



Inappropriate Sinus Tachycardia in Patients Recovered from Covid 19

Dr. Abdullah Ansari¹, Dr. Mirza Atif Baig², Dr. Ayesha Raof^{3*}, Dr Rishabh Chormalle⁴

1. MBBS, MD, PGDCC. Department of Cardiology. Shadan Institute of Medical Sciences, Hyderabad. India
2. MBBS, DNB. Associate Professor. Department of Orthopaedics, Shadan Institute of Medical Sciences, Hyderabad. India.
3. MBBS, DCP. Department of Internal Medicine, Shadan Institute of Medical Sciences, Hyderabad. India
4. MBBS, Junior Resident, Department of General Medicine, ESIC Hospital, Hyderabad, India

Corresponding Author: Dr. Ayesha Raof, MBBS, DCP. Department of Internal Medicine, Shadan Institute of Medical Sciences, Hyderabad. India

Copy Right: © 2021 Md. Ayesha Raof, this is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Received Date: September 16, 2021

Published date: October 01, 2021

Abstract

INTRODUCTION: *The new infection SARS-CoV-19 has been linked to a variety of cardiovascular abnormalities like myocarditis, cardiomyopathy and heart failure. In this study, we aim to identify the probability of covid-19 being responsible for causing tachycardia in patients infected and recovered from SARS-CoV-19.*

METHODS: *A multicentre prospective study was conducted for 3 months on patients recovered completely from Covid 19. Various diagnostic investigations like 2D Echo, ECG, CBP, TSH, LFT, PFT, Electrolytes were performed to rule out other causes of tachycardia. After ruling out other causes of tachycardia, random 100 patients were included in the study and compared for the incidence of tachycardia, and for age and gender-based differences using student's t test.*

RESULTS: *27% of the participants were diagnosed with tachycardia without any evidence of cardiac disease or any other etiological factors. The mean HR of the younger group was found to be higher i.e., 95.19 than that of the elder group which was found to be 89.51. The incidence of tachycardia was found to be statistically significant in younger individuals when compared to the older group. The gender difference was not statistically significant.*

CONCLUSION: *The Incidence of Tachycardia among the patients recovered from Covid-19 is seen in more than 25% of the population under study. The incidence of tachycardia is observed to be more common amongst the younger individuals when compared to the elderly group. What are the factors that may play a significant role in the causation of tachycardia in the young has to be studied. Furthermore, any factor that may play a role in maintaining the sinus rhythm in the elderly has to be studied. Once the answer to these questions is found, unnecessary treatment with rate controlling drugs in the young can be avoided.*

KEYWORDS: *COVID-19, Tachycardia, post covid arrhythmias, post viral cardiac complications.*

Introduction:

The novel viral infection namely Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), generally referred to as Covid-19 has infected a whopping 105.3 million people around the world as of February 2021 since its outbreak in December 2020. [1]. Although the most significant manifestation of covid-19 is respiratory distress, cardiac complications have been observed in patients who are known to have cardiovascular conditions as well as in patients without any prior CVD disease. Myocarditis, heart failure, arrhythmias and Acute coronary syndrome are some of the encountered cardiac complications of the Covid-19. [2]. Tachycardia at rest and upon exertion has been noted in patients recovering from Covid-19 since the beginning of the pandemic. [3]. Possible reasons behind this complication is believed to be deconditioning [4], impaired lung and heart function, cardiac arrhythmias, thyroid problems, anaemia, autonomic dysfunction and anxiety. [5]. The American Heart Association has defined Tachycardia as a heart rate of ≥ 100 bpm, which can be a normal physiologic response to a systemic process or a manifestation of underlying pathology [6]. The current prospective cross-sectional study was carried out in order to determine the incidence of tachycardia in patients recovering from covid-19 as a complication of the infection.

Methods and Materials:

A multicentric prospective study was carried out for the duration of 2 months starting from February 1 2021 to March 31st 2021 in which a total of 115 patients who were confirmed to have been infected with covid-19 through polymerase chain reaction test and were recovered from the infection were selected provided they fell into the following eligibility criteria.

INCLUSION CRITERIA:

1. Post-covid non-hypertensive patients
2. Patients without any history of arrhythmias.
3. Age >20 and <50

EXCLUSION CRITERIA:

1. Patients above 50 years of age.
2. Known case of Hypertension
3. Patients on beta-blockers or any other rate controlling drug.
4. Patients with arrhythmias other than tachycardia

5. Patients who needed ICU admission during Covid-19 treatment.

6. Patients who needed steroids for treatment of Covid-19

To obtain the demographic details (age, sex and race) and medical comorbidities of the subjects, their medical records were systematically obtained and evaluated. Comorbidities were recorded including any history of Coronary artery disease, Atrial Fibrillation, COPD, Liver Disease, Chronic Kidney Disease, Myocardial Infarction, Congestive Heart Failure, Hypertension and Diabetes. Vitals, laboratory tests, anti-viral medications, steroids, antibiotics or any other medication received during hospitalization were also documented.

All the patients had an electrocardiogram done to document the heart rate and rhythm. The participants whose electrocardiogram showed tachycardia underwent other necessary investigations including 2D-Echo, CBP, TSH, Electrolytes, PFT and LFT to rule out other etiological causes of tachycardia like the hyperthermia, anaemia, hypertension, hyperthyroidism, electrolyte imbalances or any other cause. Chest X ray was done to know out nay underlying lung pathology like pneumonia, pulmonary edema or pneumothorax. Postural hypostatic tachycardia syndrome was ruled out by tilt table test. Complete drug history was taken to rule out any medications causing tachycardia like anticholinergics, catecholaminergics, recent withdrawal of beta blockers etc. Personal history was taken like intake of alcohol, caffeine, tobacco or cocaine which is known to cause tachycardia. History regarding chronic pain or stress was also taken to rule out physiological causes of tachycardia. 15 patients having one of the above-mentioned causes of tachycardia were excluded from the study.

The data obtained were spread in an excel sheet. We then calculated the incidence of tachycardia due to covid-19 among our subjects and compared the incidence among different age groups, as well as against the two genders. Incidence of tachycardia was also correlate with the different medications taken during the active phase of the disease. SPSS Version 20 was utilized for these statistical analyses and a P value of less than 0.05 was considered to be statistically significant.

RESULT:

In our study, among the 100 participants selected, most of them were asymptomatic and came for the routine follow up. Only 11 patients had palpitations on exertion, 4 patients complained of chest discomfort, 6 patients had symptoms of light headedness and 37 patients complained of generalized weakness. There were no participants with symptoms of cough, syncopal attacks or dyspnea on exertion.

Table 1: Presenting Symptoms of the population under study.

Symptoms	Percentage
Asymptomatic	42
Palpitations	11
Chest discomfort	4
Light headedness	6
Generalized Weakness	37

In the group under study, 41 patients were of the age group of 20-35 years and 59 patients were found to be aged between 36-50 years. They were divided into two groups based on the age for comparison of the age-based differences in the results. With respect to gender, 69% participants were male and 31% participants were females. Both the groups had more males than females [figure 1], Group A had 28 males and 13 females whereas the Group B had 41 males with 18 females.

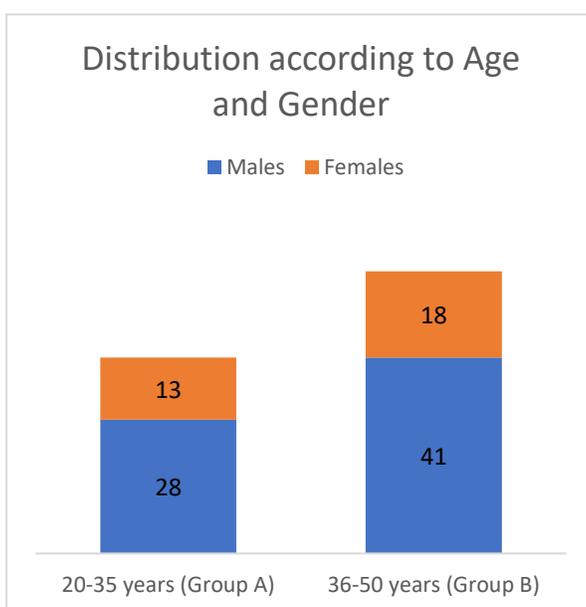


Figure 1: Distribution of participants according to Age and Gender:

Upon conducting investigations for tachycardia, the Heart rate (HR) of 27 participants was found to be more than 100 beats per min(bpm) while the rest of them (73) had their heart rate within the normal limits (less than 100 bpm). Among the 27 individuals diagnosed with tachycardia, 13 belonged to the group A whereas 14 belonged to the Group B, depicted in the Table no. 1. The P value was found to be P=0.015.

Table no. 2: Depiction of the HR:

	HR < 100bpm	HR>100bpm	Total
20-35	28	13	41
36-40	45	14	59
Total	73	27	100

The average HR of both the groups were calculated and it was found that the younger group showed an average HR of 95.19 while the elder group B had an average HR of 89.51 bpm.

Additionally, the average HR of males and females in both the groups were calculated separately which revealed that the average HR of males in the group A was 93.67 and that in the group B was 89.17 with a P value of 0.049. On the other hand, the average HR of females in the group A was 98.46 and that in the Group B was found to be 90.11 with a P value of 0.057.

Table no. 3: Depiction of Average HR of males and females in the both the groups:

	Males	Females	P value
20-35	93.67	98.46	0.208
36-50	89.17	90.11	0.767
P value	0.049	0.057	

Table 4: Medication history was taken and recorded. The results are as shown below.

Medication	Percentage
Doxycyclin 100 mg	100
Paracetamol 500 /650 mg	100
Levocetirizine +/- Montelukast	100
Ivermectin 12mg	78
Vitamin C	100
Multivitamins	100

Medication history revealed that all the patients received Doxycyclin 100 mg along with paracetamol and levocetirizine with or without montelukast during the active phase of the disease. Supportive medications included Vitamin C and multivitamin tablets. 78% of the study population received Ivermectin 12 mg for 5 days, while the remaining group did not receive Ivermectin. As this was the only difference in the medication history, incidence of tachycardia in patients receiving Ivermectin was also calculated to ensure that the tachycardia was not due to Ivermectin.

Table 5: Depiction of HR in patients taking Ivermectin

Group	HR<100	HR>100
20-35 years	22	11
36-50 years	33	12
P value	0.113	0.306

In patients taking Ivermectin, a total of 23 patients had tachycardia out of a total of 78 patients accounting to about 29.48%. The p value for the differences in the heart rate in different age group was not statistically significant.

Discussion:

Tachycardia is a complication seen in patients recovering from severe acute respiratory syndrome. [7] There are many scholarly articles that link viral infections to tachycardia. But one of the most important elements in diagnosing tachycardia is exclusion of all the known causes of tachycardia before labeling it as post viral tachycardia. 27 patients among the 100 patients recovered from Covid-19 who were included in our study in accordance with our eligibility criteria were found to have tachycardia. Since the CBP, ESR, LFT, TSH, LDH, CK, CRP tests of these individuals were found to be under normal limits, it is suggestable that an ongoing disease was highly unlikely among them. Moreover, normal results for Chest ray, normal blood gas levels and negligible lung function impairment implies that any pulmonary defect can be easily ruled out as the significant cause for tachycardia in these subjects while performing normal activities. This result is in accordance with the outcomes of the study conducted by Suet-Ting Lau et al. [7]

Even though the participants were known to be free of any cardiac abnormalities, upon presenting with palpitations, they underwent 2D Echo in an attempt to rule out any newly developed cardiac disease such as valvular heart disease as in the case presented by Ansari et al. [8] or any other heart pathology as various studies have been published lately that attribute many cardiac complications like heart failure, arrhythmias and myocardial infection to covid-19 infection. [9,10,11] All the known causes of tachycardia were ruled out using multiple tests.

In this study, the number of individuals clinically diagnosed with tachycardia with respect to the sample size is quite significant with a P value of 0.015 which was calculated employing the student's T test. Therefore, the outcome of our study suggests that the probability of the viral infection Covid-19 being attributable for the development of tachycardia in these patients is statistically significant. The reason for tachycardia in patients recovered from Covid -19 disease is poorly understood. The reason might be intrinsic sinus nodal hyperactivity along with the autonomic perturbations which are modulated by the

neurohumoral responses.[12] This post viral tachycardia might also be due to primary sinus node abnormality which is characterized by intrinsically high heart rate along with hypersensitivity of the beta-adrenergic receptors. It may also be coupled with depressed efferent cardiovagal reflex. [13] A case report by Sawalha K et al [14] on inappropriate sinus tachycardia following viral illness attribute it to a physiological response following the viral infection.

Comparing the two age groups, Group A and Group B, it can be seen that the incidence of tachycardia post-covid is more common among the younger population than the older one. P value obtained was less than 0.05 indicating that the difference in the incidence of tachycardia was statistically significant. The reason for higher incidence of tachycardia amongst the younger individuals is poorly understood. Though growing evidence has been linked to infections and tachycardia, age related tachycardia has not been the central focus of numerous clinical studies. As such, very limited data is available as to why younger individuals have higher incidence of tachycardia when compared to the elderly. If this tachycardia is considered as a physiological response, it should have had equal incidence in all the age groups. Younger individuals might have increased stress due to personal and work load that might have contributed to this difference. The factor influencing the activity of the sinus node at different ages has to be studied if this difference is significant.

Gender differences have the potential to affect the diagnosis and management of several medical conditions including cardiac arrhythmias.[15] Most of the research has only a minority of the females as the subject and this has to be improved so that the actual incidence can be correctly calculated. Even though there was significant difference in the incidence of tachycardia in different age groups, gender-based difference was clinically insignificant.

All patients included in the study have received Tablet doxycyclin 100 mg twice daily for a total of 5 days. Doxycyclin has antiviral and anti-inflammatory activities by dampening the cytokine storm to decrease the lung damage caused by the virus.[16] There is no data linking doxycyclin to causation of tachycardia. The TIPTOP trial has shown that early short term doxycyclin therapy in patients with acute myocardial infarction and left ventricular dysfunction prevents the ominous progression to adverse remodeling. [17] Additionally, Doxycyclin has also shown to protect the heart muscles after heart attack and decreases the susceptibility to arrhythmias [18] Based on these, it is unlikely that doxycyclin might have contributed to the tachycardia in these patients.

Paracetamol is known to be cardiotoxic only at very high doses. The cardiotoxic effect of paracetamol is related to the liver damage and it is shown that paracetamol has no direct cardiotoxic effect. [19] As the population under study had normal liver function tests and other cardiovascular investigations were normal, the role of paracetamol in the causation of tachycardia is less likely.

Some of the Antihistaminics were shown to cause prolongation of QT interval and Torsades de pointes. But these effects were seen only with the withdrawn formulations like terfenadine and astemizole. These

effects were shown only at far higher toxic levels and when combined with other enzyme inhibitors and not at the usual therapeutic doses used. Most of the preparations had no arrhythmogenic potential.[20]

Ivermectin is an antiparasitic medicine which has shown to decrease the SARS Covid 19 infection by 5000-fold at 48 hours in invitro studies. [21] A case report by Sparsa A has shown that Ivermectin has caused tachycardia and asthma in an elderly lady.[22] There are no large studies that has focused on the incidence of tachycardia in patients taking Ivermectin. In the present study, there was no significant difference in the heart rates among the age groups or different genders.

According to Suet-Ting Lau et al [7], patients with severe disease and complications during the treatment, prolonged hospital stay along with confinement during recuperation stage could undergo physical deconditioning. The Quality of Life might be impaired affecting physical as well as psychological well-being of the individuals, leading to anxiety.

Due to absence of any cardiac, pulmonary, thyroid and hematological issues in our cases, it can be inferred that the evident tachycardia can be attributable to physical deconditioning as well as the anxiety which could have developed as a result of fighting and recovering from the virus.

Conclusion

From the outcomes of our study, it is seen that tachycardia can be a complication of covid 19 disease. It is seen that the incidence of tachycardia is significantly higher in younger age group when compared to the elderly group. There was no significant difference between the genders in the incidence of tachycardia. Medications also had no significant role in the causation of tachycardia. Based on our results, we can conclude that SARS Covid 19 may be responsible for the causation of tachycardia.

Reference

1. <https://www.who.int/publications/m/item/weekly-epidemiological-update---9-february-2021>, COVID-19 Map.In: Johns Hopkins Coronavirus Resource Center [Internet]. [cited 9 Apr 2020]. Available: <https://coronavirus.jhu.edu/map.html>. Accessed 11 June 2020.
2. Babapoor-Farrokhran S, Gill D, Walker J, Rasekhi RT, Bozorgnia B, Amanullah A. Myocardial injury and COVID-19: possible mechanisms. *Life Sci.* 2020;253:117723. <https://doi.org/10.1016/j.lfs.2020.117723>.
3. Liu K, Fang Y-Y, Deng Y, Liu W, Wang M-F, Ma J-P, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J.* 2020;133(9):1025–31. <https://doi.org/10.1097/CM9.0000000000000744>.

4. Raven PB, Welch-O'Connor RM, Shi XO. Cardiovascular function following reduced aerobic activity. *Med Sci Sports Exerc* 1998 (July); 30(7):1041 – 52.
5. Hasser EM, Moffitt JA. Regulation of sympathetic nervous system function after cardiovascular deconditioning. *Ann N Y AcadSci* 2001; 940:454 – 68.
6. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am CollCardiol*. 2016 Apr 5;67(13):e27-115
7. Lau ST, Yu WC, Mok NS, Tsui PT, Tong WL, Cheng SW. Tachycardia amongst subjects recovering from severe acute respiratory syndrome (SARS). *Int J Cardiol*. 2005;100(1):167-169. doi:10.1016/j.ijcard.2004.06.022
8. Ansari A, Raouf A, Baig MA, Aamir M. “A Case Report of Covid-19 Associated Mitral Stenosis: A Causative Association?” *MAR Cardiology* 2.6 (2021)
9. Bader, F., Manla, Y., Atallah, B. et al. “Heart failure and COVID-19”. *Heart Fail Rev* 26, 1–10
10. Coromilas EJ, Kochav S, Goldenthal I, Biviano A, Garan H, Goldberg S et al. “Worldwide Survey of COVID-19-Associated Arrhythmias”. *CircArrhythmElectrophysiol*. 2021 Mar;14(3):e009458. doi: 10.1161/CIRCEP.120.009458. Epub 2021 Feb 7. PMID: 33554620; PMCID: PMC7982128.
11. Modin D, Claggett B, Sindet-Pedersen C, Lassen MCH, Skaarup KG, Jensen JUS et al. “Acute COVID-19 and the Incidence of Ischemic Stroke and Acute Myocardial Infarction”. *Circulation*. 2020 Nov 24;142(21):2080-2082. doi: 10.1161/CIRCULATIONAHA.120.050809. Epub 2020 Oct 15. PMID: 33054349; PMCID: PMC7682795.
12. Olshanky b, Sullivan RM. Inappropriate Sinus Tachycardia. *J Am Coll Cardiol*. 2013,61,793-801.
13. Morillo CA, Klein GJ, Thakur RK, Li H, Zardani M, Yee R. Mechanism of inappropriate sinus tachycardia: role of sympathovagal balance. *Circulation* 1994, 9, 873-877.
14. Sawalha K, Habash F, Vallurupalli S and Paydak H. Inappropriate Sinus Tachycardia following Viral Illness. *Clin Pract*. 2021,11 ,219-222.
15. Ehdaie A, Cingolani E, Shehata M, Wang X, Curtis AB, Chugh SS. Sex differences in cardiac Arrhythmias. *Circulation: Arrhythmias and Electrophysiology*. 2018.11:e005680
16. Malek AE, Granwehr BP and Kontoyiannis DP. Doxycycline as a potential partner of Covid-19 therapies. *ID cases*. 2020 jun 6;21:e00864

17. Giampaolo Cerisano, Piergiovanni Buonamici, Renato Valenti, Roberto Sciagrà, Silvia Raspanti, Alberto Santini, Nazario Carrabba, Emilio Vincenzo Dovellini, Roberta Romito, Alberto Pupi, Paolo Colonna, David Antoniucci, Early short-term doxycycline therapy in patients with acute myocardial infarction and left ventricular dysfunction to prevent the ominous progression to adverse remodelling: the TIPTOP trial, *European Heart Journal*, Volume 35, Issue 3, 14 January 2014, Pages 184–191, <https://doi.org/10.1093/eurheartj/eh420>
18. Fana XZ, Zhu HJ, Wu X, Yan J, Xu J, Wang DG. Effects of doxycycline on cx43 distribution and cardiac arrhythmia susceptibility of rats after myocardial infarction. *Iran J Pharm Res*. 2014 Spring;13(2):613-21. PMID: 25237357; PMCID: PMC4157037.
19. Ralapanawa U, Jayawickreme KP, Ekanayake EM, Dissanayake AM. A study on paracetamol cardiotoxicity. *BMC Pharmacol Toxicol*. 2016 Jul 14;17(1):30. doi: 10.1186/s40360-016-0073-x. PMID: 27411502; PMCID: PMC4944443.
20. Olasińska-Wiśniewska A, Olasiński J, Grajek S. Cardiovascular safety of antihistamines. *Postepy Dermatol Alergol*. 2014 Jun;31(3):182-6. doi: 10.5114/pdia.2014.43191. Epub 2014 Jun 13. PMID: 25097491; PMCID: PMC4112269.
21. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antivir Res*. 2020;178:104787.
22. Sparsa A, Bonnetblanc JM, Peyrot I, Loustaud-Ratti V, Vidal E, Bédane C. Effets secondaires de l'ivermectine utilisée dans le traitement de la gale [Systemic adverse reactions with ivermectin treatment of scabies]. *Ann Dermatol Venereol*. 2006 Oct;133(10):784-7. French. doi: 10.1016/s0151-9638(06)71044-4. PMID: 17072195.