Abstract

Objectives: to investigate the prognostic value of levels of VEGF in patients with sepsis in the intensive care setting regarding the clinical course and final outcome. Moreover, to compare this prognostic value of VEGF levels with other commonly used biochemical markers for prognosis of sepsis (CRP and Microalbuminuria) and with the APACHE IV and SOFA scoring systems. ***Design:*** A prospective, randomized, single center study. ***Setting:*** Critical Care Department (medical/surgical ICU).***Patients:*** 40 critically ill patients admitted to the Critical Care Department with a diagnosis of sepsis. ***Measurements:*** VEGF concentrations (measured by ELISA) were measured on admission and 48 hours later. CRP levels and Microalbuminuria concentrations were measured on admission to the ICU. APACHE IV score was calculated on admission and 72 hours later and SOFA score was calculated at baseline and subsequently thereafter every day until ICU discharge or death or up to a total of 28 days. Clinical outcome (duration of stay in the ICU, need for mechanical ventilation, need for inotropic/vasopressor support, need for haemodialysis, and final outcome of survival/mortality rates) were recorded for all patients. ***Results:*** The median VEGF 1 concentration in critically ill septic patients was775 ng/l and this was significantly (approximately 6-fold) higher than the median VEGF concentration in healthy subjects 137.5 ng/l, **(*P* =0.001).)**. The median VEGF 2 level for all patients after 48 hours of ICU admission was 850 (normal value less than 200 ng/l), approximately 7 fold higher than that in healthy subjects also, **(*P*= 0.000)**.but there was no significant correlation between VEGF 1 and VEGF 2 , **(*P*= 0.272)** .The median VEGF 1 level was significantly higher in patients who required mechanical ventilation 800 ng/l than those who did not require it 470 ng/l, **(*P* = 0.002)**.While there were no significant differences seen in the median VEGF 2 levels between patients who did not require mechanical ventilation 850 ng/l and those who required it 830 ng/l, **(*P* = 0.871)**. There were significant differences seen in the median VEGF 1 levels between patients who required inotropic / vasopressor support 810 ng/l and those who did not require it 460 ng/l, **(*P* = 0.006)**, also there were significant differences seen in the median VEGF 2 levels between patients who required inotropic / vasopressor support 900 ng/l and those who did not require it 830 ng/l, **(*P* = 0.024)**. The median VEGF 1 levels was significantly higher in patients who required renal supportive therapy (hemodialysis) 850 ng/l versus those who did not require it 830 ng/l, **(*P* = 0.008)**.However there were no significant differences seen in the median VEGF 2 levels between patients who required renal supportive therapy (hemodialysis) 850 ng/l and those who did not require it 830 ng/l, **(*P* = 0.378)**. VEGF 1and VEGF 2 levels were significantly correlated with C-reactive protein (CRP) level at ICU admission, **(r = 0.475 , r = 0.631) ,** (***P* < 0.002, *P* < 0.001)** respectively .also VEGF 1and VEGF 2 levels were significantly correlated with Alb/Creat ratio (Microalbuminuria**)** level at ICU admission, **(r = 0.623 , r = 0.607) ,** (***P* < 0.001, *P* < 0.001)** respectively. also VEGF 1and VEGF 2 levels were significantly correlated with APACHE IV score **(r = 0.397 , r = 0.410) ,** (***P* < 0.011, *P* < 0.034)** respectively. But not with SOFA score, **(r = 0.153 , r = 0.291) ,** (***P* < 0.345, *P* < 0.133)** respectively. Insignificant correlation was found between VEGF 1 level and the length of stay in the ICU, **(r = 0.015), (*P* = *0.927).***but significant correlation was found between VEGF 2 level and the length of stay in the ICU,**(r = 0.448), (*P* = 0.015)**. The median VEGF1 concentration in non survivors was (810 ng/l)and this was significantly higher (approximately 2 fold greater) than that in survivors (470 ng/l), **(*P* 0.001)**. However no significant difference between the median VEGF 2 concentration in non survivors (740 ng/l) and the median VEGF 2 concentration in survivors (880 ng/l), **(*P* 0.268).** ROC analysis of the data indicated a sensitivity of 85.15% and a specificity of 92.3% when VEGF concentration of 410 ng/l was taken as a predictor of ICU mortality.

Conclusion: VEGF concentrations were elevated early in patients who were admitted to the ICU with sepsis when compared to healthy controls, VEGF concentrations were significantly higher in patients who needed organ supportive measures (mechanical ventilation, inotropic / vasopressor support and haemodialysis) during their ICU stay, VEGF levels were significantly higher in ICU non-survivors than in survivors. VEGF concentrations demonstrated a significant correlation with CRP concentrations, Alb/Creat ratio (Microalbuminuria**)** and APACHE IV score, but not with SOFA score . These findings indicate that VEGF might be used as a potential useful marker for evaluation of septic patients when admitted to ICU and for prediction of their adverse outcomes.

Key words: sepsis; VEGF; CRP; Microalbuminuria, APACHE IV score; SOFA score; clinical outcome.