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# Severe Covid Illness with Normal Heart Rate- An Unusual Phenomenon: Findings from a Hospital Based Observational Study

**1. Suhail Mantoo (First author)**
**Assistant Professor, Department of Internal Medicine, SKIMS Soura**
**mantoosuhail@yahoo.com**
**2. Arif Rehman Sheikh (Second/Corresponding author)**
**Senior Resident, Department of Internal Medicine, SKIMS, Soura**
**ess_arif@yahoo.com**
**3. Umar Hafiz,**
**Associate Professor, Department of Geriatrics, SKIMS Soura,**
**drumarhafiz@gmail.com**
**4. Afshan Shabir,**
**Assistant Professor, Department of Geriatrics, SKIMS**
**drafshanshabir@gmail.com**
**5. Nazia Mehfooz,**
**Assistant Professor, Department of Pulmonary Medicine, SKIMS Soura,**
**nazia_skims_rm@yahoo.com**
**6. Muzaffar Bindroo,**
**Assistant Professor, Department of Rheumatology, SKIMS Soura,**
**bindroomuzaffar@gmail.com**
**7. Farhana Siraj,**
**Assistant Professor, Department of Internal Medicine, SKIMS Soura,**
**bagdadifarhana6@gmail.com**
**8. Mudasir Qadri,**
**Associate Professor, Department of Internal Medicine, SKIMS Soura,**
**drsmudasir@yahoo.co.in**
**9. Ajaz Nabi Koul,**
**Additional Professor, Department of Internal Medicine, SKIMS Soura,**
**ajazkoul@yahoo.com**
**10. Mushtaq Dangroo,**
**Additional Professor, Department of Rheumatology, SKIMS Soura,**
**drmushtaq_01@yahoo.co.in**
**11. FayazSofi,**
**Professor,Department of Rheumatology, SKIMS Soura,**
**fayazkanjwal@rediffmail.com**
**12. Sanaullah Shah,**
**Professor, Department of Pulmonary Medicine, SKIMS Soura,**
**sonaullah_shah@yahoo.co.in**
**13. Rafi Jan,**
**Professor, Department of Pulmonary Medicine, SKIMS Soura,**
**rafiahmadjan@gmail.com**

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## Abstract

**Background:** Patients having severe covid-19 illness usually develop tachycardia as an integral part of systemic inflammatory response syndrome associated with this disease and presence of tachycardia has even been proposed as a prognostic marker in these patients. However, we observed that a significant proportion of patients do not develop tachycardic response. We aimed to investigate the prevalence of this non-tachycardic response in severe covid illness and discern the possible reasons for this phenomenon.

**Methods:** It was an observational, prospective-design study conducted at a leading tertiary referral center of north India. Patients hospitalized with severe covid illness were recruited for this study and were divided into two cohorts: patients with a tachycardic response and those with a non-tachycardic response. Different clinical and laboratory parameters were compared between two groups.

**Results:** Among 120 patients with severe covid illness included in the study, only 42 patients (35%) had tachycardia at presentation while as 78 patients (65.0%) had no tachycardia. 8 patients had absolute bradycardia with a heart rate of <60 beats per minute. Univariate regression analysis of different laboratory and clinical features between the groups with and without tachycardia did not show any statistically significant results, implying that these parameters are not primarily responsible for cardiovascular response in terms of tachycardia in these patients.

**Conclusion:** Tachycardia may not be seen in all patients with severe covid illness despite having hypoxemia and clinicians need to be aware of this phenomenon.


**Keywords:** Covid-19, Severe Covid Illness, tachycardia

## Introduction

Since the first instances of COVID 19 illness were reported from China at the end of 2019, the pandemic has affected all seven continents, with more than 600 million cases being documented worldwide so far [1]. A number of variants of the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) have been found so far that may differ in epidemiological parameters [2]. The knowledge about the different aspects of this disease is ever emerging and much more is known about this disease than before.

Central to the disease pathophysiology is acute hypoxemic respiratory failure resulting from involvement of lungs, which is responsible for death in majority of the patients. Apart from pulmonary involvement, Covid-19 can cause myriad of extrapulmonary manifestations as well which have been reported in literature in last 2 years [3].

In dealing with hospitalized Covid-19 patients with hypoxemic respiratory failure, we noted that significant proportion of these patients do not develop tachycardia, which by definition is seen in

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systemic inflammatory response syndrome (SIRS) associated with severe covid illness. Rather these patients had a normal heart rate, with some of them showing a bradycardic response.

To investigate this peculiar feature, this study was designed so as to know the prevalence of non-tachycardic response to severe covid illness in our hospital and to discern the possible factors responsible for this phenomenon.

## Materials & Methods

### Participants

This study was conducted at a large tertiary referral hospital of North India. All consecutive patients admitted to this hospital between December 2020 to March 2021 with a diagnosis of severe covid pneumonia were screened for eligibility into the study. Severe covid illness was defined as per CDC criteria, as patients who have oxygen saturation less than 94% at room air, a PaO2/FiO2 (arterial partial pressure of oxygen to fraction of inspired oxygen) ratio of less than 300 mm Hg, respiratory rate of greater than 30 breaths/min, or lung infiltrates greater than 50%. Patients with SpO2 <90% at room air at the initial presentation to the hospital were considered eligible for the study. Patients who were detected positive for SARS-CoV-2 during their inpatient hospitalization for other reasons were not included in the study. Patients who were younger than 18 years of age, who were on drugs known to alter heart rate, or had pre-existing medical conditions known to cause profound effects on resting heart rate were excluded from the study. Also, the patients with non-sinus rhythm on initial electrocardiogram (ECG) and the patients who died or left against medical advice were also excluded from the final analysis.

### Methods

Data regarding the initial presentation for the study patients was obtained from the case records of the patients. Data obtained included demographics, covid 19 related symptoms at presentation, duration of symptoms prior to presentation, pre-existing comorbidities like hypertension, diabetes mellitus, hypothyroidism, chronic lung diseases and others; drug history and pre-hospital treatments for covid-19. Vital signs at presentation including pulse rate, blood pressure and saturation at room air were noted. The findings of initial basic laboratory investigations including complete blood count, renal and liver function tests & arterial blood gas analysis were recorded. The findings of initial ECG and chest X-ray films were also noted.

The included patients were followed for the initial five days of their hospital stay and the data regarding pulse rate, blood pressure, supplemental oxygen requirement and treatment received during these days were recorded and any change in pulse rate during these days was noted thereof.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

### Statistical analysis

The data was compiled in Microsoft excel and later on analyzed through SPSS software version 22.0. Categorical variables were expressed as frequencies and proportions while as continuous variables were described as mean. We compared the characteristics of patients who had a tachycardia at presentation (defined as pulse rate of >100 beats per minute), with those who had a no tachycardiac. We used Students t-test for comparing continuous variables and Chi square test for comparing categorical variables. A two tailed p-value of less than 0.05 was regarded statistically significant.

## RESULTS

During the stipulated time, 148 patients were initially screened for eligibility into the study. 28 patients were excluded as they met the exclusion criteria for the study. Thus, a total of 120 patients were considered for the final analysis. The mean age of patients in our study was 59.63 years (SD=13.59). 45 patients among the study population were females, constituting 37.5% of the total. Table 1 shows demographics, associated comorbidities and different clinical and laboratory parameters of the study population. Some of the notable observations made from this table are as follows: hypertension is the most common underlying comorbidity in these patients; most of the patients present to the hospital late in the course of their illness, and most patients have neutrophilia and relative lymphopenia at presentation.

**Table 1: Baseline characteristics of Study population**

| **Variable** | **Frequency/ mean** | **%age/ standard deviation** |
|---|---|---|
| **Demographics** | | |
| Age (years) | 59.63 | 13.59 |
| Male Sex | 75 | 62.5 |
| **Comorbidities** | | |
| Hypertension | 82 | 68.30 |
| Diabetes mellitus | 43 | 35.80 |
| Chronic lung disease | 9 | 7.50 |
| Hypothyroidism | 17 | 14.10 |
| Malignancy | 7 | 5.80 |
| Chronic kidney/liver disease | 9 | 7.50 |
| Others | 12 | 10.0 |

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

| **Clinical & Lab parameters** | | |
|---|---|---|
| Duration of symptoms at presentation (days) | 6.08 | 2.69 |
| Pulse rate at admission (beats per minute) | 94.13 | 20.0 |
| Haemoglobin (g/dl) | 12.62 | 1.93 |
| Total leucocyte count (per cubic millimetre) | 9.29 | 4.48 |
| Neutrophils (percent of total leucocyte count) | 81.29 | 12.7 |
| Lymphocytes (percent of total leucocyte count) | 12.7 | 11.7 |
| Platelet Count (per cubic millimetre) | 175.78 | 115.66 |
| BUN (mg/dl) | 28.05 | 19.20 |
| Serum Creatinine (mg/dl) | 1.59 | 2.42 |
| Serum bilirubin (mg/dl) | 0.87 | 1.05 |

80 patients (66.67%) had fever at presentation, but only 24 patients among them had tachycardia, stressing the fact that 70% of patients with fever had relative bradycardia. Table 2 shows variation of initial pulse rate with fever at presentation.

| **Table 2: Variation of initial pulse rate in patients with fever at presentation (N=80)** | | |
|---|---|---|
| **Pulse rate (beats per minute)** | **Frequency** | **Percentage** |
| < 60 | 8 | 10 |
| 60-100 | 48 | 60 |
| >100 | 24 | 30 |

Among 120 patients with severe covid illness included in the study, only 42 patients (35%) had tachycardia at presentation while as 78 patients (65.0%) had no tachycardia. 8 patients had absolute bradycardia with heart rate of <60 beats per minute. We compared the different clinical and laboratory parameters between the group of patients with initial tachycardiac response with the group who had non-tachycardiac response but found no considerable difference in these variables as shown in table 3, implying that these parameters are not primarily responsible for cardiovascular response in terms of tachycardia in these patients.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

| Table 3: Clinical characteristics of patients with tachycardic versus non-tachycardic response to severe covid illness | | | | | |
|---|---|---|---|---|---|
| **Variable** | **Patients with Tachycardia (N=42)** | | **Patients with No Tachycardia (N=78)** | | **P-value** |
| | **n/mean** | **%age/ SD** | **n/mean** | **%age/SD** | |
| **Demographics** | | | | | |
| Age(years) | 57.73 | 11.60 | 60.65 | 14.52 | 0.26 |
| Male sex | 25 | 59.52 | 50 | 64.10 | 0.62 |
| **Co-morbidities** | | | | | |
| Hypertension | 28 | 66.67 | 54 | 69.23 | 0.77 |
| Diabetes mellitus | 15 | 35.71 | 28 | 35.89 | 0.99 |
| Chronic lung disease | 1 | 2.38 | 8 | 10.25 | 0.11 |
| Hypothyroidism | 9 | 21.42 | 8 | 10.25 | 0.09 |
| Malignancy | 3 | 7.10 | 4 | 5.12 | 0.66 |
| Chronic kidney/liver disease | 5 | 11.90 | 4 | 5.12 | 0.18 |
| **Clinical & Lab parameters** | | | | | |
| Duration of symptoms at presentation (days) | 5.64 | 2.76 | 6.32 | 2.73 | 0.21 |
| Pulse rate at admission (beats per minute) | 114 | 10.04 | 83.14 | 14.90 | <0.001* |
| Initial PaO2/FiO2 | 216.69 | 47.46 | 223.4 | 45.49 | 0.44 |
| Day 3 pulse rate(beats per minute) | 89.26 | 13.48 | 87.54 | 10.70 | 0.44 |
| Day 3 FiO2 | 0.60 | 0.18 | 0.56 | 0.17 | 0.23 |
| Day 5 pulse rate(beats per minute) | 85.98 | 11.72 | 85.44 | 10.6 | 0.79 |
| Day 5 FiO2 | 0.60 | 0.18 | 0.55 | 0.16 | 0.06 |
| Haemoglobin (g/dl) | 12.95 | 1.86 | 12.45 | 1.96 | 0.17 |

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

| | | | | | |
|---|---|---|---|---|---|
| Total leucocyte count (per cubic millimetre) | 9.57 | 4.63 | 9.14 | 4.39 | 0.61 |
| Neutrophils (percent of total leucocyte count) | 79.36 | 15.02 | 82.46 | 11.23 | 0.20 |
| Lymphocytes (percent of total leucocyte count) | 14.84 | 14.62 | 11.46 | 9.61 | 0.13 |
| Platelet Count (per cubic millimetre) | 178.5 | 81.72 | 174.29 | 131 | 0.85 |
| BUN (mg/dl) | 25.08 | 16.57 | 31.42 | 25.49 | 0.14 |
| Serum Creatinine (mg/dl) | 1.27 | 0.56 | 2.05 | 3.91 | 0.20 |
| Serum bilirubin (mg/dl) | 0.96 | 1.43 | 0.81 | 0.76 | 0.45 |

We also compared variation of initial heart rate with the degree of hypoxemia in these patients as shown in table 4, but there was no substantial association between these two variables.

**Table 4: Variation of initial pulse rate in study population with severity of hypoxemia (N=120)**

| **Initial PaO2/FiO2 ratio** | **Number of patients with pulse rate ≤100/min (n=78)** | **Number of patients with pulse rate >100/min (n=42)** | |
|---|---|---|---|
| 200-300 | 60 | 30 | **P value=0.08** |
| 100-199 | 15 | 11 | |
| <100 | 3 | 1 | |

## Discussion

This study provides important observations regarding the cardiovascular response to hypoxemia in patients hospitalized with severe Covid-19 illness. Patients with severe covid illness having respiratory failure have multiple reasons for developing tachycardia. These include hypoxemia, stress and anxiety associated with the disease and fever seen in many patients with severe covid illness. In our study cohort, wherein only hypoxemic patients were included, 65.6% of patients had no tachycardia at presentation. We also compared different parameters between the patients

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

who did not develop tachycardia with those who did, but we found no statistical difference between the two groups implying that the illness per se is responsible for a dampened cardiovascular response in these patients.

The acute cardiovascular reaction to hypoxemia is mediated primarily by hypoxic activation of the peripheral chemoreceptors leading to sympatho-activation and indirectly to vagal withdrawal, both of which trigger a tachycardiac response [4]. The preservation of vital functions in cases of well-compensated profound hypoxemia is caused by this cardiovascular compensation [5]. The correlation between hypoxemia and tachycardia seems to be linear in most patients early in their illness [6]. In our study, all included patients had hypoxemia at presentation, but only 34.4% patients had tachycardia and there was no notable correlation between the degree of hypoxemia and the development of tachycardiac response. Previous study by Kumar et al., also had noted that 51.3% of the study patients had a non-tachycardic response, but the authors have not mentioned as how many patients had hypoxemia among them [7]. This significant observation may have multiple reasons: the heart rate response to hypoxia is known to vary enormously among healthy individuals [8]. Additionally, since the ventilatory response and heart rate response to hypoxemia are directly correlated, people who do not have dyspnea may also not have significant tachycardia at the time of presentation [9]. The "silent hypoxemia" phenomenon, which refers to the absence of dyspnea even in the presence of significant hypoxemia, has been observed in some COVID-19 patients. The absence of compensatory tachypnea and tachycardia in these individuals has been postulated to be caused by aberrant autonomic regulation of breathing [10]. Age and co-morbid diseases also affect the cardiovascular response to hypoxemia in terms of tachycardia. It is well known that sympathetic nervous system responses to hypoxic stress decline with ageing [11,12]. The extent or tolerance of sympathetic nervous system activation caused by systemic hypoxia may also be constrained in patients with underlying pulmonary or cardiovascular conditions [13]. However, in our study, there was no significant difference between the mean age and underlying comorbidities of patients with a tachycardiac or non-tachycardiac response, indicating that this may not be predominant reason for the presence of blunted hemodynamic response to hypoxemia in our cohort of patients.

Also, in our study, more than 80% patients had fever at presentation, which again is expected to generate a tachycardiac response in these patients. However, 70% of patients with fever in our

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study had a non-tachycardiac response. This phenomenon of relative bradycardia has been previously described in covid as well as other some other infections with varying frequencies [14,15,16]. A number of explanations for this phenomenon of relative bradycardia have been put forth, including the direct impact of pathogenic organisms on the myocardial tissue, an imbalance in sympathovagal activation, impaired signal transduction, the modulation of autonomic activity by various cytokines via sensory feedback, and ponto-sensory interactions, which result in increased vagal tone and reduced sympathetic response [16,17,18].

In conclusion, absence of a tachycardiac response in hospitalized covid 19 patients is quite common but the literature is scarce about the same. Further studies are warranted to know the possible reasons of this dampened cardiovascular response and the impact of such a phenomenon on the outcome of such patients.

**Limitations of study**

This was a hospital based single center study and the sample size was small. Much of the observations are made based on data which was collected retrospectively. Absence of simultaneous measurement of respiratory rate at the time of presentation to hospital precludes the hypothesis of silent hypoxemia being the reason for blunted cardiovascular response in these patients. Finally, absence of clinical outcome measures in our study impedes to derive important implications of our study in day-to-day management of such patients.

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