Variation of laboratory analyzes according to severity of illness in patients with COVID-19

Farrukh Saidov*, *Shokhida* Naimov, *Nilufar* Akhmedova, *Zarif* Ruziyev, *Sukhrob* Nurulloyev, and *Dildora* Madaripova

Bukhara State Medical Institute, Bukhara, Uzbekistan

Abstract. The Covid-19 disease is a new, unexplored problem for mankind. In a short time, the epidemic of the new coronavirus infection has spread to more than 200 countries. Changes in blood parameters are important for understanding the pathogenesis of this disease and for improving the treatment and diagnosis of COVID-19. The patients with coronavirus infection were evaluated according to the severity of the clinical symptoms and peripheral blood analysis. The general blood analysis showed that in the group of critically ill patients there was an increase in the number of leukocytes at the expense of neutrophils with segmental nuclei and rod nuclei. High reliable values of neutrophils and lymphocytes in peripheral blood were obtained as the most important predictors of severity of illness and risk of lethal outcome in patients.

1 Introduction

In December 2019, yet pathogenic human coronaviruses, 2019 novel coronavirus was recognized in Wuhan, China, and has caused serious illness and death. The ultimate scope and effect of this outbreak is unclear at present as the situation is rapidly evolving. Common symptoms of SARS include fever, cough, dyspnea, and occasionally watery diarrhea [1,11]. Of infected patients, 20% to 30% required mechanical ventilation and 10% died, with higher fatality rates in older patients and those with medical comorbidities. Human-to-human transmission was documented, mostly in health care settings. All three CoVs are listed in the WHO Blueprint list for priority pathogens for research because of their epidemic potential and lack of effective treatments. SARS-CoV was first identified in humans in Guangdong, China, in November, 2002 and subsequently spread rapidly worldwide to 29 countries, resulting in 8098 human SARS cases with 774 deaths (9.6% mortality) [2,13].

The ongoing SARS-CoV-2 outbreak has rapidly evolved and spread globally. As of Feb 29, 2020, there have been 83,652 laboratory confirmed cases of COVID-19, with 2791 deaths (3.4% mortality). Outside China, there have been 4691 cases reported from 51 countries with 67 deaths [3,12]. Infection of humans with SARS-CoV typically causes an influenza-like syndrome of malaise, rigors, fatigue and high fevers. In two-thirds of infected patients, the disease progresses to an atypical pneumonia, with shortness of breath and poor oxygen exchange in the alveoli. Many of these patients also develop watery diarrhea with active virus

* Corresponding author: gulnoza7767@gmail.com

shedding, which may increase the transmissibility of the virus. Respiratory insufficiency leading to respiratory failure is the most common cause of death among those infected with SARS-CoV[4]. Consistent with these clinical observations, the host cell-surface receptor for SARS-CoV, angiotensin-converting enzyme 2 (ACE2), is detected in the lungs and gastrointestinal tract[5,9,10]. Damage to the lungs of patients who are infected with SARS-CoV seems to occur directly, by viral destruction of alveolar and bronchial epithelial cells and macrophages, as well as indirectly, through production of immune mediators, although the exact role of these direct and indirect mechanisms remain controversial. Viral load, as determined from titres in nasopharyngeal aspirate, decreases 10–15 days after the onset of symptoms, even though clinical disease and alveolar damage worsen, indicating that the host immune response is responsible for some of the pathology in SARS-CoV-infected patients(6,7). However, nasopharyngeal viral titres do not necessarily reflect viral loads in the lungs, and high concentrations of virus have been detected in several organs at autopsy, including the lungs, intestine, kidneys and brain(8).

A complete blood count is a routine diagnostic test in patients with COVID-19. The number of leukocytes in peripheral blood more than 10-12x109/l is an important evidence in favor of a severe course of SARS-CoV-2 infection. Even lower values do not exclude bacterial co-infection of the disease. Leukocytosis more than 14x109/l or leukocytopenia less than 3x109/l is an indicator of the severity of SARS-CoV-2 and indicates an unfavorable prognosis.

Neutrophil granulocytes are the first to migrate to the inflammatory zone after being stimulated by various chemicals released from damaged tissue. Stimulants of different origins (endogenous and exogenous) are recognized by a set of special neutrophil receptors, which also increase the migration and activation of new circulating neutrophils. This is followed by the release of potentially cytotoxic products such as reactive oxygen species, proteases, and various cytokines that mediate inflammation [2,3,]. According to a 2020 study, patients with ARDS due to SARS-CoV-2 had higher levels of neutrophil granulocytes in their blood, which predicted poor outcomes [13]. Clinical symptoms of coronavirus infection correspond to the clinical presentation of acute respiratory diseases.

The purpose of the study: to evaluate changes in clinical symptoms and general blood tests according to the severity of the disease in patients with COVID-19.

Material and method: In 2020, an analysis of disease characteristics and hematological indicators was carried out among patients of the Multidisciplinary Medical Center of Bukhara Region who were treated with coronavirus infection during the pandemic. A total of 89 mild, moderate, and very severe patients were studied at BVKTTM from June to November 2020 to evaluate general blood tests and clinical symptoms according to the severity of the disease. Patients "Methodological recommendations. Based on the criteria of the classification "Prophylaxis, diagnosis and treatment of the new coronavirus infection COVID-19" (version 10.0 February 8, 2021 and version 11.0 May 7, 2021) were included in the study. Patients SpO2<95%; t≥38˚C; NOS>22, as well as bilateral pneumonia were selected based on 25% changes (the presence of CT results of lung examination). SpO2≤93% in patients; t≥39˚C; NOS≥30 criteria were considered severe. General blood analysis, erythrocyte index, thrombocyte index and leukoformula were checked in all patients. Also, from biochemical blood tests, total protein, ALT, AST, AChTV, fibrinogen, prothrombin time and SRO were examined. Statistical analysis of data was carried out on the basis of Microsoft Excel 2007. The statistical confidence value was set based on Student's criterion.

2 Results

Patients with COVID-19 were divided into 3 groups according to the severity of the disease. 32 patients were divided into 1 group with mild symptoms, 2 groups with 30 patients with

moderate symptoms and 3 groups with 27 patients with very severe symptoms. Patients were analyzed according to sex, age, TVI and body temperature. There was no difference between groups according to gender. The average age of the patients in the 3 groups was 62±4.2, and the indicators of the 1st and 2nd groups were 55±3.4 and 59±2.8, and had a reliable difference (p1-2 = 0.05* p1-3 = 0 ,05*).The body weight index was also 32.4±6.3 in the very heavy group of patients, and a reliable value was reached compared to 28.9±5.5 in the 1st group of patients (p1-3 = 0.05*).

The meeting of clinical signs of the patients involved in the study is presented in the following figure (Figure 1). Out of 89 patients, 48% had respiratory failure, 33% had respiratory failure, and 19% had respiratory failure. Patients with sepsis and DIC syndrome were not included in the study.

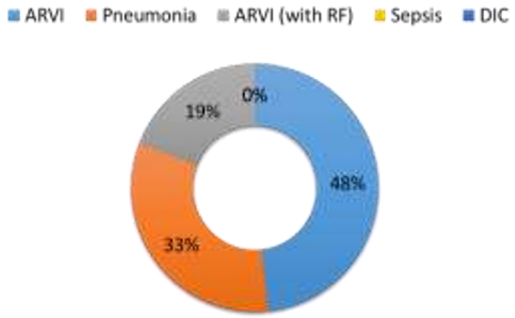

Fig. 1. The incidence rate of clinical signs of COVID-19, %

The frequency of clinical signs in the examined patients is presented in the table below. Cough was detected in 17 (53.1%) patients in group 1, and in 20 (66.7%) and 22 (81.5%) patients in groups 2 and 3. Also, there was no statistical difference between the groups in the clinical signs of shortness of breath and fatigue. Muscle pain, on the other hand, was 92.6% in the group of very severe patients, 18.7% and 53.3% in mild and moderate patients, respectively, and a statistical value was reached (<0.05) (Fig. 1).

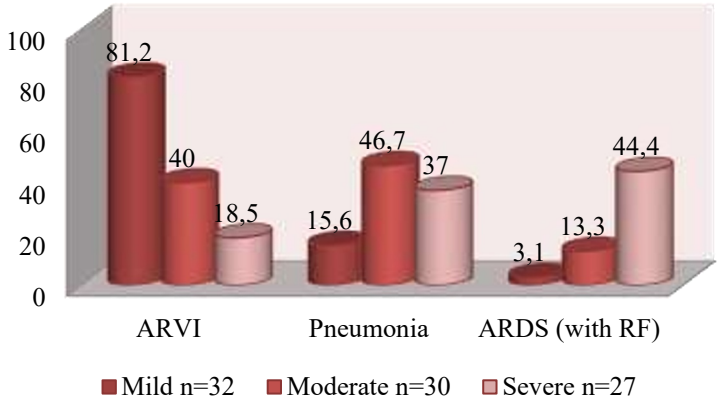

Fig. 2. Incidence of clinical forms in patients with COVID-19 according to the severity of the disease.

When the patients were studied according to the clinical forms of coronavirus infection, among the total 89 patients, 81.2% of the A group had ARVI (upper respiratory tract infection) and 3.1% of the C group. The incidence of pneumonia without respiratory failure

in moderate V groups and very severe C groups was 46.7% and 13.7%, respectively, and acute respiratory distress syndrome with respiratory failure was 4 (13.3%) and 12 (44.4 %) was recorded in patients (Fig. 1).

Table 1. The rate of comorbidities according to the severity of the disease.

Diseases	**1 group n=32 Abs,%**	**2 groups n=30 Abs,%**	**3 groups n=27 Abs,%**	**The importance of differences**
	1	**2**	**3**	
IHD	6 (18.7)	10 (33.3)	17 (62.9)	ND
AP	8 (25)	11 (36.6)	14 (51.8)	<0.05
DM type2	2 (6.3)	8 (26.7)	16 (59.2)	ND
IHD+AH	3 (9.4)	6 (20)	11 (40.7)	ND
AH+DM type2	1 (3.1)	4 (13.3)	5 (18.5)	ND
YIHD+DM type 2	2 (6.3)	3 (10)	8 (29.6)	<0.05

According to the severity of comorbidities in patients, 8 (25%) patients in group 1 had more arterial hypertension comorbidities compared to ischemic heart disease, diabetes mellitus, and other comorbidities (r<0.05). In the analysis of placental diseases of very severe patients, the cases of the combination of UIC and UIC with QD 2 were found in 17 (62.9%) and 8 (29.6%) patients, respectively (r<0.05). In general, comorbidities were found more in the group of patients with very severe disease compared to mild disease.

Table 2. Results of erythrocyte and platelet index from peripheral blood analyzes according to the severity of acute exacerbations.

Signs	**Control healthy group n=25 4 groups**	**1 group n=32 Abs,%**	**2 groups n=30 Abs,%**	**3 groups n=27 Abs,%**	**The importance of differences**
	4	**1**	**2**	**3**	
Erythrocyte indexes					
MCV, fl	87.6±0.7	88.9±1.2	90.8±1.4	88.0±1.6	R1-2=0.150
MCH, pg	32.1±0.1	31.8±0.7	31.6±0.8	31.3±0.7	R1-2=0.03
MCHC, g\dL	33.9±1.2	32.9±0.2	32.7±0.3	31.2±0.4	R1-2=0.04 R1-3=0.01
RDW,%	13.1±0.2	13,23±0.3	13.62±0.4	14.89±0.5	R1-3=0.05
Platelet index					
PDW, fl	12.56±0.4	11.59±0.5	11.78±0.8	12.21±0.5	R1-2=0.08
MPV, fl	9.6±0.1	9.3±0.3	9.5±0.2	9.7±0.2	R1-3=0.02
PCT	23.8±1.3	21.3±1.5	23.7±2.1	25.7±1.3	R1-3=0.05
Platelet, 109 /l	268.6±11.2	304.7±16.1	318.6±25.1	265.8±18.4	R1-2=0.09
Erythrocyte, 1012/l	4.25±0.03	4.32±0.08	4.12±0.12	4.01±0.01	P1-3=0.03
Hemoglobin, g/l	130.1±1.43	139.4±3.2	120±3.6	110.4±3.5	P1-3=0.01
Ht, %	41.8±0.34	42.7±1.3	37.2±1.7	40.1±1.1	R1-2=0.027
Leukocyte, 109/l	4.1±1.2	9.3±1.4	12.1±1.5	13.2±1.1	P1-3=0.01
ECR mm\s	4.2±0.5	25.1±3.2	32.5±4.2	33.1±3.7	R1-3=0.03

Total blood and biochemical blood tests were different in our examined patients. General and biochemical blood analysis were obtained from the day of admission of the patients to the hospital, therefore corresponding to the acute period of the disease. In the general blood

analysis, the number of leukocytes according to the severity of the disease (9.3±1.4; 13.2±1.1 P1-3=0.01) and an increase in the amount of EC (25.1±3.2; 33.1±3.7 P1-3=0.03) was observed and a statistically reliable value was achieved. In particular, left shift of SOE and leukocyte count was higher in patients with very severe novel coronavirus infection than in mild patients.

An increase in the number of lymphocytes during the course of the disease compared to those with a mild course was also noteworthy. These results are associated with insufficient immune response in critically ill patients (Table 2).

A decrease in the amount of total protein and albumin is characteristic in patients with coronavirus infection, and in mild patients65.8±3.2 and average of 56.4±3.1 in critically ill patients, statisticallyA confidence value of p1-3 < 0.01 was reached. Albumin content also tended to decrease accordingly.46±2.4 and 36±2.3,p1-3 < 0.01; p2-3 < 0.06 equaled the statistically reliable value.

Also, changes in fibrinogen and AChTV levels were consistent with disease severity. In this case, 3.87 in 1 group of patients± 1.2 and22.4± 3.2 in 2 groups of patients3.4± 1.5 and26.8± 3.4, and in 3 groups of patients,3.01± 1.7 and39.1± 3.5 results were obtained and a statistically reliable difference was obtained (p1-2 < 0.01; p1-3 < 0.05; p2-3 < 0.05).

Similarly, SRO is moderate in mild coronavirus patientswas 12.3±2.3 and reached 36.3±0.8 in very heavy walkers (p1-3 < 0.001). Thus, the results of the study showed a several-fold increase in the inflammation index compared to normal groups and intergroup values.

According to instrumental examinations, lung damage on CT was 29% in groups 1, and 67% and 71% of lung damage were found in severe and very severe patients, respectively, and this was a reliable difference (p1-2 < 0.001; p1-3 < 0.001).

Table 3. Results of biochemical blood analyzes and instrumental examination according to the severity of COVID-19 disease.

Signs	**1 group n=32 Abs,%**	**2 groups n=30 Abs,%**	**3 groups n=27 Abs,%**	**The importance of differences**
	1	**2**	**3**	
Total protein, g\l	65.8±3.2	57.1 ± 3.3	56.4±3.1	p1-2 < 0.01 p1-3 < 0.01
Albumin, g\l	46±2.4	39±1.2	36±2.3	p1-2 < 0.01 p1-3 < 0.01 p2-3 < 0.06
Total bilirubin, μmol\l	9.18±1.2	8.6±1.3	11±1.3	ND
ALT	27.8 ± 3.1	24.4±2.8	25.5±4.6	ND
AST	27.9 ± 5.2	23.3±4.7	32.5±5.6	ND
Fibrinogen	3.87± 1.2	3.4± 1.5	3.01± 1.7	p1-2 < 0.01 p1-3 < 0.05 p2-3 < 0.05
ATT	22.4± 3.2	26.8± 3.4	39.1± 3.5	p1-2 < 0.012 p1-3 < 0.01 p2-3 < 0.01
Prothrombin time, sec	10.60± 2.2	13.2± 2.3	16.2± 2.1	p1-2 < 0.012 p1-3 < 0.01 p2-3 < 0.01
SRP	12.3±2.3	25.6±1.2	36.3±0.8	p1-2 < 0.012 p1-3 < 0.001 p2-3 < 0.001
Lung damage according to CT data, %	28.8%	67.5%	71.1%	p1-2 < 0.001 p1-3 < 0.001

3 Conclusion

Thus, taking into account the variational methods of statistics, different clinical and laboratory indicators were obtained in patients with mild, severe and very severe course of COVID-19. In the laboratory analyzes taken from the patient's 1-day hospitalization, leukocytosis, increased monocytes, increased EChT, lymphocytopenia, C-reactive protein, AChTV, and prothrombin time were revealed.New arrivalCOVID-19Although the pandemic period of the infection has been more than three years, this disease remains relevant to this day due to its constant impact on the health system of the whole world.

COVID-19in the patients with a mild course, mainly arterial hypertension, in the group of patients with a severe and very severe course, accompanying diseases such as diabetes mellitus and IUD were noted at a high level and a statistically reliable value was reached (r1-3<0.05).COVID-19according to the results of laboratory analysis in patients, an increase in the number of leukocytes due to neutrophils with segmental nuclei and rod nuclei (r<0.05) and a decrease in the reliable absolute number of lymphocytes in peripheral blood (r<0.05) were observed in very severe patients. According to the results of the research, ferritin level, absolute number of neutrophils and lymphocytes in peripheral blood are the most important parameters that predict the severity of the disease and the risk of lethal outcome in patients.

References

1. E. De Wit et al., Nature reviews microbiology **14(8)**, 523-534 (2016)
2. J. S. M. Peiris et al., New England Journal of Medicine **349(25)**, 2431-2441 (2003)
3. WHO. Outbreak of the coronavirus disease (COVID-19), https://www.who.int/emergencies/diseases/novel-coronavirus-2019
4. J. S. Peiris, K. Y. Yuen, A. D. Osterhaus, K. Stohr, N. Engl. J. Med. **349**, 2431–2441 (2003)
5. I. Hamming et al., J. Pathol. **203**, 631–637 (2004)
6. K. H. Chan et al., Emerg. Infect. Dis. **10**, 294–299 (2004)
7. T. Mazzulli et al., Emerg. Infect. Dis. **10**, 20–24 (2004)
8. A. Giacomelli, L. Pezzati, F. Conti, D. Bernacchia, M. Siano, L. Oreni, S. Rusconi, C. Gervasoni, A. L. Ridolfo, G. Rizzardini et al., Self-reported olfactory and taste disorders in SARS-CoV-2 patients: A cross-sectional study. Clin Infect Dis ciaa330 (2020)
9. S. Recalcati, J Eur Acad Dermatol Venereol **26** (2020)
10. Y. Cao, L. Li, Z. Feng, S. Wan, P. Huang, X. Sun, F. Wen, X. Huang, G. Ning, W. Wang, Cell Discov. **6(11)** (2020)
11. Z. M. Abdurakhmanov, B. Y. Umarov, M. M. Abdurakhmanov, Rational Pharmacotherapy in Cardiology **17(4)** (2021)
12. A. K. Ashirmetov, I. R. Mavlyanov, Z. I. Mavlyanov, G. Z. Zharylkasynova, Health Risk Analysis **4** (2020)
13. A. R. Oblokulov, G. E. Niyozov, International Journal of Pharmaceutical Research **12(4)** (2020)
14. A. N. Sharipovna, S. G. Tulkinzhanovna, M. M. Hayatovna, G. N. Odiljonovna, International Journal of Current Research and Review **13(2)**, 127-131 (2021)
15. L. L. Ivanova, Scientific notes SSGA **4**, 130-138 (2012)
16. A. R. Masalimova, *The content and technology of corporate training of mentors: pedagogical component: teaching aid* (KFU Publishing House, Kazan, 2015)