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Conduction System Disease in Victims of COVID-19

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ABSTRACT

Background: Electrophysiological-related manifestation of COVID-19 is a matter of debate in the literature nowadays. A wide spectrum of arrhythmias was observed among patients who have been infected with COVID-19.

Objectives: This study discussed the prevalence of arrhythmias and conduction system disease in patients with COVID-19.

Method: In this retrospective study, demographic and electrocardiographic data of 432 expired COVID-19 patients who had been admitted to Faghihi Hospital of Shiraz University of Medical Sciences from August 2020 until December 2020 were reviewed.

Results: Atrioventricular nodal block (AVB) was found in 40(9.3%) patients. Furthermore, 28(6.5%) of them suffered from the first degree of AVB, and 12(2.8%) suffered from complete heart block (CHB). Among 189 cases (59.0%) ST-T changes agreed with myocardial infarction or localized myocarditis. Findings of myocardial injury including fragmented QRS and prolonged QTc were observed among 91 (21.1%) and 28 (6.5%) respectively. In victims of COVID-19, conduction disease was not related to any comorbidities. Fragmented QRS, axis deviation, presence of S1Q3T3, and poor R wave progression were significantly related to conduction system abnormalities in victims of COVID-19 (P-value > 0.05)

Conclusion: Our findings can serve in future studies that aim to develop a risk stratification method for susceptible COVID-19 patients. The myocardial injury appears to role significantly in COVID-19 morbidity and mortality. Consequently, we recommend health policymakers consider separate catheterization laboratories that provide service only to COVID-19 patients.

KEYWORDS: COVID-19, Conduction system, ECG, Atrioventricular block, Iran

INTRODUCTION

The first studies of COVID-19 considered it to be predominantly a respiratory disease (1). However, more recent evidence highlights multiple organ system involvements in COVID-19 patients, including coagulation system disorders like pulmonary thromboembolism, acute kidney injury, hepatocellular injury, and cardiac and central nervous system complications (2-4). The cardiac complications include thromboembolic events, heart failure, heart block, acute coronary syndrome, myocarditis, arrhythmias, and sudden cardiac death (5).

Electrophysiological-related manifestation of COVID-19 is a matter of debate in the literature nowadays. A wide spectrum of arrhythmias was observed among patients who have been infected with COVID-19. (6). Moreover, multiple case reports introduce atrioventricular block as a potential manifestation of COVID-19 (7). Furthermore, previous studies have been reported several conduction system abnormalities including T-wave change, QTc interval prolongation, and arrhythmias among COVID-19 patients. Moreover, in-hospital mortality risk increased with increasing abnormal ECG scores (8). In another study investigating the association between electrocardiographic features and mortality in COVID-19 patients in a large tertiary care hospital in Northern Nevada, the prevalence of AVB was 11.8%. Another article conducted a rigorous patient-level analysis to determine the association of acute malignant cardiac arrhythmias, such as tachy- or bradyarrhythmias, and mortality in hospitalized patients with COVID-19. The prevalence of AVB was 3.5%. Among them, 2 were associated with MI, 2 had metabolic abnormalities, suggesting that refractory shock was primarily responsible for conduction block, and 1 patient had AV block in the setting of non–ST-segment–elevation myocardial infarction and newly depressed left ventricular ejection fraction (9-11). However, no association between the presence of AVB and mortality was reported in these articles.

As presented before, the knowledge of electrophysiological abnormalities and particularly atrioventricular blocks is largely based on very limited data. The present paper aims to describe electrocardiographic abnormalities in demised COVID-19 patients.

METHODOLOGY

Patient selection

This study is a descriptive investigation that retrospectively reviewed 432 expired COVID-19 patients who were admitted to Faghihi Hospital of Shiraz University of Medical Sciences from August 2020 until December 2020. all the expired patients of COVID-19 who were over 18 years old were studied. Those who were known cases of cardiovascular disease were excluded. Faghihi Hospital, located in Shiraz, Fars Province, is one of the major tertiary teaching hospitals and is responsible for the treatments for COVID-19 assigned by the government. COVID-19 was confirmed in these patients by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) RNA detection with the nasal and pharyngeal swab, performed at admission or during hospitalization.

Data collection

Electronic demographic and on-paper medical records were evaluated. The data was gathered into a planned-out questionnaire. The questionnaire included demographic data, underlying diseases, and ECG factors. The data was collected by six independent practitioners. ECGs were interpreted by two cardiologists blinded to the patients' information and confirmed by an electrophysiologist. Cardiologists interpreted ECGs basic parameters like rhythm, rate, axis, hypertrophy, enlargement, relatively new findings on COVID-19 (ST elevation and atrioventricular conductance disturbances), repolarization variants (J elevation, early repolarization, Brugada pattern, U wave, QTc prolongation, QT dispersion (QTD), the slope of the terminal part of T wave (T-slope), depolarization abnormalities (Bundle Branch Block, low voltage QRS, poor R wave progression, and fragmented QRS (fQRS), QRS duration prolongation), and ECG pulmonary patterns such as S1Q3T3. All ECGs were taken by the hospital's employed and trained technicians who were blinded to the purpose of the study and the patient's medical information using "Electrocardiogram Dena650" produced by "SAADAT company, Tehran, Iran".

Statistical analysis

All statistical analyses were performed by Statistical Package for the Social Sciences (SPSS), version 19.0 (IBM corp.), for windows. Categorical variables were shown as frequency and percentages, and continuous variables as mean (SD). The Chi-square test was performed to assess the relationships between ECG parameters and patients' medical conditions with his-Purkinje system disease. A two-sided P-value less than 0.05 was considered statistically significant.

RESULTS

Among the 432 demised patients, 261(60.4%) were male with a mean age of 67.02 ±14.44 years (28-96). The most prevalent comorbid diseases were Hypertension (47.9% - 207 cases), Diabetes mellitus (36.3% - 157 cases) and heart diseases (35.2% - 158 cases). The prevalence of other co-morbidities is as follow in order of frequency: coronary disease (18.5%- 80 cases), Hyperlipidemia (12.5% - 54 cases), lung disease (8.6% - 37 cases), chronic kidney disease (6.3% - 27 cases).

Regarding heart rate and rhythm, sinus tachycardia (HR>100) and bradycardia (HR<60) were noticed in 100 (23.1%) and 9 (2.3%) patients respectively. Furthermore, abnormal rhythms were noted in 66 (15.2%) patients. The most prevalent arrhythmia was AF (12.5%). Reviewing Electrocardiographic findings, AVB was found in 40(9.3%) patients. Twenty-eight (6.5%) of them suffered from first-degree AVB, and 12(2.8%) suffered from CHB. Among 189 cases (59.0%) ST-T changes agreed with myocardial infarction or localized myocarditis. Findings of myocardial injury including fragmented QRS and prolonged QTc were observed among 91 (21.1%) and 28 (6.5%) respectively. Other conduction system abnormal findings were Bundle Branch Blocks (BBB). The various ECG-related factors demonstrated in table 1. To describe more precisely, the left bundle branch block was seen in 25 (5.8%) patients and the right bundle branch block was seen in 50 (11.6%) patients. Pulmonary diseases- related findings including S1Q3T3, poor R progression, axis deviations, and low voltage ECG were reviewed and the prevalence was 14.4% (62 patients), 41.0% (177 patients), 21.7% (94 patients), and 11.3% (49 patients) respectively. Myocardial injury findings such as fragmented QRS and prolonged QTc were assessed with the prevalence of 21.1% (91 patients), 6.5% (28 patients). Primary electrical cardiac diseases such as prominent J wave, Brugada pattern, and early repolarization were detected with a prevalence of 4.4% (19 patients), 1.2% (5 patients), and 4.2% (18 patients).

Table1. Prevalence of ECG parameters in victims of COVID-19

ECG parameters		Frequency (N = 432)	Percent
Fragmented QRS	Yes	91	21.1
	No	314	78.9
ST-T change	Yes	189	59.0
	No	243	56.3

Rhythm	Sinus rhythm	366	84.7
	AF	54	12.5
	others	12	2.8
Rate	Bradycardia (HR<60)	9	2.1
	Normal (60<HR<100)	323	74.8
	Tachycardia (HR>100)	100	23.1
Axis deviation	Normal	338	78.2
	Left	29	6.7
	Right	65	15.0
Hypertrophy	No	383	88.7
	LVH	36	8.3
	RVH	6	1.4
	RAE	4	0.9
	LAE	3	0.7
AVB	Yes	40	9.3
	No	392	90.7
QTc 1	<500	281	65.0
	>500	150	34.7
QTc 2	Male AND >440 OR Female AND >460	28	6.5
	others	403	93.3
QTd	<28	377	87.3
	>28	55	12.7
J wave	Yes	19	4.4
	No	427	95.6
U wave	Yes	45	10.4
	No	387	89.6
Brugada pattern	Yes	5	1.2
	No	427	98.8
Early repolarization	Yes	18	4.2
	No	414	95.8
BBB	Normal	356	82.4
	LBBB	25	5.8
	RBBB	50	11.6
T slope	<30	16	3.7
	30-60	405	93.8
	>60	11	2.5
S1Q3T3	Yes	62	14.4
	No	370	85.6
Low voltage QRS	Yes	49	11.3
	No	383	88.7
PRP	Yes	177	41.0
	No	255	59.0

MI: Myocardial Infarction, AVB: Atrioventricular block, , LVH: left ventricular hypertrophy, RVH: right ventricular hypertrophy, RBBB: right bundle branch block, LBBB: left bundle branch block, QTc: corrected Q-T interval, QTd: Q-T interval dispersion, T slope: T-wave terminal slope, PRP: Poor R wave Progression.

Table 2 demonstrate the correlation of comorbidities and conduction system disease in victims of COVID-19, conduction disease was not related to any underlying medical condition.

Table2. Association of patients' medical conditions and conduction system disease in victims of COVID-19

Medical condition		Patients without HPD (N=317)	Patients with HPD (N=108)	P value
Sex	Female	125 (73.1)	46 (26.9)	0.654
	Male	196 (75.1)	65 (24.9)	
IHD	Yes	57 (71.3)	23 (28.8)	0.477
	No	260 (75.4)	85 (24.6)	
DM	Yes	113 (72.0)	44 (28.0)	0.357
	No	204 (76.1)	64 (23.9)	
Renal disease	Yes	42 (79.2)	11 (20.8)	0.501
	No	275 (73.9)	97 (26.1)	
Lung disease	Yes	23 (62.2)	14 (37.8)	0.078
	No	292 (75.6)	94 (24.4)	
Hyperlipidemia	Yes	38 (70.4)	16 (29.6)	0.503
	No	279 (75.2)	92 (24.8)	
CKD	Yes	19 (70.4)	8 (29.6)	0.648
	No	298 (74.9)	100 (25.1)	
HTN	Yes	151 (72.9)	56 (27.1)	0.504
	No	165 (76.0)	52 (24.0)	
HTN: hypertension, DM: diabetes mellitus, IHD: ischemic heart disease, HLP: hyperlipidemia, CKD: chronic kidney disease.				

Distribution of different parameters of ECG displayed in table 3. Assessing ECG parameters in conduction system disease in victims of COVID-19, ST-T changes, fragmented QRS, axis deviation, presence of S1Q3T3, and poor R wave progression were significantly related to conduction system disease in victims of COVID-19 (P-value > 0.05)

Table3. ECG parameters in conduction system disease in victims of COVID-19

ECG parameters prevalence		Patients without HPD (N=317)	Patients with HPD (N=108)	P value
Fragmented QRS	Yes	53 (58.2)	38 (41.8)	<0.001
	No	268 (78.6)	73 (21.4)	
ST-T change	Yes	125 (66.1)	64 (33.9)	0.001
	No	196 (80.7)	47 (19.3)	
Rhythm	Sinus rhythm	279 (76.2)	87 (23.8)	0.095
	AF	34 (63.0)	20 (37.0)	
	others	8 (66.7)	4 (33.3)	
Rate	Bradycardia (HR<60)	5 (55.6)	4 (44.4)	0.069
	Normal (60<HR<100)	234 (72.4)	89 (27.6)	
	Tachycardia (HR>100)	82 (82.0)	18 (18.0)	
Axis deviation	Normal	283 (83.7)	55 (16.3)	<0.001
	Left	14 (48.3)	15 (51.7)	
	Right	24 (36.9)	41 (63.1)	
QTc 1	<500	211 (75.1)	70 (24.9)	0.728
	>500	110 (73.3)	40 (26.7)	
QTc 2	Male AND >440	300 (74.4)	103 (25.6)	0.999
	Female AND >460	21 (75.0)	9 (25.0)	
QTd	<28	276 (73.2)	101 (26.8)	0.190
	>28	45 (81.8)	10 (18.2)	
J wave	Yes	13 (68.4)	6 (31.6)	0.592
	No	308 (74.6)	105 (25.4)	

U wave	Yes	32 (71.1)	13 (28.9)	0.592
	No	289 (74.7)	98 (25.3)	
Early repolarization	Yes	15 (83.3)	108 (26.1)	0.581
	No	306 (73.9)	108 (26.1)	
T slope	<30	12 (75.0)	4 (25.0)	0.714
	30-60	302 (74.6)	103 (25.4)	
	>60	7 (63.6)	4 (36.4)	
S1Q3T3	Yes	38 (61.3)	24 (38.7)	0.018
	No	283 (76.5)	87 (23.5)	
Low voltage QRS	Yes	42 (85.7)	7 (14.3)	0.057
	No	279 (72.8)	104 (27.2)	
PRP	Yes	121 (68.4)	56 (31.6)	0.025
	No	200 (78.4)	55 (21.6)	
MI: Myocardial Infarction, AVB: Atrioventricular block, LVH: left ventricular hypertrophy, RVH: right ventricular hypertrophy, RBBB: right bundle branch block, LBBB: left bundle branch block, QTc: corrected Q-T interval, QTd: Q-T interval dispersion, T slope: T-wave terminal slope, PRP: Poor R wave Progression.				

DISCUSSION

Reviewing past literature, there is mounting evidence in support of the association between influenza pneumonia and heart diseases and it has been reported that influenza infections have been associated with a six-fold increased risk of acute MI (12, 13). It is likely that COVID-19 also, directly and indirectly, affects the cardiovascular system and the heart in particular (14). This topic discusses the prevalence of arrhythmias and conduction system disease in patients with COVID-19.

Triggers of Arrhythmia in Coronavirus Disease 2019 have not been specified yet. However, potential reported triggers are as follows (15). First, electrolyte imbalance caused by complications of COVID-19 including diarrhea, acute kidney injury, or severe sepsis is the notable cause (16). Second, SARS-CoV-2-induced myocardial injury due to upregulation of ACE2 receptor during the viral invasion and severe hypoxia-induced myocyte necrosis is another potential cause of arrhythmias (17). Besides, acute myocardial infarction due to demand/supply imbalance and arterial thrombotic event secondary to hypercoagulable state can cause acute arrhythmias (18-21). In addition, Stress-induced cardiomyopathy owing to physiological stress and cytokine storm about sepsis and high inflammatory state is another potential mechanism triggering arrhythmias (15, 22-24). Moreover, prolonged QTc-inducing malignant ventricular arrhythmias and channelopathies induced by off-label medical therapy and antiviral therapy could be introduced as direct triggers of arrhythmias (25-29).

The most remarkable result to emerge from the data was the prevalence of advanced AVB in victims of COVID-19. This prevalence was not yet assessed in expired CPVID-19 patients however, the reported range of prevalence of AVB in COVID-19 patients was from 3 to 12 percentages in different articles (8, 30). All types of AVBs were 40(9.3%) prevalent in our study. Among those with AV block, 12(2.8%) cases suffered from third-degree (Complete Heart Block). CHB has been assumed to be a rare ECG feature of COVID-19 and this novel finding was only been reported in a few case studies (31-33).

Another interesting result was the high prevalence of fragmented QRS, prominent J wave, and ST-T wave change. These parameters can be directly related to myocardial injury induced by SARS-CoV-2 infection. In addition, the high incidence of S1Q3T3 and LBBB in this study could be an indicator of pulmonary involvement in COVID-19 victims. S1Q3T3 is a relatively specific pattern for pulmonary thromboembolism and a potential cause of death (21, 34-37).

Moreover, assessing ECG parameters in conduction system disease in victims of COVID-19, ST-T changes, fragmented QRS, axis deviation, presence of S1Q3T3, and poor R wave progression were significantly related to conduction disease in victims of COVID-19. possible suggestive of new-onset myocardial infarctions during the infection, increasing the risk of mortality (38-40). This may indicate that COVID-19 adversely affects cardiac myocardial tissue more than how it was taken for granted. Besides, our study provides further evidence for the observed ST-T waves changes in COVID-19 patients, suggestive of myocardial infarction or localized myocarditis (41, 42).

In line with previous studies, the most prevalent arrhythmia was atrial fibrillation (43, 44). It is alerting that we witnessed these findings in patients who had no evidence of arrhythmia before their admission. Therefore, we suggest future studies scope on the mechanism of arrhythmogenicity of COVID-19.

LIMITATIONS

This is a single-center study, conducted retrospectively. Unfortunately, assessing the presence of myocarditis was not possible due to the absence of data on serum markers and echocardiographic examination for most of our enrolled patients.

CONCLUSION

To the best of our knowledge, this study is the first study that exclusively assessed expired COVID-19 patients and cleared AVB prevalence among them. Our findings can serve in future studies that aim to develop a risk stratification method for susceptible COVID-19 patients. The myocardial injury appears to role significantly in COVID-19 morbidity and mortality. Consequently, we recommend health policymakers consider separate catheterization laboratories that provide service only to COVID-19 patients.

ABBREVIATIONS

Abbreviations COVID-19: Coronavirus; ECG: Electrocardiogram; SUMS: Shiraz University of Medical Sciences; BBB: Bundle branch block; PRP: Poor R wave progression; fQRS: Fragmented QRS; STEMI: ST-segment elevation myocardial infarction; AVB: Atrioventricular conduction block; T slope: Slop of the terminal part of T wave; QTc: Corrected QT; QTD: QT dispersion; HTN: Hypertension; DM: Diabetes Mellites; IHD: Ischemic heart disease; CKD: Chronic kidney disease.

DECLARATIONS

Ethics approval and consent to participate

Written informed consent was obtained from the patients in our study. The purpose of this research was completely explained to the patient and was assured that their information will be kept confidential by the researcher. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the ethical committee of Shiraz University of Medical Sciences.

Availability of data and materials

Written informed consent was obtained from the patients regarding the publication of this study. There is no identifying information in this article.

Competing interests

The authors declare that they have no competing interests.

Informed Consent

Written informed consent was obtained from the patients. A copy of the written consent is available for review by the Editor of this journal.

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