International Journal of Current Research and Review
DOI: https://doi.org/10.31782/IJCRR.2022.141901

Research Article

IJCRR
Section: Healthcare

Copyright@IJCRR

Alteration of Hematological and Biochemical Parameters to Predict Severity in SARS-CoV-2 Infection

Shrewastwa Mukesh Kumar[1], Acharya Viyatprajna[2], Aggrawal Kavita[3]

[1]Assistant Professor, Department of Biochemistry, Nepalgunj Medical College, Kohalpur, Nepal; [2]Professor, Department of Biochemistry, KIMS & PBH, Bhubaneswar, India; [3]Associate Professor, Department of Biochemistry, KIMS & PBH, Bhubaneswar, India.

ABSTRACT

Introduction: SARS- CoV-2 global pandemic has fired the world into a notable health catastrophe, with over 187,348,181 cases and 4,044,898 deaths as of July 10 2021. Many studies have been conducted to determine the clinical, biological, and radiological characteristics of COVID-19 for better identification of infected people at an early stage and stop disease development to an advanced state.

Objectives: The aim & objective of our study was to take advantage of the biochemical and haematological parameters in predicting the prognosis and mortality in disease severity COVID-19 patients.

Methods: This single-centre retrospective, observational study was supervised to have all the admitted patients (n = 90) possessing COVID-19 Polymerase chain reaction (PCR) positive, and assessed those for prognosis and disease outcome by taking advantage of several biochemical and haematological markers.

Results: Out of 90 patients, 53(58.89%) had mild to moderate disease that were included in non-severe group; 37(41.11%) had severe to critical disease, of which 17 died and 20 survived. Advanced age, presence of comorbidities and infection were risk factors for advancement to severe disease. The existence of statistically significant abnormalities in the following parameters were strongly related with advancement to severe disease: white blood cells (WBC, p=0.002), neutrophils (p=0.001), lymphocytes (p=0.001), C-reactive protein (CRP, P<0.001), D-dimer (P<0.001), Lactate dehydrogenase (LDH, p<0.001), Ferritin (P<0.001), creatinine (p=0.001), aspartate aminotransferase (AST, P=0.012), procalcitonin (P<0.001) and alanine aminotransferase (ALT, P=0.001) during both admission and hospitalization.

Conclusion: The inflammatory markers, biochemical parameters and haematological indices are a good guide for predicting the severity and disease outcome of corona virus disease.

Key Words: Acute respiratory distress syndrome (ARDS), C-reactive protein(CRP), Lactate dehydrogenase(LDH), Fibrin degradation product (FDP or D-dimer), White blood cells (WBC), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST)

INTRODUCTION

Caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), otherwise known as the COVID-19 pandemic is the largest pandemic of the century. It is an up surging disease that is spreading promptly worldwide and alarms the bio security of all countries[1,2], with the number of cases outstripping 187,348,181 and death of more than 4,044,898 people. The two most overwhelmed countries are the United States of America and India, with a death toll of 622,821 in the USA and 408,072 in India as of July 10, 2021.The infection rate was 24,035 cases per million populations.

The COVID-19 pandemic in Nepal is part of the worldwide pandemic of coronavirus disease. In Nepal, the first case was approved as Covid-19 positive test on 23 January 2020 when a 31-year-old student had returned to Kathmandu from Wuhan on 9 January.[3]It was also the first noted case of COVID-19 in South Asia.[4] Nepal's first case of local transmission was approved on 4th April in Kailali District. The number of cases confirmed in the different regions of our country was 652,002 including 9,400 deaths in July 12, 2021.

This alarming viral transmission and mortality have prompted the publication of many studies to determine clinical, biological, radiological, and genetic predictors for the

Corresponding Author:
Mukesh Kumar Shrewastwa, Assistant Professor, Department of Biochemistry, Nepalgunj Medical College, Kohalpur, Nepal.
E-mail: mshrewastwa55@gmail.com

ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)

Received: 01.07.2022 **Revised:** 15.07.2022 **Accepted:** 05.08.2022 **Published:** 05.10.2022

progression to severe and fatal forms of the coronavirus disease.[5]Acknowledgement of these predictors would make it possible to differentiate the risk and conduct the intervention studies to triage the patients.

Clinical (comorbidities, acute respiratory distress syndrome [ARDS]), Demographic (advanced age, male sex) and radiological predictors have been broadly comprehensive in many studies.[5–7]Biological (lymphopenia, hyperferritinemia, serum C-reactive protein [CRP] levels) predictors [5, 8] have been described but remain mainly unreported/under-reported in western region of Nepal. A simple and potent index to evaluate the severity and decide the prognosis of new crown pneumonia is urgently needed at this stage of coronavirus disease.

Lymphocytes take part in a pivotal role in maintaining the body's immune homeostasis and inflammatory response. The knowledge regarding the mechanisms involving in changes in these blood biochemical indexes is contemplated to give an effective approach for the treatment of COVID-19. In addition, the promotion, protection and maintenance of lymphocyte counts may promote the treatment and prevention strategy regarding development of new crown pneumonia in COVID-19 patients.

We retrospectively analyzed the patients admitted to Nepalgunj Medical College & teaching hospital, Kolhapur who had been cured of COVID-19 and discharged from the hospital between January 1, 2020, and August 30, 2020 because all the literature published regarding COVID-19 patients are mainly concentrated on hospitalized patients, with many patients still being under hospitalization or under treatment. We propose the prediction reliability and accuracy of this study are higher because the clinical end point has been accomplished in these patients.

The main objective of our study was to report the haematological and biochemical abnormalities in Nepalese patients with COVID-19 and to determine the prediction efficacy of parameters that can help to distinguish those likely to develop severe COVID-19. We expect that the findings of this study can give helpful information for early decision-making and treatment for severe COVID-19 patients.

STUDY DESIGN AND METHODS

A retrospective, observational and single-centre study was approved by institutional review committees of Nepalgunj medical college & teaching hospital, Kolhapur of ethical clearance letter number:743/077-078 and was planned to be conducted at Nepalgunj medical college & teaching hospital, Kolhapur which was started from 1 January, 2020 till 30 August 2020 and including all patients who were diagnosed as COVID-19 positive via on a reverse-transcriptase polymerase chain reaction (RT-PCR, Kit Maccura Biotechnology) assay using a nasopharyngeal swab specimen.

A total of 90 patients were recruited which were divided into two groups: 37 severe patients and 53 non-severe patients that were randomly taken without age and gender matched. Severely ill patients were defined as those admitted to the ICU with one of the following signs: respiratory rate more than 30 breaths/min, oxygen saturation less than 93% at room air, ARDS, or requirement of mechanical ventilation.[9] Non-severe patients were those with mild or moderate forms of COVID-19 according to World Health Organization criteria.[9] This study reports the clinical presentation, demographic characteristics, laboratory findings, and outcomes of incident cases of COVID-19 admitted to the intensive care unit (ICU) from 1 January, 2020 till 30 August 2020.The time frame was chosen to have a minimum follow-up of 15 days for all patients. The nadir and peak haematological and biochemical parameters were taken by following patients from admission to their last blood test.

Statistical analysis

Normally distributed continuous variables were expressed as means ± standard deviation [SD] whereas variables not normally distributed were expressed as medians (interquartile range [IQR]); categorical variables were presented as counts (%). The Kolmogorov-Smirnov test was used to assess the normality of distribution of continuous variables. Baseline demographic, clinical, and biological characteristics were compared among severe and non-severe patients. We used the Student's t-test (parametric distribution) or Mann-Whitney's U test (nonparametric distribution) for continuous variables and the chi-squared or Fisher's exact test for categorical variables to compare differences between the two groups. Statistical analyses were performed using SPSS version 20.0 (IBM SPSS) and p-value below 0.05 was considered statistically significant for two-tailed.

RESULT

Out of 90 PCR positiveCOVID-19 patients, 53 (58.89%) were admitted to general wardwhereas37 (41.11%) patients were severe due to corona diseases who required treatment in the ICU. During treatment of severe covid-19 patients in ICU, 20 survived and 17 died. Gender-wise, males had a higher preponderance for the disease.

The age and comorbidities of the patients were statistically significant associated with disease severity ($P<0.05$) and the age of maximum number of patients belonging to severe group was old age. Marginally greater than half of the patients (47 [52.22%]) had comorbidities, with hypertension (34 [37.78%]) being the most common, followed by diabetes (29 [32.22%]) and kidney disease (16 [17.79%]).

The most common symptoms were weakness (74 [82.22%]), followed by fever (71 [78.89%]) and headache (64[71.11%]). The further symptoms (cough, pharyngalgia, Expectoration, dyspnea, myalgia, dizziness, chills and diarrhoea) were observed in our series less frequently (Table 1)).

17 deaths (45.94%) occurred in the severe group, out of which 12 (32.43%) patients underwent invasive mechanical ventilation and 5 (13.51%) had sudden cardiorespiratory arrest under non-invasive ventilation. The causes of death were principally due to development to severe ARDS alone (4 [10.8%]) or associated with acute kidney injury (10 cases [27.02%]), septic shock (2 [5.4%]), and cirrhotic decompensation (1 [2.70%]). Other complications that the severe patients developed were thromboembolic events (4 [10.81%]), arrhythmia (7 [18.9%]) and pneumothorax (4 [10.81%]).

In univariate analysis, severe patients had statistically significant association with age (P<0.05). With increasing age, the percentage of covid-19 with severe symptoms were increased and more comorbidities, dominated by hypertension (16 [43.20%] versus 18 [34%], P<0.001), diabetes (13 [35.1%] versus 16 [30.2%], P<0.003) and kidney disease (8 [21.6%] versus 8 [15.1%], P<0.001).High levels of white blood cells (WBC), neutrophils, CRP, D-dimer, lactate dehydrogenase (LDH), ferritin, creatinine, alanine aminotransferase (ALT), procalcitoninand aspartate aminotransferase (AST), both on admission and during hospitalization, were statistically significant strongly associated with development to severe forms (Tables 2, 3 and 4) whereas decrease in count of lymphocyte number (lymphopenia) was statistically significant associated with advancement to severe forms.

In binary logistic regression step 1, higher levels of LDH were independently associated with severe covid-19 group (odds ratio (OR) per SD 0.971 [95% CI: 0.959-0.983]; P<0.01) in comparison to non-severe group and in step2, higher levels of LDH were independently associated with severe covid-19 group (odd ratio (OR) per SD 0.962 [95% CI: 0.959-0.983]; P<0.01) after adjusting procalcitonin in comparison to non-severe group.(Table 5)

DISCUSSION

The third type of coronavirus, known as SARS-CoV-2, identified in the last two decades after SARS-CoV1 and Middle East respiratory syndrome (MERS)-CoV, detected in 2003 and 2012, respectively.[10, 11] 8,096 people were infected by SARS-CoV-1 infection which caused the death of 774 people in 2002–2003. MERS-COV was culpable for a localized epidemic in the Middle East in 2012 which case-fatality rate was 38%.

We reported the clinicobiological profile of COVID-19 disease in the Midwestern region of Nepal having a sample of 90 patients. The demographic characteristics in our study showed that progressive age is a factor that predisposes patients to COVID-19 and develops advancement to severe disease and death which was supported by many studies.[12,13,14]

Zhou et al. demonstrated in their study that age greater than 50 years was strongly related to the existence of ARDS and age greater than 65 years was linked with mortality.[13] But, progressive age was also noted as key independent predictor of mortality in SARS and MERS.[15,16] The age associated comorbidities noted in our study population are severity and prognostic factors as showed by many studies, like Zhou et al. and Wu et al. whereas hypertension and diabetes were significantly related to the existence of ARDS in a multivariate analysis and with the existence of mortality in a univariate analysis.[12,13,14] The reason for the relation between Covid-19 virus infections associated mortality and age would be impaired cellular immune function and a longer duration of inflammation in elderly people.[12]

In our study, gender was not statistically significant associated factor influencing the severity of COVID-19 which is not in congruence with the work of Irani authors.[17] But, some study showed that male gender was as a factor influencing the increasing severity of COVID-19.[18]

The clinical signs manifested by our patients, as well as their frequencies and rates, were close to previousstudies.[5,14] It is clear that COVID-19 disease is statistically significantly associated with morbidity, especially in patients with chronic diseases, somewhat one-fifth of them require supportive care in medical ICUs [19], which are particularly limited in most developing countries such as those in Africa. In addition, in spite of the implementation of optimal supportive interventions, the inpatient mortality rate goes on above 1.4%, come to 6.4% in the population aged over 60 years old.[20, 21]

The biological profiles of our study participants are similar to that has been reported in the literature, with the existence of lymphopenia in severe patients upon admission and further an aggravation of lymphopenia during their stay. Many hypotheses have been constructed to explain the molecular mechanism for pathogenesis of lymphopenia in the context of SARS-CoV-2 infection.

A Chinese study described the characteristics of the haemogram and lymphocyte subpopulations in 166 non-severe patients' and286 severe patients. Severe patients had a significantly raised neutrophil/lymphocyte ratio and upraised markers of inflammation (CRP, ferritin, interleukin-6, interleukin-8, and interleukin-10). In addition, there was disparity in the lymphocyte immune response in severe patients, who possessed higher CD4 lymphopenia, higher CD4-naïve cells and CD4 suppressor T cells, and less CD4 memory cells and regulatory T cells, in comparison to non-severe patients.[22] Rodriguez et al. have proposed that COVID-19 virus have effect on lymphocytes, principally T cells, perhaps diminishing CD4 and CD8 cells.[18] The viral particles proliferate via

the respiratory mucosa, first by utilizing the ACE2 receptor at membrane of ciliated bronchial epithelial cells and then infecting other cells. This phenomenon causes a cytokine storm in the body and provokes a series of immune responses, which induce changes in peripheral WBCs and immune cells such as lymphocytes.[23] This concept has been determined by Henry et al. in their meta-analysis: the number of lymphocytes, principally CD4 lymphocytes, may provide as a biological predictor of severity and mortality; in the case of COVID-19, they also described the hypothesis that survival can be based on the ability to build up lymphocytes that are killed by the virus.[24] The same authors also described statistically significant rise in ferritin and CRP levels in patients with suspected severe COVID-19 which are in line with our study.

The rise in CRP levels in blood reflects the extent of the systemic inflammatory syndrome observed in severe forms of the disease, which is followed with a huge release of inflammatory cytokines creating a "cytokine storm" culpable for acute tissue damage with the onset of severe ARDS and subsequent multi-systemic failure.[24] The statistically significant rise of LDH levels in blood found in our study which is consistent with the findings of Liu who correlated LDH, lymphocyte, neutrophil, and CRP abnormalities with severe COVID pneumonia.[14,25] The raised ferritin levels in blood are likely due to secondary phagocytic lymphohistiocytosis and severe cytokine release syndrome.[26, 27] In our study, raised D-dimer level in blood was also significantly associated to severity group of COVID-19 patients and was the cause of coagulopathy with thromboembolic complications in 4.44% of our patients. Anaemia and thrombocytopenia were not statistically significant in my study.

Myocardial damage, as mentioned biologically by elevated troponin and creatine phosphokinase levels in blood suggestive of viral myocarditis, which has been reported by others, was not reported in our study of severe patients' group.[28,29] However, the stay was affected by the significantly distinct difference of the median nadir of WBC, lymphocytes, and Neutrophils, as well as the median peak of neutrophil, WBC, CRP, ferritin, procalcitonin, LDH, D-dimer, ALT, AST, creatinine, and urea levels. This determines the manifestation of complications of the severe form of COVID-19 including the following: bacterial super infection, severe ARDS secondary to the cytokine storm, thromboembolic disease, and organ dysfunction (which is believed to be multifactorial [comorbidities, the cytokine storm of COVID-19, the rejuvenation environment]), leading to death. This is in affirmation with other authors. [5–31]

In binary logistic regression step 1, 1unit increased in levels of LDH was independently associated with increased severity by 0.971 times in severe covid-19 group (P<0.01) in comparison to non-severe group and in step 2, 1 unit increased in levels of LDH was independently associated with increased severity by 0.962 times in severe covid-19 group P<0.01) after adjusting procalcitonin in comparison to non-severe group

Our study reinforces these data by describing the experience in our least developed country, which commenced confinement measures at an early stage of the crisis, hence influence the progress of this pathology. We expect that the findings of this study can give helpful information for early decision-making and treatment for severe COVID-19 patients

The limitations of our study were as follows: the single-centre retrospective study design, which increases the chance of selection bias and impacts the generalizability of data; the absence of evaluation of immunological parameters (CD4, CD8, interleukin-6, interleukin-8, interleukin-10) studied by the other studies which could help us to properly analyse the inflammatory characteristics of our patients; the small sample size; and missing data from some pauci-symptomatic patients and patients who died at a given time. This limits the in-depth statistical analysis needed to stratify the maximum risks associated with the pathology.

CONCLUSION

Majority of the studies being done on Chinese population, there may be a bias due to ethnicity, epigenetic and environmental factors. By observing the changes in biochemical and haematological parameters, repeat CT scans and invasive procedures can be obviated in hospitalized patients to monitor prognosis.

ACKNOWLEDGEMENT

We acknowledge the support of the Department of Biochemistry and Medicine, Nepalgunj Medical College, Kohalpur, Nepal in this study.

Conflict of interest: None

Author contribution: Shrewastwa MK - Study planning, execution, statistical analyses and article writing; Acharya V- Article writing, review and overall supervision; Agrawal Kavita -Article review.

Source of Funding: Self-funded

REFERENCES

1. Matuizzi C, Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak? Ann Transl Med. 2020; 8: 48. https://doi.org/10.21037/atm.2020.02.06 PMID: 32154288
2. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020; 579: 265–269. https://doi.org/10.1038/s41586-020-2008-3 PMID: 32015508

3. Shrestha R, Shrestha S, Khanal P; Kc B. "Nepal's first case of COVID-19 and public health response". J Travel Med. 2020 May 18:27 (3): ISSN 1195- 1982. PMC 7107523. PMID 32104884 .
4. "Nepal Reports South Asia's First Confirmed Case Of Deadly Coronavirus". NDTV.com. Archived from the original on 24 January 2020. Retrieved 21 May 2020.
5. Placais L, Richer Q.COVID-19: clinical, biological and radiological characteristics in adults, infants and pregnant women. An up-to date review at the heart of the pandemic. Rev Med Interne. 2020; 41: 308–318. https://doi.org/10.1016/j.revmed.2020.04.004 PMID: 32334862.
6. Elchazli RM, Toraih EA, Elgaml A, EI-Mowafy M,EI-Mesery M, Amin MN, et al. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: A meta-analysis of 6320 patients. 2020; 15(8). https://doi.org/10.1371/ journal.pone.0238160.
7. Iftimie S, Lopez-Azcona AF, Vicente-Miralles M,RiuF,Joven J, Camps J, et al. Risk factors associated with mortality in hospitalized patients with SARS-CoV-2 infection. A prospective, longitudinal, unicenter study in Reus, Spain. 2020. https://doi.org/10.1371/journal.pone.0234452.
8. Rossi PG, Marino M, Formisano D,Venturelli F, Vicentini M, Grilli R, et al. Characteristics and outcomes of a cohort of COVID-19 patients in the Province of Reggio Emilia, Italy. 2020. https://doi.org/10.1371/journal.pone.0238281.
9. Peng F, Tu L, Yan Y, Hu P, Wang R, Hu Q, et al. Management and treatment of Covid-19: the Chinese experience. Can J Cardiol.2020. Available from https://doi.10.1016/j.cjca.2020.04.010 PMID: 32439306
10. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med. 2003; 348: 1953–1966.https://doi.org/10.1056/NEJMoa030781 PMID: 12690092
11. Zaki AM, Van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med. 2012; 367: 1814–1820. https://doi.org/10.1056/NEJMoa1211721 PMID: 23075143
12. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult in-patients with COVID-19in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3 PMID: 32171076
13. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020. https://doi.org/10.1001/jamainternmed.2020.0994 PMID: 32167524
14. Kantri A, Ziati J, Khalis M, Haoudar A, Ei Aidaoui K, Daoudi, et al. Hematological and biochemical abnormalities associated with severe forms of COVID-19: A retrospective single center study from Morocco. PLOSONE.2021.https://doi.org/10.1371/journal.pone.0246295
15. Choi KW, Chau TN, Tsang O, Tso E, Chiu MC, Tog WL et al. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med. 2003; 139: 715–723. https://doi.org/10.7326/0003-4819-139-9-200311040-00005 PMID: 14597455
16. Hong KH, Choi JP, Hong SH, Lee J , Kwon JS, Kim SM, et al. Predictors of mortality in Middle East respiratory syndrome (MERS).Thorax. 2018; 73:286–289. https://doi.org/10.1136/thoraxjnl-2016-209313 PMID: 28724637
17. Javanian M, Bayani M, Shokri M, Babazadeh A, Yeganeh B, Mohseni S, et al. Clinical and laboratory findings from patients with COVID-19 pneumonia in Babol North of Iran: a retrospective cohort study. Rom J Intern Med. 2020. Available from: https://doi.org/10.2478/rjim-2020-0013 PMID: 32396143
18. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel-coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395: 507–513. https://doi.org/10.1016/S0140-6736(20)30211-7 PMID: 32007143
19. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutie´rrez-Ocampo E, Villamizar-Pena R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020; 34:101623. https://doi.org/10.1016/j.tmaid.2020.101623 PMID: 32179124
20. Shim E, Tariq A, Choi W, Lee Y, Chowell G. Transmission potential and severity of COVID-19 in South Korea. Int J Infect Dis. 2020; 93: 339–344.https://doi.org/10.1016/j.ijid.2020.03.031 PMID: 32198088
21. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: amodel-based analysis. Lancet Infect Dis. 2020; 20: 669–677. https://doi.org/10.1016/S1473-3099(20) 30243-7 PMID: 32240634
22. Qin C, Zhou L, Hu Z, Zhang S, Yang S, TaoY, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan,China. Clin Infect Dis. 2020. Available from: https://doi.org/10.1093/cid/ciaa248 PMID: 32161940
23. Rodriguez-Morales AJ, MacGregor K, Kanagarajah S, Patel D, Schlagenhauf P. Going global—travel and the 2019 novel coronavirus. Trav Med Infect Dis. 2020; 33: 101578. https://doi.org/10.1016/j.tmaid.2020.101578 PMID: 32044389
24. Henry BM, Santos 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. Clin Chem Lab Med. 2020. Available from: https://doi.org/10.1515/cclm-2020-0369 PMID: 32286245
25. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020; 63: 364–374. https://doi.org/10.1007/s11427-020-1643-8 PMID: 32048163
26. Velavan TP, Meyer CG. Mild versus severe COVID-19: laboratory markers. Int J Infect Dis. 2020; 95:304–307. https://doi.org/10.1016/j.ijid.2020.04.061 PMID: 32344011
27. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokinestorm syndromes and immunosuppression. Lancet. 2020; 395: 1033–1034. https://doi.org/10.1016/S0140-6736(20)30628-0 PMID: 32192578
28. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019(COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis. 2020. https://doi.org/10.1016/j.pcad.2020.03.001 PMID: 32169400
29. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020; 323: 1061–1069. https://doi.org/10.1001/jama.2020.1585 PMID: 32031570
30. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020; 5: 428–430. https://doi.org/10.1016/S2468-1253(20)30057-1 PMID: 32145190
31. Yan L, Zhang HT, Goncalves J, Xiao Y, Wang M, Guo Y, et al. An interpretable mortality prediction model for COVID-19 patients.Nature Machine Intelligence. 2020; 2: 283–288.

Table 1: Demographic and clinical characteristics of patient

Variable	Disease severity		P- value
	Severe(n=37)	Non-severe(n=53)	
Age(years)			
0- <15 yr	0	1 (1.9%)	
≥15-<40 yr	11(29.7%)	26(49.1%)	0.021
≥40- <65 yr	12 (32.4%)	20 (37.7 %)	
≥65 yr	14 (37.8%)	6 (11.3%)	
Sex			
Male	20(54.1%)	28(52.8%)	0.909
Female	17 (45.9%)	25 (47.2%)	
Comorbidities			
Yes	27(73%)	20 (37.7%)	0.001
No	10 (27%)	33 (62.3%)	
Hypertension	17(45. 9 %)	8(15.1%)	0.002
Diabetes	18(48.6%)	10(18.9%)	0.003
Cerebral infarction	2(5.4%)	2(3.8%)	0.712
Respiratory disease	7(18.9%)	5(9.4%)	0.193
Liver Disease	6(16.2%)	5(9.4%)	0.334
Kidney disease	8(21.6%)	8(15.1%)	0.425
Cardiac disease	5(13.51%)	4(7.55%)	0.353
Asthma	3(8.11%0	4(7.55%)	0.922
Malignancy	1(2.70)	1(1.90)	0.796
Symptoms			
Fever	30(81.1%)	41(77.4%)	
Cough	25(67.6%)	34(64.2%)	
Pharyngalgia	23(62.2%)	31(58.5%)	
Expectoration	12(32.4%)	18(34.0%)	
dyspnea	8(21.6%)	11(20.8%)	
Dizziness	5(13.5%)	6(11.3%0	
Headache	25(67.6%)	39(73.6%)	
Weakness	31(83.8%)	43(81.1%)	
Chills	8(21.6%)	9(17.0%)	
Diarrhea	4(10.8%)	5(9.4%)	
Myalgia	7(18.9%)	9(17.0%)	
Complications			
ARDS	11(29.73%)	0	
Arrythmia	7(18.91%)	0	
Pneumothorax	4(10.81%)	0	
Thromboembolic disease	4(10.81%)	0	
Septic shock	2(5.40%)	0	
Death	17(45.94%)	0	
Causes of death			
ARDS+AKF	10(27.02%)	0	
ARDS	4(10.8%)	0	
Septic shock	2(5.40%)	0	
Decompensated cirrhosis	1(2.70%)	0	

P values were calculated by the Student's t-test or Mann-Whitney U test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables. Data are shown as frequencies (%). ARDS: acute respiratory distress syndrome.

Table 2: Hematological laboratory findings of patients during admission

Parameters	Severe(n=37)	Non-severe(n=53)	P-value
Hemoglobin (gm/dl)	12.8(11.3-13.7)	13.3(12.2-14.6)	0.544
Platelets (x 10^9/L)	212(167-312)	225 (185-287)	0.584
Neutrophils (x 10^9/L)	4.91(3.42-6.85)	3.59(2.26-4.88)	0.001
White blood cells (x10^9/L)	7.88(6.21-9.75)	6.54(4.50-7.92)	0.002
Lymphocytes(x10^9/L)	0.981(0.70-1.32)	1.64(1.20-2.15)	0.001

P values were calculated by the Student's t-test or Mann-Whitney U test for continuous variables and chi-squared test or Fisher's exact test for categorical variables.
Data are shown as medians [quartiles].

Table 3: Biochemical laboratory findings of patients during admission

Parameters	Severe	Non-severe	P-value
CRP(mg/L)	19(15 - 40)	12(8 - 16.5)	<0.001
D-dimer (ng/ml)	1.22(0.62 - 1.95)	0.50(0.295 - 0.71)	<0.001
Urea(mmol/L)	5.2(3.9-6.5)	3.4(2.9-4.7)	0.489
Creatinine(µmol/L)	84(72-107)	67(61-76)	0.001
Ferritin(µg/L)	646.1(384.2-2290)	131(43-230)	<0.001
LDH(IU/L)	332 (264 -405)	204 (172 - 250)	<0.001
ALT (IU/L)	39(24-60)	24(21-30)	0.001
AST (IU/L)	38(25-61)	23(18-33)	0.012
Troponin(ng/ml)	0.004 (0.002-0.105)	0.002(0.001-0.004)	0.29
Procalcitonin(ng/ml)	3.00 (1.8 – 6.0)	0.56 (0.245- 1.355)	<0.001

P values were calculated by the Student's t-test or Mann-Whitney U test for continuous variables and chi-squared test or Fisher's exact test for categorical variables.
Data are shown as medians [quartiles].

Table 4: Blood profiles during inpatient stay (nadir and peak of laboratory findings)

		Severe(n=37)	Non-severe(n=53)	P-value
NADIR	Hemoglobin(g/L)	12.0 (10.2-13.1)	13.1 ((12.3-14.2)	0.000
	White blood cells (x10^9/L)	7.22(5.7-9.5)	5.42(4.5-6.16)	0.001
	Neutrophils (x 10^9/L)	5.38(3.35-7.53)	3.10(2.40-3.9)	0.001
	Lymphocytes (x10^9/L)	0.62(0.38-1.18)	1.61(1.24-2.1)	0.001
PEAK	White blood cells (x10^9/L)	9.8(6.8-18.6)	6.01(5.41-7.10)	0.001
	Neutrophils (x 10^9/L)	7.49(4.85-15.71)	3.58(2.46-4.39)	0.001
	CRP(mg/L)	32 (20-72)	15(8-36)	<0.001
	D-dimer (ng/ml)	1.91(0.79- 4.72)	0.60(0.319-0.89)	<0.001
	Urea(mmol/L)	7.90(5.6-12.42)	3.8(3.4-4.6)	0.680
	Creatinine(µmol/L)	107(81-283)	68(63-82)	0.001
	Ferritin(µg/L)	2099(841-2950)	91.21(31-239)	0.001
	LDH(IU/L)	411(272-655)	223(179-304)	<0.001
	ALT (IU/L)	54(34-118)	33(21-54)	0.001
	AST (IU/L)	36(49-102)	25(20-55)	0.018
	Troponin(ng/ml)	0.03(0.008-0.16)	0.03(0.008-0.16)	0.830
	Procalcitonin(ng/ml)	3.92 (2.10 – 6.78)	0.68 (0.345- 1.55)	<0.001

P values were calculated by the Student's t-test or Mann-Whitney U test for continuous variables and chi-squared test or Fisher's exact test for categorical variables.
Data are shown as medians [quartiles].

Table 5: Binary logistic regression estimates for the Odds ratio (OR) of Covid-19 severe group individuals using non-severe group as reference.

		β	S.E.	Wald	df	Sig.	Exp(β)
Step 0	Constant	.359	.214	2.814	1	.093	1.432

		β	S.E.	Wald	df	Sig.	Exp(β) or odd ratio	95% C.I.forEXP(β)	
								Lower	Upper
Step 1[a]	LDH1	-.029	.006	21.594	1	.000	.971	.959	.983
	Constant	8.315	1.725	23.226	1	.000	4085.480		
Step 2[b]	LDH1	-.039	.012	10.017	1	.002	.962	.939	.985
	Procalcitonin	-1.576	.509	9.585	1	.002	.207	.076	.561
	Constant	14.114	4.012	12.375	1	.000	1347633.103		

a. Variable(s) entered on step 1: LDH1.

b. Variable(s) entered on step 2: Procalcitonin.

β = coefficient of regression