Research Article

Effect of comorbidities on patients with severity of coronavirus disease 2019

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ABSTRACT

INTRODUCTION: COVID-19, a novel coronavirus outbreak, started in China. The clinical spectrum of COVID-19 disease is varied; it has been noted that patients with pre-existing comorbidities are more vulnerable to more severe disease.

OBJECTIVE: To measure the percentage of comorbidities in patients with COVID-19 and the association between the severity, measured by O2 saturation and the extent of lung involvement by chest CT scan, and having one or more co-morbidities.

METHODS: This is a cross-sectional study involving 270 patients confirmed with coronavirus disease 2019 by polymerase chain reaction (PCR) conducted at the medical and respiratory diseases outpatient clinics between 11 December 2020 and 31 September 2021. Demographic characteristics, oxygen saturation, and extent of lung involvement by computed tomography (CT) findings were analyzed according to the presence and number of comorbidities.

RESULTS: Out of 270 patients included in this study, 130 (48.14%) have at least one comorbidity. Hypertension was the most common comorbidity, 97 (35.9%), followed by diabetes mellitus, 58(21.5%). The most common chest involvement score measured by CT scan was score 2 (5-25% involvement) in patients with or without comorbidities, 80 (61.54%) and 96 (68.57%), respectively, with a p-value of 0.263. Oxygen saturation < 94 was more common in the group with comorbidity than without, 65.38% and 53.57%, respectively, with a p-value of 0.048. SPO2 was lower in those with more than one comorbidity than in those with only one (p-value 0.009). Females were more common than males in all types of comorbidities.

CONCLUSION: Comorbidities are common in patients with COVID-19. Hypertension and diabetes mellitus were the most common comorbidity in patients with COVID-19. Oxygen saturation was lower in the group with comorbidity than without and even lower in those with more than one comorbidities than those with only one.

Key words: COVID-19, comorbidities, hypertension, diabetes mellitus, Iraq.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease that has spread throughout the world.[1] According to the World Health Organization (WHO), coronavirus is a large family of viruses that can infect birds and mammals, including humans.[2] Since the outbreak and the global spread of acute respiratory syndrome in Wuhan, China, in late December 2019,[3] the WHO announced COVID-19 as a pandemic in March 2020.[4]

Increases in transmission appear to be driven by four factors: the circulation of more transmissible Variants of Concern (VOCs), relaxation of public health social measures originally intended to control transmission, increases in social mixing, and the number of people who remain susceptible.[5]

Although most patients have mild symptoms and a good prognosis, COVID-19 can develop into severe illnesses, including pneumonia, pulmonary oedema, acute respiratory distress syndrome, multiple organ failure, or even death.[6] Therefore, finding the related factors of disease severity in clinical practice is vital.

Studies indicated that people <65 years old have minimal risks of COVID-19 death even in pandemic epicentres; it is remarkably uncommon in people <65 years without underlying

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predisposing conditions. Male sex and comorbidities[7] (hypertension is the most common, followed by diabetes mellitus and cardiovascular diseases)[8] are other risk factors for poor prognosis associated with COVID-19. Interestingly, more cases of COVID-19 patients with comorbidities are reported.[9]

The patients who were admitted to the intensive care unit (ICU) had a higher number of comorbidities (72.2%) than those not admitted to the ICU (37.3%), suggesting that comorbidities may be risk factors for adverse outcomes.[10] Researchers in China studied 344 patients in the ICU with COVID-19; 133 died on the 28th day with a median survival of 25 days, 141 patients had hypertension, and many had different comorbidities.[11] Another study showed that COVID-19 patients with a history of hypertension, obesity, chronic lung disease, diabetes, and cardiovascular disease have the worst prognosis and often end up with deteriorating outcomes such as ARDS and pneumonia. In addition, elderly patients in long-term care facilities, chronic kidney disease patients, and cancer patients are at risk for contracting the virus and significantly increased risk of death.[12]

In this study, we are reporting the demographic features of the COVID-19 patients with comorbidities presented to the outpatient clinic at Al-Imammain Al-Kadimain Medical City from 11 December 2020 to 31 September 2021, and to measure the association between comorbidities and the severity of the disease measured by the extent of the lesion on chest CT scan and the O2 saturation by oximetry.

METHODS

Setting and study design: A cross-sectional study involving 270 patients confirmed with COVID-19 by polymerase chain reaction (PCR) was conducted at the medical and respiratory diseases outpatient clinics at Al-Imammain Al-Kadimain Medical City in Baghdad from 11 December 2020 to 31 September 2021.

Ethical consideration: The ethical committee of Al-Karkh Health Directorate approved the study's proposal. The author took the acceptance of the hospital administration to do the research at the outpatient clinics and the patient participation in this research.

Case definition: inclusion and exclusion criteria: We included adult patients who visited the outpatient's clinics during the studied period with a diagnosis of COVID-19. The diagnosis of COVID-19 was based on clinical suggestion and confirmed by positive PCR. We excluded patients who had incomplete data from this study.

Sampling: we enrolled only patients who presented to the clinics during our consultancy duties, one day a week during the studied period.

Definitions of the outcomes: The diagnosis of COVID-19 infection was made by a positive PCR on a nasopharyngeal swab that was taken by inserting a flexible fine-shafted polyester swab inserted into the nostril and back to the nasopharynx and left in place for a few seconds, then withdrawn slowly in a rotating motion. The tip of the swab is detached from the shaft, put into a vial containing 2–3 ml of virus transport medium and sent to the laboratory for analysis.

Demographic characteristics of each participant were taken, including age, gender, duration of symptoms, and comorbidities. These comorbidities included hypertension, diabetes mellitus, ischaemic heart disease, stroke, asthma, and malignant diseases. The comorbidities were diagnosed based on the history, and patients were asked to provide medical records to support the diagnosis, like medical reports, medical prescriptions, or laboratory results, whenever possible.

Two parameters determined the severity of COVID-19 were used in our study; the oxygen saturation measured by pulse oximetry and the extent of lung involvement determined by computed tomography of the chest. Oxygen saturation of 94 % and above were considered normal. The extent of lung involvement was divided into five scores; ***score 1*** when less

than 5 < of the lungs had been involved, ***score 2*** when 5-25 % involved, ***score 3*** when 26-49 % involved, ***score 4*** when 50-74 % involved, and ***score 5*** when more than 75 % involved.[13] The chest CT scan was interpreted by an experienced chest radiologist from our hospital.

Procedure: Patients were grouped into two; those with at least one comorbidity and those without any. In each group, we calculated the mean age and duration of symptoms, the distribution of the gender, O2 saturation and the score of lung involvement. Then, we regrouped the participants into two groups; those with only one risk factor and those with more than one. Similarly, associations with age, gender, duration of symptoms, O2 saturation, and CT score were measured. Statistical tools were applied to test the statistical significance of any differences.

Statistical Analysis: Statistical package for social sciences version 24 (SPSS v24) used to analyze data. Continuous variables are presented as means with standard deviation. At the same time, the categorical variables are presented as numbers and percentages. A T-test for two independent variables was used to test the significance of the difference in mean between the two study groups. The Chi-square test for independence was used to test the significance of the association between categorical variables. The level of significance was set at a p-value < 0.05.

RESULTS

In this study, the total number of participants was 270 patients. Females were 145 (53.7%), and males were 125 (46.3%). The mean age was 52.2 ±15.1 years, and the mean duration of symptoms was 7.5±3.2 days. Hypertension was the most common comorbidity reported in 97 patients (35.9%), diabetes mellitus in 58 patients (21.5%), and IHD in 19 patients (7%), while CVA, asthma, and malignancy were reported in only 2, 5, 4 patients respectively. For O2 saturation and the extent of lung involvement by Chest CT scan, see table 1.

We found that 130 (48.1%) patients with COVID-19 have comorbidities. The mean age of them was 58.77±12.65 years, p-value <0.001. Female was higher than male in those with comorbidities, 77(59.23%) than 53 (40.77%) in male, with a p-value of 0.029. See table 2

The highest chest CT score in the group with comorbidities and without was in score 2 (5-25% involvement of the lungs), 80 (61.54%) and 96 (68.6%), respectively, followed by score 3 (26-49% lung involvement), 29 (22.3%) and 31 (22.1%) respectively. However, these figures showed no statistically significant difference. In Covid-19

Table 1 | Demographic, comorbidities, CT Scores, and SpO2 levels of all patients.

Variable	Category	N	%
Age (Y)	Mean±SD	52.2±15.1	
Gender	Male	125	46.3
	Female	145	53.7
Duration of symptoms (d)	Mean±SD	7.5±3.2	
Hypertension	Yes	97	35.9
	No	173	64.1
Diabetes	Yes	58	21.5
	No	212	78.5
IHD	Yes	19	7.0
	No	251	93.0
CVA	Yes	2	0.7
	No	268	99.3
Asthma	Yes	5	1.9
	No	265	98.1
Malignancy	Yes	4	1.5
	No	266	98.5
CT Score of chest involvement	<5 %	0	0.0
	5-25 %	176	65.2
	26-49 %	60	22.2
	50-74 %	33	12.2
	≥75%	1	0.4
SpO2 Level	≥94%	111	41.1
	<94%	159	58.9

Table 2 | Demographic characteristics of patients according to the presence or absence of comorbidities.

Variables	With Comorbidity 130 (48.1%)	Without Comorbidity 140 (51.9%)	P value
Age(y) Mean±SD	58.77±12.65	46.16±14.73	<0.001
Gender:			0.079
Male	53(40.77%)	72(51.43%)	
Female	77(59.23%)	68(48.57%)	
DoS(d) Mean±SD	7.76±3.44	7.34±3.04	0.293

DoS: Duration of the symptoms, (y): years, (d): days.

Table 3 | Relation of extent of CT chest findings of patients to the presence or absence of comorbidities.

	Comorbidity		
	Yes	No	P value
Total (%)	**130 (48.14%)**	**140 (51.86%)**	
CT Score(S)			0.353
S 1 (<5%)	0 (0)	0 (0)	
S 2 (5-25%)	80 (61.54%)	96 (68.57%)	
S 3 (26-49%)	29 (22.3)	31 (22.1)	
S 4 (50-74%)	21(16.15)	12 (8.7)	
S 5 (≥75%)	0 (0%)	1 (0.7)	
SpO2 Level			0.041
≥94%	45 (34.6)	65 (46.43)	
< 94%	85 (65.4)	75 (53.57)	

Table 4 | CT score and SpO2 level of patients according to the number of comorbidities.

	Comorbidity		
	One	More than one	P value
Total (%)	**79 (60.7 %)**	**51 (39.3)**	
CT Score(S)			0.521
S 1 (<5%)	0 (0)	0 (0)	
S 2 (5-25%)	51(64.56%)	29(56.86%)	
S 3 (26-49%)	15(21.13%)	14(27.45%)	
S 4 (50-74%)	13(16.46%)	8(15.69%)	
S 5 (≥75%)	0(0%)	0 (0)	
SpO2 Level			0.079
≥94%	32(40.5%)	13(25.5%)	
< 94%	47(59.5%)	38(74.5%)	

patients with comorbidities, 45 (34.6%) had an SpO2 of ≥ 94% and 85 (65.4%) had SpO2< 94 %. In patients without comorbidities, 65 (46.43%) had SpO2 of ≥ 94%, and 75 (53.57%) had SpO2 of <94%. This difference was statistically significant, with a p-value of 0.041. See table 3

Seventy-nine patients (60.77%) reported one comorbidity, and 51 (39.23%) more than one. Score 2 lung involvement (5-25% lung involvement) was reported in 51 (64.56%) patients of one comorbidity group and 29 (56.86%) of more than one comorbidities group. For other CT lung scores, see table 4. These differences were statistically non-significant, with a p-value of 0.73. In patients with at least one comorbidity, 32 (40.5 %) had an O2 saturation of ≥ 94%, and 47 (59.5 %) had a saturation of <94%. While in those with more than one comorbidity, 13 (25.5%) had an O2 saturation of ≥ 94%, and 38 (74.5%) had a saturation of <94%. These differences were statistically significant, with a p-value of 0.009. See table 4.

Table 5 shows the distribution of patients with hypertension, diabetes mellitus, IHD, CVA, Asthma, or malignancies according to the mean age, duration of the symptoms, CT score, and level of O2 saturation in addition to gender. Hypertension, diabetes, and IHD were statistically significant associations with old patients. The mean level of O2 saturation was lower in patients with hypertension than those without; this difference was statistically significant with a p-value of 0.001. Other differences were statistically non-significant.

DISCUSSION

The increasing number of COVID-19 and the extensive geographical involvement have caused widespread concern worldwide.[13] In our study on 270 patients with COVID-19, 129 patients have at least one comorbidity (47.7%). Studies have shown different rates of comorbidities in patients with COVID-19. It ranges from as low as 15.8 % in a study from China[15] to as high as 37.8 % in a study from Maynmar[14] and 46.4 % in a study from Wuhan, China.[10] In Thailand[16] and Singapore,[17] studies have reported 25 and 28.3 %. These differences in the rate of comorbidities among different studies may be attributed to the differences in study designs, the severity of the disease, sample size and characteristics of the participants, and the possible geographic effect.

In our study, the mean age of the patients with comorbidities was 58.77 ± 12.65 years, higher than that for patients without comorbidities, 46.16 ± 14.73 years, with a p-value <0.001. This difference is expected because diseases like hypertension, diabetes mellitus, and coronary heart disease are more common in older people,[18] who are more susceptible to COVID-19.[19] Kavya et al. in their study[20] have reported that the mean age of COVID-19 patients with comorbidities was 55.9±10.20 years.

In group with comorbidity, we found that female was higher than male, 78 patients

Table 5 | Distribution of each comorbidities according to age gender duration of symptoms and Ct score and SpO2 level

Variables N (%)		Hypertension		Diabetes		IHD		CVA		Asthma		Malignancy	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
		79 (35.9)	173(64.1)	58 (21.5)	212(78.5)	19(7)	251(93)	2(0.7)	268(99.3)	5(1.9)	265(98.1)	4(1.5)	266(98.5)
Age (y)	Mean±SD	60.7±11.4	47.5±14.9	57.2±11.2	50.9±15.8	62.4±10.2	51.5±15.2	56.5±52.2	26.2±15.1	52.0±13.3	52.2±15.2	63.0±12.0	52.1±15.1
	P	<0.001		0.004		0.002		0.689		0.973		0.152	
DoS (d)	Mean±SD	7.6±3.4	7.5±3.2	7.4±3.7	7.6±3.1	8.4±3.8	7.5±3.2	6.5±7.6	2.1±3.2	5.8±3.9	7.6±3.2	6.5±3.9	7.6±3.2
	P	0.84		0.785		0.250		0.649		0.225		0.518	
CT Score	Mean±SD	27.1±17.7	23.9±15.5	26.6±18.3	24.6±15.8	25.8±14.6	25.0±16.5	12.5±25.2	10.6±16.4	19.0±12.4	25.2±16.4	32.5±22.2	25.0±16.3
	P	0.134		0.410		0.842		0.277		0.405		0.361	
SpO2 Level	Mean±SD	90.1±6.6	92.4±4.9	90.7±6.1	91.9±5.5	90.1±5.0	91.7±5.7	93.5±4.9	91.6±5.7	91.8±2.9	91.6±5.7	94.5±1.3	91.6±5.7
	P	0.001		0.167		0.234		0.636		0.938		0.546	
Gender													
Male	N (%)	38(39.2)	87(50.3)	24(41.4)	101(47.6)	6(31.6)	119(47.4)	0 (0)	125 (46.6)	1(20.0)	124(46.8)	1(25.0)	124(46.6)
Female	N (%)	59(60.8)	86(49.7)	34(58.6)	111(52.4)	13(68.4)	132(52.6)	2(100.0)	143(53.4)	4(80.0)	141(53.2)	3(75.0)	142(53.4)
	P	0.079		0.397		0.182		0.188		0.234		0.389	

(60.5%) versus 51(39.5%). Males and females have similar susceptibility to SARS-CoV-2; however, males are more likely to have higher severity and mortality.[21] In addition, screening of cardiovascular risk factors was similar in men and women with IHD.[22] Our result in this regards may be due to the sample we included in this study.

In this study, hypertension was the most common comorbidity reported in 79 (35.9%) patients, Followed by diabetes mellitus in 58 (21.5%), and IHD in 19 (7%); these results go with Dwi's study[23] which showed that among those with COVID-19 and a history of chronic disease, the most common was hypertension in 38% and followed by diabetes mellitus in 27.6%.

Population-based surveillance conducted by the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET) reported that out of 1479 patients with COVID-19, 12% have clinical data of underlying medical conditions; hypertension in 49.7%, diabetes mellitus in 28.3%, and cardiovascular diseases in 27.8%.[24] The presence of comorbidities in our study, 129 (40.8 %), is more than that reported by COVID-NET, this may be due to sample size differnces between the studies or way of approving the presence of comrbidities. There are reports that over 86% of COVID-19 deaths involved at least one comorbidity, according to the New York State Department of Health in which hypertension 55.4%, diabetes 37.3%, and Coronary artery disease 12.4% (25). So hypertension and diabetes mellitus are common comorbidities in different severity groups of COVID patients. ?? In our study, patients with COVID-19 reported fewer rates of asthma, malignant diseases, and CVA, 3.6%, 2.2%, and 2.2%, respectively. Ye Minn in his study,[14] also reported lower rates of malignant diseases (1.2%) and stroke (4.8%), and similarly, Shima[26] reported asthma in 3.6%, malignant diseases in 2.2 % and CVA in 2.2 %.

In groups with and without comorbidities, we found score 2 (5-25 %) was the commonest CT score of chest involvement, reported in 80 (61.54%) and 96 (68.6), respectively, followed by score 3 (26-49%) in 29(22.3%) and 31(22.1%), respectively. These differences showed a non-significant statistical association with a p-value of 0.353. Similarly, Ammar, in his study from Iraq,[27] found a score 2 (5-25%) was the commonest lung involvement in the CT scan of the chest, followed by a score 3 (26-50%) and in both genders.

The oxygen saturation lower than 94 % was commoner in the group with comorbidity than in the group without, 85 (65.4%) and 75(53.6%), respectively, and this difference was statistically significant with a p-value of 0.041. This association indicates that the severity of COVID-19 measured SPO2 % severe cases was more with comorbidity. It has been proposed that the clinical severity of COVID-19 should depend on the presence of any of the following criteria: a partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) ratio <300 mm Hg, a respiratory rate >30 per min and peripheral oxygen saturation (SpO2) <94% or lung

infiltrates > 50%.[28] A meta-analysis[29] proposed a potential association between comorbidities and the risk of severe COVID-19; compared with patients with non-severe disease, patients with severe infection are prone to have one or more comorbidities.

To study the effect of the number of comorbidities on the severity of COVID-19, we grouped the participants into two; those with at least one comorbidity and those with more than one. In both groups, we found that score 2 (5-25%) CT chest involvement was the commonest, followed by score 3; however, no statistical significance was detected, see table 5. This may indicate that the extent of CT chest involvement is not affected by the number of comorbidities. There are limited data about the relationship between CT chest manifestation and comorbidities; however, Kavya study[20] showed a significant association between CT chest manifestation and comorbidities irrespective of the number of comorbidities. This may be attributed to the timing at which CT examination is performed as consolidation with or without ground glass changes will be seen in the 2nd and 3rd weeks of the infection course.[27] In studying the association between oxygen saturation and the number of comorbidities, we found that the more the number of comorbidities, the lower the SPO2; 47 (59.5%) in the group of at least one comorbidity and 38 (74.5%) in the group of more than one comorbidity. This difference was statistically non-significant, with a p-value of 0.079. In parallel, Cegan[30] showed a high rate of admission to hospital and ICU and mortality rate in patients with two comorbidities, irrespective of the age of the patients. Also, Wei-Jie[31] stated that a higher number of comorbidities correlated with poorer clinical outcomes.

The limitations of this study:

1. It is cross-sectional, making assessing the causality between comorbidity and severe outcomes difficult.
2. Confounding factors, like obesity and smoking, are not addressed.
3. Other parameters measuring severity, like mortality rate admission to the ICU, are not studied due to limited time and resources.

CONCLUSION

In conclusion, this study showed that comorbidities are common in patients with COVID-19, and hypertension and diabetes mellitus are the most common associated chronic medical illness. Lower oxygen saturation was more in patients with comorbidity, and this association is more when the patient has more than one comorbidity. The extent of lung involvement measured by chest CT scan has shown a statistically non-significant association with comorbidities.

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Abbreviations list: Acute respiratory distress syndrome (**ARDS**), Cerebrovascular accident (**CVA**), Computed tomography (**CT**), Coronavirus disease 2019 (**COVID-19**), COVID-19-Associated Hospitalization Surveillance Network (**COVID-NET**), Days (**D**), Duration of the symptoms (**DoS**), intensive care unit (**ICU**), Ischemic heart Disease (**IHD**), Oxygen (**O2**), Polymerase chain reaction (**PCR**), Severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**), Statistical package for social sciences version 24 (**SPSS v24**), Variants of Concern (**VOCs**), World Health Organization (**WHO**), Years (**Y**).

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