SOFA Score as a Predictor of Mortality in Critically Ill Cirrhotic Patients

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Abstract: Scoring systems have been developed to predict outcome of patients admitted to ICU as well as to prioritize admission to ICU. The objective of this study is to evaluate SOFA score in prediction of outcome of critically ill cirrhotic patients in comparison with APACHE II and MELD scoring systems. Method: a hundred cirrhotic patients admitted to ICU were enrolled in the study. SOFA, APACHE II and MELD scores were collected during the first 24 hours of ICU admission. The patients were classified into two main groups according to outcome; Survivor and Non-Survivor. Result**:** This study showed that the mean for initial SOFA score, APACHE II score and MELD score were significantly higher in non-survivor group in comparison to survivor one. Discrimination was highest for SOFA score (area under ROC curve 1.00, p=0.001) compared to both APACHE II score (area under ROC curve 0.933, p=0.001) and MELD score (area under ROC curve 0.899, p=0.001).Conclusion**:** This study concluded that the initial SOFA score can predict short term prognosis in critically ill cirrhotic patient admitted to ICU in comparison to APACHE II and MELD scoring systems. We believe that SOFA score within the first 24 hours of ICU admission represents a highly significant prognostic tool to evaluate mortality in critically ill cirrhotic patients.

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Key words: : SOFA score, ICU mortality, Critically ill cirrhotic patients

1. Introduction

Liver cirrhosis represents the final common pathway of virtually all chronic liver disease and is characterized by an accumulation of extracellular matrix rich in fibrillar collagen (Jang, 2009).

The common used scoring systems for predicting the outcome in critically ill cirrhotic patients are Child–Pugh score (Pugh, 1973), Sequential Organ Failure Assessment (SOFA) (Vincent, 1996), Model for End-stage Liver Disease (MELD) (Kamath, 2001), and Acute Physiology, Age, Chronic Health Evaluation II (APACHE II)(Knaus, 1985).

The sequential organ failure assessment (SOFA) score has been created in order to take into consideration the changing severity over time of the process of organ dysfunction/failure. It has been claimed that the clinical complexity of a multimodal event such as the multi-organ failure syndrome needed to be described quantitatively and as objectively as possible over time. Therefore, the SOFA score has been designed to report morbidity and to objectively quantify the degree of dysfunction/failure of each organ daily in critically ill patients (Vincent, 1996).

The aim was to quantify the severity of the patients' illness based on the degree of Organ dysfunction, serially over time. Although severity of illness scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE II) are based on the first 24 hrs of intensive care unit (ICU) admission, the (SOFA) scoring system takes into account the time course of a patient's condition during the entire ICU stay (Vincent, 1996).

The Sequential Organ Failure Assessment (SOFA) score is designed to evaluate the function of six major organ systems (i.e., cardiovascular, respiratory, renal, hepatic, central nervous system, and coagulation) over time. The score is obtained on the day of admission and each of the following days in the ICU. Because the SOFA score monitors daily changes in organ function, it can evaluate the patient's response to treatment, and sequential changes in the SOFA score (e.g., increasing or decreasing) can predict the eventual outcome of the ICU stay (Marino, 2007).

It was stated that one of the criteria for a system that defines the degree of Organ dysfunction is that it should be based on a limited number of simple but objective variables that are easily and routinely measured in every institution. With a total of 6 variables, the SOFA score contains fewer variables than most other ICU severity of illness scoring systems, such as APACHE II (Vincent, 1996).

Both retrospective and prospective studies showed that high SOFA scores were associated with increased mortality, and that different patient groups may acquire different patterns of organ dysfunction. Sequential assessment of organ dysfunction during the first few days of ICU admission is a good indicator of prognosis. Both

the mean and highest SOFA scores are particularly useful predictors of outcome. Independent of the initial score, an increase in SOFA score during the first 48 hours in the ICU predicts a mortality rate of at least 50% (Marino, 2007).

Aim of study:

The aim of the study was to evaluate SOFA score as a predictor of mortality in critically ill cirrhotic patients in comparison to APACHE II and MELD scoring systems.

2.Patients and Methods:

The local ethics committee approved the study protocol. Formal consent was obtained either from the patient or the next of kin if the patient was incompetent.

- Pediatric patients ≤ 18 years of age.
- Uremic patients undergoing renal replacement therapy.
- Patients who had undergone liver transplantation.

The following data were collected for each patient on the 1st day of admission:

→ Demographics.

→ Reason for ICU admission.

→ Acute diagnosis.

→ SOFA score.(Table1)

→APACHE, MELD AND CHILD POUGH SCORE

And finally, the duration of hospitalization and the outcome of each patient were recorded.

Table (1): Showing Sequential Organ Failure Assessment (SOFA) Score

	Points				
Variables	**0**	**1**	**2**	**3**	**4**
PaO_2/FiO_2 (mmHg)	>400	≤400	≤300	≤200*	≤100*
Platelets ($10^3/\mu L$)	>150	≤150	≤100	≤50	≤20
Billrubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	≥12
Creatinine (mg/dL) or Urine Output (mL/day)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200
Glasgow Coma Score†	15	13–14	10–12	6–9	<6
Hypotension	None	Mean BP <70 mmHg	Dopa ≤5 or Dobu (any dose)‡	Dopa >5 or Epi ≤0.1 or Norepi ≤0.1‡	Dop >15 or Epi >0.1 or Norepi >0.1‡

*Values obtained during respiratory support.
†In patients who are sedated, use the best estimate of what the GCS would be without sedation.
‡Adrenergic agents administered for at least one hour. Doses expressed in µg/kg/min.
Dopa = Dopamine, Dobu = dobutamine, Epi = epinephrine, Norepi = norepinephrine.

Scoring Method:

1. Use the *most abnormal value* for each variable in a 24-hour period.
2. If a single value is missing, use the mean value of the sum of the results immediately preceding and following the missing value.
3. Add the corresponding points for all 6 parameters to obtain the final score (range = 0–24).

Statistical Analysis

Diagnosis of cirrhosis was based on a combination of physical findings and biochemical and sonar findings. Severity of liver disease on ICU admission was graded using Child-Pugh and SOFA scoring systems.

Continuous variables were summarized using means and standard error. The primary analysis compared hospital survivors with non-survivors. All variables were tested for normal distribution using the Kolmogorov–Smirnov test. Student's *t*-test was employed to compare the means of continuous variables and normally distributed data; otherwise, the Mann–Whitney *U*-test was employed. Categorical data were tested using the chi-square test. Finally, risk factors were assessed with univariate analysis, and variables that were statistically significant ($p < 0.05$) in the univariate analysis were included in multivariate analysis by applying a multiple logistic regression based on forward elimination of data.

3. Results

1-Regarding demographic data

Table (2): showing statistically insignificant difference between both groups regarding age, gender.

Table 2	Fate	Mean ± Std. Deviation		P VALUE
Age	Survivor	59.73 ± 5.71		0.625
	Non-Survivor	58.91 ± 9.24		
Gender		Male	Female	0.27
	Survivor	23	15	
	Non-Survivor	45	17	

2-Regarding assosiated comorbidities (DM,HTN, HCC)data

Table (3): showing statistically insignificant difference between both groups regarding DM, HTN and HCC occurrence

Table 3	Fate	Mean ± Std. Deviation		P VALUE
DM		No DM	DM	0.589
	Survivor	23	15	
	Non-Survivor	44	18	
HTN		No HTN	HTN	0.589
	Survivor	33	5	
	Non-Survivor	51	11	
HCC		No HCC	HCC	0.485
	Survivor	30	2	
	Non-Survivor	50	8	

3-Regarding lab data

Table (4) mean values of laboratory data with Standard deviation are

Table 2	N	Mean ± Std. Deviation
BUN	100	38.6 ±23.30 mg/dl
Na	100	130.03 ± 7.35 mmol/l
K	100	4.41 ± 725 mmol/l
AST	100	70.23 ±57.95 U/L
ALT	100	35.90 ±23.95 U/L
Albumin	100	2.05±0.44 g/dl
Bilirubin	100	6.70±5.88 mg/dl
Hb	100	8.79±1.43 g/dl
WBC	100	10.43±6.15 thousands/cmm
Platelets	100	120.46±71.87 thousands/cmm
PT	100	18.54±2.70
INR	100	1.67±0.26
PH	100	7.35±0.10
PO2	100	83.06±17.75
PCO2	100	26.36±5.81
HCO3	100	16.77±4.80
Hct	100	24.90±6.65
Creatinine	100	0.96±6.65 mg/dl

Table (5): Univariate analysis for laboratory data

Table 5	Fate	Mean ± Std. Deviation	P VALUE
BUN (mg/dl)	Survivor	24.50 ± 15.34	0.0001
	Non-Survivor	47.30 ± 23.19	
Na (mmol/l)	Survivor	135.42 ± 5.55	0.0001
	Non-Survivor	126.72 ± 6.31	
K (mmol/l)	Survivor	4.29 ± 0.39	0.20
	Non-Survivor	4.48 ± 0.86	
AST (U/L)	Survivor	54.86 ± 33.98	0.037
	Non-Survivor	79.64 ± 67.18	
ALT (U/L)	Survivor	36.86 ± 28.05	0.75
	Non-Survivor	35.30 ± 21.29	
Albumin (g/dl)	Survivor	2.23 ± 0.44	0.0001
	Non-Survivor	1.93 ± 0.40	
Bilirubin (mg/dl)	Survivor	3.53 ± 2.20	0.0001
	Non-Survivor	8.65 ± 6.57	
Hb (g/dl)	Survivor	8.96 ± 1.27	0.35
	Non-Survivor	8.68 ± 1.52	
WBC (1000/cmm)	Survivor	9.23 ± 4.78	0.12
	Non-Survivor	11.16 ± 6.78	
Platelets (1000/cmm)	Survivor	135.71 ± 88.93	0.09
	Non-Survivor	111.11 ± 57.91	
PT	Survivor	16.88 ± 1.30	0.0001
	Non-Survivor	19.56 ± 2.83	
INR	Survivor	1.51 ± 0.13	0.0001
	Non-Survivor	1.77 ± 0.27	
PH	Survivor	7.41 ± 0.07	0.0001
	Non-Survivor	7.32 ± 0.11	
PO2	Survivor	86.28 ± 12.43	0.15
	Non-Survivor	81.08 ± 20.18	
PCO2	Survivor	27.18 ± 6.08	0.27
	Non-Survivor	25.85 ± 5.63	
HCO3	Survivor	18.41 ± 4.21	0.0001
	Non-Survivor	15.76 ± 4.90	
Hct (g%)	Survivor	25.26 ± 6.39	0.672
	Non-Survivor	24.67 ± 6.85	
Creatinine (mg/dl)	Survivor	0.77 ± 0.22	0.0001
	Non-Survivor	1.08 ± 0.23	

As described Non-Survivor group had significantly higher serum creatinine, BUN, serum bilirubin, PT and INR in comparison to Survivor group. The Non-Survivor group had a significantly lower serum sodium level, serum albumin, blood PH and HCO3.
There were statistically insignificant differences between both groups regarding values of ALT, Hb, Hct, WBCs, PLT, PO2 and PCO2.

4-Regarding scoring systems

I-The mean values of scoring systems used and their SD are shown in table (6):

Table 6	N	Mean ± Std. Deviation
APACHE II	100	25.40 ± 10.62
SOFA	100	10.51 ± 4.61
MELD	100	23.37 ± 7.96
CHILD	100	3.00 ± 0.00

II- validity of each scoring system

Comparison between the 2 groups was done for validation of each scoring systems and showed the same extreme significance of higher SOFA, APACHE II, MELD with extremely significant p values (0.0001 for each) The Non-Survivor group had a significantly longer duration of hospital stay than the Survivor group.

Table (7) validity of each scoring system

Table 7	Fate	Mean	Std. Deviation	P VALUE
APACHE	Survivor	15.44	3.62	0.0001
	Non-Survivor	31.50	8.69	
SOFA	Survivor	5.21	1.49	0.0001
	Non-Survivor	13.75	2.24	
MELD	Survivor	16.81	4.38	0.0001
	Non-Survivor	27.38	6.92	

III-regarding predictive value

Table (8): Shows all scoring systems studied in this study were highly predictive of poor outcome in cirrhotic patients at different cut-off points as studied by ROC curve analysis (Figure 1):

Table 8	Area under the curve	Mean of Cut off point	P value	PPV	NPV	Sensitivity	Specificity	
APACHE	0.933	19.5	0.0001	86%	77%	87%	82%	
SOFA	1.000	10.5	0.0001	80%	85%	88%	100%	
MELD	0.899	18.5	0.0001	79%	92%	91.9%	77%	

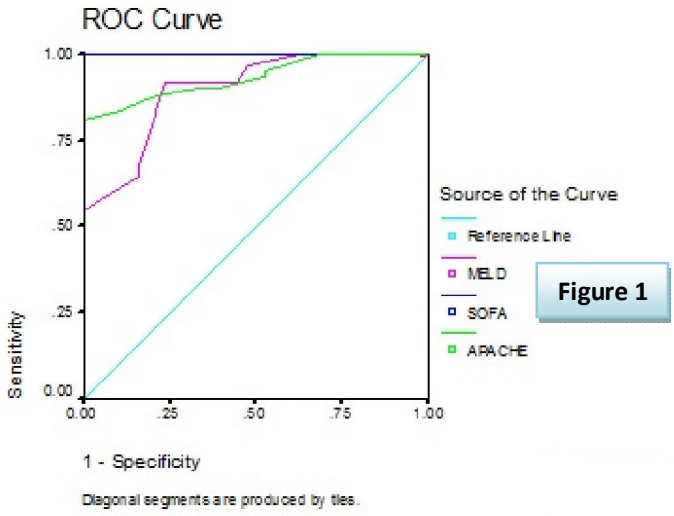


Figure 1

IV-scoring systems and length of stay in the hospital

The mean duration of hospital stay in the whole studied population was 11.6± 6.58 days with least of 3 days and maximum 30 days.

There were 62% non-survival cases and 38 % survival as described for overall population in this study. There was a significant positive correlation between SOFA score and the LOS as the R= 0.3 and p value = 0.008 as shown in figure (2):

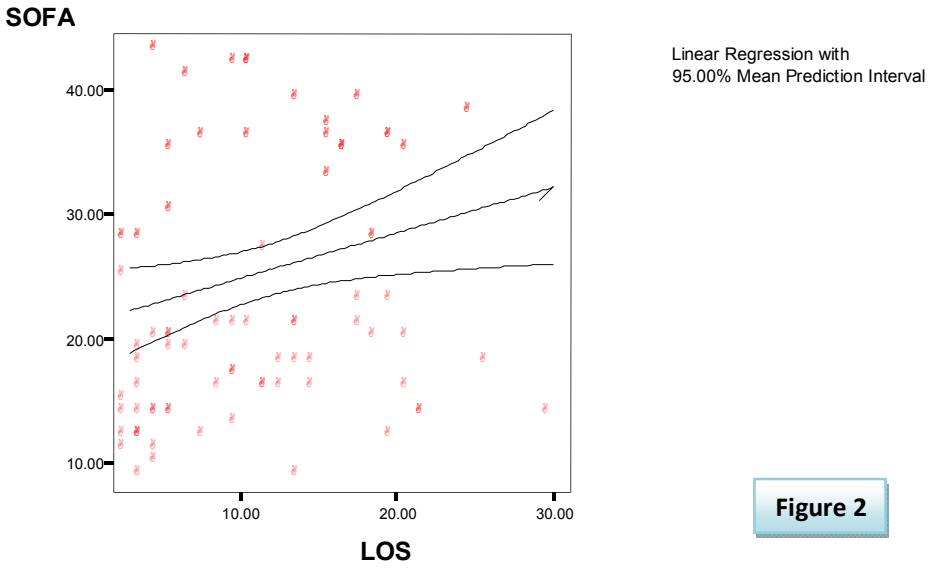


Figure 2

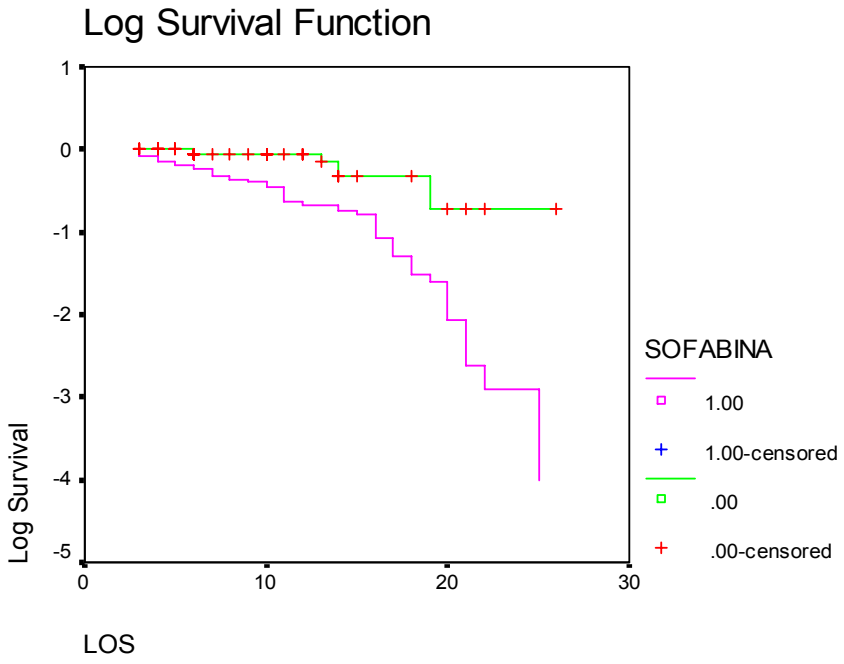
V-scoring system predictive death rates

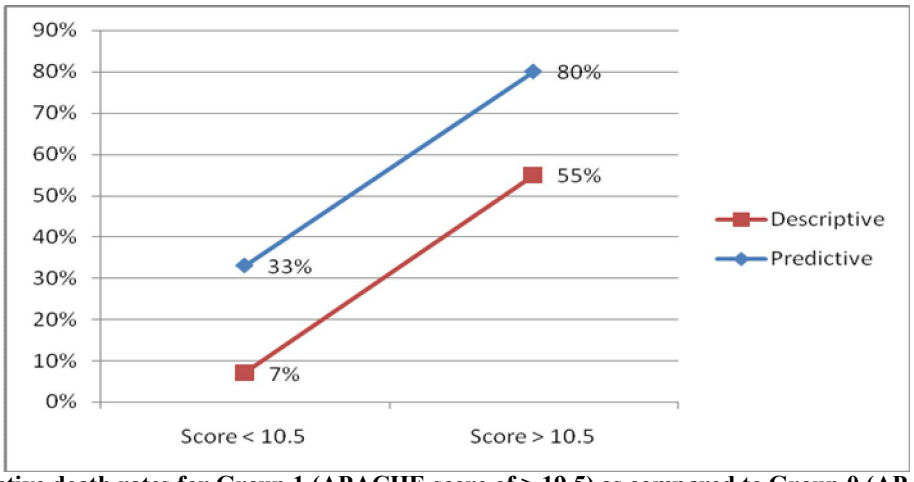
The predictive death rates for Group 1 (SOFA score of > 10.5) as compared to Group 0 (SOFA score of < 10.5) was significantly higher

80 % at 19th day in group 1 (**SOFA score of > 10.5**)

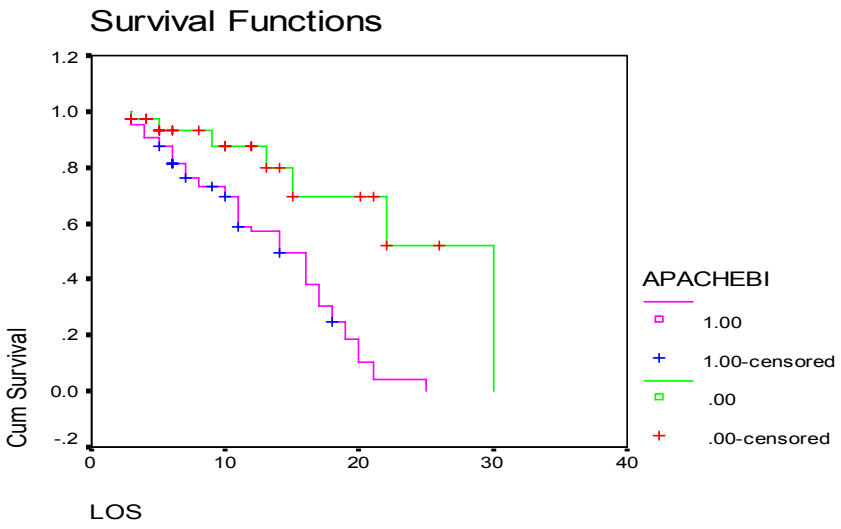
33% at 18th day in group 0 (**SOFA score of < 10.5**)

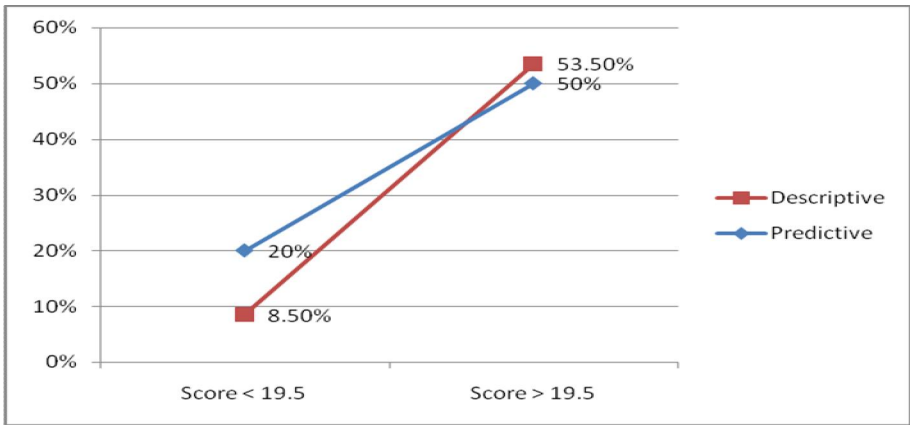
p value was 0.0001



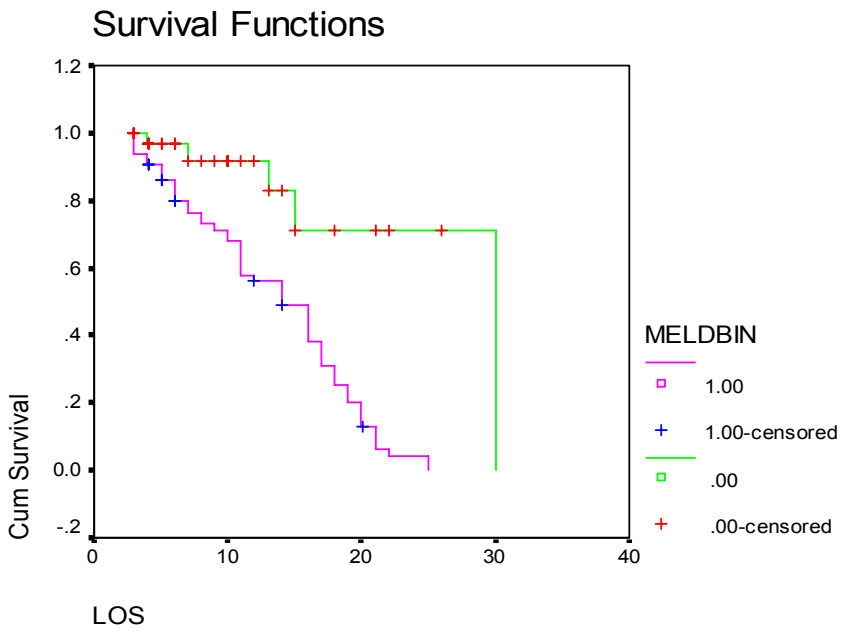


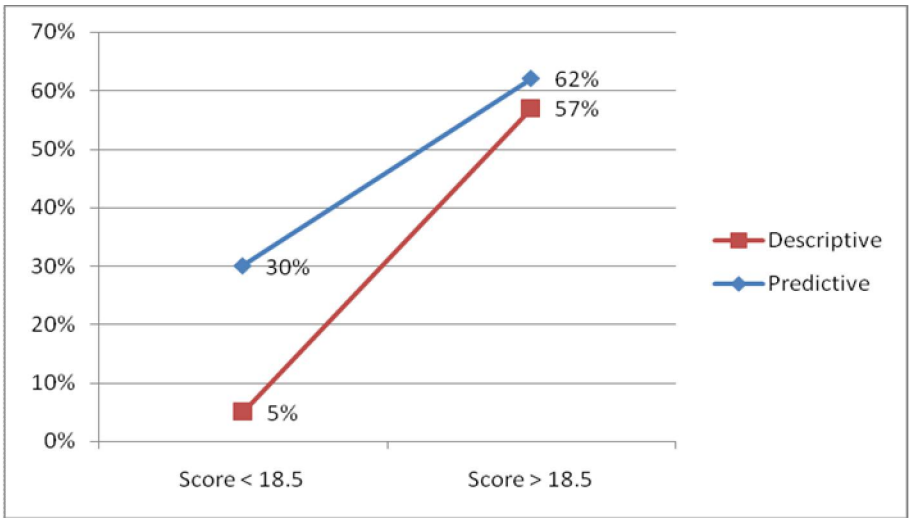
The predictive death rates for Group 1 (APACHE score of > 19.5) as compared to Group 0 (APACHE score of < 19.5) was significantly higher
50 % at 13th day in group 1 (**APACHE score of > 19.5**)
20% at 13th day in group 0 (**APACHE score of < 19.5**)
p value was 0.0002





The predictive death rates for Group 1 (MELD score of > 18.5) as compared to Group 0 (MELD score of < 18.5) as shown in figures (9-A, 9-B) was significantly higher
62 % at 16th day in group 1 (**MELD score of > 18.5**)
30% at 18th day in group 0 (**MELD score of < 18.5**)
p value was 0.0001





4. Discussion

The overall mortality rate in this investigation was 62%, and is in agreement with previous reports indicating that cirrhotic patients admitted to an ICU have a very poor prognosis (Ismair, 2001; Menon, 2001; Petrides, 1994; Hillebrandt, 2002; Houglum, 1997; Cotezee, 1980). The cause of liver cirrhosis was hepatitis C virus and most cases of ICU admission were due to hematemesis, hepatic coma and SBP. This study identified that SOFA Score on the first day of ICU admission was prognostically significant variable for critically ill cirrhotic patients. SOFA Score was highly predictive of poor outcome in cirrhotic patients at a cut-off point of 10.5 as studied by ROC curve analysis

There was statistically insignificant difference between both groups regarding age, gender distribution, DM, HTN and HCC occurrence on both groups. The Non-Survivor group had significantly higher serum creatinine level, higher BUN, serum bilirubin, PT and INR in comparison to Survivor group. The Non-Survivor group had a significantly lower serum sodium level, serum albumin, blood PH and HCO3 There were also statistically insignificant differences between both groups regarding values of ALT, Hb, Hct, WBCs, PLT, PO2 and PCO2. This study showed that the mean for initial SOFA score, APACHE II score and MELD score were significantly higher in non-survivor group in comparison to survivor one. Discrimination was highest for SOFA score (area under ROC curve 1.00, p=0.001) compared to both APACHE II score (area under ROC curve 0.933, p=0.001) and MELD score (area under ROC curve 0.899, p=0.001).

Several studies have verified the importance of SOFA Score when assessing the prognosis of cirrhotic patients. ***Shrestha et al*** (2011) conducted a study to compare Acute Physiology and Chronic Health Evaluation (APACHE) III score with initial Sequential Organ Failure Assessment (SOFA) score to predict ICU mortality where they found that both mean APACHE III and initial SOFA score were significantly ($p<0.001$) higher in non survivors when compared to survivors and a positive and strong correlation was seen between initial SOFA score and APACHE III score. Similar results were seen in studies by ***Ferreira*** (2001) ***et al***, ***Acharya et al*** (2007) and ***Chen et al*** (2006)**.** Discrimination was good for both APACHE III (area under ROC curve 0.895) and initial SOFA score (area under ROC curve 0.881). Area for initial SOFA was 0.917 in a study by ***Chen et al*** (2006) and 0.79 in a study by ***Ferreira et al*** (2001)**.** In our study, the area under ROC curve for initial SOFA score was 1 and this may be due to the very bad general condition of cirrhotic patients. They concluded that initial SOFA score had better calibration and performed better to predict non survivors when compared with APACHE III score, So initial SOFA score can be used as a simple, economical yet reliable tool to predict outcome in ICU and can help clinicians for better utilization of limited and expensive ICU resources.

Acharya et al (2007) conducted a study to evaluate the Sequential Organ Failure Assessment (SOFA) Score in predicting outcome in ICU patients with SIRS. They found that the non survivors had high initial, mean and highest SOFA scores as compared to survivors. The initial SOFA score > 11 predicted a mortality of 90 %. Similarly, mean SOFA score of > 7 predicted a mortality of 73.9% and high SOFA score > 11 predicted a mortality of 87.5%. Area under receiver operating characteristic (ROC) curve for mean SOFA was 0.825, for high SOFA was 0.817 and for initial SOFA was 0.708. They concluded that the SOFA score was able to predict outcome in ICU patients with SIRS. Initial SOFA, Mean SOFA and Highest SOFA, all correlated well with the mortality. The SOFA scoring system can help the ICU physicians in admitting patients, monitoring the clinical course, assessment of organ dysfunction, predicting mortality, and for transferring patients out from the ICU and thus in proper utilization of ICU resources also in developing countries where the resources are limited.

Halim et al (2009) conducted a study to determine and compare the validity of the SOFA and MSOFA scores with the Acute Physiology and Chronic Health Evaluation II (APACHE II) score for predicting mortality in surgical patients treated in the ICU. This study showed that the mean APACHE II score and MSOFA were all higher in non-survivors than in survivors. Discrimination was less satisfactory for APACHE II and acceptable for both initial SOFA and initial MSOFA. Mean and maximum values of SOFA and MSOFA showed even better discrimination values with AuROC=0.92; $p\leq0.001$, and AuROC=0.91; $p\leq0.001$ for mean SOFA and max SOFA respectively, and AuROC=0.90; $p\leq0.001$, AuROC=0.90; $p\leq0.001$ for mean MSOFA and max MSOFA respectively. They concluded that SOFA and MSOFA scoring systems are better than APACHE II system in predicting mortality in ICU surgical patients. Serial measurements of SOFA and MSOFA score significantly improve their predictive accuracy.

Wehler et al (2001) conducted a study to assess and compare the prognostic accuracy of the Child-Pugh classification, the Acute Physiology and Chronic Health Evaluation (APACHE) II system and the Sequential Organ Failure Assessment (SOFA) for predicting hospital mortality in patients with cirrhosis when used 24 hours after admission to a medical intensive care unit (ICU). Prospective data were recorded on 143 patients. Cumulative mortality rates were 36% in the ICU, 46% in the hospital, and 56% at 6-month follow-up. By using the area under receive operating characteristic (AUROC) curves, the SOFA showed an excellent discriminative power (AUROC 0.94), which was clearly superior to the APACHE II

(AUROC 0.79) and the Child-Pugh system (AUROC 0.74).They concluded that the discriminatory power of the SOFA to predict short-term mortality in critically ill patients with cirrhosis is clearly superior to the APACHE II and Child-Pugh systems They also believe that the SOFA may improve the physician's estimate of prognosis and, therefore be useful in clinical decision making aimed at using medical resources appropriately as well as providing patients and families with objective information.

Eric Levesque et al (2012) conducted a study on three hundred and seventy-seven cirrhotic patients admitted to the ICU between May 2005 and March 2009 at Paul Brousse University Hospital to assess the predictive value of prognostic scores with respect to mortality and to identify mortality risk factors. ROC curve analysis demonstrated that SOFA (0.92) and SAPS II (0.89) scores calculated within 24 h of admission predicted ICU mortality better than the Child–Pugh score (0.79) and MELD scores (0.79–0.82). They concluded that for cirrhotic patients admitted to the ICU, SAPS II, and SOFA scores predicted ICU mortality better than liver-specific scores.

5. Conclusion

This study concluded that the initial SOFA score can predict short term prognosis in critically

ill cirrhotic patient admitted to ICU in comparison to APACHE II and MELD scoring systems. We believe that SOFA score within the first 24 hours of ICU admission represents a highly significant prognostic tool to evaluate mortality in critically ill cirrhotic patients.

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