

ABSTRACT

Background . Myocardial dysfunction frequently accompanies severe sepsis and septic shock. Whereas myocardial depression was previously considered a preterminal event, it is now clear that cardiac dysfunction as evidenced by biventricular dilatation and reduced ejection fraction is present in most patients with severe sepsis and septic shock. Myocardial depression exists despite a fluid resuscitation-dependent hyperdynamic state that typically persists in septic shock patients until death or recovery. Cardiac function usually recovers within 7–10 days in survivors. Myocardial dysfunction appears to be due to circulating depressant factors (e.g. tumor necrosis factor alpha and IL-1 β) . It was hypothesized that the Toll-like receptor 4 (TLR4) mediates myocardial dysfunction in sepsis through activation of cytokine production by monocytes/macrophages and through an increase in NO and TNF production by the myocytes themselves.

Objective: To correlate between the Toll-like receptor concentrations and myocardial dysfunction, clinical course and outcome of septic patients.

Methods: A total of 20 septic patients were enrolled into the study, 10 of them developed myocardial depression during ICU stay and the other 10 patients were without myocardial depression. Excluded from our study the patients known to have cardiac problems and those on immunosuppressive therapy. All included patients were subjected to the measurements of TLR4, TNF- α , IL-1 β and Troponin I which were withdrawn at day 1 of ICU admission. Length of ICU stay, Need for organ supportive measures (Inotropic/Vasopressor support and/or Mechanical ventilation) and final outcome were reported for all patients until ICU discharge or demise or up to a total of 28 days. APACHE II score was calculated within the first 24hrs of ICU admission and SOFA score was recorded daily throughout the study period.

Results:

- Toll-like receptor-4 concentrations were significantly elevated in patients who were admitted to the ICU with septic criteria(the higher concentrations were detected in patients with the diagnosis of septic shock at ICU admission).
- TLR-4 concentrations were significantly higher in patients who needed inotropic/vasopressor support during their ICU stay than those who did not require it.(P value=0.015).
- TLR-4 concentrations were significantly higher in patients who developed impaired ventricular function during their ICU stay than those without ventricular dysfunction.(P value=0.006).
- TLR-4 concentrations were significantly correlated with IL-1 β .(P value=0.04).
- TLR-4 concentrations were significantly higher in patients who died in the ICU than those who survived.(P value=0.024).

Conclusion: Toll-like receptor-4 may be a potentially useful prognostic test for the evaluation of septic patients when admitted to the ICU and for the prediction of their

adverse outcomes (e.g. impaired ventricular function, haemodynamic compromise with need for inotropic/ vasopressor support and mortality).

Key words: Toll-like receptor-4, TNF- α , IL-1 β , Myocardial depression, sepsis.