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# Implication of inflammatory markers in post COVID syndrome

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**Abstract**---Post-COVID syndrome was described in the context of a survey of prolonged COVID-19 symptoms for the first time in 2020, run by the Patient-Led Research Collaborative, citizen's scientist group. Symptoms persisting for more than three weeks after the diagnosis of COVID-19 fall into the category of post-COVID syndrome. The most common post-COVID symptoms include fatigue, dyspnea, olfactory and gustatory dysfunction, chest pain, myalgia, and sleep and mental disorders. The pathogenesis of post-COVID syndrome is multi-factorial. Underlying chronic, low grade inflammation has been theorized for pathogenesis. Available data shows conflicting results regarding the implication of inflammatory markers in full clinical spectrum and its long-term outcome.

**Keywords**---post COVID, myalgia, D-dimer, C reactive protein (CRP).

**Introduction**

Post-COVID syndrome was described in the context of a survey of prolonged COVID-19 symptoms for the first time in 2020, run by the Patient-Led Research Collaborative, citizen's scientist group. Symptoms persisting for more than three weeks after the diagnosis of COVID-19 fall into the category of post-COVID syndrome. The most common post-COVID symptoms include fatigue, dyspnea, olfactory and gustatory dysfunction, chest pain, myalgia, and sleep and mental disorders.

The pathogenesis of post-COVID syndrome is multi-factorial. Underlying chronic, low grade inflammation has been theorized for pathogenesis. Available data shows conflicting results regarding the implication of inflammatory markers in full clinical spectrum and its long-term outcome.

### **Aims and objective**

Our aim was to know whether subjects with Post covid syndrome have higher blood levels of inflammatory markers, after mild to moderate COVID-19.

### **Study design**

Analytical cross sectional study.

### **Materials and Methods**

Total cases= 120

- Cases of mild- moderate COVID-19 were included. Patient with COVID-19 was classified as PCS (Prolonged Covid Syndrome) if signs and symptoms persisted beyond 12 weeks.
- Neutrophil count, NLR, CRP, D-dimer levels were assessed.

### **Results**

Most common symptom of PCS overall was fatigue (in 44% cases) while least common was reported to be myalgia (in 12% cases). The distribution of symptoms was similar for both sexes. Neutrophil count, NLR and CRP showed the best correlation with PCS. Inflammatory markers like CRP, NLR, Ferritin and D-dimer were raised proportionately higher among the patients with prolonged covid.

### **Conclusion**

Post Covid syndrome i.e. Prolonged COVID is an important health issue which should not be ignored. It should always be taken into due consideration as it has a major impact on quality of life.

### **Original article**

#### **Introduction**

COVID-19 is a deadly virus which has become a global disease burden and has become the focus of many researches as per the need of the time. Post-COVID syndrome (PCS) was described for the first time in spring 2020 in the context of a survey of prolonged COVID-19 symptoms, run by the Patient-Led Research Collaborative, citizen's scientist group<sup>1</sup>. Soon after the first COVID-19 cases evolved, they observed that COVID-19 patients had symptoms persisting for several weeks after acute infection<sup>1</sup>. Long- Covid or Post-COVID syndrome is increasingly recognized as a new clinical entity in the context of SARS-CoV-2 infection. Symptoms persisting for more than three weeks after the diagnosis of

COVID-19 fall into the category of post-COVID syndrome. The most common post-COVID symptoms include fatigue, dyspnea, olfactory and gustatory dysfunction, chest pain, myalgia, and sleep and mental disorders<sup>1-4</sup>. Symptoms may last for several months and disrupt work activities. Evidences of long-COVID symptoms involving various organ systems are rapidly growing in literature. In recent months, our knowledge on post-COVID syndrome has expanded, mainly due to the recognition of new clinical manifestations, including rare neurological and thromboembolic complications, while the long-term consequences of the disease remain largely unknown. Its incidence ranges from 10% to 35%, however, rates as high as 85% have been reported among patients with a history of hospitalization<sup>5-7</sup>. As of now, we have not known much about the pathogenesis of Prolonged COVID. Currently it is a Poorly known entity. The pathogenesis of post-COVID syndrome is multi-factorial and more than one mechanism may be implicated in several clinical manifestations. Underlying chronic, low grade inflammation has been theorized for its pathogenesis. Available data shows conflicting results regarding the implication of inflammatory markers in full clinical spectrum and its long-term outcome<sup>8</sup>. Further research is also imperative to elucidate the pathogenesis of post-COVID syndrome.

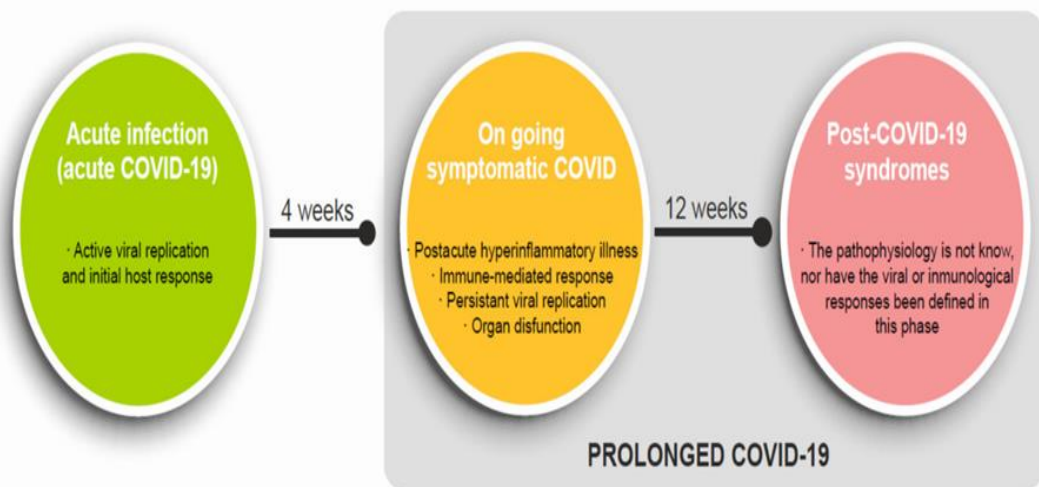


Figure 1 showing natural history of PCS

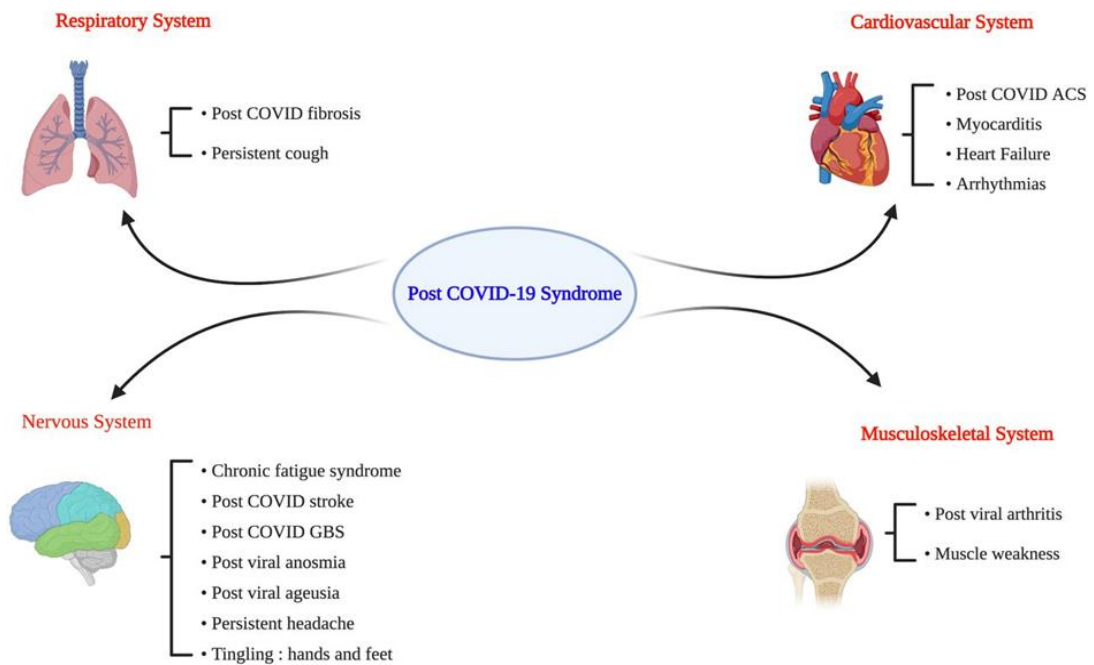


Figure 2 showing various presentation of PCS

### Aims and Objectives

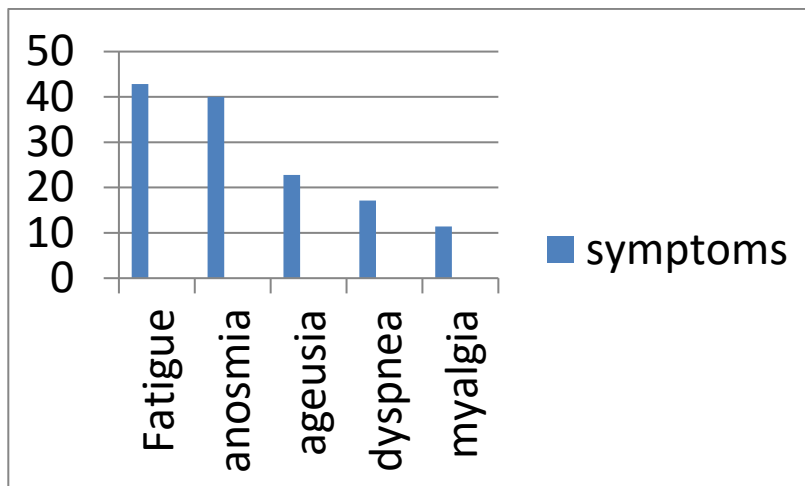
- Our aim was to know whether subjects with PCS have higher blood levels of inflammatory markers, after mild to moderate COVID-19.

### Materials and Methods

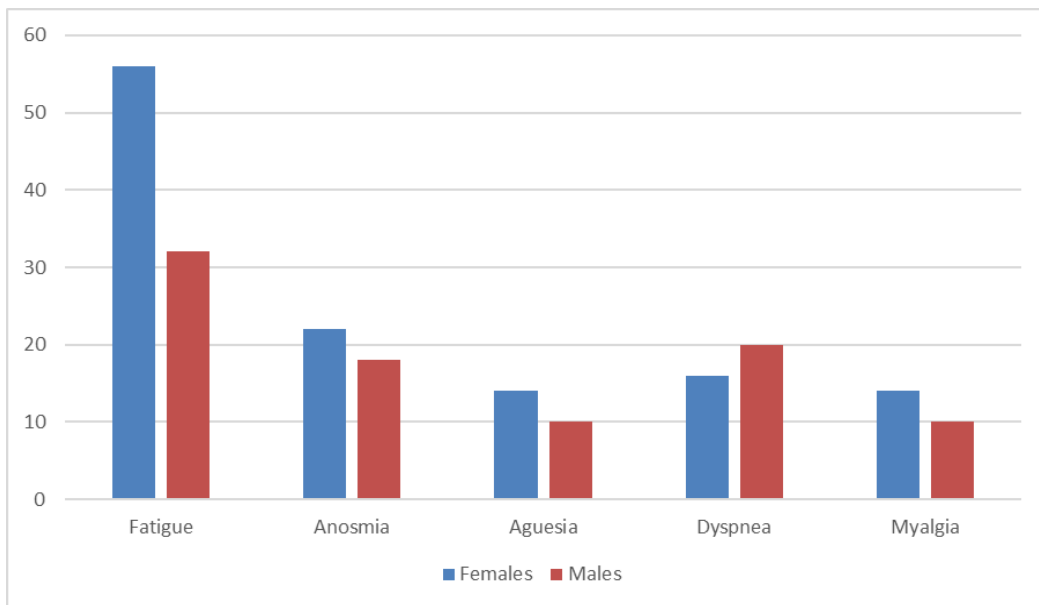
- Study type- Analytical cross sectional study
- Total cases= 120
- Cases of mild- moderate COVID-19 were included
- Epidemiological data (age, sex, BMI, smoking, co-morbid status) and clinical variables of acute COVID along with blood levels of inflammatory markers were obtained.
- A patient infected with COVID-19 was classified as PCS (Prolonged Covid Syndrome) if signs and symptoms persisted beyond 12 weeks.
- Neutrophil count, NLR, CRP, D-dimer levels were assessed.
- Multivariate analyses were performed.

### Observations and Results

- Mean age of presentation was 45.7 years. Slightly male predominance was noted with 60% males (n=72), 40% females (n=48) affected in study. Most common symptom of PCS overall was fatigue (in 44% cases) while least common was reported to be myalgia (in 12% cases) (Graph 1)



Graph 1 showing prevalence of symptoms among patients of PCS



Graph 2 showing gender wise distribution of symptoms in patients of PCS

Inflammatory marker such as C Reactive protein (CRP) was elevated in 40 cases (Table 1) while ferritin was increased in 20 patients only (Table 3). Neutrophil to lymphocyte ratio (NLR) in PCS patients was raised in 32 cases while 52 patients without PCS also showed raised neutrophil to lymphocyte ratio (Table 2). Observation in D DIMER levels were somewhat similar like NLR and Ferritin as 27 cases with PCS had elevated D DIMER and 22 were having low normal values (Table 5).

	Patients with PCS (n=49)	Patients without PCS (n=71)
CRP levels high	40	24
CRP levels low-normal	09	47
P-Value	<0.00001	

Table 1 showing correlation of CRP levels with PCS

	Patients with PCS (n=49)	Patients without PCS (n=71)
NLR levels high	32	19
NLR levels low-normal	17	52
P-Value	<0.001	

Table 2 showing correlation of NLR levels with PCS

	Patients with PCS (n=49)	Patients without PCS (n=71)
Ferritin levels high	20	07
Ferritin levels low-normal	29	64
P-Value	<0.001	

Table 3 showing correlation of Ferritin levels with PCS

	Patients with PCS (n=49)	Patients without PCS (n=71)
D-dimer levels high	27	12
D-dimer levels low-normal	22	59
P-Value	<0.001	

Table 4 showing correlation of D-dimer levels with PCS

## Discussion

PCS affected 54.17% of women and 31.94% of men ( $p=0.015$ ). Among the acute symptoms, women presented a higher frequency of fatigue (56.2% vs 31.9%). Most common symptom of PCS overall was fatigue (in 44% cases) while least common was reported to be myalgia (in 12% cases)<sup>9</sup> it was similar finding in other studies. The distribution of symptoms was similar for both sexes. Neutrophil count, NLR and CRP showed the best correlation with PCS. Inflammatory markers like CRP, NLR, Ferritin and D-dimer were raised proportionately higher among the patients with prolonged covid<sup>10</sup>.

These were markers commonly done in all countries including INDIA during COVID time but their implication in PCS is not yet widely published. Patients with deranged levels of inflammatory markers had 4-5 fold increased risk of PCS. Patients with raised CRP or NLR had a 10-17 fold increased risk of PCS<sup>11</sup>. There are multiple mechanisms whereby SARS-CoV-2 infection can engender or exacerbate persistent fatigue and/or cognitive impairment. It is also recognized that systemic sequelae including endothelial dysfunction, hyperinflammation, autoimmunity, latent viral reactivation, multi-organ pathology, and autonomic

nervous system dysfunction can interact with the foregoing in a synergistic manner. However there are not too much studies to compare results as this is an evolving issue and long term follow up is not present.

### **Conclusion**

Post Covid syndrome i.e. Prolonged COVID is an important health issue which should not be ignored. It should always be taken into due consideration as it have a major impact on quality of life. High risk individuals should be screened for early detection and prevention.

### **Future research scope**

The evolving data indicate a multi-factorial pathogenesis, namely inflammation, nervous system dysfunction, endothelial damage, and thromboembolism as the main pathogenetic mechanisms. It is expected that as the long-term complications of COVID-19 unfold, more evidence will be available to guide therapeutic management. Further research is needed in order to elucidate the incidence, clinical spectrum, pathogenesis, and prognosis of this new clinical entity.

### **Limitations of the study**

Absence of sufficient evidence based data and researches on Post covid syndrome hence need correlation. However, large samples studies are necessary to define the cut-off points for biomarkers levels at which the diagnosis of PCS could be established.

### **Conflict of interest**

All authors declare there is no conflict of interest.

### **Source of funding - Nil**

### **References**

1. Patient-Led Research Collaborative. Report: What Does COVID-19 Recovery Actually Look Like? An Analysis of the Prolonged COVID-19 Symptoms Survey by Patient-Led Research Team. Available online: <https://patientresearchcovid19.com/research/report-1/> (accessed on 7 May 2021).
2. Writing Committee for the COMEBAC Study Group; Morin, L.; Savale, L.; Pham, T.; Colle, R.; Figueiredo, S.; Harrois, A.; Gasnier, M.; Lecoq, A.L.; Meyrignac, O.; et al. Four-month clinical status of cohort of patients after hospitalization for COVID-19. *JAMA* 2021. [CrossRef]
3. Alpert, O.; Begun, L.; Garren, P.; Solhkhah, R. Cytokine storm induced new onset depression in patients with COVID-19. A new look into the association between depression and cytokines—Two case reports. *Brain Behav. Immun. Health* 2020, 9, 100173. [CrossRef] [PubMed]

4. Dicipinigaitis, P.V.; Canning, B.J. Is there (will there be) a post-COVID-19 chronic cough? *Lung* 2020, 198, 863–865. [CrossRef]
5. Covid-19-Long-Term-Health-Effects. Available online: <https://www.gov.uk/government/publications/covid-19-long-termhealth-effects/covid-19-long-term-health-effects> (accessed on 7 May 2021).
6. Carvalho-Schneider, C.; Laurent, E.; Lemaïgnen, A.; Lemaïgnen, A.; Beaufile, E.; Bourbao-Tournois, C.; Laribi, S.; Flament, T.; Ferreira-Maldent, N.; Bruyère, F.; et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset. *Clin. Microbiol. Infect.* 2021, 27, 258–263. [CrossRef] [PubMed]
7. Becker, R.C. COVID-19 and its sequelae: A platform for optimal patient care, discovery and training. *J. Thromb. Thrombolysis* 2021, 1–8. [CrossRef]
8. World Health Organization. Coronavirus Disease (COVID-19) Situation Reports. Available online: <https://www.who.int/emergencies/situation-reports>
9. Ceban F, Ling S, Lui LMW, Lee Y, Gill H, Teopiz KM, Rodrigues NB, Subramaniapillai M, Di Vincenzo JD, Cao B, Lin K, Mansur RB, Ho RC, Rosenblat JD, Miskowiak KW, Vinberg M, Maletic V, McIntyre RS. Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. *Brain Behav Immun.* 2022 Mar;101:93-135. doi: 10.1016/j.bbi.2021.12.020. Epub 2021 Dec 29. PMID: 34973396; PMCID: PMC8715665.
10. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19 - A systematic review. *Life Sci.* 2020 Aug 1;254:117788. doi: 10.1016/j.lfs.2020.117788. Epub 2020 May 13. PMID: 32475810; PMCID: PMC7219356.
11. Maamar M, Artime A, Pariente E, Fierro P, Ruiz Y, Gutiérrez S, Tobalina M, Díaz-Salazar S, Ramos C, Olmos JM, Hernández JL. Post-COVID-19 syndrome, low-grade inflammation and inflammatory markers: a cross-sectional study. *Curr Med Res Opin.* 2022 Jun;38(6):901-909. doi: 10.1080/03007995.2022.2042991. Epub 2022 Mar 9. PMID: 35166141; PMCID: PMC8935459.