University of Thi-Qar Journal of Science (UTJsci)
E-ISSN: 2709-0256, P-ISSN: 1991-8690, Vol. 10, No. 2, Dec. 2023

Association between the Demographic Characteristics of Patients and the Severity of COVID-19

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Received 2023-07-22, Revised: 2023-08-05, Accepted: 2023-08-12, Published: 2023-12-24

***Abstract*—The relationship between obesity and COVID-19 is controversial. In addition, the disease's relationship to sex and re-infection is not fully understood. This study investigated the demographic characteristics of 120 patients in the age range from 27 to 70 years old, without chronic disease, which were infected with COVID-19 and treated at Al-Hussein Teaching Hospital in Thi-Qar Province/Southern of Iraq. In this study, the male increased non-significantly than female 55.83% 44.17% respectively. The infected females had a higher BMI (29.1 ± 6.07kg/m2) than males (26.7 ± 5.99 kg/m2); 12.5% of the male patients and 0.83% of the female patients were previously infected with COVID-19; and 12.5% of the patients and 7.5% of female patients were previously vaccinated against COVID-19. The study noted a positive relationship between BMI and disease severity in both male and female patients and that males had a higher percentage of severe disease than females. The study identified age and BMI had association with disease severity, which COVID-19 occurred more in males than females, and that 80% of patients were not vaccinated against COVID-19.**

Key Words: BMI, COVID-19, COVID-19-Vaccination, Re-infection, Severity.

I. Introduction

SARS-CoV-2, which has led to an emerging and rapidly evolving global situation, was first isolated and identified in the Hubei province of Wuhan, China, in December 2019 [1]. The disease that has rapidly grown into a pandemic is caused by severe acute respiratory syndrome coronavirus-2 [2]; as of 4/8/2023, it had infected 759.407.939 million people globally and 2.465.545 million in Iraq according to the European Centre for Disease Prevention and Control, the Centers for Disease Control and Prevention, causing the deaths of 6.866.421 million people globally and 25.375 in Ira https://www.worldometers.info/coronavirus/country/iraq/. According to the study Otuonye *et al*., [3], the initial outbreak appeared to be a result of zoonotic transmission from bats. However, as the outbreak continued, human-to-human transmission was confirmed [4]. COVID-19 patients have a wide range of clinical signs and symptoms that range from being absent (asymptomatic infections) to mild or moderate infection with symptoms such as dry cough, fever, abdominal pain, fatigue, pains, and aches, with sore throat, headache, difficulty breathing, diarrhea, loss of sense of smell and/or taste, conjunctivitis, and skin rash also noted [5]. In contrast, in those who have severe or critical disease, more serious symptoms develop, such as acute respiratory distress syndrome (ARDS), multiple organ failure, and eventually death [6]. A recent study proposed numerous mechanisms by which obesity ectopic fat might enhance the risk of severe COVID-19 [7].Our study was motivated by observations in hospital intensive care units that patients with a body mass index (BMI) above 35 kg/m2 were associated with a poorer prognosis. The abnormal secretion of cytokines, such as IL-6, that comprise 10-35% of adipocyte secretion in normal status, tumor necrosis factor-alpha, and interferons characterizes the chronic low-grade inflammation present in abdominal obesity; this may impair the immune response and have effects on lung and bronchial parenchyma. IL-6 is secreted by adipocytes and is thought to be one reason why obese individuals have higher endogenous levels of CRP and body temperature [7], [8]. The patient's age was also of interest, as surveys showed that patients aged ≥ 65

https://doi.org/10.32792/utq/utjsci/v10i2.1093

years had higher mortality rates. These patients also had a low lymphocyte count or a high ratio of neutrophils to lymphocytes (NLR). With age, the gradual decrease in the ability to maintain redox homeostasis will increase the risk of excessive immune response and lung damage in response to a viral infection, as has been shown with SARS-CoV-1/2 infections [9], [10]. Sex is also an important factor, as the prevalence of disease is higher in males than in females. This can be attributed to steroid hormone differences between males and females, which influence various aspects of immunity. In addition, the X chromosome harbors some immune regulatory genes (i.e., toll-like receptor 7, TLR7), and their products can lower viral loads and inflammation in females [11].

II. Materials and Methods

A. Collection of Data

This study involved 120 patients with COVID-19 infection, of which 67 were male and 53 were female and their age ranged from 27 to 70 years. The study excluded patients with chronic disease and pregnant women. The patients were divided into three groups according to age, BMI index, the BMI were classified according to WHO, https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations, and the disease severity, also the severity was determined by physios depending hospital protocol such as CT scan and clinical symptoms.

B. Inclusion and Exclusion Criteria

The current study included patients with COVID-19 of both sexes up to 70 years old, who were hospitalized in the Thi-Qar Health Directorate, with the exception of patients with chronic diseases and pregnant women.

C. Statistical Analysis

The collected demographic data were statistically analyzed using the Statistical Package for Social Sciences version 26. Age and BMI were analyzed using an independent sample *t*-test, whereas the other non-parametric data were analyzed both descriptively and using a non-parametric chi-square at a p value of < 0.05 and t test at a p value of < 0.05.

III. Results

A. Association between Sex and other Demographic Characteristics of COVID-19 Patients

The present study revealed a statistically non-significant difference in the mean age of male and female patients. In the current study, patients were divided into three age groups: 27-40, 41-55 and 56-70, years; the results showed that COVID-19 infection was distributed at a rate of 7.5%, 25%, 35%, and 32.5% in each age group, respectively, also, revealed a significant difference according to age groups, in addition revealing that patient above 36 years old account for a high proportion of COVID-19 infections. BMI was significantly higher in female patients (29.1 ± 6.07 kg/m2) than in male patients (26.7 ± 5.99 kg/m2). Regarding previous COVID-19 infection, the study noted a significantly higher percentage of previous infection in male patients than in female patients (33.33% compared with 1.67%), and regarding vaccination, the study recorded a non-significantly higher percentage of vaccinated male patients than female patients (43.33% compared with 36.67%), as shown in Table 1.

Table 1: Association between sex and demographic characteristics in COVID-19 patients.

Characterization		Sex	Mean ± SD	Range	p value
Sex	Age	Male	56.1 ± 12.3	27 – 70 years	0.884
		Female	55.8 ± 8.60	28 – 70 years	
	BMI	Male	26.7 ± 5.99	17.7 – 41.1 k/m^2	0.031*
		Female	29.1 ± 6.07	20.7 – 42.2 k/m^2	
Age Groups In years	27 – 40		9	7.50	< 0.01**
	41 – 55		46	38.33	
	56 - 70		65	54.17	
Previous COVID-19 Infection	Yes	Male	15 (12.5)		0.01**
		Female	1 (0.83)		
	Non	Male	52 (43.33)		
		Female	52 (43.33)		
Vaccination Status	Yes	Male	15 (12.50)		0.462
		Female	9 (7.50)		
	Non	Male	52 (43.33)		
		Female	44 (36.67)		

B. *Association between Severity of Disease and Demographic Characteristics of COVID-19 patients*

The present study revealed a statistically significant difference at $p < 0.05$ for disease severity: in male patients, 49.25% had critical infection status, 14.93% had severe infection status, and 35.82% had moderate infection status compared with 1.89%, 26.42%, and 71.70% in female patients, respectively. Regarding previous infection, 18.75% of patients with previous infection had critical infection status, 18.75% had severe infection status, and 62.5% had moderate infection status, whereas in patients who had no previous infection, the corresponding values were 29.81%, 20.19%, and 50.0%, respectively. With regard to vaccination status, the study recorded that 41.76% of vaccinated patients had critical infection status, 0.0% had severe infection status, and 58.33% had moderate infection status, whereas in unvaccinated patients, the corresponding values were 25.0%, 25.0%, and 50.0%, respectively. Regarding BMI, the study noted a non-significant difference at $p < 0.05$, as shown in Table 2.

Table 2: Association between severity of disease and demographic characteristics of COVID-19 patients

Characteristic		Moderate		Severe		Critical		p value
		No.	%	No.	%	No.	%	
Sex	Male	24	35.82	10	14.93	33	49.25	< 0.001
	Female	38	71.70	14	26.42	1	1.89	
Total		62	51.67	24	20.00	34	28.33	
Previous infection	Yes	10	62.50	3	18.75	3	18.75	< 0.001
	Non	52	50.00	21	20.19	31	29.81	
Total		62	51.67	24	20.00	34	28.33	
Vaccination	Yes	14	58.33	0	0.00	10	41.67	
	No	48	50.00	24	25.00	24	25.00	
Total		62	51.67	24	20.00	34	28.33	
BMI	Normal weight	18	36.00	14	28.00	18	36.00	0.069
	Over weight	19	61.29	5	16.13	7	22.58	
	Obesity	25	64.10	5	12.82	9	23.08	
Total		62	51.67	24	20.00	34	28.33	

IV. Discussion

The present study reports that COVID-19 patients of 36 years old or older accounted for 92.5% of total infections, and those patients of 49 years old or older accounted for 67.5% of total infections. Since April 2020, the trends across age groups have been largely consistent over time. The study of Caramelo *et al*., [12] showed that elderly individuals above 60 years old present the highest risk for COVID-19, even more so than with any common disease. Accordingly, younger adults (30-39 years old) seem to experience some protection. Additionally, a study reported a more than one-third increase in mortality risk in the elderly, which was mediated by poor lung function, muscle weakness, high blood pressure, and multiple LTCs. Among older participants, these factors were more common and closely associated with higher COVID-19 mortality. These results have significant clinical and public health ramifications. Firstly, the occupational and behavioral factors of younger adults may lead to a greater risk of contracting COVID-19. Younger adults make up a significant proportion of workers in frontline jobs, such as childcare, retail stores, social services, public transportation, and highly exposed industries such as entertainment, restaurants, and personal services [13], where the control of prevention strategies may be difficult or even impossible. In addition, it is more difficult for younger adults to follow community mitigation strategies, such as avoiding group gatherings and social distancing [14]. In our opinion, the primary mechanism fundamental to the high reproduction numbers in 27–49-year-old is that, at a population level, adults between the ages of 27 and 49 normally have the most contact with other adults aged 20 or older, who are at higher risk of contracting COVID-19 than younger individuals; furthermore, there are increased mobility trends for these age groups. Because individuals over 50 years old are often less mobile and socialize more with other people susceptible to diseases, such as COVID-19, than individuals younger

than 50 years old, most infections are transmitted to them through younger family members.

Regarding sex, the present study recorded an infection rate of 55.83% in male patients and 44.17% in female patients. The present results were in line with an Italian study performed by Borghesi and Marold, [15], involving 783 patients, which reported 67.94% of infections in males and 32.06% in females, and that males aged 50 or older and females aged 80 or older had the highest risk of severe lung disease development. Moreover, a study of Lau *et al*., [16] performed in the USA showed that males have a higher risk of COVID-19 infection than females (58% in males and 42% in females); additionally, the severity of disease measured using CRP and IL-6 was higher in males compared to females. In USA, a study revealed that among 1983 patients, 51.2% were male and 48.8% were female; these percentages are higher than the results obtained in this study and previous studies [17]. This similar incidence of COVID-19 in women and men, which contrasts with previous studies, may be due to the prevalent viral strain that may have crossed sex boundaries; additionally, the study included immunosuppressed patients, CVD patients, and diabetic and pulmonary patients, with approximately 50% being vaccinated and non-vaccinated patients, respectively. In contrast, a Turkish study performed by Arslan *et al*., [18] of 58811 COVID-19 patients in Istanbul that collected data from March 11, 2020, to 31 August, 2021, showed the infection percentage was 52.02% in females and 47.98% in males.

The innate and adaptive immune response has been proposed as the cause of biologic sex differences leading to the bias of COVID-19 infection in males compared with females. Subsets of immune cells show sex-specific patterns and regulation of gene expression [19]. Moreover, immune regulation is subdued by sex chromosomes, as the incomplete inactivation of the X chromosome is associated with female-biased vaccine efficacy in autoimmune diseases [20]. Finally, sex hormones, including testosterone and estrogen, have a direct impact on the function of immune cells. Collectively, the biological and immunological differences between the sexes suggest that men may be more susceptible to COVID-19 infection due to reduced immune responses, while women are potentially protected by a robust immune response [21]. The study of Mustafa *et al*., [22] revealed that the cellular and humoral immune response in females is much higher after viral infections and vaccinations. T cells play an essential role in the cell-mediated immune response, with CD4+ T cells regulating the response of B cells to produce antibodies and CD8+ T cells responsible for killing infected cells and reducing the viral burden .

Regarding vaccination, the present results show that 80% of infected patients were not previously vaccinated against COVID-19, while 20% of patients were vaccinated. The present result is similar to that of Tenforde *et al*., [17], which involved 1983 hospitalized patients from twenty-one hospitals, of which 15.8% of patients were previously vaccinated and 84.2% were non-vaccinated. Vaccination has been reported to be beneficial for individuals who have previously been infected. In several studies, the full vaccination and booster vaccination doses were noted to provide further protection against re-infection in individuals infected with COVID-19 [23].

With regard to re-infection, the current study recorded that 13.3% of the study population were previously infected with COVID-19 and that all re-infected patients were unvaccinated. This is higher than the percentage recorded in previous studies; the study of Arslan *et al*., [18] reported that 0.07% of their population were previously infected, and the study of Islam *et al*., [24] revealed that among 41408 patients, 473 (1.14%) were re-infected, of which 60.9% were non-vaccinated. In current study, the high rate of re-infection in this study may be due to several factors, including: the fact that most of the study population did not receive the vaccine for COVID-19 and all re-infected patients were non-vaccinated; the percentage of vaccinated people who did not complete the full course of vaccine doses and the booster dose; and the fact that the COVID-19 omicron strain differs to a high degree from previous strains of the virus, such as alpha, beta, and gamma, in its mode of transmission, symptoms, clinical signs, morbidity, and mortality. Alternatively, the reason for this difference may be the small sample size in the current study, as compared to the size of samples in previous studies. Acquired immunity after primary infection with the COVID-19 virus was studied in rhesus monkeys; four Chinese macaques were infected with SARS-CoV-2, and two were re-infected 28 days after the initial infection with the same viral dose after recovery. For certain viral loads, the swabs tested negative after re-infection. In addition, the autopsy of a re-infected monkey showed no viral replication and no histopathological changes. Moreover, sera from three monkeys showed neutralizing activity against SARS-CoV-2 in vitro, indicating the production of protective antibodies [25]. This result reinforces the findings of the current study, as the short period of time between the first and second infections with the same viral strain and dose is non-pathogenic and ineffective, while the length of time and the change in the viral strain and dose may be influential, as found in the current study.

V. Conclusion

The current study concludes that men are more susceptible to infection than women, the infection rate increases with age, people who have a large body mass have a greater rate of exposure than those who have a normal body mass, and vaccination against the virus provides a high rate of protection against re-infection.

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I would like to thank the Covid-19 patients for allowing me to collect samples despite their illness, and I would also like to thank the staff of the Imam Hussein Teaching Hospital laboratory for providing assistance during the sample collection period.

Statement of Data Availability

All data obtained in this study are available at main text.

Ethical Approval

The thesis project has been approved according to the decision of the Research Committee in the Thi-Qar Health Directorate (issue No. 208/2022 on 15/8/2022) and facilitation task issued by the Thi-Qar Health Directorate, Department of Training and Development (issue No. 617 on 17/8/2022), which are attached to the document of University of Thi-Qar /College of Science (issue No. 3/11/982 on 17/7/2022), where the patient's consent is taken verbally when reviewing hospitals designated for Covid-19 patients.

Conflict of Interest

Authors declare that they have no conflict of interest.

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