Journal of Microbiology and Infectious Diseases / JMID
2011; 1 (3): 101-109
doi: 10.5799/ahinjs.02.2011.03.0024

ORIGINAL ARTICLE

Prognostic value of cytokines (TNF-α, IL-10, Leptin) and C-reactive protein serum levels in adult patients with nosocomial sepsis

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ABSTRACT

Objectives: The purpose of this trial was to investigate in patients with sepsis, the correlation between prognosis of disease and factors, which influence prognosis like gender, focus of infection, bacterial growth in blood culture, growing pathogens in addition to serum levels of cytokines (TNF-α, IL-10, leptin) and C-reactive protein.

Material and methods: Forty-six adult patients with sepsis and 55 healthy adults as control group were enrolled in this study. Serum cytokine (TNF-α, IL-10 and leptin) levels were determined by ELISA method and C-reactive protein (CRP) levels were measured by nephelometric method. Serum cytokine and CRP levels on day 0 (initial), day 3 and day 5 were compared in surviving sepsis patients and patients who died because of sepsis.

Results: Serum IL-10 level on day 0 (initial) of adult patients who died as a result of sepsis was found to be higher than surviving patients and the difference was statistically significant (p=0.025). On 3rd day of treatment, serum TNF-α and CRP levels of patients who dies because of sepsis were higher than values of surviving patients (for TNF-α p=0.033, for CRP p=0.026). In adult patient group with sepsis who died on the 5th day of treatment, serum TNF-α level was significantly higher than levels in surviving patients (p=0.030).

Conclusion: It was determined that in patients who died due to sepsis, initial serum IL-10 level, TNF- α and CRP levels on 3rd day of treatment and finally on 5th day of treatment, only serum TNF- α level was higher than surviving patients. We believe that determining serum TNF-α and IL-10 levels in patients with sepsis before and during treatment will help clinicians to clarify prognosis and enable them to implement appropriate treatment modifications. *J Microbiol Infect Dis 2011; 1(3):101-109*

Key words: Sepsis, cytokines, CRP, prognosis

Nozokomiyal sepsisli erişkin hastalarda serum sitokinleri (TNF-α, IL-10, Leptin) ve C-Reaktif protein düzeylerinin prognostik değeri

ÖZET

Amaç: Bu çalışmada sepsisli hastalarda prognoza etki eden yaş, cinsiyet, infeksiyon odağı, kan kültüründe üreme ve etken bakteri gibi faktörlerle sitokinlerden TNF-α, IL-10, leptin ve C-reaktif protein serum düzeylerinin prognozla ilişkisinin araştırılması amaçlandı.

Gereç ve yöntem: Çalışmaya 46 erişkin sepsisli hasta ile kontrol grubu olarak ise 55 sağlıklı erişkin dahil edildi. Serum sitokin (TNF-α, IL-10 ve leptin) düzeyleri ELISA yöntemiyle, C-reaktif protein (CRP) düzeyleri ise nefelometrik yöntemle saptandı.

Serum sitokin ve CRP düzeyi sepsili ölen hasta grubu ile yaşayanlar arasında başlangıç (0.gün), 3. ve 5.günlerde istatistiksel olarak karşılaştırıldı.

Bulgular: Sepsisten ölen erişkin hastalarda başlangıç (0. gün) serum IL-10 düzeyi, yaşayan hastalarinkinden istatistiksel olarak daha yüksek saptandı (p=0.025). Sepsisten ölen hastalarda, tedavinin 3. gününde serum TNF-α ve CRP düzeyleri yaşayan hastalardan daha yüksekti (TNF-α için p değeri=0.033, CRP için p=0.026). Sepsili erişkin hasta grubunda tedavinin 5. gününde ölen hastalarda serum TNF-α düzeyi yaşayan hastalardan daha yüksekti (p=0.03)

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Received: 08.12.2011, Accepted: 21.12.2011

Sonuç: Sepsisli erişkin hastalrda tedavi başlangıcında serum IL-10 düzeyinin, tedavinin 3. gününde TNF-α ve CRP düzeyinin, tedavininin 5. gününde ise sadece serum TNF- α düzeyinin prognostik olduğu belirlendi. Sepsisli hastalarda serum TNF-α ve IL-10 düzeylerinin tedavinin başlangıcında ve tedavi esnasında saptanması hastaların prognozunun belirlenmesinde ve uygun tedavi değişikliklerinin yapılmasında klinisyene yol gösterici olabilir.

Anahtar kelimeler: Sepsis, sitokin düzeyleri, CRP, prognoz.

INTRODUCTION

Sepsis is a leading clinical syndrome among emergency infection conditions which carry a very high mortality rate. Pathogenesis of sepsis is quite complicated. Sepsis is one of the leading causes of hospitalizations in intensive care units. It leads to prolongation of hospitalization and increase in costs related both to hospital and to intensive care unit.[1]

Nosocomial sepsis is the leading cause of death in intensive care units. Sepsis is an inflammatory process during which various mediators (like cytokines) play a certain role between microorganisms and immune system of the host. During this process, presence of bacteria or endotoxine in the circulation leads to a release of small signalling proteins called cytokines. Cytokines are abundantly released in cases of sepsis, multiple organ failure, trauma and following burn injuries. During sepsis, there is a continuous interaction between proinflammatory (e.g. TNF-α) cytokines and antiinflammatory cytokines (e.g. IL-10).[2- 6]

Main factors which affect prognosis in sepsis are hypotermia, underlying diseases, age, pathogens leading to sepsis, focus of sepsis, severity of sepsis (sepsis, septic shock, multiple organ failure), appropriateness of antimicrobial treatment, initiation time of antimicrobial treatment, cytokines (TNF-α, IL-10, IL-6 etc.) and coagulation factors.[8-12]

The aim of this trial, which was carried out in adult patients diagnosed with nosocomial sepsis in intensive care units, is to identify prognostic value of prognostic factors like age, gender, focus of infection, and pathogens leading to sepsis and in addition, to determine prognostic value of serum cytokine levels like TNF-α, IL-10, leptin which play an important role in pathogenesis of sepsis and levels of C-reactive protein (CRP).

MATERIALS AND METHODS

This trial was realized between June 2005 and August 2007 in Ankara Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology and Gülhane Military Medical College, Department of Infectious Diseases and Clinical Microbiology. Ethical Committee approval was obtained from participating centers and informed consent forms were signed by patient and controls.

For this trial, adult patient group with sepsis was composed of patients hospitalized in intensive care units and/or clinics of Infectious Diseases of Ankara Education and Research Hospital and Gülhane Military Medical College and diagnosed as nosocomial sepsis.

In order to compare data of patient group, a control group of healthy volunteers was enrolled. Control group were selected from healhty subjects without any underlying diseases. All data of patient and control group was documented on related monitoring forms in Excell format. In patients with sepsis, risk factors preceding sepsis, age, gender, focus of infection (pneumonia, catheter-associated infection, intraabdominal infection, urinary system infection etc.), positivity of blood culture, response to treatment and mortality rates were documented on patient report forms.

Patient and control group

Forty six adult cases with a diagnosis of sepsis and 55 healthy adult control group were enrolled in this trial. Sepsis patients were diagnosed both clinically and by laboratory findings in accordance with ACCP/SCCM criteriae.[7,8] APACHE II score was calculated in patients with sepsis. In order to determine focus of infection in patients, cultures from various sources like blood, urine, deep tracheal aspirate, abcess material were obtained before treatment was initiated. In all patients, sepsis developed 72 hours after referral to hospital and therefore, cases were considered as nosocomial sepsis.

In patients hospitalized in intensive care units and diagnosed with nosocomial sepsis, ampirical antimicrobial treatment against possible pathogens was initiated during the first 6 hours, after blood samples were obtained. When pathogen was isolated, ampirical antimicrobial treatment was re-evaluated based on antimicrobial sensitivity results.

Methods

Blood samples from adult patients with sepsis were obtained on day 0 (before treatment) plus on 3rd and 5th days of treatment; only one blood sample was obtained from healthy control group.

Blood samples were centrifuged and stored in deep-freeze at -80°C. Serum CRP, TNF-α, IL-10, leptin levels were measured on day 0 (before treatment) plus on 3rd and 5th days of treatment. Measurement of CRP level was performed by nephelometric method using high sensitive CRP kit (Dade Behring, Germany) in accordance with recommendations of the manufacturer. Serum TNF-α, IL-10, leptin levels were measured by ELISA method using commercial kits (Biosource, Belgium) in accordance with recommendations of the manufacturer. All cytokine evaluations were performed in Gülhane Military Medical College Laboratory of Department of Immunology.

Statistical analysis

Statistical analysis were realized in Ankara University Medical Faculty Department of Biostatistics. All data of patient and healthy control group were entered into SPSS 11.5 Windows program. In the statistical evaluation, Kolmogorow–Smirow normal scatter test, Mann-Witney U test and Chi-square tests were utilized. In order to evaluate prognostic (mortality or survival) prediction value of statistically significant parameters in patients who died from sepsis and in surviving sepsis patients, ROC curve was established. Area under the curve was tested to determine significance. In order to determine the effect of variables (age, gender, sepsis group, and cytokines (CRP, TNF-α, IL-10, leptin) on mortality, multiple logistic regression analysis (Hosmer and Lemeshow tests) was performed. $p<0.05$ value was considered as statistically significant.

RESULTS

Demographic and statistical data of adult patients and control group

In the adult patient group, 16 (34.7%) were women and 30 (5.2%) were men; mean age of men was 60,4 ± 19,60 and mean age of women was 66.9 ± 13.7. In the control group, 23 (41.8%) were men, 32 (58.1%) were women; mean age of men was 38.2 ± 12.3 and mean age of women was 37.7 ± 11,6. Mean age of patient group was 62.8 ± 17.8 and mean age of healthy control group was 37.9 ± 11.8. In the trial, blood samples from adult patients with sepsis were obtained on day 0 (before treatment) plus on 3rd and 5th days of treatment; only one blood sample was obtained from healthy control group.

At the admission (day 0), 3rd day and 5th day serum TNF-α, IL-10 and C-reactive protein levels in sepsis patients displayed statistically significant differences in comparison to control group ($p<0.001$). There was no statistically significant difference between patient and control groups in terms of leptin levels ($p>0.001$). Results are shown on Table 1. Mortality was seen in 30 of 46 sepsis patients (65.2%). While growth was determined in blood cultures of 11 sepsis patients (24%), no growth was observed in any of the cultures [(blood, catheter, deep trecheal aspirate (DTA), etc] in 26 patients (56.5%).

Examination of prognostic factors in patients with sepsis

APACHE-II scores: APACHE II score were higher in patients who died than surviving patients (27.9 ± 8.42 for patients who died and 19.6 ± 6.85 for surviving patients, respectively). There was statistically significant difference between patients who died and surviving patients in terms of APACHE II scores ($p<0.05$).

Underlying diseases in patients with sepsis: The underlying diseases were diabetes mellitus (n=2), hypertension (n=8), and cerebrovascular disease (n=3) in patients who died. The underlying diseases were diabetes mellitus (n=5), hypertension (n=20), and cerebrovascular disease (n=6) in surviving patients. There was not statistically significant difference between patients who died and surviving patients in terms of underlying diseases ($p>0.05$).

Focus of sepsis: Patients who died and surviving patients were compared in terms of focus of sepsis. No statistical comparison could be performed due to various numbers of foci of infection; percentage ratios were determined (Table 2).

Growth rate in blood culture and growing pathogens: In 11 of 46 sepsis patients (24%) growth was seen in blood cultures. Gram positive bacteria which grew in blood cultures (n=6) are methicillin resistant *Staphylococcus aureus* (MRSA, n=3), methicillin sensitive *Staphylococcus aureus* (MSSA, n=1), coagulase negative staphylococcus (CNS, n=1), enterococcus species (n=1), respectively. Gram-negative bacteria which grew in blood cultures (n=5) were *E.coli* (2), *Pseudomonas aeruginosa* (2), *Enterobacter species* (spp.) [1] and *Acinetobacter* spp. (1), respectively. Growth in blood cultures was determined in 5 of 30 patients (16.6%) who died from sepsis and in 6 of 16 surviving sepsis patients (37.5%). In blood cultures of patients who died from sepsis, Gram positive bacteriae were isolated in 3 and Gram-negative bacteriae were isolated in 2 patients. In blood cultures of surviving patients, Gram-positive bacteriae were isolated in 3 and Gram negative bacteriae were isolated in 3 patients. When died and surviving patients were compared in terms of growth rate for blood cultures and growing pathogens; there was no statistically significant difference between among two group (p=0.228).

Table 1. Comparison of age, gender, TNF -α, IL-10, leptin and CRP levels on day 0, day 3 and day 5 of patients with sepsis and control group [median (min-max)]

Variables	Patient	Control	p value
Age, yrs	68 (21-86)	36 (20-66)	<0,001
Gender F/M number (%)	17 (37%) /29 (63%)	31 (56.4%)/24 (43.6%)	0,052
TNF – α, day 0	27.76 (13.69-169.89)	12.35 (9.30-24,47)	<0,001
TNF- α, day 3	26.88 (14.20-87.07)	12.35 (9.30-24.47)	<0,001
TNF- α, day 5	24.61 (15.55-71.62)	12.35 (9.30-24.47)	<0,001
IL-10, day 0	3.24 (1.01-198.84)	0.60 (0.24-2.77)	<0,001
IL-10, day 3	2.39 (0.60-28.58)	0.60 (0.25-2.77)	<0,001
IL-10, day 5	1.76 (0.38-25.25)	0.60 (0.25-2.77)	<0,001
Leptin, day 0	3.03 (0.78-120.17)	4.72 (0.29-29.06)	0,424
Leptin, day 3	1.50 (0.33-83.39)	4.72 (0.29-29.06)	0,004
Leptin, day 5	1.29 (0.38-26.30)	4.72 (0.29-29.06)	0,002
CRP, day 0	140 (18-313)	3.02 (3-31)	<0,001
CRP, day 3	104 (4.58-238)	3.02 (3-31)	<0,001
CRP, day 5	87.60 (3.02-195)	3.02 (3-31)	<0,001

Table 2. Foci of sepsis in patients with sepsis.

Focus of sepsis	Surviving patients (n= 16)	Patients who died (n=30)
Pneumonia, n (%)	5 (31.2)	12 (40)
Catheter infection, n (%)	2 (12.5)	3 (10)
İntraabdominal infection, n (%)	0	3 (10)
Urinary system infection, n (%)	6 (20)	4 (25)
Skin, soft tissue infection, n (%)	2 (12.5)	1 (3.3)
Central nervous system infection, n (%)	1 (6.25)	1 (3.3)
Mixt infection, n (%)	0	1 (3.3)
No focus determined, n (%)	2 (12.5)	3 (10)

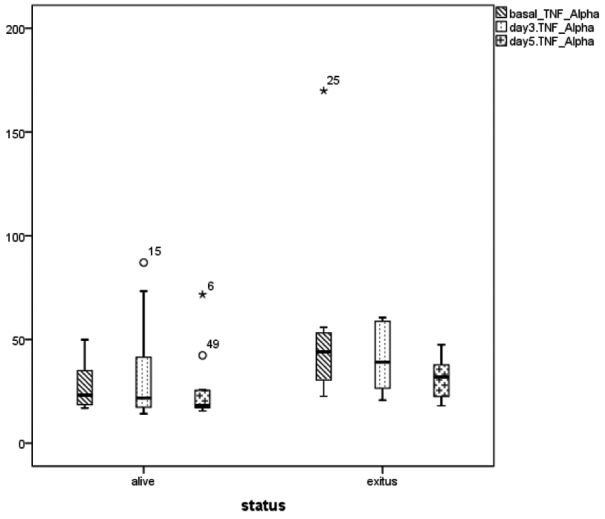

Figure 1. Serum TNF-α values according to treatment responses in patients with sepsis (i.e, alive and exitus).

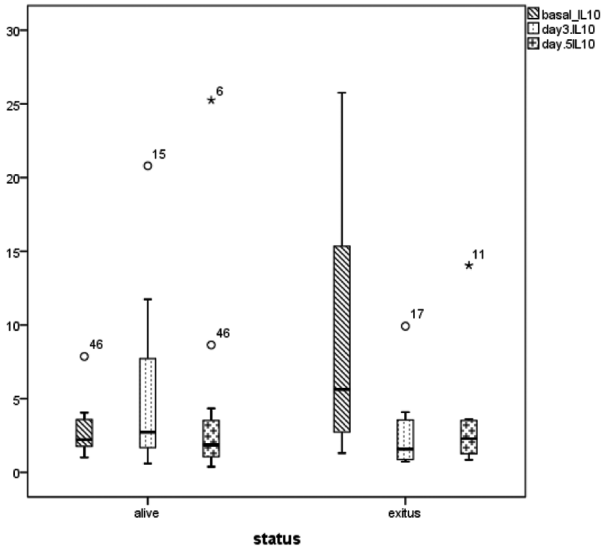

Figure 2. Serum IL-10 values according to treatment responses in patients with sepsis (i.e, alive and exitus)

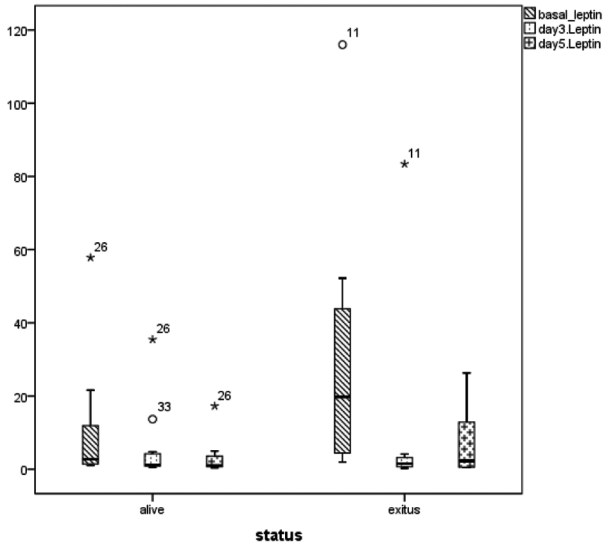

Figure 3. Serum leptin values according to treatment responses in patients with sepsis (i.e, alive and exitus)

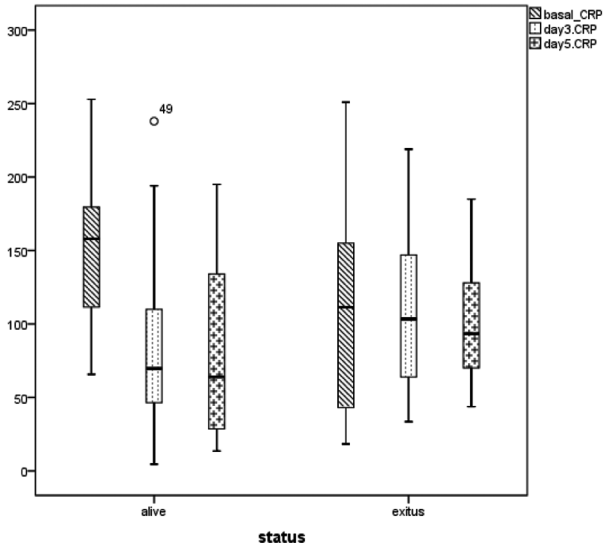

Figure 4. Serum CRP values according to treatment responses in patients with sepsis (i.e, alive and exitus)

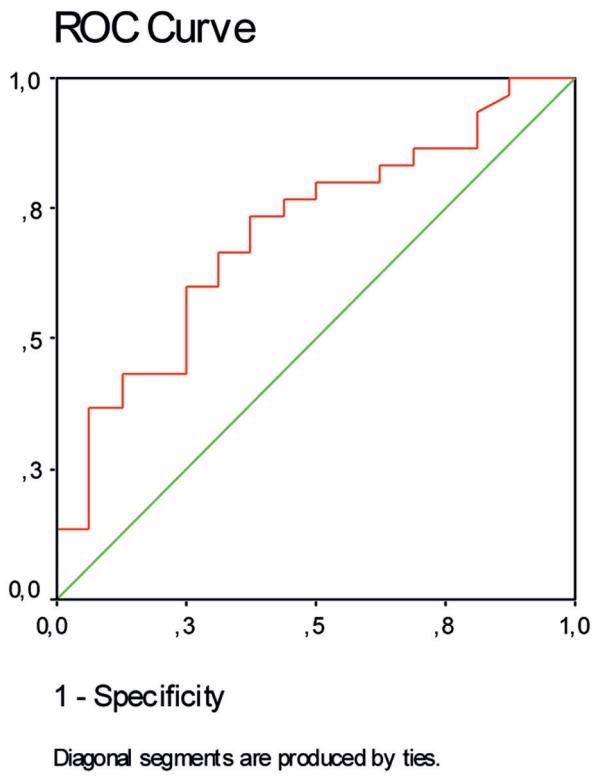

Figure 5. ROC curves showing the sensitivity and specificity of IL-10 for sepsis at the admission.

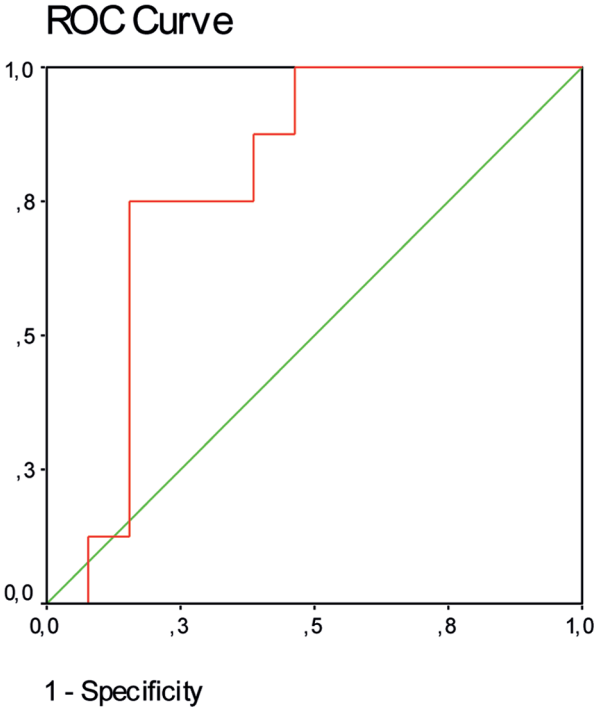

Figure 6. ROC curves showing the sensitivity and specificity of TNF-α on 5th treatment day.

Comparison of serum CRP, TNF-α, IL-10, leptin levels of patients who died from sepsis and surviving sepsis patients.

Patients with sepsis were classified into two groups according to treatment responses; namely surviving patients and patients who died. In the patient group with sepsis, serum CRP, TNF-α, IL-10, leptin levels on day 0, day 3 and day 5 were statistically compared between surviving patients and patients who died. In the patient group with sepsis, initial (day 0, at the admission) serum IL-10 levels of patients who survived after treatment and patients who died showed a statistically significant difference (p=0.025); other parameters were not significantly different. At the admission (day 0) serum IL-10 levels of patients who died from sepsis was high as compared to surviving patients (IL-10 median value in patients who died: 3.65 pg/ ml, in surviving patients; median: 2.13). In patients with sepsis, there was a significant difference in serum TNF-α and CRP levels of patients who died on 3rd treatment day and surviving patients (for TNF-α p = 0.033, for CRP p=0.026); other parameters were similar. Serum TNF-α and CRP levels on 3rd treatment day was high in patients who died from sepsis in comparison to surviving patients (In patients who died; TNF-α level median value: 41.7 pg/ml, CRP level median: 113 mg/dl, in surviving patients; TNF-α level median: 21.4 pg/ml, CRP level median: 75.5 mg/dl). In adult patient group with sepsis, statistically significant difference on 5th treatment day was observed only for serum TNF-α levels between surviving patients and patients who died (for TNF-α p=0.03). Serum TNF-α level was higher in patients who died (in patients who died; TNF-α level median was 31.8 pg/ml, in surviving patients; TNF-α level median was 17.7 pg/ml). At the admission (day 0), day 3 and day 5 TNF-α, IL-10, leptin and CRP values according to treatment responses in patients with sepsis (i.e, alive and exitus) is shown in Figure 1, Figure 2, Figure 3, and Figure 4, respectively.

Evaluation of prognostic value of serum TNF-α and IL-10 in patients who died from sepsis and in surviving patients

A ROC curve was created for this evaluation. Significance value (if any) of area under the curve was tested. It was determined that initial (day 0) serum IL-10 levels had a differential value in predicting mortality (Area under the curve: 0.73; area

under the curve was significant). Cut-off value was determined by Youden index. In sepsis, initial IL-10 levels over 2.37 pg/ml had a sensitivity value of 73.3% and a specificity value of 62.5% in predicting mortality. Figure 5 contain ROC curves showing the sensitivity and specificity of IL-10 for sepsis at the admission.

In patients who died from sepsis, TNF-α levels on 5th treatment day were higher than surviving patients. Serum TNF-α levels on day 5 was shown to have a differential value for predicting mortality (Area under the curve: 0.78). Cut-off value was determined by Youden index. In sepsis, TNF-α levels above 25.82 pg/ml on day 5 of treatment was found to have a sensitivity value of 75% and a specificity value of 84.6% in predicting mortality. Figure 6 contain ROC curves showing the sensitivity and specifity of TNF-α on day 5 th treatment day.

Logistic regression analysis

For this analysis age, sepsis group, serum TNF-α, IL-10, CRP, leptin on day, 0, day 3 and day 5 were determined as variables for multiple statistical model. When logistic regression analysis is performed in terms of patient and control group; it was determined that among cytokines on day 0, IL-10 level is also an independent risk factor (p=0.001, odds ratio (95% CI) :46.88 (5.24-419.41).

For day 3, serum CRP level was an independent risk factor (p=0.015, Odd ratio (95% CI) :1.28 (1.05-1.57). For day 5, serum CRP level was determined as an independent risk factor (p<0.001, Odds ratio (95% CI):1.18(1.07-1.31)

Among variables according to treatment responses (gender, sepsis group, TNF-α, IL-10, CRP, leptin), serum TNF-α level on day 5 was an independent risk factor for mortality (p=0.044, Odds ratio (95% CI):14.84). For TNF-α values over 25.82 ng/ml, mortality risk was increased by 14.84-fold.

DISCUSSION

Despite current technological, pharmacological and surgical developments in a number of diseases, mortality ratio related to sepsis is still too high.[11] Sepsis is a complex inflammatory response syndrome which incorporates immune and coagulation systems. Interrelation of cytokines which mediate interaction between host and microorganism has an important role in clinical course and prognosis of sepsis. In the pathogenesis of sepsis, cytokines can be classified as proinflammatory (e.g.,TNF-α) and antiinflammatory (e.g., IL-10), according to their inflammatory activities.[3,8]

Main factors which affect prognosis in sepsis are hypothermia, underlying disease, age, pathogens causing sepsis, focus of sepsis, severity of sepsis (sepsis, septic shock, multiple organ failure), appropriateness of antimicrobial treatment, cytokines (IL-10, IL-6, TNF-α) and coagulation factors.[8-11] Cytokines have an important role in the cascade and prognosis of sepsis. Among cytokines, TNF-α is a proinflammatory cytokine and it's released from Th1 subgroup of T helper lymphocytes and from macrophages. It plays an important role in acute inflammatory response and high serum levels are associated with mortality. High serum TNF levels in Gram- negative bacteriemia is an indicator for poor prognosis.[8]

IL-10 is an antiinflammatory cytokine and is released mainly by Th2 subgroup of T helper lymphocytes. IL-10 has multiple functions. IL-10, in collaboration with PGE2, inhibits proinflammatory cytokine synthesis. It plays an important role in the control of immune reactions during systemic infections. Elevated IL-10 levels are an indicator for severe acute phase reaction related to macrophage activation. High IL-10 levels are correlated with CRP and neopterin levels. In addition, there exists a correlation between IL-10 level and proinflammatory cytokines TNF-α, IL-6 and IL-8 levels.

IL-10 decreases synthesis of IL-1, IL-6 and TNF-α in monocytes and it supress interferon-γ release from Th1 lymphocytes.[8-12] Plasma IL-10 level is also correlated with severity of septic shock. In severely ill patients with systemic inflammatory response syndrome, changes in IL-6 and IL-10 levels indicate poor prognosis.[12] In several trials, higher IL-10 and IL-4 (antiinflammatory cytokines) levels are reported in patients who died from sepsis, in comparison to surviving patients.[2,8,11,12]

In our trial, relation between prognosis and gender, growth in blood culture, Gram-positivity or negativity of growing pathogen, cytokines (TNF-α, IL-10, leptin) and CRP levels in sepsis patients was investigated. In prognosis of pa-

tients with sepsis, no relation was determined between prognosis and gender, growth rate in blood culture and Gram-positive or negative of growing pathogen.

Leptin is a cytokine, which is released from adipose tissues and has a role in energy balance. Malnutrition decreases resistance against infections by supressing immune function. In animal studies, it has been shown that lowered fasting leptin levels increase sensitivity to endotoxic shock. Leptin in sepsis has stimulatory actions on hematopoetic, immunmodulatory and hepatocyte functions and acts as an acute phase reactant. It stimulates monocyte activation and proliferation in addition to release of IL-6 ve TNF-α from monocytes.13,14 Riquelme et al. conducted a trial on patients with secondary peritonitis and showed that serum leptin levels under 10 ng/ml indicate to poor prognosis in secondary peritonitis with a moderate to severe course.[15] In our trial, there was no statistically significant difference between patient group with sepsis and control group in terms serum leptin levels. In addition, it was shown that serum leptin levels do not possess any prognostic value in sepsis patients.

In our country Heper et al.[16] investigated diagnostic and prognostic value of serum C-reactive protein, procalcitonin, TNF–α and IL–10 in 39 patients with community acquired sepsis, severe sepsis and septic shock. In this trial, procalcitonin levels of patients who had severe sepsis (septic shock) and died due to sepsis was found to be significantly high at all measurements during first 72 hours. Insistently high procalcitonin levels for 72 hours is regarded as an indicator for poor prognosis. In this trial, C-reactive protein levels did not show any significant difference between the groups and was reported to have no value as an indicator for prognosis. TNF–α level did not show significant difference between sepsis and severe sepsis groups but in patients who died, high levels were observed at early stages (referral to hospital and during first 24 hours). IL–10 level was reported to be significantly high in patients with severe sepsis and in patients who died during all measurements. In the trial, it was reported that initially, procalcitonin and IL–10 are beneficial in differentiation of sepsis and severe sepsis; on the other hand, TNF– α and IL–10 levels are beneficial in determining poor prognosis. Likewise in our trial, serum TNF–α and IL–10 levels are found to be related to poor prognosis, similar to trial of Heper et al.16. Özbalkan et al.4 reported that IL-10 peak levels in surviving patients with no sepsis are lower than patients who died. Gogos et al.[1] also reported statistically significant high levels of IL – 10 and TNF–α in patients who died from sepsis.

Seki et al.[18] investigated the role of procalcitonin, CRP, IL-6, IL-8 and IL-10 in determining diagnosis and prognosis in sepsis. In this trial, serum CRP level at a threshold of 7.5mg/dl and higher is reported to be 100% sensitive and 95% specific for diagnosis of sepsis; similarly, procalcitonin level at a threshold of 0.5 ng/ml and higher is reported to be 95% sensitive and 98% specific for diagnosis of sepsis. Changes in IL-10 levels at various time intervals (day 1, 4 and 7) was found to be statistically insignificant while IL-6 levels between day 1 and 4 revealed statistically significant differences. As a result, it was reported that IL-6 and procalcitonin are sensitive parameters in determining prognosis.

Csontos et al.[19] reported that in patients with sepsis due to burn injuries, serum IL-10 levels in patients who died were higher than serum levels of surviving patients. Lorenta et al.[20] showed that serum IL-10 levels are higher in patients who died from sepsis in comparison to surviving patients but they also stated that serum TNF-α levels were lower. Frink et al.[21] reported high plasma IL-10 levels in patients with multiple organ dysfunction (MODS). Our results are in accordance with the results of studies reported in the literature.

In this trial age, serum IL-10 and TNF-α levels are determined as prognostic factors in sepsis patients. Mean age in patients who died from sepsis was higher than those of surviving patients. In adult patients with sepsis, initial (day 0, pre-treatment) serum IL-10 levels and serum TNF-α levels in 3rd and 5th days of treatment were determined to be prognostic for mortality. In pateints who died from sepsis, serum TNF-α ve IL-10 levels were found to be higher than surviving patients and the difference was statistically significant. Logistic regression analysis revealed that according to treatment response, TNF-α is an independent risk factor for mortality. When logistic regression analysis was performed in terms of patient and control groups; age and serum IL-10 level on day 0, serum CRP level on day 3, and CRP on day 5 were independent risk factors.

In conclusion, we believe that in patients with sepsis, determining serum TNF-α and IL-10 levels at the beginning and during treatment will prove to be helpful for clinicians in determining prognosis and in implementation of appropriate treatment changes.

ACKNOWLEDGEMENTS

This study was supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) with the project number SBAG-2841.

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