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# Validity of systemic inflammatory response syndrome (SIRS) criteria, interleukin-6 and (MELD) score as prognostic tools in cirrhotic patients with acute renal failure admitted to Emergency Department in Suez Canal University Hospital, Egypt

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**Abstract**
Systemic inflammatory response syndrome (SIRS) is the body's response to an infectious or noninfectious insult. Cirrhotic patients are predisposed to infection due to an impaired immune function acute kidney injury (AKI), is a frequent problem, in cirrhotic patients. Renal failure following sepsis has been observed in 1 third of patients with cirrhosis and ascites the prognosis for patients with cirrhosis and renal failure is poor: Acute kidney injury (AKI), is a relatively frequent problem, occurring in approximately 20% of hospitalized patients with cirrhosis. The prognosis for patients with cirrhosis and renal failure is poor, this extremely poor outcome is probably related to the combination of liver and renal failure, as well as to associated complications.To evaluate the outcome of the acute kidney injury in cirrhotic patients by using SIRS, IL-6 and value of MELD score in order to early diagnosis and treatment to improve outcome and to decrease short term mortality.as prognostic tools. Cross sectional observational study with prospective data collection**.** Data collected from 72 cirrhotic patients with acute kidney injury. All patients were followed up for 3 months and outcome was recorded. The 3 months mortality was 58.33%. 59.7% of the patients express SIRS criteria on admission to Emergency Department. SIRS criteria were significantly correlated with both ER mortality and 3 month mortality**,** serum level of IL-6 was 157.53 ± 191.59 pg/ml, there was significant relation between ER mortality, overall mortality and presence of infection and IL-6 levels. The mean MELD score was 30.32 ± 5.01, and Expected 3 month mortality according to MELD score ranged between "6% - 71.3%". There was significant relation between ER and overall mortality and MELD score. Value of IL-6>36.5 pg/ml has sensitivity of 83.3%, specificity of 80%, SIRS score>2 has sensitivity of 47.62%, specificity of 93.33%, in prediction of overall mortality among cirrhotic patients with acute renal failure, Value of MELD score>28 has sensitivity of 80.95%, specificity of 80%, in prediction of overall mortality among cirrhotic patients with acute renal failure.

**Keywords:** SIRS, interleukin-6, (MELD) Score, cirrhotic, renal failure

## Introduction

Acute kidney injury (AKI), is a relatively frequent problem, occurring in approximately 20% of hospitalized patients with cirrhosis [1].

Patients with advanced cirrhosis commonly develop disturbances in renal function, such as sodium retention, water retention, and renal failure, among them; renal failure is the most relevant in clinical practice [2]. Because its appearance usually entails a very poor prognosis, several factors predisposing to the development of renal failure in patients with cirrhosis have been identified, including spontaneous bacterial peritonitis, large-volume paracentesis without intravenous administration of albumin, and treatment with several drugs, such as non-steroidal anti-inflammatory drugs or aminoglycosides [2].

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In patients with cirrhosis, acute renal failure is mainly due to pre-renal failure (caused by renal hypoperfusion) and tubular necrosis. The main causes of pre-renal failure are “true hypovolemia” (induced by hemorrhage or gastrointestinal or renal fluid losses), sepsis, or type 1 hepato-renal syndrome (HRS). Acute tubular necrosis is mainly due to an ischemic insult to the renal tubules. The most common condition leading to ischemic acute tubular necrosis is severe and sustained prerenal failure [3].

Despite advances in intensive care, and new treatment facilities, renal failure in patients with cirrhosis is a serious event with a poor prognosis [4].

The prognosis for patients with cirrhosis and renal failure is poor. The overall survival rate is approximately 50% at 1 month and 20% at 6 months. This extremely poor outcome is probably related to the combination of liver and renal failure, as well as to associated complications. However, survival rates can differ according to the type of renal failure [5]. The hepato-renal syndrome is associated with the worst prognosis. The great majority of patients with the

hepato-renal syndrome have a poor short-term outcome unless they undergo liver transplantation. Mortality is higher with type 1 hepato-renal syndrome than with type 2 (median survival, 1 month vs.6 months [5].

There is growing evidence that systemic inflammation is one of the key factors causing circulatory disorders, including impaired effective arterial blood volume leading to renal hypo-perfusion and failure [4].Bacterial infection represents one of the most frequent complications in patients with cirrhosis , as a result of multiple abnormalities in the defensive mechanisms against bacteria and because the release of cytokines and vasodilators is a well-known feature of all bacterial infections it may be hypothesized that renal failure in patients with cirrhosis may be induced also by bacterial infections [6].

Renal dysfunction develops in 33% of patients with infection. the pathogenesis of renal dysfunction in the setting of infection is related to worsening splanchnic and systemic vasodilatation leading to a further decrease in effective arterial blood volume, with the consequent activation of neurohumoral systems (renin-angiotensin-aldosterone) that leads to renal vasoconstriction and renal dysfunction associated with increases in inflammatory cytokines as tumor necrosis factor and interleukin 6 (TNF, IL-6) [1].

The diagnosis of Systemic Inflammatory Response Syndrome ( SIRS) and sepsis and evaluation of its severity is complicated, however, the early diagnosis and stratification of the severity of sepsis is very important, increasing the possibility of starting timely and specific treatment and save patients from multiple organ dysfunctions especially impairment of kidney function [3].

Because of extremely high mortality rates of cirrhotic patients with acute renal failure and the promising new treatment and restricted medical resources investigators and physicians require a reliable tool to risk stratify and monitor the patients during practice and clinical trials [7]. It has been a challenging issue for physicians to elaborate reliable tools for predicting outcome. The principal goal is to establish a single score resulting from the sum of a subset of individual variables (predictive variables), each being supposed to weight on the progression of the disease. Among a series of new prognostic scores reported in the literature, MELD (for Model for End Stage Liver Disease) score was proposed as a most promising alternative to Child–Pugh score [5].

The Model for End-Stage Liver Disease (MELD) score has emerged as a useful tool that estimates mortality in patients awaiting liver transplantation it was implemented on February 26, 2002, by the United Network for Organ Sharing (UNOS) as criteria for organ allocation in patients with chronic disease awaiting liver transplantation [7].

The success of the MELD score is based not only on its accuracy in predicting prognosis, but also on the fact that it is objective, reproducible, and readily available in all settings. Its superiority over other existing prognostic indexes is likely due to the fact that it includes a variable that estimates the degree of renal dysfunction (serum creatinine), because renal function is known to accurately predict prognosis in patients with cirrhosis [8].

This study aims to help in identify the role of SIRS and IL-6 (as an inflammatory cytokine) and highlighting the prognostic value of MELD score in cirrhotic patients presented with acute renal failure in order to early diagnosis and treatment to improve outcome and to decrease short term mortality.

**Material and Methods**

**Study Design and Site** Cross sectional observational study with prospective data collection.

**Study population:** All patients admitted to Emergency Department at Suez Canal University Hospital with definite liver cirrhosis & fulfilling criteria of acute renal failure. Acute renal failure is defined as an increase in serum creatinine levels of more than 50% of the baseline value, to above 133 μmol/L (1.5 mg/dL) [4]. Patients could have acute renal failure on admission or develop it during hospitalization.

**Inclusion criteria:** Patients age > 18 years, males and females, confirmed liver cirrhosis clinical, biochemical, and radiological parameters, Serum creatinine levels of more than 50% of the baseline value, to above (1.5 mg/dL) & at least 1 normal serum creatinine level assessment during the month before inclusion or, normal serum creatinine levels during the final assessment before inclusion.

**Exclusion criteria:** Absence of information on baseline renal functions, chronic renal impairment or failure, evidence of hepatocellular carcinoma, refusal to participate in the study.

**Sample size:** Sample size was calculated using the following equation:

N= (Zα)2 *PQ/D2
Zα = Apercentile of standard normal distribution= 1.96
D2= width of the confidence interval =0.01
P= prevelance of acute renal failure in cirrhotic patients = 25% [1].
Sample size = 72 patients

**Data collection** data collected in pre-organized data sheet by the researcher; the following variables were studied:

**A)Medical history** recorded upon inclusion, diagnosis of cirrhosis confirmed clinically, biochemically, or

radiological and acute renal failure was diagnosed by: elevated serum creatinine levels of more than 50% of the baseline value, to above (1.5 mg/dL), and absence of criteria of chronic renal failure, Current medical events (infection, bleeding, ascites, and paracentesis) were recorded. Treatments administered within the last month and 48 hours before enrollment were reviewed carefully, any use of contrast medium also biochemical and bacteriological parameters within 48 hours before admission were reviewed.

**B) Clinical evaluation**: of the patients carried out upon arrival to Emergency Department regarding vital signs (pulse, blood pressure, respiratory rate and temperature), general examination, and various body systems examination, Severity of liver disease was assessed according to model for end-stage liver disease (MELD) which shows its usefulness in determining the prognosis of groups of patients with chronic liver disease. It incorporates 3 widely available laboratory variables including the International Normalized Ratio (INR), serum creatinine, and total serum bilirubin, the higher the MELD score the worst the prognosis of the patient. By using the MELD score patients will be assigned a score from 6 to 40, which equates to an estimated 3 month survival rate from 90% to 7 % respectively (appendix 2)[9].

-Patients were examined for the presence and number of SIRS criteria which were defined by the American College of Chest Physicians/ Society of Critical Care Medicine ACCP/SCCM Consensus Conference:

1. Systemic Inflammatory Response Syndrome (SIRS) was defined as the presence of two or more of the following: (1) tachycardia >90 beats per minute; (2) tachypnea 20 breaths per minute PaCO2 level of less than 32 mm Hg or hypoxia oxygen saturation <90% ; (3) hyperthermia >38°C or hypothermia <36°C ; and (4) leukocytosis >12,000/µL, leucopenia <4,000/µL , or >5% bands) .
2. Sepsis was defined as two or more criteria for SIRS plus documented or presumed source of infection.
3. Severe sepsis was defined as sepsis plus organ dysfunction (altered mental status, oxygen saturation <90%, acute renal failure, and abnormal liver enzyme in the absence of explainable liver disease).
4. Septic shock was defined as severe sepsis plus hypotension refractory to initial fluid therapy. (American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, 1992).

**C) Investigations:** Blood and urine samples were drawn on arrival to Emergency Department in all enrolled patients for: Complete blood count, Coagulation profile (PT, INR), Serum electrolytes (Na, K,), Serum creatinine, Serum bilirubin, Random blood sugar, Arterial blood gases analysis, Urine analysis (protein, casts, pus and RBCs), and Serum IL-6 analysis:

Venous blood samples were taken in the hospital. Serum samples will immediately deep frozen and kept at -70C until assay. Commercial ELISA kits will be used. Assay range: 7-500 pg/ml. Both the researcher and the clinical pathologist will be blinded to samples Pelvic-abdominal ultrasound.

**D) Follow up:** During hospitalization: Patients followed up daily during the period of hospitalization after ED admission The course of renal failure, urinary output daily, complications of liver cirrhosis (ascites, gastro-intestinal bleeding , encephalopathy and sepsis ) have been diagnosed and managed according to the guidelines.

After discharge: A telephone call with the patient or with his family was conducted to inquire about the patient's 3 months survival status.

**E) Outcome**:The primary outcome was 3 month mortality. This was noticed during the hospitalization period or after discharge by telephone call.

**Data analysis & management:** Data collected throughout history, clinical examination and laboratory investigations was coded, entered and analyzed using Microsoft Excel software. Gathered data will be presented using (Statistical Package for Social Sciences) (SPSS) software program version 13.0 for analysis. According to the type of data, the following tests was used to test differences for significance; Chi square, t test, and one-way ANOVA with least significant difference. Chi square test and non-parametric tests was used to compare categorical variables. P value was set at <0.05 for significant results.

Laboratory investigations and interventions' budget was covered as a part of the health service provided in Emergency Department in Suez Canal University Hospital.

**Ethical consideration**

1) Approval of Research ethics committee.
2) Singing written informed consent from participants.
3) Confidentiality of data.
4) Explanation of our study to the participants.
5) An informed consent will be taken from each patient.

**Results**

A total of 72 patients who were admitted to Emergency Department at Suez Canal University Hospital with definite liver cirrhosis and fulfilling criteria of acute renal failure were included into the study.

Value of IL-6>199.5 pg/ml has sensitivity of 100%, specificity of 89.66%, positive predictive value of 70%,

negative predictive value of 100% and positive likelihood ratio of 9.67 and negative likelihood ratio of 0 in prediction of mortality in emergency department among cirrhotic patients with acute renal failure.

**Table 1.** Personal characteristics and presenting complaints among the studied patients (n=72).

| | | Number | Percent |
|---|---|---|---|
| **Age** | 40 – | 8 | 11.11% |
| | 50 – | 35 | 48.61% |
| | 60 – | 22 | 30.56% |
| | 70 – 80 | 7 | 9.72% |
| | Mean ± SD | 57.09 ± 7.71 | |
| | Range | 40 – 80 | |
| **Sex** | **Male** | 43 | 59.8% |
| | **Female** | 29 | 40.2% |
| **Residence** | **Urban** | 42 | 58.33% |
| | **Rural** | 30 | 41.67% |
| **Presentations** | | | |
| **DLOC *** | | 31 | 43.06% |
| **Hematemesis and melena** | | 13 | 18.06% |
| **Jaundice** | | 3 | 4.17% |
| **Abdominal pain** | | 20 | 27.78% |
| **Dyspnea** | | 2 | 2.78% |
| **Ascites** | | 23 | 31.94% |
| **Hematuria** | | 1 | 1.39% |
| **Diabetic foot infection** | | 2 | 2.78% |

#Patient may be presented with more than one complaint
*Disturbed level of consciousness

**Table 2.** Baseline clinical findings and laboratory parameters among the studied patients (n=72).

| | | Number | Percent |
|---|---|---|---|
| **Airway** | **Patent** | 64 | 88.89% |
| | **Intubated** | 8 | 11.11% |
| **Ascites** | **No** | 4 | 5.56% |
| | **Minimal** | 3 | 4.17% |
| | **Moderate** | 45 | 62.5% |
| | **Tense** | 20 | 27.77% |
| **Lower limb edema** | **Yes** | 68 | 94.44% |
| | **No** | 4 | 5.56% |
| **Encephalopathy** | **No** | 28 | 38.89% |
| | **Grade I** | 9 | 9.78% |
| | **Grade II** | 2 | 2.78% |
| | **Grade III** | 9 | 9.78% |
| | **Grade IV** | 24 | 33.33% |
| | | **Mean ± SD** | **Range** |
| **Total bilirubin** | | 5.01 ± 4.96 | 0.67 – 30 |
| **Direct bilirubin** | | 3.57 ± 4.35 | 0.3 – 21.9 |
| **Hemoglobin (g/dl)** | | 8.77 ± 1.68 | 5 – 12.3 |
| **Total leucocytic count** | | 8741.67 ± 5113.27 | 2500 – 20000 |
| **INR** | | 2.17 ± 0.61 | 1.16 – 3.9 |
| **Serum creatinine** | | 3.59 ± 1.75 | 2 – 9.7 |
| **Serum Na** | | 126.08 ± 8.06 | 112 – 148 |
| **Serum K** | | 4.49 ± 0.78 | 3.1 – 6.7 |

**Table 3.** Infection and shock with expected cause of renal injury among the studied patients (n=72).

| | | Number | Percent |
|---|---|---|---|
| **Presence of infection** | **Yes** | 36 | 50% |
| | **No** | 36 | 50% |
| **Source of infection (n=36)** | **UTI *** | 7 | 19.44% |
| | **Strangulated hernia** | 2 | 5.56% |
| | **Spontaneous bacterial peritonitis** | 13 | 36.11% |
| | **Chest infection** | 2 | 5.56% |
| | **Bed sores** | 1 | 2.78% |
| | **Acute cholecystitis** | 2 | 5.56% |
| | **Septic peritonitis** | 5 | 13.89% |
| | **Cholangitis** | 1 | 2.78% |
| | **Diabetic foot infection** | 3 | 8.33% |
| **Presence of shock** | **Yes** | 27 | 37.5% |
| | **No** | 45 | 62.5%% |
| **Type of shock (n=27)** | **Hypovolemic shock** | 8 | 29.62% |
| | **Septic shock** | 19 | 70.37% |
| **Expected cause of renal injury** | | | |
| **Cholestasis** | | 2 | 2.78% |
| **Hepatorenal syndrome** | | 39 | 54.17% |
| **Postrenal cause** | | 4 | 5.56% |
| **Severe sepsis** | | 19 | 26.39% |
| **Hypovolemia and hypoperfusion** | | 8 | 11.11% |

Urinary tract infection *

**Table 4.** IL-6 among different groups of patients according to outcome.

| | | IL-6 (pg/ml) Mean ± SD | p-value |
|---|---|---|---|
| **ER mortality** | **No** | 86.15 ± 131.62 | 0.001* |
| | **Yes** | 453.25 ± 87.28 | |
| **Overall mortality** | **No** | 28.68 ± 35.05 | 0.001* |
| | **Yes** | 249.57 ± 204.63 | |
| **ICU admission** | **No** | 152.75 ± 196.46 | 0.7 (NS) |
| | **Yes** | 169.1 ± 183.38 | |
| **Infection** | **No** | 23.33 ± 20.4 | 0.001* |
| | **Yes** | 291.7 ± 192.36 | |
| **Shock** | **No** | 57.21 ± 64.23 | 0.001* |
| | **Yes** | 324.74 ± 216.35 | |
| **Type of shock** | **Hypovolemic** | 92.25 ± 168.03 | 0.001* |
| | **Septic** | 461.5 ± 80.79 | |

*Statistically significant difference
NS: no statistically significant difference

**Table 5.** MELD score among different groups of patients according to outcome.

| | | MELD score Mean ± SD | p-value |
|---|---|---|---|
| **ER mortality** | **No** | 28.89 ± 4.27 | 0.001* |
| | **Yes** | 36.21 ± 3.29 | |
| **Overall mortality** | **No** | 27.2 ± 3.8 | 0.001* |
| | **Yes** | 32.55 ± 4.58 | |
| **ICU admission** | **No** | 30.1 ± 5.12 | 0.6 (NS) |
| | **Yes** | 30.8 ± 4.85 | |
| **Infection** | **No** | 28.47 ± 4.53 | 0.001* |
| | **Yes** | 32.17 ± 4.84 | |
| **Shock** | **No** | 29.49 ± 4.29 | 0.09 (NS) |
| | **Yes** | 31.7 ± 5.86 | |
| **Type of shock** | **Hypovolemic** | 27.8 ± 3.39 | 0.002* |
| | **Septic** | 34 ± 5.84 | |

*Statistically significant difference
NS: no statistically significant difference

**Table 6.** SIRS score among different groups of patients according to outcome.

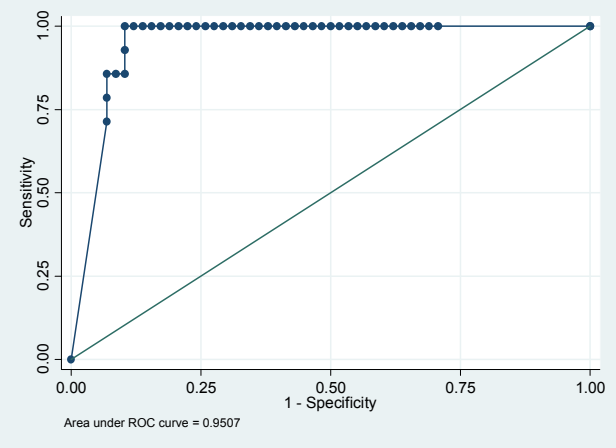
| | | SIRS score Mean ± SD | p-value |
|---|---|---|---|
| **R mortality** | **No** | 0.71 ± 1.27 | 0.001* |
| | **Yes** | 3.86 ± 0.36 | |
| **Overall mortality** | **No** | 0.53 ± 1.01 | 0.002* |
| | **Yes** | 1.88 ± 1.88 | |
| **ICU admission** | **No** | 1.45 ± 1.7 | 0.3 (NS) |
| | **Yes** | 1 ± 1.64 | |
| **Infection** | **No** | 0.4 ± 0.94 | 0.001* |
| | **Yes** | 2.19 ± 1.85 | |
| **Shock** | **No** | 0.16 ± 0.6 | 0.001* |
| | **Yes** | 3.26 ± 1.02 | |
| **Type of shock** | **Hypovolemic** | 2.4 ± 1.17 | 0.01* |
| | **Septic** | 3.76 ± 0.44 | |

*Statistically significant difference
NS: no statistically significant difference

Value of MELD score>32 has sensitivity of 92.8%, specificity of 79.3%, positive predictive value of 52%, negative predictive value of 97.9%, positive likelihood ratio of 4.49 and negative likelihood ratio of 0.09 in prediction of mortality in emergency department among cirrhotic patients with acute renal failure.

Value of SIRS score>2 has sensitivity of 100%, specificity of 86.21%, positive predictive value of 63.6%, negative predictive value of 100%, positive likelihood ratio of 7.25 and negative likelihood ratio of 0.00 in prediction of mortality in emergency department among cirrhotic patients with acute renal failure.

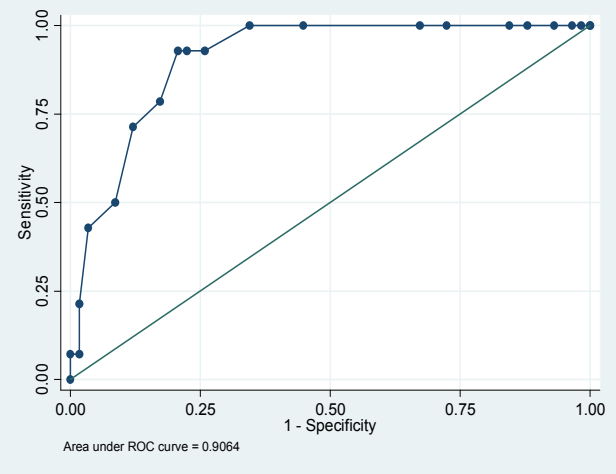
**Graph 1.** ROC curve analysis for predictive characteristics of IL-6 in prediction of ER mortality among cirrhotic patients with ARF




| IL-6 value | >199.5 pg/ml |
|---|---|
| Sensitivity (95% CI) | 100% (76.7 – 100) |
| Specificity (95% CI) | 89.66% (78.8 – 96.1) |
| PPV | 70% |
| NPV | 100% |
| +LR | 9.67 |

Area under the curve: 95%
Standard error: 0.0228
95% confidence interval: 0.906 – 0.995
P-value = 0.001* (Statistically significant)

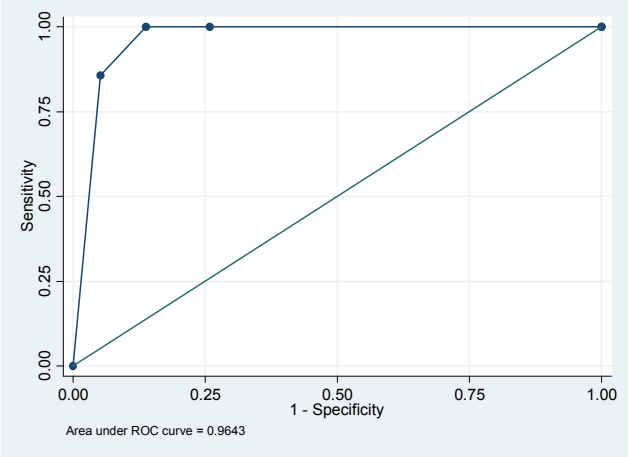
**Graph 2.** ROC curve analysis for predictive characteristics of MELD score in prediction of ER mortality among cirrhotic patients with ARF




| MELD score | > 32 |
|---|---|
| Sensitivity (95% CI) | 92.8% (66.1 – 98.8) |
| Specificity (95% CI) | 79.3% (66.6 – 88.8) |
| PPV | 52% |
| NPV | 97.9% |
| +LR | 4.49 |
| -LR | 0.09 |

Area under the curve: 91%
Standard error: 0.035
95% confidence interval: 0.838 – 0.975
P-value = 0.001* (Statistically significant)

**Graph 3.** ROC curve analysis for predictive characteristics of SIRS score in prediction of ER mortality among cirrhotic patients with ARF




| | |
|---|---|
| SIRS score | > 2 |
| Sensitivity (95% CI) | 100% (76.7 - 100) |
| Specificity (95% CI) | 86.21% (74.6 – 93.8) |
| PPV | 63.6% |
| NPV | 100% |
| +LR | 7.25 |
| -LR | 0.00 |

Area under the curve: 96%
Standard error: 0.018
95% confidence interval: 0.929 – 0.999
P-value = 0.001* (Statistically significant)

## Discussion

Renal failure is a common occurrence in patients with cirrhosis. It is caused by a variety of factors, some specific to cirrhosis, and others affecting the general patient population. Renal failure in cirrhosis carries a worse prognosis; mortality is especially high with Hepatorenal syndrome (HRS) [10].

The aim of the current study was to evaluate the outcome of the acute renal failure in a series of cirrhotic patients by using systemic inflammatory response syndrome (SIRS) criteria, IL-6 and model for end-stage liver disease (MELD) score as prognostic tools.

We had our study on 72 cirrhotic patients presented to Emergency Department (ED) Suez Canal University Hospital with acute renal failure. All patients were evaluated in the (ED), and followed up during hospitalization and up to 3 months after hospital discharge.

Our study shows that the mean age group of the studied patients was 57.09 ± 7.71 years ranging from 40 to 80 years, males were (59.8%) , and 58.33% came from urban areas .This agreed with Belcher et al., 2012 who reported that the mean age was 55.1± 9.3 years (71% were males)[11].

In accordance, Rocco and Soares, 2010 studied 304 cirrhotic patients , (62.5%) of them were males with mean age 54 years [12].

It was found by Choi et al. found that cirrhotic patients with higher severity of cirrhosis, developed renal dysfunction much more, and that was statistically significant [13]. And this was emphasized by Cardenas et al. who stated that sever liver cirrhosis is an independent factor of the development of acute renal failure [2].

We also found that 62.5% of the studied patients presented by moderate ascites, while 27.77% presented by tense ascites and 33.33% presented by hepatic encephalopathy grade 4.basic laboratory data showed that mean total bilirubin was 5.01 ± 4.96 range ( from 0.67 to 30 mg/dl), mean hemoglobin was 8.77 ± 1.68 , total leucocytic count ( TLC) ranging from 2500 to 20000. Mean of INR in the studied group was 2.17 ± 0.61 ranging from (1.16-3.9). In our study we reported that mean serum sodium was (126.08 ± 8.06 mEq/dl) ranging from 112 – 148 mEq/dl. Alessandria C et al. reported that low serum sodium levels in cirrhosis are associated with severe ascites and high frequency of hepatic encephalopathy, spontaneous bacterial peritonitis, and Hepatorenal syndrome [8].

We noticed that mean serum creatinine level was 3.59 ± 1.75 ranging from 2–9.7 mg / dl. Alessandria C et al. reported that Serum creatinine concentration is a parameter that should be included in the prognostic assessment of patients with decompensated cirrhosis, but should be combined with other specific parameters of liver function, such as bilirubin, albumin, and the international normalized ratio (INR) for prothrombin time [8]. Botta et al. noticed that elevated serum creatinine level is a markers of higher risk of death among cirrhotic patients [14].

Serum creatinine (S Cr) measurement remains the most practical and widely accepted method for estimating renal function in clinical practice in patients with cirrhosis and is the basis of existing definitions of AKI. The prognostic impact of renal function in liver disease is reflected by the inclusion of S.Cr in the Model for End-Stage Liver

Disease (MELD) score, which is used to prioritize patients for liver transplantation [15].

Our results showed that the most common cause of acute renal failure was (HRS) 54.17% followed by sever sepsis 26.39%, hypovolemia and hypoperfusion accounts for 11.11% .This is in accordance with the study done by Schepke et al., 2006, who found that 40% of the studied patients had Hepatorenal syndrome (HRS) [16]. In contrast Botta et al. found that the most frequent cause of acute renal failure in cirrhotic patients was renal failure associated with infections (46%), followed by hypovolemia-related renal failure (32%), and HRS accounts for only (13%) [14].

Nadim MK et al. reported that the incidence of sepsis in cirrhosis is estimated to be at least 30–50% of hospital admissions. Once admitted, between 15% and 35% of cirrhotic patients develop nosocomial infections compared with an infection rate of 5–7% in the general hospital population [15].

In our series 50% had infection, the most common source of infection was spontaneous bacterial peritonitis about (36.11%), followed by septic peritonitis, and urinary tract infection 13.89% and 19.44% respectively. this agreed with Wu et al., who reported that patients who developed ARF were more likely to have had infection, especially septicemia [17]. Botta et al., stated that the most common source of infection was SBP (32.9%), followed by respiratory tract infection (20.7%) and urinary tract infection (10.3%) [14]. Also Bonnel et al. reported that the most common infection were SBP (25%), UTI (20%), and pneumonia (15%). Bacterial overgrowth and translocation from the GIT are important steps in the pathogenesis of SBP and bacteremia. This pathogenic process leads to increased levels of endotoxins and cytokines that trigger an excessive inflammatory host response a cause for septic shock, multi-organ dysfunction and death [18].

The present study showed that only 27 patients (37.5%) had shock, 19 patients were diagnosed as septic shock and 8 patients had hypovolemic shock.

Botta et al. in their study found that the most common cause of renal failure in cirrhotic patients were infection followed by volume depletion and hypovolemic shock accounting to almost two thirds of all cases . They noticed that, in most cases, renal failure in patients with infection occurs in the absence of septic shock [14].

We reported that mortality rate in the ER was 19.44%, while 3 months mortality was 58.33% .Wu et al. reported in his retrospective study that mortality rate in cirrhotic patients with ARF was much higher than in those patients without ARF (72% vs. 13%, $p < 0.001$) [17].

In the study of Thabut et al. reported that the in-hospital mortality of cirrhotic patients with acute renal failure was almost 50%, confirming the very poor outcome of acute renal failure in patients with cirrhosis [4]. the impact of acute renal failure on liver cirrhosis was done by Cholongitas et al. it included 74 studies (43 prospective and 31 retrospective) , they reported that the mortality rate in AKI group at 1,3, and 12 months were 58%, 69% and 63% respectively . Prognostic indicators were studied in 37 studies (2548 patients). The most frequent variables that were independently associated with prognosis were age, child class, MELD score, hepatic encephalopathy and sepsis [19].

In the present study 29 (from 72 patients) 40.2% presented at inclusion with SIRS criteria as defined in patients and methods. 15 patients fulfilled 4 SIRS criteria, while 7 patients fulfilled 3 SIRS criteria, and also 7 patients fulfilled 2 criteria. Presence of SIRS was significantly correlated with the presence of infection ($p= 0.001$) , and presence of shock ( $p= 0.001$).

Hartleb M et al., 2012 , in their study enrolled 101 cirrhotic patients, 52 ( 51.5%) of them fulfilled the criteria of SIRS diagnosis, 50 (49.5%) of them had SIRS on admission and 2 of them develop SIRS during their hospital stay . they reported that there was significant correlation between SIRS and bacterial infection as ( 38.5%) of cirrhotic patients with SIRS have bacterial infection while only 6.1% of cirrhotic patients without SIRS had bacterial infection [20] . Thabut et al., 2007, Found that 34 (from 83 patients) 41% presented at inclusion with SIRS criteria, the majority of patients (32 patients) fulfilled 2 SIRS criteria [4].

In the present study we found that SIRS significantly correlated with ER mortality ( $p= 0.001$), SIRS score > 2 has 100% sensitivity and 86.21% specificity in prediction of ER mortality, while it showed ( 97.62%) sensitivity and (93.33%) specificity in prediction of 3 months mortality with significant correlation ( $p=0.002$) .

This was in agreement with Cazzaniga et al. showed that there was a close correlation between SIRS and in-hospital death. The prediction of death by SIRS was independent of the severity of liver disease (estimated with MELD score) and of the age of patients. This suggests that SIRS plays an active role in worsening patient conditions increasing his/her risk of death.

In the study by Thabut et al. performed on cirrhotic patients with renal failure all patients who died had SIRS on admission or developed it during hospitalization. The presence of SIRS showed strong association with poor survival ($p= 0.001$) both at hospital or 2 months after hospital discharge [4].

Hartleb M et al. in their study showed that the mortality rate was 11 out of 101 cirrhotic patients . 15.4% of the SIRS-positive and 6.1% of the SIRS-negative patients [20].

It was concluded by Schepke M et al. that the presence of SIRS criteria alone had no prognostic value for either in hospital mortality or 1-year mortality. The authors concluded that organ dysfunction, rather than SIRS criteria, was a better predictor of mortality [14].

In the present study result showed that IL -6 ranging from ( 7 to 500 pg/ml ) mean was 157.53 pg/ml and median was 54.11 pg/ml. there is significant correlation with ER mortality ($p = 0.001$), and 3 months mortality .

Albillos et al. showed that many cirrhotic patients with ascites had an increased release of tissue necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6), two cytokines that mediate systemic inflammation [21].

In the present study we reported significant correlation between plasma IL -6 and ER mortality and overall 3 months mortality ($p= 0.001$). Lee et al., 1996, reported that the plasma IL-6 significantly increased in cirrhotic patients than healthy one ($p<0.01$), they found that IL-6 progressively increased in relation to the severity of liver dysfunction [22].

In our study the mean MELD score was 30.32 ranging from (18 to 42) and median was 29. there is significant correlation between MELD score and ER and 3 months mortality ( $p= 0.001$), the value of MELD score > 32 has sensitivity of 92.8% , specificity of 79.3% in prediction of mortality in ER , while MELD score > 28 has sensitivity of 80.95% and specificity of 80% in prediction of 3 months mortality in cirrhotic patients with acute renal failure .

This agreed with Belcher et al., 2012, who reported that the median MELD score was 26.3 at time of enrollment. Thabut et al. reported that the mean MELD was 30. Botta et al. confirmed the prognostic ability of the MELD scoring system for both short and medium term survival, in a European series of cirrhotic patients. He reported that the MELD scoring system is correlated with the degree of liver functional impairment. Their results showed that both the MELD and Child-Pugh scores had similar accuracy in evaluating the progressive worsening of the clinical condition of cirrhotic patients [4, 11,14].

**Conclusions from our work:-** The mean age of the studied patients was 57.09 ± 7.71 years. The mean serum creatinine level was 3.59 ± 1.75 mg/dl ranging from 2 – 9.7 mg /dl. The mean serum Na was 126.08 ± 8.06 mEq/dl.

We reported that 50% of the studied patients had infection, the most common source of infection was SBP account for 36.11%.

The most common cause or renal impairment in the studied patients was (HRS) accounts for 54.17%, followed by sepsis 26.39%.

About 19.44% of the studied patients died in the Emergency Department before admission, while overall mortality (3 months mortality) was 58.33%.

Mean serum level of IL-6 was 157.53 ± 191.59 pg/ml, there was significant relation between ER mortality, overall mortality and presence of infection and IL-6 levels. Value of IL-6>36.5 pg/ml has sensitivity of 83.3%, specificity of 80%, in prediction of overall mortality among cirrhotic patients with acute renal failure.

A twenty nine patients presented with SIRS criteria, 15 of them express SIRS score = 4. There is significant relation between presence of SIRS criteria and infection, ER and overall 3 months mortality. Value of SIRS score>2 has sensitivity of 47.62%, specificity of 93.33%, in prediction of overall mortality among cirrhotic patients with acute renal failure.

The mean MELD score was 30.32 ± 5.01, and Expected 3 month mortality according to MELD score ranged between" 6% -71.3%". There was significant relation between ER and overall mortality and MELD score. Value of MELD score>28 has sensitivity of 80.95%, specificity of 80%, in prediction of overall mortality among cirrhotic patients with acute renal failure.

**Recommendations:** Early diagnosis and treatment of infection in cirrhotic patients.

SIRS criteria is considered a prognostic tool in predicting mortality in cirrhotic patients.

Interleukin -6 should be used as a diagnostic tool for detection of infection and also as prognostic tool in cirrhotic patients with acute renal failure.

MELD score should be used as a prognostic tool in cirrhotic patients with acute renal failure.

Improvement of Hepatorenal syndrome therapeutics may be added as a bridge for liver transplantation as mortality is high in those patients.

Further research in that era

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