Original Article

Clinical, Hematological And Inflammatory Markers Profile In COVID-19 Patients At Tertiary Care Centre

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Abstract

Background: The ongoing pandemic of severe acute respiratory syndrome by coronavirus-2 (SARS-CoV-2) continues to pose several diagnostic and therapeutic challenges. Assessing clinical, demographic, biochemical, haematological and inflammatory parameters have thus become important for investigating the COVID-19 cases.

Materials and Methods: A total of 505 Covid-19 positive cases were included in this study to compare their haematological, biochemical and inflammatory parameters among mild, moderate and severe cases who were categorized as per ICMR guidelines and Institute guidelines.

Results: In our study 54% patients belonged to >50 years of age group. Different Haematological values were studied for statistical significance where White blood cell count (WBC), Neutrophil count, Neutrophil lymphocyte ratio (NLR), Absolute neutrophil count (ANC), Lymphocyte count and Absolute lymphocyte count (ALC) showed statistical significance with p value <0.05. Among inflammatory markers C-reactive protein (CRP), coagulative marker D-Dimer and biochemical parameters such as S.Ferritin and lactate dehydrogenase (LDH) levels showed statistical significance with p value <0.05.There was no significant change in the Hemoglobin, Monocyte, Absolute monocyte count (AMC), Lymphocyte monocyte ratio (LMR) and platelet count.

Conclusion: According to the findings of our study, WBC, neutrophil, lymphocyte, neutrophil lymphocyte ratio, CRP, D-dimer, LDH and serum ferritin played an essential part in risk stratification models that serves as clinical predictors of severity in COVID-19 patients.

Keywords: Biomarkers, Covid-19, CRP, NLR, WBC.

Introduction

Coronaviruses (CoV's) are large group of viruses belonging to the Coronaviridae family with a single-stranded RNA genome [1]. The ongoing pandemic of severe acute respiratory syndrome caused by coronavirus-2 (SARS-CoV-2) continues to pose several diagnostic and therapeutic challenges [2]. First reported case was from Wuhan, China in December 2019. The World Health Organization on February 11, 2020 officially named this infection as coronavirus disease 2019 (COVID-19) and the virus as SARS CoV-2. It was declared as a pandemic on March 11, 2020.

As of April 2022, there have been approximately more than 510 million cases worldwide with more than 6.25 million reported deaths. In India more than 43 million cases have been reported with the death tally crossing over 520,000 [3]. In India, the first case was reported on 30 January 2020 in Kerala [4].

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Access this article online

Quick Response Code:

Website: www.pnrjournal.com

DOI: 10.47750/pnr.2022.13.03.131

How to cite this article: Swathi M, Eswari V, Sumanth Kumar B, Clinical, Hematological And Inflammatory Markers Profile In COVID-19 Patients At Tertiary Care Centre, J PHARM NEGATIVE RESULTS 2022;13: 875-882.

COVID-19 infection is accompanied by an aggressive inflammatory response with the release of large amounts of pro-inflammatory cytokines in an event known as "cytokine storm."[5] Several studies analysing cytokine profiles from COVID-19 patients suggest that the cytokine storm is directly related to lung injury, multi-organ failure, and unfavourable prognosis [6,7].

In SARS-CoV-2 viral infections, haematological, biochemical and inflammatory parameters often change which helps in monitoring the infectious process and also indicates the degree of its severity[8,9].The parameters include neutrophil count, NLR, S.Ferritin, lymphocyte count, platelet counts, Hemoglobin level, D-dimer status, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Cytokines, blood glucose, gamma-glutamyl transferase (GGT) and lactate dehydrogenase levels(LDH) [8,9].The aim and objective of the present study is to review the Case files of 505 COVID-19 positive patients and compare their haematological, biochemical and inflammatory parameters among Covid-19 patients and also with the degree of severity conducted at tertiary care centre, Kanchipuram, Tamilnadu.

MATERIALS AND METHODS:

This retrospective study was approved by Institutional ethical committee (66A/Path/IEC/2021) conducted for a period of 6 months starting from March 2021 till August 2021 in the clinical pathology and biochemistry lab at tertiary care centre, Kanchipuram, Tamilnadu. A total of 505 Covid-19 positive cases along with pre-existing comorbidities were included in this study to compare their haematological, biochemical and inflammatory parameters and to compare with the severity of the disease.The severity was classified as mild, moderate, and severe as per Indian Council of Medical Research (ICMR) and Institutional guidelines [12]. All the records of these patients were extracted and a detailed review was done for demographic details, clinical, hematological, biochemical and inflammatory parameters.

Statistical analysis:

Data was collected and tabulated in a Microsoft excel spreadsheet. Data was compared and analysed for statistical significance. P values < 0.05 is considered significant. The results are expressed in Mean ± Standard Deviation (S.D.) Descriptive analysis was carried for quantitative variables, frequency and proportion for categorical variables. Data's were represented using appropriate diagrams like bar diagram, pie diagram and box plots. The mean differences along with their 95% confidence intervals (CI) was presented. One way ANNOVA test was used to assess statistical significance by using IBM SPSS version 22.

RESULTS:

Out of 505 Covid-19 positive cases, 329 (65%) were males and 176 (35%) were females. The majority of the patients were over the age of 50 years (271 patients). In terms of clinical features, all patients presented with fever and 457 patients (90%) experienced loss of taste and smell. Fatigue was present in 393patients (78%), while breathlessness and cough were present in 169patients (33%). Among the comorbidities, Diabetes mellitus (DM) and Hypertension (HTN) were found in 363patients (72%) and 360 patients (71%), respectively. Dyslipidaemia was observed in 155patients (30.8%). The mortality rate was10% (48patients).In terms of disease severity, 257patients (51%) fell into the mild category, 185 patients (37%) into the moderate category, and 63patients (12%) into the severe category (Table 1).

Table 1: Distribution of demographic and clinical features of study group

N=505	Value/N& (%)	Mean±SD	Min-Max	95% CI
Gender				
Male	329 (65%)	-	-	-
Female	176 (35%)			
Age				
<=20	5 (1%)			
21-30	33 (7%)	52.02±14.66	19-69	50-54
31-40	84 (17%)			
41-50	112 (22%)			
>50	271 (53%)			

Clinical feature				
Fever	505 (100%)			
Breathlessness	169 (33%)	-	-	-
Cough	169 (33%)			
Loss of taste/smell	457 (90%)			
Fatigue	393 (78%)			
Acute gastroenteritis	4 (1%)			
Comorbidities				
Diabetes mellitus	363 (72%)			
Hypertension	360 (71%)			
COPD	26 (5%)	-	-	-
Cardiovascular diseases	37 (7%)			
Dyslipidaemia	155 (30.8%)			
Carcinoma	1 (0.2%)			
Mortality	48 (10%)	-	-	-
Respiratory rate				
12-23	257 (51%)			
24-29	185(37%)	22.06±6.28	2-39	21-22
≥30	63(12%)			
SPO_2				
>=90%	442 (88%)	91.73±5.5	70-97	92-94
<90%	63(12%)			
Severity				
Mild	257 (51%)	-	-	-
Moderate	185 (37%)			
Severe	63 (12%)			

In terms of haematological parameters, White blood cell count (WBC) (p value-0.0184), Neutrophil count (p value <0.0001), Neutrophil lymphocyte ratio (NLR) (p value <0.0001) and Absolute neutrophil count (ANC) (p value 0.0014) were raised significantly with the severity of disease. Lymphocyte count (p value <0.0001) and Absolute lymphocyte count (ALC) (p value 0.0328) was significantly reduced in severe cases. There was no significant changes in Haemoglobin (p value 0.121), Monocyte (p value 0.2798), Absolute monocyte count (AMC) (p value 0.6544), Lymphocyte monocyte ratio (LMR) (p value 0.1187) and Platelet count (p value 0.13) (Table 2).

Table 2: Comparison of Hematological parameters between severity groups

Haematological markers	Severity	Mean	SD	Min-Max	95% CI	P value
WBC	Mild (257)	7.65	6.9	2.2-14.6	7.1-9.5	**0.0184**
	Moderate (185)	8.75	4.39	4.6-18.6	7.8-8.3	
	Severe (63)	10.19	6.04	6.6-23	8.6-11.7	

	Total (505)	8.86	5.77	2.2-23	7.0-8.5	
Neutrophil	Mild (257)	74.27	13.5	20-80	72-77	**<0.0001**
	Moderate (185)	76.11	13.2	37-92	74-76	
	Severe (63)	84.56	11.15	50-100	82-86	
	Total (505)	78.3	9.2	20-100	74-78	
Lymphocyte	Mild (257)	22.96	12.5	1-45	20-24	**<0.0001**
	Moderate (185)	19.88	13.3	2-35	18-22	
	Severe (63)	12.67	8.1	2-15	12-18	
	Total (505)	18.5	11.3	1-45	10-14	
Monocyte	Mild (257)	3.68	2.93	1-10	3.1-3.6	0.2798
	Moderate (185)	3.49	2.654	2-15	3.3-4.0	
	Severe (63)	3.03	2.78	1-15	2.3-3.7	
	Total (505)	3.4	2.7	1-15	2.5-3.5	
ANC	Mild (257)	6.01	4.94	1.2-24.3	6.13-7.58	**0.0014**
	Moderate (185)	6.86	5.25	1.16-26.3	5.4-6.64	
	Severe (63)	8.86	5.74	2.15-58.9	7.41-10.3	
	Total (505)	7.24	5.31	1.2-58.9	5.2-9.8	
ALC	Mild (257)	1.59	1.3	0.06-13.1	1.32-1.64	0.0328
	Moderate (185)	1.40	0.91	0.16-6.60	1.37-1.64	
	Severe (63)	1.09	0.84	0.16-4.92	0.88-1.31	
	Total (505)	1.36	1.01	0.06-13.1	1.1-1.61	
AMC	Mild (257)	0.27	0.36	0.02-1.55	0.24-0.33	0.6544
	Moderate (185)	0.29	0.22	0.03-1.42	0.24-0.30	
	Severe (63)	0.31	0.35	0.03-3.49	0.21-0.40	
	Total (505)	0.29	0.31	0.02-3.49	0.26-0.35	
NLR	Mild (257)	5.17	6.58	0.01-13.9	5.36-6.98	**<0.0001**
	Moderate (185)	6.84	6.68	0.66-28.5	4.88-6.81	
	Severe (63)	11.52	10.1	0.40-30.2	8.98-14.1	
	Total (505)	7.84	7.78	0.01-30.2	6.5-12.5	
LMR	Mild (257)	8.7	6.98	0.53-55	7.45-9.16	0.1187
	Moderate (185)	8.3	7.08	0.25-52	7.64-9.70	

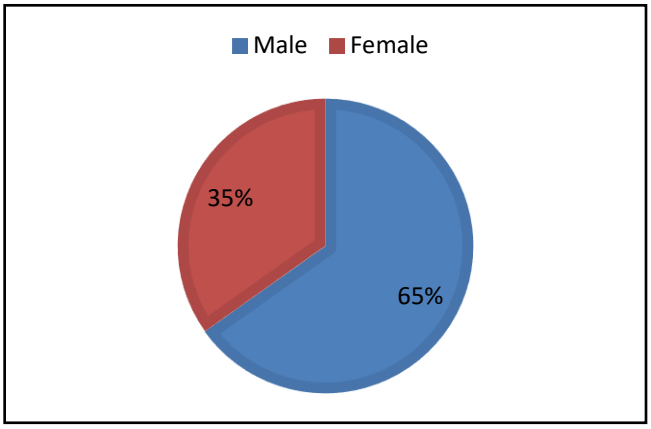
	Severe (63)	6.63	5.2	1.5-25	5.32-7.94	
	Total (505)	7.87	6.42	0.25-55	5.65-8.70	
Hb	Mild (257)	12.9	2.36	3.9-17.3	12.3-15.2	0.121
	Moderate (185)	11.5	2.15	4.0-18.3	12.1-14.9	
	Severe (63)	11.9	3.1	5.4-18.0	11.9-15.1	
	Total (505)	12.55	2.53	3.9-18.3	11.5-14.6	
Platelet	Mild (257)	2.61	0.98	1.24-4.29	3.8-4.6	0.13
	Moderate (185)	3.47	1.01	1.93-6.56	3.7-5.1	
	Severe (63)	4.1	0.86	2.01-7.17	3.1-6.1	
	Total (505)	3.39	0.95	1.24-7.17	3.4-4.8	

Among inflammatory markers C-reactive protein (CRP) (p value <0.0001) and D-Dimer level (p value 0.0001) was significantly elevated in patients with moderate and severe disease. Among biochemical parameters S.Ferritin (p value <0.0001) and lactate dehydrogenase (LDH) levels (p value <0.0001) were increased in moderate and severe cases when compared to the mild category (Table 3).

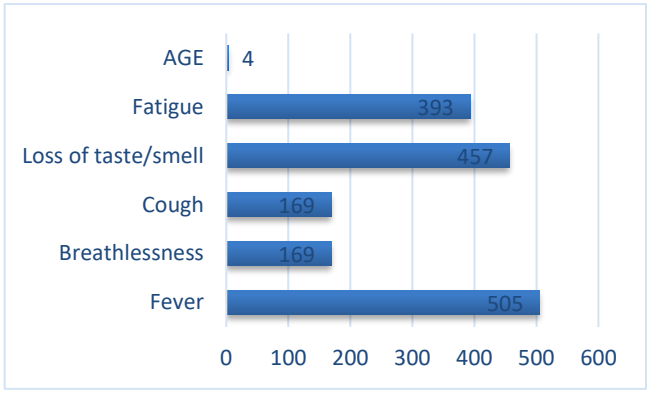
Table 3: Comparison of inflammatory and biochemical markers among severity groups

Inflammatory & Biochemical markers	**Severity**	**Mean**	**SD**	**Min-Max**	**95% CI**	**P value**
CRP	Mild (257)	38.42	16.2	1.1-84	32.8-44.1	**<0.0001**
	Moderate (185)	72.8	12.9	10.6-95.8	70.9-74.6	
	Severe (63)	79.49	17.6	30.1-235	67.5-91.5	
	Total (505)	63.57	15.56	1.1-235	45.5-85.2	
D-Dimer	Mild (257)	0.52	0.55	0.5-3.3	0.55-1.58	**0.0001**
	Moderate (185)	1.54	1.84	0.5-5.9	0.62-1.66	
	Severe (63)	4.56	2.53	1.1-8.8	1.74-3.69	
	Total (505)	2.20	1.64	0.5-8.8	1.5-2.64	
LDH	Mild (257)	331.5	160	200-505	311-351	**<0.0001**
	Moderate (185)	391.7	62.7	203-899	366-400	
	Severe (63)	428	191.5	211-958	389-476	
	Total (505)	383.73	138.06	200-958	352-391	
S.Ferritin	Mild (257)	311.5	143.8	11.7-589.3	293-329	**<0.0001**
	Moderate (185)	873.7	155.2	107.7-1150	851-896	
	Severe (63)	977.2	652.1	303.4-1952	811-1143	
	Total (505)	720.8	317.03	11.7-1952	752-885	

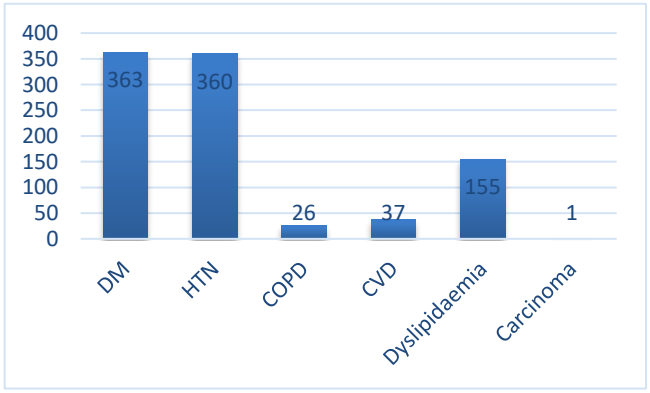
A total of 48 patients (10%) with comorbidities expired due to viral pneumonitis, acute respiratory distress syndrome (ARDS) and respiratory failure.



Graph 1: Gender Distribution



Graph 2: Distribution of Clinical Features



Graph 3: Distribution of Comorbidities

Discussion:

The prevalence of COVID-19 cases has seen a global increase. Assessing clinical, demographic, biochemical, haematological and inflammatory parameters have thus become important for investigating the COVID-19 cases. Likewise, our study included Clinical features, hematological, biochemical and inflammatory parameters as mentioned before for investigation of the COVID 19 positive cases.

Till date, features such as epidemiological, clinical, laboratory, radiological and treatment data of COVID-19 patients have been described in many studies in which most of the laboratory findings were seen as the significant differences between mild, moderate and severe cases [10,11]. In our study, all the patients presented with fever and fatigue. Majority of the patients experienced loss of taste and smell, while few presented with cough and breathlessness. According to the study by Eren Usul and Yang et al, had mentioned fever, cough, expectoration, sore throat, fatigue as major clinical symptoms and diarrhea, chest tightness, headache, pharyngalgia, shortness of breath and rash as less common symptoms during COVID-19 hospitalization[12,13].

In patients with severe disease, a significant increase inWBCs may point towards clinical worsening and increased risk of a poor outcome [14]. Our data indicated that the increase in WBCs is driven by elevated neutrophils, as decreasing trends were observed for lymphocytes and monocytes. In COVID-19 it has been further hypothesized that survival may be dependent on ability to replenish lymphocytes which are killed by the virus. As such, lymphocyte count, especially may serve as a clinical predictor of severity and prognosis [15]. Macrophages and monocytes play an important role in innate and adaptive immune response against microbial and viral pathogens through their phagocytic activity, production of cytokines and activation of lymphocytes [16].

In our study, the mean with standard deviation value of NLR among COVID patients was 7.84±7.78. Among the classified COVID patients, based on severity, patients in mild category had mean with standard deviation value of 5.17±6.58, while patients in moderate category had mean with standard deviation value of 6.84±6.68. The patients in severe category had mean with standard deviation value of 11.52±10.1.The NLR is considered to be an important inflammatory marker which aids in evaluation of progression and prognosis of COVID-19 and an increased value usually indicates poor prognosis[17].Likewise, the obvious difference in NLR between severe and non-severe patients during hospitalization in this study also confirmed the above data[18].In the study by Zhang et al., Yan et al., and Wang et al. concluded that an elevated NLR upon admission to hospital was an independent predictive marker of severe pneumonia in COVID-19 patients.[19-21]There was no significant changes in Hemoglobin, Monocyte, Absolute monocyte count (AMC), Lymphocyte monocyte ratio (LMR) and Platelet count.

C-reactive protein (CRP) an acute phase reactant was also found to be significantly elevated in our study.In the study done by Nurshad Ali et al and Huang Y et al, CRP was considered as an early predictor of COVID 19 severity. A cut off of >10 mg/L is estimated to be a predictor of poor outcome [22,23].

Another parameter to be significantly elevated was D-Dimer

which is a coagulative marker. Yumeng Yao et al and Poudel A et al considered D-Dimer value as an accurate biomarker for predicting mortality in patients with COVID 19[24,25]. Our study also showed significant elevation of biochemical parameters, S.LDH and S.ferritin levels in COVID 19 patients. Yihui Huang et al and Szarpak L et al concluded LDH levels to be an independent risk factor and predictor of mortality in patients with COVID 19[26,27]. Karanvir Kaushal et al concluded serum ferritin levels to be a prognostic biomarker in COVID-19 patients, however few studies showed minimal role of ferritin in predicting ICU admission and need for ventilation[28-30].

Conclusion:

COVID-19 is a disease with a wide range of symptoms that vary with age and comorbidity factors. Biomarkers play an important role in early assessment, diagnosis, monitoring, prognosis of the condition and patient care. Furthermore, clinical evaluation is critical at every stage, and biomarkers must be meaningfully integrated into bedside decision making. Biomarker panels, as opposed to single biomarkers, deliver more trustworthy results. According to the findings of our study, several hematological, biochemical, and inflammatory markers play an essential part in risk stratification models that may can serve as clinical predictors of severe and fatal COVID-19. Hence we recommend that clinicians regularly monitor these variables in hospitalized patients with respiratory distress as signals for probable progression to critical illness.

References

1. Pal M, Berhanu G, Desalegn C, Kandi V. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): an update. Cureus. 2020 Mar 26;12(3).
2. Bchetnia M, Girard C, Duchaine C, Laprise C. The outbreak of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): A review of the current global status. Journal of infection and public health. 2020 Nov 1;13(11):1601-10.
3. https:/www.worldometers.info/coronavirus/
4. Kakar A, Nundy S. COVID-19 in India. Journal of the Royal Society of Medicine. 2020 Jun;113(6):232-3.
5. Cheng B, Hu J, Zuo X, Chen J, Li X, Chen Y, Yang G, Shi X, Deng A. Predictors of progression from moderate to severe coronavirus disease 2019: a retrospective cohort. Clinical Microbiology and Infection. 2020 Oct 1;26(10):1400-5.
6. Dotan A, Muller S, Kanduc D, David P, Halpert G, Shoenfeld Y. The SARS-CoV-2 as an instrumental trigger of autoimmunity. Autoimmunity reviews. 2021 Apr 1;20(4):102792.
7. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Critical reviews in clinical laboratory sciences. 2020 Aug 17;57(6):389-99.
8. Biamonte F, Botta C, Mazzitelli M, Rotundo S, Trecarichi EM, Foti D, Torti C, Viglietto G, Torella D, Costanzo F. Combined lymphocyte/monocyte count, D-dimer and iron status predict COVID-19 course and outcome in a long-term care facility. Journal of translational medicine. 2021 Dec;19(1):1-0.
9. Słomka A, Kowalewski M, Żekanowska E. Coronavirus disease 2019 (COVID–19): A short review on hematological manifestations. Pathogens. 2020 Jun;9(6):493.
10. Ghazanfari T, Salehi MR, Namaki S, Arabkheradmand J, Rostamian A, Chenary MR, Ghaffarpour S, Ardestani SK, Edalatifard M, Naghizadeh MM, Mohammadi S. Interpretation of hematological, biochemical, and immunological findings of COVID-19 disease: biomarkers associated with severity and mortality. Iranian Journal of Allergy, Asthma and Immunology. 2021 Feb 11;20(1):46-66.
11. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19–A systematic review. Life sciences. 2020 Aug 1;254:117788.
12. Usul E, Şan İ, Bekgöz B, Şahin A. Role of hematological parameters in COVID-19 patients in the emergency room. Biomarkers in Medicine. 2020 Sep;14(13):1207-15.
13. Yang L, Xie X, Tu Z, Fu J, Xu D, Zhou Y. The signal pathways and treatment of cytokine storm in COVID-19. Signal transduction and targeted therapy. 2021 Jul 7;6(1):1-20.
14. Bain W, Yang H, Shah FA, Suber T, Drohan C, Al-Yousif N, DeSensi RS, Bensen N, Schaefer C, Rosborough BR, Somasundaram A. COVID-19 versus non–COVID-19 acute respiratory distress syndrome: comparison of demographics, physiologic parameters, inflammatory biomarkers, and clinical outcomes. Annals of the American Thoracic Society. 2021 Jul;18(7):1202-10.
15. Henry BM, De Oliveira MH, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clinical Chemistry and Laboratory Medicine (CCLM). 2020 Jul 1;58(7):1021-8.
16. Wu J, Zha P. Proactive Body Temperature Management Protocol and Lifestyle Interventions as Predictable Cures for COVID-19 Disease: Curative Protocols Discovered from a Century of Medical Discoveries.
17. Elahi A, Masoudi A, Hemmati H. Diagnostic and Prognostic Blood Biomarkers in COVID-19. International Journal of Medical Investigation. 2022 Mar 10;11(1)
18. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. International immunopharmacology. 2020 Jul 1;84:106504.
19. Zhang H, Cao X, Kong M, Mao X, Huang L, He P, Pan S, Li J, Lu Z. Clinical and hematological characteristics of 88 patients with COVID-19. International journal of laboratory hematology. 2020 Dec;42(6):780-7.
20. Yan X, Li F, Wang X, Yan J, Zhu F, Tang S, Deng Y, Wang H, Chen R, Yu Z, Li Y. Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: a retrospective cross-sectional study. Journal of medical virology. 2020 Nov;92(11):2573-81.
21. Wang C, Deng R, Gou L, Fu Z, Zhang X, Shao F, Wang G, Fu W, Xiao J, Ding X, Li T. Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters. Annals of translational medicine. 2020 May;8(9).
22. Ali N. Elevated level of C-reactive protein risk for severity of COVID-19. J Med Virol. 2020;92(11):2409-2411.
23. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, Jiang X, Li X. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. Journal of medical virology. 2020 Jul;92(7):856-62.
24. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, Chen X, Chen S, Yu K, Huang Z, Hu B. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. Journal of intensive care. 2020 Dec;8(1):1-1.
25. Poudel, A., Poudel, Y., Adhikari, A., Aryal, B.B., Dangol, D., Bajracharya, T., Maharjan, A. and Gautam, R., 2021. D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19. Plos one, 16(8), p.e0256744.
26. Huang Y, Tu M, Wang S, Chen S, Zhou W, Chen D, Zhou L, Wang M, Zhao Y, Zeng W, Huang Q. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: A retrospective single center analysis. Travel medicine and infectious disease. 2020 Jul;36:101606.
27. Szarpak L, Ruetzler K, Safiejko K, Hampel M, Pruc M, Kanczuga-Koda L, Filipiak KJ, Jaguszewski MJ. Lactate dehydrogenase level as a COVID-19 severity marker. Am J Emerg Med. 2021 Jul 1;45:638-9.
28. Kaushal K, Kaur H, Sarma P, et al. Serum ferritin as a predictive

biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. J Crit Care. 2022;67:172-181.
29. Ahmed S, Ahmed ZA, Siddiqui I, Rashid NH, Mansoor M, Jafri L. Evaluation of serum ferritin for prediction of severity and mortality in COVID-19-A cross sectional study. Annals of medicine and Surgery. 2021 Mar 1;63:102163.
30. Payán-Pernía S, Gómez Pérez L, Remacha Sevilla ÁF, Sierra Gil J, Novelli Canales S. Absolute lymphocytes, ferritin, C-reactive protein, and lactate dehydrogenase predict early invasive ventilation in patients with COVID-19. Laboratory medicine. 2021 Mar;52(2):141-5.