Original Research Article

Evaluating laboratory parameters for diagnostic accuracy in COVID-19 patients in a tertiary care Government Hospital in Greater Noida, UP, India

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Received: 11-07-2021 / Revised: 07-08-2021 / Accepted: 15-10-2021

Abstract

Introduction: The occurrence, development, mechanism of prognosis and immune status of patients with COVID-19 are still unclear. Timely identification of virus carriers is vital not only to prevent their spread but also to more efficiently control disease progression. **Objective**: In this study, we have assessed the hematological characteristics of the patients. This study aimed to evaluate the accuracy of laboratory parameters in predicting cases with positive RT-PCR for COVID-19. **Material and Methods**: This was a cross sectional study that included 67 RTPCR +ve and 69 RTPCR -ve cases over a period of 5 weeks. The blood samples were collected from symptomatic patients presented to the cough OPD of the hospital and undergoing RT-PCR testing for Covid-19 between 9am to 4 pm on consecutive working days till the sample size requirement was met. On the day of swab sampling, blood sampling was done for each participant included in our study as mentioned in the sampling method above. All tests were performed in an appropriate autoanalyser after complying internal quality control. **Results:** The mean age of patients included in this study was 34.1 (24.05) years. The mean CT value among RTPCR positive patients was 22.7 (SD 4.99) with mean(SD) values of PCT, ferritin, D-dimer, LDH and CRP was 1.30 (SD 2.52), 197.2 (SD 284.40), 1.7 (SD 2.08), 353.5 (SD 186.43) 20.5 (SD 37.58) respectively . On the other hand the mean(SD) value of PCT, ferritin, D-dimer, LDH and CRP was 0.045 (SD 0.073), 84.6 (SD 137.51), 1.1 (SD 1.70), 328.5 (SD 99.84) and 5.7 (SD 16.67) respectively in the RTPCR negative patients. The sensitivity and specificity for procalcitonin analysis among these patients were 97% with CI (93.8-100) followed by serum ferritin with 82%, CI (70-94) and CRP levels were having just 77.3%, CI (61.2-93.4). **Conclusion:** In the current study, the AUC of procalcitonin and serum ferritin were above 0.80; thus, they are effective markers and have very good predictive value for predicting COVID-19. The mean values in the RTPCR positive patients were significantly high for the biochemical markers namely procalcitonin, ferritin and CRP whereas the mean levels of total protein and albumin were significantly lower among RTPCR positive patients compared to RTPCR negative patients. It seems that these blood laboratory parameters could be used in screening cases with positive RT-PCR for COVID-19. However, serum LDH, D Dimer, and vitamin D3 levels or liver function tests, renal function tests remain insignificantly linked with covid-19 positivity rate in this study.

Keywords: COVID-19, serum LDH, Procalcitonin, RT-PCR.

Introduction

In the early stages of covid-19disease, symptoms of severe acute respiratory infection occur, with some patients rapidly developing acute respiratory distress syndrome (ARDS) and other serious complications, which are eventually followed by multiple organ failure[1].

Therefore, early diagnosis and timely treatment of critical cases is very crucial. At present, the occurrence, development, mechanism of prognosis and immune status of patients with COVID-19 are still unclear. Timely identification of virus carriers is vital not only to prevent their spread but also to more efficiently control disease progression. To the best of our knowledge, while most published articles have discussed the clinical features and imaging findings of COVID-19, few studies have addressed the diagnostic and prognostic value of abnormal laboratory findings [2]. Irrespective of its inherent definition[3], the contributory role of laboratory medicine is far beyond etiological detection and it is now almost undeniable that this branch of medical science is effectively involved in epidemiologic

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surveillance, determination of prognosis, patient follow-up, and, last but not least, therapeutic monitoring of a wide range of human diseases, including COVID-19[4,5].

In this study, we have assessed the hematological characteristics of the patients. The role of clinical laboratory data in the differential diagnosis of severe forms of COVID-19 has not been definitely established. This study aimed to evaluate the accuracy of laboratory parameters in predicting cases with positive RT-PCR for COVID-19.

Material and Methods

This was a cross sectional study that included 67 RTPCR +ve and 69 RTPCR -ve cases over a period of 5 weeks. The blood samples were collected from symptomatic patients presented to the cough OPD of GIMS, Greater Noida and undergoing RT-PCR testing for Covid-19 between 9 am to 4 pm on consecutive working days till the sample size requirement for RT-PCR negative patients was met. Any positive patient was included in the RTPCR +ve group during screening. Sampling of RT-PCR positive patients was done on the day of new admissions to the isolation ward of GIMS, Greater Noida to meet the required number of RTPCR +ve patients. On the day of swab sampling, blood sampling was done for each participant included in our study as mentioned in the sampling method above. About 2 ml of venous Blood was collected in EDTA vial for CBC estimation and 2 ml of blood was collected in citrate vial for doing D-dimer. For Biochemical analysis, 3 ml of blood was collected in plain vial. All tests were performed in an appropriate autoanalyser after complying with internal quality control. Test results were received from the lab for research purpose and all enrolled patients were provided with the reports. This study was approved by the institutional ethics committee with reference no. …….

The data were collected and collated in Microsoft Excel sheet. Data were presented as frequencies and percentages for qualitative and categorical variables. Mean with standard deviation or median with interquartile range was reported for continuous variables depending upon their distribution type. Appropriate statistical tests were applied for identifying significant statistical difference in the distribution of variables included in our study.

Differences in the blood laboratory parametrers levels between the RT-PCR positive and negative patients were assessed using Student's t-test. Receiver operating characteristic (ROC) curve and AUC were used to analyze the optimal cut-off for prediction of positive RT-PCR cases. In this study, AUC 0.9 to 1 is defined as excellent accuracy, 0.8 to 0.9 as very good, 0.7 to 0.8 as good, 0.6 to 0.7 as sufficient, 0.5 to 0.6 as bad, and < 0.5 as poor (useless test). All statistical analyses were carried out at 5% level of significance and p-value 0.05 was considered significant.

Results

The mean age of patients included in our study was 34.1 (24.05) years with 33.1 (SD 32.05) in RTPCR negative patient and 35.1 (SD 11.40) in RTPCR positive patients. The frequency of male versus female patient included in this study were 60:40 while percentage of male and female patients who were RTPCR positive were 28% and 21% respectively. The mean CT value among RTPCR positive patients was 22.7 (SD 4.99) with mean(SD) values of PCT, ferritin, D-dimer, LDH and CRP was 1.30 (SD 2.52), 197.2 (SD 284.40), 1.7 (SD 2.08), 353.5 (SD 186.43) 20.5 (SD 37.58) respectively . On the other hand the mean(SD) value of PCT, ferritin, D-dimer, LDH and CRP was 0.045 (SD 0.073), 84.6 (SD 137.51), 1.1 (SD 1.70), 328.5 (SD 99.84) and 5.7 (SD 16.67) respectively in the RTPCR negative patients. The mean values in the RTPCR positive patients were significantly high for the biochemical markers namely procalcitonin, ferritin and CRP whereas the mean levels of total protein and albumin were significantly lower among RTPCR positive patients compared to RTPCR negative patients. (Table 1).

The sensitivity and specificity for procalcitonin was 97% with CI (93.8-100) followed by serum ferritin with 82%, CI (70-94) and CRP levels with 77.3%, CI (61.2-93.4). However, LDH, D Dimer, and vitamin D3 levels or Liver function tests, Renal function tests remain insignificantly linked with covid positivity rate among this cohort. (table 2,2 and fig.2,2)

Table 1: Comparison of biochemical parameters between RTPCR negative and RTPCR positive study participants

	RTPCR -ve			RTPCR +ve			
Variable	N	Mean	Std. Deviation	N	Mean	Std. Deviation	P value
Age	68	33.1	32.05	67	35.1	11.40	0.63
T. Bilirubin	69	0.6	0.34	67	1.3	5.44	0.31
D. Bilirubin	69	0.5	0.89	67	0.4	0.24	0.09
I. Bilirubin	69	0.1	0.83	67	0.9	5.44	0.20
ALT	69	46.2	37.86	67	50.2	46.14	0.58
AST	69	36.5	26.85	67	46.5	40.20	0.09
ALP	68	205.8	56.46	67	244.7	175.48	0.08
Total Protein	69	7.6	0.46	67	7.1	0.65	**<0.01**
Albumin	69	4.6	0.42	67	4.4	0.53	**<0.01**
Creatinine	69	1.1	0.19	67	1.1	0.45	0.40
Urea	69	23.6	6.50	67	26.7	11.90	0.07
Uric acid	69	5.5	1.88	67	5.5	2.44	0.98
Procalcitonin (PCT)	67	0.045	0.07	17	1.29	2.52	**<0.01**
Ferritin	69	84.6	137.51	53	197.2	284.36	**<0.01**
Vit D3	69	18.8	12.39	61	20.9	14.97	0.36
D-Dimer	58	1.1	1.70	37	1.7	2.08	0.14
LDH	69	328.5	99.84	62	353.5	186.43	0.33
CRP	69	5.7	16.67	61	20.5	37.58	**<0.01**

Table 2: Table showing area under curve of selected biochemical lab parameters

Area Under the Curve					
Test Result Variable(s)	**Area**	**Std. Error**	**P value**	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
Ferritin	**0.820**	0.061	<0.001	0.700	0.940
LDH	0.624	0.113	0.174	0.402	0.846
PCT	**0.971**	0.017	0.000	0.938	1.000
CRP	0.773	0.082	0.003	0.612	0.934
Vit D3	0.521	0.105	0.816	0.315	0.728

Table 3: showing area under curves of different liver function test parameters

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error	P value	95% Confidence Interval	
				Lower Bound	Upper Bound
T. BIL	0.514	0.050	0.785	0.415	0.612
D. BIL	0.359	0.047	0.005	0.266	0.452
I. Bil	0.714	0.045	<0.001	0.625	0.802
ALT	0.502	0.050	0.972	0.403	0.600
AST	0.544	0.050	0.376	0.446	0.642
ALP	0.505	0.051	0.925	0.404	0.605
Total protein	0.265	0.043	0.000	0.180	0.350
Albumin	0.312	0.047	0.000	0.221	0.403

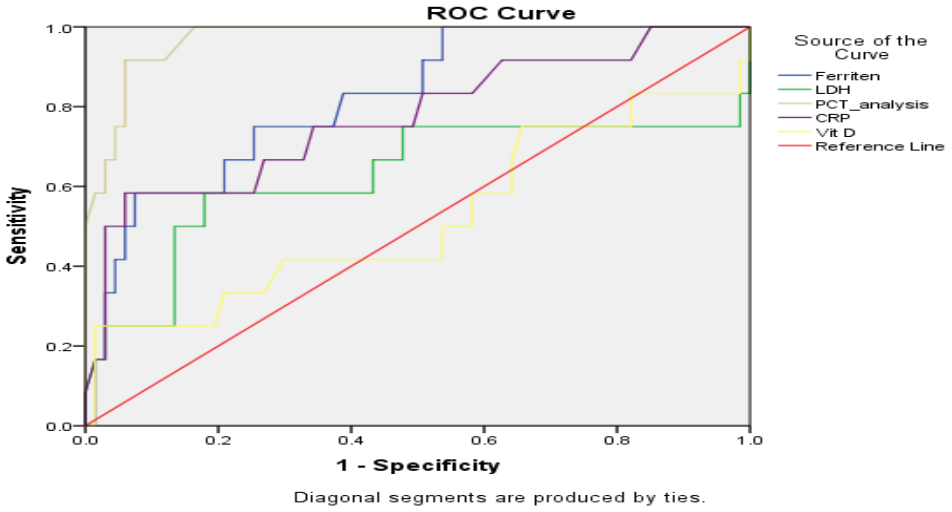

Fig 1: ROC curves showing sensitivity and specificity of different inflammatory laboratory parameters

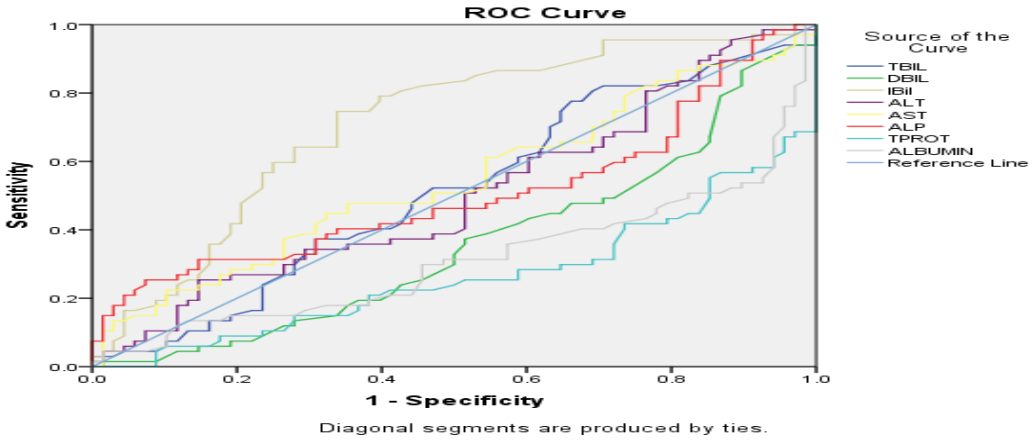

Fig.2: ROC curves showing sensitivity and specificity of liver function parameters

On correlation regression analysis, we observed that CT values of RT-PCR test were found to be negatively correlated with D-Dimer values. PCT analysis were correlated with ferritin, CRP and LDH. Ferritin values were correlated with PCT, LDH, and CRP. D-dimer were correlated only with CT values in negative manner. LDH levels were correlated with PCT, CRP and ferritin values. CRP levels were correlated with PCT, ferritin and LDH levels. vitamin D3 levels were not found to be correlated with any inflammatory markers in this study. (Table 3)

Table 4: Correlation analysis of selected biochemical lab parameters

		CTValue	Procalcitonoin (PCT)	Ferritin	Vit D3	D-Dimer	LDH	CRP
CT Value	Pearson Correlation	1	0.185	0.145	.038	-0.439*	0.108	0.179
	P value		0.610	0.359	.801	0.019	0.476	0.235
	N	50	10	42	46	28	46	46
Procalcitonin (PCT)	Pearson Correlation	0.185	1	0.243*	-.141	0.023	0.776**	0.621**
	P value	0.610		0.031	.203	0.853	<0.001	<0.001
	N	10	84	79	83	65	83	83
Ferritin	Pearson Correlation	0.145	.243*	1	-.115	0.104	0.296**	0.253**
	P value	0.359	0.031		.206	0.317	0.001	0.005
	N	42	79	122	122	95	122	122
Vit D3	Pearson Correlation	0.038	-0.141	-0.115	1	0.028	-0.017	0.073
	P value	0.801	0.203	0.206		0.785	0.852	0.414
	N	46	83	122	130	95	130	129
D-Dimer	Pearson Correlation	-0.439*	0.023	0.104	.028	1	0.156	0.118
	P value	0.019	0.853	0.317	.785		0.130	0.254
	N	28	65	95	95	95	95	95
LDH	Pearson Correlation	0.108	0.776**	0.296**	-.017	0.156	1	0.663**
	P value	0.476	<0.001	0.001	.852	0.130		0.000
	N	46	83	122	130	95	131	130
CRP	Pearson Correlation	0.179	0.621**	0.253**	.073	0.118	0.663**	1
	P value	0.235	<0.001	0.005	.414	0.254	<0.001	
	N	46	83	122	129	95	130	130

*. Correlation is significant at the 0.05 level (2-tailed), **. Correlation is significant at the 0.01 level (2-tailed).

Discussion

Fan et al.[6] analyzed the hematological indices of COVID-19 infected patients between the intensive care unit (ICU) and non-ICU patients. They showed lymphopenia and raised lactate de-hydrogenase (LDH) were associated with higher rate of ICU admissions. Many patients with MERS-CoV had liver function abnormalities with elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), and LDH [7]. Also laboratory data on SARS have shown that most patients had elevated CRP levels, lymphopenia, leukopenia, and elevated levels of aminotransferase, LDH and creatine kinase[8]. A series of recently published articles have reported the epidemiological and clinical characteristics of patients with COVID-19 disease, but data regarding the laboratory characteristics of infected individuals are limited[9-11].

Chen et al., found that LDH had significantly increased in most patients, while albumin had decreased, but ALT and AST showed no significant changes[1]. The mentioned values were also reported for patients with MERS-CoV, where elevated ALT, AST and LDH was observed. Another study indicated that 2–11% of patients with COVID-19 had liver comorbidities and 14–53% of cases had abnormal ALT and AST levels during progression of COVID-19 disease[12]. Furthermore, Shi et al. studied patients whose COVID-19 diagnosis was confirmed by computed tomography (CT) scan while in the subclinical phase and found that incidence of AST abnormality among these patients was significantly lower than those diagnosed after the onset of symptoms[13]. Therefore, liver injury is more prevalent in severe cases compared to mild cases of COVID-19. In another report, Yang et al. found no difference in the incidence of abnormal liver function between survivors (30%) and non-survivors (28%)[9]. Liver damage in mild cases of COVID-19 is often transient and can return to normal without any special treatment[12].

In the present study, ROC curve was used to analyze the specificity and sensitivity of different variables in suspected COVID-19 patients. The AUC of laboratory parameters such as ALT, CRP, AST, LDH, and D dimer indicated that they could not be used to predict the presence of COVID-19 disease, while those of ferritin and procalcitonin were above the reference line of ROC curve, indicating that they were good predictors of the disease. The data in contrast with results reported by Wang et al.[14] and Gao et al.[5]. In the current study, the AUC of CRP, ALT, LDH, were below 0.80; thus, they are not effective and have poor predictive value for predicting COVID-19. It seems that, some blood laboratory parameters could be used in screening cases with positive RT-PCR for COVID-19.

It has also been reported that some COVID-19 patients have increased prothrombin time (PT) together with prolonged activated partial thromboplastin time (aPTT). Adding to these abnormalities, elevated D-dimers further support the occurrence of coagulopathy which is an important indicator of disease progression. It was previously established that inflammation-related parameters are highly elevated in acute phases. COVID-19 makes no exception to this rule, whereby the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin are increased in the sera of these patients, albeit with different values. It is worth mentioning that while the diagnostic value of ferritin and procalcitonin is superior to CRP, the latter may potentially be of greater value than the former for predicting disease progression. Li et al. detected ferritin levels above the upper limit of the reference range in 49 out of 54 (90.7%) COVID-19 patients and showed that the ferritin levels decreased as hs-CRP decreased, but they were significantly higher than the upper reference range for at least 5 days after hs-CRP returned to normal[15]. Previous studies have shown that soluble CD-163 (sCD-163), which represents the activation of macrophages, increases parallel to ferritin during the acute inflammation stage [16], suggesting that ferritin measurement may provide diagnostic value and can be used for diagnostic purposes in COVID-19[17,18].

As presented, increased levels of lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (Bil) and decreased levels of albumin are among the most common abnormal laboratory findings in COVID-19 patients. Changes were not limited to the indicated parameters since elevated creatine kinase (CK) and increased creatinine (Cr) were also demonstrated in earlier studies. Knowing that the primary site of the SARS-CoV-2 attack is the lower respiratory tract together with the fact that LDH is an important marker of lung damage (19) may explain, at least partly, why this enzyme's level is elevated in most COVID-19 patients[20-22]. The emergence of severe disease due to the injury of non-pulmonary organs may also instigate abnormal values of kidney- and liver-related biochemical parameters. Guan et.

al. reported that ALT and AST levels in COVID-19 patients were elevated in 21.3% and 22.2% of cases, respectively[23], which may mirror virus-mediated liver impairment. The results of a recent study also revealed that 2–11% of COVID-19 patients had liver comorbidities and 14–53% had abnormal levels of ALT and AST[24]. Analysis of creatinine in 149 cases demonstrated that 28.8% of COVID-19 patients had an increased levels, representing SARS-CoV-2's ability to induce kidney injury[25].

The prognostic significance of laboratory tests is not limited to the valuable data represented by simple CBC examinations, as increased PT and D-dimer values may be indicative of a worse prognosis[20]. Tang et al. reported a significant difference in the occurrence rate of coagulopathy in terms of disseminated intravascular coagulation (DIC) between COVID-19 patients who died of the disease compared to those who survived (71.4% vs 0.6%)[26].In a study reporting the results of 13 severe of 140 COVID-19 patients, increased procalcitonin values were 25% vs 0% in ICU patients compared to non-ICU patients, respectively[20]. A study by Zhang et al. on 140 COVID-19 patients, including 58 severe cases, further supported the previous data. They reported that increased levels of D-dimer along with elevated procalcitonin and CRP levels could help clinicians effectively discriminate between severe and non-severe COVID-19 cases [27]. Taken together, t PT and D-dimer values coupled with follow-up of altered patterns of procalcitonin and CRP levels may provide a simple and rapid method of predicting disease prognosis.Notably, it has been reported that hyperferritinemia can activate macrophages [28,29], which increases the secretion of pro-inflammatory cytokines, and the subsequent inflammation is mainly responsible for organ damage. Although ferritin is a positive acute phase reactant and serum level of this intracellular protein increases during inflammation, dying cells may also release ferritin. Thus, it is reasonable to assume that higher serum ferritin levels in severely affected COVID-19 patients might indicate a greater extent of organ damage.Liu et al. also reported that albumin was significantly lower in a progression group than an improvement/stabilization group (36.62 vs 41.27 g/l, P = 0.006)[30]. In agreement, Huang et al. introduced decreased albumin along with increased LDH, ALT, and total bilirubin levels as appropriate biomarkers with the ability to discriminate between severe and non-severe groups[20]. In a large cohort of 1099 patients from 552 hospitals, Guan et al. reported a higher degree of abnormal liver aminotransferase levels in patients with severe disease than non-severe subjects[23].

Although lab diagnostics efficiently contribute to the early identification of SARS-CoV-2 infection, there is evidence that laboratory medicine may also provide essential assistance to discriminate between severe and non-severe COVID-19. The large variations in the clinical features of the disease, spanning from asymptomatic to fatal, necessitates the identification and application of novel laboratory biomarkers to rapidly and economically predict COVID-19 prognosis[31].

Conclusion

In the current study, the AUC of procalcitonin and serum ferritin were above 0.80; thus, they are effective and have very good predictive value for predicting COVID-19. It seems that, these blood laboratory parameters could be used in screening cases with positive RT-PCR for COVID-19. However, serum LDH, D-Dimer, and vitamin D3 levels or liver function tests, renal function tests remain insignificantly linked with covid positivity rate in this study.

Considering the significant findings in laboratory parameters evaluated in this study, one can hope to model or predict the results of coronavirus testing based on routine laboratory tests. Based on the findings of this study serum procalcitonin and serum ferritin have very good accuracy in predicting cases with positive RT-PCR for COVID-19. However, serum LDH, D Dimer, and vitamin D3 levels, liver function tests, renal function tests remain insignificantly linked with covid positivity rate among this cohort.

References

1. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395(10223):507-513.
2. Lippi G., Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin. Chem. Lab. Med. (CCLM) 2020;1(ahead-of-print)
3. Lippi G., Plebani M. A modern and pragmatic definition of Laboratory Medicine. Clin. Chem. Lab. Med. (CCLM) 2020;1(ahead-of-print)
4. Lippi G., Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin. Chem. Lab. Med. CCLM. 2020;1(ahead-of-print)
5. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic Utility of Clinical Laboratory Data Determinations for Patients with the Severe COVID-19. Journal of Medical Virology. 2020.
6. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE,Tan GB, et al. Hematologic parameters in patients with COVIDâ ˇA˘R19 infection. American Journal of Hematology.
7. Al Ghamdi M, Alghamdi KM, Ghandoora Y, Alzahrani A,Salah F, Alsulami A, et al. Treatment outcomes for patients with Middle Eastern Respiratory Syndrome Coronavirus (MERS CoV) infection at a coronavirus referral center in the Kingdom of Saudi Arabia. BMC infectious diseases. 2016;16(1):174.
8. Wang J-T, Sheng W-H, Fang C-T, Chen Y-C, Wang J-L,Yu C-J, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. Emerging infectious diseases. 2004;10(5):818.
9. Rodriguez-Morales AJ, Cardona-Ospina JA, GutiÃl'rrez-OcampoE,Villamizar-PenaR,Holguin-RiveraY,Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Medicine and Infectious Disease.2020:101623.
10. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020.
11. Kui L, Fang Y-Y, Deng Y, Liu W, Wang M-F, Ma J-P, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chinese medical journal. 2020.
12. Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: management and challenges. The Lancet Gastroenterology &Hepatology. 2020.
13. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. The Lancet Infectious Diseases. 2020.
14. Wang Y, Liu Y, Liu L, Wang X, Luo N, Ling L. Clinical outcome of 55 asymptomatic cases at the time of hospi-tal admission infected with SARS-Coronavirus-2 in Shen-zhen, China. The Journal of Infectious Diseases. 2020.
15. Li Y., Hu Y., Yu J., Ma T. Retrospective analysis of laboratory testing in 54 patients with severe-or critical-type 2019 novel coronavirus pneumonia. Lab. Invest. 2019;2020:1–7.
16. Colafrancesco S., Priori R., Alessandri C., Astorri E., Perricone C., Blank M., Agmon-Levin N., Shoenfeld Y., Valesini G. sCD163 in AOSD: a biomarker for macrophage activation related to hyperferritinemia. Immunol. Res. 2014;60(2–3):177–183.
17. Shoenfeld Y. Corona (COVID-19) time musings: Our involvement in COVID-19 pathogenesis, diagnosis, treatment and vaccine planning. Autoimmun. Rev. 2020

18. Bataille S., Pedinielli N., Bergougnioux J.-P. Could ferritin help the screening for COVID-19 in hemodialysis patients? Kidney Int. 2020.
19. Jurisic V., Radenkovic S., Konjevic G. The actual role of LDH as tumor marker, biochemical and clinical aspects. Adv. Cancer Biomarkers Springer. 2015:115–124.
20. Huang C., Wang Y., Li X., Ren L., Zhao J., Hu Y., Zhang L., Fan G., Xu J., Gu X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497–506.
21. Liu Y., Yang Y., Zhang C., Huang F., Wang F., Yuan J., Wang Z., Li J., Li J., Feng C. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci. China Life Sci. 2020;63(3):364–374.
22. Zhou F., Yu T., Du R., Fan G., Liu Y., Liu Z., Xiang J., Wang Y., Song B., Gu X. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020
23. Guan W.-J., Ni Z.-Y., Hu Y., Liang W.-H., Ou C.-Q., He J.-X., Liu L., Shan H., Lei C.-L., Hui D.S. Clinical characteristics of coronavirus disease 2019 in China. N. Engl. J. Med. 2020
24. Zhang C., Shi L., Wang F.-S. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol. Hepatol. 2020.
25. Yang W., Cao Q., Qin L., Wang X., Cheng Z., Pan A., Dai J., Sun Q., Zhao F., Qu J. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang. J. Infect. China. 2020.
26. Tang N., Li D., Wang X., Sun Z. Abnormal Coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J. Thromb. Haemost. 2020.
27. Zhang J.-J., Dong X., Cao Y.-Y., Yuan Y.-D., Yang Y.-B., Yan Y.-Q., Akdis C.A., Gao Y.-D. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020.
28. Kernan K.F., Carcillo J.A. Hyperferritinemia and inflammation. Int. Immunol. 2017;29(9):401–409.
29. R. Piero, B. Onorina, C. Paolo, I. Annamaria, S. Yehuda, Severe hyper-inflammatory COVID-19, another piece in the puzzle of the“ htperferritinemic syndrome, Rheumatol Point View (2020).
30. Liu W., Tao Z.-W., Lei W., Ming-Li Y., Kui L., Ling Z., Shuang W., Yan D., Jing L., Liu H.-G. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Med. J. Chin. 2019:2020.
31. Pourbagheri-Sigaroodi A, Bashash D, Fateh F, Abolghasemi H. Laboratory findings in COVID-19 diagnosis and prognosis. Clin Chim Acta. 2020;510:475-482.

Conflict of Interest: Nil Source of support: Nil