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RESEARCH LETTER

Evidence of diagnostic value of ferritin in patients with COVID-19

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The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic forces medical personnel to search for alternative early diagnosis methods of the patient's condition [1]. An essential element of the diagnosis of a patient with COVID-19 is to understand the impact of various laboratory tests on the severity of the disease. An example of this research can be determining the level of ferritin, which is considered an indicator of the body's iron supply. As iron levels fall, the blood ferritin levels fall [2]. The concentration of 1 μg/L corresponds to 8 mg of iron in the reserve pool [3]. When healthy, 20% of the body's iron is bound to ferritin. Ferritin bound iron accounts for 95% of the hepatic iron stores. According to World Health Organization, adult women's norm ranges from 15 to 150 μg/L, for men from 15 to 200 μg/L [4]. Moreover, ferritin is considered an acute phase protein, so its concentration also increases inflammation and infections. This limits the possibility of using its determination to assess systemic iron resources, even in terms of the diagnosis of COVID-19 severity [5, 6]. Abbaspour et al. [7] showed that ferritin is a crucial mediator of immune dysregulation via direct immune-suppressive and pro-inflammatory effects, contributing to cytokine storm.

The present study aimed to determine the usefulness of ferritin as a predictor of a patient's severity with COVID-19 in a performer systematic review and meta-analysis. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [8] and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines for reporting systematic reviews and meta-analyses of observational studies [9].

Three authors (L.S., J.S., and S.B) independently searched relevant literature. The current Pubmed, Embase, Cochrane, Web of Science, Scopus (from database inception to November 10, 2020) was explored. The whole search strategy used free words, including "ferritin" AND "COVID-19"

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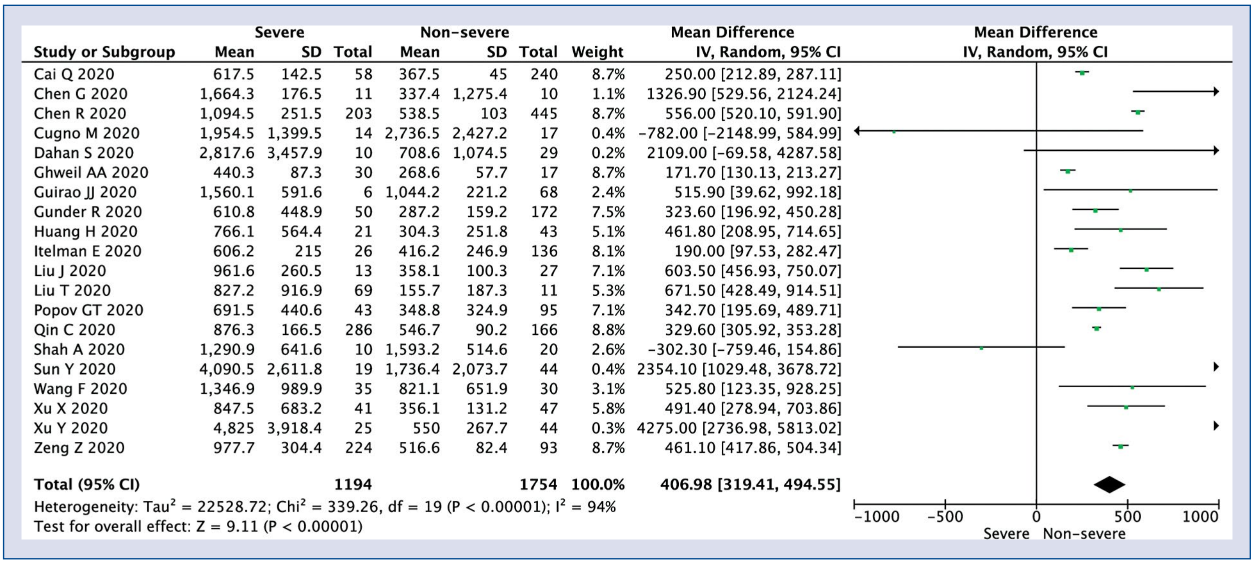

Study or Subgroup	Severe Mean	Severe SD	Severe Total	Non-severe Mean	Non-severe SD	Non-severe Total	Weight	Mean Difference IV, Random, 95% CI
Cai Q 2020	617.5	142.5	58	367.5	45	240	8.7%	250.00 [212.89, 287.11]
Chen G 2020	1,664.3	176.5	11	337.4	1,275.4	10	1.1%	1326.90 [529.56, 2124.24]
Chen R 2020	1,094.5	251.5	203	538.5	103	445	8.7%	556.00 [520.10, 591.90]
Cugno M 2020	1,954.5	1,399.5	14	2,736.5	2,427.2	17	0.4%	−782.00 [−2148.99, 584.99]
Dahan S 2020	2,817.6	3,457.9	10	708.6	1,074.5	29	0.2%	2109.00 [−69.58, 4287.58]
Ghweil AA 2020	440.3	87.3	30	268.6	57.7	17	8.7%	171.70 [130.13, 213.27]
Guirao JJ 2020	1,560.1	591.6	6	1,044.2	221.2	68	2.4%	515.90 [39.62, 992.18]
Gunder R 2020	610.8	448.9	50	287.2	159.2	172	7.5%	323.60 [196.92, 450.28]
Huang H 2020	766.1	564.4	21	304.3	251.8	43	5.1%	461.80 [208.95, 714.65]
Itelman E 2020	606.2	215	26	416.2	246.9	136	8.1%	190.00 [97.53, 282.47]
Liu J 2020	961.6	260.5	13	358.1	100.3	27	7.1%	603.50 [456.93, 750.07]
Liu T 2020	827.2	916.9	69	155.7	187.3	11	5.3%	671.50 [428.49, 914.51]
Popov GT 2020	691.5	440.6	43	348.8	324.9	95	7.1%	342.70 [195.69, 489.71]
Qin C 2020	876.3	166.5	286	546.7	90.2	166	8.8%	329.60 [305.92, 353.28]
Shah A 2020	1,290.9	641.6	10	1,593.2	514.6	20	2.6%	−302.30 [−759.46, 154.86]
Sun Y 2020	4,090.5	2,611.8	19	1,736.4	2,073.7	44	0.4%	2354.10 [1029.48, 3678.72]
Wang F 2020	1,346.9	989.9	35	821.1	651.9	30	3.1%	525.80 [123.35, 928.25]
Xu X 2020	847.5	683.2	41	356.1	131.2	47	5.8%	491.40 [278.94, 703.86]
Xu Y 2020	4,825	3,918.4	25	550	267.7	44	0.3%	4275.00 [2736.98, 5813.02]
Zeng Z 2020	977.7	304.4	224	516.6	82.4	93	8.7%	461.10 [417.86, 504.34]
Total (95% CI)			**1194**			**1754**	**100.0%**	**406.98 [319.41, 494.55]**

Heterogeneity: $Tau^2 = 22528.72$; $Chi^2 = 339.26$, $df = 19$ ($P < 0.00001$); $I^2 = 94\%$

Test for overall effect: $Z = 9.11$ ($P < 0.00001$)

Figure 1. Forest plot of ferritin levels in severe versus non-severe groups. The center of each square represents the odds ratio for individual trials, and the corresponding horizontal line stands for a 95% confidence interval (CI). The diamonds represent pooled results; SD — standard deviation.

OR "SARS-CoV-2". The reference lists of all eligible trials and reviews were screened for additional citations. Publications were restricted to the English language.

Twenty studies reported ferritin levels in severe and non-severe patient groups. Polled analysis showed that it significantly correlated higher ferritin levels with the more severe condition of the COVID-19 patient (MD: 406.98; 95% CI: 319.41–494.55; $p < 0.001$; I^2: 94%; Fig. 1). Detailed characteristics of the studies included in the meta-analysis are presented in **Supplementary Digital Content**. Higher ferritin levels were also associated with more frequent hospitalization in intensive care unit conditions (MD: 748.96; 95% CI: 444.45–1053.48; $p < 0.001$; I^2: 89%), and higher mortality in COVID-19 patients (MD: 594.43; 95% CI: 345.7–843.17; $p < 0.001$; I^2: 99%; **Supplementary Digital Content**).

In conclusion, this systematic review and meta-analysis show a close correlation between ferritin levels and the state of the COVID-19 patient. Higher ferritin levels were associated with a more severe patient condition, more intensive care unit exposure, and higher mortality.

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Conflict of interest: None declared

References

1. Dzieciatkowski T, Szarpak L, Filipiak KJ, et al. COVID-19 challenge for modern medicine. Cardiol J. 2020; 27(2): 175–183, doi: 10.5603/CJ.a2020.0055, indexed in Pubmed: 32286679.
2. Evrin T, Demirel B, Szarpak L, et al. Galectin-3: a novel blood test for the classification of patients with COPD. An observational study. Dis Emerg Med J. 2019; 4(3): 77–82, doi: 10.5603/demj.a2019.0016.
3. Salman Z, Yılmaz T, Mehmetçik G. The relationship between ferritin levels and oxidative stress parameters in serum of β-thalassemia major patients. Arch Biochem Biophys. 2018; 659: 42–46, doi: 10.1016/j.abb.2018.09.020, indexed in Pubmed: 30287235.
4. Dopsaj V, Martinovic J, Dopsaj M, et al. Gender-specific oxidative stress parameters. Int J Sports Med. 2011; 32(1): 14–19, doi: 10.1055/s-0030-1267930, indexed in Pubmed: 21086243.
5. Henry BM, de Oliveira MH, Benoit S, et al. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020; 58(7): 1021–1028, doi: 10.1515/cclm-2020-0369, indexed in Pubmed: 32286245.
6. Katipoğlu B, Sönmez LÖ, Vatansev H, et al. Can hematological and biochemical parameters fasten the diagnosis of COVID-19 in emergency departments? Dis Emerg Med J. 2020, doi: 10.5603/demj.a2020.0039.
7. Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. J Res Med Sci. 2014; 19(2): 164–174, indexed in Pubmed: 24778671.
8. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015; 350: g7647, doi: 10.1136/bmj.g7647, indexed in Pubmed: 25555855.
9. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000; 283(15): 2008–2012, doi: 10.1001/jama.283.15.2008, indexed in Pubmed: 10789670.