Conduction System Disease and Atrioventricular Block in Victims of COVID-19 in Iran

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Abstract

Background

More recently, a growing body of literature on COVID-19 has investigated the electrophysiological issues presetting as a disease manifestation of COVID-19 and highlight the spectrum of arrhythmias observed in patients with COVID-19 infection. This Study discuss the prevalence of arrhythmias and conduction system disease in patients with COVID-19.

Method

electrocardiographic data and comorbidity data of 432 expired COVID-19 patients admitted to Faghihi Hospital of Shiraz University of Medical Sciences from August 1st until December 1st were reviewed.

Results

AVB was found in 40(9.3%) patients. 28(6.5%) of the patients suffered from 1st degree AVB, and 12(2.8%) suffered from CHB. Changes in ST-T wave compatible with myocardial infarction or localized myocarditis appeared in 189(59.0%) patients. Findings compatible with myocardial injury such as fragmented QRS, and prolonged QTc were assessed with prevalence of 21.1% (91 patients), 6.5% (28 patients). In victims of COVID-19, conduction disease was not related to any underlying medical condition. 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, Table 3)

Conclusion

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

Introduction

In December 2019, a cluster of pneumonia cases was reported in Wuhan, Hubei province, China, caused by a novel coronavirus, SARS-CoV-2, that triggered the respiratory infection, COVID-19. Due to the rapid transmission rate of COVID-19, WHO declared a pandemic on March 11th, 2020 [1].

The first studies of COVID-19 considered it to be predominantly a respiratory disease. However, more recent evidence highlights multiple organ system involvements in COVID-19 patients, including coagulation system disorder, acute kidney injury, hepatocellular injury, and cardiac and central nervous
system complications [2]. The cardiac complications include thromboembolic events, heart failure, heart block, acute coronary syndrome, myocarditis, arrhythmias, and sudden cardiac death [3].

More recently, a growing body of literature on COVID-19 has investigated the electrophysiological issues presetting as a disease manifestation of COVID-19 and highlight the spectrum of arrhythmias observed in patients with COVID-19 infection [4]. Moreover, multiple case reports introduce atrioventricular block as a potential manifestation of COVID-19 [5–13]. In a retrospective study about the prognostic significance of electrocardiography findings in patients with COVID-19, T-wave change (31.7%), QTc interval prolongation (30.1%), and arrhythmias (16.3%) were three most common found ECG abnormalities and atrioventricular block were presented in 3.9% of the patients [14]. First-degree atrioventricular block (AVB) was seen in 10 patients (3.3%) and second degree AVB Mobitz type I was found in 2 patients (0.7%). In-hospital mortality risk increased with increasing abnormal ECG scores. [14] In another study investigating 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 these patients, 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 [15]. 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 1st until December 1st. The inclusion criteria were all the admitted patients with age > 18. 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 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 collected from by six independent practitioners. ECGs interpreted by two cardiologists blinded to the patients’ information and confirmed by an electrophysiologist. Cardiologists interpreted ECGs Basic ECG 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 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). 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) and with age range of 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) was noticed in 100 (23.1%) and 9 (2.3%) patients respectively. 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. 28(6.5%) of the patients suffered from 1st degree AVB, and 12(2.8%) suffered from CHB. Changes in ST-T wave compatible with myocardial infarction or localized myocarditis appeared in 189(59.0%) patients. Other conduction system abnormal findings were Bundle Branch Blocks (BBB). Left bundle branch block was seen in 25 (5.8%) patients and right bundle branch block was seen in 50 (11.6%) patients. Moreover, findings compatible with pulmonary diseases such as S1Q3T3, poor R progression, Axis deviations, and low voltage ECG were reviewed and the prevalence were 14.4% (62 patients), 41.0% (177 patients), 21.7% (94 patients) and 11.3 (49 patients) respectively. Findings compatible with myocardial injury such as fragmented QRS, and prolonged QTc were assessed with 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 reviewed with prevalence of 4.4% (19 patients), 1.2% (5 patients) and 4.2% (18 patients) (Table 1)
Evaluating the association of patients’ medical conditions and conduction system disease in victims of COVID-19, conduction disease was not related to any underlying medical condition. (Table 2)

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, Table 3)

**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 six-fold increased risk of acute MI [16, 17]. It is likely that COVID-19 also directly and indirectly affects the cardiovascular system and the heart in particular [3]. This topic discuss the prevalence of arrhythmias and conduction system disease in patients with COVID-19.

Triggers of Arrhythmia in Coronavirus Disease 2019 have not yet been specified yet. However, potential reported triggers are as follows [18]. First, electrolyte imbalance caused by COVID-19 symptoms such as diarrhea and complications such as acute kidney injury or severe sepsis are notable causes [19]. Second, SARS-CoV-2-induced myocardial injury due to upregulation of ACE2 receptor during viral invasion and severe hypoxia-induced myocyte necrosis are another potential causes on arrhythmias [20]. Besides, acute myocardial infarction due to demand/supply imbalance and arterial thrombotic event secondary to hypercoagulable state can cause acute arrhythmias [21, 22]. In addition, Stress-induced cardiomyopathy owing to physiological stress and cytokine storm in relation to sepsis and high inflammatory state is another potential mechanism triggering arrhythmias [18]. 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 [23].

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 [13, 14]. All types of AVBs were 40(9.3%) prevalent in our study. Among those with AV block, 12(2.8%) cases suffered from 3rd 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 [5, 7, 9].

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, 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 [24].

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. This may indicate that COVID-19 adversely affects cardiac myocardial tissue more than how it was taken as 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 [25].

Compatible with previous studies, the most prevalent arrhythmia was atrial fibrillation [26]. 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.

**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. Myocardial injury appears to role significantly in COVID-19 morbidity and mortality. Consequently, we recommend health policymakers to consider separate catheterization laboratories that provide service only to COVID-19 patients.

**Limitations**

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

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**Authors’ contributions**

MHN, STH, SA, AA contributed in analyzed the data, and interpreted the results, wrote the manuscript drafting. MHN, STH contributed in interpretation the results and designed the study. NDE, AM, FM, OM, HE, and MT contributed in interpretation the results wrote the manuscript drafting. All authors have read and approved the manuscript.

**Ethics approval and consent to participate**

This study was approved by the ethics committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1400.270). All methods were performed in accordance with the relevant guidelines and regulations.

**Availability of data and materials**

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Tables**

**Table 1.** 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    |
|                  | Yes | No |        |
|------------------|-----|----|--------|
| **U wave**       | 45  | 387| 10.4   |
| **Brugada pattern** | 5   | 427| 1.2    |
| **Early repolarization** | 18  | 414| 4.2    |
| **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.** 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.

**Table 3.** 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.