



Serum Ferritin Levels In Inflammation: A Retrospective Comparative Study In COVID-19 And Non COVID-19 Infections.

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ABSTRACT: AIMS & OBJECTIVES- SARS-CoV-2 infection has spread worldwide, and insights in its pathogenic mechanism have been evolving through investigation. The role of ferritin as a marker of inflammation is already known, and whether it changes differently between COVID and non-COVID patients remains unclear. The aim of this retrospective analysis is to understand whether the inflammatory process in these two types is different.

MATERIAL & METHODS - The present study was designed as a retrospective comparative study. Total 30 patients were enrolled. 15 were affected by SARS-CoV-2, who had been admitted between period of February 2020 and April 2020 (group A) along with 15 patients admitted for non COVID infections with SARSCoV-2 negative swab (group B). Patients were compared for serum ferritin levels.

RESULT - There is a significant correlation between serum Ferritin levels and COVID 19 infection.

CONCLUSION-Our study found association between serum ferritin levels and COVID 19 infection. The data suggest that the role of iron metabolism appears to be directly involved in COVID 19 infection. Our finding suggests the use of ferritin as a marker for COVID infection.

KEYWORDS – Ferritin, SARSCOV 2, Inflammation, COVID 19, iron.

INTRODUCTION –

Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is the pathogen that causes coronavirus disease 2019 (COVID-19). The current evidence showed that severely ill patients tend to have a high concentration of pro-inflammatory cytokines, such as interleukin (IL)-6, compared to those who are moderately ill. Recently, increasing studies indicate that the “cytokine storm” may contribute to the mortality of COVID-19¹

. The body contains iron in the form of ferritin, which is an intracellular protein composed of 24 subunits circling an iron core containing 4000–4500 iron atoms. Ferritin is an intracellular protein composed of 24 subunits surrounding an iron core containing 4000–4500 iron atoms. Ferritin is a mediator for immune dysregulation, especially in hyper-ferritinemia, with direct immune suppressive and pro-inflammatory effects that cause cytokine storms. The cytokine storm syndrome causes dangerous outcomes in covid-19 disease. Normal Ferritin levels in blood in adults are in range of 30–400 ng/mL. Covid-19 disease is an infectious disease that has been declared a global public health emergency by the WHO. Serum ferritin levels are closely linked to severe covid-19 disease. Treatment with iron chelators is one potential method for lowering serum ferritin levels in the body².

Material and methods:

The present study was designed as a retrospective observational study. Patients were recruited from a hospital located in central maharashtra, India. A total of 30 patients were enrolled in the study.

Group I – 15 patients diagnosed with COVID-19 infection made up group A (8 male, 7 female, mean age 54.4). In group A, all patients were positive for 2019-ncov by real time RT-polymerase chain reaction from nasopharyngeal swab.

Group II – The second cohort, 15 patients (8 male, 7 female, mean age 52.06 yrs) with double negative nasopharyngeal swab for SARS-COV-2 admitted from August 25 to September 15, 2020 to the same setup for acute non covid 19 infections composed group.

Inclusion Criteria:

Patients between the age of 30 yrs to 70 yrs.

Patient admitted in the same centre during February 2020 to April 2020

Patients having clinical features suggestive of infections

Exclusion Criteria:

Patients above the age of 70 yrs and below the age of 30 yrs.

Patients with diagnosed comorbidities.

Patients with chronic illness.

Study Design:

The present study was retrospective observational study conducted to evaluate and compare the serum ferritin levels in covid 19 and non covid 19 infections. This study focused on the analysis of common determinants and laboratory results obtained in the days following hospital admission. Data was analyzed to compare S. Ferritin levels between the two groups—COVID-19 versus nonCOVID-19. In our study, we evaluated the hypothesis of serum ferritin as a marker of SARS-CoV2 infection, which could be a simple and useful laboratory test to identify and monitor the inflammatory process in COVID-19 patients.

Statistical analysis :

Data were expressed as mean \pm standard deviation. Comparison of the categorical or numeric variables between groups was carried out using a Chi-square test or Student's t-test separately. The multivariate regression model was used to rule out possible mutual association of traditional risk factors (including age, sex, covid status) with cases and control groups. The sensitivity, specificity, and predictive values of DELC in two genders and age groups 40 to 70 years old) were compared. A P value of <0.05 was analysis was conducted using Statistical Package for Social Sciences [SPSS] for Windows Version 22.0 Released 2013. Armonk, NY: IBM Corp.

Results :

Fig.1: Comparison of mean age between Covid positive subjects (Group A) and Covid negative subjects (Group B) respectively

Age	Mean	SD	Unpaired t test	p value, Significance
Covid Positive subjects (Group A)	54.46	16.07		
Covid Negative subjects (Group B)	52.06	17.11		

p >0.05 – no significant difference * p<0.05 – significant **p<0.001 – highly significant

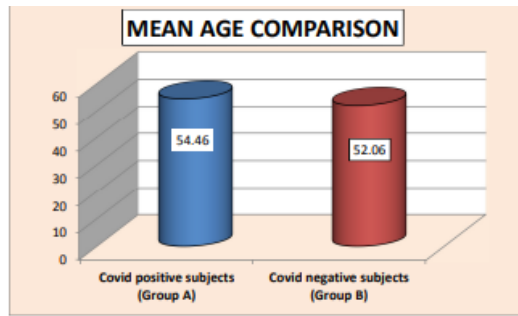


Fig.2 : Comparison of gender between Covid positive subjects (Group A) and Covid negative subjects (Group B) respectively

Gender	Male n (%)	Female n (%)	Unpaired t test	p value, Significance
Covid Positive subjects (Group A)	8 (53.3%)	7 (46.7%)	Chi = 0.0	p = 1.000
Covid Negative subjects (Group B)	8 (53.3%)	7 (46.7%)		

p >0.05 – no significant difference * p<0.05 – significant **p<0.001 – highly significant

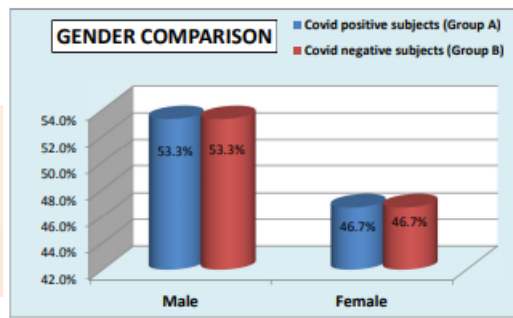
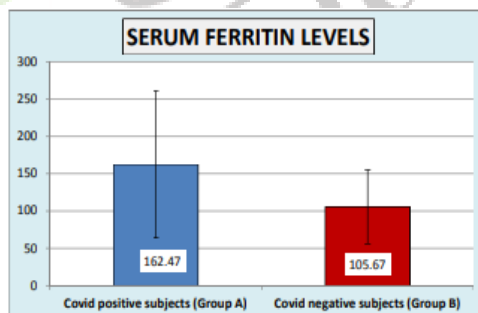


Fig3: Comparison of mean serum ferritin levels between Covid positive subjects (Group A) and Covid negative subjects (Group B) respectively

Serum ferritin levels	Mean	SD	Unpaired t test	p value, Significance
Covid Positive subjects (Group A)	162.47	98.63	t =2.034	p = 0.046*
Covid Negative subjects (Group B)	105.67	49.7		

p >0.05 – no significant difference * p<0.05 – significant **p<0.001 – highly significant



All the statistical results collected revealed that there was weak correlation between the ages of covid positive patient and serum ferritin levels, there was weak correlation between genders of covid positive patient and serum ferritin levels, where as there was strong positive relation between the covid positive and non covid positive serum ferritin levels.

DISCUSSION: In December 2019, a new coronavirus was identified as responsible agent for cases of severe pneumonia, the pathogenic mechanism of which has been crucial topic of investigation. Acute inflammatory process has been postulated to be responsible for manifestations of disease. Ferritin is an acute phase reactant, and as such, is generally elevated in inflammatory responses of any type. Serum ferritin has been long studied as a marker of iron metabolism, however, its application as biomarker of inflammation presented high importance in the context of COVID-19 progression, as demonstrated by previous studies in the field³ Ferritin production occurs when intracellular iron concentration augments, with iron being stored in the form of ferritin and subsequently expelled from the cell. Intracellular iron accumulation occurs in two main modalities: hyperexpression of Transferrin receptor 1 which internalizes

transferrin, and hepcidin⁴ Ferritin is a key mediator of immune dysregulation, especially under extreme hyperferritinemia, via direct immune-suppressive and pro-inflammatory effects, contributing to the cytokine storm. A possible strategy to decrease ferritin levels might be the treatment with iron chelators. Deferoxamine may be a good candidate, since is a non-toxic iron chelator clinically approved by the FDA and is effective for long-term iron chelation therapy in beta-thalassemia⁵ We studied serum ferritin, at the days of hospital admission, a series of SARS-CoV-2 infected patients and we observed a strong correlation between serum ferritin and overall mortality.

Limitation of the study : We would like to state that with solely one ethnic population, rel

atively small sample size, and single centre design in this study, the result may not be generalized. Therefore, we suggest more longitudinal studies on large samples in both academic and non academic hospitals.

Conclusion: Even if ferritin is considered an acute-phase protein, its role in monitoring inflammation is still not clear and, for this reason, it is not used routinely. The role of iron metabolism in COVID infection is increasing even without an accurate interpretation, and our study seems to confirm this observation. Hyperinflammation in COVID19 patients evaluated the high levels of serum ferritin in the first seven days of hospitalization as a predictor for the cytokine storm syndrome, serum ferritin as a biomarker for potential progression to critical illness in COVID 19 . However, our finding suggests the use of ferritin values as a marker for COVID infection.

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