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Original Article

Internal Medicine Section

Electrocardiographic Changes among Moderate and Severe COVID-19 Patients in a Tertiary Care Teaching Hospital at Shahdol, Madhya Pradesh, India: A Record-based Study

RUPESH KUMAR GUPTA[1], JEETENDRA SHARMA[2], ROOPA AGRAWAL[3], RUPESH SAHU[4], SANTENNA CHENCHULA[5], PRADEEP KUMAR PATHAK[6]

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ABSTRACT

Introduction: Electrocardiographic (ECG) abnormalities in Coronavirus Disease 2019 (COVID-2019) patients are largely unknown. ECG changes in COVID-19 disease may guide to initiate therapeutic anticoagulation, more so in moderate and severe disease.

Aim: To identify various ECG changes in moderate and severe COVID-19 patients and to ascertain the association between initial ECG changes and disease outcome.

Materials and Methods: This was retrospective record-based study was conducted in the Department of Internal Medicine, Birsa Munda Medical College, Shahdol, Madhya Pradesh, India, on 216 patients with laboratory-confirmed COVID-19 in a tertiary care teaching hospital from March 2021 to June 2021. Demographic and clinical data including ECG were extracted from medical records of the patients and if needed, the patients were followed-up till outcome. COVID-19 disease severity was considered based on oxygen saturation at room air (moderate: 94%-90%; severe: <90%). Data were entered using the Epicollect5 mobile application to minimise errors.

Results: A total of 216 patients were included (35 to 54 years), the majority were male. Mortality rate was 46.3%. Total 57.4% of ECG changes were classified as abnormal. Sinus tachycardia was the most common abnormality followed by ischaemic changes. Left axis deviation in ECG was more commonly seen than right axis deviation. Total 53.2% of patients with abnormal ECG findings and 36.9% with normal ECG findings died. Mortality was very high in patients with ischaemic changes.

Conclusion: COVID-19 patients with ischaemic changes in ECG were significantly associated with increased mortality. Hence, early detection of these changes in COVID-19 patients is vital and will help primary care physicians to intervene early and help in deciding therapeutic anticoagulation requirements in patients with COVID-19.

Keywords: Coronavirus disease 2019, Ischaemic changes, Oxygen saturation, Therapeutic anticoagulation

INTRODUCTION

Being first reported in December 2019, COVID-19 infection caused by the Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) virus, increased in numbers dramatically throughout the world forcing World Health Organisation (WHO), to declare it as a global pandemic. With the start of the second wave in India, it has been very clear that mortality in COVID-19 infection is highly associated with comorbidities and multiorgan involvement. In a study of COVID-19 patient, it had been shown that in hospital mortality was very high with cardiovascular involvement [1]. A wide range of cardiovascular events such as myocardial injury, acute coronary syndromes, cardiac arrhythmias, and heart failure are associated with COVID-19 [2,3].

In a study comprising 138 hospitalised COVID-19 patients, cardiac injury was reported in 7.2% of patients [4]. Increased expression of Angiotensin converting enzyme 2 (ACE 2) receptors in cardiac pericytes, cardiac myocytes apoptosis caused by loading of intracellular calcium due to hypoxia and excessive release of various cytokines were probable mechanism of cardiac injury in COVID-19 [5]. The best, non invasive and cost-effective tool to detect earlier cardiac involvement in COVID-19 is ECG changes. Earlier studies had already described various ECG abnormalities in viral illnesses. ECG changes noticed during Swine flu (H1N1) 2009 pandemic were for short period of time and these changes were not related to patient's earlier conditions or further outcome [6]. Uptill today, no significant ECG abnormalities have been explained in COVID-19 patients. Still today incidence and prevalence of ECG abnormalities in COVID-19 patients is not known [7]. ECG changes in COVID-19 may also guide us to initiate therapeutic anticoagulation. As guidelines suggest that, therapeutic anticoagulation is reserved for patients who developed features of thromboembolism (like raised D dimer levels), hence, signs of ischaemia and/or infarction in ECG may guide us to initiate therapeutic anticoagulation [8]. Knowledge of early ECG changes will enable the primary care physician to become alert for upcoming possible catastrophe. The present study was conducted with objectives to identify various ECG changes in moderate and severe COVID-19 patients and to ascertain the association between initial ECG changes and disease outcome.

MATERIALS AND METHODS

The present study was designed as retrospective record-based study conducted in the Department of Internal Medicine, Birsa Munda Medical College, Shahdol, Madhya Pradesh, India. Data was collected from 1st March 2021 to 30th June 2021. Analysis time period Feb 2022 to May 2022. Study was approved by Institutional Ethics and Review committee (IERC/21/09/02). The study has been conducted in accordance with the ethical principles mentioned in the Declaration of Helsinski (2013).

Inclusion criteria: Patients tested positive for SARS-CoV-2 on Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) with moderate or severe disease, having ECG recorded early at admission, at an associated hospital of Government medical college were included. Informed consent was taken from all the participants.

Exclusion criteria: Those not consenting were excluded. The authors did not put any stringent exclusion criteria, so as to avoid bias and increase generalisability.

Sample size calculation: Sample size was calculated using formula for estimation of proportion. Since the disease was new at the time of study, there was not enough data on ECG changes, hence, through consultation with senior consultants and an intelligent guess, authors expected 15% abnormal ECG findings among the moderate to severe COVID-19 patients. With 95% confidence, 5% absolute precision and adding 10% for non response, the final sample size was calculated to be 216. Universal sampling was done. The authors collected data for 216 important subjects.

Study Procedure

From the hospital records, data was abstracted for patients satisfying inclusion criteria. Data was abstracted in data abstraction form having concerned variables. Data was entered at the time of data collection itself by the consultants, with the help of the Epicollect5 mobile application to minimise errors of data entry. Primary outcome variable was whether the patient was discharged from the hospital or died. If the patient leaves the hospital without any information, it is considered as considered 'Discharged Against Medical Advice' (DAMA). The authors have counted 'DAMA' patients under 'discharged' for analysis. Other variables include age, gender, symptoms with duration, clinical data (SpO_2, Pulse, Systolic and Diastolic BP) and ECG analysis (as described below) was done. Primary source of data was hospital records. The outcomes as documented in the records were taken and those still in the hospital were followed-up until either discharge or death in the hospital (outcome). Those patients with oxygen saturation between 93%-90% at room air were considered as having moderate disease and those with less than 90% at room air were considered as having severe COVID-19 disease [9].

Electrocardiographic (ECG) analysis: All 12-lead electrocardiograms recorded as early as possible after admission (as standard protocol 1 millivolt equals to 10 millimeters and speed of ECG paper will be 25 mm/s) then offline analysis was done [10]. ECG was evaluated by consultants from the internal medicine department. The considered parameters were rate, rhythm (sinus, supraventricular or ventricular), QTc (using Bazett formula), various conduction abnormalities like atrioventricular block, bundle branch block, or fascicular block and ST-T segment deviation. Height difference (in millimetres) was measured between baseline TP segment and J point as ST segment alterations. In the proper clinical context, ST-segment Elevation Myocardial Infarction (STEMI) is considered when at least two contiguous leads with ST-segment elevation ≥2 mm in men or ≥1.5 mm in women in chest leads and/or ≥1 mm in the other leads. Non ST Segment Elevation Myocardial Infarction (NSTEMI) is considered with depression of similar measurement along with chest pain and/or positive cardiac biomarker, if available. T wave was considered normal if voltage ≥0.1 mV and remained upright in all leads except in lead III, aVR and V1. Abnormal Q waves were considered when its depth was >25% of QRS complex or >2 mm depth below isoelectric line or >40 ms width [11]. Left Ventricular Hypertrophy (LVH) was labelled when it follows Sokolow-Lyon criteria (depth of S wave in V1+height of R wave in V5 or V6 ≥35 mm or height of R wave in aVL ≥11 mm) [8]. Electrocardiogram was considered abnormal, if any of the following changes like significant ST segment deviations, abnormal T wave, LVH, tachyarrhythmias or bradyarrhythmias. Patients with sinus rhythm without above described changes were considered as normal.

STATISTICAL ANALYSIS

Chi-square and Fischer's-exact test was used to analyse association between qualitative variables. Percentages and proportions were used as descriptive tools for categorical variables. Mean and standard deviations were used for describing numerical data. The p-value <0.05 was taken as being statistically significant. Analysis was done by MS Excel and Epi info 7.

RESULTS

In total, the authors studied 216 patients with complete clinical data and ECG changes. The authors excluded those with incomplete data. Descriptive statistics of the patient sample are explained in [Table/Fig-1]. The mean (SD) age of the study sample was 50.12 (13.8) years, ranged from 15 to 90 years. Median (IQR) age was 50 (39-60) years. About 62% (134/216) of the patients were male. The majority belonged to 35 to 64 years age group (154/216, 71.2%), and 37/134 (28.7%) males belonged to the middle age-group of 45 to 54 years in which the majority (25/82, 30%) of females were also present. Patients of extreme age group were very less in number in either gender.

Age group (in years)	Female	Percentage (%)	Male	Percentage (%)	Total (N)	Percentage (%)
15-24	2	2.44	0	0	2	0.93
25-34	8	9.76	16	11.94	24	11.11
35-44	15	18.29	34	25.37	49	22.69
45-54	25	30.49	37	27.61	62	28.70
55-64	15	18.29	28	20.90	43	19.91
65-74	10	12.20	17	12.69	27	12.50
75-84	4	4.88	02	1.49	6	2.78
85-94	3	3.66	0	0	3	1.39
Total	82	37.96	134	62.03	216	100

[Table/Fig-1]: Age and gender-wise distribution of study sample.

[Table/Fig-2,3] shows that nearly 70% (152/216) of patients in the sample belonged to the severe disease category and the rest 30% (64/216) were moderate disease. Out of 216 patients, a total of 100 (46.3%) patients died while 109 (50.5%) were discharged fairly from the hospital, whereas 3.2% (7/216) patients were considered DAMA. The authors have considered 'DAMA' patients as 'discharged' for analysis.

Outcome	Frequency (n)	Percentage (%)
Discharged	109	50.5
Discharged Against Medical Advice (DAMA)	7	3.2
Died	100	46.3
Grand Total	216	100

[Table/Fig-2]: Disease outcome wise distribution of study sample.

S. No.	Disease severity	Frequency (n)	Percentage (%)
1	Moderate disease	64	29.6
2	Severe disease	152	70.4
	Total	216	100

[Table/Fig-3]: Distribution according to disease severity.

[Table/Fig-4] summarises overall ECG changes in which 57.4% (124/216) (95% CI 50.52%-64.09%) were classified as having abnormal ECG. Sinus tachycardia was the commonest abnormality followed by ischaemic changes (STEMI, NSTEMI and T wave inversion. Left axis deviation in ECG was more commonly seen than right axis deviation (35/216 vs 6/216).

S. No.	ECG	Frequency (n)	Percentage (%)
1	Normal	92	42.6
2	Abnormal	124	57.4
	Total	216	100

[Table/Fig-4]: Distribution according to ECG status.

[Table/Fig-5] presents ECG changes in moderate and severe category patients. Rhythm disturbances like atrial fibrillation/flutter were seen in only one patient of severe category, while none of the patients in the moderate category developed the same. Similarly, right and left bundle branch block was found in only severe category patients. Left axis deviation was more in moderate category patients (11/64, 17.18%) as compared to severe category (24/152, 15.8%). Ischaemic events suggested by STEMI/NSTEMI and localised T wave inversion were very commonly noticed in severe category patients. Localised T wave inversion was found in 39/152 (25.7%) patients in the severe group and 9/64 (14%) in the moderate group. One patient (1/152, 0.6%) developed STEMI and eight patients (8/152, 5.3%) developed NSTEMI, seen only in severe category patients. A tall peaked T wave in ECG was seen in 5/152 (3.3%) vs 1/64 (1.5%) in severe and moderate groups respectively. About 53% (34/64) of moderate COVID-19 patients had abnormal ECG whereas 59.2% (90/152) of severe COVID-19 patients had abnormal ECG. However, the difference was not statistically significant (p=0.409).

ECG changes	COVID-19 disease group according to severity		Total (%) N=216
	Moderate disease n=64	Severe disease n=152	
Normal sinus rhythm	41	93	134 (62.0)
Sinus tachycardia	18	49	67 (31.0)
Sinus bradycardia	5	7	12 (5.6)
Atrial fibrillation/flutter	0	1	1 (0.5)
RBBB	0	1	1 (0.5)
LBBB	0	1	1(0.5)
Right axis deviation	2	4	6 (2.8)
Left axis deviation	11	24	35 (16.2)
LVH	3	6	9 (4.2)
RVH	3	5	8 (3.7)
STEMI	0	1	1 (0.5)
NSTEMI	0	8	8 (3.7)
Localised T wave inversion	9	39	48 (22.2)
Tall peaked T wave	1	5	6 (2.8)

[Table/Fig-5]: ECG changes in moderate and severe COVID-19 diseases.
RBBB: Right bundle branch block; LBBB: Left bundle branch block; LVH: Left ventricular hypertrophy; RVH: Right ventricular hypertrophy; STEMI: ST elevation myocardial infarction; NSTEMI: Non ST elevation myocardial infarction

When the authors looked for the association between ECG changes and disease outcome [Table/Fig-6], 53.2% (66/124) of patients with abnormal ECG findings died, while 36.9% (34/92) with normal ECG findings died (p=0.018). Nearly 57% (38/67) of patients with sinus tachycardia died, while 43.3% (29/67) survived (p=0.0039) [Table/Fig-7]. Mortality was very high in patients developing Ischaemic changes in ECG. Only one patient with ECG signifying NSTEMI changes, survived, while the rest of the patients died (p=0.026). Nearly 60% (29/48) of the patients with localised T wave inversion died, while 39.6% (19/48) survived (p=0.026). Four out of six patients with tall peaked T wave died, the rest survived. Five out of eight patients with Right ventricular hypertrophy (RVH) died (p=0.476), while two out of nine patients with LVH died (p=0.181).

ECG change		Outcome		Total (N)	p-value*
		Discharged	Died		
ECG	Abnormal	58	66	124	0.018
	Normal	58	34	92	
Total		116	100	216	

[Table/Fig-6]: Association between overall ECG changes and disease outcome (*Chi-square test).

ECG changes	Outcome		Total	p-value
	Discharged n=116	Died n=100		
Sinus tachycardia	29	38	67	0.039*
Sinus bradycardia	8	4	12	0.354
Atrial fibrillation/flutter	0	1	3	-
RBBB	1	0	1	-
LBBB	1	0	1	-
Right axis deviation	4	2	6	0.688
Left axis deviation	18	17	35	0.853*
LVH	7	2	9	0.181
RVH	3	5	8	0.476
STEMI	0	1	1	0.463
NSTEMI	1	7	8	0.026
Localised T wave inversion	19	29	48	0.026*
Tall peaked T wave	2	4	6	0.419

[Table/Fig-7]: Association between different ECG changes and disease outcome (*Chi-square test, rest Fischer's-exact test).
RBBB: Right bundle branch block; LBBB: Left bundle branch block; LVH: Left ventricular hypertrophy; RVH: Right ventricular hypertrophy; STEMI: ST elevation myocardial infarction; NSTEMI: Non ST elevation myocardial infarction

DISCUSSION

With this retrospective study, the authors aimed to identify various ECG changes in moderate and severe COVID-19 patients and to ascertain the association between initial ECG changes and disease outcome. Commonest abnormality was sinus tachycardia (31%), followed by localised T wave inversion (22.2%) and left axis deviation (16.2%). Approximately, 57% were classified as having abnormal ECG with one or more abnormalities. Those who died had statistically significant association with having sinus tachycardia, NSTEMI and localised T wave inversion. It is well-known fact that respiratory symptoms associated with COVID-19 is primarily due to ACE2 expression in the type 2 lung alveolar cells; however, over 7.5% of myocardial cells also express the ACE2 receptor [12]. While these receptors are responsible for most of the cardiac symptoms also, the aetiology of the cardiovascular symptoms in COVID-19 is likely multifactorial [12-16].

Hypoxic injury, cytokine storm, and thromboembolism caused by COVID-19 virus will lead to various cardiac abnormalities and fatal outcome. These abnormalities can be picked easily and early by looking various ECG changes like rhythm disturbances, ischaemic events, axis deviation, etc. Here, the authors analysed the data of 216 patients with moderate to severe COVID-19 infection admitted to the tertiary care centre and key issues related to their ECG changes are discussed ahead.

The most common ECG abnormality encountered was Sinus tachycardia and it was more frequent among those who died (38%) as compared to those who survived (25%) (p=0.039). Serious rhythm disturbances like atrial fibrillation/flutter was seen in one patient. Earlier studies showed that commonest supraventricular tachycardia seen in COVID-19 patient was sinus tachycardia and fever, pain, anxiety, hypoperfusion and reduced oxygenation were the usual causes. Second most common supraventricular tachycardia was atrial fibrillation [17-19].

New York hospital study showed that 14.3% of COVID-19 patients present with atrial fibrillation at the time of admission and 10.1% patients developed, during hospitalisation [20]. One more study showed that, in patients with severe COVID-19 infections, who required mechanical ventilation 22% of them developed atrial fibrillation [21]. In the present study, mortality was 57% in patient with sinus tachycardia and 100% with atrial fibrillation. Outcome in COVID-19 patients was depends on various factors, but sinus tachycardia and atrial fibrillation were independently responsible for the severity of illness and its poor outcome [17].

The authors did not find any patients with malignant ventricular arrhythmia like Ventricular tachycardia/Ventricular fibrillation (VT/VF) in the present study, probably due to the fact that these findings were terminal events and the authors were considering initial ECG changes.

Next common finding was ischaemic changes characterised by ST-T changes included STEMI/NSTEMI/localised T wave inversion. Severe viral infections can cause a systemic inflammatory response syndrome that increases the risk of plaque rupture and thrombus formation, resulting in either an ST-elevation MI or non ST-elevation MI [22]. One study showed that cardiac injury suggested by ST-T changes like ST segment elevation or depression or T wave inversion and pathologic Q waves was seen in patients with COVID-19 infections [23-28]. Another study noted that in COVID-19 patients who required ICU admissions, 40% had ST-T changes [29]. Mortality among patients with ischaemic changes was also very high in the present study as compared to those discharged (p=0.026). One more study showed that ST-T changes were observed in nearly 41% of COVID-19 patients and most of these changes were due to cardiac damage and responsible for more critical care unit admission, increased ventilator support and very high mortality [17,21].

Axis deviation in ECG was not very common in the present study and was seen in 18% of patients. Left axis deviation was found more common than right axis deviation however, it was not statistically significant (p=0.853). Precise mechanism for left axis deviation might be ischaemia, left ventricular overload or hypertrophy. Right axis deviation was due to right ventricular strain in patients presenting with acute lung injury due to consolidation or pulmonary embolism [26]. In the present study, mortality seems to be very high in patients with axis deviation in ECG. One study founded axis deviation to be in 11% of patients and was more often among non survivors [30].

More of those with abnormal ECG died, as compared to those with normal ECG's at admission, and the finding was statistically significant, suggesting to the physician to become alert on finding abnormality in ECG on initial admission. The authors tried to make the sample as representative as possible with not much exclusion criterion, hence a balanced interpretation on generalisability could be expected.

Limitation(s)

Old ECG records of the patients were not available, hence it cannot be commented upon that the current ECG changes have occurred afresh or were pre-existing.

CONCLUSION(S)

Sinus tachycardia was the commonest ECG finding followed by ischaemic changes associated with infarction (localised T wave inversion) which were associated with very high mortality, followed further by left axis deviation. Early detection of these changes even before worsening of oxygenation will help in addition of anti-ischaemic and anticoagulant drugs in full therapeutic doses to avoid probable mortality. The authors found significant association between abnormal ECG at admission and risk of death in moderate to severe COVID-19 patients. Prospective, larger studies are recommended in future, for other better causal evidences.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Internal Medicine, Birsa Munda Medical College, Shahdol, Madhya Pradesh, India.
2. Assistant Professor, Department of Internal Medicine, Birsa Munda Medical College, Shahdol, Madhya Pradesh, India.
3. Associate Professor, Department of Paediatrics, Bundelkhand Medical College Sagar, Madhya Pradesh, India.
4. Associate Professor, Department of Community Medicine, Chhindwara Institute of Medical Science, Chhindwara, Madhya Pradesh, India.
5. Assistant Professor, Department of Pharmacology, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India.
6. Assistant Professor, Department of Orthopaedics, Birsa Munda Medical College Shahdol, Madhya Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Rupesh Kumar Gupta,
Ward 14, Sarda Colony, Shahdol-484001, Madhya Pradesh, India.
E-mail: neolog.raj@gmail.com

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