Abstract

Objectives: to investigate the prognostic value of circulating Serum angiopoietin-2 level in patients with sepsis in the intensive care setting regarding the clinical course and final outcome. Moreover, to compare this prognostic value of circulating Serum angiopoietin-2 level with the APACHE II and SOFA scoring systems. ***Design:*** A prospective, randomized, single center study.

Setting: Critical Care Department (medical/surgical ICU), Cairo University Hospitals.

Patients: 30 critically ill patients admitted to the Critical Care Department, Cairo University Hospitals with a diagnosis of sepsis. ***Measurements:*** *Serum angiopoietin-2 level concentrations* (measured by ELISA), measured on admission to the ICU. APACHE II score was calculated once (in the first 24h of ICU admission) 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 current study showed that the Serum angiopoietin-2 level concentrations were significantly higher (approximately 5-folds) in septic patients compared to healthy subjects **(0.9(0.3-2.6) ng/ml**, *P < 0.001),* and the Serum angiopoietin-2 level concentrations were significantly higher in patients with septic shock at their ICU admission *(28.1(3.7-72.6)* ng/ml) than those with severe sepsis *(16.45(2.7-39.7)* ng/ml) or those with sepsis *(2.8(1.0-9.0) ng/ml), P < 0.001* for both. In this study, there was no significant correlation between Serum angiopoietin-2 level concentrations and age *(P = 0.675) or sex (P = 0.289).*There were also no significant differences seen in the Serum angiopoietin-2 levels between patients who were operated or not *(P = 0.363).* In the present study, the median Serum angiopoietin-2 concentration in patients who were ventilated *[11.75 (6.2-34) ng/ml]* was significantly **(P = 0.001)** higher than that in patients who were not ventilated *[5.5 (3.25 – 7.75)* ng/ml], Serum angiopoietin-2 level was also significantly higher in patients who required inotropic/vasopressor support **[12.13 (6.2-34) ng/ml] P < 0.001)** or renal support **([19.5 (15-34) ng/ml]** versus**[7.75 (3.25-14.25) ng/ml] P = 0.011)** when compared with non-supported patients . Our study revealed insignificant negative correlation between the Serum angiopoietin-2 level and the length of stay in the ICU *(r = - 0.15, P =0.429).* In the current study, the Serum angiopoietin-2 concentration was significantly correlated with SOFA score *(r = 0.715, P <0.001),* and with APACHE II score *(r = 0.756, P = 0.001).* There was approximately 2-fold significant increase in median circulating angiopoietin-2 concentrations in patients who died in the ICU **[14.25 (7.6-34) ng/ml]** when compared with survivors **[6.75 (3.25-15 ng/ml],** *P < 0.001* and, the sensitivity and specificity for prediction of ICU mortality was 100%, for both. In the present study, Receiver operator characteristic analysis used in our study revealed that a serum angiopoietin-2 value of **7.775 ng/ml** was superior to a SOFA score value of **4.75** and an APACHE II score value of **20.5** for predicting ICU mortality. As the sensitivity and specificity were **92%** and **65%** for pserum angiopoietin-2, **77% and 88%** for SOFA score and **77%** and **82%** for APACHE II score. In our study, in an attempt to use the serum angiopoietin-2 concentration as a predictor of ICU morbidity (patients who survived but not recovered, were still morbid and needed longer duration of ICU stay) by using the ROC curve analysis, the best cutoff value for serum angiopoietin-2 to predict ICU morbidity was **9.125 ng/ml**, with a sensitivity of **80%** and a specificity **of 83%.**

Conclusion: Circulating Serum angiopoietin-2 levels were elevated early in patients who were admitted to the ICU with sepsis when compared to healthy controls, Serum angiopoietin-2 level concentrations were significantly higher in patients who needed organ supportive measures (mechanical ventilation, inotropic/vasopressor support and haemodialysis) during their ICU stay, Serum angiopoietin-2 levels were significantly higher in ICU nonsurvivors than in survivors. Circulating angiopoietin-2 concentrations demonstrated a significant correlation with SOFA score, APACHE II score, and with length of ICU stay. These findings indicate that Serum angiopoietin-2 levels 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; serum angiopoietin-2; prognostic marker; cell necrosis; apoptosis; APACHE II score; SOFA score; clinical outcome.