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Significance of biochemical parameters in assessment of the status of COVID-19 positive patients: An overview

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Abstract. *COVID-19 is an infection induced by the SARS-CoV-2 virus, that has resulted in a worldwide sanitary crisis. COVID-19 has a wide variety of clinical features, ranging from asymptomatic infection to minor to severe pneumonia. Different laboratory markers get altered in these patients, according to recent studies, and are therefore valuable as biomarkers to detect disease development and identify patients who may present a severe and/or deadly clinical condition. This article reviews biochemistry and immunology biomarkers that are changed in COVID-19 positive individuals, as well as inflammatory markers, and their influence on liver, heart, kidney and pancreatic functions markers' levels, as well as their significance in the disease's progression.*

Key words: *biochemical markers, COVID-9, coronavirus infection, laboratory diagnosis, severe acute respiratory syndrome (SARS-CoV-2), acute kidney injury, cytokines*

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Значення біохімічних показників для оцінки стану хворих на COVID-19: Огляд літератури

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Резюме. *Коронавірусна хвороба (COVID-19) має широкий спектр клінічних ознак від безсимптомного інфікування до важкої пневмонії. Згідно з останніми дослідженнями, пацієнти з COVID-19 мають широкий спектр лабораторних змін, що може бути корисним для виявлення розвитку захворювання та ідентифікації пацієнтів високої групи ризику. У цьому огляді літератури розглядаються потенційні біологічні та імунологічні маркери COVID-19, їх значення у прогресуванні захворювання та вплив на показники функцій печінки, серця, нирок та підшлункової залози.*

Ключові слова: *біохімічні маркери, COVID-19, лабораторна діагностика, важкий гострий респіраторний синдром (SARS-CoV-2), гостре пошкодження нирок, цитокіни.*

Introduction. In December 2019, the Chinese city of Wuhan was the site of uncommon pneumonia cases, which were later identified as a new coronavirus in January 2020. This has suddenly escalated into a major worldwide health security threat [1]. This virus is made up of the same components as a beta coronavirus, single chains of positive RNA from the huge group. It is a member of the Coronaviridae family and can infect humans as well as other animals such as mammals. The coronavirus disease of 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which quickly spread over the world and on March 11, 2020, was proclaimed a pandemic by the World Health Organization (WHO) [2].

The virus's entry mechanism into host cells has been related to the angiotensin II-converting enzyme (ACE2), which can act as a receptor for certain proteins released by the SARS coronavirus when positioned in the cell membrane. The distribution of ACE2 in the body is linked to whether the disease affects cells and tissues. This protein is expressed by epithelium, lung epithelium, intestinal tract epithelial cells, circulatory endothelium, and smooth muscle cells, among others [3]. ACE2, which decreases the functioning of the angiotensin-converting enzyme (ACE) and protects against acute respiratory distress syndrome (ARDS), regulates the angiotensin-renin system. The ACE2 encoding genes is a class 1 transmembrane glycoprotein with 805 amino acids as well as a single catalytic domain with a molecular mass 120 kDa that is found on chromosome X. Similar to ACE, ACE2 comprises two domain names: an amino-terminal catalytic subunit as well as a carboxy-terminal subunit. The catalytic subunit and the ACE amino subunit share 41.8 % of their sequence [4].

SARS-CoV-2, HCoVOC43, HCoV-NL63, HCoV-HKU1, MERS-CoV, SARS-CoV, and HCoV-229E are seven viruses of the coronavirus family that can cause serious illnesses in humans. These are mammalian viruses with singular contained RNA, a round form, conspicuous appendages of spiked glycoproteins called protein S on the membrane surface, and structural proteins such nucleocapsid (protein N), the envelope (protein E), nucleocapsid (protein N) and matrix (protein M) on the envelope surface [5]. The spikes (S) glycoproteins of the virus function as attaching proteins and are therefore incredibly important because they allow the virus to enter the host cells. S1 and S2 are the two subunits of protein S, which is a trimeric protein. The receptor-binding domain (RBD) of S1 attaches to the target cell and connects to an ACE2 domain [6]. It increases higher levels of angiotensin II when it interacts, which might cause local vasoconstriction. It also attaches to receptors on pulmonary and blood vessel cells, producing pulmonary impairment and scattered alveolar injury, putting a film over them but also developing fibrosis and respiratory discomfort in extreme cases [7].

In persons with a demographic clinical history symptom, COVID-19 is confirmed through laboratory tests and radiographic investigations. COVID-19 disease can present itself in a variety of ways, ranging from asymptomatic to mild, moderate, or severe symptoms, including pneumonia [8]. Flu and sneezing, coughing are the most common symptoms on a worldwide scale.

The research has been done to prove that several metabolic parameters change as a result of COVID-19 infection, and this has been linked to the disease's se-

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verity and, in rare situations, its association with regard to the patients' prognosis. The research facility characteristics, as well as other demographic and socioeconomic factors patients' clinical data may allow them to be classified in the early stages of the process, therefore identifying those who is likely to develop a life-threatening illness and allowing them to be treated enhance their clinical treatment and explore appropriate therapeutic options strategies. The impact of biochemical biomarkers (liver, heart, kidney, pancreatic as well as inflammatory) in COVID-19 patients, as well as their consequences for disease progression, are investigated in this study.

Impact of the clinical laboratory in the evaluation of biochemical markers in COVID-19 positive people. Clinical laboratories play an important role in virus diagnosis, patient follow-up (monitoring their progress), and pandemic monitoring by analysing serological markers in their blood. Verified SARS-CoV-2 laboratory tests are essential for timely COVID-19 treatment because they aid in the clinical decision-making process for decreasing infections and identifying asymptomatic individuals. As a result, timely separation and effective treatment are facilitated, as well as the risk of contagion is reduced [9].

A number of laboratory markers can be used to determine the symptoms of the condition and predict whether it will develop toward more serious disorders such as multiple organ failure (MOF), disseminated intravascular coagulation (DIC) as well as acute respiratory distress syndrome (ARDS) [10]. Hypoalbuminemia, creatinine, absolute neutrophilia, thrombocytopenia, increased liver enzymes, and nonspecific inflammatory markers including C-reactive protein (CRP) as well as Interleukin 6 (IL-6) have all been related to a poor prognosis. Despite the aforementioned, critical progression predictors such as lymphopenia, elevated D-dimer, and ferritin levels should be included in the marker profile, as should LDH, troponin and CPK [11].

Inflammatory Response Markers. Table 1 presents the laboratory findings of parameters associated with inflammation in individuals diagnosed with COVID-19, based on the intensity of the clinical condition.

Table 1

Inflammatory markers according to the seriousness of the COVID19 infection on admission

Parameter	Number of patients	Biological Range	Severity of the Infection			P value	Reference
			Total cases	Mild Cases	Serious cases		
Lactate dehydrogenase (U/L)	138	120-240	261	212	435	S	21
	99	120-250	336	-	-	-	28
	41	≤ 245	286	281	400	S	14
	40	-	304	221	462	NS	13
	12	114-240	605	-	-	-	29
	174	135-225	267	246	336		23
C-Reactive Protein (mg/dl)	73	0-5	51.4				28
	12	<10	41.1				29
	156	0-5	54.2	28.7	46.6	S	30
	452	0-1	44.1	33.2	57.9	S	15
Procalcitonin (ng/mL)	138	<0.05	49	22	27	S	21
	99	0-5	0.5				28
	12	0-0.5	0.81				29
	118	0-5	0.07	0.05	0.1		30
Interleukin-1β (pg/mL)	452	0-5	5.0	5.0	5.0	NS	15
Interleukin-6 (pg/mL)	99	0-7	7.9				28
	452	0-7	21.0	13.3	25.2	S	15
Interleukin 10 (pg/mL)	452	0-9.1	5.4	5.0	6.6	S	15

An increased immune response in COVID-19 patients causes an inflammatory response described as a 'cytokine storm,' which destroys multiple tissues and contributes to the patient's deteriorating health [12]. Lymphopenia and increased proinflammatory cytokines have been found to be more common in severe COVID-19 individuals than in milder cases, with higher serum concentrations of IL10, IL2, IL6, and IFN- present in extreme cases. In this respect, the neutrophil-to-CD8+ T cell ratio (N8R), as well as a neutrophil-to-lymphocyte ratio (NLR), have been proven to be useful diagnostic factors in critically ill patients [13]. Moreover, it was revealed that cytokines (IL-10, IL-2, IL-4, IFN-, as well as TNF-α) attain their maximum levels in serum 3 to 6 days after the onset of the disease, excluding IL-6. When compared to the milder cases, significant increases in serum levels of IL-6 and IL-10 were only found 4 to 6 days after the initiation of the disease in the critically ill group. Around 4 to 6 days after the initiation of the sickness were huge increases in serum levels of IL-2 and IFN- detected in the critically ill group [13].

According to Huang et al., plasma concentrations of IL2, IL7, IL10, GCSF, IP10, Monocyte Chemoattractant Protein-1 (MCP1), Tumor Necrosis Factor (TNF α) as well as macrophage Inflammatory Protein-1 alpha (MIP1A) were higher in ICU patients than in non-ICU patients [14]. The bulk of extreme cases had higher levels of infection-related biomarkers (procalcitonin, CRP and serum ferritin) as well as inflammatory cytokines (IL-6, IL-2R, IL-10, IL-8 and TNF-α), according to Qin et al. [15]. The plasma C-reactive protein (CRP) is generated by the liver and triggered by an inflammatory response such as IL-6. Regardless of the lack of accuracy, it is used as a biomarker in clinical settings for a range of inflammatory problems, and a rise in its levels is connected to illness intensity. This protein has the potential to affect phagocytic cell activity and can activate complement via the conventional route, implying that it could be involved in the opsonisation of pathogenic pathogens and damaged cells [16]. C-reactive serum concentrations in COVID-19 patients were measured and divided into four categories in a survey. Initial (3 days), progression (7 days), peak findings (12 days), and healing are the stages of computed tomography (CT) (16 days). The very ill group (n=6) had greater levels of CRP in the development phase than the milder group. (n=21), but the difference was not statistically significant. differences between peak and recovery stages [17]. In addition, Liu et al. [18] reported that the C-reactive protein levels in the progression were substantially higher. (10.6 mg/L vs. 10.6 mg/L in the recovery/stabilization group (38.9% vs. 38.9% in the recovery/stabilization group)). The progression group's albumin levels (41.27 g/L) were significantly lower than the recovery group's (36.62 g/L) [18]. In the multivariate analysis, both albumin (OR, 7.353; CI 95%: 1.098–50.000; P = 0.003) and CRP (OR, 10.530; CI 95%: 1.224–34.701, P = 0.028) were revealed to be risk factors for illness progression. The plasma concentrations of these proteins (albumin, CRP) fluctuate by at least 25% in the acute phase in response to certain cytokines generated during various types of inflammatory processes including some degree of tissue damage [19].

Furthermore, an elevation of the lactate dehydrogenase enzyme (LDH), which is used as a marker of lung tissue death, is one of the most common biochemical abnormalities in COVID-19 patients on admission to the hospital. Unlike patients in critical condition [13, 20, 21], where there is a significant difference in the amount of the modification in very ill patients [14, 22-24], patients with moderate infection have LDH values that are within the reference limits, according to multiple studies.

According to Yuan et al. [25] findings, patients with severe clinical problems had considerably greater serum concentrations of LDH and IL-6 in the first six days of hospitalisation in comparison to the moderate group, which thereafter dropped dramatically in both groups of patients, about day 6 to 9 days. The elimination of viral mRNA was linked with a drop in serum concentrations of CK or LDH, suggesting that a constant reduction in LDH or CK levels is likely to suggest a good reaction to the journey of illness in COVID-19 positive patients [25]. In patients with severe pneumonia, the early viral condition precedes (between 5 and 9 days) a phase of systemic immunological hyperresponsiveness, which is likely exacerbated by the cytokine storm or macrophage activation syndrome (MAS). This is especially frequent in patients having ARDS, where increased CRP and higher ferritin levels are critical for detecting MAS and are elevated in many severe pneumonia cases due to COVID-19. The poor life expectancy of ARDS is connected to a long-term increase in IL-6 and IL-1 levels. Higher acute phase reactants are linked to a higher rise in pro-inflammatory cytokines like IL-6, which are evidently higher in deceased than in one still living throughout the clinical course, and which rise with the severity of the disease [26]. In the univariate analysis (38), it was easy to combine it to a higher risk of in-hospital death in patients with increased IL-6, procalcitonin as well as LDH, where it was noted that LDH concentrations gets elevated in both groups (deceased and one still living) in the initial stages of the disease, but reduced by day 13 among the one still living [26].

Increased amounts of cytokines cause a cytokine storm. Interleukins such as IL-6, IL-2, IL-10, IL-7 and TNF α as well as cytokines, together with several additional indicators, such as granulocyte colony-stimulating factor (G-CSF), is an interferon-inducible protein (IIP). This condition, on the other hand, is likewise characterised by a drop in CD8+ and CD4+ T cells, as well as a decrease in the number of CD8+ and CD4+ T cells expression of the interferon-inducible protein (IFN)by CD4+ T cells [27]. Furthermore, larger amounts of G-CSF have been discovered in ICU patients, which is linked to a more severe condition.

Cardiac biomarkers. Advanced age, previous cardiovascular disease, and a more severe presentation of pneumonia are all risk factors for cardiac disease during the COVID-19 infection. 1) Pro-inflammatory responses of atherosclerosis-mediating cytokines (IL-7, IL-22, IL-6, CXCL10), which consequently lead to endothelial dysfunction via inflammatory cytokines, are examples of systemic processes.; 2) activation of pro-coagulation elements; and 3) tissue damage attributing to thrombosis and ischemia are among the elements that cause these events [26, 28-30]. As a result, complications, as well as direct and indirect heart injury, contribute to minor elevations in high-sensitivity troponin I indicators (hsTn) or pro B type natriuretic hormone N-terminal peptide (NT-proBNP) in patients in hospitals [31].

Table II shows the laboratory findings of parameters related to cardiovascular, liver, and kidney function on the admission of COVID-19 infected people, grouped by the severity of the clinical condition. In endothelial cells, vascular smooth muscle cells, cardiac tissue, ACE2 expression has been discovered [32], implying that SARS-CoV-2 can infect cardiomyocytes through the binding of ACE2 with spike protein. ACE2 causes a protein surge, which has a negative impact on cardiovascular health thus affecting the renin-angiotensin-aldosterone system (RAAS) and producing a myocardial infarction injury [33].

A meta-analytic review of 28 studies with 4,189 patients COVID-19 individuals who were extremely unwell presented with Troponin and creatinine levels are much elevated. Myoglobin, NT-proBNP, and kinase-MB (CK-MB), sudden cardiac damage (troponin increase) was shown to be extra prevalent. In comparison, As compared to their weaker versions, it is more common in those with serious conditions. Predominantly, during the study, the levels of hsTnI and NT-proBNP rose, only in non-one still living during the hospitalisation [34].

Churchill et al. [35] investigated the occurrence as well as the attenuation of left ventricular dysfunction utilizing 2 D echo, in 93 subjects with hypertension (60%), obesity (50%) and diabetes (41%). 88% of the patients got admitted to the ICU required life support and 71% needed vasopressors The average values of highly sensitive troponin (hsTn) and natriuretic peptide were 51 ng/L and 1.643 pg/mL, respectively, in these 93 patients. A total of 48 % of the 50 patients with a troponin level of 50 ng/L had left ventricular dysfunction.

On the other hand, Huang et al. [14] reported that hsTnl concentrations risen dramatically in five cases (12.2 %) who had been diagnosed with virus-related cardiac damage. It also was shown that the aspartate aminotransferase (AST) enzyme levels rose in 62% of ICU patients compared to only 25% of those who were not in the ICU. Furthermore, in an analysis of univariate data, Zhou et al. [26] found that subjects with increased ALT, creatine kinase and high-sensitivity cardiac troponin I had a higher risk of death, whereas hsTnl increased rapidly in the group of deceased as of day 16 after the onset of the disease. In the same manner, Deng et al. [36] that most individuals were having standard troponin concentrations on admission, but that these levels increased in 37.5 % of cases throughout hospitalisation, notably in deceased. In fact, the troponin levels rose dramatically in the week leading up to death.

According to Chen et al. [28], 76 % of patients (n=99) had an abnormal myocardial zymogram, with CK elevation in 13 patients and LDH elevation in 75 cases, with one case having both abnormal CK (6280 U/L) and LDH (740 U/L).

Liver biomarkers. Elevated levels of alanine aminotransferase (ALT), total bilirubin, and aspartate aminotransferase (AST) are frequent in critically serious individuals, indicating the involvement of liver impairment in these patients than with less severe forms of illness. In one of the studies, Chen et al. reported 43 patients with COVID-19 who had a liver impairment, with AST or ALT levels over the normal levels, and one illustration had substantial hepatic function damage, with ALT of 7590 U/L and AST of 1445 U/L values, respectively (18). Cai et al. studied that on admission, approximately 90% of individuals with abnormal liver tests were mild and while during their hospitalization, around 24% had ALT and GGT levels that were more than three times the upper limit [37]. There was a slight increase in AST and total serum bilirubin (TBIL) to more than 3 times the upper limit of normal (12 % and 15%, respectively), but ALP levers were not increased. Gong et al. [38] looked at 12 subjects who had laboratory abnormalities like lymphopenia, hypoalbuminemia, and neutrophilia. The researchers concluded that a combination of hypoalbuminemia, lymphopenia, and elevated LDH, as well as CRP and concentrations, indicated significant severe pulmonary damage on being admitted to the hospital.

Post-mortem hepatic histopathological analysis of 51 years old COVIDpositive man revealed that there was a mild portal and lobular activity and microvascular steatosis which indicated that liver injury could either have been caused by medication and SARS-CoV-2 infection [26]. Furthermore, immune-mediated inflammatory reactions contributed to hepatic damage, finally leading to liver damage in critically serious subjects. Because problems can produce hypoxia and shock, hepatic ischemia and hypoxiareperfusion dysfunction can develop. This discovery is consistent with prior findings of autopsy performed on SARS-CoV-2 patients [39].

Kidney Biomarkers. ACE-2 is significantly observed on the brush border of proximal tubular cells in the kidneys, according to findings. Its activity in renal endothelium and mesangial cells, on the other hand, has yet to be defined [32]. Kidney disease in COVID-19 individuals might appear as Acute kidney injury (AKI), proteinuria or hematuria, all of which increase the risk of death. It's uncertain if ARL is caused mostly by he-

modynamic abnormalities and release of cytokine, or as a result of the virus's toxic effects [40].

Renal histopathology studies of six COVID-19 patients who died in Wuhan, China, revealed impairment of renal function, as well as varying degrees of acute tubular necrosis, luminal brush boundary separation, and vacuole degeneration in different locations of the six samples. Overall, findings revealed that the infection is primarily responsible for lymphocyte infiltration as well as severe acute tubular necrosis. Immunohistochemical examination was used to examine the antigen of the viral nucleocapsid protein (NP), which was found in the renal tubular tissue samples [41]. Although acute kidney disease was documented in subjects who are serious, it was found that both seriously ill and moderate cases of acute renal failure had normal serum creatinine and cystatin C levels (n =178). Despite the fact that 23.6% of patients had a lower eGFR (estimated glomerular filtration rate), 2.8 % of patients were having elevated BUN levels and no one had a higher serum creatinine level. Regardless of whether they were admitted to the ICU or not, no patients acquired acute kidney damage, according to these findings. Surprisingly, 45 (54.2%) of the 83 patients without a history of kidney illness who were exposed to a regular urine test while hospitalised showed an abnormality. Proteinuria, hematuria, and leukocyturia were all found to be abnormal, although no one had acute renal insufficiency (ARI) during the trial. These renal changes were most likely caused by the nephrotoxicity of medications taken prior to admission to the hospital, but the potential that they were caused by the viral infection cannot be discounted [42].

In conversely, a research of 59 cases hospitalised in a Wuhan COVIDhospital (having 28 seriously ill cases and three deaths) revealed that 63 % had proteinuria, with 64 % had urine protein on admission, implying that renal impairment was already present before or at the time of admission. Patients with high blood urea nitrogen (BUN) levels experienced an increase in 43 % of cases within 2 to 10 days, and two-thirds of deceased patients had obviously high levels before their death. An elevated level of creatinine was found in 19% of the patients (11 of 59). Finally, all patients' computed tomography scans (100%) revealed a radiological abnormality in the kidneys [23].

Cheng et al. discovered that 44 % of 701 hospitalised patients had proteinuria and hematuria, with at least 26.7 % having both, came with hematuria on admission, with a 15.5 % and 14.1 % frequency of elevated creatininemia and uremia, respectively. 3.2 % of participants had ARI during the study period [22]. 3.2 % of participants had ARI during the study period [22]. Furthermore, the Cox regression revealed that increased concentrations of BUN, base serum creatinine (>133 μmol/L) and, as well as AKI stage 2 or higher, proteinuria of any level, and hematuria of any levels, are all unrelated predisposing factors for in-hospital mortality [22]. Wang et al. [21] also found that when the illness progressed and the patient outcome worsened, the blood concentrations of creatinine and urea elevated. Increased gradually before death, reaching significant levels ($p < 0.05$) on days 13 and 17 after the illness began. The findings bear the notion that renal impairment exists widespread in COVID-19 positive people and is one of the reasons for disease seriousness, leading to multiple organ collapse as well as death [43, 44]. As a result, tracking the functioning of the kidney would be critical in the early treatment of renal failure with continuous therapy, as well as clinical management of infected patients.

Pancreatic Biomarkers. In certain COVID-19 patients, minor pancreatic damage has been identified [45], which may be described in part with a variety of processes, including SARS-direct CoV-2's cytotoxic effects, as well as secondary and general immunologic inflammatory cell reactions. Furthermore, in cells within the pancreas and exocrine glands, the SARS CoV-2 ligand of ACE 2 is widely expressed, this can trigger inflammation and destruction to the islets, culminating in rapid diabetes, making pancreatic enzymes like amylase or lipase beneficial for follow-up [45].

In the study involving 212 patients, the post-infection pancreatic damage was investigated [45]. In light cases, 1.85 percent (1 of 54) had elevated amylase and lipase levels, whereas in severe cases, 17.91 percent (12 of 64) and 16.41 percent (11 of 64) had elevated amylase and lipase levels, respectively. Five critically ill patients (7.46%) had alterations on computed tomography, primarily localized pancreas enlargement or pancreatic duct dilatation, but no acute necrosis [46]. In this context, the research found that members of a family had acute pancreatitis linked to SARS-CoV-2, ruling out alternative causes of pancreatitis. On admission, one patient had 173 U/L of Pancreatic amylase levels (a 47-year-old woman), but it quickly rose to > 1500 U/L after 11 hours. The amylase level went from 85 U/L on admission day to 934 U/L on day six in a second instance (68-year-old woman), and a 5-point modified Glasgow acute pancreatitis severity score indicated severe acute pancreatitis [47].

Wang et al. found that 17 % of COVID-19-related pneumonia patients (n=52) were having high lipase or amylase levels, with 5 patients with pre-existing diseases such, diabetes, hypertension or heart disease [45]. Other gastrointestinal disorders can cause an increase in pancreatic enzymes, as found in COVID-19 positive patients by the researchers [48], leading De-Madaria et al. [50] to suggest that pancreatic injury in COVID-19 patients be determined using imaging basis such as magnetic resonance imaging (MRI) or computed tomography (CT).

Discussion. COVID-19 is a serious public health concerns issue on a worldwide scale that has been linked to a number of issues that affect the health of the patient as well as hospital expenses. As a result, clinical laboratories can contribute to the development of biomarkers that can be used to distinguish the likelihood of serious patients, speeding up medical judgment-making

[12, 35]. With the known risk factors like (sex of the patient, ages, and connections to the pathologies such as hypertension, diabetes and obesity) [16], it's crucial to use biomarkers that enable the differentiation of disease progression and the prediction of which patients may need sophisticated medical procedures, allowing for a more focused utilization of medical resources. Patients suffering from critical conditions, per the research, have a variety of changes in their biochemical markers and, in some cases, septic shock and ARDS develop quickly, followed by multiple organ damage [28]. Increased levels of high-sensitivity troponin I and IL-6 have been reported in critical COVID-19 patients in this scenario [51, 52].

Serum creatinine and other kidney function indicators were found to be within the reference range in most cases [13, 14, 24, 28, 29, 42], it was reported that there was no statistically significant difference among the mean values of patients who had mild and severe symptoms on getting admitted (Table II). The non-surviving patients, on the other hand, exhibited a gradual rise (on day 10 after getting admitted) over the reference range during their hospitalisation, peaking prior a few days they died. In critically unwell people, BUN levels grew in a similar way during their hospitalisation. As a result, these parameters could be used to determine a patient's prognosis during their hospitalisation. In mild COVID-19 positive patients, renal impairment remained mild, and the patient was not identified as having ARI. However, in severe cases, 43 out of 65 patients were diagnosed with ARI [34]. Because of their increasing age and increased occurrence of associated conditions such as hypertension and diabetes, End-stage renal disease (ESRD) individuals are particularly prone to severe COVID-19 infections [40]. While respiratory complaints seem to be the most common in COVID-19, heart dysfunction is particularly important since it increases the risk of infection with SARS-CoV-2 and the progression of the disorder. Cardiac insufficiency is one of the most common and serious SARS-CoV-2 consequences, as it elevates the possibility of death thus causing quickly increasing severe myocarditis [24]. Regardless of any previous conditions, the intensity of the acute sickness and its overall course, cardiac issues can persist even after recovery [53]. Biomarkers like CK-MB, troponin I, myoglobin and BNP are elevated in the case of a severe form of the disease, indicating the extent of the damage. Although the values of these parameters in moderate and critical cases of patients are normal during admission [24, 36], patients who die later have an exacerbated increase in these cardiac indicators. This is the situation with troponin I increasing in some critically serious individuals throughout hospitalisation and just before death [35]. Certain markers, on the other hand, are shown to elevate in severe instances in comparison with moderate ones, but they rarely reach the reference values as seen in Table 2.

Table 2

Biochemical markers related to heart, liver and kidney functions according to the seriousness of the COVID-19 infection on admission

Parameter	Number of patients	Biological Range	Severity of the infection			P value	Reference
			Total cases	Mild Cases	Serious cases		
Troponin I (pg/mL)	138	<26.2	6.4	5.1	1.1	S	21
	150	2-28	-			S	24
	41	≤28	3.4	3.5	3.3		14
Troponin I (g/mL)	12	0-0.1	0.95				29
Creatinine kinase-MB (U/L)	138	<25	14	13	18	S	21
Creatine kinase-MB (ng/mL)	12	0-2.37	2.0	-	-	-	29
Myoglobin (ng/mL)	99	0-146.9	67.9	-	-	-	28
	12	0-110	43.9	-	-	-	29
	65	0-106	58.6	21.6	63.4	-	23
	150	0-146.9	-	-	-	-	24
Natriuretic peptide (pmol/L)	4	0-23.1	43.9	-	-	-	29
Alanin aminotransferase (U/L)	138	9-50	24	23	35	S	21
	99	9-50	39	-	-	-	28

Continuation of Table 2

Parameter	Number of patients	Biological Range	Severity of the infection			P value	Reference
			Total cases	Mild Cases	Serious cases		
Aspartat aminotransferase (U/L)	138	15-40	31	29	52	S	21
	99	15-40	34	-	-		28
	41	≤ 40		34	44	NS	14
	12	0-45	40				29
	50	0-40	24.2	22	46.3	S	44
Gamma-glutamyltranspeptidase (U/L)	417	≤ 49	34.1	-	-	S	37
Total bilirubin (mmol/L)	138	5–21	9.8	9.3	11.5	S	21
	701		12			NS	22
	41		11.7	10.7	14	NS	14
Total bilirubin (μmol/L)	50	0–18.8	10.2	10	10.6	NS	44
	12	3-22	8.2				29
	40		10.3	8.8	13.2		13
Alkaline phosphatase (U/L)	417	≤ 135	61			S	37
Albumin (g/L)	99	40-55	31.6				28
	41		31.4	34.7	27.9	S	14
	12	40-50	37.7				29
Blood urea nitrogen (mmol/L)	138	2.8–7.6	4.4	4.0	5.9	S	21
	99	3.6–9.5	5.9				28
	12	3.2–7.1	5.4				29
Serum creatinine (μmol/L)	138	64–104	72	71	80	S	21
	99	57–111	75.6				28
	41	≤133	74	73	79	NS	14
Proteinuria (+)	83	Negative	35%	28%	58%		42
	128	Negative	59%	55%	66%		23
	442	Negative	44%				22
Hematuria (+)	83	Negative	29%	22%	53%		42
	128	Negative	44%	44%	45%		23
	442	Negative	27%				22

An elevation of concentrations of inflammatory markers in serum is proportional to the strength of the infection, exceeding the standard value by up to 12 times in some cases, perhaps due to liver tissue damage or as a side effect of pharmacological treatment given to patients who develop liver injury during their hospitalisation [38]. As a result, it is suggested that patients using hepatotoxic medications or those with preexisting hepatic problems have their ALT, bilirubin, and albumin levels measured at least once during their therapy [53].

In addition, Individuals with COVID-19 can be distinguished from those with pneumonia or a respiratory ailment that is similar to COVID-19 by having eosinopenia and an increased high-sensitivity C-reactive protein (hs-CRP). (helping with the diagnosis) [54]. Furthermore, raised LDH, is amongst the most commonly changed biochemical biomarkers on admission, and a rise in specific cytokines (IL-2, TNF α, IL-6) [55] throughout the advancement stage may keep you informed for illness follow-up (see Table 1).

In SARS-CoV, infected patients, serum levels of pro-inflammatory cytokines (IFN-, IL-6, IL-61, IL-12 as well as TGF-dv) but also chemokines (IL-8, CXCL10, CXCL9, and CCL-2) were greater than in healthy individuals. in previous cases of pneumonia caused by SARS-CoV infection (2003) [56]. Several differences between groups of more severe cases were discovered in a COVID-19 meta-analysis. In compared to the one still living, non-one still living exhibited significantly higher leukocyte, total bilirubin, creatine kinase, serum ferritin, and interleukin 6 (IL-6) levels and significantly lower lymphocyte and platelet counts [57].

In terms of pancreatic function, elevated lipase and amylase levels are linked to serious instances, suggestive of pancreatic damage pancreatic injury revealed by computed tomography in critically ill individuals [46].

A review of the literature finds several flaws, including the fact that the evidence is currently limited to a single group of people, which may leave out important factors such as epidemiological characteristics, strain virulence, viral genome mutations, social and cultural norms, and other countries' socioeconomic and hygienic conditions, all of which can affect the virus [58]. We expect that more scientific information reflecting these distinctions and sources of variability will be accessible soon. Other downsides observed were that few of the research [13, 14, 20] were examined, didn't include the population's standard ranges [18], biomarker follow-up was not always done during the hospitalisation period, or there was no information available.

Other analytical technologies like proteomic studies have aided in the search for possible biomarkers for the different expressions depending on the seriousness of COVID-19 patients' medical condition, including complement factors, pro-inflammatory factors modulators of inflammation, and coagulation factors. Such observations, together with discrepancies in conventional laboratory data, may assist in the diagnosis of potentially infectious pathogens and help in therapeutic targets [59].

Previous studies have suggested that COVID-19 patients with various complications (inflammation, co-infection, and thrombosis) can be classified based on analytical patterns, with personalised therapy potentially contributing to lower early mortality rates (OR 0.144; CI: 0.03-0.686; p = 0.015) in patients, implying that each situation necessitates a therapeutic focus tailored to the type of altered pattern [60].

To summarise, Clinical laboratories are important in the SARS-CoV-2 outbreak, not just for diagnosis but also for COVID-19 patient prognosis, assessing the severity of metabolic disease, and promoting the establishment of clinical decision support systems in order to customize medicine to the physiological changes that patients are experiencing. Similarly, laboratories provide for better utilization of hospital environment resources in important tools of systems of health, giving the result of faster and more efficient reaction times. These approaches, however, should be re-evaluated on a regular basis defined as the latest and credible information authored in many countries, as well as the introduction of newer technology into clinical laboratories to improve specificity in the quest for biological indicators.

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Authors contribution.

Jankar JS: the study concept, literature search, data analysis and interpretation, manuscript writing and editing, and was a major contributor in writing the manuscript;

Harley KN, Waghmode AH: the manuscript writing and editing. All authors reviewed the final draft of the paper.

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