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Laboratory Tests and Muscle Thickness Predict Mortality among Septic Patients in ICU

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Abstract

Sepsis is a clinical syndrome defined by a systemic response to infection. With progression to sepsis-associated organ failure or hypotension mortality increases. Improvement in sepsis recognition and treatment has led to a reduction in 28 day- and in-hospital mortality. Muscle wasting in the critically ill patients is up to 2% per day and delays patient recovery and rehabilitation; it is linked to inflammation, organ failure and severity of illness. Adult patients admitted with severe sepsis and critically ill in the medical ICU were studied. The primary outcome was the mortality among the study population; Laboratory investigations and muscle thickness of the upper limb of biceps and forearm were the secondary outcome. Out of 91 patients, 58 (63.7%) died. analysis showed that muscle thickness and laboratory investigations were variables associated with high mortality. Patients with decreased upper limb thickness and low platelets count (on admission) were found to be clear predictor of mortality in severely septic patients. Early identification of the predictors of mortality should enable us to do necessary interventions toward surviving the severe sepsis.

Keywords: Sepsis, mortality, critically ill

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1. Introduction

Sepsis is currently one of the important problems in medicine due to its complexity from pathophysiologic, clinical, and therapeutic viewpoints. Sepsis is an important cause of hospitalization and a major cause of death in the Intensive Care Units (ICUs) worldwide [1]. The systemic, deleterious host response to infection is defined as sepsis. If not treated early, it can progress to severe sepsis and lead to tissue hypo perfusion and hypotension called septic shock. [2]. In western countries, septic patients account for as much as 25% of ICU bed utilization and the pathology occurs in 1–2% of all hospitalizations. The mortality rates of sepsis range from 12.8% for sepsis and 20.7% for severe sepsis, to up to 45.7% for septic shock [3]. Sepsis biomarkers may provide information beyond what is available using other metrics and could therefore help inform clinical decision-making and potentially improve patient management. For example, more timely and appropriate antibiotic therapy could be administered and unnecessary antibiotics avoided if biomarkers were available that could accurately diagnose sepsis early [4]. Critically ill patients with sepsis are at increased risk for reduced muscle strength and impaired exercise tolerance after discharge [5]. This weakness is a result of muscle wasting due to immobility, sepsis, organ dysfunction, drugs and systemic inflammation [6].

2. Materials and Methods

After obtaining Institutional Ethical Committee approval and written informed consent from the patients or their relatives, this observational study was carried out at El-Minia University Hospital. Adult Patients over 20 years old of both sex admitted to the ICU with severe sepsis and those patients who developed sepsis in ICU were enrolled in this study (total number of patients was 91 of both sexes). Patients with Psychiatric disorders, refusal to give informed consent and patients with noninfectious causes were excluded from the study. The included patients suffered from systemic inflammatory response syndrome (SIRS) with suspected or proven microbial etiology. SIRS includes the presence of at least two of the following:

- Body temperature >38°C or <36°C,
- Heart rate >90/min,
- Respiratory rate >20 breaths/min or hyperventilation with a $PaCO_2$ <32 mmHg,
- White blood cell count >12,000/mm^3 or <4000/mm^3, or with >10% Immature neutrophils.

Severe sepsis was defined as sepsis associated with organ dysfunction .All patients were followed up until discharge or death. Outcome was defined as mortality or discharge improved. At the end of the study patients were

classified into group A (survivors) and group B (non survivors) .The primary outcome is the incidence of mortality among septic patients while the secondary outcome is which predictor is more sensitive for outcome in septic patients.

2.1. Parameters assessed (for survivors and non- survivors patients

Muscle depth (cm) by ultrasound were measured on days 1, 3, 7 and 14 of the study. Technique described by Akirov et al., 2007 Muscle depth differences (cm) was measured using a SonositeMTurbo™ ultrasound machine with a 5 MHz linear array transducer. Muscle depth change was assessed over the bicep and forearm. Participants were supine with measurements made on the right side of the body, on the bicep and forearm to mark a halfway point on the limb from which the ultrasound measurement would be made. Markings were made in indelible ink to ensure that the same site would be measured throughout the patient's ICU stay. The average of three measurements for each site was used; up to a 0.2cm, difference was accepted. The mean value from the bicep and forearm was combined to provide a daily total muscle depth (cm). A substantial amount of ultrasound gel was applied to ensure that the probe could rest gently on the skin without compressing muscle or distorting underlying soft Tissue [7]. Biceps the elbow was flexed to 90 degrees and a point on the skin was marked between the tip of the olecranon and the acromion with indelible ink. With the elbow extended and the patient in a supine position, the forearm was supinated. The ultrasound probe was applied at the pen mark on the upper arm to obtain a cross-sectional (axial) view, which included the humerus, biceps and brachialis muscle, subcutaneous tissue and skin. Forearm The patient's arm was extended and forearm kept in supinated position. A point between the antecubital skin crease and the ulnar styloid was marked with indelible pen. The ultrasound probe was applied at the pen mark on the radial (lateral) side of the forearm to obtain a cross-sectional (axial) view, which included the radius. The thickness of the flexor compartment was measured anteriorly between the superficial fat-muscle interface and the interosseous membrane; radial or lateral side of the forearm.

2.1.1. Laboratory assessment

I. Routine investigations as platelets count, renal function tests (urea and creatinine), serum electrolytes (Na and k). (Measured on admission to ICU).
II. Albumin level (measured in 1st 24hr in ICU).

2.2. Statistical analysis

The gathered data underwent coding, tabulation, and statistical analysis. Using the Statistical Package for Social Sciences (SPSS) application. Specifically software version 20. 2-sample Wilcoxon test for inter group comparison and Mann–Whitney test for between groups comparisons for measured variables for muscle thickness. Independent Samples T Test (for between groups comparisons) for lab data of the studied cases as platelets, RFT, electrolytes, and Serum Albumin. To test the Statistical significance of the difference in the mean values of measurable variables with respect to mortality, Student's t-test was done. $P < 0.05$ was taken as statistically significant [12].

3. Results and discussion

Total number of patients was 91 of both sexes; non-survivors were 58 while survivors were 33 patients. Muscle thickness of biceps and forearm in the studied patients, biceps thickness was 22, 21,19and 17 in days1, 3,7,14 respectively, and forearm thickness was 22,21,20,19 in the same days respectively as illustrated in table (1). Table (2) illustrated that there was statistical significant decrease in non-survivor group more than survivor group as regard thickness of biceps and forearm. Table (3)demonstrates laboratory investigations done on 1st day of admission ,the mean Platelet 150 ± 671 X10*3/ul ,urea22.8 ± 9.8 mg/d, creat 1.3 ± 0.6 mg/d, Na140.5 ± 5.1 mmol/L ,k 3.9 ± 0.5 mmol/L, Serum Albumin2.8 ± 0.5(g/dl). Table (4) comparison between survivors and non-survivors as regard lab data. Both groups were comparable regarding urea, creat , Na ,K and Serum Albumin measured on admission As illustrated in table (4). There was statistical significant decrease in platelets count measured on admission in non-survivors more than survivors as p-value was 0.001. Sepsis is a global healthcare problem with increasing. Incidence and high mortality attributed mainly to an Aging population with increased comorbidity including immunocompromised state and active malignancy [8]. Studies investigating the temporal relationship between death in sepsis patients after ICU admission are even more sparse. Apparently, one-third of all sepsis deaths occurs within 3 days of ICU admission. Muscle wasting during critical illness is a multi-factorial process thought to be a consequence of sepsis and inflammation, disuse atrophy, severity of illness [9]. As illustrated in our results there was statistical significant decrease in non-survivor group more than survivor group as regard thickness of biceps and forearm.

Our results were in the same context with Hadda et al., 2018 who measured Muscle thickness of 70 patients with sepsis at the level of the mid-arm and mid-thigh using bedside USG on days 1, 3, 5, 7, 10 and 14 and then weekly till discharge or death. Patients were followed up for 90 days after discharge. The muscle thickness (mean ± SD) at the level of the mid-arm and mid-thigh on day 1 was 23.13 ± 4.83 mm and 31.21 ± 8.56 mm, respectively. The percentage muscle thickness [median (min, max)] decline at the mid-arm and mid-thigh was 7.61 (− 1.51, 32.05) % and 10.62 (− 1.48, 32.06) %, respectively on day 7 as compared to baseline ($p < 0.001$). The decline in muscle thickness at the mid-arm and mid-thigh were higher among non-survivors compared to survivors at all-time points. In addition, the decline in muscle thickness was significantly higher among patients with worse outcome at day 90. Patients with ICU-acquired weakness also had significantly higher decline in muscle thickness ($p < 0.05$). Early decline (from day 1 to day 3) in muscle thickness was associated with in-hospital mortality.so he concluded that critically ill patients with sepsis exhibit a gradual decline in muscle thickness of both the arm and thigh. Decline in muscle thickness was associated with in-hospital mortality [10].

Table 1. Descriptive statistics of biceps and forearm muscle thickness of the studied case

	Muscle thickness		Descriptive statistics
Biceps muscle (m)	**Day1**	Median (IQR)	22 (13-29)
	Day 3	Median (IQR)	21 (12-28)
	Day 7	Median (IQR)	19 (10-27)
	Day 14	Median (IQR)	17 (7-27)
Forearm muscle (m)	**Day 1**	Median (IQR)	22 (15-30)
	Day 3	Median (IQR)	21 (14-28)
	Day 7	Median (IQR)	20 (13-25)
	Day 14	Median (IQR)	19 (10-25)

Table 2. Comparison between survivors and non-survivors as regard muscle thickness

Muscle thickness		**Survivors (N =33)**	**Non survivors (N =58)**	**P value**
Mean biceps thickness	Median (IQR)	20 (12-25)	13 (10-20)	<0.001*
Mean forearm thickness	Median (IQR)	21 (13-22)	15 (11-17)	<0.001*

Mann-Whitney Test for muscles thickness
– *: Significant level at P value < 0.05

Table 3. Descriptive statistics of lab data of the studied cases

Lab data (T-TEST) (N=91)		**Descriptive statistics**
Platelet (X10*3/ul)	Mean ± SD (Range)	150 ± 671 (85:325)
urea (mg/d)	Mean ± SD (Range	22.8 ± 9.8 (5:49
creat (mg/d)	Mean ± SD (Range)	1.3 ± 0.6 (0.53.7)
Na (mmol/L)	Mean ± SD (Range)	140.5 ± 5.1 (132:149)
k (mmol/L)	Mean ± SD (Range)	3.9 ± 0.5 (3:5.1)
Serum Albumin	Mean ± SD (Range)	2.8 ± 0.5 (1.9:4)

Table 4. Comparison between survivors and non-survivors as regard lab data

Lab data		**Survivors (N =33)**	**Non survivors (N =58)**	**P value**
Platelet (X10*3/ul)	Mean ± SD (Range)	227 ± 49 (96:325)	106.3 ± 20.1 (85:190)	0.001*
urea (mg/d)	Mean ± SD (Range)	22.6 ± 9.9 (9:49)	23 ± 9.8 (5:49)	0.65
creat (mg/d)	Mean ± SD (Range)	1.3 ± 0.6 (0.5:3.7)	1.4 ± 0.5 (0.5:3.5)	0.93
Na (mmol/L)	Mean ± SD (Range)	140± 4.9 (133:149)	141 ± 5.2 (132:149)	0.42
k (mmol/L)	Mean ± SD (Range)	3.9 ± 0.5 (3:5)	3.9 ± 0.5 (3:5.1)	0.58
Serum Albumin	Mean ± SD (Range)	2.8 ± 0.5 (1.9:4)	2.8 ± 0.5 (1.9:4)	0.93

Independent Samples Test for Lab data
– *: Significant level at P value < 0.05

USG has a potential to identify patients at risk of worse in-hospital and post-discharge outcomes. Regarding laboratory tests (measured on admission) our results showed no statistical difference between survivors and non survivors as regard renal function tests, serum electrolytes, and albumin level, while platelets count was significantly decreased in non-survivor group more than survivors. In consistence with our results Anilkumar et al.,2017 selected Adult patients with severe sepsis in the medical ICU. The primary outcome was the mortality among the study population. Baseline demographic, clinical, and laboratory data were recorded upon inclusion into the study. Risk factors associated with mortality were studied by univariate analysis. The variables having statistical significance were further included in multivariate analysis to identify the independent predictors of mortality. Out of eighty patients, 54 (67.5%) died. He found that serum albumin ,Serum levels of creatinine or sodium and potassium were not found to have association with mortality while tachycardia, hypotension, elevated C-reactive protein (CRP) and lactate. In association with our results regarding platelets yang et al., 2023 studied retrospective observational study of patients with sepsis admitted to our hospital from January 2017 to September 2021 to explore the predictive value of platelet count at admission for mortality. A total of 290 patients with sepsis were included in this study. Multivariate logistic regression analysis was used to evaluate the risk factors for mortality and construct a predictive model with statistically significant factors [11]. When Compared with survivors, non-survivors tended to be much older and had significantly higher acute physiology and chronic health evaluation II and sequential organ failure assessment scores ($P < .001$). The platelet count was significantly lower in the non-survivor group than in the survivor group ($P < .001$). Multivariate logistic regression analysis indicated that age ($P = .003$), platelet count ($P < .001$) and lactate level ($P = .018$) were independent risk factors for mortality in patients with sepsis. In their study, platelet count at admission as a single biomarker showed good predictability for mortality in patients with sepsis.

4. Conclusions

Patients with decreased upper limb thickness and low platelets count (on admission) were found to be clear predictor of mortality in severely septic patients. Early identification of the predictors of mortality should enable us to do necessary interventions toward surviving the severe sepsis.

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