

## POST COVID COMPLICATIONS AMONG COVID-19 PATIENTS TREATED AT A TERTIARY CARE CENTRE OF WESTERN RAJASTHAN.

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### ABSTRACT:

**INTRODUCTION:** Majority have mild disease and recover from acute COVID disease, significant proportion of patients had variety of complications beyond the acute phase. This study aimed to determine the spectrum of post COVID complication among treated COVID patients.

**Material and Methods:** This descriptive observational study was conducted jointly by Department of Community Medicine and General Medicine at a tertiary care centre of western Rajasthan. 'Post- COVID-19 complications' were defined as persistent symptoms and/or delayed complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms or positivity by RT-PCR. A total of 831 patients treated at this hospital during the 1<sup>st</sup> wave of COVID were evaluated for possible post COVID sequelae.

**Results:** Most of the patients were <40 years age. Among patient not requiring admission, the common complication were weakness / fatigue (21.2%), breathlessness (12%), persistent cough (8.6%), prolonged loss of smell / taste (3.2%). Among patients requiring admission, common complications were continuous breathlessness (51.5%), anxiety /depression (36.2%), lack of sleep (13.8%), weakness / fatigue (22.9%). More serious complications included uncontrolled Diabetes (9.1%), arrhythmia (5.3%), uncontrolled hypertension (3.8%) deep venous thrombosis (2.6%), and Myocardial infarction (0.9%). Serious complications like continued breathlessness thrombo-embolic events were more common among elderly patients.

**Conclusion:** Multi-organ sequelae of COVID-19 after the acute disease phase are being identified. Multi disciplinary approach is required for early identification and management of these varieties of post-COVID ailments.

**Key words:** COVID, Corona, Post COVID, Long COVID.

### INTRODUCTION:

COVID-19 disease caused by SARS-CoV-2, first identified in December 2019, spread rapidly throughout the world causing significant morbidity and mortality, leading WHO to declare it pandemic on 11 March 2020 (1). COVID- 19 had lead to wide range of manifestations ranging from

mild upper respiratory tract infection symptoms like fever, cough, and dyspnea to acute respiratory failure and multi organ manifestations that may lead to mortality (2–

progress to ARDS (6). Patients who have cardiopulmonary or metabolic comorbidities (e.g., diabetes mellitus), autoimmune diseases, or immune-suppression have a higher risk of death (3). Most patients get cured without lung damage, a significant number of patients will suffer residual sequelae (6). Scientific evidence is evolving on the long-term effects of COVID-19, which can affect multiple organ systems (7).

**Post-COVID conditions** are a wide range of new, returning, or ongoing health problems people experience **four or more weeks** after

first being infected with the virus that causes COVID-19. (8,9) Even people who did not have COVID-19 symptoms after they were infected can have post-COVID conditions (8).

Post COVID complains reported include shortness of breath, fatigue, Difficulty concentrating (“brain fog”), prolonged Cough, Chest or stomach pain, Headache, palpitations, Joint or muscle pain, Diarrhea, Sleep problems, Rash, Mood changes, Change in smell or taste etc. (5,8,10–12) Despite the abundance of journal articles published on acute COVID-19 infection, the clinical picture of post- COVID-19 and its sequelae are still under investigation (2,13). To provide insight to understand and manage post-COVID-19 sequelae, present study aimed to identify various post COVID complications among patients recovered from COVID.

### **Material and methods:**

This descriptive observational study was conducted jointly by Department of Community Medicine and General Medicine at the largest tertiary care centre of western Rajasthan. This hospital was among the Rajasthan to start testing for COVID by RT-PCR test and had conducted 363,384 tests during 1<sup>st</sup> wave by Jan 2021, of which 37,314 had turned out positive. Looking at the emerging post COVID complications, Post COVID OPD and IPD were started in this hospital. For study purpose ‘Post- COVID-19 complications’ were defined as persistent symptoms and/or delayed or long-term complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms or positivity by RT-PCR. A total of 831 patients treated at this hospital during the 1<sup>st</sup> wave of COVID were recruited for the study. These patients were recruited from from IPD (340 patients), Post COVID OPD (219 patients) or telephonic contact of patients treated previously (272 patients). A pre designed Semi structured proforma was used to collection information from these post COVID patients. Information from admitted post COVID patients was obtained from patient’s case sheets.

### **Results:**

Most of the patients studied in post COVID

period belonged to <30 years (23.5%) and 50-59 years (21.4%). 19.7% patients were in 60-69 years and 56 (6.7%) were  $\geq 70$  years (Table 1). Most of the patient were male (67.4%) and 32.6% were females. This difference reflects the difference in COVID positive cases, which are recorded more in males (Table 2).

Among patient not requiring admission, the most common complication seen was weakness / fatigue in 104 (21.2%) followed by continued breathlessness (12%). Other common complications prolonged cough (8.6%), prolonged loss of smell / taste (3.2%). Psychological complications include lack of sleep (10.2%), anxiety /depression (2.8%). Among more serious complications include uncontrolled Diabetes (2.2%) and uncontrolled Hypertension (0.4%) and Deep venous thrombosis (0.6%). Cardiac complications include arrhythmia (0.8%) and Myocardial Infarction (0.2%).

Among patients requiring admission (IPD), the most common complication seen was continuous breathlessness (51.5%), followed by post viral pneumonitis (36.2%). Psychological complications include anxiety /depression (36.2%) and lack of sleep (13.8%). Other complications include weakness / fatigue (22.9%). Among more serious complication, uncontrolled Diabetes (9.1%), uncontrolled hypertension (3.8%) deep venous thrombosis (2.6%), Acute renal failure (2.6%), stroke (0.6%). Cardiac complications include arrhythmia (5.3%) and Miocardial infraction (0.9%). Other rare complication include Thyroid dysfunction (1 OPD, 1 IPD), weight loss (1 OPD, 3 IPD), electrolyte imbalance ( IPD-1), MODS (IPD-2), Sepsis (IPD-5) (Table 3).

Weakness / fatigue were the most common complication among all age groups. Continued breathlessness and post viral pneumonitis were more common among older age group. Lack of sleep was more common among younger age group, while anxiety/depression and prolonged cough were equally common among all age groups. Prolonged loss of taste/smell were seen

exclusively among younger age patients (<50 years). More serious complications like Deep venous thrombosis, uncontrolled or new onset diabetes and hypertension, stroke and MI were relatively more common among older age patients (Table 4).

**Table 1: Age distribution of study subjects**

Age group (years)	N	Percentage
<30	195	23.5
30-39	125	15.0
40-49	113	13.6
50-59	178	21.4
60-69	164	19.7
≥70	56	6.7
<b>Total</b>	<b>831</b>	<b>100.0</b>
<b>Mean ± SD</b>	<b>46.35 ± 17.12</b>	

**Table 2: Gender distribution of study subjects**

Gender	N	Percentage
Male	560	67.4
Female	271	32.6
<b>Total</b>	<b>831</b>	<b>100.0</b>

**Table 3: Post COVID complications among OPD and IPD patients**

Clinical feature	OPD / Contact (N=491)		IPD (N=340)		Total (N=831)	
	N	%	N	%	N	%
Weakness / fatigue	104	21.2	78	22.9	182	21.9
Breathlessness	59	12.0	175	51.5	234	28.2
Post viral pneumonitis	3	0.6	123	36.2	126	15.2
Lack of sleep	50	10.2	47	13.8	97	11.7
Prolonged cough	42	8.6	19	5.6	61	7.3
Anxiety / depression	14	2.8	123	36.2	137	16.5
Prolonged loss of smell/taste	16	3.2	4	1.2	20	2.4
Uncontrolled DM	11	2.2	31	9.1	42	5.1
Uncontrolled HTN	2	0.4	13	3.8	15	1.8
DVT	3	0.6	9	2.6	12	1.4
Headache	6	1.2		0.0	6	0.7
Arrhythmia	4	0.8	18	5.3	22	2.6
ARF	0	0	9	2.6	9	1.1
Newly Dx HTN	0	0	4	1.2	4	0.5
Newly Dx DM	0	0	9	2.6	9	1.1
CVA / Stroke	0	0	2	0.6	2	0.2
ACS / MI/ CAD	1	0.2	3	0.9	4	0.5
Others	2	0.4	12	3.6	14	1.7

**Table 4: Post COVID complications in different age groups**

Clinical feature	<30 years (N=194)	30-50 years (N=239)	50-70 years (N=315)	>70 years (N=83)
Weakness / fatigue	40 (20.6%)	61 (25.5%)	70 (22.2%)	11 (13.3%)
Breathlessness	24 (12.4%)	54 (22.6%)	122 (38.7%)	34 (41%)
Post viral pneumonitis	8 (4.1%)	31 (13%)	62 (19.7%)	25 (30.1%)
Prolonged cough	20 (10.3%)	20 (8.4%)	18 (5.7%)	5 (6%)
Anxiety/Depression	27 (13.9%)	36 (15.1%)	58 (18.4%)	16 (19.3%)
Lack of sleep	37 (19.1%)	26 (10.9%)	27 (8.6%)	6 (7.2%)
Prolonged loss of smell/taste	16 (8.2%)	4 (1.6%)		
DVT	1 (0.5%)	1 (0.4%)	7 (2.2%)	3 (3.6%)
Arrhythmia	6 (3.1%)	6 (2.5%)	9 (2.9%)	1 (1.2%)
Uncontrolled HTN		3 (1.3%)	10 (3.2%)	2 (2.4%)
Newly Dx HTN		1 (0.4%)	3 (1%)	
Uncontrolled DM	1 (0.5%)	5 (2.1%)	29 (9.2%)	7 (8.4%)
Newly Dx DM		1 (0.4%)	6 (1.9%)	2 (2.4%)
Headache	2 (1%)	1 (0.4%)	3 (1%)	
ARF		2 (0.8%)	2 (0.6%)	5 (6%)
CVA / Stroke			2 (0.6%)	
ACS / MI/ CAD			2 (0.6%)	2 (2.4%)
Others	2 (1%)	2 (0.8%)	5 (1.5%)	1 (1.2%)

**Discussion:**

Most COVID-19 patients survived the acute phase, but a significant proportion of these patients developed variety of health problems. Most of the patients in present study belonged to <40 years (37.5%). Male : Female ratio was 2.1:1. Mahmud R et al also had similar findings with most patients (60%) younger than 40 years of age and ratio of male and female patients of 1.4:1. (4) In another similar study patient's age ranged from 25 to 75 years with mean age of 43.2 years (6). Cellular damage, inflammatory cytokine production, and a pro-coagulant state induced by SARS-CoV-2 infection is proposed to contribute to post COVID sequelae (7).

Fatigue was the most common complain (>20%). Similar studies have reported fatigue in upto 63% patients recovered from COVID. (4,5,7,10,13) Formation of pro-inflammatory cytokines, interleukins (IL-1, TNF-α and Toll-like receptors), and interferon gamma within the

hypothalamus might lead to the development of post-viral fatigability (4,14) Dyspnea during exertion was noted in 28.2% cases in present study. Studies have reported Dyspnea in post covid patients ranging from 7% to 43.4% (4,7,13). Pre-existing respiratory disease, higher body mass index, older age had been associated with post COVID dyspnea. (7) Persistent cough had been reported in 8.5% to 15.4% patients (4,7) similar to 7.3% cases in present study. Thrombotic complications were seen in many patients. Deep venous thrombosis was seen in 1.4% of cases. Increases in complement level, coagulation and tissue factors, plasminogen activating factor I, and von Willebrand factor are responsible for modifying the hemostatic environment, and held responsible for these thromboembolic issues (3)

Acute cardiac events were seen in 0.5% of patients. High levels of circulating cytokines and mediators of toxic response, including IL-6, TNF- $\alpha$ , nitric oxide, have been described in pathogenesis of cardiovascular complications(5,15). Thrombo-inflammatory mechanism including endothelial injury, complement activation, platelet activation and platelet-leukocyte, interactions, neutrophil extracellular traps, release of pro-inflammatory cytokine and disruption of normal coagulant are held responsible for cardiac complications(3,7) Cardiac Arrhythmia was found in 2.6% patients. Studies have reported arrhythmia in upto 1.3% cases (4,13). COVID-19 causes arrhythmias due to increased catecholaminergic state caused by cytokines (IL-6, IL-1 and TNF- $\alpha$ ), that prolongs ventricular action potentials by modulating cardiomyocyte ion channel expression (16).

Acute Kidney Injury occurred in 2.6% of admitted post COVID patient. Studies have reported AKI in upto 5% of all hospitalized patients and 20–31% of critically ill patients (7,17). Uncontrolled sugar level in known diabetics occurred in 9.1% of cases requiring admission, while New onset DM was found in 2.6% of admitted cases. Another similar study 0.6% (4) consequences of direct viral injury, immunological and inflammatory damage (7). New onset HTN was seen in 1.2% of IPD patients similar to finding of other studies (4)

Neurological manifestation have been reported in past studies in upto 36.4% patients (18). Persistent loss of taste or smell was noted in 2.4% of post COVID patients in present studies. It had been reported in upto 13.1% from other regions (4,7). Loss of smell / taste could be due to neurotropic infection to the gustatory or olfactory systems (19). Headache was reported by 0.7% of patients in present study. Other similar studies have reported headache in 0.6 to 70.3% even after 6 weeks (3,4,7). Two patients (0.6%) were admitted with Stroke in post COVID period. Its etiology is considered multifactorial, including direct viral infection, systemic inflammation, neuroinflammation, neuro-degeneration and microvascular thrombosis (7,20). Risk of stroke has been associated with old age and comorbidities (21).

Psychological disturbance (anxiety / depression) was noted in as many as 16.5% patients, especially among those requiring admission. In a meta-analysis stress was identified as the most prevalent mental health sequele (48.1%)(5). Depression (26.9%-46.9%) (5) and anxiety (21, 8%) (22) were reported in many patients. In another study, anxiety/ depression was reported in 23% patients (7). In yet another study, psychological distress, like post-traumatic stress disorder, anxiety, depression lack of concentration and were noted in approximately 30% cases (7) and sleep difficulties in 26% cases. Lack of sleep was seen in 11.6% patients in present study. Sleep disturbance have been reported in 5.9% - 20% patients. (4,5) It has been related to emotional distress and increased stress responsivity, probably due to shortness of breath and low blood oxygen levels. (5)

Quarantine and isolation measures were adopted globally to prevent spread of disease, that lead to abrupt change in people's lifestyles, causing panic and anxiety (22). All these complications have developed or were severe in those with symptomatic / severe COVID disease, thus the best way to prevent post-COVID conditions is vaccination against COVID-19 that protects against severe disease (8). Also COVID patients need to be followed up with regular check up. Experts have suggested evaluation with serial PFTs and 6MWTs for patients with persistent

dyspnea, and HRCT chest at 6 and 12 months (7). Evaluation of COVID-19 survivors after hospital discharge can be based on the severity of acute COVID. Clinical assessment and chest X-ray in all patients at 12 weeks, along with consideration of PFTs, 6MWTs, sputum sampling and echocardiogram have been recommended (23). An early clinical assessment for respiratory, psychiatric and thromboembolic sequelae, as well as rehabilitation needs, is also recommended at 4–6 weeks after discharge for those with severe acute COVID-19, defined as those who had severe pneumonia, required ICU care, are elderly or have multiple comorbidities.(23) Multidisciplinary rehabilitation team care to deal with these complications have also been recommended (5).

## CONCLUSION:

The multi-organ sequelae of COVID-19 after the acute disease phase are being identified. Regular follow-up is required even after recovery for early identification and management of these post-COVID ailments. Prioritization of post COVID care needs to be considered for those at high risk for post- COVID complications, including elderly patients and those with comorbidities or those who had severe illness during acute COVID-19. A comprehensive multidisciplinary rehabilitation program seems essential with specific recommendations regarding physical activity, nutrition, psychological care, and regular follow up.

**Limitation:** Patients treated at this tertiary level hospital were included, thus proportion of complication may not be applicable to entire population developing COVID as most patients are asymptomatic. This was a cross sectional study and it is expected that many patients would have developed problems after our contact. Thus prospective study with multiple follow up could better estimate the burden of post COVID complications.

**Conflict of interest:** Nil

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