ELECTROCARDIOGRAPHIC FOLLOW-UP OF PATIENTS RECOVERED FROM COVID-19 INFECTION. A CASE-CONTROL STUDY IN SULAIMANI CITY

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ABSTRACT

Background

Electrocardiography (ECG) is one of the simplest, informative and valuable method to assess cardiac abnormalities associated with different illnesses especially during acute viral infections. The role of ECG was confirmed during previous pandemics in identifying various cardiac abnormalities. During covid-19 pandemic cardiac problems was of special concern, it appeared as second cause of mortality and morbidity after respiratory system complications

Objectives

To identify ECG abnormalities after recovery from mild to moderate SARS-COV-2 infection.

Materials and Methods

This preliminary case control study was conducted over a period of eight months from February 2021-December 2021 in the Internal Teaching Hospital and private clinic sector in Sulaimani city- Iraq. The study recruited 163 patients recovered from mild to moderate covid-19 disease and was compared to 100 matched control non infected group. Patients with severe covid-19 disease, history of heart failure and those with cardiac electrical conduction diseases were excluded from the study. Following ECG parameters were assessed among studied groups: heart rate (HR), P-R interval, R-R interval, QRS dispersion, corrected QT (QTc) and any sort of ST change. Evidence and types of arrhythmias were taken into account.

Results

The mean age ± SD (standard deviation) of participants were (48.98 ± 13.7 SD). Regarding gender distribution, ninety-nine (99/163) of the studied cases were female (60.7%) while 64 (64/163) (39.3%) were male. Majority of studied group were cigarette smoker (122/163 vs 41/163) and only 6.1% of them were regular alcohol drinker. The study demonstrated a significantly shorter QRS dispersion among recovered group compared to the control group (15.38 ± 8.29 SD vs 17.94 ± 11.9 SD) with a P- value of 0.04. Additionally, the mean corrected QT interval (QTc) was significantly lower in covid-19 recovered group compared with control group with P-value of <0.001 (406.94 vs 440.77). Meanwhile, no statistically significant changes were noted in P-R interval, R-R interval, heart rate, ST segment changes and any kind of arrhythmias between the studied and controlled groups.

Conclusion

This study concluded that three months after recovery from mild to moderate SARS-COV-2 infection did not demonstrate significant remanent changes compared to non-infected control group.

Keywords: *SARS-COV-2, Electrocardiography, and Pneumonia.*

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INTRODUCTION

An outbreak of pneumonia caused by a new coronavirus occurred in Wuhan, Hubei province in December 2019, and has spread rapidly throughout the China [1]. The pathogen for this type of respiratory infection was originally called 2019- novel coronavirus (2019-nCov) but has subsequently been officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization (WHO). After the disease spread to Europe and United States, on March 2020 the World Health Organization (WHO) has declared a pandemic status.[2].

Although respiratory system is the main site of infection, indeed the cardiac complications of COVID-19 draw the cardiologist's attention to outline the correlation between cardiovascular risk and a respiratory virus infection[3].Many reports confirm that more severe cases of this infection are in those patients with underlying concomitant diseases like hypertension (HTN), diabetes mellitus (DM), and atherosclerotic cardiovascular diseases (CVD)[4]. Similarly, Cohort studies of hospitalized patients in China estimated that cardiac injury occurs in 7-17% of patients hospitalized with the disease [5,1,6] .

Many determinants are contributed to promote inflammatory state in patients with COVID-19 infection like release of inflammatory cytokines, increase free radicals, sympathetic hyperactivation, increased thrombophilia, tachycardia and hypoxia [7]. There are reports which suggest evidence of acute myocarditis and heart failure (HF) in Middle East respiratory syndrome-related coronavirus (MERS-CoV), given that MERS-CoV and SARS-CoV-2 have similar structure and pathogenicity, this novel virus might also cause acute and chronic damage to cardiovascular system [7].

Angiotensin- converting enzyme 2 (ACE2) is a membrane bound aminopeptidase that has an important role in both immune and cardiovascular systems, it is involved in heart function and in certain diseases like HTN and DM. In addition, ACE2 has been identified as a functional receptor for corona virus infection and is highly expressed in the lungs and heart. It is worth to be mentioned that, it is the binding of the viral spike to ACE2 which trigger the disease, therefore, ACE2 related signaling pathway might also has role in myocardial injury[8].

Electrocardiography (ECG) remains the simplest and the most practical method for screening the possible cardiac abnormalities [9]. Its prognostic value has been confirmed in previous population-based studies for patients with underlying cardiovascular abnormalities especially HTN. Hence, ECG can be considered as a good diagnostic modality particularly during this pandemic[10] .It gives important information for identifying chronic and acute cardiac diseases through changes in the ECG strip including tachyarrhythmia, bradyarrhythmia, electrical conduction disorders and ST segment and T wave changes. To our knowledge, till now there is no study outlining the prevalence of ECG abnormalities in those patients who recovered from SARS-CoV2 infection in our region.

The rationale of this study is that acute viral infections may lead to secondary organ damages including cardiac manifestations so the aim is to find out any effect of SARS-CoV2 infection on ECG in patients after recovery from the infection.

MATERIALS AND METHODS

This preliminary observational case control study was conducted from February 2021 to December 2021 in the Internal Teaching Hospital and private clinic sector in Sulaimani city- Iraq. The study was approved by the Ethical Committee of College of Medicine, University of Sulaimani number 13 on 19th February 2023. All participants provided with informed consent. A total number of 163 patients of both genders (males and females) with ages (20-75) were recruited in this study. Additional one hundred patients were taken as matched control group who had no history of covid-19 infection and their ECG strips were interpreted. SARS-CoV-2 infection was confirmed in all recruited patients by either positive nasopharyngeal swab or pulmonary infiltrations by high resolution pulmonary computed tomography (HRCT).

Severity of covid-19 infection was classified according to National Institute of Health updated guideline march 2023 into the following groups:

Asymptomatic or presymptomatic infection: individuals who test positive SARS-CoV-19 using a virological test.

Mild illness: individuals who have any various signs and symptoms of covid-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but do not have shortness of breath, dyspnea, or abnormal chest imaging.)

Moderate illness: Individuals who show evidence of lower respiratory disease during clinical

assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO2

) ≥94% on room air at sea level.

Severe illness: Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.

Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ

dysfunction. 11

Patients with severe COVID-19 infection, those who were admitted at intensive care unit, with bundle brunch blocks and patients with HF were excluded from the study.

Vital signs: pulse rate, blood pressure, respiratory rate and body temperature were checked, anthropometric measures were recorded including body weight (Kg) by sensitive electronic balance and height(m) by fixed scale meter on the wall. Then body mass index was measured using the formula (BMI: kg/m2).

ECG measurements:

ECG was obtained from all eligible patients 3 months after their recovery from SARS-CoV-2 infection. All standard ECGs were recorded with speed of 25 mm/ second, voltage of 1 mV/10 mm and 0.05-150 Hz filter setting. All ECG recordings were scanned, after which the scans were magnified by Photos Window Viewer. Analyzed ECGs were blinded to clinical data of patients and then the second review was performed by another cardiologist for further confirmation.

The following ECG parameters were calculated: heart rate (HR)(beats/minute), R-R interval (msec) (interval between two successive R waves), P-R interval (msec) (interval between start of P wave to the beginning of Q wave, QRS duration (msec) (interval from the beginning of Q wave to the end of S wave) and QRS dispersion (duration of the most widened QRS minus duration of the narrowest QRS), QT measured (QTm) (msec) (time between start of Q wave to end of T wave), corrected QT (QTc) (msec) (QTm corrected by heart rate according to the Bazett's formula) (QTc = QTm / √RR), presence of ST segment abnormalities (Yes or No),). Evidence of arrhythmia and its type were taken into account as well.

Data Entry and Analysis:

Data had entered into excel sheet, after Data clearance had transferred to Statistical Package for Social Science (SPSS) version 23 for analysis. Frequency and percentages were determined for categorical variables and mean with standard deviations used for quantitative data. Association between categorical variables determined by Chi square test. P- values equal or less than (0.05) were regarded statistically significant.

RESULTS

In this study 163 patients were investigated. They underwent cardiac assessment with electrocardiogram record 3 months after a course of infection ranging from mild to moderate covid-19 disease. Their ECG record parameters were compared to the ECG of 100 control cases. Patients in the control group had no history of being infected with covid-19 virus. Age of participants were ranged from 22-75 years with mean age of (48.98 ± 13.7). Regarding gender distribution, ninety-nine (99/163) of the studied cases were female (60.7%) while 64 (64/163) (39.3%) were male. Cigarette smoking constitutes (122/163) (74.8%) while (41/163) (25.2%) were non-smoker. Minority of participants were alcohol drinkers (10/163) (6.1%) and majority (153/163) (93.9%) were non-drinker. Hypertension was the commonest associated chronic diseases (44.17%) (72/163) followed by diabetes mellitus (38.65%) (63/163) then hyperlipidemia (27%) (44/163) among the studied patients. Table 1 showed patients characteristics.

The mean P-R interval in covid 19 recovered group was (158.53 msec ± 20.4 SD) which was almost similar to the controlled group P-R interval (158.8 msec ± 25.88 SD) with no statistically significant P-value 0.93. Regarding R-R interval, the mean interval in covid 19 recovered patients was close to the mean of control group (755.95 msec ± 136.1 SD) vs (764.98 msec ± 134.6 SD) with non-significant statistically association, P- value of 0.6. Statistically significant correlation was found in QRS dispersion, it was greater (17.94 ± 11.9 SD) in controlled patients compared to covid 19 recovered patients (15.38 ± 8.29 SD), P value of 0.04. Table 2 comparing the mean between cases and controls. The mean heart rate was similar in covid recovered patients and in control group (83.13 ± 15.17 SD) (80.25 ± 13.82 SD) respectively, with P- value of 0.1, which

indicates no statistically significant difference between two groups. Regarding incidence of arrhythmias, sinus bradycardia was present in 3 enrolled covid-19 recovered patients (1.8%) while not present in control group, sinus tachycardia was similarly occurred in both groups (37/163 vs 22/100) (22.6% vs 22.0%). Any sort of significant ST segment deviation from the baseline were more observed in covid-19 recovered group compared to the control group (30/163 vs 11/100) (18.4% vs 11%).

As shown in figure number, the mean corrected QT interval (QTc) was significantly lower in covid-19 recovered group compared with control group with P value of <0.001 (406.94 vs 440.77).

Table 1. showed patients characteristics.

Variables	Study group		Control group	
	No.	%	No.	%
Age				
<45 years	66	40.5%	35	35%
45-65 years	70	43%	46	46%
≥65 years	27	16.5%	19	19%
Mean ± SD	48.98± 13.7			
Gender				
Male	64	39.3%	45	45%
Female	99	60.7%	55	55%
Chronic diseases				
DM	63	38.65%	30	30%
Hypertension	72	44.17%	42	42%
Hyperlipidemia	44	27%	32	32%
ASCVD	30	18.4%	10	10%
Thyroid disease	30	18.4%	14	14%
Chronic kidney disease	6	3.7%	2	2%
Cigarette smoker				
Yes	122	74.8%	68	68%
No	41	25.2%	32	32%
Alcohol drinker				
Yes	10	6.1%	13	13%
No	153	93.9%	87	87%

Table 2. comparing the mean between cases and controls.

Diagnosis		PR (msec)	RR (msec)	QRS dispersion	HR b/m
Control	**N**	100	100	100	100
	Mean	158.80	764.98	17.94	80.25
	Std. Deviation	25.88	134.63	11.90	13.82
COVID 19 Cases	**N**	164.00	163.00	164.00	163.00
	Mean	158.53	755.95	15.38	83.16
	Std. Deviation	20.40	135.61	8.29	15.17
Total	**N**	264.00	263.00	264.00	261.00
	Mean	158.63	759.38	16.35	82.05
	Std. Deviation	22.59	135.05	9.87	14.71
P- Value		**0.93**	**0.60**	**0.04**	**0.12**

Table 3. Association between ST change and Arrythmia in cases and controls.

			Diagnosis		Total
			Control	COVID 19 Cases	
ST change	**Depressed or Elevated**	Count	11	30	**41**
		%	11.0%	18.4%	**15.5%**
	Normal	Count	89	134	**223**
		%	89.0%	82.2%	**84.5%**
arrythmia	**No Arrythmia**	Count	78	124	**202**
		%	78.0%	76%	**77%**
	Sinus tachycardia	Count	22	37	**59**
		%	22.0%	22.6%	**22.3%**
	Sinus Bradycardia	Count	0	3	**3**
		%	0.0%	1.8%	**1.1%**
Total		Count	100	163	**263**
		%	100.0%	100.0%	**100.0%**

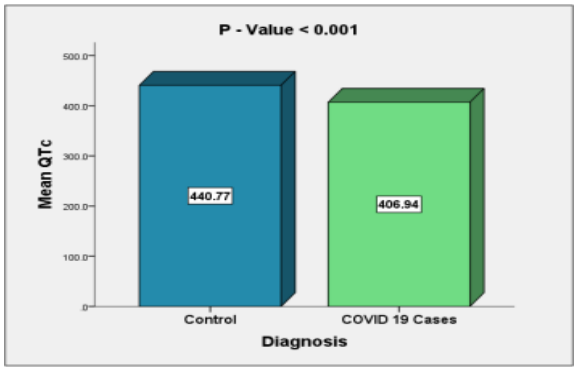

Figure 1. comparison of the Mean QTc between cases of COVID and control.

DISCUSSION

Several bacterial infections were followed by chronic changes and residual cardiac complications like in rheumatic carditis, chagas' disease and toxoplasma cardiomyopathy. Moreover, virus myocarditis was a well-known complication after recovery from the convalescent period of some viral infection (12).

Electrocardiograph is a useful, non-invasive and available tool to recognize various cardiac conditions especially those related to myocardial damage. The main aim of this study was to find out cardiac electrical changes in patients who recovered from mild to moderate covid-19 disease. To the best of my knowledge, it is the first study to follow up ECG parameters in these group of patients.

In the current study the overall ECG measurements did not show any significant differences between studied and control groups except for the corrected QT interval and QRS dispersion.

Despite paucity of data in recovered covid patients, in previous studies: tachycardia was present in the majority of recently hospitalized patients for acute covid-19 infection. The prevalence of tachycardia was highest during the first week of admission whilst they noticed a gradual decrease of heart rate in the second and third weeks of their stay (76 (62.8%), 55 (45.4%), and 43 (35.5%) respectively) and tachycardia was present in 38.8% of the followed-up patients after their discharge from hospital, (13). however in our study after recovery from mild to moderate covid-19 infection the frequency of tachycardia was almost comparable to the controlled group (22.6%), no statistically significant correlation (P- value 0.12) was noted, and no relevant tachycardia was recorded. Meanwhile, comparing to the incidence of tachycardia in SARS recovered

patient, Yu CM, et al., noticed that 40% of the studied patients had persistent tachycardia during out-patient follow up notwithstanding of it is benign course. 14 Additionally, Lau et al mentioned that tachycardia at rest or on exertion was observed among SARS recovering patients. The definite cause was unclear, but anxiety, autonomic dysregulation, pulmonary related causes were among their possible explanation [(15)].

Contrary to sinus tachycardia, sinus bradycardia was noticed only in few (1.8%) in covid-19 recovered patient (and none in controlled group) and is consistent with a study done by C-M Yu et al, which showed bradycardia was relatively transient even with sever acute respiratory syndrome [(13)].

A predictable inverse correlation is present between PR duration and the heart rate. This physiological adaptation by sympathetic stimulation keeps atrioventricular synchrony and optimizes left ventricular filling during an increase of heart rate.16 Except for acute rheumatic fever, all other febrile illnesses are associated with shortening of PR interval [(17)]. The recovered patients enrolled in the study showed no statistically significant prolongation of mean PR interval when compared to the controlled group (158.8 vs 158.5, P- value 0.930), apparently could be due to negligible long-standing residual effect of covid infection on the AV conduction system in the recovered group.

The ST segment represent the starting of ventricular repolarization, it is usually isoelectric. Although common cardiac pathologies like myocardial inflammation or ischemia are among the most common causes for the ST deviation from the baseline, but still non-pathological occasions may be responsible for the change. Alteration in ST segment was noted in covid-19 recovered group in 18.3% (30/164), which was resemblant to our control group, 11% (11/100) and was statistically non-significant. On the other hand, Leonardo et al noted ST segment elevation/depression in 6% (95/78) of patients recovered from mild to moderate covid infection during their post discharge follow up [(18)].

A higher incidence of myocardial involvement in covid-19 infection compared to other viral infections was postulated. Consequently, a more disturbance in ventricular conduction will be and it is partially demonstrated by QRS dispersion. The relationship of prolonged QRS dispersion with in-hospital mortality and post discharge sudden death was assumed by Harbalioglu H. et al, and additionally, Antonio et al. described the association of increased QRS dispersion and mortality when covid-19 infection was compared to other acute respiratory infections[(19)]. Contrarily to them, in our retrospective follow up there was a statistically significantly shorter QRS dispersion (P value 0.04) in covid-19 recovered group (15.38 msec+-8.29 SD) compared to the controlled group (17.94 msec +- 11.9 SD). Furthermore, H. Deniz et al specified that measured ECG parameters were improved during followed up recovery period compared to acute stage of infection [(20)].

An important indicator of ventricular dysrhythmias is heterogenicity of ventricular repolarization which is indicated by QT duration. Several viral infections are associated with prolonged QT interval like dengue, human immune deficiency virus and more recently covid-19 infections [(21)]. Moreover, in the absence of infection, elevated C reactive protein and systemic inflammation have also been associated with prolonged QT interval [(22)]. In our study, QTc was higher in controlled group while numerically shorter in covid-19 recovered patients (440.77 vs 406.94). in harmony with our result, a study done by H. Diaz et al in Turkey, they concluded that no statistically significant difference was observed between the two groups (active infection and recovered) (426.1±23.6 msec vs. 422.5±26.2 msec; p=0.237) despite the longer QTc in recorded ECG during first week of their illness [(20)].

Conclusion

Despite documentation of correlation of some ECG parameters change with prognosis and likelihood of increasing mortality in patients severely infected with SARS-COV infection during active infection stages and short-term recovery period, this study concluded that three months after recovery from mild to moderate SARS-COV-2 infection do not demonstrate significant remanent changes compared to non-infected control group.

REFERENCES

1. Dawei Wang, Bo Hu, Chang Hu, Fangfang Zhu, Xing Liu, Jing Zhang et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020 (3)17;323(11):1061-1069.

2. Peng Zhou, Xing-Lou Yang, Xian-Guang Wang, Ben Hu, Lei Zhang, Wei Zhang. et al. A pneumonia outbreak associated with a new coronavirus of probable bat

origin. Nature. 2020;(12) 588(7836):E6.

3. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;(2)15;395(10223):507-513.

4. Wei-Jie Guan, Zheng-Yi Ni, Yu Hu, Wen-Hua Liang, Chun-Quan Ou, Jian-Xing He, et al. China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;(4)30;382(18):1708-1720.

5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet.2020; (2)15;395(10223):497-506.

6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; (3) 28;395(10229):1054-1062.

7. Wang H, Yang P, Liu K, Guo F, Zhang Y, Zhang G, et al. SARS coronavirus entry into host cells through a novel clathrin-and caveolae-independent endocytic pathway. Cell Res. 2008;18(2):290-301.

8. Turner, A. J., Hiscox, J. A. & Hooper, N. M. ACE2: from vasopeptidase to SARS virus receptor. Trends Pharmacological sciences. 2004; 25(6):291-4

9. Lanza, G.A.; De Vita, A.; Ravenna, S.E.; D'Aiello, A.; Covino, M.; Franceschi, F., et al. Electrocardiographic findings at presentation and clinical outcome in patients with SARS-CoV-2 infection. Europace 2021 Jan 27;23(1):123-129.

10. Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram: Prevalence, incidence and mortality in the Framingham study. Ann Intern Med. 1969 Jul; 71(1):89–105.

11. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Clinical spectrum of SARS-CoV-2 infection. NIH 2023, https://www.covid19treatmentguidelines.nih.gov/

12. Balemann WH. Virus and the Heart. Circulation. 1971 Nov; 44(5): 950-6.

13. C-M Yu, R S-M Wong, E B Wu, S-L Kong, J Wong, G W-K Yipet al. Cardiovascular complications of severe acute respiratory syndrome. Postgraduate Medical Journal. 2006 Feb; 82(964):140–144.

14. Shaobo Shi, Mu Qin, Bo Shen, Yuli Cai, Tao Liu, Fan Yang,et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol: 2020 Jul 1;5(7):802-810.

15. Xiong TY, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. Eur Heart J. 2020 May 14;41(19):1798-1800.

16. Carruthers S, McCall B, Cordell B, Wu R. Relationships between HR and PR interval during physiological and pharmacological interventions. Br J Clin Pharmacol. 1987 Mar; 23(3):259–265.

17. David D. Rutstein, Walter Bauer, Albert Dorfman, Robert E. Gross, John A. Lichty, et al. Jones Criteria (modified) for guidance in the diagnosis of rheumatic fever: report of the committee on standards and criteria for programs of care. Circulation 1956;13:617–620.

18. Leonardo A. Sechi1, Gianluca Colussi, Luca Bulfone, Gabriele Brosolo, Andrea Da Porto, Maddalena Peghin, et al. Short-term cardiac outcome in survivors of COVID-19: a systematic study after hospital discharge. J Am Heart Assoc. 2022;11: e023473.

19. Harbalioglu H, Omer Genc, Gokhan Alici, Alaa Quisi, Abdullah Yildrim. Features on ECG During Admission May Predict In-hospital Events for COVID-19 Patients. Konuralp Medical Journal 2021;13(S1): 401-410.

20. Deniz H, Deniz F. Effects of COVID-19 infection on ECG parameters in outpatients. Eur Heart J. 2022 Oct; 43(Suppl 2): ehac544.393

21. Rosemary Aparecida Furlan-Daniel, Luis Felipe Silveira Santos, Tufik José Magalhães Geleilete, Carolina Baraldi Araujo Restini, Reinaldo Bulgarelli Bestetti. Abnormalities in electrocardiographic ventricular repolarization in patients with dengue virus infection. J Infect Dev Ctries. 2019 Aug 31;13(8):759-763.

22. Pietro Enea Lazzerini, Maurizio Acampa, Pier Leopoldo Capecchi, Mohamed Hammoud, Silvia Maffei, Stefania Bisogno, et al. Association between high sensitivity C-reactive protein, heart rate variability and corrected QT interval in patients with chronic inflammatory arthritis. Eur J Intern Med. 2013 Jun;24(4):368-74.