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Tumor Necrosis Factor in Critically ill Patients and Its Relation to Outcome

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Abstract— The purpose of this study was to predict the outcome of critically ill patients by change of TNF serum level comparing it with q SOFA and APACHE II scores. It included 150 critically ill patients were admitted toAssuit University Hospitals ICUs. All patients underwent carful medical history, clinical examination, abdominal us and ECG. Serum samples were collected for TNF and routine investigations included renal and liver function tests, CBC, ABG, and LDH.There was significant correlation between short term mortality and serum levels of TNF,APACHE IIandqSOFA scores as (P were 0.005, 0.01, 0.002 respectively). TNF and qSOFA had significant correlation with Long-term mortality (P were 0.006, 0.001 respectively) but APACHE IIhad insignificant correlation with Long-term mortality as (P was 0.059). TNF and APACHE II had significant correlation with hospital stay length (P were 0.001, 0.001 respectively) while q SOFA had insignificant correlation with hospital stay length as (P was 0.6). This study concludes that TNF is good predictors for mortality (short and long term) and the duration of hospital stay.

KEYWORDS: ICU, critically ill patients, TNF, APACHE II, q SOFA.

INTRODUCTION

ICU patients are critically ill as they arephysiological instable and have many comorbidities e.g., malignancy, heart diseases… beside other factors include the age and severity of the disease which may end with death in hours, they need accurate assessment of the diseases severity for death prediction (1)(2).

In ICU there are many severity scoring systems for mortality and morbidity prediction like APACHE and SOFA. They include monitor parameters and clinical data (3) (4). Q SOFA score is sensitive for detection of the patientshaving infection especially sepsis, q SOFA score is easyand simple score consist of three factors (respiratory rate, GCS, SBP) (5).APACHE II score which consist of twelve physiological items calculated at admission within twenty-four hours is used for mortality prediction (6).

Tumor necrosis factor is Cytokines which has an important role in cell signaling and immunity against infection and inflammationis generated by many cells, including immune cells like macrophages, B lymphocytes(8) (9). TNF level is changed in sepsisand itcan produce fever, inflammation, apoptotic cell death and inhibit viral replication, thischange is seen in various human diseases as cancer, inflammatory bowel diseases (7).

PATIENTS AND METHODS

Patients

An observational descriptive studyconducted in accordance with the Declaration of Helsinki and approved by the local Clinical Research Ethics Committee. It included 150 eligible critically ill patients were admitted to ICU from January 2018 to January 2019.Their mean age was 61 years, 64% of them were males. We excluded from the study patients who refused to participate in this study, patients on immune modulating drugs and patients with significant functional compromise. All patients underwent carful medical history, clinical examination, abdominal us and ECG.

Biochemical Analysis

Serum samples were collected for TNFa measurement by ELIZA (SimpleStep ELISA® technology) and routine investigations included renal and liver function tests, CBC, ABG, and LDH.

At ICU admission, all patients were evaluated;APACHE II and quick SOFA scores were calculatedand correlated with ICU mortality, hospital stay period and long-term mortality.

Statistical analysis

Data wascollected, codedand analyzed using SPSS version 21*. Suitable statistical tests for data analysis and interpretation (Means, standard deviations, percentages, independent T-test, Chi-square test,regressionand correlation analysis) were done. ROC curve was done for TNF, APACHE II and q SOFA scores.Significance was considered when p-value ≤ 0.05.

RESULTS

The demographic data and main clinical characteristics of the patients are shown in table (1).

Table 1: Demographic data and clinical characteristic of the patients

		All patients (150)
Sex	**Male**	95 (64%)
	Female	55 (36.7%)
Mean age (± SD)		61.6 ± 11.4
Acute kidney injury		57 (38%)
Respiratory disease		44 (29%)
Septic shock		18 (12%)
Liver diseases		74 (49%)
Cardiac diseases		89 (59%)

Amongst the included 150 patients; 18 patients (12%) died within 21 days (short term mortality) and 12 patients (8%) died after six months(The long-termmortality).

The descriptive analysis of blood investigations is shown in table (2).

Table 2: the descriptive analysis of blood investigations

Test	Mean ± SD
WBC	11.53 ± 5.7
RBC	4.62 ± 0.88
PLT	239.7 ± 94.5
HGB	12 ± 2.2
HCT	40 ±32
Total bilirubin	0.95 ± 1.3
Direct bilirubin	0.25 ± 0.47

Total protein	7.2 ± 1.6
Albumin	3.7 ± 1.2
ALT	110 ± 271
AST	154 ± 311
Alkaline phosphate	105 ±53
Prothrombin time	15.1 ± 5.6
Prothrombinconc	73.9 ± 24.3
INR	1.2 ± 0.8
LDH	442 ± 330
BUN	11 ± 9.2
Creatinine	142.6 ± 125.3
Mg	2.05 ± 1.8
NA	137 ± 4.4
K	4.1 ± 0.67
Calcium	9.6 ± 1.7
TNF	20 ± 18.6

The mortality (short and long- term) and length of hospital stay were correlated to TNF and scores (APACHE and q SOFA) (table 3).

Table 3: correlation of mortality (short and long -term) and length of hospital stay to TNF and scores

		Length of hospital stay	Short term mortality	Long term mortality
TNF	**r**	0.526	0.421	0.354
	P	0.001	0.005	0.006
APACHE II	**R**	0.307	-0.490	0.240
	P	0.001	0.01	0.059
q sofa	**R**	0.042	-0.425	0.528
	P	0.604	0.002	0.001

TNF was the most impressible predictor for short term mortality.Q SOFA score was the most sensitive predictor for the long-term mortality while APACHE II was the best predictor for length of hospital stay table (4)

Table 4: logistic regression regarding mortality(short and long -term), hospital stay length and q SOAF, APACHE II scores and TNF:

		P. value	Exp (B)	95% C.I for EXP(B)	
				Lower	Upper
Short term mortality	**TNF**	**0.033**	0.968	0.940	0.997
	APACHE II	0.001	0.863	0.791	0.942
	q SOFA score	0.692	0.842	0.359	1.976
Long term mortality	TNF	0.038	1.034	1.002	1.067
	APACHE II	0.860	0.995	0.902	1.090
	q SOFA score	**0.028**	2.810	1.119	2.056
Hospital stay length	TNF	0.005	1.046	1.014	1.080
	APACHE II	**0.004**	1.147	1.045	1.259
	q SOFA score	0.172	0.492	0.178	1.361

The maximum AUCs for prediction of the mortality were 0.795, 0.757 and 0.7 for APACHE II, TNF and q SOFA respectivelyfigure (1, 2, 3).

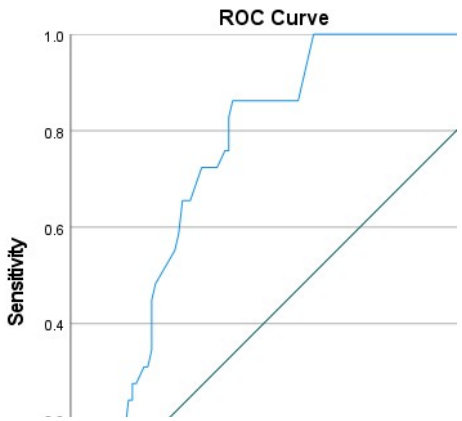

Figure 1: ROC curve of APACHE II for prediction of mortality (sensitivity 86%, specificity 47%).

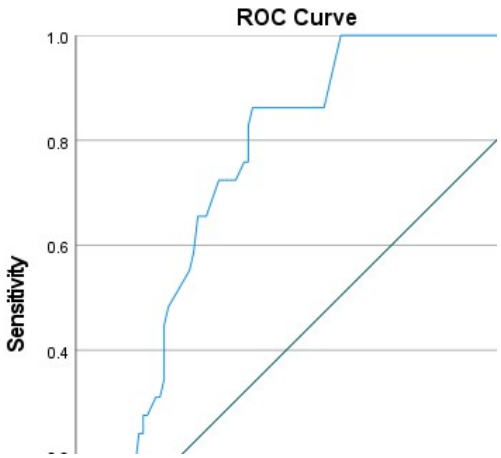

Figure 2: ROC curve of TNF for prediction of mortality (sensitivity 93%, specificity 48%).

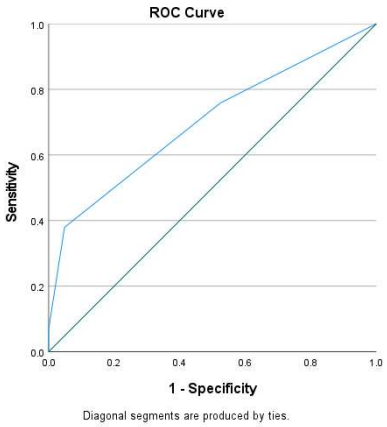

Figure 3: ROC curve of q SOFA for prediction of mortality (sensitivity 75%, specificity 52%).

DISCUSSION

The diseases of the ICU patients are associated with systemic inflammation (Cytokine storm) which leads to tissue damage either by direct effects of on cell function or as a result ofhypo perfusion resulting in immune exhaustion,secondary infections and failure of the organs(10).
Inthe current study, we evaluated 150 patients who were admitted to Assuit university hospitals ICU from January 2018 to January 2019. There was significant correlation between the short-term mortality and APACHE II, q SOFA andTNFwhichmatchedwith previous studies' results (10) (11).

In our study acute kidney injury developed in 38% of the patients and this agreed with (12).Twenty-nine (29%) of the patients had respiratory diseases and 12% of them developed shock this agreed with (13).
In this study there was significant correlation between the long-term mortality and q SOFA score, TNF while there was no significant correlation between long term mortality and APACHE IIthis agreed with other studies' results(10)(14).
TNF and APACHE II had significant correlation with hospital stay length while q SOFA had insignificant correlation with hospital stay length this were the same results provided by previous studies(15)(16)(17).

CONCLUSION

TNFlabored at Assuit University Hospitals ICUs is a sensitive predictor for mortality(short and long -term)and hospital stay duration.

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