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BRIEF REPORT

Evaluation of diabetes mellitus in patients with sepsis

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ABSTRACT

Background: Diabetes mellitus is a prevalent disease worldwide and infection is a major problem in diabetics. This study investigated the frequency of diabetes mellitus and its associated factors in patients with sepsis.

Patients and methods: This is a descriptive cross-sectional study including 300 randomly selected cases admitted to Rasoul-e-Akram Hospital with the diagnosis of sepsis between March 2003 and February 2006.

Results: Of 300 septic patients, 158 (52.7%) had diabetes mellitus with the mean age (± standard deviation) of 52.7±28.4 years. The most common site of infection was respiratory tract. Evaluation of the outcome of patients in two diabetic and non-diabetic groups demonstrated a statistical difference (p=0.001). Mortality rate increased with aging, delay in therapy commencement and the number of SIRS criteria (p=0.001). Evaluation of the mortality rate in 3 diabetic groups (blood glucose> 250, 180-250 and <180 mg/dl) demonstrated a statistical difference (P= 0.001).

Conclusion: Aging can increase the rate of sepsis and its associated mortality in both diabetic and non-diabetic patients. Mortality of sepsis is more in diabetics when compared with non-diabetics. Severity of disease (further SIRS criteria) increases mortality and tight control of blood glucose may be associated with better prognosis.

Keywords: *Diabetes mellitus, Sepsis, Systemic Inflammatory Response Syndrome (SIRS).*
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INTRODUCTION

Diabetes mellitus (DM) is a prevalent disease worldwide and infection is a major problem in diabetics (1). Infection is one of the most important causes of hyperglycemia and is responsible for 30% of diabetic ketoacidosis attack.

DM induces immune deficiency through multiple mechanisms. Increased blood sugar disturbs the function of phagocytes (chemotaxis, immigration of inflammatory cells and their accumulation in inflammation site). In 25% of patients with DM type I, defects in complement and decreased T-lymphocytes are also reported. In the other hand, hormonal disturbances and cytokine changes inhibit the insulin release and by causing hyperglycemia enter the patients in the ketoacidotic phase (2). Frequency of urinary tract infections, respiratory infections (including tuberculosis), cholecystitis, necrotizing fasceitis, foot ulcers, AIDS and hepatitis are higher in diabetic than non-diabetics patients (3). In theory it is expected that the prevalence of sepsis will be higher in diabetic patients than non-diabetics.

Previous studies have shown not only the higher prevalence of infections but also special infections in diabetic patients. In the present study, we

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evaluated the frequency of DM and factors associated with its outcome in patients with sepsis.

PATIENTS and METHODS

This is a descriptive cross-sectional study including 300 randomly selected subjects admitted to Rasoul-e-Akram hospital with the diagnosis of sepsis between March 2003 and February 2006.

All clinical and laboratory data were collected in a data sheet. Clinical data included age, sex, temperature, respiratory rate, pulse rate, site of infection, other associated diseases, duration of symptoms before treatment, past history of DM and their outcome. Laboratory data included fasting blood sugar and leukocyte count.

Sepsis was diagnosed in the presence of more than one of the following clinical findings and the probability of an infectious origin: 1) body temperature higher than 38.8ºC or lower than 36.8ºC 2) heart rate higher than 90/min, 3) hyperventilation evidenced by respiratory rate higher than 20/min, 4) WBC count higher than 12,000 cells/ml or lower than 4000 cells/ml (4).

DM defined as random blood glucose concentration of 200mg/dl or higher in the presence of polyuria, polydipsia and weight loss or fasting plasma glucose ≥126 mg/dl or 2-hour plasma glucose ≥200mg/dl during an oral glucose tolerance test (5). Patients with hyperglycemia during hospital stay without history of DM were omitted because of the probability of stress hyperglycemia.

All figures are expressed as mean ± standard deviation (SD). Data were analyzed using SPSS software (version 10.0, SPSS Inc., USA).

RESULTS

During the study period (2003-2006), 300 septic patients had been admitted to Rasoul-e-Akram hospital with the mean age of 57.2 ± 28.4 years (a range, 10 days to 95 years). Table 1 represents the frequencies of different age groups in diabetics.

Table 1. Frequency of diabetes mellitus in different age groups of patients with sepsis

Age (years)	Diabetics (%)	Total (%)
<20	10 (6.3)	58 (19.3)
20-40	10 (6.3)	26 (8.7)
40-60	15 (9.5)	31 (10.3)
60-80	88 (55.7)	129 (43.0)
80-100	35 (22.2)	56 (18.7)
Total	158	300

One hundred-fifty eight (52.7%) patients had DM. Most of the cases aged 60-80 years (55.7%), followed by >80 years old patients (22.2%). Totally, 62.3% of diabetic patients were male.

The most common sites of infection were respiratory system (128 patients, 42.7%), urinary tract (96 patients, 32%), wound infection (15 patients, 5%), gastrointestinal infections (10 patients, 3.3%), cellulites (4 patients, 1.3%) and unknown source (47 patients, 15.7%).

Eighty-two patients (27.3%) had no other accompanied diseases. Associated diseases were cerebral vascular attack (CVA) in 46 (15.3%), heart failure in 39 (13%), chronic renal failure in 67 (22.3%), immune deficiency in 17 (5.7%), acute renal failure in 15 (5%), chemotherapy in 28 (9.3%), multiple trauma in 3 (1%) and cirrhosis in 3 patients (1%). Outcome of patients are shown in table 2. Mortality in <20 years old patients was 39%, however, in 20-40, 40-60, 60-80, and >80 years old patients it was 63%, 46%, 67% and 70%, respectively.

Delay in therapy commencement was associated with a higher mortality rate so that 14-day gap (between onset of symptoms and treatment) resulted in 82% deaths, however, in patients with 7-14 and <7 days gap the associated mortality rates were 70% and 58%, respectively (p=0.001).

Table 2. Outcome of diabetic and non-diabetic patients with sepsis

Outcome	Non-diabetics (%)	Diabetics (%)	Total (%)	P-value
Discharge	89 (62.7)	32 (22.3)	121 (40.3)	0.001
Death	53 (37.3)	126 (79.8)	179 (59.7)	0.001
Total	142	158	300	

Patients' mortality according to leukocyte count, number of Systemic Inflammatory Response Syndrome (SIRS) criteria and mean plasma glucose level are shown in table3.

Table 3. Outcome of septic patients according to the leukocyte count, number of SIRS criteria and mean plasma glucose

	Number	Death (%)	P-value
Leukocyte count (/ml)			
<4000	50	34 (72.0)	
4000-10000	95	48 (50.5)	0.001
>10000	155	97 (62.5)	
Number of SIRS criteria			
2	88	16 (18.2)	
3	156	116 (74.4)	0.001
4	56	47 (83.9)	
Mean plasma glucose (mg/dl)			
>250	67	65 (97.0)	
180-250	55	46 (83.6)	0.001
<180	36	15 (41.7)	

DISCUSSION

This study showed that 52% of 300 patients admitted by sepsis had DM, hence, of any 2 patients with sepsis, 1 was diabetic. Furthermore, 26% of patients aged less than 46 years old.

The prevalence of DM was first studied by the Institute of Nutrition and Nutritional Sciences during 1976-1977 in Iran. They reported a prevalence of 0.6-5 in 1000 in children and 2-10% in adults. In 1993, Endocrine Research Center and Institute of Nutrition and Nutritional Sciences of Shahid Beheshti Medical University reported a prevalence of 7.2% in >30 years old population of Tehran and 1.4% in >10 years old population of Isfahan (6). Therefore if the maximum prevalence of DM in general population is 10%, the prevalence of DM in patients with sepsis in our study (52%) will be quite high.

Prior investigators demonstrated that age of patients (more than 65 years old) was a risk factor for septicemia (7,8) and the rate of septicemia was higher in diabetics (9). Our results revealed not only the higher prevalence of DM among septic patients but also showed mortality increased with aging. This is in agreement with previous reports (9-11). Similarly, respiratory and urinary tract were the commonest sites of infection in diabetics (8,10,12-15).

Approximately 20-35% of patients with severe sepsis and 40-60% of patients with septic shock die within 30 days (1,14). This study showed 60% mortality rate with a statistically significant difference between mortality in septic diabetics (80%) and non-diabetics (37%). Jakubowska et al. reported a mortality rate of 88.3% in diabetics compared with 33.3% of non-diabetics (10).

Delay in therapy aggravates the outcome of septic patients. Mortality rate was lower in patients treated in less than 7 days of onset of the symptoms. Thus, immediate and appropriate treatment of infection with suitable antibiotics can improve the prognosis and outcome of patients with DM.

According to Opal et al there was no association between leukocyte count and prognosis of patients (13). In theory, leukocytosis is an immune response and normal leukocyte count and leukopenia can be considered as a marker of unresponsiveness and it could be correlated with poor prognosis. The prognosis of patients with leukopenia was worse than other groups in this study.

Although some studies have shown that the severity of sepsis affects the prognosis of patients and the evolution of septic shock augments the mortality of patients (from 40% to 60%) (11,13), some other studies disclaimed any correlation between the number of SIRS criteria and the prognosis (15,16). In theory, the number of SIRS criteria was increased by accelerating the severity of sepsis, so it should have influence on patients' outcome. Our study shows an association between the number of SIRS criteria on admission and final outcome in septic diabetic patients.

The main problem of diabetic patients is hyperglycemia. Different researches have focused

on this point to evaluate the relationship between the levels of plasma glucose and progression of different infections in diabetic patients, most of which have shown a prominent correlation between the tight control of plasma glucose and the outcome of patients with sepsis (17-23). Other investigators suggested that intensive insulin therapy placed critically ill patients with sepsis at increased risk of serious adverse events related to hypoglycemia (23). In our experience, the mortality of patients in whom the level of blood glucose was <180 mg/dl (42%), was less than 50% of those with a blood glucose level of >250 mg/dl (97%).

In conclusion, diabetic patients are at an increased risk of sepsis than non-diabetics and the risk is even higher with aging. Other underlying diseases like chronic renal failure, immune deficiency and malignancies will also increase the prevalence of sepsis. Uncontrolled blood glucose, delay in treatment, leukopenia, and further SIRS criteria worsen the prognosis of patients. Strict control of blood glucose, and early and effective treatment of infection (specially respiratory and urinary infections) decrease the prevalence and the mortality of sepsis.

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