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A COMPARATIVE STUDY ON THE LEVEL OF FERRITIN IN PATIENTS INFECTED WITH COVID-19 AND THE CORRELATION TO THE SEVERITY OF THE DISEASE

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Abstract:
Objective: The objective of this study was to evaluate the ferritin levels in patients with COVID-19 disease as well as to correlate its levels with patient conditions so as to determine its usefulness as a measure of the disease burden.

Materials: This study accumulated information on 96 positive COVID 19 cases that were treated in hospitals in Thi-Qar province and identified medical records between November 2022 and December 2023. The information was also obtained through a questionnaire survey of the isolation hospitals. They were sub-categorized into: mild, moderate and severe diseases based on the severity of the disease.

Results: The study was able to show that there were high ferritin levels in COVID-19 cases with mild disease being the lowest. About 59% of the patients were males, 62.5% had mild disease, 31.25% moderate disease whereas 6.25% had a severe disease and needed invasive mechanical ventilation. Assessment of markers of inflammation may be useful in the management of COVID-19 infection since high levels of ferritin in the inflammatory response may have its application.

Conclusions: The outcomes of this research stress it is possible to use serum ferritin to assess the severity of disease in patients with COVID-19. High levels of ferritin within the patient were also correlated with an increase in the severity of the disease, which can assist practitioners in the early stage of detecting and managing severely ill patients.

Keywords: COVID-19 severity, ferritin levels, the underlying inflammation, Hyperferritinaemia.

Introduction

The human ferritin molecule contains two structural components, ferritin heavy chain (FTH) and ferritin light chain (FTL) [1]. The FTH chain has ferroxidase activity and converts Fe2+ into Fe3+. The Fe3+ ion subsequently migrates towards the nucleation site on the FTL chain and thus contributes to the process of iron oxidation and core formation in a regulated manner. The assembled ferritin units resemble a spherical shape with an encaged core having outer wall

and inner wall dia of 12 and 8nm, respectively It Is This spherical enclosure which is stable between pH 3-9 and called as nano cage isolates the iron inside the core from the external environment, shielding the body from the damaging effects of too much free iron. About 5000 iron atoms can be sequestered by a single ferritin molecule.

. Serum ferritin concentrations reflect iron store status in healthy individuals, where low levels signify iron shortage and high levels denote iron overload [2]. Serum ferritin serves as a clinical diagnostic for evaluating iron deficiency or excess. Ferritin is an acute-phase protein that is increased and raised during both infectious and non-infectious inflammation, hence significantly influencing its assessment in inflammatory contexts. Consequently, supplementary biomarkers such as soluble transferrin receptor or transferrin saturation are employed to evaluate iron status, which is less affected by inflammation. [1, 3-5]. Hyperferritinaemia is a biomarker for inflammation-driven disorders and is observed in various diseases.

This is said to be associated with extrication or leakage from compromised intracellular reserves leading to iron overload [5, 6]. It has been established that excess iron can support the growth of viruses like hepatitis C, human immunodeficiency virus, and even SARS-CoV-2 [7, 8]. Accumulation of excess iron can lead to enhanced creation of fibrin chains and a hypercoagulable state leading to coagulopathy in moderate to critically ill Covid-19 patients [9]. One of the studies suggests that SARS-CoV-2 adheres to hemoglobin which leads to mobilisation of iron [10, 11]. This Theory has been disproved. Iron chelation therapy in COVID-19 is highly debated and more studies are required to better understand the individual health impact of this therapy [12, 13].

In 2019, a novel coronavirus emerged in Wuhan, China [14] resulting in its worldwide dissemination and designation as a global epidemic by the World Healthcare Organization (WHO) in March 2020 [15, 16]. The disease, characterized by varying severity and clinical presentation, affects respiratory and acute respiratory systems, releases pro-inflammatory mediators, and activates the immune system, with the cytokine storm being the leading cause of COVID-19 mortality [17-19]. The current study aims to clarify the relationship between ferritin levels in the serum of patients infected with the Coronavirus and the severity of the disease.

Materials and methods

This study obtained data on 96 patients suffering from COVID-19 from two hospitals located in Thi-Qar province. Medical records were reviewed, and data from the hospitalizations covering the period of 1st November 2022 to 31st December 2023 was collected from the hospitals.

The data was obtained through the use of a prepared questionnaire while the information was sourced from COVID-19 isolation hospitals in the city of Nasiriya for the period November 2022 till the end of December 2023. WHO measures were implemented to establish the presence of COVID-19 [20]. Confirmed COVID-19 cases were defined as a positive result from a polymerase chain reaction (PCR) assay of nasal and pharyngeal swab specimens. Only instances confirmed by PCR were included in the analysis. EMR was used to get laboratory results. All laboratory examinations conducted were in consistent with the clinical consumption of the patients. Current investigations were composed of complete blood count and other

routine tests including CRP and ferritin assay, and chest films for radiological query.
COVID-19 admission severity was evaluated based on Report of the WHO-China Joint Mission on COVID-19 [21].
-Mild illness included non-pneumonia as well pneumonia cases.
-Moderate illness was attended by little intolerable breathlessness, respiratory ingrate of 30 per min, or below blood saturation of 93 percent.

-In the severe or critical category, patients presented with respiratory failure, septic shock, and/or one or more multiple organ dysfunction or failure.

Results

The current study included 96 patients with coronavirus disease, and the data was collected from isolation hospitals for Corona patients from November 2021 to the end of April 2022. Ferritin values were used; thus, patients were classified into 3 groups according to severity of coronavirus disease and ferritin value: Patients with mild disease had the lowest average ferritin level of 327.27 ng/ml, followed by patients in the moderate group with an average ferritin level of 555 ng/ml. The severe group had an average ferritin level of 817.6 ng/ml. The study demonstrated that ferritin levels were elevated in COVID-19 patients, according to Table (1).

Table (1): Age and Sex distribution with Ferritin value in patients

Age of patient (year)	Number of cases		Total	Percentage%	Value of Ferritin
	Male	Female			
31- 40	16	21	37	38.94	237-903
41- 50	29	8	37	38.94	277-985
51- 60	9	4	13	13.68	465-983
61- 70	5	4	8	8.42	300-1000
Total	59	37	96	100	

Based on the available data, it has been observed that there is a higher likelihood of males (59%) being infected with COVID-19 compared to females (37%), as shown in Figure 1.

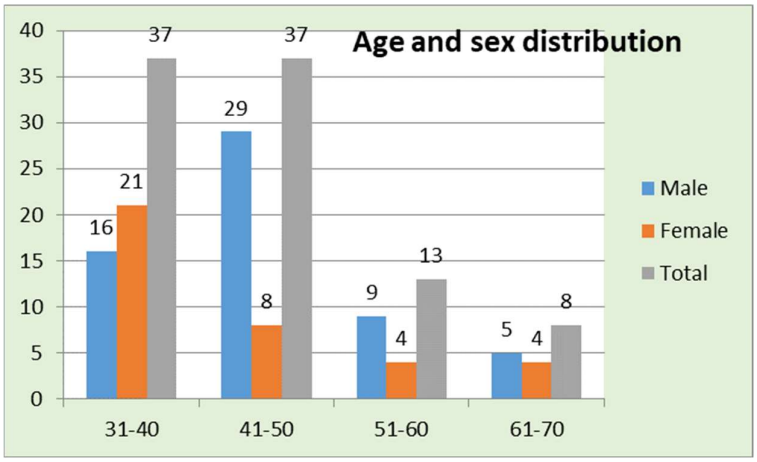

Figure (1): Age and sex distribution in patients with COVID-19

In our study, 62.5% (n=60) of the patients were considered to have a mild COVID-19, 31.25% (n=30) were considered to have moderate disease, and the remaining 6.25% (n=6) presented with severe disease, which required invasive ventilation (Table 2) and Figure 2. In the context of the inflammatory response to COVID-19, it has been observed that an elevation in ferritin levels is associated with an increase in inflammatory markers such as CRP. This correlation can potentially aid in the diagnosis of COVID-19 infection.

Table (2): COVID – 19 severities in 96 patients

COVID- 19 severity	Frequency	percent
Mild	**60**	**62.5%**
Moderate	**30**	**31.25%**
Severe	**6**	**6.25%**

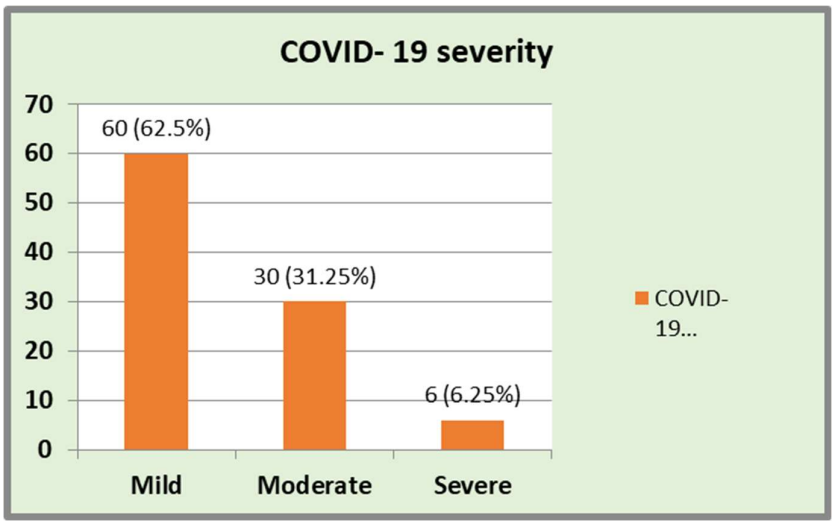

Figure (2): COVID – 19 severities in 96 patients

Discussion

Ferritin plays a crucial role in immune dysregulation, particularly in extreme Hyperferritinaemia, contributing to the cytokine storm syndrome [22, 23]. This syndrome has

been linked to fatal COVID-19 outcomes, suggesting that disease severity is dependent on it. Elevated serum ferritin levels in individuals with diabetes increase their risk of severe complications from COVID-19 [24]. This suggests that ferritin levels may be a significant factor influencing COVID-19 severity [25, 26]. The findings of the present study on ferritin levels in individuals with confirmed Covid-19 virus have been reported, and these findings are in line with numerous previous studies [27-29]. There is a growing body of evidence indicating that advanced age and being male are significant factors associated with an increased susceptibility to COVID-19 and higher mortality rates [30-32]. Our study revealed a higher susceptibility of males to Coronavirus infection and a correlation between age and mortality rates, aligning with extensive research conducted in various countries. Among the 1591 patients hospitalized to the intensive care unit in the Lombardy region of Italy, a substantial majority of 82% were male [33]. Various factors have been suggested to elucidate the gender disparity in COVID-19, including variations in smoking and alcohol consumption patterns, alongside social and psychological attributes. Inflammation, encompassing the acute-phase response, is marked by several physiological and metabolic alterations that transpire promptly following tissue injury. The alteration in concentrations of several plasma proteins, referred to as "acute phase proteins," serves as a crucial indicator of the acute-phase response. Ferritin is frequently utilized as a biomarker in clinical practice [34]. Comprehensive studies have been performed on serum ferritin as an indicator of iron metabolism [35]. Nonetheless, it has emerged as a significant biomarker for inflammation in relation to COVID-19 progression, as evidenced by the present study and previous investigations in this domain [36]. Ferritin is a protein that generally exhibits elevated levels during inflammatory responses [37].

Conclusion

According to the most recent study, the majority of COVID-19 virus-infected individuals Laboratory tests revealed high levels of ferritin in the blood for both sexes o those men receiving treatment in the hospital f. This finding may contribute to the diagnosis of COVID-19 infection; thus, patients with COVID-19 should have their levels regularly evaluated for signs of disease progression. A thorough understanding of the disease's overall prognosis and inflammatory state can be gained by tracking ferritin levels.

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