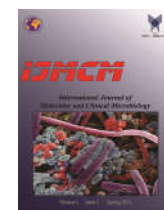# International Journal of
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Examining the frequency of clinical and paraclinical indicators of cancer patients with Sepsis

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ABSTRACT

Cancer is one of the most important diseases of current century and the second cause of death after cardiovascular diseases. Various factors are effective in the occurrence of malignancy and one of the most important factors is blood infection. The present study was aimed to investigating the frequency of clinical and paraclinical indicators of cancer patients with symptoms of sepsis. This cross-sectional study, 100 cancer patients' referred to the emergency department of Imam Khomeini Hospital in Sari city with signs of sepsis were selected. Finally, the information obtained from the questionnaires was entered into SPSS-18 software and the collected information was statistically analyzed using descriptive statistics (prevalence and mean) and T-test. Among the patients, 57% were men and 43% were women. 56% had sepsis, 42% had severe sepsis and only 2% had septic shock. *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), Acinetobacter and *Candida albicans* (*C. albicans*) were the most prevalent causes of sepsis. Blood pressure in most patients is lower than normal and 26% of patients have a history of diabetes. The highest frequency of cancer was related to stomach and small intestine cancer, and neutropenia was present in all types of cancer except leukemia and lymphoma. The results of this study showed that many non-specific parameters for cancer diagnosis should be taken into consideration by emergency department specialist and should not be easily interpreted from symptoms such as fever, diabetes, decrease or increase in neutrophils and white blood cells. Forgiveness.

1. Introduction

Cancer is one of the most important causes of death in the world. According to the GLOBOCAN report, more than 16 million new cases of cancer have been registered in the world during 2021 (Sung et al., 2021). According to the available reports, cancer is the second leading cause of death in Iran after cardiovascular diseases. Although the exact statistics of the number of cancer cases in the country are not available, it is estimated that more than one hundred thousand new cases of cancer are diagnosed in the country every year. This is despite the fact that most of the reliable national studies have shown that due to the epidemiological transmission process and the accelerated aging process of the country's

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population, the incidence and mortality of cancer will increase significantly in the coming years (Roshandel et al., 2019).

The significant occurrence of cancer and the growing trend of its prevalence and occurrence in the country make planning to ensure the physical, social and mental health of these patients necessary during the initial treatment and in the period after. In other words, only cancer treatment without paying attention to the prevention and treatment of side effects cannot be enough, because due to the aggressive nature of cancer treatments, there are many side effects that can threaten the patient's quality of life and even his life. Chemotherapy is one of the complicated but common treatments for most malignancies. Each of these complications can expose the patient to the risk of various infections and their widespread development, because practically the neutropenia created will lead to a severe weakness of the body's immune system in the appropriate inflammatory response to infections. As studies have shown, infection in these patients can lead to sepsis and finally to 2-21% mortality (Oun, Moussa and Wheate 2018, Moore et al., 2018). Studies have shown that despite significant advances in the treatment and care of sepsis, this complication is one of the main causes of death in the world and even in developed countries. Based on the ranking of causes of death in the United States, sepsis is the tenth cause of death (Rathour et al., 2015; Hoyert et al., 1999).

Although studies indicated that 54-65% of sepsis cases occur in the context of chronic diseases, but cancer alone is known as one of the most important independent causes. In a way that more than 17% of all sepsis cases occur in cancer patients (Martin et al., 2006; Alberti, 2005). The incidence of sepsis in some cancers, including pancreatic cancer, leukemia, lung, lymphoma, and brain, has been higher than other types (Danai et al., 2006). In addition to the incidence, mortality due to sepsis will also increase in the field of cancer. It has been estimated that this rate among cancer patients is about 1.5-4 times that of non-cancer patients (Danai et al., 2006; Drumheller et al., 2016; Zhou et al., 2014). One of the reasons for higher mortality in this group is the higher incidence of severe sepsis among cancer patients compared to other patients. So that more than 12% of all

sepsis cases in cancer patients will turn into severe sepsis (Danai et al., 2006).

Despite the high incidence and mortality caused by sepsis in cancer patients, studies revealed that the care and treatment of these patients is not enough (Clarke et al., 2015). Based on this, recently researchers showed great interest in identifying patients at risk of sepsis more accurately. In this regard, a study indicated that identifying and monitoring the health of seemingly low-risk individuals can improve the outcome of sepsis in cancer patients (Moon and Chun, 2009). Considering the relationship between sepsis and cancer, the researchers designed the present study with the aim of investigating the frequency of clinical and paraclinical indicators of cancer patients who referred to Imam Khomeini Hospital in Sari with the Sepsis panel, and they hope that its results can pave the way for providing better care to Cancer patients are at risk of sepsis.

2. Materials and Methods

In this descriptive-cross-sectional study, 100 cancer patients with sepsis who referred to Imam Khomeini Hospital in Sari city were examined. Patients with AIDS and patients who were discharged without a doctor's order, as well as patients who did not want to participate in this study were excluded from the statistical population. Due to the limited number of cancer patients referred to the emergency department, all eligible cancer patients who had referred to Imam Khomeini Hospital in Sari were included in the study after giving informed consent. Non-randomized sampling technique was applied and all outcomes were recorded during the patients' stay in the hospital.

This study was approved by the Ethics Committee of Mazandaran University of Medical Sciences, and a questionnaire including age, gender, tumor type, tumor stage, place of residence, weight, height, blood pressure, history of diabetes, history of cardiovascular diseases, chemotherapy (diet), duration of treatment, other treatments, history of cancer recurrence, history of neutropenia, smoking, age of onset (diagnosis) of cancer, history of COPD, time of initiation of empirical antibiotic treatment, means of referral to emergency room, body temperature, history of SIRS , history of other chronic diseases (specifying the type), history of

chipping, marital status, type of health insurance, distance from the last chemotherapy treatment, normal blood pressure of the person, result of blood culture, pulse, antibiotic prophylaxis, history of allergies, history of receiving Immunosuppressive drugs, history of HIV infection, duration of previous/current neutropenia, patient's occupation, family history of cancer in first-degree relatives, time from entering the ED to the diagnosis of sepsis, type on infection, time from the onset of symptoms to receiving antibiotics, functional status of the patient (independent, dependent), to some extent independent), history of receiving antibiotics, history of bone marrow transplantation, type of antibiotic prescribed, history of receiving radiotherapy, use of steroid drugs, suspected causes of infection, level of consciousness and its changes, changes in blood pressure and body temperature, triage, number of blood cells (in the last tests available), blood sugar, length of last hospitalization, number of chemotherapy drugs, main symptoms led to referral, duration of fever, hemoglobin level, chest radiography report was designed and completed by patients or patients' companions.

2.1. Statistical analysis

Descriptive statistics were used to estimate the mean and standard deviation, median and interquartile range of quantitative variables. Qualitative variables were described in the form of numbers and percentages according to the levels of the variables. Single-variable tests such as independent T-test and chi-square were used to check single-variable relationships and Multivariate Logistic Regression analysis was used to check the independent effect size of each variable. A P value of less than 0.25 was used to select eligible variables for multivariate analysis. All statistical tests were performed in a two-sided manner and the level of statistical significance was defined as less than 0.5.

3. Results

Investigations showed that among the 100 cancer patients examined, 57% were men and 43% were women, and no significant difference was observed between different genders and the incidence of sepsis. But both cases of septic shock occurred in males, and severe sepsis was also significantly higher in males ($P<0.05$). In terms of age groups, people over 69 years old and people in the age range of 49 to 58 years had the highest frequency with a significant difference ($P<0.05$). The time of cancer diagnosis among the examined patients ranges from less than 2 months to more than 24 months (Fig. 1) ($P<0.001$).

In terms of systolic pressure, 15% had a systolic pressure greater than 140, 25% had a pressure of 120-140, and 60% had a systolic pressure less than 12 ($P=0.023$), and 12% had a diastolic pressure greater than 90, and 22% had a pressure of 90, 80 and 66% had diastolic pressure less than 80 ($P=0.001$). The results of clinical examination and microbiological tests showed that 56% of patients had sepsis, 42% had severe sepsis, and 2% had septic shock ($P=0.000$). Of all patients, 26% of all patients had chemotherapy in the last month and 69% in the last 2 months, and only 5% had no chemotherapy ($P<0.001$).

Figure 2 showed the distribution of types of sepsis in different cancers. The results have shown that the most cases of sepsis in stomach and small intestine, breast and colon cancer, the most cases of severe sepsis in acute lymphoid leukemia, and colon and septic shock in larynx and pancreas cancer with a significant difference more than other cancers. (Fig. 2) ($P>0.05$).

Chest x-ray in different types of sepsis showed that in sepsis and severe sepsis, the number of normal cases was more than abnormal with a significant difference, and in septic shock both cases, the chest X-ray was abnormal with a significant difference ($P=0.238$).

The survey showed that the number of neutrophils was high in 15%, normal in 45% and low in 40% of patients. The number of cancer patients who had high neutrophils was less than the average and low level patients and there was a significant difference. The results of Fisher's exact test showed that the status of neutrophils was related to the status of sepsis. Neutrophils at a low level were more in the group of severe sepsis and septic shock (neutrophils in outcomes ($P=0.038$), neutrophils in all cancer patients ($P=0.000$)).

Also, in this study, it has been determined that there is a significant relationship between diabetes, chemotherapy, history of neutropenia, the amount of platelets, leukocytes, blood pressure, average pulse of the patient, history of

hospitalization in the emergency department, fever in the last three months, body temperature and antibiotic use. The steroid drugs and types of sepsis were not observed (P=0.072) and none of the patients were HIV positive (P>0.05). The survey showed that in the whole sample, the variable value of BMI is equal to 20.4050. Using analysis of variance, there is a difference between the averages BMI of people in different outcome groups. The group with severe sepsis had a lower BMI level (P=0.032).

In this study, 100 blood samples were cultured, and in 35 cases, the culture results were positive. *E. coli*, *P. aeruginosa*, Acinetobacter and *C. albicans* were the most important causes of sepsis. In two patients with septic shock, the genus Acinetobacter was reported and both patients died in different hospital departments. Two other positive blood cultures were related to patients with severe sepsis. In this study, a number of patients were not sampled and in some cases sampling was not applicable.
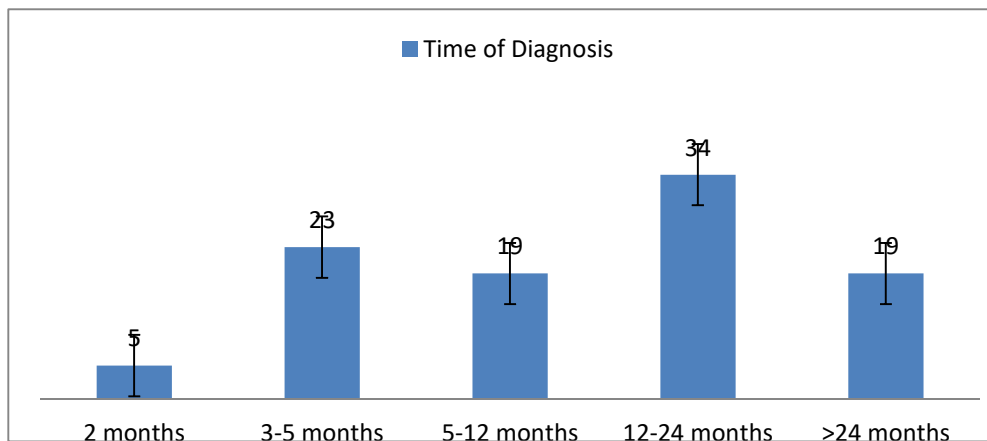
3.1. Blood culture results

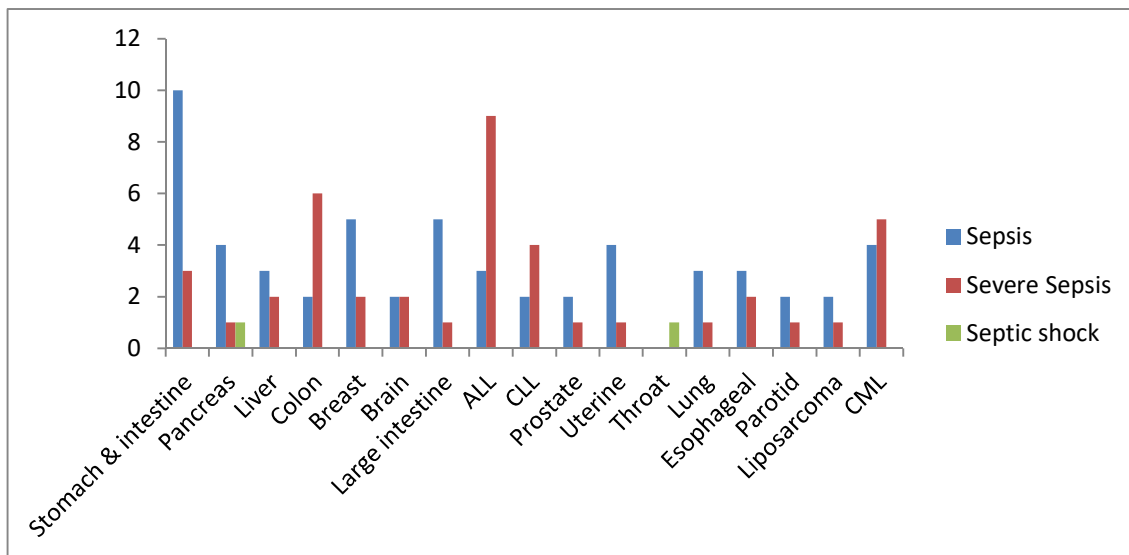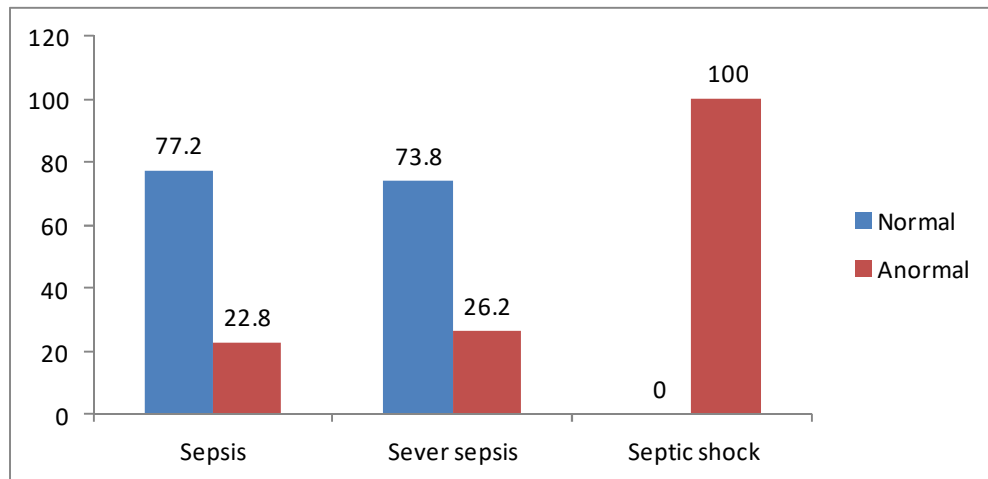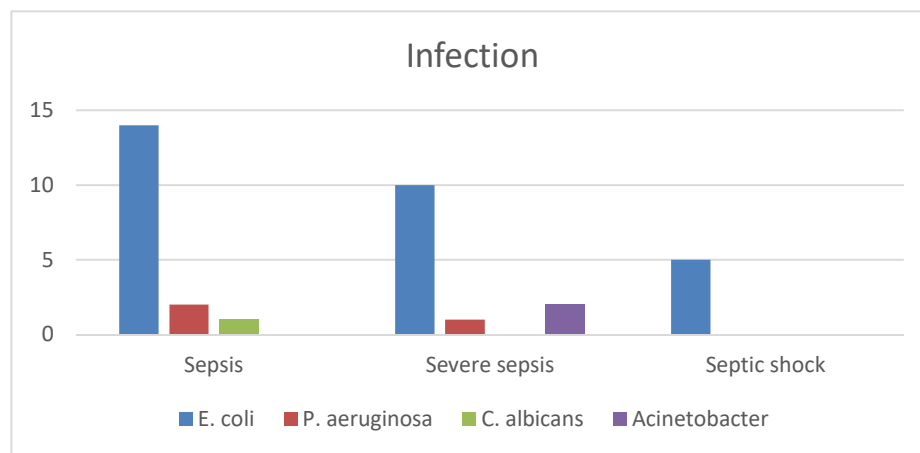**Figure1.** The time of cancer diagnosis among the examined patients.

Figure 2. The distribution of types of sepsis in different cancers.

Figure 3. Examining the condition of the chest radiography according to sepsis status.

Figure 4. Types of infections in patients with different types of sepsis

4. Discussion

In the present study, the frequency of clinical and paraclinical indicators of sepsis, severe sepsis and septic shock in cancer patients was investigated. Bacterial infection in the body causes various degrees of disease including septicemia, sepsis, severe sepsis and septic shock. Among the above-mentioned complications, only in the case of septicemia, the diagnosis is laboratory-based, and in most cases, blood cultures are positive in terms of bacterial contamination. But in the forms of sepsis, severe sepsis and septic shock, the diagnosis is often clinical (Angus and Van der Poll, 2013). Sepsis is the body's systemic response to invading microorganisms, including bacteria and fungi, and is one of the most important hospital infections. Sepsis is the second most common cause of death in patients with non-cardiovascular diseases hospitalized in the intensive care unit and one of the ten main causes of death among all hospitalized patients. In intensive care patients, the rate of sepsis is very variable (Moore et al., 2018; Rathour et al., 2015; Hoyert et al., 1999; Martin et al., 2003) and their mortality rate ranges from 20% for sepsis, up to 40% for severe sepsis, and up to 60% for septic shock (Fleischmann et al., 2016). In this study, about 100 patients with sepsis, severe sepsis and septic shock were evaluated and it was found that 56% had sepsis, 42% had severe sepsis and only 2% had septic shock. In this study, clinical factors such as blood

pressure, pulse, heart rate, body temperature and paraclinical factors such as blood sugar measurement, immune cell count of sepsis patients were examined.

In a recent study, 60% of patients with cancer and sepsis had significantly lower blood pressure than normal. Orthostatic hypotension can be acute or chronic. Affected patients may experience lightheadedness, blurred vision, confusion, weakness, fatigue, or syncope. In less common cases, there is a possibility of neck and shoulder pain, orthostatic dyspnea and chest pain. Blood pressure is expected to be much lower in the form of septic shock than in the form of sepsis and severe sepsis. In this study, we have only had two cases of septic shock, in terms of systolic and diastolic blood pressure, it was in the lower than normal range.

It has also revealed in a recent study that the amount of pressure drop in severe sepsis is significantly higher than in sepsis. In septic shock and severe sepsis, the toxin of microorganisms causes a disorder or failure in the smooth muscle of the vascular wall, which is known as vasodilatation shock. This type of pressure drop usually does not respond to treatments and causes failure of various body organs.

Diabetes is one of the most common chronic diseases in the society and it causes immune deficiency through several mechanisms and increases the prevalence of various infections. In addition, infection can cause hyperglycemia and ketoacidosis attacks in these patients (Venot et al., 2015). In this study, an attempt was made to investigate the prevalence of diabetes in patients with sepsis and the factors related to these patients, and the results showed that 26% of people with sepsis had a history of diabetes. The results of Fisher's exact test showed that the diabetes condition was not related to the type of outcome (sepsis, severe sepsis and septic shock), which means that with the increase in the spread of the disease and the progression of the disease from the stage of sepsis to the stage of septic shock, there is a change in the amount Blood sugar does not develop, and the underlying disease of diabetes does not play a role in the development of the disease. Contrary to our study, Barati and his colleagues in 2016 investigated the blood sugar level in patients diagnosed with sepsis in Hazrat Rasool Akram (PBUH) Hospital in Tehran and showed that

52% of 300 patients with sepsis had have also been related to diabetes, and the difference in blood sugar in different groups was significant. This study showed that with increasing age, the risk of sepsis and death due to it increases in diabetic and non-diabetic groups. Also, the death caused by sepsis in diabetics is more than in non-diabetics and quick treatment can reduce mortality. It increases as the severity of the disease increases, while accurate blood sugar control can improve the prognosis of the disease (Barati et al., 2008).

Schuetz et al., investigated the relationship between sepsis and diabetes in a review study. In the study of these researchers, it was shown that diabetes reduces the activity of neutrophils and immune cells, and also reduces the production of immune cytokines, thus making the body prone to sepsis and other infections. In a similar study, Delamaire et al., reported the effect of hypoglycemia in reducing neutrophil activity, reducing phagocytosis, reducing chemotaxis and reducing bacterial death (Schuetz et al., 2011). In various studies, the prevalence of diabetes has been reported between 0.5% and 11% (Wild et al., 2004), but in a recent study, 26% of people with sepsis also had diabetes at the same time, and this indicates a significant relationship between sepsis and the incidence of diabetes ($P<0.05$).

Patients with cancer, due to the use of immune system balancing drugs such as alemtuzuma, imatinib and rituximab, all the protective barriers of the body against the entry of microorganisms, both from the outside and inside the body, are distorted. The results of the recent study also showed that 26% of the total sample had chemotherapy in the last month and 69% in the last 2 months, and only 5% had no chemotherapy. The results of Fisher's exact test showed that chemotherapy had a significant relationship with the type of sepsis.

The main problem in chemotherapy is the reduction of specific and non-specific immune cells, which are the main factor in the fight against infections. In this study, the number of neutrophil cells in patients with sepsis was significantly lower than healthy people, which could be due to cancer and the use of chemical drugs. Neutropenia is one of the special medical emergencies and one of the reasons for the hospitalization of patients with immune deficiency, especially those receiving drugs that

weaken the immune system and is a side effect of chemotherapy (Wild et al., 2004). In this study, about 43% of the patients with cancer had a lower than normal level of neutrophils and it has a significant difference compared to healthy people. Of course, in patients with acute and chronic lymphoid leukemia, the amount of white blood cells was significantly higher than normal, which is consistent with the results of other studies. In terms of comparison between different outcomes, the greatest decrease in the number of leukocytes has been observed in patients with sepsis. Considering the role of neutrophils in the immune system, neutropenia can be one of the causes of sepsis and the progression of sepsis to septic shock. The above findings indicate that diabetic people are more at risk of sepsis than non-diabetic people and this risk increases with age. In addition to diabetes, various factors such as chemotherapy, use of steroid drugs and low levels of white blood cells increase the incidence of sepsis. Fever, low blood pressure and decreased platelets can be symptoms of sepsis in cancer patients. According to the results obtained in this study, it is suggested that cancer patients and even healthy people should be screened annually for symptoms such as fever, rapid breathing, blood pressure, blood cell count, and blood sugar level. Since diabetic patients are susceptible to infection due to the physiological conditions of the body, they should take necessary care in this regard. It is also suggested that the use of steroid drugs should be completely controlled because if not controlled, it may have irreparable side effects for the patient.

Acknowledgements

Conflicts of interest

The authors declare that there are no conflicts of interest.

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