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ORIGINAL ARTICLE

Ferritin-Haemoglobin Ratio as a Predictor of Severity and Fatal Outcome in Patients with COVID-19

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Abstract

Background/Aim: Although ferritin and haemoglobin were well-studied for adverse outcome prediction in COVID-19 patients, a ferritin-haemoglobin ratio (FHR) was studied poorly. The study aimed to evaluate the prognostic ability of FHR at hospital admission in hypertensive and non-hypertensive patients with COVID-19.

Methods: The study included 135 patients hospitalised for COVID-19-associated pneumonia. The 78.5 % of patients were hypertensive.

Results: FHR at admission was higher in patients with critical condition (39.8 [17.1–83.0]) than in patients with moderate (22.0 [12.1–32.1], p = 0.01) and severe condition (34.6 [15.1–64.5], p = 0.01). FHR was higher in patients who required supplemental oxygen (40.4 [29.4–47.8]) than in patients without the need for supplemental oxygen (22.0 [18.0–25.5]) (p = 0.001). FHR at admission was higher in non-survivors (40.1 [24.6–95.9]) than in survivors (24.5 [21.6–28.4]) (p = 0.047). FHR showed weak discriminative ability for the prediction of severe/critical conditions in hypertensive patients (AUC = 0.636, p = 0.015) and all (hypertensive and non-hypertensive patients) patients (AUC = 0.658, p = 0.001), whereas FHR had an acceptable discriminative ability in non-hypertensive patients (AUC = 0.764, p = 0.015). There was an acceptable discriminative ability of FHR for in-hospital mortality prediction in hypertensive patients (AUC = 0.717, p = 0.029). Patients with FHR > 33.98 (Youden index, 0.39) had higher odds of severe/critical clinical condition (OR: 4.57; 95 % CI: 1.87–11.18; p = 0.001). FHR of > 37.64 (Youden index, 0.55) was associated with higher in-hospital mortality among hypertensive patients (OR: 12.06; 95 % CI: 2.44–59.71; p = 0.002). There was no difference in AUC for the discriminative ability of FHR regarding severe/critical condition (p = 0.296) and mortality (p = 0.663) in hypertensive and non-hypertensive patients.

Conclusion: FHR at admission of > 33.98 is a predictor of severe/critical COVID-19 in both hypertensive and non-hypertensive patients. FHR of > 37.64 is a predictor of in-hospital mortality in hypertensive patients. There was no significant difference in the discriminative ability of FHR between hypertensive and non-hypertensive patients.

Key words: COVID-19; Hypertension; Ferritin-haemoglobin ratio; Severity; Mortality.

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Introduction

The COVID-19 pandemic is related to health, economic and social crises with a significant impact on all spheres of human life.[1] As of 14 June 2023, WHO reported over 767 million confirmed cases of COVID-19, including almost 7 million deaths.[2] The case fatality rate of COVID-19 in the general population is 1.0 %, whereas in hospitalised patients it's 13.0 %.[3]

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COVID-19 results in a hyperinflammatory state and cytokine storm leading to tissue damage, acute respiratory distress syndrome and multi-organ failure.[4] Serum ferritin is a well-known inflammatory biomarker, however, there are some doubts about whether serum ferritin causes or reflects inflammation.[5] It's hypothesised that elevated serum ferritin levels may be due to passive release from cell damage.[6] Multiple studies and meta-analyses showed that serum ferritin levels are higher in patients with severe/critical COVID-19 than in mild/moderate COVID-19 and this biomarker may be used as a predictor of severity.[7-10] Also, serum ferritin is found to be a considerable predictor of mortality in COVID-19 patients.[11-14]

A positive association between the mean serum ferritin levels and high blood pressure was found.[15] Hypertensive patients present with far higher ferritin levels compared to non-hypertensive patients.[16]

Haemoglobin level is another laboratory parameter that may reflect COVID-19 severity. It was found that haemoglobin level is significantly lower in COVID-19 patients with severe disease compared to those with mild disease.[17] Patients with anaemia are more likely to develop severe pneumonia associated with COVID-19.[18] Also, the decrease in haemoglobin levels during the short period might be a predictor of worsening pneumonia in COVID-19 patients.[19] Numerous studies showed that haemoglobin level positively correlates with blood pressure.[20-22]

Severe COVID-19 is accompanied by low haemoglobin levels along with increased serum ferritin.[23] Ferritin-haemoglobin ratio is known to be an important prognostic factor in patients with advanced non-small-cell lung cancer.[24] Also, it was found that the ferritin-haemoglobin ratio is an independent risk factor for mortality in patients with COVID-19.[25]

Thus, hypothesis was made that a ferritin-haemoglobin ratio may be better predictor of COVID-19 severity and mortality than ferritin and haemoglobin separately. Considering the fact that hypertension impacts the levels of both haemoglobin and ferritin, it's reasonable to study the predictive ability of the ferritin-haemoglobin ratio in hypertensive and non-hypertensive patients.

The aim of this study was to evaluate the prognostic ability of the ferritin-haemoglobin ratio in hypertensive and non-hypertensive patients hospitalised for COVID-19.

Methods

This was a prospective study. Hospitalised patients with COVID-19-associated pneumonia were included from March to June 2021. The research was conducted at the Ivano-Frankivsk Central City Hospital and Ivano-Frankivsk City Hospital No 1.

One hundred thirty-five adult patients were enrolled in the study. Pneumonia was confirmed by either chest computed tomography or chest X-ray. Coronavirus SARS-CoV-2 was confirmed in each patient with either PCR or ELISA test (IgM level assessment). All patients were not vaccinated for COVID-19.

Among 135 patients, 106 (78.5 %) were hypertensive (arterial hypertension was diagnosed prior to hospital admission). The diagnosis of arterial hypertension was established according to the criteria of the 2018 European Society of Cardiology Guideline.[26]

The severity of COVID-19-associated pneumonia was assessed according to the Protocol of Medical Care for Treatment of Coronavirus Disease (COVID-19).[27] A severe clinical condition was defined in the presence of at least one of the following characteristics: respiratory rate ≥ 30 breaths per minute, oxygen saturation ≤ 93 % and pulmonary infiltrates occupying > 50 % of the lung area. The critical condition was defined in the presence of at least one of the followings: acute respiratory distress syndrome, sepsis, altered consciousness and multiple organ dysfunction syndrome. Also, the severity of pneumonia at the moment of hospital admission was assessed using the following scores: CURB-65 and pneumonia severity index (PSI).

Besides the conventional laboratory tests (complete blood count, urine analysis, fasting glucose, biochemical profile), ferritin level was assessed. The samples were taken at the moment of hospital admission.

A consent form was signed by each participant before recruitment into the study. All of the procedures in the study met bioethical standards according to the Helsinki Declaration. The consent of the Ethics Committee of the Ivano-Frankivsk National Medical University (No 134/23) was obtained.

Statistical processing was performed using the software MedCalc and MS Excel. The Shapiro-Wilk test was used to evaluate the distribution of variables. The mean with the 95 % confidence interval (CI) was calculated for variables with normal distribution. The median value with the interquartile range was calculated for variables with abnormal distribution. Categorical variables were shown as an absolute numbers with a percentage. Independent T-test, Mann-Whitney U test, Fisher exact test, One-way ANOVA with post-hoc Tukey's test, Kruskal-Wallis test with post-hoc Dunn's test were used. Odds ratio (OR) was calculated. Receiver operating characteristic (ROC) curves were built and the area under the curve (AUC) was calculated. Sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratio and Youden index were calculated. Also, a comparison of AUCs was performed. A p-value of < 0.05 was considered significant.

Results

Characteristics of hypertensive and non-hypertensive patients are shown in Table 1.

Table 1: Characteristics of hypertensive and non-hypertensive patients with COVID-19 at hospital admission

Characteristic	Hypertensive patients (n = 106)	Non-hypertensive patients (n = 29)	p-value
Age in years	68.4 ± 1.7	59.1 ± 4.9	< 0.001*
Gender			
Male	41 (38.7 %)	12 (41.4 %)	0.790**
Female	65 (61.3 %)	17 (58.6 %)	
BMI, kg/m^2	27.1 [24.6-32.0]	26.8 [24.5-31.1]	0.17***
PSI, points	70.0 [57.0–82.0]	54.0 [45.8-68.5]	< 0.001***
CURB-65	1.0 [0.0–1.0]	1.0 [0.0–1.0]	0.220***
SpO_2, %	94.5 [92.0–96.0]	95.0 [94.8–96.0]	0.260***

*BMI: body mass index; SpO_2: peripheral oxygen saturation; PSI: pneumonia severity index; *: Independent T-test; **: Fisher exact test; ***: Mann-Whitney U test;*

The median length of inpatient stay was similar in hypertensive and non-hypertensive patients (13.0 [10.0–16.0] days vs 14.0 [9.0–16.0] days, p = 0.86). Among hypertensive patients, 47 (44.3 %) had a moderate clinical condition, 46 (43.4 %) developed a severe clinical condition and 13 (12.3 %) developed a critical clinical condition. Among non-hypertensive patients, 16 (55.2 %) had a moderate clinical condition, 9 (31.0 %) developed a severe clinical condition and 4 (13.8 %) developed a critical clinical condition.

Supplemental oxygen was required by 50 (47.2 %) hypertensive patients and 12 (41.4 %) non-hypertensive patients. Continuous positive airway pressure therapy was used in 10 (9.4 %) hypertensive patients and 2 (6.9 %) non-hypertensive patients. Mechanical ventilation was used in 5 (4.7 %) hypertensive patients and none non-hypertensive patients. Twelve (11.3 %) hypertensive patients and 2 (6.9 %) non-hypertensive patients died during the inpatient stay.

Levels of ferritin, haemoglobin and the ferritin-haemoglobin ratio at the moment of hospital admission in hypertensive and non-hypertensive patients are shown in Table 2.

Table 2: Levels of ferritin, haemoglobin and ferritin-haemoglobin ratio at the moment of hospital admission in patients with COVID-19

Characteristic	Hypertensive patients (n = 106)	Non-hypertensive patients (n = 29)	p-value
Ferritin, ng/mL	349.0 [176.0-572.5]	349.0 [189.0-746.5]	0.92*
Haemoglobin, g/dL	13.1 [12.1–14.2]	13.1 [12.4-14.0]	0.84*
Ferritin-haemoglobin ratio	25.7 [22.0–33.1]	25.8 [20.8–41.6]	0.89*

**: Mann-Whitney U test;*

The ferritin-haemoglobin ratio at the moment of hospital admission depending on the disease severity is shown in Table 3.

Table 3: Ferritin-haemoglobin ratio at the moment of hospital admission in patients with COVID-19

Patients	Moderate condition[1]	Severe condition[2]	Critical condition[3]	p
Hypertensive (n = 106)	22.2 [12.0–32.3]	29.9 [13.7–50.0] 1/2: p = 0.08	43.0 [31.0–96.0] 1/3: p = 0.01 2/3: p = 0.13	0.020*
Non-hypertensive (n = 29)	22.4 ± 5.8	59.0 ± 26.1 1/2: p = 0.003	31.0 ± 47.9 1/3: p = 0.79 2/3: p = 0.14	0.004**
All patients (n = 135)	22.0 [12.1–32.1]	34.6 [15.1–64.5] 1/2: p = 0.01	39.8 [17.1–83.0] 1/3: p = 0.01 2/3: p = 0.53	0.001*

**: Kruskal-Wallis test, post-hoc Dunn's test; **: ANOVA, post-hoc Tukey's test;*

The ferritin-haemoglobin ratio at the moment of hospital admission was higher in patients with the need for supplemental oxygen during an inpatient stay compared to patients that didn't require supplemental oxygen (Table 4).

Table 4: Ferritin-haemoglobin ratio at the moment of hospital admission depending on the need for supplemental oxygen during the inpatient stay in patients with COVID-19

Patients	Necessity of supplemental oxygen		p-value
	Yes	No	
Hypertensive (n = 106)	39.3 [24.1–46.4]	39.3 [24.1–46.4]	0.020*
Non-hypertensive (n = 29)	53.5 [28.6–70.1]	53.5 [28.6–70.1]	0.003*
All patients (n = 135)	**40.4 [29.4–47.8]**	**40.4 [29.4–47.8]**	**0.001***

**: Mann-Whitney U test;*

Among hypertensive patients, the ferritin-haemoglobin ratio at the moment of hospital admission was higher in deceased patients (45.9 [39.3–96.7]) than in survivors (24.4 [12.8–41.8]) (p = 0.02). Among all patients, the ferritin-haemoglobin ratio at hospital admission was higher in deceased patients (40.1 [24.6–95.9]) than in survivors (24.5 [21.6–28.4]) (p = 0.047).

The discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio at hospital admission for the prediction of severe/critical clinical conditions and death are shown in Figure 1 and Table 5. Ferritin and ferritin-haemoglobin ratio showed acceptable discriminative abilities for the prediction of severe/critical clinical condition development in non-hypertensive patients, whereas these parameters had weak discriminative abilities in hypertensive patients. The haemoglobin levels failed to show a sufficient predictive discriminative ability for the prediction of severe/critical clinical condition in both hypertensive and non-hypertensive patients. However, ferritin level and ferritin-haemoglobin ratio at the moment of hospital admission showed acceptable discriminative abilities for the prediction of in-hospital mortality in hypertensive patients, but these parameters didn't have sufficient discriminative abilities in non-hypertensive patients. However, the haemoglobin levels showed excellent discriminative abilities for in-hospital mortality in non-hypertensive patients.

The predictive abilities of the ferritin-haemoglobin ratio at hospital admission are shown in Table 6. The ferritin-haemoglobin ratio had a low Youden index for the prediction of severe/critical clinical conditions in hypertensive patients and death in non-hypertensive patients. However, the Youden index was acceptable for the prediction of

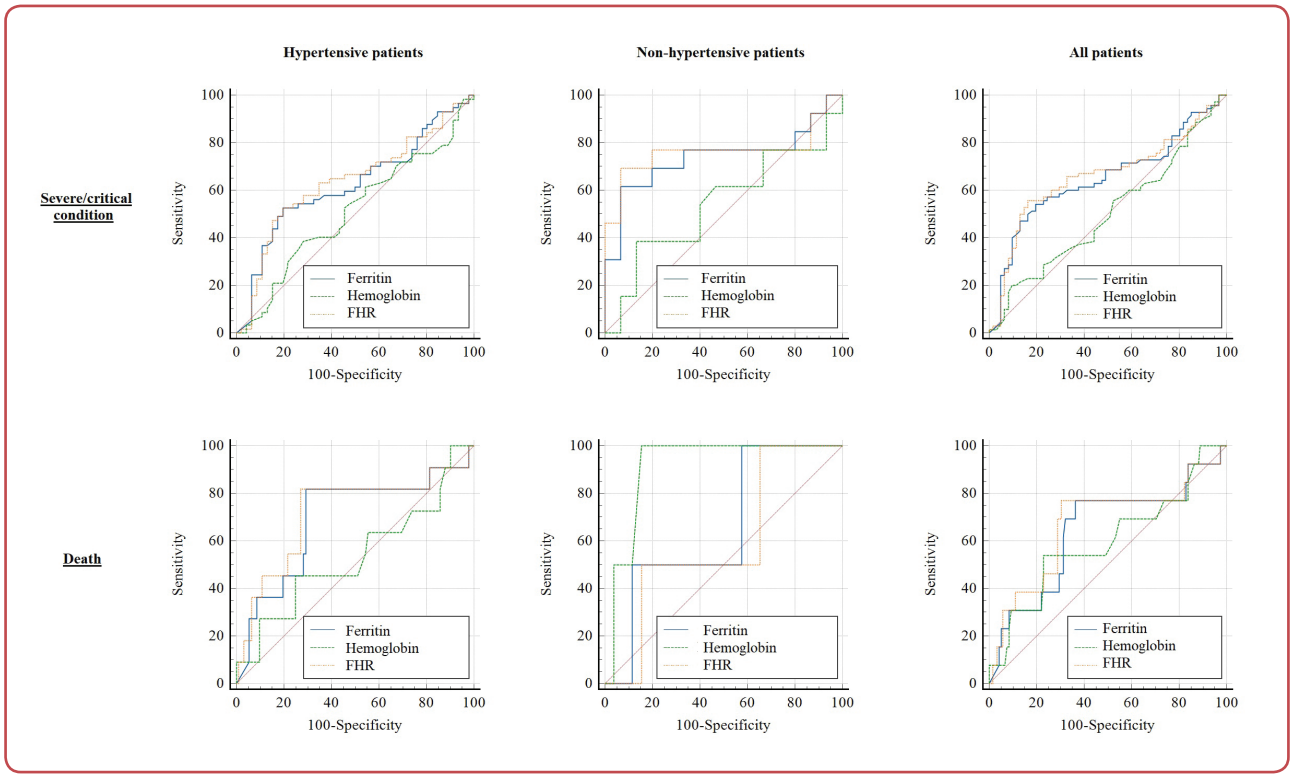

Figure 1: ROC-curves of discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio for the prediction of severe/critical clinical conditions and death in patients with COVID-19

Table 5: Parameters of AUCs for discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio for the prediction of severe/critical clinical conditions and death in patients with COVID-19

Parameter	Hypertensive patients		Non-hypertensive patients		All patients	
	AUC; SE	p-value	AUC; SE	p-value	AUC; SE	p-value
Severe/critical clinical conditions						
Ferritin	0.628; 0.056	0.021	0.745; 0.106	0.020	0.653; 0.049	0.002
Haemoglobin	0.510; 0.057	0.863	0.541; 0.117	0.726	0.501; 0.051	0.986
FHR	0.636; 0.056	0.015	0.764; 0.109	0.015	0.658; 0.049	0.001
Death						
Ferritin	0.701; 0.091	0.027	0.648; 0.249	0.552	0.651; 0.087	0.083
Haemoglobin	0.543; 0.105	0.681	0.913; 0.067	< 0.001	0.600; 0.094	0.287
FHR	0.717; 0.100	0.029	0.596; 0.259	0.711	0.668; 0.094	0.075

AUC: area under the curve; FHR: ferritin-haemoglobin ratio; SE: standard error;

Table 6: Predictive abilities of ferritin-haemoglobin ratio at the moment of hospital admission in patients with COVID-19

Patients	Youden index	Optimal cut-off value	Se, %	Sp, %	LR+	LR-	PPV+, %	PPV-, %
Severe/critical clinical conditions								
Hypertensive (n = 106)	0.33	> 33.98	52.63	80.43	2.69	0.59	76.9	57.8
Non-hypertensive (n = 29)	0.63	> 33.55	69.23	93.33	10.38	0.33	90.0	77.8
All patients (n = 135)	**0.39**	**> 33.98**	**55.71**	**83.61**	3.40	0.53	79.6	62.2
Death								
Hypertensive (n = 106)	0.55	> 37.64	81.82	72.83	3.01	0.25	26.5	97.1
Non-hypertensive (n = 29)	0.35	≤ 11.24	50.00	84.62	3.25	0.59	20.0	95.7
All patients (n = 135)	**0.46**	**> 35.21**	**76.92**	**69.49**	**2.52**	**0.33**	**21.7**	**96.5**

LR+, positive likelihood ratio; LR-, negative likelihood ratio; PPV+, positive predictive value; PPV-, negative predictive value; Se, sensitivity; Sp, specificity;

severe/critical clinical conditions in non-hypertensive patients and death in hypertensive patients.

The probability of severe/critical clinical condition in hypertensive patients was 76.9 %, if the ferritin-haemoglobin ratio was > 33.98 at the moment of hospital admission and 42.2 % if this parameter was lower than this value (OR: 4.57; 95 % CI: 1.87–11.18; p = 0.001). If the ferritin-haemoglobin ratio at admission in non-hypertensive patients was > 33.55, the probability of severe/critical clinical condition was 90.0 %; in patients with a ferritin-haemoglobin ratio below this value, the probability of severe/critical clinical condition was 22.2 % (OR: 31.50; 95 % CI: 3.02–328.94; p = 0.004). Among all patients (hypertensive and non-hypertensive) with a ferritin-haemoglobin ratio of > 33.98, severe/critical clinical condition developed in 79.6 %; in patients with a ferritin-haemoglobin ratio below this cut-off value, the probability of severe/critical condition was 37.8 % (OR: 6.42; 95 % CI: 2.81–14.65; p < 0.001).

The mortality rate in hypertensive patients with a ferritin-haemoglobin ratio of > 37.64 was 26.5 %; in hypertensive patients with a ferritin-haemoglobin ratio below this value, in-hospital mortality was 2.9 % (OR: 12.06; 95 % CI: 2.44–59.71; p = 0.002). Among all patients (hypertensive and non-hypertensive) with a ferritin-haemoglobin ratio of > 35.21, the in-hospital mortality rate was 21.7 %; in patients with a ferritin-haemoglobin ratio below this cut-off value, the in-hospital mortality rate was 3.5 % (OR: 7.59; 95 % CI: 1.97–29.24; p = 0.003).

AUCs for discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio for the prediction of severe/critical clinical conditions and death are compared in Tables 7 and 8. The ferritin-haemoglobin ratio showed better discriminative abilities for the prediction of severe/critical clinical conditions than the haemoglobin level. Despite a higher value of AUC of ferritin-haemoglobin ratio for the prediction of adverse outcomes in hypertensive patients and all patients, statistical significance was not met.

Discriminative abilities of the ferritin-haemoglobin ratio were compared between hypertensive and non-hypertensive patients. There was no significant difference in AUC representing

Table 7: Comparison of AUCs for discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio for the prediction of severe/critical clinical conditions in patients with COVID-19

Parameter	Hypertensive patients		Non-hypertensive patients		All patients	
	AUCs diff; SE	p-value	AUCs diff; SE	p-value	AUCs diff; SE	p-value
Ferritin vs haemoglobin	0.113; 0.077	0.139	0.197; 0.179	0.269	0.145; 0.076	0.055
Haemoglobin vs FHR	0.125; 0.082	0.125	0.223; 0.172	0.195	0.157; 0.071	0.028
Ferritin vs FHR	0.012; 0.011	0.244	0.026; 0.022	0.235	0.012; 0.009	0.202

AUC: area under the curve; FHR: ferritin-haemoglobin ratio; SE: standard error; diff: difference;

Table 8: Comparison of AUCs for discriminative abilities of ferritin, haemoglobin level and ferritin-haemoglobin ratio for the prediction of death in patients with COVID-19

Parameter	Hypertensive patients		Non-hypertensive patients		All patients	
	AUCs diff; SE	p-value	AUCs diff; SE	p-value	AUCs diff; SE	p-value
Ferritin vs haemoglobin	0.159; 0.169	0.347	0.260; 0.289	0.369	0.047; 0.158	0.768
Haemoglobin vs FHR	0.183; 0.160	0.252	0.317; 0.309	0.304	0.074; 0.150	0.623
Ferritin vs FHR	0.024; 0.028	0.381	0.058; 0.037	0.122	0.027; 0.024	0.262

AUC: area under the curve; FHR: ferritin-haemoglobin ratio; SE: standard error; diff: difference;

discriminative abilities regarding severe/critical conditions (difference, 0.128; p = 0.296). Also, AUC representing discriminative abilities regarding in-hospital mortality was similar in hypertensive and non-hypertensive patients (difference, 0.121; p = 0.663).

Discussion

Presented study showed that an increase in the ferritin-haemoglobin ratio at the moment of hospital admission was associated with a more severe clinical condition during the in-patient stay. Patients with the need for supplemental oxygen during the in-patient stay had a higher ferritin-haemoglobin ratio at admission. Also, deceased patients had a higher ferritin-haemoglobin ratio at admission than survivors.

In this study, the ferritin-haemoglobin ratio showed a weak discriminative ability for the prediction of severe/critical condition in hypertensive patients and all patients, whereas this parameter had an acceptable discriminative ability in non-hypertensive patients. There was an acceptable discriminative ability of the ferritin-haemoglobin ratio for in-hospital mortality prediction in hypertensive patients, but this parameter showed an insufficient discriminative ability for the prediction of in-hospital mortality in non-hypertensive and all patients. This study showed somewhat higher AUCs of ferritin-haemoglobin ratio for the prediction of adverse outcomes in hypertensive patients and all patients, but statistical significance was not met. The optimal cut-off value of the ferritin-haemoglobin ratio for the prediction of severe/critical clinical condition among all patients was 33.98, patients with the ferritin-haemoglobin ratio above this value had higher odds of severe/critical clinical condition. Patients with a ferritin-haemoglobin ratio of > 35.21 had higher in-hospital mortality with Youden index of 0.46. There were no significant differences in AUCs for the ferritin-haemoglobin ratio regarding the prediction of severe/critical condition and in-hospital mortality between hypertensive and non-hypertensive patients.

The predictive ability of the ferritin-haemoglobin ratio is poorly studied nowadays. The study performed by Raman et al showed that the ferritin-haemoglobin ratio was an independent risk factor for mortality (HR: 12.293 [3.147–48.028]) with an optimal cut-off value of 31 (Sensitivity, 85 %; Specificity, 71.6 %),[25] which corresponds to presented findings.

Multiple studies showed that ferritin may be used as a predictor of adverse outcomes in COVID-19 patients. Dahan et al noted that patients with severe COVID-19 had higher levels of ferritin than patients with non-severe disease.[9] According to

the research performed by Alrooms et al, ferritin was found to be an independent predictor of in-hospital mortality.[11] Chicamy et al showed that a ferritin level of 651.02 ng/mL is the optimal cut-off criterion; ferritin levels higher than this value is associated with poor outcome in COVID-19 patients (HR = 8.84, [95 % CI: 3.59–21.73]).[28] Maghfirah et al noted that the cut-off ferritin value for the mild/moderate condition was 153.89 ng/mL and the cut-off ferritin value for mortality was 1145.54 ng/mL.[29] The study conducted by Lino et al showed that ferritin had an AUC of 0.79 ($p < 0.001$) for the cut-off of 1873.0 ng/mL with a sensitivity of 68.4 % and specificity of 79.3 % in predicting in-hospital mortality.[14] The research performed by Deng et al showed that ferritin level at admission may be used as an independent factor for predicting in-hospital mortality in patients with COVID-19 in the intensive care unit; its discriminative capacity with an AUC of 0.822 was higher than one of procalcitonin and C-reactive protein.[30] Shakaroun et al concluded that initial ferritin levels were highly predictive of ICU admission, the need for mechanical ventilation and in-hospital mortality.[13]

Plenty of studies showed that haemoglobin level is another important predictor of severity and mortality in COVID-19 patients. Jha et al concluded that anaemia correlated with COVID-19 severity.[31] According to the research conducted by Tao et al, anaemia was an independent risk factor associated with the severe illness of COVID-19.[32] Zuin et al concluded that anaemia represents a major comorbidity in about 25 % of COVID-19 patients and it is associated with about 70 % higher risk of short-term mortality.[33] The study performed by Dinevari et al showed that anaemia was independently associated with mortality (OR: 1.68; 95 % CI: 1.10–2.57), ventilator requirement (OR: 1.74; 95 % CI: 1.19–2.54) and the risk of intensive care unit admission (OR: 2.06; 95 % CI: 1.46–2.90) in COVID-19 patients.[12]

Presented study showed that the ferritin-haemoglobin ratio had a higher AUC for the discriminative ability for the prediction of severe/critical condition development compared to haemoglobin level. However, the difference in AUCs for the ferritin-haemoglobin ratio and ferritin level was statistically insignificant.

Conclusion

The ferritin-haemoglobin ratio at hospital admission of > 33.98 was a predictor of severe/critical COVID-19 in both hypertensive and non-hypertensive patients. The ferritin-haemoglobin ratio of > 37.64 may be used as a predictor of in-hospital mortality in hypertensive patients. There was no significant difference in the discriminative ability of the ferritin-haemoglobin ratio between hypertensive and non-hypertensive patients.

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Conflict of interest

None.

References

1. Panneer S, Kantamaneni K, Palaniswamy U, Bhat L, Pushparaj RRB, Nayar KR, et al. Health, economic and social development challenges of the COVID-19 pandemic: strategies for multiple and interconnected issues. Healthcare 2022;10(5):770. doi:10.3390/healthcare10050770.
2. WHO. WHO COVID-19 dashboard [Internet]. World Health Organization. 2023. Available from: https://covid19.who.int/ [Accessed 19-Jun-2023].
3. Alimohamadi Y, Tola HH, Abbasi-Ghahramanloo A, Janani M, Sepandi M. Case fatality rate of COVID-19: a systematic review and meta-analysis. J Prev Med Hyg 2021;62(2):E311-E320.
4. Tan LY, Komarasamy TV, Rmt Balasubramaniam V. Hyperinflammatory immune response and COVID-19: a double edged sword. Front Immunol 2021;12:742941. doi:10.3389/fimmu.2021.742941.
5. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. Metallomics 2014;6(4):748-73.
6. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood Rev 2009;23(3):95-104.

7. Bozkurt FT, Tercan M, Patmano G, Bingol Tanrıverdi T, Demir HA, et al. Can ferritin levels predict the severity of illness in patients with COVID-19? Cureus 2021;13(1):e12832. doi:10.7759/cureus.12832.
8. Kaushal K, Kaur H, Sarma P, Bhattacharyya A, Sharma DJ, Prajapat M, et al. Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. J Crit Care 2022;67:172-81.
9. Dahan S, Segal G, Katz I, Hellou T, Tietel M, Bryk G, et al. Ferritin as a marker of severity in COVID-19 patients: a fatal correlation. Isr Med Assoc J 2020;22(8):494-500.
10. Ahmed S, Ansar Ahmed Z, Siddiqui I, Haroon Rashid N, Mansoor M, Jafri L. Evaluation of serum ferritin for prediction of severity and mortality in COVID-19- A cross sectional study. Ann Med Surg (Lond) 2021;63:102163. doi:10.1016/j.amsu.2021.02.009.
11. Alroomi M, Rajan R, Omar AA, Alsaber A, Pan J, Fatemi M, et al. Ferritin level: A predictor of severity and mortality in hospitalized COVID-19 patients. Immun Inflamm Dis 2021;9(4):1648-55.
12. Faghih Dinevari M, Somi MH, Sadeghi Majd E, Abbasalizad Farhangi M, Nikniaz Z. Anemia predicts poor outcomes of COVID-19 in hospitalized patients: a prospective study in Iran. BMC Infect Dis 2021;21(1):170. doi:10.1186/s12879-021-05868-4.
13. Shakaroun DA, Lazar MH, Horowitz JC, Jennings JH. Serum ferritin as a predictor of outcomes in hospitalized patients with Covid-19 pneumonia. J Intensive Care Med 2023;38(1):21-6.
14. Lino K, Guimarães GMC, Alves LS, Oliveira AC, Faustino R, Fernandes CS, et al. Serum ferritin at admission in hospitalized COVID-19 patients as a predictor of mortality. Braz J Infect Dis 2021;25(2):101569. doi:10.1016/j.bjid.2021.101569.
15. Hafeez L, Puri S, Chahabra S, Patel N, Singal KK, Thakr N. Association between serum ferritin levels and elevated blood pressures: A case control study. Eur J Mol Clin Med 2022;9(2):78-81.
16. Singh H, Kaur M, Bedi GK, Sibia RPS, Kaur D. Evaluation of serum ferritin levels in patients of hypertension. Int J Clin Biochem Res 2020;7(3):317-9.
17. Lippi G, Mattiuzzi C. Hemoglobin value may be decreased in patients with severe coronavirus disease 2019. Hematol Transfus Cell Ther 2020;42(2):116-7.
18. Chen C, Zhou W, Fan W, Ning X, Yang S, Lei Z, et al. Association of anemia and COVID-19 in hospitalized patients. Future Virol 2021:10.2217/fvl-2021-0044. doi:10.2217/fvl-2021-0044.
19. Anai M, Akaike K, Iwagoe H, Akasaka T, Higuchi T, Miyazaki A, et al. Decrease in hemoglobin level predicts increased risk for severe respiratory failure in COVID-19 patients with pneumonia. Respir Investig 2021;59(2):187-93.
20. Ghosh T, Rehman T, Ahamed F. Relationship between hemoglobin and blood pressure levels in the context of chronic morbidity among older adults residing in a developing country: a community-level comparative cross-sectional study. Cureus 2021;13(11):e19540. doi:10.7759/cureus.19540.
21. Atsma F, Veldhuizen I, de Kort W, van Kraaij M, Pasker-de Jong P, Deinum J. Hemoglobin level is positively associated with blood pressure in a large cohort of healthy individuals. Hypertension 2012;60(4):936-41.
22. Lee SG, Rim JH, Kim JH. Association of hemoglobin levels with blood pressure and hypertension in a large population-based study: the Korea National Health and Nutrition Examination Surveys 2008-2011. Clin Chim Acta 2015;438:12-8.
23. Kronstein-Wiedemann R, Stadtmüller M, Traikov S, Georgi M, Teichert M, Yosef H, et al. SARS-CoV-2 infects red blood cell progenitors and dysregulates hemoglobin and iron metabolism. Stem Cell Rev Rep 2022;18(5):1809-21.
24. Lee S, Jeon H, Shim B. Prognostic value of ferritin-to-hemoglobin ratio in patients with advanced non-small-cell lung cancer. J Cancer 2019;10(7):1717-25.
25. Raman N, Kv P, Ashta KK, Vardhan V, Thareja S, J M, et al. Ferritin and hemoglobin as predictors of fatal outcome in covid-19: two sides of the same coin. J Assoc Physicians India 2021;69(8):11-2.
26. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021–104.
27. Ministerstvo Okhorony Zdorovia Ukrainy. Derzhavnyi Ekspertnyi Tsentr [Internet]. Protokol «Nadannia medychnoi dopomohy dlia likuvannia koronavirusnoi khvoroby (COVID-19)» [cited 20-Jun-2023]. Available from: https://www.dec.gov.ua/wp-content/uploads/2023/05/protokol-covid2023.pdf. Ukrainian.
28. Chicamy YA, Safitri A, Nindrea RD. Serum ferritin levels for the prediction of mortality among COVID-19 patients in an Indonesia's national referral hospital. OAMJMS 2022;10(B):1056–61.
29. Maghfirah AI, Widaningsih Y, Bahrun U. Correlation of serum ferritin levels and COVID-19 severity in Makassar. JMBI 2022;4(1):1-5.
30. Deng F, Zhang L, Lyu L, Lu Z, Gao D, Ma X, et al. Increased levels of ferritin on admission predicts intensive care unit mortality in patients with COVID-19. Med Clin (Barc) 2021;156(7):324-31.
31. Jha M, Tak ML, Gupta R, Sharma P, Rajpurohit V, Mathur P, Gaur N. Relationship of anemia with COVID-19 deaths: A retrospective cross-sectional study. J Anaesthesiol Clin Pharmacol 2022;38(Suppl 1):S115-S119.
32. Tao Z, Xu J, Chen W, Yang Z, Xu X, Liu L, et al. Anemia is associated with severe illness in COVID-19: A retrospective cohort study. J Med Virol 2021;93(3):1478-88.