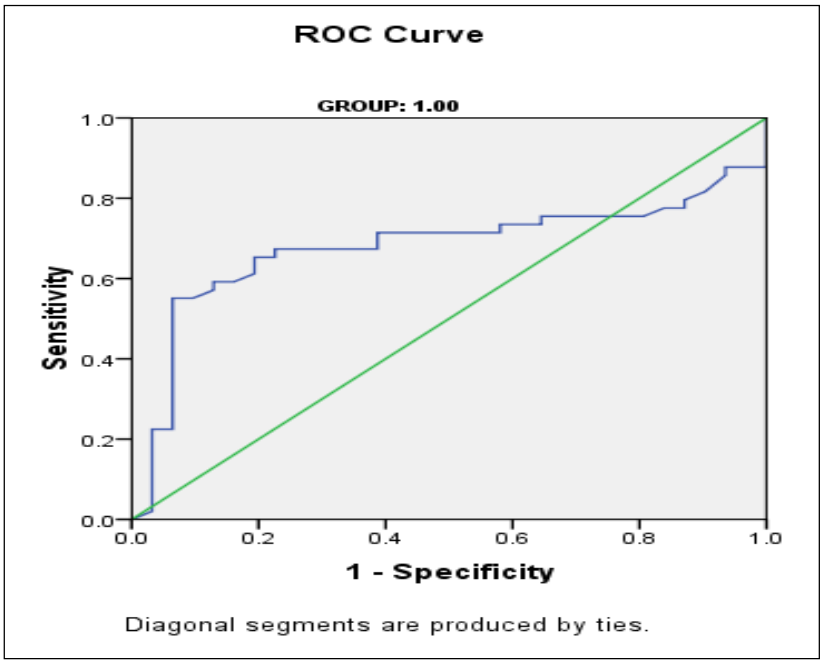

Figure (5): Cut off value for fibrinogen to predict survival

Cut off value of fibrinogen to predict severe or critical ISS:

Fibrinogen at 332 was predictive to ISS 4 or ISS 5 with AUC 0.98 and sensitivity 100% with specificity 98% a lower cut off value of 247 was sensitive by 100% and specific by 75% and p values was 0.0001 for each as shown in table (12).

Table (12): Cut off value for fibrinogen to predict severe or critical ISS:

Test Result Variable (s): Fibrinogen				
Area	Cut off value	P-value	Sensitivity	Specificity
0.985	**332**	0.0001	100%	98%
0.985	**247**	0.0001	100%	75%

Estimation of Logarithmic Fibrinogen Levels:

Through rigorous statistical modeling, we examined the correlation coefficients and the effect of independent variables—hemoglobin (Hb), Injury Severity Score (ISS), and base excess (BE)—to develop an equation for estimating the logarithmic fibrinogen level, which accounts for potential sample dilution:

Estimated Log Fibrinogen = 3.188 + 0.243 Hb - 0.019 Hb^2 + 0.019 BE - 0.05 ISS + 0.0002 ISS^2

When we compared the estimated log fibrinogen values with the measured values, we found a strong, significant direct correlation (R = 0.75, p = 0.0001), as illustrated in **Scatterplot Chart [9]**.

Note: The estimated fibrinogen values were analyzed earlier in the results and consistently demonstrated the same level of significance when correlated with other clinical parameters, further supporting the reliability of the equation.

Subsequent multiple regression analysis, which assessed the relative contributions of Hb, BE, and ISS in refining the predictive model, showed that this equation provides the best correlation with the actual log-measured fibrinogen levels (R = 0.75, p = 0.0001), as confirmed in **Scatterplot Chart [9]**.

4. Discussion:

Fibrinogen is a pivotal coagulation factor that is often critically reduced in patients with severe trauma [4]. It typically decreases rapidly following major traumatic hemorrhage [6], often preceding the decline of other coagulation factors [5].

Despite its clinical significance, fibrinogen is not measured as a routine part of standard

clotting assays, making its assessment is challenging in trauma settings. This study sought to evaluate the utility of three commonly altered laboratory parameters—hemoglobin (Hb%), Injury Severity Score (ISS), and base excess (BE)—in estimating fibrinogen levels, with the goal of predicting the need for urgent plasma transfusion.

Fibrinogen levels showed a clear correlation with systolic blood pressure, consistently increasing as blood pressure rise. This suggests that a decline in fibrinogen, whether measured or estimated, is a hallmark of shock in trauma patients.

Lower systolic blood pressure, along with elevated heart rate and respiratory rate, continues to serve as significant indicators of hemorrhagic shock, with a notable correlation to hemoglobin levels.

Our study also found that fibrinogen levels directly correlated with systolic blood pressure (SBP) and inversely with BE, both of which are key indicators of shock in trauma patients. Similarly, Christoph J et al. (2013) identified shock and substantial tissue injury as major drivers of trauma-induced coagulopathy (TIC), resulting in a profibrinolytic state via the activation of the protein C pathway [8].

Our multiple regression analysis identified Hb%, ISS, and BE as the sole independent variables capable of reliably predicting fibrinogen levels in trauma patients. These findings are consistent with prior research, including a study by Christoph J et al., which demonstrated the feasibility of estimating fibrinogen levels in the emergency department using point-of-care assays [8]. Their retrospective study derived an equation using the same three parameters; however, variations in the equations observed in the two studies may be attributable to differences in patient characteristics and study design. While Christoph J work was retrospective, our study was prospective, which may contribute to some discrepancies in the results.

Acidosis and hypothermia are known to exacerbate trauma-induced coagulopathy (TIC), with profound effects on fibrinogen synthesis and metabolism [10]. These findings are supported by the results of our study, which identified critical or low fibrinogen levels in 81% and 63% of shocked patients, respectively. This underscores the importance of early recognition of fibrinogen deficiency in trauma patients, as prompt intervention, such as plasma transfusion, can be life-saving.

Our study highlights the potential of using routine laboratory parameters to predict fibrinogen levels, providing a valuable tool

for clinicians in managing trauma patients, particularly those at risk for coagulopathy. Further research, including larger multicenter studies, is warranted to validate these findings and explore their broader clinical application.

In cases of severe trauma, plasma fibrinogen levels are often depleted before the effects of intravenous fluid resuscitation can dilute them [8, 11, 12, 13-14]. Moreover, fibrinogen levels usually tend to decrease earlier and more frequently than other coagulation factors, such as prothrombin time, activated partial thromboplastin time, and platelet count, in severely injured patients [15]. This early depletion of fibrinogen highlights the importance of assessing fibrinogen levels as a predictor of mortality in trauma patients, especially in critical care and emergency situation.

In the present study, we demonstrated that lower fibrinogen levels upon admission were associated with longer ICU stays and higher mortality rates. This aligns with other research that has reported a trauma-induced coagulopathy (TIC) in 25–35% of injured patients on arrival to ER [15, 16]. Established TIC is known to significantly increase the risk of massive transfusion (MT), extended ICU and hospital stays, and higher mortality rates [15].

A multicenter retrospective Japanese study found that 25% of severe trauma patients (with an Injury Severity Score [ISS] ≥16) had reduced plasma fibrinogen concentrations on ER admission [4, 6–8]. Critically low fibrinogen levels (≤1.0 g/L) and low fibrinogen levels (1.0–1.8 g/L) were observed in 21% and 44% respectively, in patients admitted with severe trauma who received massive transfusions MT. [8, 11, 12, 13-14]. Hypofibrinogenemia has been found as an independent predictor of both mortality and massive transfusion MT requirements in severe trauma patients [8, 11, 12, 13-14].

In agreement with Christoph J et al., who statistically analyzed and suggested that the following parameters Hb %, ISS, and BE, can estimate fibrinogen levels in patients with severe trauma on admission, our findings align with theirs. In their study, these three parameters accounted for approximately 51% of the variability in observed fibrinogen concentrations. In our research, Hb%, BE, and ISS were shown to be reliable parameters for estimating fibrinogen levels in trauma patients, with a strong correlation (75%) to measured fibrinogen concentrations

In our study, a plasma fibrinogen threshold of 2.22 g/L was found to correlate strongly with survival. This finding is consistent with earlier guidelines that suggested that

measured fibrinogen level of 1.0 g/L as the critical level in bleeding post traumatic patients [17]. More recent guidelines recommend maintaining fibrinogen levels above 1.5–2.0 g/L in severe trauma patients. Several retrospective studies have also identified fibrinogen levels ≤1.9 g/L on ER admission as independent predictors of mortality and massive bleeding [18]. Based on these insights, our study supports a critical fibrinogen threshold of 2.0 g/L, which closely matches the cut-off value for measured fibrinogen levels found in our research.

Schlump and colleagues have shown that fibrinogen level can be easily estimated in trauma patients in the ER. Hemorrhage, injury severity, and metabolic acidosis are primary factors that deplete fibrinogen levels, in addition to other iatrogenic and endogenous factors that contribute to its reduction [19].

The limitations of this study include the relatively small sample size and the short follow-up period.

5. Conclusions:

A fibrinogen cutoff value of 222.5 mg/dL was found to predict survival in trauma patients with a sensitivity of 67%, specificity of 78%, and a p-value of 0.007.

Furthermore, a fibrinogen threshold of 332 mg/dL effectively predicted severe injury (ISS 4 or ISS 5), showing an area under the curve (AUC) of 0.98, sensitivity of 100%, and specificity of 98%. A lower cutoff of 247 mg/dL also proved highly sensitive (100%) and specific (75%).

This study demonstrates that it is feasible to risk-stratify patients for low or critical fibrinogen levels using hemoglobin (Hb), Injury Severity Score (ISS) and base excess (BE), all of which are rapidly available in ICU.

This research highlights the importance of estimation and mathematical calculation of fibrinogen level before waiting of laboratory results so that cryoprecipitate and fibrinogen can be given to the severely traumatized patient at ER or ICU.

I would like to express my sincere gratitude to Dr. Nadia Mohamed for her invaluable support in proofreading this article. I also wish to acknowledge the excellent statistical analysis performed by our colleague, Dr. Moataz Elhalag, who provided us with the equation for estimating fibrinogen level.

6. References:

1. **Mosesson MW.** Fibrinogen and fibrin structure and functions. Journal of Thrombosis and Haemostasis. 2005 Aug; 3(8):1894-904.

2. **Gama S.** Low fibrinogen levels: How to maximize accuracy when using an optically derived method. Journal of Applied Hematology. 2016 Oct 1; 7(4):148.
3. **Schlimp CJ, Schöchl H.** Fibrinogen Assays. In Trauma Induced Coagulopathy 2016 (pp. 227-235).
4. **Chambers LA, Chow SJ, Shaffer LE.** Frequency and characteristics of coagulopathy in trauma patients treated with a low-or high-plasma-content massive transfusion protocol. American journal of clinical pathology. 2011 Sep 1; 136(3):364-70.
5. **Hayakawa M, Gando S, Ono Y, Wada T, Yanagida Y, Sawamura A.** Fibrinogen level deteriorates before other routine coagulation parameters and massive transfusion in the early phase of severe trauma: a retrospective observational study. In Seminars in thrombosis and hemostasis 2015 Feb (Vol. 41, No. 01, pp. 035-042).
6. **Winearls J, Campbell D, Hurn C, Furyk J, Ryan G, Trout M, et al.** Fibrinogen in traumatic haemorrhage: a narrative review. Injury. 2017 Feb 1; 48(2):230-42.
7. **Solomon C, Collis RE, Collins PW.** Haemostatic monitoring during postpartum haemorrhage and implications for management. British journal of anaesthesia. 2012 Oct 16; 109(6):851-63.
8. **Schlimp CJ, Voelckel W, Inaba K, Maegele M, Ponschab M, Schöchl H.** Estimation of plasma fibrinogen levels based on hemoglobin, base excess and Injury Severity Score upon emergency room admission. Critical care. 2013 Aug; 17(4):R137.
9. **Cohen MJ, Kutcher M, Redick B, Nelson M, Call M, Knudson MM, et al.** Clinical and mechanistic drivers of acute traumatic coagulopathy. The journal of trauma and acute care surgery. 2013 Jul; 75(101):S40.
10. **Martini WZ.** Coagulopathy by hypothermia and acidosis: mechanisms of thrombin generation and fibrinogen availability. Journal of Trauma and Acute Care Surgery. 2009 Jul 1; 67(1):202-9.
11. **White NJ, Martin EJ, Brophy DF, Ward KR.** Coagulopathy and traumatic shock: characterizing hemostatic function during the critical period prior to fluid resuscitation. Resuscitation. 2010 Jan 1; 81(1):111-6.
12. **Hayakawa M.** Dynamics of fibrinogen in acute phases of trauma. Journal of Intensive Care. 2017 Dec;5(1):3.

13. **Charbit B, Mandelbrot L, Samain E, Baron G, Haddaoui B, Keita H, et al.** The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. Journal of Thrombosis and Haemostasis. 2007 Feb; 5(2):266-73.
14. **Rourke C, Curry N, Khan S, Taylor R, Raza I, Davenport R, et al.** Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes. Journal of Thrombosis and Haemostasis. 2012 Jul; 10 (7):1342-51.
15. **Schöchl H, Cotton B, Inaba K, Nienaber U, Fischer H, Voelckel W, et al.** FIBTEM provides early prediction of massive transfusion in trauma. Critical Care. 2011 Dec; 15(6):R265.
16. **Tauber H, Innerhofer P, Breitkopf R, Westermann I, Beer R, El Attal R, et al.** Prevalence and impact of abnormal ROTEM® assays in severe blunt trauma: results of the 'Diagnosis and Treatment of Trauma-Induced Coagulopathy (DIA-TRE-TIC) study'. British journal of anaesthesia. 2011 Jun 23; 107(3):378-87.
17. **Inaba K, Karamanos E, Lustenberger T, Schöchl H, Shulman I, Nelson J, et al.** Impact of fibrinogen levels on outcomes after acute injury in patients requiring a massive transfusion. Journal of the American College of Surgeons. 2013 Feb 1; 216(2):290-7.
18. **Bouzat P, Ageron FX, Charbit J, Bobbia X, Deras P, Nugues JB, et al.** Modelling the association between fibrinogen concentration on admission and mortality in patients with massive transfusion after severe trauma: an analysis of a large regional database. Scandinavian journal of trauma, resuscitation and emergency medicine. 2018 Dec;26(1):55.
19. **Schlump CJ, Cadmore J, Solomon C, Redl H, Schöchl H.** The effect of fibrinogen concentrates and factor XIII on Thromboelastometric in 33% diluted blood with albumin, gelatine, hydroxyethyl starch or saline in vitro. Blood Transfusion. 2013 Oct;11(4):510.