SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Hematological Variations in Patients with COVID-19 in Marrakesh, Morocco

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DOI: 10.36347/sasjm.2021.v07i06.011 | **Received:** 21.03.2021 | **Accepted:** 28.04.2021 | **Published:** 11.06.2021

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Abstract **Original Research Article**

Introduction: Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) is a strain of coronavirus that causes coronavirus disease 2019 (COVID-19), an infectious disease that started as an epidemic in Wuhan, China and turned into a Pandemic infecting over 20M people worldwide and affecting billions of others through measures of social distancing and the socio-economic impacts it brings about. The aim of our study is to determine hematologic biomarkers that could be used in screening for a diagnosis, as well as monitoring the evolution of COVID-19 infections; leading to a more favorable outcome, especially in severe cases. ***Methods:*** This is an observational, descriptive and prospective study of 41 patients with RT-PCR positive diagnoses of COVID 19 who in the period from April, 2020 to May 5, 2020, were admitted the Mohamed Sixth University Hospital of Marrakesh. The patients were allocated to two groups according to the severity of the disease. The tests analyzed were white blood cells plasma level's (WBCs), neutrophil count, lymphocyte count, hemoglobin, platelets, prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer, fibrinogen, C-reactive protein (CRP), Ferritin and lactate dehydrogenase (LDH). ***Results:*** Of 41 patients with COVID-19 twelve (29.6%) patients were defined as severe cases and twenty-nine (70.4%) were non-severe cases. There were numerous differences in blood routine parameters between the two groups. Compared to non-severe patients, leukocyte count, neutrophil counts, LDH, Ferritin and CRP were significantly higher. There were no significant differences in hemoglobin or lymphocyte counts in between the two groups. As well as APTT and the levels of d-dimers and fibrinogen. ***Conclusion:*** The following results prove to be relevant in assessing the disease since they can be used as markers for the more severe cases and allow us to adapt the therapeutic conduct following the needs of each individual patient.

Keywords: COVID 19, Hematological variations, Morocco, SARS Cov2.

INTRODUCTION

Sars-Cov-2 infected more than 7.039.918 people worldwide and had a death toll of 404 000 as of June 9, 2020 (Organization, 1961). After the initial epidemic in China, it spread to dozens of other countries, and was declared by the World health Organization as a pandemic on January 30th 2020.

Coronavirus disease (Covid-19) is caused by a new pathogen Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) which can generate an acute respiratory distress syndrome [1].

In Morocco, the first imported case was detected on March 2nd, 2020. According to the Moroccan Health Ministry, as of June 09, 2020, Morocco had over 8400 confirmed cases of COVID19 infection, with a case-fatality rate of 2, 47 %. SARS-CoV-2 was confirmed using real-time reverse transcriptase-polymerase chain reaction (RT-PCR), detected on the respiratory samples of these patients.

During this pandemic, the most important questions raised concern patients and clinicians to understand how the disease is spreading, what its clinical presentation with a severity profile is and which assessment or diagnostic measures should be used to plan different treatments [2].

The aim of our study is to outline the forecasters of the disease's progression and outcome through the hematological parameters performed in our context.

METHODS

Study design: We conducted a descriptive study on patients confirmed to have COVID 19 between April 16, 2020 and May 5, 2020 in the Mohamed Sixth University Hospital of Marrakesh. All cases were diagnosed through a real-time reverse-transcriptase–polymerase-chain-reaction (RT PCR) assay of the nasal and the pharyngeal swabs. We excluded the patients under 18 years of age and those admitted for COVID-19 illness despite negative test results.

The clinical outcomes (discharges, mortality) were monitored up to May 19, 2020, the final date of follow-up. Day one is the first day of admission, and subsequent days after admission were based on this calculation. We have collected laboratory data for 14 days after admission. We have based this time limit on the fact that most patients were recovered or were deceased after the defined time interval.

The patients were then put into two groups of patients, those admitted to the intensive care unit (ICU) and those who were not, in over 14 days of hospitalization.

We analyzed the white blood cells plasma level's (WBCs), neutrophil count, lymphocyte count, hemoglobin, platelets, prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer, fibrinogen, C-reactive protein (CRP), Ferritin and lactate dehydrogenase (LDH) in the two groups, with the objective of highlighting statistically significant differences which could be useful for the prediction of the prognosis of ICU and non-ICU COVID19 patients.

DATA COLLECTION

Demographic, epidemiological, and outcome data was extracted from the hospital electronic patient records using standard data collection. For each patient, blood samples were collected at the time of admission and in subsequent days during their hospitalization, for hematological and biochemistry investigations.

Complete blood counts were performed by Sysmex XN4000 (Sysmex, Japan). While the coagulation tests (prothrombin time, activated partial thromboplastin time, D-dimer, and fibrinogen) were performed by Sysmex CS-2100i. Chemistry assays were measured on Roche Cobas 6000 (Roche Diagnostic, Basel, Switzerland).

STATISTICAL ANALYSIS

The data collected was computerized and statistically analyzed using the SPSS program (Statistical Package for Social Science) version 15.0. Qualitative data were represented as frequencies and percentages. Quantitative data were represented as mean and standard deviation or median and interquartile range (IQR). Quantitative data was compared using the Student's t test or Mann–Whitney's U - test. The test results were considered significant when p value < 0.05.
Confidentiality and anonymity were respected during the data collection and analysis.

RESULTS

Demographic characteristics and outcome: The study population involved 41 hospitalized patients with confirmed COVID-19. The median age was 56 years IQR [22-90]. Male patients represent 61%; 29% (9 men and 3 women) were admitted in an intensive care unit (ICU) due to them developing an acute respiratory distress.

Compared with patients who were not admitted to ICU care (n=29), the severe group was significantly older (median age 65,5 vs 52 years, p=0.02). There was no significant difference between the ICU group and non-ICU group in gender (p=0.305).

Thirty-eight patients (92, 68%) were discharged from the hospital; those who did not receive intensive care were released after 10 days of hospitalization. A total of five patients (4 males and 1 female) were deceased, they had all required ICU support during their hospitalization period. The median age of the non-survivors was 70 [56-85] and the mean time from admission to death was 18 days (Table 1).

Laboratory findings in patients with COVID19 on admission: Tables 1 and 2 present the laboratory data of patients with COVID-19 for the ICU group and non-ICU group on admission to the hospital.

There were numerous differences in blood routine parameters between the two groups including higher white blood cell, neutrophil counts and prothrombin time (PT) as well as higher levels of ferritin, lactate dehydrogenase and c-reactive protein.

Patients with COVID-19 in ICU group had higher leucocyte counts ($p < 0.05$), higher neutrophil counts (6,72 vs 4,30× 109/L; $p < 0.05$), prolonged prothrombin times (71 vs 90 %; $p < 0.05$), higher ferritin (21352,90 vs 296,36; P = 0,013), higher LDH (546,32 vs 294,59; $p< 0.05$). The level of CRP was significantly higher in the ICU group (143,25 ± 81,55 mg/L) than in the non-ICU group (17,43 ± 22,52 mg/L) ($t = 2.660$; $p =0,002$).

There were no significant differences in neither hemoglobin nor lymphocyte counts in between the two groups. As well as APTT and the levels of d-dimers and fibrinogen.

Dynamic changes of laboratory findings in patients with COVID-19: We notice a synchronized steady decline in the Hemoglobin count in both groups. With much lower values in ICU group of patients. A growing trend was found in platelet count from severe patients during hospitalization. Over the follow-up period, platelet count decreased to reach the initial value. In non-severe patients the median count of platelet remained stable at a much lower level.

In ICU patients, the median count of lymphocyte was below the lower limit (1.5 × 109 /L) of normal range in the early stage of hospitalization, and reached the lower limit until day 9 after admission. Despite a slight ascent from day 3 after admission, lymphocyte count in non-severe patients was above the lower limit and generally increased during the follow-up.

Neutrophil count noticed a significant increase in ICU patients Compared to their Non-ICU counterparts that had continuously lower counts after each consequent test (Figure 1).

We notice a slight increase in APTT time and PT time shown to be prolonged in ICU patients group; with much stable trend in Non-ICU patients group.

D-dimers and fibrinogen on admission were higher in the ICU patient group than those in the Non-ICU group and generally increased during the follow-up (Figure 2).

Table-1: Demographic characteristics of patients with COVID19 and cell blood count findings at admission

		Overall (n=41)		**ICU patients (n=12)**		**Non ICU patients (n= 29)**		**P value**
		Median (IQR)	**No. (%)**	**Median (IQR)**	**No. (%)**	**Median (IQR)**	**No. (%)**	
DEMOGRAPHIC CHARACTERISTICS								
Age		56,00 (22-90)		65,5 (29-85)		52,00 (22-90)		0,02
Gender	**Male**		25 (61)		09 (75)		16 (55,2)	0,305
	Female		16 (39)		03 (25)		13 (44,8)	
OUTCOME								
Discharged			38(92,68)		7 (58,33)		29 (100,0)	0,002
Deceased			5 (12,19)		5 (41,67)		0 (0,0)	
CELL BLOOD COUNT FINDINGS AT ADMISSION								
Hb (g/dl)		13,6 (9,8-17,4)		13,2 (9,8-15,3)		13,7 (11,2-17,4)		0,064
	< 10		01 (2,4)		01 (8,3)		00(0,0)	
	10-12		06 (14,6)		03(25,0)		03(10,3)	
	>12		34(82,9)		8(66,7)		26(89,7)	
WBC (G/L)		7,23 (2,41-18,8)		14,15 (9,5- 18,8)		5,05 (2,41- 7,69)		0,031
	<4		3 (7,3)		0(0,0)		3 (10,3)	
	4--10		31 (75,6)		8 (66,7)		23(79,3)	
	>10		7 (17,1)		4 (33,3)		3 (10,3)	
ANC (G/L)		4,97 (1,42-16,6)		6,72 (4,59-10,63)		4,30 (1,42- 16,6)		0,005
	≤1,5		01 (2,4)		00 (0,0)		01 (3,4)	
	>1,5		40(97,6)		12(100,0)		28(96,6)	
ALC (G/L)		1,56 (0,43-5,40)		1,11 (0,43-2,75)		1,85 (0,61- 5,40)		0,085
	<0,5		1 (2,4)		1 (2,4)		0 (0,0)	
	0,5-1		10(24,4)		4 (33,3)		6 (20,7)	
	>1		30(73,2)		7(58,)		23(79,3)	
Platelets (G/L)		205 (53- 571)		224 (53- 396)		203 (98- 571)		0,656
	<100		1 (8,3)				1 (3,4)	
	100-150		0 (0,0)					
	>150		11 (91,7)					

WBC: White blood count, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count

Table-2: Coagulation parameters and biochemical findings at admission

	Overall (n=41)	**ICU patients (n=12)**	**Non ICU patients (n= 29)**	**P value**
COAGULATION PARAMETERS (Mean±SD)				
PT (%)	85,35 (14,36)	71,76 (15,16)	90,79 (9,98)	0,001
APTT (s)	27,84 (3,54)	26,37 (3,62)	28,45 (3,42)	0,168
D-dimers (ug/mL)	7,03 (14,12)	12,59 (19,22)	1,47 (1,46)	0,266
Fibrinogen (g/L)	4,43 (1,63)	4,77 (1,66)	4,10 (1,6)	0,532
BIOCHEMICAL FINDINGS (Mean±SD)				
Ferritin (ng/mL)	689,70 (711,68)	1352,90 (1005,83)	296,36 (334,927)	0,013
CRP (mg/L)	54,43 (74,52)	143,25 (81,55)	17,43 (22,52)	0,011
LDH (U/L)	375,32 (205,14)	546,88 (214,02)	294,59 (146,37)	0,002
PT: Prothrombin time, APTT: activated partial thromboplastin time, CRP: Creactive protein, LDH: Lactate dehydrogenase				

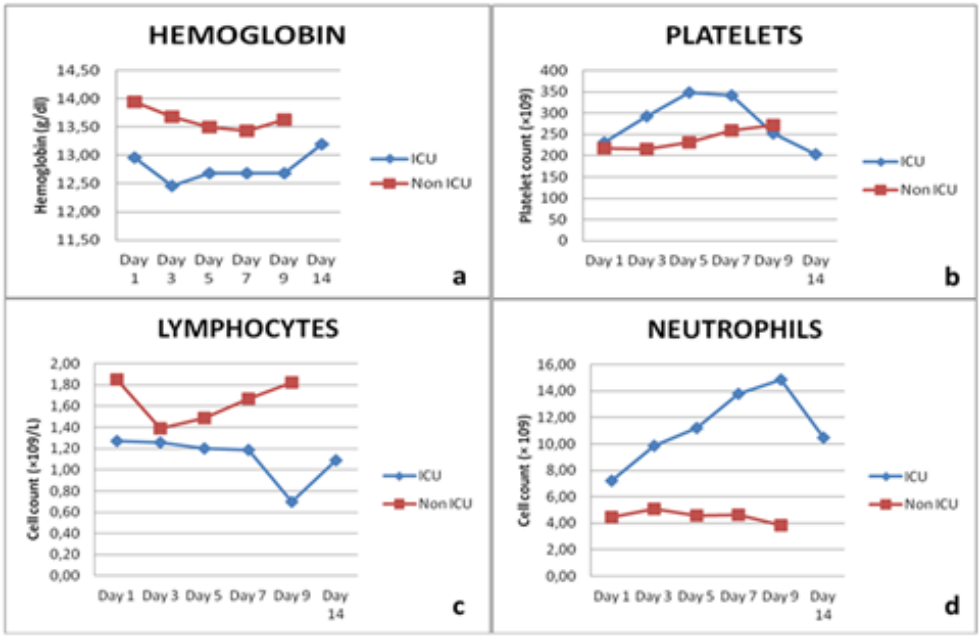

Fig-1: Evolution of cell blood count in ICU and non ICU groups

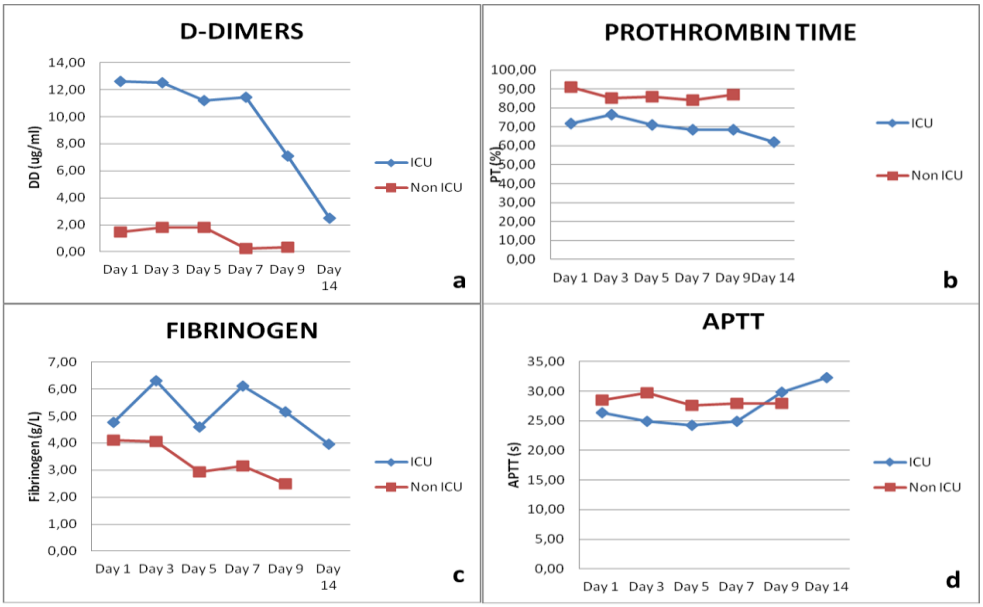

Fig-2: Dynamic profile of coagulation parameters in ICU and non ICU patients

DISCUSSION

Fast and accurate detection of SARS-CoV-2 is essential to control the outbreak of COVID-19. Nucleic acid detection is one of the main methods of laboratory diagnostics. Quantitative reverse transcription PCR (RT-qPCR) is a molecular biological diagnostic technology based on nucleic acid sequences. The complete sequences of the SARS-CoV-2 genome are available at GenBank. Thus, SARS-CoV-2's nucleic acid can be detected by RT-qPCR or by sequencing viral genes from nasopharyngeal and oropharyngeal swabs, stool, sputum, or blood samples [3].

Suspected and confirmed cases should be treated in designated hospitals with effective conditions of isolation and protection. Suspected cases must be treated in a room and isolated and confirmed cases can be treated in the same ward. In addition, critical cases should be admitted to the intensive care unit as soon as possible [4]. General treatment strategies include resting and supportive care, ensuring adequate energy intake, maintaining a stable internal environment (water, electrolytes and other internal environmental factors) and monitoring vital signs (heart rate, pulse, blood pressure, blood saturation) oxygen, respiratory rate, etc [4].

According to recent reports, the clinical manifestations of COVID-19 are heterogeneous [5]. Upon admission, 20-51% of patients with at least one comorbidity were reported, the most common being diabetes (10-20%), hypertension (10-15%) and other cardiovascular and cerebrovascular diseases (7-40%) [6]. unfortunately, there was a lack of information in our data to investigate this part of comorbidities.

The current study included 41 patients; the patients were then put into two groups in term of the severity of the disease. Thus, there was a mild group (29 patients) and the severe group admitted in intensive unit care (12 patients) followed up for one-month data. We evaluated longitudinal laboratory parameters in patients with COVID 19, and we reported the results of cell blood count, coagulation function and blood biochemistry.

Furthermore, the patients admitted to the ICU were older of age and nine of them were men. This suggests that age and gender can be risk factors for poor outcome. This data confirms the recent report that demonstrated that SARS Cov2 infection is more likely to affect males [1]. As of March 16, a total of 4,226 cases of COVID-19 had been reported in the United States, with the number of reports increasing to 500 or more per day as of March 14. Of the 2,449 patients of known age, 6% were aged 85 or older, 25% were 65 to 84 years old, 18% were between 55 and 64 years old, 17% were 45 to 54 years old and 29% were between 20 and 44 years old, while only 5% of cases occurred in people aged 0 to 19 years [7].

A total of 12 ICU patients and 29 non-ICU patients underwent blood routine examinations on admission. There were many differences in the parameters of blood routine between non-ICU group and ICU group as the Hemoglobin count was less than 12 in ICU patient compared to the non-ICU patients. Similarly, the WBC count was significantly associated with the low count of less than 4 G/L in the ICU patients as compared to non-ICU patients. These findings are supported by another study where severe non-ICU patients and severe ICU patients underwent blood routine examinations on admission. There were many differences in the parameters of blood routine between severe non-ICU group and severe ICU groups [7].

The current study finding showed that hemoglobin level are greater than 12G/L in overall patients, however, in ICU patients there is a decline in HB with less than 10G/L but no significant association was observed ($p=0.064$) these findings are similar in a context that hemoglobin value was significantly lower in COVID-19 patients with severe disease, compared with those with milder forms [8].

In this study the Absolute neutrophil count (ANC), Absolute lymphocyte count (ALC) were observed to be more than 1.5 G/L, greater than 1 G/L respectively in all covid-19 patients. However, there is significant association between them ($p<0.05$). These findings were consistent with another study finding where the neutrophil count was high and patients with COVID-19 had lower counts of leucocytes, lymphocytes, but also had higher neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR), which were compared with controls ($p< 0.001$) [7].

Of our ICU patients with COVID19 infection, five of 12 patients (42%) had lymphopenia on admission. Qin C et Al showed that lymphopenia was detected in 85% of several cases, and its depth is associated with the increased need for intensive care [9, 10].

Similarly, Tan Li et al. demonstrated that lymphopenia is an indicator of prognosis. In fact, the majority of severe cases presented lymphocyte levels <5% at the onset of the illness, requiring hospitalization in the intensive care unit, with a high mortality rate [11].

On the other hand, a meta-analysis with 1779 COVID-19 patients reported that thrombocytopenia increased the risk of severe COVID-19 [12]. Tissue damage to the lung caused by the inflammatory reaction can cause consumption of platelets and megakaryocytes resulting from platelet aggregation in the lungs and the formation of thrombi. It has been suggested that SARS-CoV-2 induces a state of disseminated intravascular

coagulopathy and further increases the consumption of platelets in the damaged lungs [12]. Similarly, no association was observed in COVID-19 patients with platelets. This is supported by other findings where the author has observed no association between platelets and the disease [13].

In term of coagulation parameters, it was clearly demonstrated that patients with severe forms had higher level of d-dimers during their disease course. This is due to the sustained inflammatory response [14]. Arachchilage et al. highlighted in a study concerning 183 patients with COVID-19 by comparing between discharged patients and deceased, that the levels of D-dimers were significantly higher in the group of non-survivors [15]. Unfortunately, not all patients in our study underwent level of d-dimers on admission, which is the origin of the insignificance of this variable (p= 0,266).

Overall patients had a PT mean SD time of85.35 + 14.36 which were significantly associated as well in all COVID patients. However, there is an increase in PT time shown to be prolonged in COVID patients. The findings were consistent with another finding where prothrombin time is prolonged and D-dimer is elevated [16]. Commonly used laboratory coagulation indicators include DD, PT, APTT. DD is a product of fibrinolytic solubilization of fibrin, and high levels of DD indicate that there is a state of hypercoagulation and secondary fibrinolysis In the body, which can be seen in an increase in the fibrinolytic activity of the body system [17].

Regarding CRP on admission, it was higher in the ICU patient group than those in the Non-ICU group and it was statistically significant as well (p< 0,05). Similar findings were seen where the author demonstrated CRP levels on admission in the moderate group were higher those in the severe group and those in the critical group were higher than those in the severe group. The difference was statistically significant [17]. Shaobo Shi et al. showed that higher CRP level waslinked to higher troponin, myocardial injury, and ARDS [18].

Another emerging biomarker for COVID 19 course is ferritin. Velavan et al. demonstrated that elevated ferritin levels due to secondary hemophagocytic lympho- histiocytosis (sHLH) and cytokine storm syndrome have been reported in severe COVID-19 patients [18]. It is a predictor of poor prognosis, as well as our current study (the mean ± SD in the ICU group: 1352, 90 (1005, 83) vs 296, 36 (334,927) in the Non-ICU group).

Accordingly in a retrospective cohort from china including 191 patients, 40% of patients admitted to the ICU had a high level of LDH [1], similar to the current study. Increased LDH was associated to ARDS and ICU support [19].

The limitation of our study is, the sample size was relatively small, which may have some impact on the statistical results We also recognize that our study was a single- center retrospective study, which may affect the generalization of the results However, this review is first on national level; and these results could prove to be helpful in the monitoring of patients leading to a more favorable outcome, especially in severe cases.

CONCLUSION

The following results prove to be relevant in assessing the disease since they can be used as markers for the more severe cases and allow us to adapt the therapeutic conduct following the needs of each individual patient.

Competing interests

The authors declare no competing interest.

Authors' contributions

All authors participated in the research design. WQ performed the data management and wrote the draft, AM performed the statistical analyses after discussion with all authors, HB revised the translation of the draft, SS and MA reviewed the manuscript and all authors approved the final the manuscript.

REFERENCES

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 17 mars 2020;323(11):1061.
2. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. Nat Med. avr 2020;26(4):506‑10.
3. Chu DKW, Pan Y, Cheng SMS, Hui KPY, Krishnan P, Liu Y. Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of Pneumonia. Clin Chem. 1 avr2020;66(4):549‑55.
4. Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, Lin R, Tang LF, Wang TL, Wang W, Wang YS. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World journal of pediatrics. 2020 Jun;16(3):240-6.
5. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. European Respiratory Journal. 2020 May 1;55(5).
6. Chen R, Sang L, Jiang M, Yang Z, Jia N, Fu W, Xie J, Guan W, Liang W, Ni Z, Hu Y. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19

patients in China. Journal of Allergy and Clinical Immunology. 2020 Jul 1;146(1):89-100.
7. Sun S, Cai X, Wang H, He G, Lin Y, Lu B, Chen C, Pan Y, Hu X. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clinica chimica acta. 2020 Aug 1;507:174-80.
8. 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.
9. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Xie C, Ma K, Shang K, Wang W, Tian DS. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clinical infectious diseases. 2020 Jul 28;71(15):762-8.
10. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y. 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 May 1;8(5):475-81.
11. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, Wang Q, Miao H. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal transduction and targeted therapy. 2020 Mar 27;5(1):1-3.
12. Liu Y, Sun W, Guo Y, Chen L, Zhang L, Zhao S, Long D, Yu L. Association between platelet parameters and mortality in coronavirus disease 2019: retrospective cohort study. Platelets. 2020 May 18;31(4):490-6.
13. Ferrari D, Motta A, Strollo M, Banfi G, Locatelli M. Routine blood tests as a potential diagnostic tool for COVID-19. Clinical chemistry and laboratory medicine (CCLM). 2020 Apr 16;1(ahead-of-print).
14. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, Zhu Y, Liu Y, Wang X, Wang L. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID- 19. Journal of medical virology. 2020 Jul;92(7):791-6.
15. Arachchillage DRJ, Laffan M. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. mai 2020;18(5):1233‑4.
16. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases With Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis. 16 mars 2020; ciaa272.
17. Long H, Nie L, Xiang X, Li H, Zhang X, Fu X. D-Dimer and Prothrombin Time Are the Significant Indicators of Severe COVID-19 and Poor Prognosis [Internet]. Vol. 2020, BioMed Research International. Hindawi; 2020
18. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. Int J Infect Dis. juin 2020; 95:304‑7.
19. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA internal medicine. 2020 Jul 1;180(7):934-43.