Cardiac Manifestations in COVID-19 Patients-Admitted in Tertiary Care Hospital of Peshawar

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ABSTRACT

Objectives: To find the frequency of CVS diseases in admitted COVID patients and its associations with outcomes.

Methodology: A cross-sectional survey was conducted at tertiary care hospitals of Peshawar from April-June 2021. All patients admitted in COVID ward and COVID ICU, consenting to participate were included. Questionnaire along with patients ECG and Echo report, Canadian classification used for angina grading and NYHA classification to classify shortness of breath.

Results: The mean age of the sample (n=75) was 60.44 years. Majority were 44 (58.66%) males and from ward 82.66%. According to responses using Canadian classification for chest pain were 61 (81.36%) class 2 angina, IN NYHA classification majority (72%) of patients had class 2 SOB. About 14.6% of patients echoed positive ECHO findings. The average stay of patients were 7.45±1.3 days. About 22.6% of mortality was noted, majority of expiry were from COVID icu (52.9%) and 69.3% of patients were discharged. About 21.33% of COVID patients had cardiac manifestations, majority were males 87.5%. 43.75% of mortality was seen in patients developing cardiac manifestations. 75% of patients that developed cardiac manifestations had multiple comorbidities, AF was reported in patients age 70 and above. NSTEMI was reported in patients with multiple comorbidities. Most of the Cardiac patients 78.66% did not have cardiac manifestations, only 16.9% of mortality was seen in patients with no cardiac manifestations.

Conclusion: Males are more prone to COVID and have more cardiac events. Age above 60 years develop more serious disease and adverse outcomes.

Keywords: COVID 19, CVS manifestations, health, patients.

I. INTRODUCTION

In early December 2019, there was a rise in unusual pneumonia cases presenting in city Wuhan, China. The cause of which was found to be SARS-CoV2 [1]. Coronaviruses comprises of large family of single positive-stranded, enveloped RNA viruses that can infect various animal species and humans. The viruses infecting humans can be classified on the basis of their pathogenicity, out of the other classes some strains having high pathogenicity are SARS-CoV, MERS-CoV, and current novel SARS-CoV2 [2].

This virus spreads via droplets in the respiratory secretions. A person can get infected by contact of mucus membrane (nose, eyes, or mouth) with the respiratory secretions of an actively infected person discharging virus particles [3].

Corona virus causes acute disease primarily involving respiratory system. SARS-CoV2 has S-spikes on its outer surface by which it binds to ACE2 receptors as an entry point in cell. This ACE2 receptors is expressed on various body cells both type 1 and type 2 pneumocytes but also on the outer surface of endothelial cells. ACE2 receptor when is activated it inversely regulates the renin-angiotensin system [4].

Many COVID 19 patients have been reported to have cardiac injury although the exact pathophysiology and mechanism of injury remains poorly understood [5].

COVID-19 induces multiple cytokines and chemokines release resulting in vascular inflammation, plaque instability, and myocardial inflammation [6]. A pre-existing cardiovascular disease (CVD) predisposes a COVID-19 infected patient with elevated risk of adverse outcomes [7]. In addition to this many studies show that patients with pre-existing coronary artery disease and/or risk factors for atherosclerotic disease are more prone to develop acute coronary syndrome ACS during acute infection phase [8].

Some previous study reports suggest direct injury to the myocytos by virus that may lead to inflammation and cardiac injury [9].

It has been suggested that the primary mechanism of SARS-CoV-2 entry into host cells is via angiotensin-converting enzyme 2 (ACE2) receptors, that are abundantly expressed on the heart and lung cells [10]. Some studies suggest systemic release of various pro inflammatory...
cytokines, such as interleukin-1 (IL-1), beta interferon-gamma (IFN-γ), macrophage inflammatory protein (MIP)-1A, tumor necrosis factor (TNF)-α and IL-6 [11]. Post-mortem study of cardiac tissue from a deceased COVID-19 patient likely suggest systemic inflammation and injury to heart [12].

Many studies show a high prevalence of cardiovascular comorbidities in hospitalized patients affected by the COVID-19 virus [13].

Many studies show that having risk factors for cardiac disease and established cardiovascular disease seems to have more vulnerability to COVID-19 and show more severe disease with worse clinical outcomes. In case report study of 138 hospitalized COVID-19 patients by [1], 14.1% had baseline cardiovascular disease, and 31.1% had hypertension. In a study of 41 patients by [3], 14.6% were having a baseline cardiovascular disease, and 14.6% were having hypertension. Whereas in a larger cohort of 416 patients by [14], 30.5% had hypertension, 10.6% had coronary artery disease, and 5.3% had cardiovascular disease. The prognostic significance of cardiovascular disease was seen in a cohort of 191 patients by [15], showing that 30% had hypertension that constituted 48% of the non-survivors, and patients already having CVD were 8% who made 13% of non-survivors.

Despite former reports, the full spectrum of CV manifestations of COVID-19 remains incompletely understood.

Although, few studies have observed cardiovascular manifestations in COVID patients, there is still an important gap in the literature.

Rationale: As the covid pandemic progress it is revealing new presentation of diseases. In Pakistan COVID has great mortality and morbidity, it is presumed that COVID patients are more prone to develop cardiac disease. Therefore, it is hypothesized that COVID leads to more heart diseases and previous CVD patients tend to have severe COVID disease and adverse clinical outcomes.

A. Aim & Objectives

The main purpose of this study was to find the frequency of Cardiac diseases in COVID-19 patients and CVS manifestations in corona cases admitted in tertiary care hospitals of Peshawar.

i. To find out spectrum of cardiac diseases occurring in COVID patients.

ii. To find if pre-existing cardiovascular disease (CVD) predisposes COVID-19 patients with elevated risk of adverse outcomes.

II. METHODOLOGY

A cross-sectional survey was conducted at tertiary care hospitals of Peshawar, Pakistan namely Kuwait teaching hospital and Lady reading hospital from April to June 2021. All patients admitted in COVID ward and COVID ICU were enrolled. All the patients consenting to participate were included.

This study was conducted in adherence with ethical policies. Their identities were concealed throughout the study period, including during the completion of the questionnaires. Each participating institute was approached for permission, before starting data collection. Informed consent was taken from all the participants, after taking verbal consent, they were provided with questionnaire. The patients admitted in wards/ICU were allowed to respond in their own time and privacy. The participation was entirely voluntary.

A self-designed questionnaire was administered and patients ecg and echo report were attached with the questionnaire.

III. FUNCTIONAL DEFINITIONS

A. Chest Pain

Canadian classification was used to grade chest pain. I. "Ordinary physical activity does not cause ... angina," such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation. II. "Slight limitation of ordinary activity." Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Walking more than 2 blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions. III. "Marked limitation of ordinary physical activity." Walking one to two blocks on the level and climbing one flight of stairs in normal conditions and at normal pace. IV. "Inability to carry on any physical activity without discomfort -anginal syndrome may be present at rest.

B. Shortness of Breath

NYHA classification was used to asses SOB Class I – No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc. Class II - Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity Class III-Marked limitation in activity due to symptoms, even during less than-ordinary activity, e.g. walking short distances (20-100 m).Comfortable only at rest. Class IV - Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

C. Ischemic Heart Disease

Also known as coronary heart disease, occurs when atherosclerosis affects the coronary arteries in the heart hence the blood flow to the heart muscle is reduced because of a partial or complete blockage of the arteries supplying it with blood, angina or a heart attack may occur.

D. Valvular Heart Disease

It is any cardiovascular disease process involving one or more of the four valves of the heart leading to structural or functional abnormality.

E. Myocarditis

Myocarditis is inflammation of the heart muscle (myocardium). The inflammation of the heart muscle causes degeneration or death of heart muscle cells. Myocarditis has many different causes and can result in a range of outcomes from mild (presenting briefly and resolving) to rapidly progressing fatal disease.

F. Pericardial Effusion

Pericardial effusion is the buildup of extra fluid in the
pericardial space. If too much fluid builds up, it can cause cardiac tamponade.

G. Heart Failure
It is defined as when the heart fails to keep up with its load.

H. Reduced Ejection Fraction
The term "ejection fraction" refers to the percentage of blood that's pumped out of a filled ventricle with each heartbeat. In heart failure patients ejection fraction is less than normal.
- HF with preserved ejection fraction (HFpEF): LVEF ≥ 50%;
- HF with a mid-range ejection fraction (HFrEF): LVEF 41-49%;
- HF with a reduced ejection fraction (HFrEF): LVEF ≤ 40%.

I. Arrhythmias
A cardiac arrhythmia is a disturbance of the electrical rhythm of the heart.
It can be classified into
- Tachy Arrhythmia having Heart Rate > 100bpm
- Brady Arrhythmia having Heart Rate <60bpm

IV. RESULTS
Our sample size was 83 but after data cleaning it came down to 75.
The mean age of sample (n=75) was 60.44+1.6 years, range 23 to 85 years. There were 44 (58.66%) males and 31 (41.33%) females. Majority of the sample was from ward 82.66% whereas 17.34% was from COVID ICU setup, most of the sample was collected from lady reading hospital (n=41, 54.64%).

Patient s treated In the ICU, compared with patients not treated in the ICU (82.6%), were older (median age, 60 years and above, range 60-77), were more likely to have underlying comorbidities.

According to responses of patients using Canadian classification for chest pain there were 61 (81.36%) class 2 angina, 7 (9.3%) class 3 and 6 (8%) class 4 angina cases. In our results, patients via NYHA classification were classified as, about 54 (72%) of patients had class 2 SOB. Patients with oxygen therapy 62 (82.66%) maintained oxygen above 92% and (17.33%) had below 92% spo2 despite oxygen therapy.

Common CVS symptoms experienced were palpitations, fatigability, intermittent claudication and syncope out of which about 8% of patients presented with palpitations, 98% of patients presented with fatigability, 1% of patients had intermittent claudication and 9% suffered from syncope.
12% of patients had positive Troponins i.e. above 0.40 cut off.
The average stay of patients came out to be 7.4533+1.3 days with max stay of 45 days to min of 2 days (range 2-45).
About 22.6% of mortality was noted in our sample, majority of expiry were from COVID icu about 52.9% and rest 47.1% were from ward.
About 69.3% of patients were discharged. Among those discharged alive (n=52), the median hospital stay was 10 days but the remaining 8% patients are still hospitalized.

About 14.6% of patients echo showed IMP LV/LV dysfunction and showed low LVEF ≤ 40%.
In our results about 82.6% of patients egs were normal and 17.3 % showed abnormal ecg patterns having arrhythmias and ST-T changes 2.6%, brady, 6% AF, 2.6% of STEMI and 5% of NSTEMI.
About 9.3% of population had an acute event and 71.4% of which occurred in three comorbidity patients.

A. Comorbidities
61.3% had Hypertension 74.6% had Diabetes type 2, 12% had CAD, 9% of patients had 3 comorbidity and 36% of patients had more than one comorbidity.
About 21.33% of COVID patients had cardiac manifestations 18.75% was from ICU and 81.25% was from ward, with an average age of 66.7 years (range 45-85), majority of which were males about 87.5% and females made 12.5%.
Average stay of patients was 8.75 days range (1-16), 43.75% of mortality was seen in patients developing cardiac manifestations.
25% of patients developing cardiac manifestation had single comorbidity whereas 75% of patients that developed cardiac manifestation had multiple comorbidities.
AF was reported in patients age 70 and above with single comorbidity (HTN or DM) or both (HTN and DM). NSTEMI was reported in patients with multiple comorbidities i.e. HTN, CAD, DM, male sex and age above 50.
About 78.66% of COVID patients did not have cardiac manifestations 16.95% of patients were from ICU and 83.05% were from ward, with an average age of 58.72 years (range 23-80), with males (50.8%) and females made 49.15%. About 62.7% of patients had single risk factor for cardiac disease, and 37.3% with multiple risk factors. Average stay of patients were 7.1 days range (1-27) and 16.9% of mortality was seen in patients.

Compared with discharge and no cardiac manifestations group, patients in death and cardiac manifestations group were older (both p < 0.001) and tended to be males (both p < 0.05). Of note, death and cardiac manifestations group had a higher rate to present with comorbidity, especially with more than one comorbidity (all p < 0.001) compared with discharge and no cardiac manifestations group.

<table>
<thead>
<tr>
<th>Cardiac manifestation</th>
<th>No Cardiac manifestation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>43.75%</td>
<td>16.9%</td>
</tr>
<tr>
<td>Length of stay</td>
<td>27</td>
<td>16</td>
</tr>
</tbody>
</table>

p-value less than 0.05 or 0.001 is significant.
Fig. 1. Cardiac manifestations seen in COVID patients.

Fig. 2. Gender wise distribution in patients that had cardiac manifestations.

Fig. 3. Mortality in COVID patients that showed Cardiac manifestations.

Fig. 4. Gender wise mortality in COVID patients that showed Cardiac manifestations.

Fig. 5. Patients maintaining SpO₂ level above 92%.

Fig. 6. Patients having acute event in the period of stay.
Fig. 7. CVS symptoms experienced by patients.

Fig. 8. Major portion of mortality of COVID patients having multiple comorbidities.

Fig. 9. Gender based mortality in COVID patients.

Fig. 10. Major portion of mortality representing COVID patients that developed cardiac manifestations.

Fig. 11. ICU/ward mortality in COVID patients.

Fig. 12. Abnormal ECG patterns observed in COVID patients.
infection is more likely to affect males and [27] that females may be less susceptible to the virus due to the protective effects of the X chromosome and sex hormones 27 and is against the finding of [1] that there was no difference in the proportion of men and women between ICU patients and non-ICU patients.

Our study supports the findings of [1] that most patients required oxygen therapy and a minority of the patients needed invasive ventilation.

Our study showed that 61.3% of patients had HTN, 74.6% had DM, 12% had CAD which is similar to the findings of the following researches by [3] that 14.6% were having a baseline cardiovascular disease, and 14.6% were having hypertension and a cohort by [14], that 30.5% had hypertension, 10.6% had coronary artery disease, and 5.3% had cardiovascular disease [14].

Our findings don’t support the findings of [1] cohort that the overall rates of severe hypoxia and invasive ventilation were higher but supports the findings of [3], rates of severe hypoxia and invasive ventilation were low, it might be due to the fact that cases in the previous study were from the early epidemic stage and the current cases are from the stage of outbreak and mid of ongoing wave.

Our study supports the findings of [24] that > 60 years old was a predictor for adverse outcomes.24 In our findings males were having more cardiac manifestations which is favored by the findings of [24] that female was found to be protective against death and adverse outcomes approximately 5-fold time increase in the risk of death as well as adverse outcomes in males. Further and detailed evaluation of the impact of different comorbidities on patients with COVID-19 is necessary and of great value to guiding proper inter-disciplinary management, especially for the elderly patients.

Our study supports the findings of recent studies by [10], [25], [26] that patients with severe cardiovascular damage and underlying cardiac insufficiency were associated with adverse events.

This study has several limitations. First, of all limited to time and finite resources. Secondly limited exposure to prevent spread and selection bias in recruiting only admitted patients.

VI. CONCLUSIONS

Present study had several limitations. First, the observational nature of this study introduces selection bias related to admitted and monitored patients with COVID-19. The incidence and severity of COVID and cardiac manifestations in non-hospitalized patients and patients with mild illness at home is unknown. Males are more prone to COVID and having more cardiac events. Age above 60 years develop more serious disease and adverse outcomes. 17.34% of patients require COVID ICU setup care, about 69.3% of patients gets discharged, 22.6% of mortality in patients having more comorbidities The average hospital stay is around 7-10 days.

Literature to date shows that more the comorbidities worse is the outcome and along with respiratory problems many CVS manifestations are seen in COVID patients.

B. LABS Values

The average creatinine levels were 0.8733 and 9.3% of patients had deranged creatinine levels above 1.1. The average CRP levels were 16.05 (range 60-3) and d dimers were around 1673.3(range 9000-100), TLC of 1.49E+04 (range 3.00E+04-5+03) all the inflammatory markers were deranged and elevated the average SGPT levels were around 45.186 (range 418-7) and RBS was on average 162.2 (range 320-52).

| TABLE II: Increase in risk factors increases the chances of cardiac disease. |
|------------------|------------------|
| S.no | Risk factors | Cardiac manifestations % |
| 1 | Risk factors 1 | 25 % |
| 2 | Risk factors 2 or more | 75 % |

V. DISCUSSION

Our study showed that 17.34% was from COVID ICU setup, about 69.3% of patients were discharged, 22.6% of mortality was present and 8% patients remain hospitalized which is against the findings of [1] that 26% required ICU care, 34.1% were discharged, 6 died (4.3%), and 61.6% remain hospitalized respectively also in Italy by [17], research showed that patients over 70 years old, especially those older than 80 years, had a higher mortality rate of 20.2%.

Our study shows that arrhythmias and shock were present in hospitalized patients which is favored by the findings of [1] i.e. major complications during hospitalization included ARDS, arrhythmia, and shock. Our result showed that 8% of patients showed palpitations which is favored by the results of study by [18] of 137 patients, that 7.3% reported palpitations as one of their symptoms.

In our study 7.9% of patients showed S-t changes, which is in favor by the research findings of [19] that ACS was noted in 33% of patients presenting with ST elevation, like wise there were case reports by [20] and [21] favoring our results that patients showed S-t changes.

Our findings are supported by [1] that most critically ill patients were older and had more underlying conditions than patients not admitted to the ICU.

Our research findings are in favor with the findings of [22] and [23] that Patients with pre-existing cardiovascular co-morbidities are presenting with severe cases of COVID-19 infection.

Our study showed that (58.66%) males got COVID which is favored by the findings of [16] showed that 2019-CoV...
REFERENCES


