



ANALYSIS OF NON-RESPIRATORY SYMPTOMS IN COVID-19 HOSPITALISED PATIENTS

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ABSTRACT Prevalence of non-respiratory symptoms, has been very commonly described nowadays with progress of coronavirus pandemic.¹ Knowledge of non- respiratory clinical manifestations may help in detecting the mild and moderate forms, which can aid in early diagnosis and rapid quarantining which will prevent community spread. With this perspective present study was undertaken to study incidence of non- respiratory symptoms, various complication related to blood, gastrointestinal, renal, dermatologic, neurologic, psychiatric and outcome in COVID- 19 patients. **Materials and Methods** :This study was a Hospital Based Prospective Observational Study which was conducted from November 2020 to November 2022 in the patients admitted in Department of Medicine at MGM Medical College and Hospital, Aurangabad. **Observation and Result**: Most commonly encountered non respiratory symptoms were fever, generalized weakness, oliguria, myalgia, anosmia, anorexia, diarrhea, headache, anxiety, arthralgia, depression, palpitation, chest pain, nausea, vomiting. **Conclusion**: Though the respiratory symptoms are found to be more common in COVID 19 patients in the study, non-respiratory symptoms were also found to be very common such as fever, fatigue, myalgia, anosmia, anorexia, diarrhea, anxiety, oliguria, dysgeusia. Complications like acute kidney injury, acute myocardial infarction, Arrhythmias, ischaemic stroke, meningitis, pancreatitis, pulmonary embolism, DVT and acute hepatitis were commonly found. Comorbidities were found to have significant relationship with the increased complications, outcome and mortality.

KEYWORDS :

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is highly transmissible coronavirus had emerged in late 2019 from the city of Wuhan has caused a pandemic COVID-19. Corona virus is a beta coronavirus which is enveloped positive-stranded RNA virus. Person to person transmission (within 6 feet) through respiratory droplets during especially coughing or sneezing is a primary source of infection². Other sources are airborne route with inhalation of particles smaller than droplets suspended in air and indirect transmission through contact with contaminated surfaces. Incubation period is generally 14 days with most cases having four to five days³. SARS-CoV-2 primarily attacks lower respiratory system causing viral pneumonia, but it may also affect the heart, gastrointestinal system, liver, kidney and central nervous system leading to multiple organ failure¹⁰. SARS-CoV-2 infection begins when the viral surface spike protein (S) binds to the human angiotensin-converting enzyme receptors (ACE2) receptor following activation of the spike protein by trans membrane protease serine 2 (TMPRSS2) which facilitates S protein priming³.

It is well established that COVID-19 most probably presented with fever and mild respiratory signs and symptoms, such as cough, shortness of breath and dyspnea. Prevalence of non-respiratory symptoms, has been very commonly described nowadays with progress of coronavirus pandemic and accumulation of scientific data from previous studies^{19,20}. Understanding the pathophysiological mechanism of corona virus in other systems of human body and its non-respiratory clinical manifestations with exploring uncommon clinical features will provide comprehensive medical knowledge for improving diagnosis and management. It is uncommon for respiratory viruses to have such widespread influences in other parts of body. Knowledge of non- respiratory clinical manifestations may help in detecting the mild and moderate forms, which can aid in early diagnosis and rapid quarantining which will prevent community spread. With this perspective present study was undertaken to study incidence of non- respiratory symptoms, various complication related to blood, gastrointestinal, renal, dermatologic, neurologic, psychiatric and outcome in COVID- 19 patients.

MATERIAL AND METHODS

The present study is a Hospital Based Prospective Observational Study which was conducted from November 2020 to November 2022 in the patients admitted in Department of Medicine at MGM Medical College and Hospital, Aurangabad. Approval of institutional ethics committee was taken prior to commencement of present study. Total 151 patients fulfilling inclusion and exclusion criteria were enrolled. Details of the study was explained to all patients in their own language and written informed consent was obtained from all.

Inclusion Criteria:

1. All patients, above 18 years of age.
2. Diagnosed with COVID 19 by Real Time Polymerase Chain Reaction (rt-PCR)
3. Diagnosed with COVID 19 by HRCT (High-Resolution Computed Tomography).

Exclusion Criteria:

1. COPD / Bronchial Asthma
2. History of Tuberculosis
3. Lung Malignancies

Statistical Analysis:

Data was entered in MS Excel and analysed using SPSS software, with chi-square test and odds ratio used to test proportions, p-value <0.05 considered significant, and results presented in visual forms like bar and pie diagrams.

OBSERVATIONS AND RESULTS:

Distribution of cases according to age and sex :

In this study, out of 151 Covid 19 patients, maximum 63 (41.72%) patients were from age group of 51-70 years, 48 (31.79%) were from age group of 31-50 years, 24 (15.89%) were from age group >70 years and only 16 (10.59%) were from age group of 19-30 years. The mean age of the patients was 46.22 ± 16.94 years. The cases were distributed according to sex, which shows the male 89 (58.94%) predominance over female 62 (41.06%).

Distribution of cases according to comorbidities : In this present

study majority of covid 19 patients reported to have comorbidities i.e diabetes 30 [19.87%], Hypertension 24 [15.89%], history of IHD 15[9.93%], obesity 22 [14.57%], hypothyroidism 11 [7.28%], Ckd 11[7.28%], cerebrovascular diseases 9[5.96%], chronic liver disease 3 [1.98%], many patients had more than one comorbidities.

Distribution of cases according to outcome: Majority of the patients 142 [94.04%] were discharged from the hospital, while 9 % [5.96%] patients died due to one or more complications.

Table 1 : Distribution Of Cases According To Non-respiratory Symptoms

Systems	Symptoms	Total Present N	Percentage (%)
Cardiovascular system	Chest pain	26	17.22
	Palpitations	28	18.54
	Breathlessness	59	39.07
Gastro- intestinal Tract	Anorexia	47	31.12
	Diarrhea	46	30.46
	Nausea, Vomiting	26	17.22
	Abdominal pain	18	11.92
	Abdominal distension	10	6.62
Neurological	Dizziness	26	17.22
	Headache	27	17.88
	Impaired consciousness	17	11.26
	Seizures	4	2.65
	Diplopia	1	0.66
Hematologic al	Petechiae	17	11.26
	Mucosal bleeding	13	8.61
	Easy bruising	12	7.95
Cutaneous	Rashes	21	13.91
	Urticaria	9	5.96
Olfactory and gustatory	Hyposmia, Anosmia	49	32.45
	Dysgeusia, Ageusia	32	21.19
Renal	Oliguria	31	27.15
	Burning micturition	9	5.96
Hepatic	Fatigue	75	49.67
	Icterus	6	3.97
Psychiatric	Anxiety	36	23.8
	depression	31	20.52
	Sleep disorder	10	6.62
	suicidal tendency	6	3.9
Musculoskeletal	Myalgia	60	39.73
	arthralgia	36	23.84
Ophthalmological	conjunctivitis	11	7.28
Miscellaneous	Fever	91	60.26

Table 1 shows distribution of cases according to non respiratory symptoms in this study majority of patients reported of having respiratory symptoms ,but even non respiratory symptoms were very common. Most commonly encountered non respiratory symptoms were fever 91 [60.26%], generalized weakness 75 [49.67%], myalgia 60 [39.73%], anosmia 49 [32.45%], anorexia 47 [31.12%], diarrhoea 46[30.46%], headache 27 [17.88%], anxiety 36[23.84%], arthralgia 36 [23.80],depression 31[20.52%], palpitation 28 [18.54%], chest pain 26 [17.22%], nausea vomiting 26[17.22%].

GRAPH 3: Distribution of patients according to non respiratory symptoms

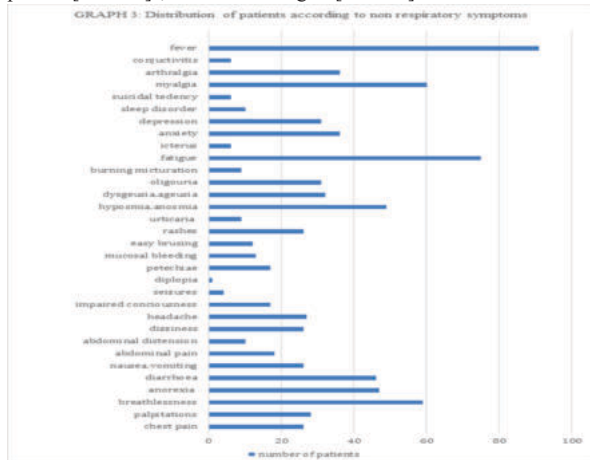


Table 2 : Distribution Of Cases According To Complications

Sr. No.	Complications	Total Present N (%)
1	Acute kidney failure	31 [15.23%]
2	Acute Myocardial infarction	7 [4.63%]
3	Arrhythmias	13 [8.61%]
4	Ischemic stroke	4 [2.65%]
5	Encephalitis/ meningitis	11 [5.96%]
6	Pancreatitis	22 [3.97%]
7.	Pulmonary embolism	3 [1.99%]
8.	Deep vein thrombosis	4 [2.65%]
9.	Acute Hepatitis	13 [8.61%]

Table 2 shows distribution of cases according to complications. Out of 151 patients complications like acute kidney injury (20.52%), acute myocardial infarction (5.96%), arrhythmias (11.92%), ischemic stroke (3.97%), meningitis (7.28%), pancreatitis (3.97%), pulmonary embolism (1.99%), DVT (2.65%) and acute hepatitis (8.61%) were found.

Many patients had more than one complications.

DISCUSSION

Coronavirus disease 2019 (COVID-19) is caused by a novel single-strand ribonucleic acid (RNA) coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARSCoV-2).⁷ It has been recognized by the World Health Organization (WHO) as an international pandemic¹². SARS-CoV-2 primary attacks the lower respiratory system causing viral pneumonia. However, extra-respiratory manifestations of SARS-CoV-2 infection have also been observed in the rapidly increasing number of COVID-19 cases. To reduce the risk of overlooking patients with COVID-19 who manifest only extra-respiratory symptoms, clinicians need to better understand the range of SARS-CoV-2 infection-related extra-respiratory manifestations. Therefore, we conducted this study to understand the range of the extra-respiratory manifestations of COVID-19 to help clinicians better understand the clinical presentations of the disease.

Several comorbidities have been identified as risk factors for severe COVID-19 disease. The most prevalent comorbidities detected in different studies were hypertension (HTN), diabetes mellitus (DM) and obesity, cardiovascular diseases, and chronic liver disease.

Age and Gender:

We recruited 151 cases in the final analysis. In this study, out of 151 covid 19 patients, maximum patients i.e. 63 [41.72%] were from the age group of 51-70 yrs, while patients in the age group of 31-50 years were 48(31.79%), in the age group of >70 years were 24 (15.84%) and that of 19-30 years were 16 (10.59%).

In the current study, covid 19 was more commonly seen in male patients i.e. 89 [58.94%] male and 62 [41.06%] female.

Non-respiratory symptoms:

Though the respiratory symptoms were more common in covid 19 patients, extra pulmonary symptoms were also found to be very common along with pulmonary symptoms.

Among the non-respiratory symptoms, most commonly patient had fever i.e 91 [60.26%], fatigue 75 [49.67%], myalgia 60 [39.73%], anosmia 49 [32.45%], anorexia 47 [31.12%].

Diarrhoea 46 [30.48], headache 27 [17.88%], anxiety 36 [23.84], arthralgia 36 [23.80%], depression 37 [20.52%], palpitations 28 [18.54%], chest pain 26 [17.22%], nausea and vomiting 26 [17.22%], oliguria 41 [27.5%] were also very commonly noticed.

A review study done by **Islam H. Elrobaa et al.**, found various symptoms as follows: diarrhea(23%), nausea and vomiting (13.7%), abdominal pain (6.6%), headache (13.1%), dizziness (16.8%), seizures (2%), acute cerebrovascular accident (2.8%), ischemic stroke(2.5%), insomnia(18.2%), ataxia (0.5%), anxiety mild (36.8%) moderate(26.7%) and severe(32.0%), depression mild(31.6%) moderate(12.3%) severe (19.3%), insomnia (18.2%), suicidal ideation (10.7%), maculopapular rash and erythema (20.4%), conjunctivitis and redness of eye (14.8%).¹⁷

Some less likely symptoms were also found in this study abdominal pain 18 [11.92%], insomnia 18 [11.92%], petechial 17 [11.26%], impaired consciousness [11.26%], mucosal bleed 13 [8.61%], Easy

bruising 11 [7.95%], conjunctivitis 11 [7.28%], abdominal distention 10 [6.62%].

Other rare symptoms were like urticaria 9 [5.96%], icterus 6 [3.97%], seizure 4 [2.65%].

Suicidal tendency 6 [3.91%], burning micturition 9 [5.96%], and diplopia 1 [0.66] were also found in some patients.

A study from **A Zhou et al** found that out of 541 patients of covid 19, 368(68%) had dry cough, cough with sputum 165(30.5%), dyspnea 89(16.5%), runny nose 3(0.6%), sore throat 38(7.0%), hemoptysis 26(4.8%), chest tightness 26(4.8%), nasal congestion 15(2.8%), fever 179(33.1%), myalgia 70(12.9%), diarrhea 49(9.1%), headache 42 (7.8%), palpitation 3 (0.6%), loss of smell and taste 8(1.5%).⁹

Another study from **Zhang et al.** showed that various gastrointestinal symptoms such as nausea (17.3%), diarrhea (12.9%), anorexia (12.2%), abdominal pain (5.8%), belching (5%), vomiting (5%) was noted were noticed in a study of 140 patients.¹⁰

A study by **Angelo V. Vasiliadi** suggested that out of 79 patients participated in this study, arthragia 29(36.7%), myalgia 41(51.9%), fatigue 60(75.9%), fever 58 (73.4%), chest pain 19(24.1%), cough 33 (41.8%), anosmia 30(38%), ageusia 28(35.4%), headache 25 (35.6%) were found.¹¹

A study from **Mao L, et al.** CNS manifestations found were, out of 214 patients, dizziness (16.8%), headache (13.1%), impaired consciousness (8%), acute cerebrovascular accidents (3%), ataxia (0.5%), anosmia (5.1%), ageusia (5.6%).⁸

A study from **Chih-Cheng Lai et al.**, reported prevalence as acute cardiac injury (8–12%), heart failure (23–52%), arrhythmia (8.9–16.7%), anorexia (26.8%), diarrhoea (12.5%), nausea/vomiting (10.2%), abdominal pain/discomfort (9.2%) Abnormal aspartate aminotransferase or alanine aminotransferase values (16.1–53.1%) acute kidney injury (overall 0.5%; 2.9–23% in severe cases), dizziness (16.8%), headache (13.1%), skeletal muscle injury (10.7%), impaired consciousness (7.5%), acute cerebrovascular disease (2.8%), ataxia (0.5%), seizures (0.5%), hyposmia (5.1–20.4%), anosmia (79.6%), dysgeusia (8.5%), ageusia (1.7%), acute conjunctivitis (31.6%) erythematous rash (15.9%), hives rash (3.4%), vesicles (1.1%), thrombocytopenia (16.4–32.3%).¹³⁵

Anosmia and dysgeusia is also a very common feature of this viral disease.

Though multiple symptoms from multiple systems were found in single patient, this data is self- explanatory about the wide range of symptoms and systems that are involved in SARS-COV 2.¹⁰

Thus we say that Covid-19 is not only respiratory but a multi system disease involving various systems at a time and presenting with wide spread symptoms.

More commonly involved systems found in this study other than respiratory were gastro-intestinal system, central nervous system and psychiatric symptoms.

Fever, anosmia, generalized weakness, fatigue, myalgia were the most commonly discovered symptoms in this study.

A study from **Sachin A Adhikia et al.** dizziness(17%), headache(13%) , impaired consciousness (16%), acute cerebrovascular disease(3%), ataxia(1%), seizures(1%), taste impairment(5.6%), smell impairment(5%), vision impairment(1.4%), nerve pain(2.3%), myalgia (11%), anorexia(30–40%), diarrhea(2–50%), nausea/vomiting(2–12%), abdominal pain(2–4%), digestive symptoms (3–23%), abnormal liver tests: Aminotransferases (14–53%), Bilirubin(10–18%).⁴

Comorbidities:

Among the 151 patient analysed in this study, many of COVID 19 patients reported to have co-morbidities i.e. Diabetes mellitus 30 [19.87%], Hypertension 24 [15.89%], history of Ischemic heart disease 15 [9.93%], obesity 22 [14.57%], hypothyroidism 11 [7.28%], CKD 11 [7.28%], Cerebrovascular diseases 9 [5.96%], Chronic

Liver disease 3[1.98%].

A study by **Angelo V. Vasiliadis** showed that out of 79 patients, 30(38%) patients had some type of comorbidity. In which 22(27.8%), cardiovascular disease 10(12.7%), diabetes mellitus 5(6.3%), hypothyroidism 5(6.3%). Many patients were found to have more than 1 co-morbidity.

Complications:

In this study, out of 151 patients 38 [25.16%] had atleast one complications. Out of 151 patients complications like acute kidney injury (20.52%), acute myocardial infarction (5.96%), arthrmias (11.92%), ischemic stroke (3.97%), meningitis (7.28%), pancreatitis (3.97%), pulmonary embolism (1.99%), DVT (2.65%) and acute hepatitis (5.96%) were found. Many patients had more than one complications.

A study by **Thomas M Drake et al.** reported that adult patients with COVID 19 developed various systemic complications with acute kidney injury (39.9%), cardiac arrhythmia (19.9%) and ARDS (28.1%) being common.

Another study **Marwan Muhammad et al.** concluded that incidence of arrhythmia was 3.1% in non icu patient and 43.8% in the icu patient.

Mortality:

Majority of the patients 142 [94.04%] were discharged from the hospital while 9 [5.96%] patients died during the hospital stay. Out of 9 patients died during the hospital stay, 8 were having comorbidities. 5 patients had multiple comorbidities. 6 were males and 3 were females. All the 9 patients died due to one or more complications leading to death. All the 9 patients were taken on invasive ventilator.

CONCLUSION :

- Though the respiratory symptoms are found to be more common in COVID 19 patients in the study, non-respiratory symptoms were also found to be very common.
- Non respiratory symptoms such as fever, fatigue, myalgia, anosmia, anorexia, diarrhea, anxiety, oliguria, dysgeusia were very commonly found.
- Complications like acute kidney injury, acute myocardial infarction, Arrthrmias, ischaemic stroke, meningitis, pancreatitis, pulmonary embolism, DVT and acute hepatitis were commonly found in this study.
- Comorbidities were found to have significant relationship with the increased complications, outcome and mortality.

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