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Laboratory Diagnostic Tests in Patients with Sepsis

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Abstract

Background: Sepsis is a syndrome involving physiological, pathological, and biochemical abnormalities caused by infection and leads to the dysfunction of various organs, including the liver and kidneys. It can lead to high mortality rates.
Objectives: This study aimed to evaluate the hepatic, renal, and coagulation diagnostic markers in patients with sepsis.
Methods: This cross-sectional analytical study was performed on patients with sepsis admitted to Abadan and Khorramshahr educational hospitals during March 21 2019-March 19, 2020. The hospital information system (HIS) collected the information of 305 patients with sepsis, including hepatic, coagulation, and renal diagnostic factors, as well as age and gender.
Results: It was observed that the mean of blood sugar (BS) (145.82 ± 105.10 mg/dL), BUN (29.64 ± 27.41 mg/dL), and creatinine (1.69 ± 1.9 mg/dL) in sepsis patients was higher than normal. In addition, the mean of diagnostic markers of the liver, including ALT (47.27 ± 76.63 U/L), AST (74.38 ± 163.96 U/L), LDH (684.69 ± 383.96 U/L), total bilirubin (1.39 ± 1.02 mg/dL), and direct bilirubin (0.60 ± 0.65 mg/dL), was higher than normal. The mean of PT (16.73 ± 9.31 sec) and INR (1.72 ± 1.53) was also higher than the normal level.
Conclusions: In hospitalized patients with sepsis, BS, renal diagnostic markers, hepatic diagnostic markers, and coagulation markers are higher than normal, indicating the destructive effect of sepsis on kidney and liver function.

Keywords: Sepsis, Hepatic Biomarkers, Renal Biomarkers, Abadan

1. Background

Sepsis is a life-threatening clinical syndrome characterized by organ dysfunction due to the patient's unregulated response to infection (1). Sepsis is defined as a syndrome involving physiological, pathological, and biochemical abnormalities caused by infection. Any infected person can potentially develop sepsis, and the incidence of sepsis is up to 1% - 2% of all hospitalized patients (2). Approximately 49 million people are affected by sepsis each year, and an estimated 11 million deaths are due to the syndrome, which accounts for 19.7% of all deaths worldwide. Sepsis is often associated with blood clotting, an important complication that contributes to organ dysfunction (3). Studies have shown that people with a history of chronic diseases, older people, males, and blacks are particularly susceptible to severe sepsis. Therefore, prevention strategies should target these vulnerable populations (4).

Infants are also at risk of disease due to a weakened immune system. Hospitalized patients are another group exposed to this disease due to intravenous injections, surgical wounds, or bedsores (5). Many people with sepsis also experience lung, kidney, and/or liver failure (6). Hepatic dysfunction is a risk factor for the progression of infection to sepsis. In addition, postoperative hepatic dysfunction is an independent risk factor for multiple organ injuries and death from sepsis. It has been observed that reducing liver damage and restoring hepatic function decreases mortality in patients with sepsis (7). Sepsis can affect the kidneys in two ways. The first is that the infection starts from the kidney, and the second is that the events due to sepsis cause kidney damage. According to the National Kidney Foundation, sepsis is one of the leading causes of acute renal injury (AKI), and some studies have shown that 32% - 48% of acute renal impairments are due to sepsis (8).

2. Objectives

Considering the destructive effects of sepsis on body organs, especially the liver, and kidneys, in this study, laboratory diagnostic markers were studied in patients with sepsis

3. Methods

3.1. Study Design and Study Population

This cross-sectional analytical study was performed on patients with sepsis admitted to Abadan and Khorramshahr educational hospitals after obtaining the necessary permits from the Ethics Committee in Biological Research of Abadan University of Medical Sciences during March 21, 2019-March 19, 2020. In this study, 305 patients with sepsis whose disease was confirmed by an infectious disease specialist and whose demographic and laboratory information were available in the hospital information system (HIS) were selected. The inclusion criteria entailed patients with sepsis whose information and tests were available in HIS, and the exclusion criteria included patients with sepsis whose information was incomplete. The data of 305 patients with sepsis admitted to Abadan and Khorramshahr educational hospitals, including hepatic, coagulation, and renal diagnostic factors, age, and gender, were collected by HIS in the checklist of patients.

3.2. Statistical Analysis

The studied variables are described using descriptive statistical methods, including frequency distribution tables, graphs, and indices of central tendency and dispersion. Moreover, one-way analysis of variance, *t*-test, and the relationships between variables were examined. The significance level in all the above tests was considered < 0.05. Data analysis was performed using SPSS 21 statistical software.

4. Results

Demographic and laboratory data of 305 sepsis patients admitted to Abadan and Khorramshahr educational hospitals during March 21 2019-March 19, 2020, were studied, of which 141 (46.2%) were women, and 164 were men (53.8%). The mean age of these patients was 43.64 ± 35.23 years. The results of this study showed that the mean blood sugar (BS) (145.82 ± 105.10) in sepsis patients was higher than normal and was abnormal in 68.8% of these patients (Table 1).

In the case of renal diagnostic markers, it was observed that the mean of BUN (29.64 ± 27.41 mg/dL) in sepsis cases was higher than normal, and it was abnormal in 45.1% of patients. Moreover, the mean of creatinine (1.69 ± 1.92 mg/dL) in patients was higher than the normal level, and it was abnormal in 38.2% of subjects (Table 1).

Regarding hepatic markers, we found that the mean of LDH (684.69 ± 383.96 U/L) in patients with sepsis was higher than the normal level and was abnormal in 86.7% of patients. The mean of total bilirubin (1.39 ± 1.02 mg/dL) was also higher than normal in studied patients and was abnormal in 52.3% of the cases. The mean of direct bilirubin (0.60 ± 0.65 mg/dL) in the study subjects was observed to be higher than normal and was abnormal in 46% of them. Furthermore, the mean AST (74.38 ± 163.96 U/L) and mean ALT (47.27 ± 76.63 U/L) levels in sepsis cases were higher than normal (Table 1).

Examining coagulation markers in patients with sepsis showed that the mean of PT (16.73 ± 9.31 sec) was longer than normal and was abnormal in 51% of these patients. The mean INR (1.72 ± 1.53) was also higher than normal and was abnormal in 42% of subjects (Table 1). The mean of laboratory markers in men and women was not significantly different (Table 2). A significant difference in the mean of PT was observed between age groups ($P = 0.03$), but no significant difference was observed in other laboratory diagnostic markers between age groups (Table 3).

5. Discussion

In this study, it was observed that the number of patients with sepsis was higher in men than women and in the age group over 75 years than in other age groups. Our study showed that the mean of hepatic diagnostic markers, including ALT, AST, ALP, total bilirubin, and direct enzymes, was higher than normal in sepsis patients. ALP levels were abnormal in 71.9% of patients with sepsis.

Liver dysfunction in sepsis cases has been reported in other studies, confirming the present results. For example, Shah et al. reported that 42% of the patients with high levels of liver enzymes who died had sepsis (9). Kobashi et al. found that 34.7% of patients with sepsis had sepsis-related hepatic damage, including 75 cases of hepatic cholestasis (48.1%). In their study, 34% were hepatocellular diseases (21.8%), and 47 cases were liver shock (30.1%) (10). In the study of Kanai et al., patients with and without bacteremia had mean AST of 68 and 84 U/L, mean ALT of 73 and 71 U/L, mean total bilirubin of 1.6 and 1.2 mg/dL, and mean direct bilirubin of 1.1 and 0.9 mg/dL, respectively (11). In a clinical trial conducted by Bakker et al. on 312 patients with septic shock, 20% of acute liver failure cases were reported within 72 hours. Acute hepatic failure was defined by at least two of the following: (a) bilirubin > 2.5 mg/dL (> 43 μmol/L), (b) serum ALT more than twice

Table 1. Mean of the Hepatic, Renal, and Coagulation Factors in Patients with Sepsis

Variables	Reference Value	Mean ± SD	Percent	Frequency
Age (y)	-	43.64 ± 35.23	-	-
BS (mg/dL)	70 - 140	145.82 ± 105.10		
Abnormal			68.8	190
Normal			31.2	86
BUN (mg/dL)	7 - 20	29.64 ± 27.41		
Abnormal			45.1	137
Normal			54.9	167
Cr (mg/dL)	0.6 - 1.3	1.69 ± 1.92		
Abnormal			38.2	116
Normal			61.8	188
Na (mmol/L)	135 - 145	138.75 ± 7.17		
Abnormal			10.4	31
Normal			89.5	267
K (mmol/L)	3.5 - 5.5	4.46 ± 0.78		
Abnormal			10.1	30
Normal			89.9	269
ALKP (U/L)	60 - 306	300.73 ± 172.47		
Abnormal			71.9	69
Normal			28	27
LDH (U/L)	200 - 500	684.69 ± 383.96		
Abnormal			86.7	26
Normal			13.3	4
Total Bilirubin(mg/dL)	0.3 - 1.0	1.39 ± 1.02		
Abnormal			52.3	47
Normal			47.7	43
Direct Bilirubin (mg/dL)	0.1 - 0.3	0.60 ± 0.65		
Abnormal			46.1	41
Normal			53.9	48
AST (U/L)	0 - 31	74.38 ± 163.96		
Abnormal			36.2	39
Normal			63.2	67
ALT (IU/L)	0 - 31	47.27 ± 76.63		
Abnormal			35.5	39
Normal			64.5	71
PT (sec)	11 - 13	16.73 ± 9.31		
Abnormal			51.5	68
Normal			48.5	64
PTT (sec)	25 - 45	38.28 ± 20.59		
Abnormal			9	12
Normal			91	120
INR	< 1.1	1.72 ± 1.53		
Abnormal			42.4	56
Normal			57.6	76

Abbreviations: BS, blood sugar; BUN, blood urea nitrogen; Cr, creatinine; ALK, alkaline phosphatase; LDH, lactate dehydrogenase; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine transaminase.

Table 2. Comparison of the Mean Hepatic, Renal, and Coagulation Factors in Patients with Sepsis by Gender

Factors	Mean ± SD		P-Value
	Male	Female	
Age (y)	45.3 ± 34.9	41.6 ± 35.5	0.36
BS (mg/dL)	153.02 ± 108.66	136.59 ± 100.42	0.20
BUN (mg/dL)	31.34 ± 28.35	27.57 ± 26.17	0.24
Cr (mg/dL)	1.77 ± 1.66	1.59 ± 2.19	0.43
Na (mmol/L)	139.12 ± 7.71	138.32 ± 6.48	0.33
K (mmol/L)	4.46 ± 0.71	4.45 ± 0.86	0.86
ALK (U/L)	323.90 ± 184.92	270.02 ± 151.27	0.13
LDH (U/L)	561.50 ± 242.47	828.41 ± 473.0	0.07
Total bilirubin (mg/dL)	1.321 ± 0.96	1.48 ± 1.09	0.44
Direct bilirubin (mg/dL)	0.60 ± 0.71	0.6 ± 0.56	0.93
AST (U/L)	68.91 ± 131.35	82.24 ± 203.49	0.69
ALT (U/L)	43.51 ± 64.46	52.16 ± 90.65	0.58
PT (sec)	17.14 ± 9.93	16.27 ± 8.61	0.59
PTT (sec)	39.60 ± 24.51	36.81 ± 15.15	0.44
INR	1.81 ± 1.69	1.62 ± 1.33	0.47

Table 3. Comparison of Mean Hepatic, Renal, and Coagulation Factors in Patients with Sepsis by Age

Factors	Mean ± SD					P- Value
	0 - 20 (y)	20 - 40 (y)	40 - 60 (y)	60 - 80 (y)	80 - 100 (y)	
BS (mg/dL)	146.14 ± 110.94	90.10 ± 20.10	147.87 ± 98.79	131.14 ± 64.70	165.48 ± 133.38	0.17
BUN (mg/dL)	31.58 ± 27.04	14.0 ± 6.37	34.21 ± 33.24	31.10 ± 28.88	23.92 ± 22.99	0.71
Cr (mg/dL)	1.75 ± 2.28	0.59 ± 0.15	2.00 ± 1.95	1.82 ± 1.71	1.39 ± 1.39	0.13
Na (mmol/L)	138.66 ± 7.36	138.25 ± 4.04	140.53 ± 7.55	138.98 ± 7.97	138.11 ± 5.51	0.62
K (mmol/L)	4.37 ± 0.76	4.09 ± 0.41	4.56 ± 1.03	4.63 ± 0.73	4.40 ± 0.76	0.06
ALK (U/L)	308.94 ± 157.39	252 ± 0	289.90 ± 175.55	254.72 ± 193.24	334.56 ± 181.19	0.56
LDH (U/L)	665.5 ± 462.40	-	810.25 ± 488.28	606.25 ± 307.82	691.66 ± 219.93	0.90
Total bilirubin (mg/dL)	1.41 ± 1.12	-	1.04 ± 0.185	1.317 ± 1.31	1.710 ± 0.99	0.32
Direct bilirubin (mg/dL)	0.59 ± 0.79	-	0.307 ± 0.11	0.56 ± 0.55	0.89 ± 0.69	0.09
AST (U/L)	70.28 ± 106.58	36.0 ± 0	37.61 ± 23.59	102.91 ± 268.35	74 ± 154.84	0.84
ALT (U/L)	49.30 ± 75.80	14.00 ± 0	15.90 ± 10.00	66.85 ± 108.59	42.04 ± 59.01	0.47
PT (sec)	15.61 ± 7.06	13.0 ± 0	13.56 ± 2.45	17.56 ± 10.36	21.74 ± 14.32	0.03
PTT (sec)	39.86 ± 26.58	28.0 ± 0	34.42 ± 8.43	38.81 ± 17.64	38.35 ± 13.73	0.86
INR	1.60 ± 1.28	1.10 ± 0	1.19 ± 0.29	1.93 ± 1.83	2.30 ± 2.16	0.14

normal, and c) PT longer than 1.5 times the control value or INR > 1.5 (12).

The results of the present study showed that the mean BUN and creatinine, as diagnostic markers of kidneys, in patients with sepsis was higher than normal. It was also observed that in the age group of 60 - 80 years, these variables were higher than in other age groups. Moreover, the BUN level was abnormal in 45.1% of people. In the study by Katayama et al., out of 514 patients with sepsis, 351 (68.3%) had stage 1 AKI (serum creatinine level > 0.3 mg/dL within 48 hours or an increase in serum creatinine ≥ 1.5 times of baseline within 7 days) (13). In a study by Fiorentino et al., of 1742 patients with septicemia, stage 2 - 3 AKI occurred in 262 patients (15%) (14). In another study by Bellomo et al., out of 192980 patients with severe sepsis in seven US states, 22% developed AKI (15). During sepsis, the kidney is affected in two ways; the first being that septicemia originates from the kidney itself, and the second is that septicemia damages the kidney (16). Sepsis is reported to be one of the leading causes of AKI, and some studies have shown that 32% - 48% of AKI cases are due to sepsis (8). In addition, acute kidney damage from any source is associated with a higher risk of sepsis. Mehta et al. found that 40% of patients developed sepsis after AKI, suggesting that AKI may increase the risk of sepsis (17). Doyle and Forni stated in their study that AKI is an independent predictor of mortality and morbidity in patients with septicemia and early detection of high-risk patients, preventive measures, and targeted therapies to reduce mortality and complications. Kidney damage is very important in patients with septicemia (18).

In the present study, we found that 51.5% of patients with sepsis had abnormal PT, and 42.4% had abnormal INR. In a study in Japan, 29% were diagnosed with sepsis-induced coagulation disorder (19). Okamoto et al. reported the prevalence of coagulation disorders in patients with sepsis to be 35% (20). In severe sepsis, dysfunction of the hemostatic system may lead to diffuse intravascular coagulation (DIC), resulting in microvascular thrombosis, perfusion, and eventually multi-organ dysfunction syndrome and death (21). Activation of coagulation decreased the regulation of anticoagulant pathways and impaired fibrinolysis, which play major roles in the pathogenesis of intravascular thrombosis in sepsis-associated DIC (22).

Our results showed that the mean of LDH enzyme in patients with sepsis was higher than normal, and 86.7% had abnormal LDH levels. Zein et al. reported that increased LDH level was commonly seen in patients with severe sepsis. It is a marker of cell injury that reflects the degree of tissue damage (23). In another study, Lu et al. demonstrated a statistical difference in 28-day mortality between the elevated and normal LDH groups. The level of serum LDH was an independent risk factor for the death of patients with sepsis. Serum LDH is probably associated with 28-day mortality in patients with sepsis (24). Algebaly et al., in 2021, concluded that LDH could be a potential inflammatory marker in the diagnosis of septic shock and is valuable for pediatric intensive care unit admission (PICU) decisions. LDH was 512 μL (406.50 - 663.00) in the septic shock group and was significantly higher than that of the control group (190 μL, range: 160.00 - 264.50) (25).

We showed that the mean BS in people with sepsis was higher than normal and in the age group of 60 - 80 years than in other ages. Furthermore, abnormal BS was observed in 68.8% of patients with sepsis. In the study of Tiruvoipati et al., 204 of the 297 (68.7%) patients had stress hyperglycemia (SH). ICU mortality rates were significantly lower in patients with SH than in others. The mean ICU and hospital stay length was higher in patients with SH than in other individuals. The presence of SH was associated with a decrease in ICU mortality, indicating that SH is protective in patients with septic shock. As a result, SH may not be harmful in severe patients with sepsis. Moreover, patients with SH had lower ICU mortality (26).

Among the limitations of this study was the small sample size. In addition, some information was not available for all patients. It is suggested that in future studies, a larger sample size of patients with sepsis be investigated, and the laboratory diagnostic markers of these patients should be compared with the healthy group. Furthermore, the relationship between these markers and the prognosis of the disease, length of hospitalization, and mortality of sepsis patients should be investigated.

5.1. Conclusions

The results of this study showed that sepsis was more common in men than in women. In hospitalized patients with sepsis, BS, renal diagnostic markers (i.e., BUN and creatinine), and hepatic diagnostic markers (i.e., ALT, AST, total bilirubin, direct bilirubin, and LDH) were higher than normal which indicates the destructive effect of sepsis on the kidneys and liver function.

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Footnotes

Authors' Contribution: Study concept and design: S. M and E. R. Acquisition of data: S. R, A. H, M. M, and Kh. K.

Analysis and interpretation of data: F. M. Drafting of the manuscript: S. R, E. R, and S. M. Critical revision of the manuscript for important intellectual content: E. R. and S. M. Study supervision: S.M and E.R.

Conflict of Interests: There was no conflict of interest.

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