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Effect of Corona Virus on Multi-Organs Diagnostics Biomarkers Among COVID-19 Positive Hospitalized Patients in Pakistan

Muhammad Tahir Ishaq[1], Muhammad Ahmad[2], Muhammad Bakhat Alam Rabbani[3], Shahid Sher[4], Fatima Iftikhar Shah[5]

[1-5]University Institute of Medical Lab Technology (UIMLT), University of Lahore, Lahore, Pakistan.

Author`s Contribution

[T,A]Conception and design, Collection and assembly of data, [B]Analysis and interpretation of the data, Statistical expertise, [S,F]Final approval and guarantor of the article

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Address of Correspondence

Shahid Sher
University Institute of Medical Lab Technology (UIMLT), University of Lahore, Lahore, Pakistan
Shahid.sheer@mlt.uol.edu.pk

A B S T R A C T

Background: COVID-19 is a pandemic that affects millions of people worldwide Pakistan. The lungs are the organs that are most affected by COVID-19. It can also affect other organs such as heart, liver and kidneys. The biomarker parameters associated with these can fluctuate with the disease, which can lead to organ failure.

Objective: The objective of this study was to assess multiple organ biomarkers in hospitalized COVID-19-positive patients within the Pakistani population and explore their correlation with the severity of the disease.

Results: In this cross-sectional study, 269 blood samples (239 males and 30 females) were collected from COVID-19 positive patients. Serum was separated from all the blood specimens for the determination of chemical analytes such as cardiac biomarker (CK, LDH), liver biomarkers (ALP, ALT, bilirubin and albumin), kidneys biomarkers (urea and creatinine), electrolytes (sodium and potassium) and inflammatory marker such as C-reactive protein (CRP) on fully automated Chemistry Analyzer COBAS C501 in the teaching hospital of University of Lahore, Pakistan.

Conclusion: In COVID-19 positive patients the level of LDH, CK and CRP were higher (abnormal) while Albumin, Urea, and Sodium showed decreased levels. These abnormal values were mostly in older patients (61-80) Albumin, creatinine and CRP showed significant p values after statistical analysis using SPSS. Thus, COVID-19 mostly effects Cardiac and Hepatic cells in comparison to other organs.

Keywords: biomarkers, electrolytes, CRP, COVID-19, patients, Pakistan.

Introduction

The term "corona" is derived from their distinctive crown-like appearance when viewed under an electron microscope, typically measuring around 150 to 160 nanometers in size. [1] Coronaviruses are enveloped viruses with an approximate size of around 100 nanometers. They are characterized by a multitude of spikes protruding from their envelope, giving the virus a distinct crown-like appearance. These viruses have a positive-stranded RNA genome ranging in size from 27 to 32 kilobases (kb), which is notably the largest among RNA viruses.[2] Outer cover comes from their host cell, hence possesses glycoprotein points.[3] The nucleocapsid of the coronavirus has a naturally occurring helical shape. However, when it becomes part of the virus's structure, it adopts a spherical form. Inside the host cell, the cytoplasm serves as the location for the replication of coronavirus RNAs.[4,5] Corona viruses including SARS-CoV gain passage into human cells through ACE2 (angiotensin converting enzyme 2), a human cell receptor. [6]

Mostly COVID-19 transmitted by inward inhalation of irresistible aerosols.[7] After the transmission of Corona virus, the incubation period of Covid-19 is around 3-14 days. Corona virus might source of infection progressed from less symptoms to deadly sickness. COVID-19 infects the Lungs and larynx in the older age patients responsive to deadly pneumonia.[8] Other indefinite side effects of COVID-19 incorporate high temperature, myalgia, cough, cold and dyspnea (without or with the diarrhea).[9] Long lasting corona symptoms can be progressed into different types of hypoxemia, problems in trachea or bronchi and ARDS (acute respiratory distress syndrome), which can lead to bacterial pneumonia.[10]

Coronaviruses primarily originate in animals. When these viruses successfully jump from animals to humans, they can trigger epidemics. In December 2019, the coronavirus was initially identified as a cause of pneumonia in Wuhan, China.[11] The disease was not confined to the China only but it rapidly affected the other regions of the world. At the start of 2020, the disease was named as COVID-19. The COVID-19 was announced as 6th public health emergency of internetional concern (PHEIC), by the World Health Organization (WHO).[12] The coronavirus was regarded as pendemic by WHO in march, 2020.[13] The pandemic of corona virus is an exceptional public health emergency which put some more burden on developing countries like Pakistan. As severity of disese the corona can cause multi organ failure like, lungs, kidneys, liver and heart or can alter their function.

We got much more information regarding clinical feathers of COVID-19, however, there is a notable gap in our understanding of abnormalities in laboratory diagnostic markers related to multiple organs, including the liver, kidneys, and heart, and their connection to the severity of the disease. The principal objective of this study was to assess multiple organ biomarkers in hospitalized COVID-19-positive patients within the Pakistani population and explore their correlation with the severity of the disease.

Methodology

A cross sectional study was conducted in the University diagnostic laboratory of University of Lahore teaching hospital, Lahore, Pakistan in May, 2021.

A total 269 samples were collected from COVID-19 positive patients. Blood specimen for the determination of chemical analytes was collected from the COVID-19 positive patients who were admitted in the teaching hospital of University of Lahore, Lahore, Pakistan.

All patients with age group of 1-80 years without the discrimination of gender were included in this study. But the patients who were already suffering from acute or chronic heart, kidney and liver diseases were excluded as per the information provided by patients or their relatives.

A convenient sample technique was used to obtain a venous blood specimen. A 3-4 ml of blood sample was collected from the COVID-19 positive patients. Sample was brought to the University Diagnostic Laboratory. Serum was separated from the whole blood through centrifugation technique.[14]

Serum samples then processed for the assessment of different biochemical analytes such as Cardiac enzymes (Creatinine Kinase CK, Lactate Dehydrogenase LDH), Liver function test (Alkaline Phosphates ALP, Alanine Aminotransferase ALT, Bilirubin and Albumin) Renal function test (Urea, Creatinine), electrolytes Sodium and Potassium Level and C-Reactive Proteins. All parameters were performed in fully automated Chemistry Analyzer COBAS C501.[15]

Data was analyzed in Statistical Software IBM SPPS. P value < 0.05 was considered significant.

Results

It was observed that 29% (69/239) male patients show high (abnormal) CK value. While in female COVID patient 20% (6/30) showed high (abnormal) CK level as shown in table I. There was a non-significance p-value 0.862.

It was noted that almost 55% (130/239) male Covid patient showed abnormal level of LDH. While 50% (15/30) female patient showed abnormal level (high) of LDH among COVID-19 positive patients as shown in table-2. p-value was 0.064, after statistical analysis which was not significant.

It was noted that ALP 13% male (31/239) showed high ALP value while 20% (6/30) female showed high ALP level as shown in table-3. The p value was 0.171 which was not significant.

48 (20%) of male patient showed abnormal (high) ALT level. While 5/30 (17 %) showed high ALT level as shown in table-4.

Table I: Gender and age wise CK values among COVID-19 patients.

		Creatine Kinase CK (Normal Range **:** 30-192U/L)					
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	7(70)	65(73)	76(68)	21(75)	169(71)	0.862
	High	3(30)	24(27)	35(31)	7(25)	69 (29)	
	Total	10(100)	89(100)	111(100)	28(100)	238(100)	
Female	Normal	1(100)	19(79)	4 (80)	-	24(80)	
	High	-	5 (21)	1(20)	-	6(20)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

There was a not-significance p-value of 0.18.

20 (8%) male COVID-19 patient showed abnormal total bilirubin level while no abnormality was seen in female COVID patients as shown in table V. The p value was 0154. which was not significant.

A result of all positive COVID-19 patients showed that out of 239 males, only 4(2%) patients showed abnormal (High) Albumin result and 30 (12%) have Low Albumin level. Out of 30 Females 3(10%) showed abnormal (Low) Albumin level as shown in table VI. There was a significance p-value of 0.005.

A result of all positive COVID-19 patients showed that out of 239 males 31(13%) showed abnormal (High) Urea value, and 33(14%) have Low Urea level. Out of 30 Female only 1(3%) have high Urea level and 13(43%) showed Low Urea level as shown in table VIII. There is a non-significance p-value of 0.809.

It was noted that, out of 239 males 12(5%) showed abnormal (High) Creatinine values while out of 30 Female COVID patients only 1(3%) showed abnormal (High) Creatinine level as shown in table-8. There was a significant p-value, which was 0.002.

In electrolytes analysis both salts (Na and K) were analyzed for all 269 COVID patients (239 males and 30 females).

It was observed that out of 239 males only 99 (41%) showed low Sodium level and 6 (2%) male patients showed high sodium level while 7 (23%) female patients showed low Sodium level. After statistical analysis it was observed that, the p-value was 0.276, which was not a significant figure and the set normal range was 125-150 mmol/L.

It was observed that out of 239 males 16 (7%) showed low potassium level while rest of male patients showed normal potassium level against the set range, which was 3.5-5.0

Table II: Gender and age wise LDH values among COVID-19 patients.

Lactate Dehydrogenase LDH(Normal Range:150-450U/L)							
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	5(50)	46(53)	45(42)	7(25)	103(44)	0.064
	High	5(50)	41(47)	63(58)	21(75)	130(56)	
	Total	10(100)	87(100)	108(100)	28(100)	233(100)	
Female	Normal	1(100)	12(50)	2(40)	-	15(50%)	
	High	0(0)	12(50)	3(60)	-	15(50%)	
	Total	1(100)	24(100)	5(100)		30(100)	

Table III: Gender and age wise ALP values among COVID-19 patients.

Alkaline phosphatase ALP (Normal Range**:** 35-300 U/L)							
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	7(70)	79(88)	95(85)	27(96)	208(87)	0.171
	High	3(30)	11(12)	16(14)	1 (3)	31(13)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Normal	1(100)	18(75)	5(100)	-	24(80)	
	High	-	6(25)	-	-	6 (20)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

Table IV: Gender and age wise ALT values among COVID-19 patients.

Alanine Aminotransferase ALT (Normal Range:1-42U/L)							
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	9(90)	76(84)	82(74)	24(86)	191(80)	0.18
	High	1(10)	14(15)	29(26)	4(14)	48((20)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Normal	1(100)	20(83)	4(80)	-	25(83)	
	High	-	4(17)	1(20)	-	5(17)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

mmol/L. In females COVID patients 23(77%) out of 30 female's patients showed normal value and only 1(3%) showed high potassium level. After statistical analysis, the p-value was 0.138, which was not a significant value.

CRP analysis was performed for all 269 COVID patients. It was observed that out of 239 males, 80 (33%) showed abnormal (High) CRP value while out of 30 Female 4 (13%) showed abnormal (High) CRP level. After statistical analysis, the p value was 0.001, which was significant.

Table V: Gender and age wise Total Bilirubin values among COVID-19 patients

		Total Bilirubin(Normal Range **:** 0.1-17 umol/L)					
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	10(100)	78(87)	104(94)	27(96)	219(92)	0.154
	High	-	12(13)	7(6)	1(3)	20 (8)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Normal	1(100)	24(100)	5(100)	-	30(100)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

Table VI: Gender and age wise Albumin values among COVID-19 patients.

		ALBUMIN(Normal Range : 35-50 g/L)					
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Low	4(40)	8(9)	10(9)	8(28)	30(12)	0.005
	Normal	6(60)	79(88)	100(90)	20(71)	205(86)	
	High	-	3(3)	1(1)	-	4(2)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Low	-	3(12)	-	-	3(10)	
	Normal	1(100)	21(87)	5(100)	-	27(90)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

Table VII: Gender and age wise Urea values among COVID-19 patient

		UREA(Normal Range =3.3-6.7 mmol/L)					
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Low	3(30)	13(14)	14(13)	3(11)	33(14)	0.809
	Normal	7(70)	75(83)	80(72)	13(46)	175(73)	
	High	-	2(2)	17(15)	12(43)	31(13)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Low	1(100)	10(42)	2(40)	-	13(43)	
	Normal	-	13(54)	3(60)	-	16(53)	
	High	-	1(4)	-	-	1(3)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

Table VIII: Gender and age wise Creatinine values among COVID-19 patients.

		CREATININE(Normal Range : 62-120 umol/L)					
Gender		**Age Group (Years)**				**Total No. (%)**	***p-value***
		1-20 **No. (%)**	21-40 **No. (%)**	41-60 **No. (%)**	61-80 **No. (%)**		
Male	Normal	10(100)	90(100)	104(97)	23(82)	227(95)	0.002
	High	-		7(6)	5(18)	12(5)	
	Total	10(100)	90(100)	111(100)	28(100)	239(100)	
Female	Normal	1(100)	23(96)	5(100)	-	29(97)	
	High	-	1 (4)	-	-	1(3)	
	Total	1(100)	24(100)	5(100)	-	30(100)	

Discussion

The pandemic of CoV-2 SARS caused by the ARS Corona Virus 2, has led to numerous cases and deaths around the world, as the new virus is spreading far more quickly and is very contagious.[16] In the clinical feature of SARS CoV2 a good knowledge has been gained.

CK in earlier times recognized as creatine phosphokinase which is located within cells found in supreme number in, myocardium, brain and skeletal muscle, lesser amounts rise in other primitive tissues. In this study we observed that, 75 (69 males, 6 females) COVID patients showed elevated level of CK, while in age wise distribution analysis, it was observed that, in age group range of (41-60 y) 35 out of 111 (31%) patients showed abnormal values. While in age group of (21-40 y) (24 out of 89) 27% showed high CK. In one of other studies, it was observed that 13/40 (33%) COVID positive patients showed elevated level of CK.[17]

Increased serum LDH value is one of the abnormal diagnostic parameters in COVID-19 patients with a severe or fatal course of disease.[18,19] Probable clinical and biological consequences of elevated LDH are pulmonary damage, as well as general organ damage.[20] In present study 21(75%) individuals belong to 61-80 years aged showed high LDH value, whereas out of 108 patients 63(58%) individuals belong to 41-60 years aged showed abnormal value, age group between 21-40 out of 87 patients 41(47%) individuals have a high LDH value, while in another study it was noted that individuals age group 61-80 (73.6%) showed high LDH level. [21]

In our study raised ALP was estimated, 31% (13 n=239) in males and 20% (6 n=30) in females while the total Bilirubin was raised 8% (8 out of 239) in males and females showed no abnormalities all were with normal Bilirubin. Whereas in another study it was noted that ALP and total Bilirubin raised in 6.1%, and 4.1% individuals. [22]

It was observed that, ALT level was elevated in 20% (48 out of 239) males and 17% (5 out of 30) in females. but other studies showed number of variations, in the present study 26 % COVID positive patients (29 out of 111) between age group of 41-60 showed high ALT level, which was abnormal ALT level. Whereas in another study it was demonstrated that high Alanine Aminotransferase (ALT) levels were reported in 11 (11/115, 9.57%) of patient.[23] Individuals who have affected with COVID-19 look have high rates of liver dysfunction. Patients relating to the stage in the development of disease before the symptoms are observed, level of ALT were high in 8.9% individuals [24], In a research instigation New York, approximately 5700 patients, 39% ALT >60U/L were reported.[25] Hepatic enzyme abnormalities are familiar in SARS patients, even though the liver injury has not been reported to be a major feature of this illness. [23,26] ALT present most common in the liver but found in plasma and in various body tissues. Its breaks into the two parts of the alanine through catalyzation [27]. On account of previous and present studies results we assumed that COVID 19 pathogenicity on liver cells (hepatocytes) is varying. SARS- CoV2-ACE2 receptors in human epithelial cells play an important role for its binding. Several studies reveal that CoV-2-SARS can also bind to the ACE2 receptor, enabling the virus to duplicate in cells.[28,29]

Hypoalbuminemia in COVID 19 patients have significance role, in present study Albumin is decreased 12% (30 out of 239) in males and 10% (3 out of 30) in females with the sample size of 269 patients. In our study the age group between 61-80 years showed 28% (8 out of 28) showed low albumin, whereas age group of 1-20 years out of 104 individuals showed low albumin. previous studies showed that Albumin is decreased in 62.9%individuals with the sample size of 4662 patients. [30]

About 15% of the patients who expired had constant renal disease in Britain. Receptor of ACE2 are found in kidneys due to occurrence of ACE2 receptors in kidneys there are chances of abnormalities in kidney function due to COVID 19, previous cohort study showed 13 % Urea and Creatinine abnormalities.[31] In our cross sectional study 13% have high Urea level and 33% have a low urea level and 5% individuals showed high creatinine level. The possible reason of this variability in both studies is study pattern in our study patients were not under observation.

In our study sodium and potassium showed some abnormalities, sodium was decreased in 41% (99 out of 239) in males and 23% (7 out of 30) in females, and potassium decrease in 7% and the individuals who showed high potassium were 10% (23 out of 239). In another studies it was found that sodium and potassium was decreased significantly in COVID 19 patients [32]. Sample delayed might cause high potassium come in serum and shows falsely high level in result, as compare to sodium only 2 % shows increase sodium level there is a possible cause for high potassium.

In our cross-sectional study we determined blood parameters abnormalities in COVID 19 positive patients. Total 269 individuals were involved in our study 89% male and 11% were females with the age group between 1-80 years. A remarkable difference was seen in laboratory parameters of COVID 19 positive patients as also in previous studies. In our study 33% males and 13% females showed high CRP level whereas in other studies 73.6% individuals showed high CRP

level [33]. Among 28 male patients 15 (53%) individuals belong to 61-80 years old showed a highest value of CRP and out of 111 patients 45 (40%) individuals showed abnormal high level of CRP belong to 41-60 years old, whereas out of 100 individuals 17(19%) showed high value of CRP in the age between 21-40 years, same findings have been observed by some other scientists globally [18,34,35]. The previous studies showed that level of CRP and the width of major lung abrasion elevated as the infection progress [36]. The level of CRP be certainly associated by lung abrasion and infection severity, near the beginning phase of CoV-19, eminent level of CRP might be a sign of lung abrasion and infection severity [36]. CRP is a blood analysis indicator for inflammation in the body formed within the liver and its intensity is deliberate via testing the blood, and are classified like an impulsive stage reactant, as inflammation progress level of CRP greater than before.

Conclusion

In COVID-19 positive patients, our study observed elevated LDH, CK, and CRP levels, alongside decreased Albumin, Urea, and Sodium levels, with a stronger effect in older individuals (61-80 years). Cardiac markers (CK and LDH) did not correlate significantly with the virus, while liver markers (ALP, ALT, bilirubin) had mostly non-significant correlations, except for albumin. Renal marker creatinine showed a significant correlation, while urea did not. Electrolytes (sodium, potassium) had non-significant correlations, and CRP showed a significant correlation. COVID-19 appeared to affect cardiac and hepatic cells more prominently, based on LDH, CK, and albumin levels.

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