The Comorbidities and it Impact on the outcome of COVID-19 Patients

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ABSTRACT

Background: The existence of associated diseases presents a major clinical challenge in the approach and management of COVID-19 patients. **Objectives**: To study the effect of common comorbidities on the severity, outcome, and duration of hospital stay among confirmed COVID-19 cases. **Methods:** Descriptive cross-sectional study. A 2574 conditions were involved in the current study. All the PCR confirmed cases in 2 COVID-19 centers at Babylon province/Iraq were included for the period from March till September 2020. A constructed questionnaire used as a method of data collection which including socio-demographic data, clinical presentation of the infection and its severity, associated comorbidities that the patient may suffer from and the duration of hospital stay and outcome. **Results:** the study shown that the mean of age 48.7 ($\pm$16.4) years, Diabetes Mellitus was the most prevalent associated comorbidity (25.0%), then hypertension with a prevalence of (23.4%), (84.0%) of the patients who had comorbidities had severe/critical illness compared to (54.1%) for patients who are free from comorbid illnesses with significant P value of (0.001), case-mortality ratio was 26.4% among patients with comorbidities compared to 10.6% among the patients free from comorbidity (P<0.001). **Conclusions:** associated diseases had significant impact on the severity of the duration and outcome of COVID-19 infection, patients with comorbidities must have additional preventive measures and they should be at the beginning in receiving the COVID-19 vaccine to prevent the deteriorations and bad consequences.

Keywords: Comorbidities, COVID-19, Hypertension, Diabetes, Babylon.

INTRODUCTION

In December 2019 COVID19 stated as pandemic by the world health organization (Ferrer, 2020) SARS-CoV-2 is the seventh   member of the family of CoVs that infects humans with severity vary from asymptomatic to severe symptoms. (Obaid et al., 200; Al Sa'ady et al., 2022; Suleman et al., 2021; Suleman & Rahman, 2020). Patients who have associated comorbidities have less favorable outcome when compared with cases without chronic diseases. COVID19 patients with a history of hypertension, obesity, chronic lung disease, diabetes, and cardiovascular disease have a negative prognosis and most often end up with more sever lower respiratory involvement as pneumonia and acute respiratory distress syndrome, chronic kidney disease (CKD) and patients with cancer were not only at risk for bad prognosis, but also increased risk of mortality among these groups (Ashraf et al., 2019; Ashraf, Ahmad & Azlizan, 2019; Yang et al., 2020).

The objectives of the present study were to estimate the prevalence of comorbidities in the confirmed COVID-19 patients and explore the effects of these comorbidities on the severity, hospitalization period and outcome of the infection.

METHODOLOGY

A descriptive cross-sectional study design was conducted at Babylon governorate hospitals, at AL- Hilla Teaching hospital, and Marjan Teaching hospital as centers of covid19 patients from the period 1st November 2020 to 31st January 2021. 2centres of covid19 which are: AL-Hilla Teaching hospital with a total bed capacity of 385, the total number of beds available for COVID-19 Patients is 106 beds (in AL-Amel isolated ward) and 20 beds for RCU, number of ventilators is 29.

Purposive sampling is used (all confirmed cases for COVID-19) (Positive PCR test) in assigned hospitals in duration between 1st March and 30th September 2020 will be enrolled in this study. The questionnaire consist of demographic characteristics (patients ID, hospital name and type, date of onset of symptoms, age, sex, occupation, date of hospital admission, smoking history, pregnancy, travel history and, contact history).

Comorbidities (Hypertension, Heart disease, Diabetes Mellitus, Malignancy, Respiratory diseases, renal diseases, cerebrovascular disease, others).

Presentation and clinical features of the infection including fever, cough, nasal congestion, shortness of breath, sore throat, chest pain, hemoptysis, nausea and vomiting, diarrhea, loss of taste or smell, fatigue, backache, and others.

The severity classification was as follows:

- a- mild case (upper respiratory tract infection)
- b- Moderate case (pneumonia no need for oxygen)
- c- Severe case (pneumonia need oxygen)
- d- Critical case (need RCU).
- e- the duration of hospitalization period.
- f- Outcome classification as: recovered, death and, others (discharge on his responsibility, referred to another hospital, disabled).

DATA ANALYSIS

According to the classification of the severity of covid19, number of days of hospitalization, and outcome. Descriptive and inferential statistics SPSS (version 23) used for achieving the study objectives. a P value (0.05) is considered statistically significant.

Administrative arrangement:

Official Approval will be granted from the Babylon Health Directorate / Iraq from Ministry of Health and the national center for training and human development.

RESULTS

Table 1: *Distribution of Cases with Comorbidities According to Severity Classification*

		Severity classification						P. Value
		Severe/ Critical		Mild/ Moderate		Total		
		No. 1700	% 66.1	No. 874	% 33.9	No. 2574	% 100	
Co-morbid Illnesses	Yes	865	84.0	165	16.0	1030	100.0	0.001
	No	835	54.1	709	45.9	1544	100.0	

Hypertension	Yes	488	81.6	110	18.4	598	100.0	0.001
	No	1212	61.3	764	38.7	1976	100.0	
Diabetes Mellitus	Yes	532	82.7	111	17.3	643	100.0	0.001
	No	1168	60.5	763	39.5	1931	100.0	
Heart Diseases	Yes	133	86.4	21	13.6	154	100.0	0.001
	No	1567	64.8	853	35.2	2420	100.0	
Respiratory Diseases	Yes	48	82.8	10	17.2	58	100.0	0.007
	No	1652	65.7	864	34.3	2516	100.0	
Renal Disease	Yes	28	90.3	3	9.7	31	100.0	0.009
	No	1672	65.7	871	34.3	2543	100.0	
Cerebrovascular disease (CVD)	Yes	37	94.9	2	5.1	39	100.0	0.002
	No	1663	65.6	872	34.4	2535	100.0	
Malignancy	Yes	18	85.7	3	14.3	21	100.0	0.070
	No	1682	65.9	871	34.1	2553	100.0	
Others	Yes	48	87.3	7	12.7	55	100.0|	0.001
	No	1652	65.6	867	34.4	2519	100.0	

This table showed (59.9%) of COVID-19 cases had no comorbidities, (20.9%) of cases had one comorbidity, and (19.2%) had more than one. The most common comorbid illnesses were Diabetes Mellitus (25.0%), hypertension (23.2%), and heart diseases (6.0%).

Table 2: *Association of COVID-19 cases to the Outcome and Number of Comorbidities.*

		Outcome								P. Value
		Death		Recovered		Other		Total		
		No.	%	No.	%	No.	%	No.	%	
No.of comorbidity	>one comorbidity	142	28.7	340	68.7	13	2.6	495	100.0	0.001.
	Only one comorbidity	130	24.3	398	74.3	8	1.5	536	100.0	
	No comorbidity	163	10.6	1363	88.3	17	1.1	1543	100.0	
	Total	435	16.9	2101	81.6	38	1.5	2574	100.0	

Table above showed there was a significant association between comorbid illnesses and severity of disease (P.value < 0.05) except malignancy.

Table 3: *Distribution of Cases with Comorbidities According to the Days of Stay in the Hospital*

		No. days of hospital stay:						P. Value
		≥ 14 days		< 14 days		Total		
		No. 248	% 9.6	No. 2326	% 90.4	No. 2574	% 100	
Co-morbid Illnesses:	Yes	125	12.1	905	87.9	1030	100.0	0.001
	No	123	8.0	1421	92.0	1544	100.0	
Hypertension	Yes	63	10.5	535	89.5	598	100.0	0.395
	No	185	9.4	1791	90.6	1976	100.0	
Diabetes Mellitus	Yes	91	14.2	552	85.8	643	100.0	0.001
	No	157	8.1	1774	91.9	1931	100.0	
Heart Diseases	Yes	15	9.7	139	90.3	154	100.0	0.536
	No	233	9.6	2187	90.4	2420	100.0	
Respiratory Diseases	Yes	7	12.1	51	87.9	58	100.0	0.468
	No	241	9.6	2275	90.4	2516	100.0	
Renal Disease	Yes	4	12.9	27	87.1	31	100.0	0.537
	No	244	9.6	2299	90.4	2543	100.0	
CVD	Yes	6	15.4	33	84.6	39	100.0	0.226
	No	242	9.5	2293	90.5	2535	100.0	
Malignancy	Yes	3	14.3	18	85.7	21	100.0	0.472
	No	245	9.6	2308	90.4	2553	100.0	
Others	Yes	6	10.9	49	89.1	55	100.0	0.746
	No	242	9.6	2277	90.4	2519	100.0	

This table shown there was a significant association between DM only (as comorbid illness) and the number of days of hospital stays (P.value < o.oo1) while not significant in other comorbid illnesses (p.value > 0.05).

Table 4: *Association of Cases with Comorbidities to the Outcome*

		Outcome								P. Value
		Death		Recovered		Other		Total		
		No. 435	% 16.9	No. 2101	% 81.6	No. 38	% 1.5	No. 2574	% 100	
Co-morbid Illnesses:	Yes	272	26.4	737	71.6	21	2.0	1030	100.0	0.001
	No	163	10.6	1364	88.3	17	1.1	1544	100.0	
Hypertension	Yes	146	24.4	438	73.2	14	2.3	598	100.0	0.001
	No	289	14.6	1663	84.2	24	1.2	1976	100.0	

Diabetes Mellitus	Yes	173	26.9	456	70.9	14	2.2	643	100.0	0.001
	No	262	13.6	1645	85.2	24	1.2	1931	100.0	
Heart Diseases	Yes	58	37.7	92	59.7	4	2.6	154	100.0	0.001
	No	377	15.6	2009	83.0	34	1.4	2420	100.0	
Respiratory Diseases	Yes	21	36.2	36	62.1	1	1.7	58	100.0	0.001
	No	414	16.5	2065	82.1	37	1.5	2516	100.0	
Renal Disease	Yes	13	41.9	17	54.8	1	3.2	31	100.0	0.001
	No	422	16.6	2084	82.0	37	1.5	2543	100.0	
CVD	Yes	16	41.0	21	53.8	2	5.1	39	100.0	0.001
	No	419	16.5	2080	82.1	36	1.4	2535	100.0	
Malignancy	Yes	9	42.9	12	57.1	0	0.0	21	100.0	0.006
	No	426	16.7	2089	81.8	38	1.5	2553	100.0	
Others	Yes	15	27.3	39	70.9	1	1.8	55	100.0	0.110
	No	420	16.7	2062	81.9	37	1.5	2519	100.0	

This table showed a significant association between comorbid illnesses and the outcome of disease (p.value <0.05).

Table 5: *Association of sex and age groups with severity classification*

			Severity						P. Value
			Severe/ Critical		Mild/ Moderate		Total		
			No.	%	No.	%	No.	%	
Gender	Male		1038	65.7	543	34.3	1581	100.0	0.598
	Female		662	66.7	331	33.3	993	100.0	
Age group	< 40		326	43.7	420	56.3	746	100.0	0.001
	≥ 40		1374	75.2	454	24.8	1828	100.0	

Table (5) showed a significant association between ages with severity (P < 0.001) and there is no significant association of gender with severity (P.0.598). (Severe/critical cases) represented

(43.7%) in patients with age group less than 40 years and (75.2%) in the age group ≥ 40 years. According to the gender, severe/critical cases in males was (65.7%) and female (66.7%).

DISCUSSION

The presence of associated comorbidities represents a great clinical challenge in the approach and management of COVID-19 infections, comorbidities need more knowledge to overcome. The main findings in the current study that the associated comorbidities were significantly related to the outcome and severity of COVID-19. A probable explanation is that chronic medical conditions increase the load and lead to more dysregulation of the major physiological functions of the immune system that may lead to higher mortality risk among COVID-19 patients. (Li et al., 2020; Suleman et al., 2023).

The current study reported that patients older than 40 years of age were at greater risk for COVID-19 as most of them acquired severe disease and the death rate was higher in this age group as illustrated in table 5. This can be explained by increased comorbid illnesses with age. Relevant studies have also showed the same and concluded that older age is a risk factor for more severe COVID-19 infection and that 80% of mortalities are occurring in patients over 60 years old. This association may be related to the less functional immune system in the elderly patients and different susceptibility to infection at variable age groups (Chen et al., 2017).

In this study, a significant association was found in table 1 and table 2; between hypertension with severity and outcome of disease as 23.2% COVID-19 patients had hypertension with higher severity compared to normotensive cases and a high case fatality rate (CFR) of 24.4%, In China, 23% of COVID-19 cases also had hypertension and the estimated CFR was 6% among these patients (Tadic et al., 2020); While another study reported that high blood pressure is the commonest associated comorbidities in patients with COVID-19, with a prevalence of 10-34% (Hussain et al., 2020).

Also other study showed that the most prevalent cardiovascular comorbidity associated with COVID-19 infection is hypertension with a prevalence of (17.1%) (Fang et al., 2020) while our study showed that the most prevalent were DM (25.0%), followed by hypertension (23.2%), and this due to missing data (past medical history), angiotensin-converting enzyme (ACE-2) inhibitors are often used by patients suffering from hypertension, which may lead to upregulating the

expression of the ACE-2 receptors and higher susceptibility to SARS-CoV-2 infection (Kumar et al., 2020).

Regarding diabetes mellitus (DM) in this study in table 3 that the death rate was higher for diabetic patients (26.9%) compared to patients with diabetes (13.6%), and disease severity was 82.7% versus 60.5% in non-diabetic cases. This agreed with a study that reported that patients with COVID-19 infection who are diabetic have a two-fold increase in mortality and higher rate of severe/critical course of COVID-19 infection compared to patients who are not diabetics (Alguwaihes et al., 2020).

Another study in Saudi Arabia revealed that the prevalence of diabetes is higher among sever hospitalized Covid-19 cases with a significantly higher mortality compared to nondiabetic patients (20.5% versus 12.3%) and that diabetics have lower survival time (Chee et al., 2020)

Patients with diabetes or hypertension have double risk to develop severe disease and require an intensive care unit (ICU) settings, Several rhetorical mechanisms may put patients with diabetes mellitus at higher risk of sever disease including the associated with immune dysfunction, increased susceptibility to infections, and reduced viral clearance. ⁽Higham⁾

According to table 4 there was significant correlation found in this study between heart diseases with severity and outcome of heart diseases with COVID-19 infection were reported with a severity and a case fatality rate (CFR). Cardiovascular disease is an independent risk factor for the severity of COVID-19 infection. COVID-19 patients with cardiovascular disease had more severe illness (Intensive care unit admission and a higher mortality rate (Liu et al., 2020).

This study reported that the prevalence of respiratory diseases among COVID19 were few and majority of them were with severe pattern as shown in table 4. Another study reported that chronic obstructive pulmonary disease (COPD) was reported in 50–52.3% of the total severe COVID-19 cases, and associated with 88% increased risk of ICU admission or death due to increased mucous production that leads to blockage of the air passages (Ejaz et al., 2020).

Table 7 shown that asthma is not directly linked to COVID-19 infections, patients with respiratory diseases and asthma show worsening of their condition during any respiratory tract infection including that of corona viruses (Chhiba et al., 2020) in contrast, another study showed that asthma is not linked to an increased risk of hospitalization, the use of asthma control inhaled

corticosteroids and systemic corticosteroids is also not associated with higher COVID-19 hospitalization (Henry, 2020).

This study concluded that most patients with renal disease acquired a severe level of covid-19 and the death rate was higher in a patient with COVID-19 and CKD (table 1). Based on a meta-analysis study, chronic kidney diseases (CKD) is associated with a higher risk of severe COVID-19. Patients with CKD should take extra precautions to reduce the exposure to a virus rich environment and limit contact with known cases or people who have signs of the disease (Trejo-Gabriel-Galán, 2020).

Our study showed that cerebrovascular disease (CVD) was another factor that affects the severity and outcome of the disease as stated in table 1. A study in Wuhan concluded that 6.8% CVD patients did not survive from COVID-19 infection (Dai et al., 2020) another study revealed that history of stroke increases the risk of death during COVID-19 by three folds [21] There are some possible explanations for the correlation between COVID-19 ischemic strokes and higher stroke severity including that viral infections may cause a direct vasculopathy (epitheliopathy) and potentiate the prothrombotic formation through several mechanisms including immune-mediated platelet activation, the associated dehydration, and infection-induced cardiac dysrhythmias (Moiseev et al., 2020).

Another finding in this study (table 4) was the significant association between underlying malignancy and COVID-19 outcome, the death rate was 42.9%, while no significant correlation with the severity of the disease was found. This disagrees with a study that showed that patients with malignancy will be more prone to severe acute SARS-CoV-2 infection and its related complications, although data related to linkage between COVID-19 infection and cancer remains limited. Another study concluded that patients with malignancies are more likely to have severe sequelae of SARS-CoV-2 infection, including higher rates of ICU admission, need for invasive ventilation and intubation, and higher mortality (Rees et al., 2020).

Most of the patients with underlying Co-morbid Illnesses had a short duration of hospitalization (<14 days) as declared in table 3. estimating how long patients remain hospitalized is a cornerstone for planning and providing sufficient beds, and related hospitalization services including medical staff and equipment that are needed, longer hospital stay is associated with high fever, bilateral pneumonia, shorter time to start lower respiratory symptoms to admission and

58

associated comorbidities mainly diabetes; there are different admission and discharge criteria that varies between countries that may affect the length of hospitalization (Wu et al., 2020).

CONCLUSION

The existence of chronic diseases are consider as factors for increase the severity of COVID-19 infection and higher mortality rate especially in older patients.

RECOMMENDATIONS

1-patients with chronic conditions must take extra precautions and preventive measures to avoid infection during the pandemic.

2-Specific attention to older patients and those with chronic disease with early screening and diagnosis.

3-priority of vaccination for older population with chronic illnesses.

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