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Comparison of Clinical Characteristics of Hospitalized Patients with and without Covid-19 in Mashhad, Iran: A Retrospective, Single-Center Experiences

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Abstract

Background: Covid-19 is known to be diagnosed with clinical manifestations such as dry mouth, fever, respiratory distress, fatigue and tiredness, decreased leukocyte, and pneumonia evidence on CT- scan. We aimed to investigate the clinical symptoms of hospitalized patients with and without Covid-19 to develop the required clinical information.

Materials and Methods: A retrospective descriptive study was conducted in 200 patients suspected of having Covid-19 infection hospitalized in Imam Reza hospital, one of the Referral Hospitals for Covid-19 patients, Mashhad, Iran. Patients' records were reviewed for demographics and clinical symptoms, and the results of laboratory tests over January and February 2020 were reviewed. The admission criterion was definitive Corona virus infection diagnosis, and the exclusion criteria were suffering from viral hepatitis, chronic liver disease, and liver malignancies. Data were analyzed using SPSS version 16.0.

Results: The prevalence of Covid-19 was revealed to be 75% among the suspected patients (71.1% in women and 77.4% in men). The average age of Covid-19 patients was 55.06± 17.23, and the average hospitalization period of Covid-19 patients was 8.22± 5.81 days. The most prevalent symptom among Covid-19 patients was fever and cold symptoms (65%), respiratory complications (17.5%), and fever (6%). The most significant laboratory findings regarding Covid-19 patients were their high NET, LDH, and CRP levels.

Conclusion: The prevalence of Covid-19 was revealed to be 77.4% among the suspected patients. The average age of Covid-19 patients was 55.06± 17.23 years. Based on the results, laboratory parameters are not sufficient for Covid-19 diagnosis due to their low sensitivity and indication, but can improve the value and diagnostic aspects of the disease if used accompanied by CT- scan.

Key Words: Covid-19, Iran, Clinical characteristics, Prevalence.

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1- INTRODUCTION

The widespread prevalence of Covid-19 has imposed considerable threats to the global economy and healthcare system (1). Despite the fact that it has not been long since the start of the new Covid-19 outbreak, major concerns have risen regarding the spread of the disease (2). Severe Covid-19 cases bring about symptoms of acute pneumonia, adult respiratory distress syndrome, and dysfunction of several organs that will eventually result in the death of patients hospitalized with respiratory tract infection symptoms (3). Recent studies indicate the highest fatality rate to be among the elderly and those with underlying diseases. Additionally, pregnant ladies and infants are also considered as high risk groups. Thus, identification of cases at risk of Covid-19 infection is of utmost importance for healthcare workers (4).

This disease is manifested with clinical symptoms such as dry mouth, fever, respiratory distress, fatigue and tiredness, decreased leukocyte, and pneumonia evidence on CT- scan. The diagnosed patients are divided into two groups of mild and severe disease based on the interpretation of their symptoms and test results (5). Although cough and fever are among the symptoms of many diseases, asymptomatic patients can also be potential infection sources (1). Patients might occasionally suffer from gastrointestinal dysfunction and diarrhea as well (6). In addition to interpretation of CT scans and clinical symptoms, the pathogenicity severity of viruses similar to Middle East respiratory syndrome coronavirus (MERS-CoV), and severe acute respiratory syndrome coronavirus (SARS-CoV) is also determined by the increase in the level of proinflammatory cytokines in the serum, indicating lung damage and infection severity (7). Based on the studies performed so far, although clinical symptoms vary in severe and mild cases of infection, the highest mortality rates are observed to be among the elderly, those with weak immune systems, and those suffering from underlying diseases, especially in some countries such as Iran (8). Anyway, patients suspected of Covid-19 are hospitalized in intensive care units and other hospital wards, and undergo chest CT scans and blood test examining the increase of white blood cells, neutrophils, and reactive proteins, and liver damage within two days. Since the aforementioned damages can result in the patient's death, all hospitalized patients must be tested for them, specifically liver damages (9). On the other hand, one of the prevalent ways of Covid-19 diagnosis is based on the glass ground theory and the rapid progression of bilateral diffuse patch infiltration in the peripheral areas of the lungs (7, 10). However, Gune et al. (2019) reported cases of Covid-19 patients with normal CT- scan results. Hence, the importance of examining clinical symptoms and laboratory tests in Covid-19 patients has been established (3, 11). The present study seeks to investigate the clinical symptoms of hospitalized patients with or without Covid-19 infection to gather more data on the Covid-19 virus.

2- MATERIALS AND METHODS

The present research is a single-center retrospective descriptive study conducted in 200 patients suspected of Covid-19 infection hospitalized in Imam Reza hospital, Mashhad. The study was conducted after obtaining a permit from the Ethics Committee of Mashhad University of Medical Sciences (ID- code: 7617884). Imam Reza Hospital is one of the two referral hospitals admitting patients infected with Covid-19 in Mashhad. All study participants were hospitalized and the required data was extracted from patients' electronic records by a trained team. All participants took the reverse polymerase chain reaction test using nasopharyngeal swab samples and

infected cases were diagnosed. Patients' records regarding demographics, clinical symptoms (fever, febrile cold, general weakness, breathing difficulty, coughing, aches and pains), and the results of laboratory tests indicating patients' neutrophils, white blood cells, blood urea levels lymphocytes, and the level of liver enzymes such as Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), and Lactate Dehydrogenase (LDH), necrotizing enterocolitis (NEC), etc. were studied for 2 months starting from January 1, 2020. Patients suffering from viral hepatitis, chronic liver diseases, and liver malignancies were excluded from the present study. The admission criteria for the study was definitive Covid-19 diagnosis as well as being hospitalized. Statistical analyses were conducted using SPSS v.16 software and p-values smaller than 0.05 were considered statistically significant.

3- RESULTS

The Covid-19 test results of 200 patients were studied in the present research. Results indicate that 75% of the patients under study (150 people) were infected with the Corona virus. The study was conducted on 124 male participants (62%) and 76 female participants (38%), the average age of the participants was 53.41±19.20 years (53.27±17.67 in men and 53.63±21.59 in women) and ranged between 1 and 93 years (**Table.1**). Results revealed that 130 participants (65%) had cold symptoms, 35 people (17.5%) had respiratory difficulty symptoms, and the rest had other symptoms. The average hospitalization period of the patients was 7.47±6.02 days (7.52±5.95 in men and 7.38±6.17 in women), and their hospitalization duration varied in a range of 0 to 34 days. The present study indicates that the prevalence of Covid-19 infection was 77.4% among men and 71.1% among women. The prevalence of Covid-19 infection was 83.1% among patients with fever and cold symptoms, 54.1% in patients with respiratory problems, 85.7% in patients with general weakness, and 50% in patients with fever and coughs (**Table.1**). The average age of Covid-19 patients was 55.06±17.23 years, ranging between 13 and 92; and the average age of healthy people was 48.76±23.70, ranging between 1 and 93 years. Besides, the hospitalization of Covid-19 patients lasted for an average of 8.22±5.81 days while the hospitalization of patients not infected with Covid-19 lasted an average of 5.20±6.11 days (**Table.1**).

The average of clinical parameters of participants with and without Covid-19 infection is demonstrated in **Table.2**, divided by laboratory information.

Average ALT-U/L was 59.17±282.01, 110.50±560.70, and 42.06±40.61, in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average AST-U/L was 58.93±224.41, 108.20±440.66, and 42.50±48.12, in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average LDH-U/L was 490.71±719.07, 492.12±638.06, and 486.50±928.40 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average CRP-mg/L was 69.26±92.49, 76.13±99.55, and 48.76±63.73 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average NET type-% was 72.84±15.43, 74.13±13.91, and 69.01±18.92 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average Lymphocyte -mcL was 19.93±19.20, 19.52±20.80, and

21.14±13.41 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average WBC-x 10^3/µL was 9.11±5.56, 9.19±5.89, and 8.89±4.45 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average Urea/mg/dL was 49.01±44.87, 51.01±47.45, and 43.02±35.79 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Average Albumin-g/dL was 3.74±0.50, 3.676±0.420, and 3.95±0.665 in total participants, participants infected with Covid-19, and participants not infected with Covid-19, respectively.

Table-1: Frequency distribution of Covid-19 in terms of demographic and contextual variables in subjects with and without Covid-19.

Variables		Total, number (%)	Result	
			Negative, number (%)	Positive, number (%)
Gender	Male	124 (62)	28 (22.6)	96 (77.4)
	Female	76 (38)	22 (28.9)	54 (71.1)
Signs	Feverish cold	130 (65)	22 (16.9)	108 (83.1)
	Respiratory problems	35 (17.5)	16 (45.7)	19 (54.3)
	Abdominal pain	2(1)	0	2(100)
	General weakness	7 (3.5)	1 (14.3)	6 (85.7)
	Fever	12 (6)	6 (50)	6 (50)
	Sore throat	1 (0.5)	0	1 (100)
	Edema	1 (0.5)	0	1 (100)
	Vomiting	1 (0.5)	0	1 (100)
	Chest pain	2 (1)	1 (50)	1 (50)
	Poisoning	1 (0.5)	0	1 (100)
	Cough	8 (4)	4 (50)	4 (50)
Age, Year, Mean (SD)		53.41 (19.20)	48.46 (23.70)	55.06 (17.23)
Duration of hospitalization		7.47 (6.02)	5.20 (6.11)	8.22 (5.81)

SD: Standard deviation.

Table-2: Frequency Distribution of Covid-19 prevalence among the participants based on laboratory data in subjects with and without Covid-19.

Parameters	Normal range	Total mean (SD)	Results	
			Positive, mean (SD)	Negative, mean (SD)
ALT, U/L	0-64	59.17 (282.01)	110.50 (560.70)	42.06 (40.61)
AST, U/L	8-40	58.93 (224.41)	108.20 (440.66)	42.50 (48.12)
LDH, U/L	12-250	490.71 (719.07)	492.12 (638.06)	486.50 (927.40)
CRP, mg/L	8-1000	69.26 (92.49)	76.13 (99.55)	48.76 (63.73)
NET type, %	40-60	72.84 (15.43)	74.13 (13.91)	69.01 (18.92)
Lymphocyte, ×103 /µl	1.1-3.2	19.93 (19.20)	21.14 (13.41)	19.52 (20.80)
WBC, x 10^3/µL	3.5-9.5	9.11 (5.56)	9.19 (5.89)	8.89 (4.45)
Urea, mg/dL	40-60	49.01 (44.87)	51.01 (47.45)	43.02 (35.79)
Albumin, g/dL	3.5-5.2	3.74 (0.50)	3.676 (0.420)	3.95 (0.665)

SD: Standard deviation. ALT: Alanine aminotransferase, AST: Aspartate transaminase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, NEC: Necrotizing enterocolitis, WBC: White blood cell.

4- DISCUSSION

150 out of 200 participants tested positive for Covid-19. The prevalence of Covid-19 was revealed to be 77.4% among male and 71.1% among female patients. Most of the participants of the study were also male. In their study, Huang et al. reported the infection rate of men to be higher than women (7). Also, the review study of Rodriguez-Morales et al. reported a higher infection rate in men which is consistent with the results of this study (12). However, results of studies conducted by Du et al. and Li et al reported the infection rate of women to be higher than men (13, 14). One of the reasons for men's higher infection rate might be women's higher sensitivity to viral infections due to the protective impacts of chromosome X and their sexual hormones (15). Men have lower immune responses and are more exposed to a variety of viral factors (16). The average age of Covid-19 patients was 55.06± 17.23 years, ranging from 13 to 92 years, and the participants with negative Covid-19 tests had an average age of 48.46 years (23.70).

In a study reviewing 19 previous studies, Rodriguez-Morales et al. reported the average age of the patients to be 51.97 years (12). The average age of the 262 patients examined in Tian at al.'s study in Beijing reported the average age of the patients to be 47.5 years which was 44.5 for mild cases and 61.4 for severe cases (17). Study results revealed high age to be a risk factor in Covid-19 infection (18). The most prevalent symptom among Covid-19 patients was fever and cold symptoms (65%), respiratory complications (17.5%), followed by coughing, fever, general weakness, chest and abdominal pains, sore throat, poisoning symptoms, swelling, and nausea. Feverish cold was observed in 83.1% of the patients. Also, sore throat, swelling, abdominal pain, and poisoning symptoms were only observed in participants who tested positive for Covid-19. According to the study of Huang et al., the most prevalent symptoms of the patients include fever (98%), coughing (76%), shortness of breath (55%), and fatigue and weakness (44%). Few patients reported symptoms such as headache, sputum, bleeding, and diarrhea (7). The study of Guan et al. on 1099 Covid-19 patients discovered that the most prevalent symptoms of the patients were fever (87.9%) and coughing (67.7%) (19). The study of Rodrigues-Morales reported the most common clinical manifestation of the patients to be coughing, fever, and shortness of breath. Besides, fever was significantly higher in adults compared to children (12). Half of Covid-19 patients examined in the study of Peiris et al. reported simple cold symptoms including sore throat, fever, and body aches (20).

The most prevalent abnormality in Covid-19 patients' laboratory parameters include lymphopenia, elevated liver enzymes (AST, ALT), elevated lactate dehydrogenase (LDH) and reactive protein-C (CRP) (12). The present study found the average white blood cells of participants infected with Covid-19 to be 9.19 and that of other patients to be 8.89. A study conducted by Guan et al. reported that 61.1% of people with severe Covid-19 infection suffered from leukopenia (21). However, the study of Qin et al. reported the average number of leukocytes to be 3.5 in the patients. This study discovered a higher leukocyte number in the 286 patients infected with Covid-19 compared to the 166 patients not infected with Covid-19 (22). On the other hand, the study of Huang et al. reported the average number of white blood cells to be 11.3 in patients with a severe case of Covid-19 as opposed to 5.7 in patients with a mild case of the disease (23). Besides, other factors such as other viral/bacterial infections and therapeutic glucocorticoids might increase or decrease WBC (24). Abnormal number

of WBCs may indicate an underlying infection; however, the reliability of white blood cell (WBC) has not been established as a biomarker in the diagnosis of Covid-19 (25). Leukocytes and lymphocytes do not undergo significant changes during the disease's incubation period and its first stage. The virus moves through the bloodstream towards lung and gastrointestinal tissues and impacts tissues expressing high levels of the angiotensin-converting enzyme (ACE2). Afterward, a cytokine storm characterized by elevated inflammatory mediators and cytokines occurs. This stage takes place on days 7-14 of the disease and after the onset of symptoms, and might be the main cause of symptom exacerbation. Peripheral blood lymphocytes reduce significantly and inflammatory factors increase in peripheral blood (12). Covid-19 disrupts lymphocyte circulation through the cell lysis mechanism and lymphoid organ atrophy, and leads to lymphopenia (26).

The present study found the mean number of lymphocytes to be below normal (19.52) in those infected with Covid-19 and in normal range (21.14) in those not infected with Covid-19. The study of Rodriguez-Morales observed Lymphopenia in 40% and the study of Wang et al. observed it in 72% of the patients (12, 27), both of which are consistent with the study's results. However, considering that Covid-19 might target Interleukin-6 (IL-6) mechanisms and lymphatic tissue, other potential causes of lymphocyte depletion must be investigated as well (28). The present study observed an increase in the neutrophils average across both sick and healthy groups which was 74.13% in the infected group and 69% in the non-infected group. The inflammatory response might stimulate neutrophil production and increase the lymphocyte apoptosis rate. Irregular immune responses and their consequent immunological abnormalities are deemed to play an important part in the viral disease severity. Inflammation increases as a result of the irregular immune response, and might lead to death. Also, patients may become infected with a bacterial infection at the same time due to immune system disorders, which can increase neutrophils (29). CRP is a beneficial inflammation marker and plays an essential part in the body's defense against invasive pathogens (30). The level of CRP is associated with the inflammation level and its concentration is not affected by factors such as gender, age, and physical condition (31). CRP promotes phagocytosis in the body and can be potentially used in the evaluation and diagnosis of infectious lung diseases (32).

The present study found the CRP level of participants infected with Covid-19 to be 13.76 and that of those not infected with Covid-19 to be 48.76. Numerous studies confirm that CRP levels are above normal in patients with positive Covid-19 test results (12, 33, and 34). Results of Tan et al. indicate that ESR and CRP evaluation can help the early identification of patients who might get a severe case of the disease. Additionally, CRP level is considerably different in recovered and deceased patients, and may be used as a potential marker for prognosis (34). CRP is one of the acute-phase proteins made by hepatocytes and is secreted into the bloodstream in response to inflammatory reactions such as cancers, infections, and chronic inflammatory diseases. This protein's production in the liver is regulated by inflammatory cytokines such as Interleukin-1 (IL-1), IL-6, and Tumor necrosis factor alpha (TNF-α) (35, 36). Given that CRP level had increased across both groups, this laboratory parameter would not be of much use in Covid-10. Some studies reported elevated LDH levels in Covid-19 patients (10, 27, 37). The present study indicates that both groups had higher than normal LDH

levels. LDH is an enzyme involved in lactate to pyruvate conversion in many bodily tissues, which increases after tissues are decomposed. Hence, elevated serum LDH manifests in a variety of clinical conditions such as heart failure, thyroid disease, cancer, hemolysis, liver disease, severe infections and sepsis, blood malignancies, etc. Ample evidence has recently been discovered indicating that serum LDH levels act as a nonspecific indicator of cell death in many diseases. Inflammatory responses reflect nonspecific responses to tissue damage, hypoxia, and necrosis, demonstrating an association between the immune system, infectious cells, and the inflammatory response (38). Given the increase in LDH levels in many clinical conditions, LDH would not be a suitable indicator for Covid-19 diagnosis, but is a suitable parameter for diagnosing the progression of the disease. In addition, examination of LDH levels along with CT increases the value and diagnostic aspect of the disease (39).

Soeters et al. reported a significant relationship between inflammatory markers such as WBC and CRP and albumin levels. The pathophysiology of hypoalbuminemia in diseases such as trauma, pancreatitis, infection, burns, and organ dysfunction is deemed to be due to decreased protein synthesis, increased capillary permeability, decreased serum albumin half-life, and decreased total serum albumin mass (40). Serum albumin levels examined in the present study were in the lower and of the normal range in Covid-19 patients and normal in patients with no Covid-19 infection. The results of the present research were consistent with the results of Aziz and Zhang's study in this regard (41, 42). Reduced albumin level is most likely a result of liver damage and might also be due to medication side-effects and systemic inflammation in Covid-19 patients (43). Evaluating albumin level may be used as a beneficial indicator in predicting the death risk in patients with a severe case of the disease (43). Yang et al., conducted a systematic review of 24 studies in 4963 patients with Covid-19 and studied the prevalence and renal impairment. Their study indicated decreased Urea in 13.7% of the patients (44). Also, Yang et al. reported this measure to be 14.1% while the present study found the mean amount of Urea in the two groups to be in the normal range while being higher in the group infected with Covid-19. Cheng at al. reported increased Urea and creatinine levels as independent risk factors for death (46).

4-1. Study Limitations

Lack of evaluation of all parameters and clinical features of patients was one of the limitations of this study.

5- CONCLUSION

The general prevalence of Covid-19 infection was revealed to be 75% among the suspected patients (71.1% in women and 77.4% in men). The average age of Covid-19 patients was 55.06±17.23, ranging between 13 and 92 years. Given the results of the study, laboratory parameters are usually not used in Covid-19 diagnosis due to their low sensitivity, but can increase the value and diagnostic aspect if used alongside CT scans. Laboratory parameters can also be used as valuable prognostic indicators in the treatment process and provide useful information about the severity, course and response to treatment. On the other hand, early diagnosis of Covid-19 in patients who are expected to undergo severe infection can facilitate the treatment process if provided with the required medical resources such as being transferred to specialized medical centers.

6- CONFLICT OF INTEREST: None.

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