

ANOMALIES BIOLOGIQUES CHEZ DES PATIENTS ALGÉRIENS HOSPITALISÉS AVEC COVID-19

MEGDAD F.Z⁽¹⁾, SAADI A.S^(1,2), ZENDJABIL M^(2,3).

1) Service de Biochimie, EHU d'Oran 1er Novembre 1954, Oran, Algérie.

2) Faculté de Médecine, Université d'Oran 1 Ahmed Benbella, Oran, Algérie.

3) Service de Biochimie, CHU d'Oran Dr Benzerdjeb, Oran, Algérie.

E-mail : megdad.fatima@hotmail.com

saadisoulef31@hotmail.com

zendjabil.mustapha@univ-oran1.dz

RÉSUMÉ :

La maladie à coronavirus 2019 (COVID-19) est due au syndrome respiratoire aigu sévère coronavirus 2 (SRAS-CoV-2) qui s'est propagé dans le monde entier. Le but de ce travail est d'étudier et de décrire les caractéristiques de laboratoire des patients algériens hospitalisés pour une infection au SRAS-CoV-2. Notre étude a porté sur 60 patients atteints de COVID-19 en mars et avril 2020. Des échantillons d'écouvillonnages pharyngés et nasaux ont été collectés pour la détection des acides nucléiques viraux SARS-CoV-2 en utilisant la réaction de polymérisation en chaîne en temps réel par transcription inverse (rRT-PCR). Nous avons collecté des données biologiques auprès des patients dès leur admission et à leur sortie de l'hôpital. Résultats : l'âge médian de tous les patients était de 49 ans avec des extrêmes allant de 18 à 88 ans et 37 (61,66%) étaient des hommes. Plusieurs différences significatives ont été notées entre les patients admis en unité de soins intensifs (n = 9) et ceux qui ne l'ont pas été (n = 51), notamment l'hyperleucocytose (1.4-fois), l'hyperneutrophilie (2.0-fois), la lymphopénie (0.3-fois), l'éosinopénie (0.02-fois), l'hypoalbuminémie (0.75-fois), l'hypocholestérolémie (0.8-fois), l'hypocalcémie (0.9-fois), ainsi que des valeurs plus élevées de CRP (6.0-fois), fibrinogène (1.8-fois), troponine I (637-fois), NT-proBNP (23.9-fois), aspartate aminotransférase (1.8-fois), alanine aminotransférase (1.4-fois), créatine kinase (2.2-fois), glucose (1.6-fois) et d'acide urique (1.9-fois). Ces biomarqueurs sont utilisés pour prédire la gravité et le pronostic de la maladie et doivent être suivis rigoureusement tout au long de l'hospitalisation pour guider les soins cliniques. Conclusion : cette étude nous a permis de déterminer le profil biologique des patients atteints de COVID-19 et de définir les anomalies biologiques associées à un risque de décès élevé dans notre population.

Mots clés : COVID-19, SARS-CoV-2, caractéristiques de laboratoire, Biochimie.

ABSTRACT: LABORATORY ABNORMALITIES IN ALGERIAN PATIENTS HOSPITALIZED WITH COVID-19.

Coronavirus disease 2019 (COVID-19) is due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which spread around the world. The aim of this study is to investigate and describe the laboratory characteristics of Algerian patients hospitalized for SARS-CoV-2 infection. Our study covered 60 patients with COVID-19 in March and April 2020. Patient pharyngeal and nasal swab specimens were collected for the SARS-CoV-2 viral nucleic acid detection using real-time reverse-transcription polymerase chain reaction (rRT-PCR) assay. We collected biological data from patients from their admission and upon discharge from the hospital. Results : the median age for all patients was 49 years with extremes ranging from 18 to 88 years and 37 (61.66%) were males. Several significant differences were noted between patients who were admitted to the intensive care unit (n=9) and those who did not (n=51), especially leukocytosis (1.4-fold), neutrophilia (2.0-fold), lymphopenia (0.3-fold), eosinopenia (0.02-fold), hypoalbuminemia (0.75-fold), hypocholesterolemia (0.8-fold), hypocalcemia (0.9-fold), as well as higher values of CRP (6.0-fold), fibrinogen (1.8-fold), troponin I (637-fold), NT-proBNP (23.9-fold), aspartate aminotransferase (1.8-fold), alanine aminotransferase (1.4-fold), creatine kinase (2.2-fold), glucose (1.6-fold) and uric acid (1.9-fold). These biomarkers are used to predict the severity and prognosis of the disease and should be followed rigorously throughout hospitalization to guide clinical care. Conclusion : this study allowed us to determine the biological profile of patients with COVID-19 and to define laboratory abnormalities associated with a high-risk of death in our population.

Key words : COVID-19, SARS-CoV-2, Laboratory characteristics, Biochemistry.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which emerged in Wuhan (China) and spread around the world [1]. SARS-CoV-2 is a betacoronavirus that is very similar to two other coronaviruses found in bats, bat-SL-CoVZC45 and bat-SL-CoVZXC21. Similarly to SARS-CoV and MERS-CoV, SARS-CoV2 may also have originated from bats [2], although the exact origin of this virus has not yet been determined. As of May 8, 2020, the latest statistics from the World Health Organization (WHO) revealed that COVID-19 has already affected more than 3.7 million people worldwide, causing up to 265,000 deaths. In Algeria, 5182 patients were diagnosed with COVID-19, with 483 deaths recorded. Although these figures are much lower than those recorded in other Mediterranean countries such as France or Italy, COVID-19 had a significant impact on our lifestyle and our health system.

Laboratory medicine has a key role in the fight against COVID-19. It is involved in the diagnosis of COVID-19 by real-time reverse-transcription polymerase chain reaction (rRT-PCR) assay and in serological surveillance by the detection of anti-COVID-19 antibodies [3]. In addition, laboratory tests play an important role in prognosis, following-up and therapeutic monitoring of patients with COVID-19 [4]. There are some studies that describe the laboratory features of patients with COVID-19 in China, United States of America and Europe. To our knowledge, no similar study has been conducted in North Africa. It is important to note that significant differences were noted in the clinical and demographic features of COVID-19 patients in different regions of the world [5]. Therefore, we sought to study and describe the laboratory characteristics of Algerian patients hospitalized for SARS-CoV-2 infection in the region of Oran.

PATIENTS AND METHODS

1. Patients

Our study includes 60 patients with COVID-19 hospitalized in the EHU Oran University Hospital (Algeria) from March to April 2020. The study was approved by the hospital and was conducted in accordance with the Helsinki guidelines [6]. SARS-CoV-2 infection was diagnosed by rRT-PCR on pharyngeal and nasal swab specimens. We collected biological data from patients from their admission and upon discharge from the hospital. On average, patients were hospitalized for 10 days. For the deceased patients, we used values from the last analysis before death.

2. Blood collection and assays

Venous blood sampling was performed in the morning. The blood was collected on tubes containing lithium heparin, tripotassium ethylenediamine tetraacetic acid (EDTA) and sodium citrate as an anticoagulant. The heparinized tubes were centrifuged within 1 hour at 2600 g for 10 minutes at room temperature, the plasmas obtained were used for biochemical assays. The whole blood contained in the EDTA tube was intended for a complete blood count tests. The sodium citrate tubes were centrifuged within 1 hour at 2500 g for 15 minutes at room temperature, the plasmas obtained were used for hemostasis tests. Biochemistry tests were performed on Advia 1800 (Siemens Healthcare Diagnostics Inc., NY, United States). Troponin I and NT-proBNP were measured on Dimension EXL 200 (Siemens Healthcare Diagnostics Inc., NY, United States), and hematology tests were carried out on Advia 2120i (Siemens Healthcare Diagnostics Inc., NY, United States) and Stago-STA Satellite (Diagnostica Stago, Inc., hereafter, Stago).

3. STATISTICAL ANALYSIS

Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were summarized as counts and percentages. All statistical analysis was performed on MedCalc statistical software (Version 19.1.13). Values of $p < 0.05$ were considered as statistically significant.

RESULTS

Our study includes 60 patients who were diagnosed with COVID-19. Mean age was 49 years with extremes ranging from 18 to 88 years, 37 (61.66%) were males. All patients received treatment with hydroxychloroquine and azithromycin. The evolution of the majority of patients was favorable. A total of 9 (15%) patients died after their admission to the intensive care unit for respiratory distress syndrome.

The laboratory results on admission and upon discharge from the hospital are reported in Table I, while, Table II summarizes frequencies and percentages of results which exceed the reference limits for each parameter.

There is a statistically significant difference between the ages of deceased patients and those who were cured with 58.75 (37-88) and 46.78 (2-83) years old respectively. By comparing the values of deceased patients ($n=9$) with those who were cured ($n=51$) at admission, we observe a leukocytosis (10.92 ± 6.12 vs $7.59 \pm 3.90 \times 10^9/L$), neutrophilia (9.66 ± 6.26 vs $4.90 \pm 3.73 \times 10^9/L$), lymphopenia (0.50 ± 0.29 vs $1.60 \pm 0.79 \times 10^9/L$), eosinopenia (0.002 ± 0.004 vs $0.13 \pm 0.33 \times 10^9/L$); a significant increase in C-reactive protein (CRP) (195.75 ± 118.38 vs 32.68 ± 58.03 mg/l), fibrinogen (8.77 ± 0.11 vs 4.92 ± 2.14 g/l), troponin I (12.74 ± 17.87 vs 0.02 ± 0.08 ng/ml), NT-proBNP (1225 ± 261.62 vs 51.25 ± 42.33 pg/ml), aspartate aminotransferase (74.78 ± 55.17 vs 40.47 ± 24.92 UI/l), alanine aminotransferase (58.67 ± 37.91 vs 41.00 ± 34.10 UI/l), creatinine kinase (201.00 ± 256.39 vs 92.00 ± 58.05 UI/l), glucose (1.96 ± 0.88 vs 1.21 ± 0.54 g/l) and uric acid (85.23 ± 14.56 vs 43.61 ± 10.00 mg/l). There is also a low level of protidemia (63.14 ± 9.74 vs 73.26 ± 8.00 g/l), albuminemia (31.25 ± 5.34 vs 41.32 ± 5.34 g/l), cholesterolemia (1.33 ± 0.19 vs 1.67 ± 0.37 g/l) and calcemia (84.88 ± 6.78 vs 93.02 ± 6.25 mg/l). Platelet count, hemoglobin level, prothrombin time and activated cephalin time, urea, creatinine, total bilirubin and alkaline phosphatase were normal for both populations.

Patients admitted to the intensive care unit presented before their death, a leukocytosis ($18.47 \pm 5.36 \times 10^9/L$), neutrophilia ($16.41 \pm 6.47 \times 10^9/L$), lymphopenia ($1.10 \pm 1.66 \times 10^9/L$), a low hemoglobin count (9.48 ± 1.94 g/dl), thrombocytopenia ($109.67 \pm 59.07 \times 10^9/L$), An allonged prothrombin time (19.33 ± 2.74 secondes) and activated cephalin time (45.12 ± 10.28 secondes), a significant increase in fibrinogen (7.7 ± 2.21 g/l), C-reactive protein (CRP) (265.14 ± 50.63 mg/l), troponin I (1.64 ± 4.29 ng/ml), NT-proBNP (1348 ± 685.39 pg/ml), urea (1.34 ± 0.70 g/l), creatinine (30.49 ± 20.02 mg/l), glucose (4.19 ± 2.24 g/l), aspartate aminotransferase (106.11 ± 65.14 UI/l), alanine aminotransferase (45.55 ± 17.36 UI/l), alkaline phosphatase (151.55 ± 103.80 UI/l), total bilirubin (59.53 ± 46.34 mg/l), direct bilirubin (56.07 ± 34.27 mg/l), creatinine kinase (330.12 ± 349.04 UI/l), with an hypoprotidemia (54.53 ± 11.74 g/l), hypoalbuminemia (19.12 ± 7.19 g/l), hypocholesterolemia (1.09 ± 0.35 g/l) and hypocalcemia (76.73 ± 11.14 mg/l).

DISCUSSION

Our study is the first to describe laboratory characteristics and their evolution in Algerian patients with covid-19. Lymphopenia

Table I. Laboratory characteristics of patients hospitalized with COVID-19 on admission and upon discharge from the hospital.

Variable	Reference values	Admission	Discharge	p-value
White blood cell count, x10 ⁹ /L	4-10	8.16 ± 4.46	9.99 ± 5.87	0.0259
Lymphocyte count, x10 ⁹ /L	1.5-4	1.43 ± 0.83	1.54 ± 0.98	0.4876
Neutrophil count, x10 ⁹ /L	1.9-7.5	5.64 ± 4.48	7.48 ± 6.48	0.0922
Monocyte count, x10 ⁹ /L	0.1-1	0.71 ± 0.43	0.67 ± 0.34	0.9666
Eosinophil count, x10 ⁹ /L	0.02-0.5	0.11 ± 0.30	0.09 ± 0.08	0.0022
Basophil count, x10 ⁹ /L	0-0.1	0.05 ± 0.03	0.06 ± 0.04	0.2313
Thrombocyte count, x10 ⁹ /L	130-400	213.97 ± 88.41	230.76 ± 124.42	0.6390
Hemoglobin, g/dl	12-18	13.03 ± 1.49	11.58 ± 1.89	0.0051
Prothrombin time, %	70-100	95.35 ± 6.49	81.31 ± 18.48	0.0018
Quicktime, seconds	Witness=13.2	13.51 ± 0.98	15.58 ± 3.35	0.0092
Activated cephalin time, seconds	Witness=31	28.90 ± 4.19	36.42 ± 9.33	0.0175
Fibrinogen, g/l	2-4	5.51 ± 2.43	6.21 ± 2.87	0.2892
Glucose, g/l	0.70-1.10	1.31 ± 0.65	2.17 ± 1.82	0.0106
Urea, g/l	0.15-0.45	0.32 ± 0.25	0.58 ± 0.64	0.0199
Creatinine, mg/l	H : 7-13 F : 5-11	10.08 ± 14.83	16.05 ± 24.63	0.0243
Sodium, mmol/l	132-146	137.51 ± 3.41	138.36 ± 3.52	0.1736
Potassium, mmol/l	3.50-5.50	3.97 ± 0.46	4.51 ± 1.06	0.0032
Chloride, mmol/l	99-109	101.33 ± 4.19	104.38 ± 4.33	<0.0001
Aspartate amino transferase, UI/l	H<50, F<35	47.65 ± 35.59	58.35 ± 53.23	0.21
Alanine aminotransferase, UI/l	H<50, F<35	44.53 ± 35.18	53.46 ± 58.00	0.28
Total bilirubin, mg/l	3-12	7.84 ± 4.09	22.24 ± 35.35	0.0075
Direct bilirubin, mg/l	<2	4.34 ± 3.55	17.39 ± 31.19	0.0077
Alkaline phosphatase, UI/l	45-129	72.87 ± 34.95	102.94 ± 84.73	0.0429
C-reactive protein, mg/l	0-6	61.04 ± 9.30	109.69 ± 112.25	0.3023
Calcium, mg/l	86-100	91.25 ± 7.10	84.22 ± 10.35	0.0936
Phosphorus, mg/l	21-51	30.96 ± 9.75	34.78 ± 22.71	0.4737
Uric acid, mg/l	H : 37-90 F : 31-78	48.33 ± 18.30	53.37 ± 27.89	0.6809
Total protein, g/l	57-82	71.53 ± 9.05	67.55 ± 13.14	0.2833
Albumin, g/l	32-48	39.42 ± 6.61	32.12 ± 13.25	0.2288
Total cholesterol, g/l	1.10-2	1.59 ± 0.36	1.41 ± 0.46	0.5460
Creatine Kinase, UI/l	H : 32-294 F : 33-211	109.21 ± 108.53	197.15 ± 244.13	0.8725
Troponin I, ng/ml	0-0.056	1.84 ± 6.77	0.96 ± 3.280.4752	
NT-ProBNP, pg/ml	0-125	218.93 ± 434.11	872.54 ± 846.92	0.4469

nia is observed in 60% of cases at admission which reflects decreased immunological response to the virus. CRP is a sensitive marker of the inflammatory response which is increased on admission and slightly more on upon discharge. It is interesting to note that the values of this protein are much higher in deceased patients than in those who were cured. Fibrinogen is also an acute phase protein associated with the inflammatory process that accompanies the disease. Troponin is associated with cardiovascular risk and therefore mortality. Thus, results show a decrease in troponin between the time of admission and discharge. In contrast, we have not seen a decrease in NT-proBNP. In addition, these two cardiac markers are significantly higher at the time of admission in patients who died, making them good prognostic markers. Transaminases are increased by more than 33,33%, especially in patients with a poor prognosis. These patients have likely liver disease before the infection. However, SARS-CoV-2 infection may also explain hepatic cytolysis. In fact, SARS-CoV-2 uses angiotensin converting enzyme 2 (ACE2) receptors to enter the body, which are found not only in the respiratory tract, but also in the gastrointestinal mucosa and

hepatic cholangiocytes. Moreover, SARS-CoV-2 was found in the stool of several patients with COVID-19 [7]. Blood glucose level is increased in our patients, especially in the 9 patients who died, diabetes is already known as a risk factor for poor prognosis in COVID-19 [8].

Analysis of several Chinese data shows that the most frequent laboratory abnormalities were lymphopenia (35–75% of cases), increased values of CRP (75–93%), LDH (27–92%), erythrocyte sedimentation rate (up to 85%) and D-dimer (36–43%). Conversely, serum albumin (50–98%) and hemoglobin (41–50%) are low [9]. In a US study including 16 patients hospitalized with COVID-19, Aggarwal et al.[10] observed hyponatremia (50%), increased values of CRP (100%), LDH (80%), and aminotransferase (38%).

At admission, several significant differences were noted between patients who were admitted to the intensive care unit and those who did not, especially leukocytosis (1.4-fold), neutrophilia (2.0-fold), lymphopenia (0.3-fold), eosinopenia (0.02-fold), hypoalbuminemia (0.75-fold), hypocholesterolemia (0.8-fold), hypocalcemia (0.9-fold), as well as higher values of CRP (6.0-fold), fibrinogen (1.8-fold), troponin I (637-fold), NT-proBNP (23.9-fold), aspartate aminotransferase (1.8-fold), alanine aminotransferase (1.4-fold), creatine kinase (2.2-fold), glucose (1.6-fold) and uric acid (1.9-fold). These biomarkers are used to predict the severity and prognosis of the disease and should be followed rigorously throughout hospitalization to guide clinical care.

Patients admitted to the intensive care unit presented a disseminated intravascular coagulation (DIC) before their death. This explains the prolongation of prothrombin time and activated cephalin time and thrombocytopenia observed. They also presented kidney failure, anemia, heart failure with a very high level of NT-proBNP, liver disease with icterus conjugated bilirubin. Since hydroxychloroquine has side effects worsening the patient's condition, such as: cardiomyopathy leading to heart failure with fatal course, conduction disorders (branch block / atrio-ventricular block) or ventricular hypertrophy, cardiac arrhythmia, anemia, thrombocytopenia, hepatobiliary disorders, bronchospasm with metabolic and nutritional disorders, treatment with hydroxychloroquine must be stopped in patients admitted to intensive care unit, in order not to worsen their condition and strict monitoring of each attack must be considered.

All patients who showin, at admission, a chronic disease such as pulmonary, cardiac disease with elevated troponin and/or NT-ProBNP, liver damage, kidney failure or diabetes, are more vulnerable to more serious complications COVID-19 disease and treatment with hydroxychloroquine is likely to worsen their condition and lead to a poor prognosis and therefore a case-by-case evaluation will be made to decide whether treatment with hydroxychloroquine should be considered or not, with daily monitoring of each parameter involved.

Unfortunately, the levels of D-dimers, procalcitonin and lactate dehydrogenase (LDH) could not be determined because the reagents were not available at the time of the study and were received only a few days later. D-dimer is used in decision making for disseminated intravascular coagulation, deep vein

Table II. Frequencies and percentages of results exceeding the reference limits for each parameter.

Variable	Admission	Discharge
White blood cell count, x10 ⁹ /L		
H/L	11(18.33%) /2 (3.33%)	17(28.33%)/1(1.66%)
Lymphocyte count, x10 ⁹ /L		
L/H	36 (60.00%)/0	30(50.00%)/1(1.66%)
Neutrophil count, x10 ⁹ /L		
H/L	12(20.00%)/6(10.00%)	16(26.66%)/1(1.66%)
Monocyte count, x10 ⁹ /L - H	8(13.33%)	7(11.66%)
Eosinophil count, x10 ⁹ /L - L	23(38.33%)	5(8.33%)
Basophil count, x10 ⁹ /L - H	3(5.00%)	7(11.66%)
Thrombocyte count, x10 ⁹ /L		
L/H	8(13.33%)/1(1.66%)	10(16.66%)/4(6.66%)
Hemoglobin, g/dl - L	13(21.66%)	31(51.66%)
Prothrombin time, % - L	0	16(26.66%)
Quicktime, seconds		
Prolonged	0	16(26.66%)
Activated cephalin time, seconds, Prolonged	5(8.33%)	25(41.66%)
Fibrinogen, g/l		
H/L	32(53.33%)/0	44(73.33%)/1(1.66%)
Glucose, g/l - H	34(56.66%)	40(66.66%)
Urea, g/l - H	5(8.33%)	14(23.33%)
Creatinine, mg/l - H	1(1.66%)	12(20.00%)
Sodium, mmol/l		
H/L	0/5(8.33%)	0/3(5.00%)
Potassium, mmol/l		
H/L	1(1.66%)/5(8.33%)	9(15.00%)/4(6.66%)
Chloride, mmol/l		
H/L	0/14(23.33%)	4(6.66%)/6(10.00%)
Aspartate aminotransferase, UI/l - H	20(33.33%)	27(45.00%)
Alanine aminotransferase, UI/l - H	20(33.33%)	22(36.66%)
Total bilirubin, mg/l		
H/L	5(8.33%)/5(8.33%)	14(23.33%)/(15.00%)
Direct bilirubin, mg/l - H	56(93.33%)	52(86.66%)
Alkaline phosphatase, UI/l - H	5(8.33%)	12(20.00%)
C-reactive protein, mg/l - H	36(60.00%)	46(76.66%)
Calcium, mg/l		
L/H	13(21.66%)/8(13.33%)	31(51.66%)/0
Phosphorus, mg/l		
L/H	1(1.66%)/4(6.66%)	8(13.33%)/8(13.33%)
Uric acid, mg/l		
H/L	1(1.66%)/2(3.33%)	1(1.66%)/3(5.00%)
Total protein, g/l		
L/H	3(5.00%)/3(5.00%)	7(11.66%)/2(3.33%)
Albumin, g/l		
L/H	10(16.66%)/0	26(43.33%)/1(1.66%)
Total cholesterol, g/l		
L/H	1(1.66%)/6(10.00%)	5(8.33%)/2(3.33%)
Creatine Kinase, UI/l		
H	3(5.00%)	9(15.00%)
Troponin I, ng/ml - H	5(8.33%)	3(5.00%)
NT-ProBNP, pg/ml - H	9(15.00%)	9(15.00%)

H : High ; L : Low.

thrombosis or pulmonary embolism and is given a high priority of testing in patients with COVID-19 [11]. Serial measurements of procalcitonin would be useful in COVID-19 patients to detect complications due to bacterial co-infections. The extrathyroidal synthesis is increased during bacterial infections, supported by high concentrations of interleukin 1 β (IL-1 β), IL-6 and tumor necrosis factor α (TNF α) [12]. Lactate dehydrogenase could be a marker for the extent of lung injuries during infections [13].

CONCLUSION

We have described here, for the first time, the main laboratory characteristics of patients hospitalized for covid-19 in the region of Oran in Algeria. This study allowed us to determine the biological profile of patients with COVID-19 and to define laboratory abnormalities associated with a high risk of death in our population. These tests can be used by clinicians to identify at admission patients with a poor prognosis who will likely require ventilatory support and/or intensive care.

CONFLICT OF INTEREST : None.

DATE D'ENVOI : 10/07/2021.

DATE D'ACCEPTATION : 20/10/2021.

DATE DE PUBLICATION : 24/03/2022.

REFERENCES

1. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020 Jul 1; 24: 91–8.
2. Jain J, Gaur S, Chaudhary Y, Kaul R. The molecular biology of intracellular events during Coronavirus infection cycle. Virusdisease. 2020 May 4;1–5.
3. Lippi G, Plebani M. The novel coronavirus (2019-nCoV) outbreak: think the unthinkable and be prepared to face the challenge. Diagn Berl Ger. 2020 26;7(2):79–81.
4. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks in. Clinical Chemistry and Laboratory Medicine (CCLM) - Ahead of print [Internet]. [cited 2020 May 6]. Available from: <https://www.degruyter.com/view/journals/cclm/ahead-of-print/article-10.1515-cclm-2020-0240/article-10.1515-cclm-2020-0240.xml>
5. Lippi G, Mattiuzzi C, Sanchis-Gomar F, Henry BM. Clinical and demographic characteristics of patients dying from COVID-19 in Italy versus China. J Med Virol. 2020 Apr 10;
6. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013 Nov 27;310(20):2191–4.
7. Zippi M, Fiorino S, Occhigrossi G, Hong W. Hypertrans aminasemia in the course of infection with SARS-CoV-2: Incidence and pathogenetic hypothesis. World J Clin Cases. 2020 Apr 26;8(8):1385–90.
8. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, and al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020 Mar 31;e3319.
9. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020 Mar 3;
10. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. Diagn Berl Ger. 2020 26;7(2):91–6.
11. Kavsak PA, de Wit K, Worster A. Emerging key laboratory tests for patients with COVID-19. Clin Biochem [Internet]. 2020 Apr 30 [cited 2020 May 7]; Available from: <http://www.sciencedirect.com/science/article/pii/S000991202030391X>
12. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. Clin Chim Acta Int J Clin Chem. 2020;505:190–1.
13. Bonetti G, Manelli F, Patroni A, Bettinardi A, Borrelli G, Fiordalisi G, and al. Laboratory predictors of death from coronavirus disease 2019 (COVID-19) in the area of Valcamonica, Italy. Clin Chem Lab Med CCLM [Internet]. 2020 Apr 28 [cited 2020 May 9];1(ahead-of-print). Available from: <https://www.degruyter.com/view/journals/cclm/ahead-of-print/article-10.1515-cclm-2020-0459/article-10.1515-cclm-2020-0459.xml>