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Cardiovascular Risks and Outcome in COVID-19 Positive Patients With Cardiovascular Disease Attending Primary Health Care Corporation in Qatar: A Retrospective Cohort Study

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Abstract

Background: Coronavirus disease (COVID-19) patients with cardiovascular disease (CVD) are at a higher risk of morbidity and mortality. This study describes the risks and outcome in COVID-19 patients with CVD attending Primary Health Care Corporationsettings in Qatar.

Objective: To report whether CVD increases the risk for hospitalization and further complications in COVID-19 patients.

Methods: Retrospective cohort study.

Results: A total of 10,178 CVD patients' data who tested positive for COVID-19 were extracted from electronic medical records on the basis of inclusion criteria and analyzed during the period of February 1, 2020 to December 31, 2020 (11 months). Among the patients included in the study, 64% (n=6527) were men and 36% (n=3651) were women; 23% (n=2299) were Qataris and 77% (n=7879) were non-Qataris. Among the selected age group of greater than 25 to less than 75 years, the median age was 50.83 years. More than half of the patients had diabetes (69.6%; n=7086) followed by hypertension (68.4%; n=6965) and dyslipidemia (45.1%; n=4590). Other comorbidities were obesity (18.3%; n=1862), kidney disease (6.5%; n=659), hematologic problems (4.2%; n=425), liver disorders (1.4%; n=142), rheumatic heart disease (1.3%; n=131) and neurologic symptoms (1.3%; n=128).

Multivariate analysis for factors associated with inpatient admissions in last 28 days for patients with CVD reported that patients with age greater than 70 years are 2.8 (1.86-4.18) times higher risk of hospital admission as compared with the patients 25-30 years of age.

Conclusion: The pre-existing CVD with age and other comorbidities predict the risk for hospitalization and further complications in patients with COVID-19. Further studies are needed to investigate the data from primary and secondary care about the long-term cardiovascular outcomes of patients who have survived COVID-19.

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INTRODUCTION

Since December 2019, Wuhan, China, has experienced an outbreak of coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Although the outbreak is likely to have started from a zoonotic transmission event associated with a large seafood market, that also traded live wild animals, it soon became clear that

efficient person-to-person transmission was also occurring.[2] In March 2020, the World Health Organization characterized COVID-19 as a global pandemic. The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure, myocarditis, and even death.[3]

COVID-19 patients with cardiovascular disease (CVD) are at a higher risk of morbidity and mortality. However, it remains unclear if the presence of cardiovascular conditions pose an independent risk or is mediated by other factors (eg, age). Cardiovascular disease was a common comorbidity in patients with COVID-19 predecessors SARS and Middle East respiratory syndrome. In SARS, the prevalence of CVD was 8% and its presence increased the risk of death 12-fold.[4] Also, tachycardia, bradycardia, arrhythmia, or even sudden cardiac death is commonly observed in patients with SARS.[5] COVID-19 contributes to cardiovascular complications, including acute myocardial injury as a result of acute coronary syndrome, myocarditis, stress-cardiomyopathy, arrhythmias, cardiogenic shock, and cardiac arrest. The higher mortality in patients with cardiovascular comorbidities may be directly attributable to underlying CVD or merely coincident with CVD.[4]

The severity and extent of cardiovascular effects of COVID-19, along with the effect of specific treatments, are not yet known and are subject to scrutiny and investigation.[6] Myocardial injury may result from direct viral myocardial infection. Recent studies have indicated that angiotensin-converting enzyme 2 is a functional receptor with a strong binding affinity to the spike protein of SARS-CoV-2, and is highly expressed in human heart. Thus, it is reasonable to hypothesize that COVID-19 induced cardiac injury might be mediated by angiotensin-converting enzyme 2.[7] At present, we cannot rule out that long-term intake of angiotensin-converting enzyme 2 inhibitors and/or angiotensin-receptor blockers may facilitate SARS-CoV-2 entry and virus replication in patients taking medication for hypertension. Conversely, it is not yet known whether the intake of angiotensin-converting enzyme 2 inhibitors and/or angiotensin-receptor blockers, when infected, is beneficial for pulmonary outcome.[8]

Hypertension has been reported as a 'risk factor' for COVID-19 but there has been a lack of clarity as to whether this means risk factor for acquiring the disease, the severity of disease, or for poor outcomes.[9] In Qatar (2012), leading causes of disease burden among the population were ischemic heart disease (11.8%), road traffic accidents, birth asphyxia, and birth trauma.[10] The prevalence of type 2 diabetes is also rising in Qatar and is associated with a higher incidence of cardiovascular events, which results in a higher rate of mortality.[11]

This study aims to report whether pre-existing CVD increases the risk for hospitalization and further complications in patients with COVID-19, attending primary health care settings in Qatar.

PATIENTS AND METHODS

Study design and setting

This was a retrospective cohort study. Qatar, a high-income Arab country in the Middle East, has invested considerably in its health care system. This includes a publicly funded primary health care service delivered by Primary Health Care Corporation (PHCC), the largest primary care provider in Qatar. At the time of undertaking this study, PHCC had 27 primary health care centers (all accredited by Accreditation Canada International) distributed across the country. Every resident in Qatar is eligible to register with a PHCC health center for a nominal annual fee and utilize its services. On July 1, 2016, the Cerner electronic medical record system became fully functional across all PHCC health centers in Qatar. Primary Health Care Corporation's laboratories are accredited by the College of American Pathologists and follow gold standard laboratory procedures for diagnosis and detection of comorbidities to ensure the highest standard of care for patients.

Data of patients with CVD who tested positive for COVID-19 were extracted from the electronic medical records of 27 health centers across the country, from February 1, 2020 to December 31, 2020. Data extraction was done by the health information management

department, PHCC. A total of 10,178 CVD patients who had their Communicable Disease Center notification forms for COVID-19 positive test, completed on Cerner electronic medical records were included in the study.

Data collection process

Communicable disease center had specific criteria for taking swabs from eligible patients attending medical facilities early in the pandemic. All patients who met the criteria, were swabbed either at the health centers or in the hospital facilities. Patients who have confirmed SARS-CoV-2 infection, by positive result on reverse transcriptase polymerase chain reaction testing of a nasopharyngeal sample, were included in the study. The study was reviewed by the PHCC Institutional Review Board and followed all regulations to ensure the protection of privacy and confidentiality of the participants. After obtaining ethical approval, data was collected from the electronic records of individual patients, which included information regarding patient demographic characteristics, comorbidities, initial laboratory tests, diagnoses during the hospital course, treatments including invasive mechanical ventilation and kidney replacement therapy, and most importantly patient outcomes.

Study population included COVID-19 positive patients with CVD, presenting to any of the 27 health centers during the study period. Inclusion criteria were as follows: a) patients who are COVID-19 positive with CVD registered under PHCC; b) patients in the age group >25 to <75 years (elderly patients, >75 years of age, will already have a few more comorbidities and hence already belong to the risk group. The need is to capture the real risk factors that lead to hospitalization and further complications from the study group); c) patients with underlying CVD; d) coronary artery disease; e) hypertension; f) arrythmias; g) heart failure. Patients with pre-existing pulmonary disease (eg, Asthma, chronic obstructive pulmonary disease), immunocompromised patients (chronic medical conditions, taking immunosuppressants), malignancies, beta-human chorionic gonadotropin in blood to check pregnancy, and patients who are registered under Qatar red crescent clinics were excluded from the study as they belong to secondary care settings. There was no sample size calculation done as all study subjects from the population, who satisfy the inclusion and exclusion criteria were included for the study.

In the data collection process, we also included the blood test results from within 6 months before the presentation, to identify patients with other undiagnosed comorbid conditions. We collected information about complete blood count, Hemoglobin A1C (HbA_{1c}), urea, creatinine, pro- B-type natriuretic peptide (BNP) proteins, estimated glomerular filtration rate, alanine amino transferase, aspartate amino transferase, and total cholesterol, low-density lipoprotein, high-density lipoprotein, ferritin, Trop T, procalcitonin, chest X ray, electrocardiogram, tread mill test, stress electrocardiogram, cardiac magnetic resonance imaging, computerized tomography angiogram, myocardial perfusion scan, and angiography wherever available.

Statistical Analyses

The statistical analyses were performed by STATA 15.1 (College Station Texas, USA). Univariate logistic regression analysis was performed for factors associated with inpatient admission, in the last 28 days, among patients with CVD. Descriptive statistics were performed for age distribution, gender, nationality, comorbidities, and study outcome parameters. $P<.05$ was considered as statistically significant.

RESULTS

A total of 10,178 CVD patients' data who tested positive for COVID-19 were extracted and analyzed from February 1, 2020 to December 31, 2020 (11 months). Table 1 shows the demographic characteristics and comorbidities of the patients who are COVID-19 positive with CVD registered under PHCC. Of these patients, 64% (n=6527) were men and 36% (n=3651) were women, 23% (n=2299) were Qatari and 77% (n=7879) were non-Qatari. Among the selected age group of >25 to <75 years, most cases were in the age group 50-60 years (32%; n=3207), followed by the age group 40-50 years (30%; n=3006) and the lowest number of patients were in the age group 25-30 years (3%; n=279). The median age

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TABLE 1. Demographic Characteristic and Clinical Histories Comorbidities

Characteristic	Number of Cases (N=10,178)	Percentage
Age distribution, y		
25-30	279	3%
30-40	1603	16%
40-50	3006	30%
50-60	3207	32%
60-70	1796	18%
>70	278	23%
Gender		
Male	6527	64%
Female	3651	36%
Nationality		
Qatari	2299	23%
Non-Qatari	7879	77%
Comorbidities		
Diabetes	7086	69.62%
Hypertension	6965	68.43%
Dyslipidemia	4590	45.10%
Rheumatic Heart disease	131	1.29%
Kidney disease	659	6.47%
Neurologic symptoms	128	1.26%
Hematologic problem	425	4.18%
Liver disorder	142	1.40%
Obesity	1862	18.29%

TABLE 2. Study Outcome in the Last 28 Days Admission

	Number of Cases (N=10,178)	Incidence/ 100
Inpatient admission	2740	26.9%
ICU admission	287	2.8%
Myocarditis	1	0.01%
Coronary artery disease	169	1.7%
Pulmonary embolism	8	0.1%
Pneumonia	1729	17%
Acute respiratory distress syndrome	51	0.5%
Asthma/COPD affects post COVID-19	293	2.9%
Cerebrovascular disease	63	0.6%

COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease; ICU, intensive care unit.

was 50.8 years. The distribution of comorbidities in the patients was as follows: more than half of the patients had diabetes (69.6%; n=7086) followed by hypertension (68.4%; n=6965), and dyslipidemia (45.1%; n=4590). Other comorbidities were obesity (18.3%; n=1862), kidney disease (6.5%; n=659), hematologic problems (4.2%; n=425), liver disorders (1.4%; n=142), rheumatic heart disease (1.3%; n=131), and neurologic symptoms (1.3%; n=128).

Table 2 describes the study outcome in the last 28 days of admission. Out of 10,178 COVID-19 cases with CVD, inpatient admission was about 27% (n=2740). About 17% (n=1729) of the patients had pneumonia and intensive care unit admission was 2.82% (n=287). About 2.9% (n=293) had asthma/chronic obstructive pulmonary disease post COVID-19, 1.7% (n=169) had coronary artery disease, 0.6% (n=63) had cerebrovascular disease, 0.5% (n=51) had acute respiratory distress syndrome, 0.08% (n=8) had pulmonary embolism, and 0.01% (n=1) had myocarditis.

Table 3 displays the laboratory test results within 6 months before to presentation, with the purpose of identifying patients with other undiagnosed comorbid conditions. According to the results, most patients had normal readings before the presentation. Serum ferritin median and interquartile range 60 (18.6-209), c-reactive protein was 7.3 (2.9-17.8), 6.8 (6-8.1) for HbA_{1c}, procalcitonin 0.09 (0.06-0.1), and NT pro-BNP 154.5 (12-297)

Table 4 describes the factors associated with inpatient admission in last 28 days. Multivariate analysis was used to predict the factor associated with inpatient admission among CVD cohort. Patients >70 years of age are 2.8 (95% CI,1.9-4.2) times more likely to have the risk of hospital admission in last 28 days, followed by patients in the age group of 60-70 years [2.3 (95% CI,1.6-3.2) times], 50-60 years [1.61(95% CI,1.16 − 2.25) times], and 40-50 years [1.40 (95% CI, 1.00-1.94) times], compared with those in the age group of 25-30 years. The risk of hospital admission and complications increase

TABLE 3. Laboratory Test Results Within 6 Months Before Presentation

	Number of Cases	Median	Mean	SD
Serum Ferritin	47	60	123.8	135.6
CRP	2130	7.3	16.9	29
HbA_{1C}	193	6.8	7.2	1.6
Procalcitonin	2	0.1	0.1	0.04
NT pro-BNP	2	154.5	154.5	201.5
Troponin- T-HS	–	–	–	–

BNP, B-type natriuretic peptide; CRP, c-reactive protein; HS, high sensitivity; SD, standard deviation.

significantly with increase in age ($P<.001$), especially in patients ≥70 years of age.

There was no significant difference in hospital admission with respect to gender distribution and Qatari vs. non-Qatari patient population (odds ratio > 1).

With respect to the association between comorbidities and hospital admission and complications, it is shown that CVD patients with kidney diseases have 1.8 (1.5-2.1) times higher risk of hospital admission as compared with the other patients, followed by neurologic symptoms [1.6 (1.1-2.2) times], hematologic problems [1.7 (1.4-2.1) times], rheumatic heart disease [1.1 (0.7-1.6) times], liver disorders [1.2 (0.8-1.7) times], diabetes [1.5 (1.3-1.6) times], hypertension [1.3 (1.2-1.5) times], obesity [1.4 (1.2-1.5) times], and dyslipidemia [0.96 (0.9 − 1.0) times].

DISCUSSION

This is a retrospective cohort study that described the cardiovascular risks and outcome in confirmed COVID-19 cardiovascular patients who were presented at the PHCC in Qatar during the study period. Among 10,178 patients, most were males with a median age of 50.83 years with symptoms. This may be due to the migration of foreign workers and predominantly male population in the region. Patients more than 70 years of age are 3.86 times more likely to have the risk of hospital admission in last 28 days compared with those in the other age groups. Older age, kidney diseases, and neurological symptoms were the major predictors of higher risk of having hospital admission and complications than the patients with other comorbidities.

The mean age of patients with confirmed COVID-19 who were diagnosed at PHCC during the study period was lower as compared with the median age of the patients with COVID-19 in a study conducted in UK (67.4 years) during the early stages of the pandemic.[12] We found that the risk of cardiovascular complications is higher in male patients with predisposing conditions such as older age, diabetes, hypertension, obesity, dyslipidemia, rheumatic heart disease, kidney disease, neurologic symptoms, hematologic problems, and liver disorders. The observation was comparable to the results of a national study conducted in UK during the early stages of the pandemic.[13] In that study male gender, older age, hypertension, obesity, diabetes, atherosclerosis associated with endothelial dysfunction, inflammation, thrombosis, and microvascular obstruction were found to be the major causes of hospitalization and complications. It was also reported that COVID-19 may lead to multi-organ dysfunction, including myocardial injury in both the presence and the absence of atherosclerotic epicardial coronary disease. In the current study, only primary care data is available for us and patients with severe illness presented directly to secondary care for prognosis and further treatment.

Hypertension is one of the major risk factors along with other comorbidities in our patient population. This is comparable to the results reported in the previous SARS-CoV-2 studies that COVID-19 patients with hypertension had a higher mortality rate and was an independent risk factor for poor prognosis.[14-16] Nishiga et al[16] reported that the proportion of COVID-19 patients with CVD,

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TABLE 4. Multivariate Analysis for Factor Associated with Inpatient Admission in Last 28 Days for Cardiovascular Patients

	Univariate analyses			Multivariate analyses		
	Odds Ratio	95% CI	*p* value	Odds Ratio	95% CI	*p* value
25-30	Reference					
30-40	1.03	0.73-1.44	0.879	0.96	0.68 — 1.35	0.817
40-50	1.54	1.11- 2.13	0.009	1.40	1.00 — 1.94	0.048
50-60	1.92	1.39-2.66	<0.001	1.61	1.16 — 2.25	0.005
60-70	2.98	2.15-4.41	<0.001	2.30	1.63 — 3.22	<0.001
>70	3.86	2.61-5.71	<0.001	2.79	1.86 — 4.18	<0.001
Male	1.02	0.93-1.12	0.645	1.03	0.93 — 1.13	0.591
Female	Reference					
Qatari	1.11	1.00-1.23	0.042	0.96	0.86 — 1.07	0.469
Non-Qatari	Reference					
Diabetes	1.52	1.37-1.67	<0.001	1.45	1.30 — 1.63	<0.001
Hypertension	1.48	1.34-1.63	<0.001	1.33	1.19 — 1.49	<0.001
Dyslipidemia	1.31	1.19-1.43	<0.001	0.96	0.86 — 1.04	0.268
Rheumatic heart disease	1.24	0.86-1.80	0.257	1.09	0.74 — 1.59	0.675
Kidney disease	2.38	2.02-2.79	<0.001	1.78	1.50 — 2.10	<0.001
Neurologic symptoms	2.13	1.50-3.04	<0.001	1.56	1.08 — 2.24	0.017
Hematologic problem	1.96	1.61-2.39	<0.001	1.74	1.42 — 2.14	<0.001
Liver disorder	1.53	1.08-2.16	0.016	1.20	0.84 — 1.72	0.317
Obesity	1.33	1.19-1.49	<0.001	1.37	1.22 — 1.54	<0.001

such as hypertension and coronary artery disease, was higher than that of patients without comorbidities, suggesting that patients with hypertension may be susceptible to SARS-CoV-2 infection.

Study outcomes in the last 28 days of admission of our participants found that only 27% had inpatient admission during the study period. 17% of them were admitted owing to pneumonia and the total intensive care unit admission was 2.8%. The pandemic has affected every part of the world. However, infection rates and case fatality rates vary widely among countries and depend on the virus variant. During our data collection period, the case fatality rate was 3.2% in the US, 7.5% in Canada, 15% in the UK, whereas in Qatar and Kuwait it was only 0.16% and 0.67%, respectively (as of August 10, 2020).[17] It has been assumed that population demographics and comorbidity burden are the key determinants of variability in case fatality rates. However, these differences alone are unlikely to fully account for the widely variable case fatality rates.[18] A previous study on COVID-19 in Qatar in February-April 2020 found that more than 90% of patients diagnosed between February 28 and April 18 were asymptomatic or had milder symptoms that did not necessitate hospitalization.[15] This was not close to the rate reported in a meta-analysis by Byambasuren et al[19] (16%, 95% CI 12%-20%), but it was around half of the percentage reported in Kuwait[15] (around 40%) and higher than the percentage reported in KSA (9%).[15,20]

We looked at the laboratory test results within 6 months before the COVID-19 presentation to identify patients with other comorbid conditions. However, in most of the cases diagnosis was either missing or in some cases the results reported that the level of serum ferritin, c-reactive protein, HbA_{1c}, procalcitonin, and BNP were all significantly higher than the normal range. This is similar to the study conducted by Khawaja et al[12] in UK.

The risk of hospital admission and complications significantly increase with increase in age ($P<.001$), especially in patients ≥70 years of age. Also, there was no significant difference in hospital admission with respect to gender distribution or Qatari vs. non-Qatari patient population (odds ratio >1). These results contradict the previous studies published in Qatar and UK.[12,15,21]

With respect to the association between comorbidities and hospital admission and complications, it was found that CVD patients with kidney disease have a higher risk of hospital admission as compared with other patients. It was followed by other comorbidities like neurologic symptoms, hematologic problems, rheumatic heart disease, liver disorders, diabetes, hypertension, obesity, and dyslipidemia. These results are in confirmation to the results from a UK study.[12]

In Qatar, as of December 31, 2020, the total number of cases were 1,43,834 and the total mortality was 245.[17] We found a very low mortality among patients with confirmed COVID-19, which may be attributed to the timely and effective response of the health system and the demographic characteristics of the infected patients. It is conceivable that right censoring with the time delay between onset of disease to death may play a part, though similarly very low mortality after the study period ended does not support this. The role played by factors, such as free access to high-quality medical care for everyone residing in Qatar, availability of a high number of critical care beds or differences in viral subtypes, needs further study.

This study outlines the cardiovascular risks and outcome in COVID-19 positive patients with CVD attending PHCC in Qatar. Patients were included from all health centers distributed in Qatar reflecting different socioeconomic backgrounds. Data were extracted from electronic medical records which were, however, incomplete for some patients. Patients with severe illness presented directly to secondary care with poor prognosis and higher risk of morbidity and mortality.

CONCLUSION

The pre-existing CVD with increasing age and other comorbidities are risk predictors for hospitalization and further complications in COVID-19 patients. Further studies are required to examine the primary and secondary care data about the long-term cardiovascular outcomes of patients who have survived COVID-19.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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Abbreviations and Acronyms: **BNP**, B-type natriuretic peptide; **COVID-19**, coronavirus disease; **CVD**, cardiovascular disease; **PHCC**, Primary Health Care Corporation; **SARS-CoV-2**, severe acute respiratory syndrome coronavirus 2

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