

Clinicodemographic Profile of the Cases Presented with Extra Pulmonary Manifestations during Covid 19 Pandemic in a Tertiary Covid Care Centre at SVPIMSR

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ABSTRACT

Aims and objectives: To study severity of COVID 19 virus on various systems in body other than pulmonary system, To foresee adverse outcome of patient who were affected with COVID 19 pneumonia with prominent extra pulmonary manifestations. **Methods:** A retrospective observational study done in 100 cases of COVID 19 positive patients admitted to SVPIMSR and developed extrapulmonary manifestations over a period of 1ST April 2020 to 31ST May 2021. **Results:** Mean age was 60.94 ± 13.91 years **and** maximum patients were in the age group of 70-79 years, predominantly male were found to have extrapulmonary manifestations, in which cardiovascular system was most commonly involved. COVID-19 patients who developed cardiovascular manifestations had multiple comorbidities. In our study overall mortality was 63% and 53% patients with cardiovascular manifestations were deceased. **Conclusion:** Patients with COVID-19 may develop extrapulmonary manifestations besides respiratory symptoms. As an emergency physician we should be very careful while managing COVID-19 patients for developing extrapulmonary manifestations. By this we can improve patient's survival and reduce mortality. This study guides us for future pandemics of SARS-CoV 2 and we can focus extrapulmonary manifestations beyond pulmonary manifestations.

Key Words: COVID 19, SARS- CoV-2, Extra pulmonary Manifestations.

INTRODUCTION

Corona virus is spherical or pleomorphic enveloped single stranded RNA virus and belongs to Coronaviridae. RNA genome extends from 26-32 kilobases in length.¹ Corona viruses are found in avian and mammalian species.

The corona virus disease-2019 (COVID-19), is caused by Severe Acute Respiratory Syndrome Corona virus 2 (SARS- CoV-2), affected millions of people across countries. Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, some will become seriously ill and require medical attention. Older people and those with underlying medical conditions like cardiovascular disease, diabetes, and chronic respiratory disease are more likely to develop serious illness.

COVID-19 is causing substantial respiratory pathology, but it can also result in several extra pulmonary manifestations.

Extra pulmonary manifestation of COVID 19 pneumonia caused by direct viral toxicity, endothelial cell damage, thrombo inflammation, dysregulation of the immune response, dysregulation of RAS and maladaptation of ACE 2 related pathogens.²

The pathogenesis of infection entails the entry in host through the attachment of its structural protein known as the S-glycoprotein to principally angiotensin-converting enzyme 2 receptors. Direct virus damage coupled with indirect effects of viral infection including thromboinflammation, dysfunction of the immune system and dysregulation of the renin-angiotensin system leads to multiple organ failure. Given that ACE 2, the entry receptor for the causative corona virus SARS-CoV 2, is expressed as in multiple extra pulmonary tissues, direct viral tissue damage is a plausible mechanism of injury.²

Extra pulmonary manifestations include myocardial dysfunction and arrhythmia, neurological dysfunction, thrombotic complications, gastrointestinal dysfunctions, endocrine system dysfunction, dermatological symptoms, haematological manifestations, renal complications etc.²

This review outlines the extrapulmonary organ specific complications.

AIMS AND OBJECTIVES:

- To study severity of COVID 19 virus on various systems in body other than pulmonary system.
- To foresee adverse outcome of patient who were affected with COVID 19 pneumonia with prominent extra pulmonary manifestations.
- To study the clinical and demographic profile of the patients who were admitted with or developed extrapulmonary manifestations during course of hospitalisation.

MATERIALS AND METHODS:

This is a retrospective observational study done in 100 cases of COVID 19 positive patients admitted to SVPIMSR and developed extrapulmonary manifestations. Patients aged more than 18 years and not more than 80 years during the study period 1ST April 2020 to 31ST May 2021 were included in the study. On admission, patients with PaO₂:FiO₂ Ratio less than 150 were excluded.

Data from the hospital information system was collected in age, gender, symptoms related to COVID-19, Co-morbidities like Hypertension, Diabetes mellitus, Ischemic heart disease (IHD), Cerebrovascular accident (CVA), chronic kidney disease, any past pulmonary disease (chronic obstructive pulmonary disease or asthma, history of pulmonary tuberculosis), liver disease, immunocompromised state, obesity and others (rheumatoid arthritis, myasthenia gravis, psychiatric illness etc), Laboratory investigations and Radiological investigations (Hb, WBC, Platelet counts, LDH, D-Dimer, Ferritin, CRP, Troponin I, IL-6 etc), Xray chest, USG abdomen, Doppler, HRCT chest plain, CT brain plain etc, Oxygen requirement and mechanical ventilation, treatment received and outcome were inquired. On admission patients with GCS > 8 and SPO2 more than or equal to 95 were included in stable patients and GCS 8 or less than 8 and patients with Oxygen requirement were included in Unstable patients. Data were entered in Microsoft excel sheet (version 16) and analysed with a statistical package for the social science software.

INCLUSION CRITERIA:

- Age > 18 years and <= 80 years
- PaO₂:FiO₂ Ratio >_ 150 on admission

EXCLUSION CRITERIA:

- Age < 18 years and > 80 years
- ARDS on admission
- PaO₂:FiO₂ Ratio < 150

KEY WORDS:

- COVID 19
- SARS- CoV-2
- Extra pulmonary Manifestations

RESULTS

We have studied 100 patients with COVID-19 admitted to our tertiary care hospital (SVPIMSR) and developed extrapulmonary manifestations for the following:

In our study, out of 100 patients, 76 were male and 24 were female. Out of 100 patients maximum numbers of patients 33 (33%) were in age group of 70 to 79 years followed by 27 (27%) patients were in age group of 60 to 69 years. Mean age was 60.94 ± 13.91 years. Median age was 63.5 years. In our study, minimum age of patient was 20 year and maximum age was 79 year. In Male minimum age was 20 years and maximum age was 78 years. In Female, minimum age was 23 years and maximum age was 79 years.

Table 1: Age wise distribution of patients

Age Group (In Years)	No.Of Patients	Male	Female
20-29	4	2	2
30-39	6	4	2
40-49	6	3	3
50-59	24	21	3
60-69	27	22	5
70-79	33	24	9
TOTAL	100	76	24

Table 2: Extrapulmonary Systems Involved

System Involved	No.Of Patients	Male	Female
Cardiovascular Manifestations	66	54	12
Gastrointestinal Manifestations	16	9	7
CNS Manifestations	8	6	2
Thrombotic Manifestations	6	4	2
Renal Manifestations	4	3	1
TOTAL	100	76	24

In our study, we found in extrapulmonary manifestations of COVID-19, cardiovascular manifestation (66%) was most common, followed by gastrointestinal manifestation (16%). Least involved system was Renal (4%).

On further evaluation, patients with above manifestations symptoms / diagnosis are as below:

In CVS, out of 66 patients 44(66.66%) patients developed STEMI, 6(9.09%) patients developed NSTEMI, 12(18.18%) patients developed new onset heart failure and 4(6.06%) patients developed new onset arrhythmias.

In GIT, out of 16 patients, 5(31.25%) patients had diarrhea, 1(6.25%) patient had vomiting, 6(37.5%) patients had loss of taste and 10(62.5%) patients had abdominal pain.

In CNS, all 8 patients developed ischemic stroke.

In thrombotic manifestations, despite thromboprophylaxis out of 6 patients 3(50%) patients developed DVT and 3(50%) patients developed PE.

In Renal manifestations, all 4 patients had Acute Kidney Injury.

Table 3: Oxygen And Mechanical Ventilation Required to Patients During Hospitalisation

Oxygen Requirement	O2	HFNC	BIPAP	INTUBATED
CVS (n=66)	56(84.84%)	22(33.33%)	25(37.87%)	53(80.3%)
GIT (n=16)	1(6.25%)	0	0	0
CNS (n=8)	6(75%)	2(25%)	1(12.5%)	7(87.5%)
Thrombotic (n=6)	6(100%)	3(50%)	4(66.66%)	5(83.33%)
RENAL (n=4)	1(25%)	0	0	1(25%)

Thus from all above data, in this study least oxygen requirement was in Gastrointestinal manifestations and maximum oxygen requirement was in Cardiovascular manifestations.

This table shows oxygen required to patients during hospitalisation. Requirement of oxygen progressively increased. For example from oxygen to HFNC, HFNC to BIPAP, BIPAP to Mechanical ventilation or Oxygen to Mechanical ventilation so here sum of patients is not 100.

Table 4: Co-Morbidities In Patients With Extrapulmonary Manifestations

Co-morbidity	Hypertension	Diabetes mellitus	IHD	CVA	Hypothyroidism/ Hyperthyroidism	Others
CVS (n=66)	39(59.09%)	39(59.09%)	11(16.66%)	6(9.09%)	Hypo 3(4.54%)	0
GIT (n=16)	3(18.75%)	2(12.5%)	0	0	0	0
CNS (n=8)	5(62.5%)	4(50%)	1(12.5%)	0	Hypo 1(12.5%)	0
Thrombotic(n=6)	1(14.28%)	0	0	0	0	0
Renal (n =4)	3(75%)	3(75%)	0	0	0	0

Here, patients may have more than one comorbidity so sum of comorbidities is not 100 or not equal to patients with specific system.

Specific Treatment According to Involved System

In AKI, out of 4 patients only 1(25%) patient needed Hemodialysis

In CVS, 19 patients were thrombolysed with streptokinase out of 44 patients with ST elevation myocardial infarction.

In Thrombotic manifestations 3 patients had developed Pulmonary Embolism and 3 patients had DVT, they were treated with Anticoagulants.

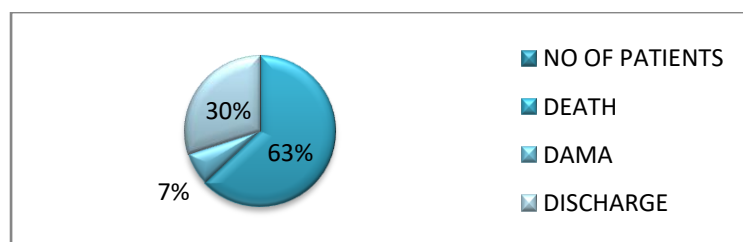


Figure 1: Outcome Of Patients With Extrapulmonary Manifestations

In our study, out of 100 patients, mortality was 63 (63%), 30 (30%) patients were discharged and 7 (7%) patients took dama.

Table 5: Outcome Based On System Involved

Outcome	Discharge	Dama	Death
CVS(n=66)	9(13.63%)	4(6.06%)	53(80.3%)
GIT(n=16)	15(93.75%)	1(6.25%)	0
CNS(n=8)	0	2(25%)	6(75%)
Thrombotic(n=6)	3(50%)	0	3(50%)
Renal(n=4)	3(75%)	0	1(25%)
TOTAL(n=100)	30	7	63

In our study, maximum mortality was seen in cardiovascular involvement 53(80.3%) followed by CNS involvement 6(75%). There were no mortality was seen in Gastrointestinal involvement 15(93.75%) patients were discharged.

Table 6: Systemwise Outcome in Patients with Extrapulmonary Manifestations of Covid-19

Pneumonia

System Involved	Stable Patients	Unstable Patients
CVS (n=66)	10	56
Discharge	6	3
DAMA	1	3
Death	3	50
GIT (n=16)	15	1
Discharge	14	1
DAMA	1	0
Death	0	0
CNS (n=8)	7	1
Discharge	0	0
DAMA	2	0
Death	5	1
Thrombotic (n=6)	4	2
Discharge	3	0
DAMA	0	0
Death	1	2
Renal (n=4)	3	1
Discharge	3	0
DAMA	0	0
Death	0	1

DISCUSSION

A) Cardiovascular manifestations:

Considering comorbidities as risk factors for the development of acute myocardial infarction, in our study, 59.09% of patients had Hypertension, comparable to Alexander Fardman et al.³ (51.8%), Nandy S et al.⁴ (58%), shao L et al.⁵ 55.6%, more than Giulio Stefanini et al.⁶ study (32.1%). In our study, patients having Diabetes were 59.09%, which was higher than the Alexander Fardman et al.³ study (31.1%) and Giulio Stefanini et al.⁶ (28.5%). In our study, 16.66% of patients already had ischemic heart disease, comparable to 20.7% in Alexander Fardman et al.³ study, Nandy S et al.⁴ study (17%) and more than Giulio Stefanini et al.⁶ study (10.71%).

Overall 44% patients had ST Elevation Myocardial Infarction which is comparable to Alexander Fardman et al.³ (50.4%).

In our study, 19 patients having STEMI out of 44 patients having STEMI were Thrombolysed by streptokinase and patients having NSTEMI and those who could not be thrombolysed were given anticoagulants, antiplatelets and statins, compared to PCI as the mainline of management in Alexander Fardman et al.³ study and Giulio Stefanini et al.⁶ study. As patients of covid-19 infection require isolation, thrombolytic therapy can be started immediately if within reperfusion time. In our study, patients were already admitted to the hospital when myocardial infarction developed and so thrombolysis could be started immediately and effectively.

In our study 18.18% patients had new onset heart failure which is comparable to study Nandy S et al.⁴ in which 23% patients had new onset heart failure and Zhou F et al.⁷ study in which 23% patients had new onset heart failure.

In our study 7.2% patients had new onset arrhythmia in which patients had new onset atrial fibrillation which is comparable to Monica RS et al.⁸ in which 6.5% patients had new onset atrial fibrillation and Tolu-Akinnawo O et al.⁹ study in which 12.7% patients had new onset atrial fibrillation.

In our study, 80.3% of patients deceased, higher than Nandy S et al.⁴ (51.2%), higher than the 39.28% of Giulio Stefanini et al.⁶ study. Only 13.63% of patients were discharged in our study, which was very less compared to the 57.1% patients in Giulio Stefanini et al.⁶ study this insimilarity may be due to number of patients in study.

Patients with cardiovascular manifestations had higher mortality due to higher incidence of coagulopathy and thromboembolic manifestations.

B) Gastrointestinal manifestations:

In our study, out of 100 patients incidence of gastrointestinal manifestations was 16%, which is comparable to study Aakriti gupta et al.² (12%-61%) and Pan, L. Et al.¹⁰ (18.6%).

In our study, 31.25% patients had diarrhea, 6.25% patients had vomiting and which is comparable to study and Pan, L. Et al.¹⁰ (34% diarrhea, 3.9% vomiting)

Gastrointestinal manifestations have not been associated with increased mortality, which is comparable to Aakriti Gupta et al.².

C) Central nervous system manifestations:

In our study, out of all patients who developed acute ischemic stroke in neurological manifestations were 8% , which is comparable to L Mao Et al.¹¹ (6.5%) and Y Li et al.¹² in which 5% patients had ischemic stroke.

D) Thrombotic manifestations:

In our study, patients who developed thrombotic complications were overall 6% despite they received prophylactic anticoagulation, which is lower than J Helms. Et al.¹³ (17-22%), J F Llitjos, et al.¹⁴ (69%). This insimilarity is due to number of patients studied and patients were studied only for thrombotic manifestations.

In our study, patients with deep venous thrombosis were 50% and pulmonary embolism were 50%. Incidence of Pulmonary embolism (50%) higher compared to J poissy Et al.¹⁵ (20.6%).

E) Renal manifestations:

In our study, 4% patients with COVID-19 developed AKI during hospitalisation which was comparable to 0.5% to 29% in Aakriti Gupta et al.² study.

In our study, patients with Renal manifestations 25% died and 75% discharged which are comparable to the study conducted by Hirsch et al.¹⁶ (Death=16.3% and discharge=60.2%).

In our study, patients with Renal manifestations overall 1% and among renal manifestations patients with AKI 25% were required Hemodialysis which is comparable to the study Hirsch et al¹⁶. (5.2% of all patients, 14.3% of those with AKI.)

F) Mortality in Stable Patients:

Patients who were stable on admission, rapidly deteriorated due to rapid progression of disease (COVID-19) and could not be survived.

CONCLUSION

Patients with COVID-19 may develop extrapulmonary manifestations besides respiratory symptoms. As a emergency physician we should be very careful while managing COVID-19 patients for developing extrapulmonary manifestations. By this we can improve patient's survival and reduce mortality. This study guides us for future pandemics of SARS-CoV 2 and we can focus extrapulmonary manifestations beyond pulmonary manifestations.

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