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Incidence of Post-Covid-19 Sequelae

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ABSTRACT:
Introduction:SARS-CoV-2, the causative agent of COVID-19, is a beta coronavirus, belonging to the subfamily Orthocoronaviridae. SARS-CoV-2 is highly transmissible as a droplet infection and via touching contaminated surfaces. In contrast to the initial misconception that COVID-19 infection resolves completely within two weeks, it is persistent beyond 4 weeks in some patients which are termed as Post COVID syndrome or long COVID syndrome. 'Long COVID syndrome' most commonly refers to symptoms persisting for more than three to four weeks after the diagnosis of COVID-19 or after the first symptom onset.
Aim of the study: The aim of the study was to assess the incidence of Post COVID sequalae.
Methodology: This is questionnaire based cross sectional study conducted between May 2021 and July 2021 with 650 individuals, at least 1month post- COVID-19 in a tertiary care centre. A questionnaire requesting demographic details and most common Post COVID sequalae were obtained from the study participants who satisfied the inclusion criteria.
Results & Discussion: Among the 650 participants,330 were excluded as they were asymptomatic. Among the participants with post COVID sequalae 171 were males, 149 were females with sex ratio of 1.4:1. Age range was between 20 to 80 years with most affected age range being 20-30 years (n=91) followed by 41-50 years(n=76). 34.7% (n=111) had comorbidities. The most common post COVID sequalae was expectoration 59.3% (n=54), anosmia 55.6% (n=54), dysgeusia 52.5% (n=42), myalgia 51.2 % (n=62), cough 50.4%(n=63).
Conclusion: This study helped to assess the incidence of Post COVID sequalae.The most common post COVID sequalae anosmia, dysgeusia, expectoration, myalgia and the least common was diarrhoea.
KEYWORDS: Post COVID-19; Post COVID syndrome; Post COVID sequalae; Long COVID syndrome; Incidence

I. INTRODUCTION:

Ever since the World Health Organization declared the COVID-19 outbreak as a global pandemic in March 2020 [1], the coronavirus disease has brought the world to a standstill, infecting more than 228 million people worldwide, with a global death toll of 4.6 million[2]. SARS-CoV-2, the causative agent of COVID-19, is a beta coronavirus, belonging to the subfamily Orthocoronaviridae[3]. It is a single-stranded RNA virus with an envelope and crown-like spokes, capable of binding with host cell receptors and attaining a high viral load in the respiratory tract (nose and pharynx). Hence, SARS-CoV-2 is highly transmissible as a droplet infection and via touching contaminated surfaces[4].

Though COVID-19 is often referred to as a respiratory infection, it is, at its core, a multi-systemic infectious disease and must be clinically approached as such[5]A wide array of manifestations affecting the respiratory, circulatory, neurological and musculoskeletal systems have been documented in previous studies[6]. Numerous countries have experienced a two-wave pattern of coronavirus cases emerging during the pandemic, with a significant change in the clinical presentation and epidemiological characteristics of the second wave in comparison to the first[7,8]. The second wave saw a rise in paediatric cases of COVID-19 with more asymptomatic and low-grade infections being reported, which could be attributed to the availability of approved vaccines against COVID[9]. Fever, myalgia, cough and shortness of breath are associated with both waves of the pandemic. Additionally, gastrointestinal symptoms such as diarrhoea, nausea/vomiting, abdominal pain and dysgeusia were also noted in the 2nd wave[8].These symptoms tend to persist even after disease resolution. The multitude of factors contributing to this pathogenesis include: the direct effects of SARS-CoV-2 on the human body, the damage caused by inflammatory mediators produced in response to the virus, the resultant

cytokine storm and the side effects of the medications used to treat the infection.

In contrast to the initial misconception that the COVID-19 infection resolves completely within two weeks, numerous troubling accounts of COVID 'long haulers' have surfaced across news outlets and social media, and increasing evidence has emerged of a 'long COVID syndrome'. Long COVID syndrome, used interchangeably with the term 'post-COVID-19 syndrome', has no standard definition at present. However, 'Long COVID syndrome' most commonly refers to symptoms persisting for more than three to four weeks after the diagnosis of COVID-19 or after the first symptom onset[10]. The persistence of an acute illness or its incomplete recovery is more often anticipated amongst the elderly, the immunocompromised and patients with pre-existing co-morbidities[11]and is widely studied. But young and middle-aged patients of COVID-19 and those with mild to moderate symptoms still remain a largely understudied group[12]. Though insufficiently documented, young adults afflicted by long COVID syndrome (which in itself contributes to increased morbidity) may be more likely to develop co-morbidities in the future. Hence, it is prudent to be wary of a possible rise in incidence of non-communicable diseases in the years to come. Neglecting the potentially debilitating effects of post-COVID syndrome amongst these individuals could further weigh down an already overburdened health care system and delay the nation's transition to normalcy. In order to tackle this situation, it is impertinent to acquire more knowledge about the extent and severity of this poorly-understood disease and its residual effects. Hence, we conduct this study to gain further insight on the incidence of post-COVID-19 sequelae.

II. METHODOLOGY:

After obtaining clearance from the IEC, this questionnaire-based, cross-sectional study was conducted between May 2021 and July 2021 to assess the incidence of persistent symptoms and sequelae seen amongst the population, post-recovery from COVID-19. 650individuals,at least 1month post- COVID-19 infectionwere randomly sampled from a tertiary care centre in Chennai, Tamil Nadu, India.330 participants were excluded as they were asymptomatic (n=320). The study questionnaire was self-made and validatedby experts in the field before distribution. It wasprepared using Google Forms for ease of circulation and to ensure that safe distancing protocols were maintained during the 2nd wave of the COVID-19 pandemic.

The questionnaire comprised of basic demographic details, co-morbidities, smoking habits, vaccination status, details regarding onset, duration of the symptoms at the time of infection and their subsequent treatment. All general, ENT, respiratory and GI symptoms experienced during the initial COVID-19 infection as well as in the post-recovery period were obtained. General symptoms such as fever, headache, myalgia and fatigue, as well as ENT symptoms like anosmia, dysgeusia, nasal congestion, sore throat, ear pain, hard of hearing, tinnitus and dizziness were noted. Cough, expectoration, dyspnoea and chest pain were amongst the respiratory symptoms discussed. The following GI symptoms-diarrhoea, constipation, vomiting, decreased appetite and mouth ulcers- were also included. In lieu of the recent increase in incidence of Mucormycosis amongst COVID patients, relevant symptoms of the same were also enquired about. Symptoms which showed a difference of ≥50%, when compared to symptoms during and after COVID were considered as significant persistence. All questions were presented in a multiple choice or checkbox format and an additional option for submitting other miscellaneous complaints was provided.

Inclusion Criteria:

1. Participants between age of 20-80 years
2. Either sex
3. COVID RT-PCR positive before start of study and participants who have acquired COVID 4 weeks prior to start of study.

Exclusion Criteria:

1. Those who were unwilling to participate
2. Participants below 20 years of age
3. Patients who acquired the coronavirus less than 4 weeks prior to the time of circulation of the questionnaire
4. Previous organic pathologies
5. Previous organic pathology related surgeries
6. Critically ill patients

III. RESULTS:

650 individuals responded to the study questionnaire (N=650), of which 360 were males and 290 were females. 330 of these participants were excluded as they were asymptomatic. Out of the 320 participants of this study (n=320), 53.4% of respondents were male (171/320) and 46.6% (149/320) were female, with a sex ratio of 1.41:1. Participants ranged from 20 to 80 years of age with the most commonly affected age group being 20-30

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years, followed by 41-50 years (as shown in Figure 1). The mean age was 39.68±16.79 years

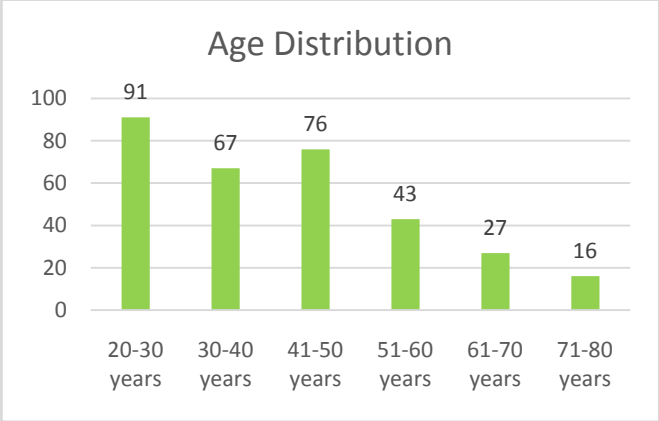

Figure 1: Age Distribution of Study Population.

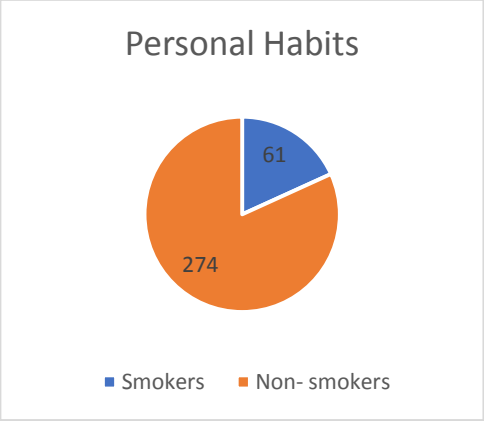

Figure 2: Smoking habits

Amongst 320 respondents, 19% were active smokers and 81% were non-smokers (shown in Fig 2). 34.7% of participants (n=111) reported to having at least one comorbidity, as depicted in (Fig 3).

Vaccination status of the study participants is shown in (Fig 4).

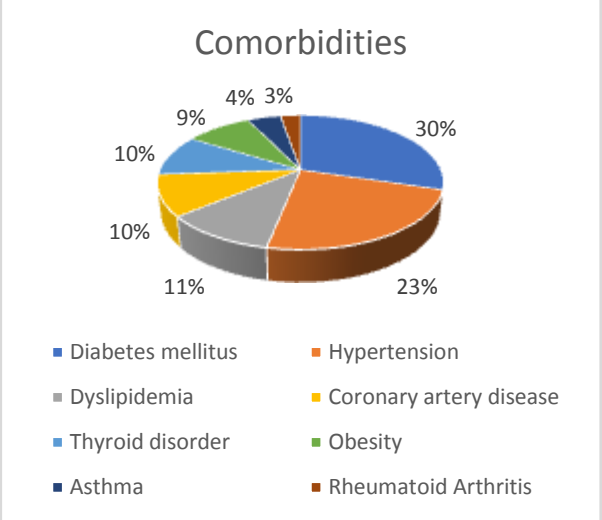

Figure 3: Prevalence of comorbidities

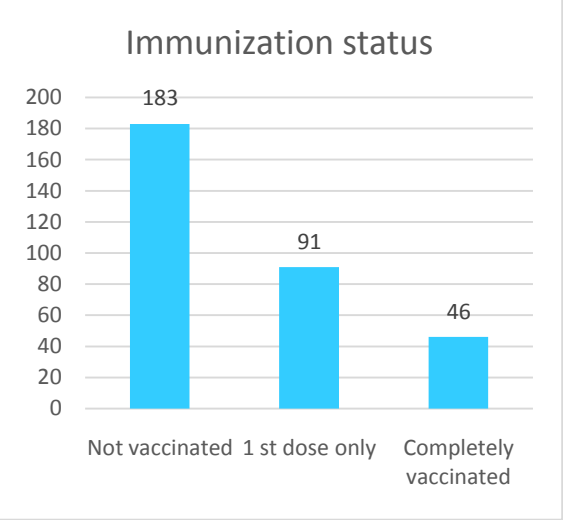

Figure 4: Vaccination status

Symptoms which showed a difference of ≥50%, when compared to symptoms during and after COVID were considered as significant persistence and are discussed in (Table-1)

Symptoms	Day of onset	No. of patients
Anosmia	Day 1-3	40% (n=39)
	Day 4-7	56% (n=54)
	Day 8-10	4% (n=4)
Dysgeusia	Day 1-3	32% (n=25)
	Day 4-7	58% (n=46)
	Day 8-10	10% (n=8)
Cough	Day 1-3	72.8% (n=91)
	Day 4-7	23.2% (n=29)

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	Day 8-10	4% (n=5)
Expectoration	Day 1-3	32% (n=29)
	Day 4-7	45% (n=41)
	Day 8-10	23% (n=21)
Mucormycosis	Day 1-3	0% (n=0)
	Day 4-7	20% (n=1)
	Day 8-10	80% (n=4)
Myalgia	Day 1-3	46.4% (n=56)
	Day 4-7	40.4% (n=49)
	Day 8-10	13.2% (n=16)

Table 1: Common clinical manifestations of COVID and their day of onset

Table 2 gives an overview of the incidence of the post-COVID sequelae and the duration of their recovery.

Symptoms	Durationof recovery	Recovery rate	Persistence rate
Anosmia	1st week	9.4% (n=4)	55.6% (n=54)
	2nd week	34.8% (n=15)	
	3rd week	55.8% (n=24)	
Dysgeusia	1st week	10.5% (n=4)	52.5% (n=42)
	2nd week	34.2% (n=13)	
	3rd week	55.3% (n=38)	
Cough	1st week	29% (n=18)	50.4% (n=63)
	2nd week	37% (n=23)	
	3rd week	34% (n=21)	
Expectoration	1st week	13.5% (n=5)	59.3% (n=54)
	2nd week	48.6% (n=18)	
	3rd week	37.9% (n=14)	
Myalgia	1st week	10.1% (n=6)	51.2% (n=62)
	2nd week	35.6% (n=21)	
	3rd week	54.3% (n=32)	

Table 2: Recovery rate and Persistence rate of symptoms post-COVID 19

The most common post COVID sequalae belonging to general symptoms, ENT, Respiratory and gastrointestinal symptoms are depicted in (figure5,6,7,8)

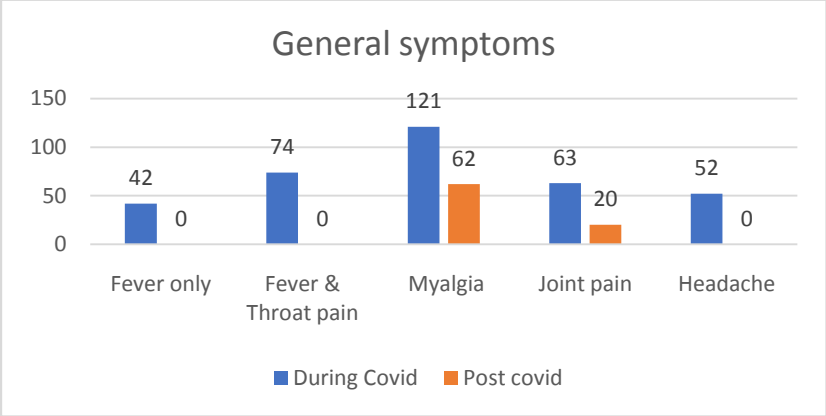

Figure 5: General symptoms during and after COVID

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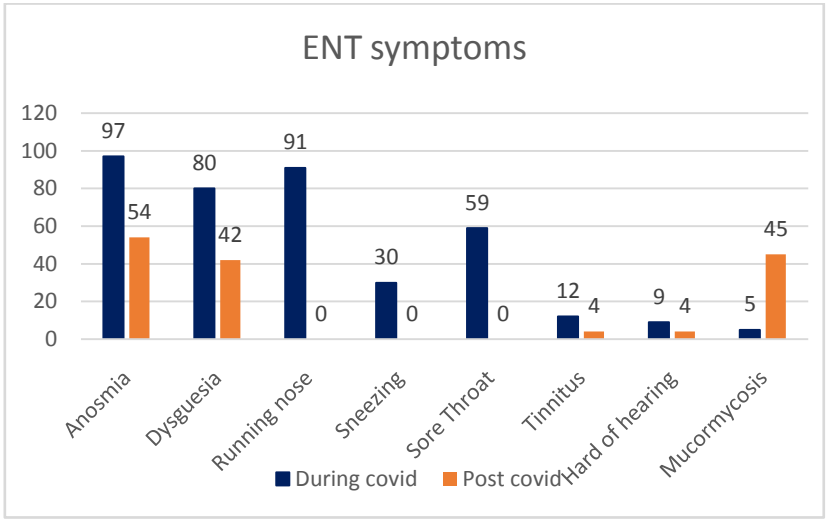

Figure 6: ENT symptoms during and after COVID

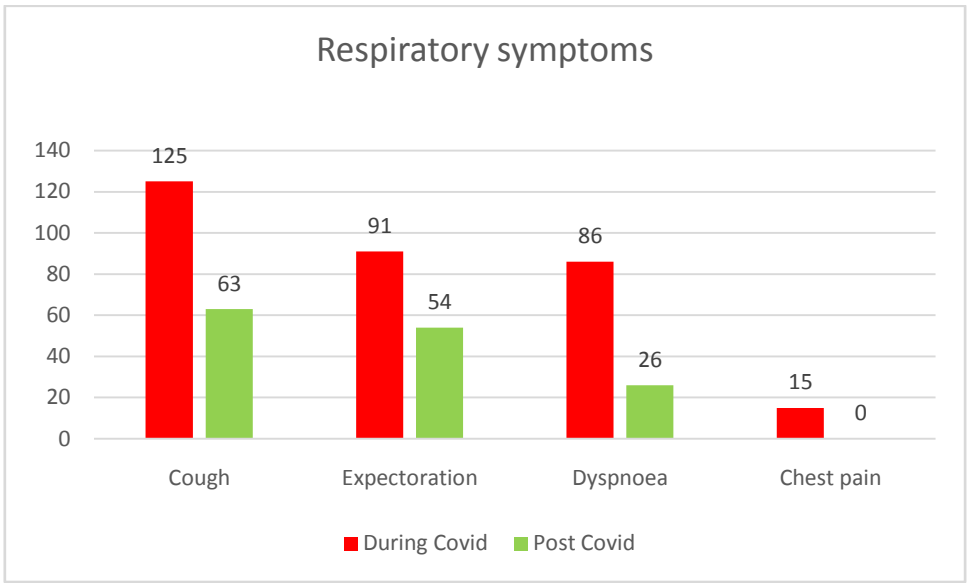

Figure 7: Respiratory symptoms during and after COVID

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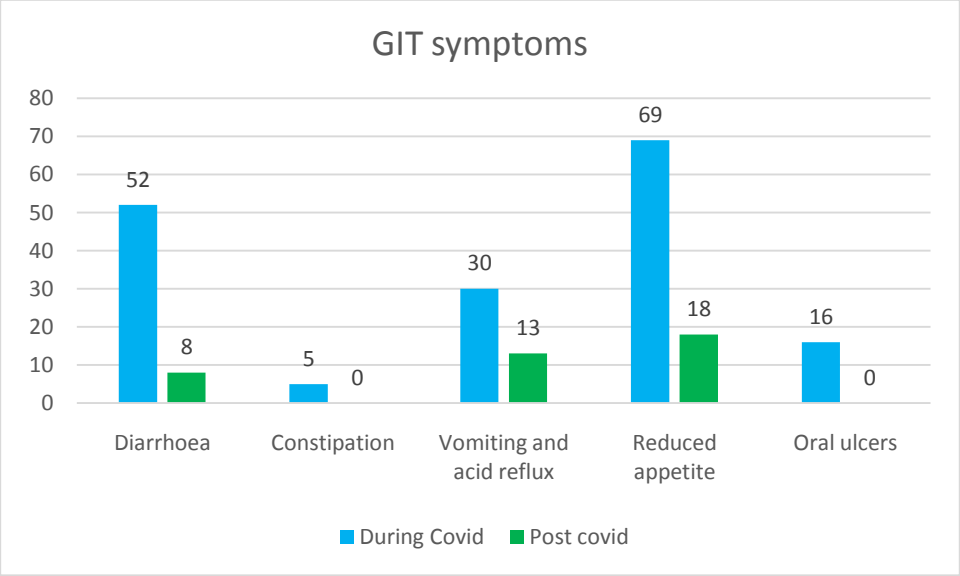

Figure 8: GIT symptoms during and after COVID

IV. DISCUSSION:

This was a prospective study conducted on 650 post COVID -19 patients, which was a telephonic questionnaire based study, similarly a study conducted by Zhou M et al it was also a prospective & questionnaire based study on 89 post COVID patients[13] , whereas study on epidemiology of post COVID syndrome by Ayoubkhani D et al was a retrospective study[14]

Age range was between 20-80 years with most common affected age group being 20-30 years (n=91, 28.4%) and the mean age of study population was 39.68±16.79 years. In a study by Daugherty SE et al on risk of clinical sequelae after the acute phase of COVID infectionthe age range was between 18 to 65 years[15] The mean age was 34.96 ± 13.4 years in a study by Panda S et al on otolaryngologic manifestation and long-term outcome in mild COVID-19.[16]

In this study there were 171 males and 149 females, with sex ratio of 1.14:1. In a study by Ganesh R et al on female predominant persistent immune dysregulation in post COVID syndrome, there was 80 females and 27 males with sex ratio of 2.9:1.[17]

28.4%(n=91) had received the 1st dose of COVID vaccine, 14.3% (n=46) were completely immunized, in which 34.7% (n=16) were people with comorbidities like diabetes, hypertension and asthma. May be because of the completely vaccinated status they had mild symptoms when compared to other participants with comorbidities. 57.1% (n=183) were not vaccinated. A study by Sharun et al, regarding beliefs and barriers associated with COVID vaccination among general population in India suggests that 68.1% of the study population accepted that vaccination against corona virus will be the better option to reduce and prevent the complications caused by the virus[18]

In this study 34.6% (n=111) had comorbidities, in which the percentages are as follows diabetes mellitus 30% (n=33), hypertension 23% (n=26), dyslipidaemia 11% (n=12), coronary artery disease 10% (n=11), thyroid disorder 10% (n=11), obesity 9% (n=10), asthma 4% (n=5), rheumatoid arthritis 3% (n=3). In study conducted by Huang C et al on 6month consequences in Covid-19 infected patients shows that 29% (n=505 had hypertension, 12%(n=207) had diabetes, 7% (n=128) had cardiovascular diseases, 3% (n=47) had cerebrovascular diseases,3% (n=44) had malignant tumour, 2% (n=31) had chronic obstructive pulmonary disorder and 2% (n=27) had chronic kidney disease.[19]

In this study we asked only about the history of smoking, in which 19% (n=61) were smokers, whereas 10.5% (n=15) were active smokers and 45.4% (n=65) were former smokers in a study on persistent symptoms after acute Covid-19 infection by Carfi A et al.[20]

The symptoms which were persistent for more than four weeks of post COVID status was myalgia 51.2% (n=62), joint pain 31.7% (n=20) in general symptoms. Otorhinolaryngological symptoms which were persistent was anosmia 55.6% (n=54), dysgeusia 52.5% (n=42), 33.3% (n=4) in tinnitus and hard of hearing 44% (n=4) During COVID infection only 1.5% (n=5) had symptoms of mucormycosis, but there was a drastic increase in the incidence of the same during the post COVID period which was 14% (n=45), which might because of the uncontrolled diabetes

mellitus, steroid therapy, prolonged oxygen therapy during their treatment course. Patients with symptoms of mucormycosis were subjected for further evaluation and management according to the hospital protocol.Gastrointestinal symptoms which were persistent are diarrhoea 15.3% (n=8), features of acid reflux 43.3% (n=12), reduced appetite 26% (n=18). Persistent respiratory symptoms were cough 50.4% (n=63), expectoration 59.3% (n=54), dyspnoea 30.2% (n=26).

The common symptoms during the acute stage of Covid-19 infection was fever, fatigue, myalgia, anosmia, dysgeusia, cough in a study by Peluso MJ et al[21] which was in accordance with this study, and the symptoms which were persistent after the acute stage of COVOID-19 are anosmia, dysgeusia, fatigue, dyspnoea, headache, difficulty in sleeping and concentration problems. Similarly anosmia, ageusia, dyspnoea, concentration problems, memory loss were found to be persistent beyond 30 days in a study by Cirulli E et al.[22] Persistence rate of altered smell and taste sensation was 11% (n=176) and 7% (n=120) in study conducted by Huang C et al[19] Diarrhoea was found to be present beyond four weeks in study by Arnold et al and Moreno-Perez et al[23,24] Cough was persistent beyond 4 weeks in study by Chopra et al(15.4%), Arnold et al (11.8%) and Moreno-Perez et al (21.3%). There has been a surge in the incidence of mucormycosis in second wave of COVID infection when compared to the first wave and the cases reported as of May 28, 2021 was found to be 14,872 cases says Raut et al in his study on rising incidence of mucormycosis during the second wave of Covid-19[25]

Day of onset of symptoms which were persistent for ≥50% when compared to symptoms during COVID infection are discussed here. Day of onset of anosmia and dysgeusia and expectoration was commonly from 4th to 7th day which was 56%(n=54), 58% (n=46) and 45%(n=41) respectively. For cough and myalgia the day of onset was between 1st to 3rd day which accounted for 72.8% (n=91) 46.4% (n=56) respectively. The day of onset of features of mucormycosis was 8th-10th day in 80% (n=4) during COVID infection. And for those who developed symptoms of mucormycosis post COVID had onset of symptoms usually between 4-5th week, which was 64.4% (n=29). Onset of anosmia was found to be reported between 4.4±1.9 days after the onset of Covid infection in study by Klopfenstein T et al.[26] It was found to be between 0-7 days with a median of 3.3 days for onset of anosmia and dysgeusia as studied by Levinson R et al.[27] Lung involvement on CT was found to be maximum at around 10th day of infection says Pan F et al[28]

For those patients who recovered from COVID within ≤4 weeks-those in their 3rd week of recovery had anosmia 55.8% (n=24), 55.3% (n=38) in dysgeusia, 54.3% (n=32) myalgia and those 2 weeks post COVID recovery had cough 37% (n=23), expectoration-48.6% (n=18). A study by Hopkins et al [29] reports that the rate of recovery for anosmia was found to be 61% between 2-3 weeks and 67% of patients recovered between 3-4 weeks. 69.5% recovered from dysosmia and dysgeusia within 3 weeks of symptoms onset in study by Sheng et al. [30] A long term follow up with pulmonary function test might be needed to evaluate the recovery from lung symptoms caused by COVID infection says Shang Y et al. [31]

V. CONCLUSION:

This study helped to assess the incidence of Post COVID sequalae which were persistent beyond 4 weeks. The most common post COVID sequalae were anosmia, dysgeusia, expectoration, myalgia and the least common was diarrhoea. The predisposing and risk factors associated with acute post COVID sequalae were not well established. Adequate vaccination cover is mandated to overcome such situation and the complications posed the COVID infection. Further prospective cohort studies with prolonged follow up might be needed to know the factors associated with Post COVID sequalae.

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