INAL RESEARCH PAPER IANGES IN PATIENTS WITH COVID-19 – OSPECTIVE OBSERVATIONAL STUDY AT IARY CARE HOSPITAL IN CHENNAI	General Medicine KEY WORDS: ECG, COVID-19, CVD					
OSPECTIVE OBSERVATIONAL STUDY AT						
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Background: A global outbreak of corona virus disease, caused by severe respiratory corona virus 2, has emerged since December 2019. However electrocardiographic manifestations of patients with COVID-19 have not been fully described. We aim to investigate ECG characteristics in COVID-19 patients and risk factors of ICU admission

Methods: This retrospective observational study included the patients with COVID-19 at the Government Kilpauk Medical College, Chennai between June 1st and 31st, 2020. Demographic, clinical and ECG characteristics were ABSTRACT collected and comparison were made between ICU and non ICU admission groups. Logistic regression was used to identify risk factors of ICU admission

Results: Among the 159 patients included ST-T abnormalities were the most common ECG feature followed by

arrhythmias. Compared with non ICU group, the ICU group showed higher heart rate and P wave duration and was more frequently associated with CVD, ST-T abnormalities, arrythmias, QTc prolongation and pathological Q waves. ST-T abnormalities and history of CVD were associated with increased risk of ICU admission

Conclusion:COVID-19 is frequently related to cardiovascular manifestations including ECG abnormalities and cardiovascular comorbidities. ST-T abnormalities and CVD at admission were associated with increased odds of ICU admission

INTRODUCTION

Corona virus disease 2019 is a disease caused by SARS Coronavirus-2 infection and its considered as a public health emergency of international concern and causing the current pandemic around the world. This virus utilizes the Angiotensin Converting Enzyme-2 as a functional receptor for cellular entry. Research demonstrates various tissues including the myocardium of heart, express the ACE-2 protein on their cellular surface. This protein has described roles in the heart function and pathophysiology of diabetes mellitus and hypertension. SARS CoV-2 might use this entry as a trajectory to invade myocardial cells and damage them. Related studies suggest other mechanisms for the perceived cardiac injury including cytokine storms and hypoxemia. Cardiac injuries correlate with a more detrimental outcome in patients with COVID-19 thus requiring adequate attention. In this study we aimed to provide the clinicians and researchers with an update on diverse patterns observed in the ECG of COVID-19 patients. Here we retrospectively investigated the patients with COVID-19 in Government Kilpauk Medical College, Chennai and described the features of ECG and identified the risk factors of admission to intensive care unit

METHODS

Patients

We retrospectively included the patients with confirmed COVID-19 admitted to Government Kilpauk Medical college, Chennai from June 1^{st} to 31^{st} , 2020.Definition of the case was based on COVID-19 guidelines of National center for disease control requiring RNA detection of the novel corona virus in nasopharyngeal swab samples and computed tomographic evidence of pulmonary involvement. The baseline characteristics were recorded on admission including age, gender, symptoms, medication history, cardiovascular comorbidities, heart rate and blood pressure. Those patients with falling oxygen saturation and progressive pulmonary

involvement were admitted to ICU

ECG COLLECTION

12 lead electrocardiogram and laboratory investigations were the main observation parameters. The criteria of parameter measurement and ECG diagnosis are based on the recommendation of American Heart Association(AHA/ACCF/HRS -2007 TO 2009). ST-T abnormalities were defined as the following criteria 1) Abnormalities in the ST segment : the ST segment was measured 80ms after the J point and significant change was described as ST segment depression >0.05mv or ST segment elevation >0.10 mv in limb leads and or >0.20 mv in chest leads 2) T wave abnormalities: high and sharp T wave: the peak of T wave >0.5mv in limb leads and >1'5mv in chest leads, low and flat T wave: the peak of T wave was < 0.1 mv in limb leads or < 0.2 mv in chest leads , bidirectional T waves, inversed T waves (inversion depth > 0.1 mv). Secondary ST-T changes caused by intraventricular conduction block, ventricular pre excitation and ventricular pacing rhythm were not included. QT interval was measured between the earliest ventricular depolarization point and the latest T wave ending point. QT interval prolongation was defined as corrected QT interval was > 450ms in male and >460ms in female. Each measurement and diagnosis were thoroughly checked by two independent experienced cardiologist

STATISTICAL ANALYSIS

Categorical variables frequency rates with percentages and continuous variables were described using median and interquartile range values. After the normal distribution test, Mann Whitney U test, chi square test were used to compare differences between ICU group and non ICU group, p value < .05 was considered statistically significant. All statistical analysis were calculated by statistical package for social sciences

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RESULTS

1.Baseline characteristics A total of 159 hospitalized patients with COVID-19 were included in this analysis. Forty eight patients were admitted or transferred to ICU since the aggravation of infection. Six patients died during hospitalization. The median age of 159 patients was 64 years (IQR - 48 - 72). About 45% patients had cardiovascular diseases. Hypertension(32%), diabetes(15%) and coronary artery disease(8%) were the most common comorbidities. Compared with patients who were not admitted to ICU (n=111), patients who received ICU care(n=48) were significantly older (70 years [55-75] vs 64 [47-67] and were more

			Total	I	ICU	Non ICU	
Ana Madicu		(n=159)		(n=48)	(n=111)	value	
Age, Median (IQR), Years		64(48 –72)		71(55- 76)	64(47-69) 0.037	
Male			81 (51)		35 (74)	46(41.4)	
Cardiovascular comorbidity			71 (45)		37(78)	24 (22)	<.001
Hypertension			51 (32)		20 (43)	31(27.9)	0.221
Diabetes			23(15)		10 (22)	13(11.7)	0.481
Hyperlipidemia			2 (1.5)		1 (4.3)	1 (0.9)	0.313
Coronary heart			12 (8)		10(22)	2 (1.8)	0.028
disease							
Previous myocardial infarction			2 (1.5)		0	2 (1.8)	>.999
Stroke			8 (5.2)		5 (10.4)	3 (2.7)	0.017
Previous PCI			8 (5.2)		5 (10.4)	3 (2.7)	0.017
	procedure			_			
Permanent pacemaker			2 (1.5)		0	2 (1.8)	>.999
Medication		r ß	4 (3.0)	+	1 (2)	3 (2.7)	0.531
receptor bl		чЧ			· (4)	0 (2.1)	0.001
Calcium ch			23 (15)	+	10 (22)	13 (11.7)	0.178
blocker	annor		10 (10)		10 (11)	10 (11.1)	0.110
ACEIs/ARB	s		14 (9)		4 (8.3)	10 (9)	>.999
Oral antidia	abetic		17 (11)	-	6 (12.5)	11(9.9)	>.999
agents							
Antiplatelet agents			6 (4.4)		2 (4.1)	4 (3.6)	<.999
		Tota	al	N	on ICU	ICU	р
		N =	159	N	/ = 111	<i>N</i> = 48	-value
ECG evalua	ation	110		10	08	110	-value 0.3
ECG evalua P wave dur		110	159 -116)	10			
		110 (101		10 (1 28	08 102-117) B	110	
P wave dur ST-T Abnormali	ation ties	110 (101 64(4	l-116) l6.5%)	10 (1 28 (2	08 102-117) 8 25.2%)	110 (92-111)	0.3
P wave dur ST-T	ation ties	110 (101 64(4	-116)	10 (1 28 (2 74	08 102-117) 8 25.2%) 4	110 (92-111) 36(75%) 82	0.3
P wave dur ST-T Abnormalii HR, ,bpm (l	ties IQR)	110 (101 64(4 76(6	1-116) 16.5%) 35–84)	10 (1 28 (2 74 (6	08 102-117) 8 25.2%) 4 85-80)	110 (92-111) 36(75%) 82 (73-95)	0.3 0.01 0.001
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block	ties IQR) ee AV	110 (101 64(4 76(6 7(4.	1-116) 16.5%) 65–84) 4%)	10 (1 (2 (2 74 (6 4)	08 102-117) 8 25.2%) 4 35–80) (3.6%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%)	0.3 0.01 0.001 0.4
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl	ties IQR) ee AV	110 (101 64(4 76(6 7(4.	1-116) 16.5%) 35–84)	10 (1 (2 (2 74 (6 4) 92	08 102-117) 3 25.2%) 4 55–80) (3.6%) 2	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96	0.3 0.01 0.001
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl msec	ties IQR) ee AV lex,	110 (101 64(4 76(6 7(4. 94(8	4%) 47–104)	10 (1 (2 (2 74 (6 4) 92 (8	08 102-117) 3 25.2%) 4 55-80) (3.6%) 2 36-104)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103)	0.3 0.01 0.001 0.4 0.2
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl	ties IQR) ee AV lex,	110 (101 64(4 76(6 7(4.	4%) 47–104)	10 (1 (2 (2 74 (6 4) 92 (8	08 102-117) 3 25.2%) 4 55–80) (3.6%) 2	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96	0.3 0.01 0.001 0.4
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl msec Abnormal (ties IQR) ee AV lex,	110 (101 64(4 76(6 7(4. 94(8 8(5.)	4%) 47–104)	10 (1 28 (2 74 (6 4) 92 (8 3)	08 102-117) 3 25.2%) 4 55-80) (3.6%) 2 36-104)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103)	0.3 0.01 0.001 0.4 0.2
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl msec Abnormal o wave	ties IQR) ee AV lex,	110 (101 64(4 76(6 7(4. 94(8 8(5.) 12(7	1-116) 46.5%) 35–84) 4%) 37–104) 0%)	10 (1 (2 (2 7 (6 4) (1 9) (8 (3) (1) (8) (7)	08 02-117) 8 55.2%) 4 55–80) (3.6%) 2 36–104) (2.7%) (7.2%) (6.3%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%)	0.3 0.01 0.001 0.4 0.2 0.04
P wave dur ST-T Abnormalii HR, ,bpm (J First-degre block QRS compl msec Abnormal o wave L AFB	ties IQR) ee AV lex,	110 (101 64(4 76(6 7(4. 94(8 8(5.) 12(7	1-116) 16.5%) 55-84) 4%) 37-104) 0%) 7.5%) 3.9%)	10 (1 (2 (2 7 (6 4) (1 9) (8 (3) (1) (8) (7)	08 02-117) 8 55.2%) 4 55-80) (3.6%) 2 36-104) (2.7%) (7.2%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%)	0.3 0.01 0.001 0.4 0.2 0.04 0.8
P wave dur ST-T Abnormalit HR, ,bpm (l First-degre block QRS compl msec Abnormal (wave L AFB RBBB	ties IQR) ee AV lex,	110 (101) 64(4 76(¢ 7(4. 94(8 8(5.) 12(7 11(¢ 5(3.) 410	1-116) 16.5%) 55-84) 4%) 37-104) 0%) 7.5%) 5.9%) 1%)	10 (1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B 35.2%) 4 358-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 4(8.3%) 2(4.2%) 398(366-	0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6
P wave dur ST-T Abnormali HR, ,bpm (1 First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB QT, msec	ties IQR) ee AV lex,	110 (101) 64(4 76(€ 7(4. 8(5. 12(7 11(€ 5(3. 410 (380)	1-116) 16.5%) 55-84) 4%) 37-104) 0%) 7.5%) 3.9%)	10 (1 (2 (2 74 (6 4) (8) (3) (3) (3) (3)	D8 0.02-117) B \$5.2%) 4 \$5-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17 885-440)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 4(8.3%) 2(4.2%) 398(366- 4 40)	0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6 0.6 0.09
P wave dur ST-T Abnormali HR, ,bpm (J First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB	ties IQR) ee AV lex,	110 (101) 64(4 76(€ 7(4. 8(5. 12(7 11(€ 5(3. 410 (38) 422	1-116) 16.5%) 55-84) 4%) 37-104) 0%) 7.5%) 5.9%) 1%)	1((1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B 35.2%) 4 358-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 4(8.3%) 2(4.2%) 398(366-	0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6 0.6
P wave dur ST-T Abnormali HR, ,bpm (1 First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB QT, msec	ation ties IQR) ee AV lex, Q	110 (101) 64(4 76(6 7(4. 8(5. 12(7) 11(6 5(3. 410 (380) 4452 (432)	1-116) 16.5%) 155-84) 4%) 37-104) 0%) 7.5%) 3.9%) 1%) 0-4 40)	1((1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B \$5.2%) 4 \$55-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17 385-440) 50(433-74) 1	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 4(8.3%) 2(4.2%) 398(366-440) 458	0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6 0.6 0.09
P wave dur ST-T Abnormali HR, ,bpm (1 First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB QT, msec Qtc, msec	ation ties IQR) ee AV lex, Q	110 (101) 64(4 76(6 7(4. 94(8 8(5.) 112(7 11(6 5(3.) 410 (380) 452 (432) 74(4	I-116) I6.5%) S5-84) 4%) 37-104) 0%) 7.5%) S.9%) 1%) D-4 40) E-475) I6.5%)	1((1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B \$5.2%) 4 \$5-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 1885-440) 50(433-74) 1 155.0%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 4(8.3%) 2(4.2%) 398(366- 440) 458 (431-484) 13 (27.1%)	0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6 0.09 0.4
P wave dur ST-T Abnormali HR, ,bpm (1 First-degre block QRS compl msec Abnormal 0 wave L AFB RBBB LBBB QT, msec Qtc, msec	ation ties IQR) ee AV lex, Q	110 (101) 64(4 76(6 7(4. 94(8 8(5.) 112(7 11(6 5(3.) 410 (380) 452 (432) 74(4	1-116) 16.5%) 55-84) 4%) 37-104) 0%) 7.5%) 5.9%) 1%) 0-4 40) 2-475)	1((1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B 35.2%) 4 355-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17 385-440) 50(433-74) 1 35.0%) 0(110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 2(4.2%) 398(366- 440) 458 (431-484) 13 (27.1%) 35(0.3 0.01 0.001 0.4 0.2 0.04 0.8 0.6 0.09 0.4
P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB QT, msec Qtc, msec Normal EC	ation ties IQR) ee AV lex, Q	110 (101) 64(4 76(6 7(4. 8(5. 8(5. 12(7) 11(6 5(3. 410 (380) (432) 74(4 85(5)	I-116) I6.5%) S5-84) 4%) 37-104) 0%) 7.5%) 3.9%) 1%) 0-4 40) 2-475) I6.5%) 33.5%)	10 (1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2	D8 0.02-117) B \$5.2%) 4 \$55-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17 385-440) 50(433-74) 1 \$5.0%) 0(5.0%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 2(4.2%) 398(366- 440) 458 (431-484) 13 (27.1%) 355 (72.9%)	0.3 0.01 0.001 0.4 0.2 0.04 0.6 0.09 0.4 0.001
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P wave dur ST-T Abnormalii HR, ,bpm (l First-degre block QRS compl msec Abnormal (wave L AFB RBBB LBBB QT, msec Qtc, msec Normal EC	ation ties IQR) ee AV lex, Q Q C G ECG	110 (101) 64(4 76(¢ 7(4. 8(5. 12(7 11)(¢ 5(3. 410 (380) (432) 74(4 85(5) 74(4) 85(5) 13(§	I-116) I6.5%) S5-84) 4%) 37-104) 0%) 7.5%) 3.9%) 1%) 0-4 40) 2-475) I6.5%) 33.5%)	10 (1) (2) (2) (2) (4) (4) (4) (5) (5) (4) (5) (5) (5)	D8 0.02-117) B \$5.2%) 4 \$55-80) (3.6%) 2 36-104) (2.7%) (6.3%) (2.7%) 17 385-440) 50(433-74) 1 \$5.0%) 0(5.0%)	110 (92-111) 36(75%) 82 (73-95) 3(6.3%) 96 (90-103) 5(10.4%) 4(8.3%) 2(4.2%) 398(366- 440) 458 (431-484) 13 (27.1%) 355 (72.9%)	0.3 0.01 0.001 0.4 0.2 0.04 0.6 0.09 0.4 0.001



DISCUSSION

This retrospective study revealed the ECG characteristics in patients with COVID-19. In our study we found that ST-T abnormalities were the most prominent ECG manifestation among the patients with COVID-19. The ST segment elevation in COVID-19 patients is mainly due to obstructive/non obstructive coronary diseases, myocarditis, pericarditis or stress cardiomyopathy(Dehghani et al., 2020; Inciardi et al., 2020). However the exact reasons for the other nonspecific ST-T abnormalities remain unclear. Infection mediated myocardial injury and prior cardiovascular abnormalities may contribute

Cardiac arrythmias were the second commonest ECG finding and should be taken seriously because some arrythmias can be life threatening. Recent studies have shown fatal arrhythmias including complete heart block, polymorphic ventricular tachycardia and ventricular fibrillation in patients with COVID-19(Kochav et al., 2020; Kir et al., 2020; Guo et al., 2020). The high prevalence of arrhythmias may be attributed to metabolic disorders, hypoxia, neurohormonal imbalance or inflammatory reaction in patients with or without prior cardiovascular disease

Although QTc prolongation was more common in ICU group there was no significant difference in values in our cohort. Drugs for treating COVID-19 were regarded as the main cause of QTc prolongation and this effect may be amplified when multiple QT prolonging drugs were used in combination. Hydroxychloroquine, lopinavir/ritonavir, and azithromycin have been confirmed to prolong the QTc interval in patients with COVID-19. Moreover some inflammatory factors (TNF-[], IL-6) and electrolyte imbalance may potentially contribute to this process. Abnormal Q wave often indicated myocardial necrosis or stun, which maybe caused by myocarditis and were associated with poor prognosis

Finally ECG changes during admission cannot be ignored or may be even more important. Although we did not re-examine the ECG for all patients because to minimize exposure of health care workers, ECG changes were observed in more than 60% of patients

CONCLUSION

The novel findings of this study are the cardiovascular disease comorbidities and ECG abnormalities were not uncommon in patients with COVID-19 and some of which are life threatening. History of cardiovascular disease and ST-T abnormalities were associated with increased odds of ICU admission. The ECG is a simple and useful screening tool which can help us promptly assess the cardiac complications while avoiding adverse cardiac events during admission

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6

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