Research Article

Correlation of Serum Ferritin Level with Severity of COVID-19 Infection: A Retrospective Cross Sectional Study in a Tertiary Care Centre, Aurangabad, India

Vijaykumar S Gulwe[1], Potu Sanjana Reddy[1*], Sanjay Govindrao Guddetwar[2], Malempati Bharadwaja[1] and Abhilash R Taware[1]

[1]Department of Medicine, MGM Medical College, Aurangabad, Maharashtra, India; [2]Department of Biochemistry, MGM Medical College, Aurangabad, Maharashtra, India

Corresponding author:
Dr Potu Sanjana Reddy
Department of Medicine,
MGM Medical College & Hospital,
Aurangabad, Maharashtra, India
E-mail: sanjana1226@gmail.com

Received: 26-Feb-2022;
Manuscript No. AMHSR-22-51597;
Editor Assigned: 01-Mar-2022,
PreQC No. AMHSR-22-51597 (PQ);
Reviewed: 09-Mar-2022,
QC No AMHSR-22-51597;
Revised: 18-Mar-2022,
Manuscript No. AMHSR-22-51597(R);
Published: 26-Mar-2022
DOI: 10.54608.annalsmedical.2022.06

Abstract

Background: COVID-19 has been declared a global public health emergency by the World Health Organization. Serum ferritin levels are closely linked to the covid-19 disease in previous studies. **Aim:** Iron metabolism undergoing significant modifications in covid-19 disease hence Serum ferritin levels can be employed in predicting severity. **Materials & Methods:** 30 SARS-CoV-2 positive patients diagnosed on Reverse-Transcriptase Polymerase Chain Reaction (RTPCR) test were enrolled. They are divided into severe and non-severe groups. Serum ferritin was measured by Chemi Luminescence Immune Assay (CLIA) in all 30 patients. **Result:** In group I on day 1 it was 308.2 ± 12.51 and on day 7 it was 311.09 ± 11.52. In group II on day 1 it was 312.9 ± 11.10 and on day 7 it was 770 ± 36.25. Statistically significant result found on day 7 between group I and II (P<0.0001) whereas no significant difference found on day 1 (P=0.2857). **Conclusion:** Inflammatory cytokine storm is associated with severity of COVID 19. Ferritin despite representing total body iron stores is linked with acute and chronic inflammatory processes. Serum ferritin can be considered in combination with clinical details and other laboratory tests in designing the patient centered treatment plans.

Keywords: COVID-19; Ferritin; CLIA

Introduction

Coronavirus disease 19 (COVID-19) has been declared a global public health emergency by the World Health Organization since its emergence in Wuhan China. Patients are either asymptomatic or with mild influenza-like symptoms. [1] It is a complex multi systemic disease involving inflammatory process which play main role in pathogenesis of multiple organ damage and responsible for outcome of COVID-19 patients. Early identification of COVID-19 patients and their prognostic markers are quite useful in management which can limit severe complications. Commonly monitored inflammatory markers in clinical practice include white blood cell count, lactate dehydrogenase, C reactive protein, fibrinogen and D-dimer. [2,3] It is an established fact that iron metabolism is involved in several patho genetic disease mechanisms including infections, various haematological and immunological disorders. [4]

Body contains iron in the form of ferritin which is an intracellular protein consisting of 24 subunits circling around iron core with 4000–4500 iron atoms. [5] Ferritin is a mediator of immune dysregulation with direct immune suppressive and pro-inflammatory effects that may cause cytokine storms. [6] Serum ferritin levels are closely linked to the covid-19 disease in previous studies and iron metabolism undergoing significant modifications can be employed in predicting severity. [7] With this objective present study was undertaken to study role of serum ferritin in assessing severity of COVID 19 infection.

Materials and Methods

Present study is a cross sectional retrospective study conducted in the department of medicine at MGM Hospital, Aurangabad from May 2021 to October 2021. Approval of institutional ethics committee was taken prior to commencement of this study. Written informed consent was obtained from all the participants.

Inclusion Criteria

30 SARS-CoV-2 positive patients diagnosed on Reverse-Transcriptase Polymerase Chain Reaction (RTPCR) test were enrolled. They are divided into two groups;

- Group I (Non-Severe): Not requiring intensive care admission or assisted respiration
- Group II (Severe): requiring intensive care admission or assisted respiration (invasive ventilation or non-invasive oxygen support.

Exclusion Criteria

Patients with acute or chronic kidney disease

Procedure

Demographic data including age, gender and clinical data with

How to Cite this Article: Gulwe VS, et al. Correlation of Serum Ferritin Level with Severity of COVID-19 Infection: A Retrospective Cross Sectional Study in a Tertiary Care Centre, Aurangabad, India. Ann Med Health Sci Res. 2022;12:S1:73-76.

symptoms, hospital stay in days and final outcome were noted in case record form in all 30 patients. Samples for ferritin blood test were obtained from venepuncture. Serum ferritin was measured by Chemiluminescence immunoassay (CLIA) on the Siemens Advia Centaur immunoassay analyserusing Cobas® 8000 analyser (Roche Diagnostics, Mannheim, Germany) with the manufacturer's recommendations. Results are expressed as nanogram of ferritin per microliter of serum (ng/mL). For internal quality control, 2 levels of manufacturer-provided controls (low and high) were run with each batch of analyte.

Normal ferritin levels [Graph 1] in blood in male are 12–300 ng/mL and in female are 10–150 ng/mL. [8] MedCalc Statistical Software version 19.1.7 was used for statistical analysis. Continuous variables were summarised as mean and Standard Deviation (SD) [Graph 2] and categorical variables as number and percentage (%). A student test was used to compare continuous variables and chi square or Fisher's exact test to compare categorical variables.

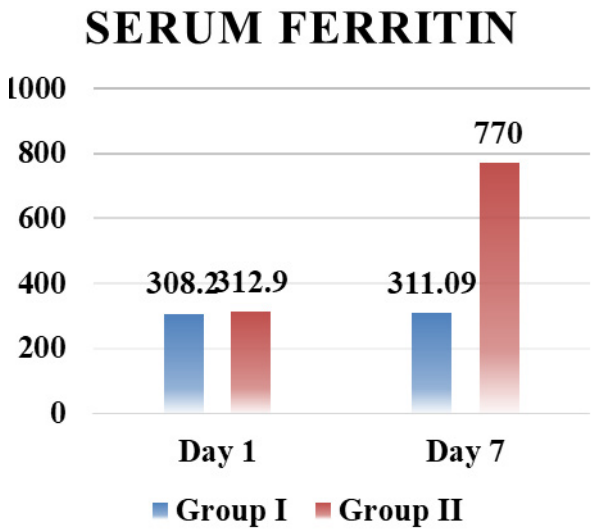
Results

Table 1 shows age and sex distribution amongst study participants. Maximum patients *i.e.* 70% (21/30) were found from 30 to 60 years age group. Male preponderance was found with 66.6% (20/30).

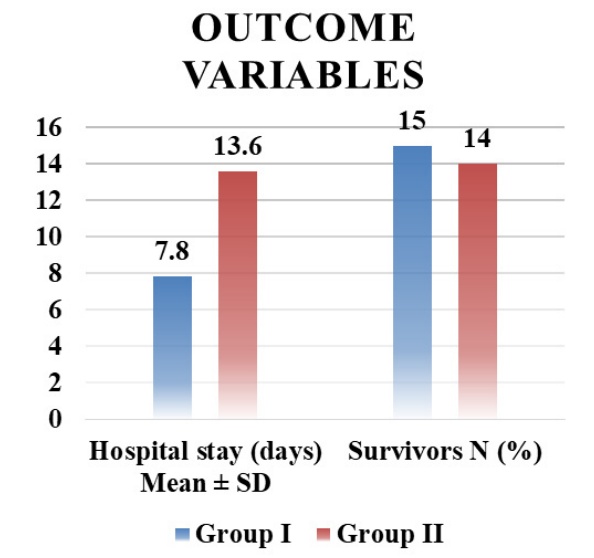
Table 2 shows symptoms distribution. In both the groups fever and cough was present in maximum patients *i.e.* 83.33% (25/30) out of total. Sore throat was present in 47% (14/30), breathlessness in 60% (18/30), nausea/vomiting in 17% (5/30) and diarrhoea in 10% (3/30).

Table 3 shows serum ferritin level. In group I on day 1 it was 308.2 ± 12.51 and on day 7 it was 311.09 ± 11.52. In group II on day 1 it was 312.9 ± 11.10 and on day 7 it was 770 ± 36.25. Statistically significant result found on day 7 between group I and II (P<0.0001) whereas no significant difference found on day 1 (P=0.2857).

Table 4 shows outcome variables. Hospital stay (days) Mean ± SD in group I was 7.8 ± 0.37 and in group II 13.6 ± 1.24. Result shows statistically significant difference (P<0.0001). In group I survivor% was 100% and in group II 93.33%



Graph 1: Serum ferritin.



Graph 2: Outcome variables.

Discussion

COVID-19 is a heterogeneous disease with unpredictable

Table 1. Age and sex distribution.

Sr No.	Age	Group I (15) Male N (%)	Group I (15) Female N (%)	Group II (15) Male N (%)	Group II (15) Female N (%)	Total N (%)
1	<30	2 -6.70%	1 -3.30%	1 -3.30%	0 0%	4 -13%
2	30 to 60	6 -20%	2 -6.70%	8 -27%	5 -17%	21 -70%
3	>60	2 -6.70%	2 -3.30%	1 -3.30%	0 0%	5 -17%
Total		10 -33.30%	5 -17%	10 -33.30%	5 -17%	30 -100%

Table 2. Symptoms distribution.

Sr No.	Clinical feature	Group I (15) N (%)	Group II (15) N (%)	Total-30 N (%)
1	Fever	12 -49%	13 -43.33%	25 -83.33%
2	Cough	11 -37%	14 -47%	25 -83.33%
3	Sore throat	8 -27%	6 -20%	14 -47%
4	Breathlessness	6 -20%	12 -49%	18 -60%
5	Nausea/Vomiting	2 -6.70%	3 -10%	5 -17%
6	Diarrhoea	1 -3.30%	2 -6.70%	3 -10%

Table 3. Serum ferritin level.

Sr No.	Serum ferritin (ng/ml)	Group I (15) Mean ± SD	Group II (15) Mean ± SD	t value	P value
1	Day 1	308.2 ± 12.51	312.9 ± 11.10	1.088	0.28
2	Day 7	311.09 ± 11.52	770 ± 36.25	46.72	<0.0001

Table 4: Outcome variables.

Sr No.	Outcome variables	Group I (15)	Group II (15)	P value
1	Hospital stay (days) Mean ± SD	7.8 ± 0.37	13.6 ± 1.24	<0.0001
2	Survivors N (%)	15 (100 %)	14 (93.33 %)	0.31

course ranging from mild self-limiting symptoms to cytokine storms. Identification of high-risk cases will enable appropriate intervention and escalation. Ferritin despite widely recognized as a representative of total body iron stores, its prognostic utility is linked with COVID-19. Present study was aimed at evaluation of these associations of ferritin with severity in coronavirus disease 2019 (COVID-19). 30 SARS-CoV-2 positive patients diagnosed on Reverse-Transcriptase Polymerase Chain Reaction (RTPCR) test were enrolled and serum ferritin in all. Results obtained were analyzed in present study maximum patients *i.e.* 21 (70%) were found from 30 to 60 years age group. Male preponderance was found with 20 (66.6%) cases out of total 30 (100%).

In the similar study by Sibtain et al. age median IQR was 59.5 (52–70) in severe group and 54 (39–68) in non-severe group. [9] Filippo et al. in a retrospective observational study involving two cohort groups of patients found in first cohort 17 patients diagnosed with COVID-19 pneumonia (11 males−64%; 6 females, mean age 68.8) and in second cohort, 30 patients (17 males−56%; 13 females, mean age 66.2). [10] Rusu et al. found out of the 72 patients, 46 (64%) were males and 26 (36%) females. [11] The average age of patients was 62 (16.8) years.

In present study in both the groups fever and cough was present in maximum patients *i.e.,* 25 (83.33%) & 25 (83.33%) respectively. Sore throat was present in 14 (47%), breathlessness in 18 (60%), nausea/vomiting in 5 (17%) and diarrhea in 3 (10%). In the similar study by Keddie et al. fever was present in 19 out of 24 non-severe and 18 out of 23 severe groups. [12] Sore throat was present in 3 out of 24 non-severe and 1 out of 23 severe groups. Breathlessness was present in 10 out of 24 non-severe and 20 out of 23 severe groups. Nausea/vomiting was present in 7 out of 24 non-severe and 2 out of 23 severe groups. Diarrhea was present in 5 out of 24 non-severe and 1 out of 23 severe groups.

In present study in group I on day 1 it was 308.2 ± 12.51 and on day 7 it was 311.09 ± 11.52. In group II on day 1 it was 312.9 ± 11.10 and on day 7 it was 770 ± 36.25. Statistically significant result found on day 7 between group I and II (P<0.0001) whereas no significant difference found on day 1 (P=0.2857). In the similar study by Sibtain et al. median ferritin being 828.5(IQR: 428.5–1386.7) and 357.5(IQR: 198.91098) ng/mL which was found to be significantly higher in the severe group compared to the non-severe cases group respectively (p value=0.005). Filippo et al. in their study found median (interquartile range) serum ferritin value as 674 (1284) ng/mL which was double the cutoff (300 ng/mL) in 9 of 17 patients (52%). Rusu et al. in their study found mean serum ferritin levels were 459 mcg/L on day 1 and 623 mcg/L on day 7.

In present study hospital stay (days) Mean ± SD in group I was 7.8 ± 0.37 and in group II 13.6 ± 1.24. Result shows statistically significant difference (P<0.0001). In group I survivor% was 100% and in group II 93.33%. In the similar study by Sibtain et al. (2021) there were a total of 86 (55%) cases in the severe category and 71 (45%) of the non-severe category survived. [9] Increased duration of hospital stay was also revealed as variables independently associated both with severity. Rusu et al. in their study found survivors were 39 (54%) out of total 72.

Inflammatory cytokine storm associated with severity of COVID 19 is characterized by abrupt and excess release of pro-inflammatory cytokines like interleukins IL-6, IL-10 and tumor necrosis factor (TNF-α). [13] Along with biochemical analysis of these plasma inflammatory markers, positive acute phase reactants like ferritin is also useful in predicting the disease progression. Ferritin occurring as a cytosolic protein in most tissues and representing total body iron store sits prognostic utility is linked with acute and chronic inflammatory processes. It is also non-specifically raised in a variety of disorders including chronic kidney disease, rheumatoid arthritis, and autoimmune disorders. [14]

Strength

Selection bias resulting from age, sex, race and socioeconomic status was eliminated.

Limitations

The main limitation of our study is that we have not considered effect of clinical parameters like blood pressure, body mass index and smoking habits. Also only symptomatic patients were enrolled.

Conclusion

On hospital admission ferritin level can be a predictor of mortality however it cannot reliably predict severity. In present study ferritin level was less on day 1 in both groups which increased on day 7 in both group but dramatic increase was observed in severe group. Owing to these statistically significant results obtained it is a useful marker of risk scarification in COVID-19 and can be considered in combination with clinical details and other laboratory tests in designing the patient centered treatment plans.

Acknowledgement

I would like to express my appreciation to Dean sir Dr. Rajesh Bohra and my Guide Dr. VijayKumar S. Gulwe MGM medical college and hospital Aurangabad. Also to record section of hospital for helping in retrieval of data of patients.

References

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395:507–513.
2. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003;31(4):1250–1256.
3. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: Guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854–87.
4. Litton E, Lim J. Iron metabolism: An emerging therapeutic target in critical illness. Crit Care. 2019;23:81.
5. Domellof M, Dewey KG, Lonnerdal B, Cohen RJ, Hernell O. The diagnostic criteria for iron deficiency in infants should

be re-evaluated. J. Nutr. 132 (12)(2002) 3680–3686.

6. Pagana KD, Pagana TJ, Pagana TN. Mosby's diagnostic & laboratory test reference 14th ed. St. Louis, Mo: Elsevier; 2019.
7. Vargas-Vargas M, Cortés-Rojo C. Ferritin levels and COVID-19. Rev PanamSalud Publica. 2020;44:e72.
8. Liu T, Zhang J, Yang Y, Ma H, Li Z, Zhang J, Yi J. The role of interleukin-6 in monitoring severe case of coronavirus disease 2019. EMBO Mol Med. 2020;12: e12421.
9. Sibtain A, Zeeshan AA, Imran S, Naveed HR, Maheen M, Lena J. Evaluation of serum ferritin for prediction of severity and mortality in COVID-19- A cross sectional study. Ann Med Surg (Lond). 2021; 63:102163.
10. Filippo B, Gaetano MC, Patrizio C. Serum ferritin levels in inflammation: a retrospective comparative analysis between COVID-19 and emergency surgical non- COVID-19 patients. World Journal of Emergency Surgery (2021) 16:9.
11. Rusu D, Blaj M, Ristescu I, Patrascanu E, Gavril L, Lungu O, et al. Outcome predictive value of serum ferritin in ICU patients with long ICU stay. Medicina. 2021;57:1.
12. Keddie, OZ, Chou MKL, Taylor RL, Heslegrave A, Garr E, Lakdawala N, et al. Laboratory biomarkers associated with COVID-19 severity and management. Clin Immunol. 2020;221:108614.
13. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020.
14. Jacobs A, Miller F, Worwood M, Beamish MR, Wardrop CA. Ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. Br Med J. 1972;4: 206–208.