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The Laboratory Diagnostic Profile of SARS−CoV−2 (COVID−19) Patients & Associated Factors

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Abstract

Background: Severe Acute Respiratory Syndrome Corona Virus 2 (SARS−CoV−2) is the novel corona virus first detected in Wuhan in 2019. nCOV belongs to the β-corona virus cluster. As the third most highly pathogenic corona virus, the clinical presentations of 2019-nCoV infection resemble those of the other two corona viruses, Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV) and Middle East Respiratory Syndrome Corona Virus (MERS-CoV). The abnormalities in the laboratory indices particularly the Blood Biochemical parameters may be associated with the severity of multiple organ dysfunction seen in COVID-19. The aim of the present project was to analyze the laboratory diagnostic profile of sars−cov−2 (covid−19) patients & to study the associated factors. **Methods**: The present hospital - based cross sectional study was conducted on all the patients who had tested positive for COVID & were admitted in Rajindra Hospital, Patiala in the time period of the July 2020 to December 2020, during the declared Corona Virus Pandemic. All the Biochemical Parameters were estimated on the automatic Analysers.**Results:** The results of the present study show abnormalities in the Renal Function Tests, Liver Function Tests, Blood sugar levels and Serum Electrolytes. Blood sugar levels and Renal function tests are significantly deranged in the patients of Covid 19 having co-morbidities like Diabetes Mellitus, Hypertension, CAD, CKD, Hypothyroidism etc**: Conclusions:** Biochemical Laboratory parameters are very important tool in management of COVID-19 patients .

Keywords:- COVID-19, Comorbidities, Biochemical Parameters.

INTRODUCTION

Corona virus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), was declared a global public health emergency on 30 January 2020. Emerging data suggests that COVID-19 has extrapulmonary manifestations and complications, subsequently leading to multi-organ failure and death. Common Cardiovascular and Renal complications reported to be associated with COVID-19 include myocardial injury, heart failure, acute kidney injury and electrolyte disturbances.[1,2]

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The number of 2019-nCOV infections is increased rapidly because of the existence of the following factors, person to person transmission through respiratory droplets, with possible transmission through aerosols under specific circumstances, the high affinity of the spike glycoprotein of 2019-nCOV for angiotensin-converting enzyme (ACE 2) receptors in human host cells, infectivity in a latent period, asymptomatic infection with atypical clinical symptoms, and insufficient attention in the early stages.[3] The most commonly observed symptoms of COVID-19 are fever, dry cough, and bilateral ground-glass opacities on chest CT scans. Some patients have muscle soreness, fatigue & diarrhea. The abnormalities in laboratory indexes, particularly blood biochemical parameters, may be associated with the severity of multiple organ dysfunction.[4] As blood biochemical changes play an essential role in evaluating the disease and prognosis and directing treatment; this present study was conducted to estimate the laboratory diagnostic profile of SARS−Cov−2 (covid−19) patients & associated with demographic profile and comorbidities like Diabetes Mellitus, Hypertension, CAD, CKD, Hypothyroidism etc.

Pathophysiology of SARS-CoV-2

The SARS-CoV-2 genetic sequence is similar to both SARS-CoV and MERS-CoV all originating in bats. Early in infection SARS-CoV-2 targets cells, such as nasal and bronchial epithelial cells and pneumocytes, through the viral structural spike protein (S) that binds to the angiotensin-converting enzyme 2 (ACE2) receptor 7. The type 2 transmembrane serine protease(TMPRSS2),present in the host cell promotes viral uptake by cleaving ACE2 and activating the SARS CoV2 S protein, which mediates coronavirus entry into host cells. 7ACE2 and TMPRSS2 are expressed in host target cells, particularly alveolar epithelial type II cells.[5,6] Similar to other Respiratory viral diseases, such as influenza, profound lymphopenia may occur in individuals with COVID-19 when SARS-CoV-2 infects and kills T lymphocyte cells. In addition, the viral inflammatory response, consisting of both the innate and the adaptive immune response (comprising humoral and cell-mediated immunity), impairs lymphopoiesis and increases lymphocyte apoptosis.[7,8] In the later stages of infection, when viral replication accelerates, epithelial-endothelial barrier integrity is compromised.In addition to alveolar epithelial cells, SARS-CoV-2 infects pulmonary capillary endothelial cells ,accentuating the inflammatory response and triggering an influx of Monocytes and neutrophils Inflamed lung tissues and pulmonary endothelial cells may result in microthrombi formation and contribute to the high incidence of thrombotic complications, such as Deep Venous Thrombosis (DVT), pulmonary embolism, and thrombotic arterial complications (eg, limb ischemia, ischemic stroke, myocardial infarction). In critically ill patients the development of viral sepsis, defined as life threatening organ dysfunction caused by a dysregulated host response to infection, may further contribute to multiorgan failure.[9] We have analysed the various biochemical biomarkers with an aim to determine the significant trend analysis shown by COVID-19 positive patients in their blood reports aiming for better identification and monitoring of the disease.

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Aims and Objectives

1) To Estimate Organ Function Tests of COVID-19 positive patients
   a) Liver Function Tests
   b) Renal Function Tests
2) To Estimate Blood Sugar levels and Serum Electrolytes of COVID-19 positive patients
3) To find the association of the above biochemical parameters with comorbidity.
4) To study demographic profile of COVID-19 positive patients.

Methodology

Study design: The study was a cross sectional, observational & descriptive study conducted in the Clinical lab of Department of Biochemistry in Rajindra Hospital (a tertiary care hospital).

Sample size: All the patients tested as COVID positive & admitted in Rajindra Hospital, Patiala in the time period July 2020 to December 2020, during the declared Corona virus pandemic were recruited the study group (n=1024).

MATERIAL AND METHODS

This hospital-based cross sectional study was conducted on 1024 COVID 19 positive patients who had tested positive by RT PCR method in the period of July to December 2020 , during the declared Corona virus pandemic. This study has been approved by the Institutional Ethical Committee of the Government Medical College, Patiala.

The Following Biochemical parameters were analysed

1. Glucose by GOD-POD Method.[10]
2. Urea by Urease method.[11]
3. S.Creatinine by Modified Jaffes Method.[12]
4. SGOT by IFCC without PLP.[13]
5. ALP by ALP-AMP Method.[14]
6. S.Bilirubin by Diazo method.[15]
7. Total Serum Proteins by Biuret method.[16]
8. Serum Albumin by BCG method.[17]
9. Serum Na+ & S.K+ by ISE method.[18]

Inclusion Criteria

All patients tested as COVID positive by RT PCR method and admitted in Rajindra Hospital Patiala's covid isolation ward in the time period of July 2020 to December 2020.

Exclusion Criteria

All patients who were suspected to be covid positive but their result outcome came out negative were excluded from this study

Statistical Analysis

The data was analysed using Microsoft Excel software 2016 and Epi- info CDC Atlanta version 7.2.2.1.6. Appropriate chi square test was applied wherever required.

RESULTS

24.4% of covid positive patients are in 51 to 60 years of age,17.6% of covid positive patients are in 41 to 50 years of age, 17.1% of covid positive patients are in 61 to 70 years of age, 12.4% of covid positive patients are in 31 to 40 years of age, 9.6% of covid positive patients are in 71 to 80 years of age,3.8% of covid positive patients are in more than 80 years of age.1.7% of covid positive patients are in 11 to 20 years of age. 0.4% of covid positive patients are in 0 to1 to years of age. 0.3% of covid positive patients are in 2 to 10 years of age. 59.8%of covid positive

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patients are males, 78.8% of covid positive patients are from urban areas and 51.4% of covid positive patients had no comorbidity.

Table 1: Demographic Profile of the Study Group.

		Number	**Percentage**
Mean Age (Years)	0-1	4	0.4
	2 – 10	3	0.3
	11 – 20	17	1.7
	21 – 30	131	12.8
	31 – 40	127	12.4
	41 – 50	180	17.6
	51 – 60	250	24.4
	61 – 70	175	17.1
	71 – 80	98	9.6
	>80	39	3.8
Gender	Male	612	59.8
	Female	412	40.2
Area of Residence	Rural	217	21.2
	Urban	807	78.8
Any Co-morbidity	Absent	526	51.4
	Present	498	48.6

Co-morbidities present in Covid Positive patients

Hypertension	22.9%
Diabetes Mellitus	29.3%
CKD	3.7%
CAD	5%
Others (Hypothyroidism etc.)	0.7%

Biochemical Parameters of the Study Group

Table 2a: Blood Sugar levels in COVID Positive Patients.

		Number	**Percentage**
1. Blood Sugar	Normal	582	56.8
	Increased	442	43.2

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Table 2(b): Comparison of Blood Sugar levels in COVID Positive Patients with comorbidities

Comorbidities		**Absent**		**Present**		**P value**
		N	**%**	**N**	**%**	
1.Blood Sugar	Normal	399	75.9	183	36.7	<0.001**
	Increased	127	24.1	315	63.3	

Blood sugar levels was increased in covid positive patients assosciated with comorbidities and was found statistically highly significant (p<0.001).

Table 3(a): Renal Function Tests in COVID Positive Patients

		Number	**Percentage**
1.Blood Urea	Normal	390	38.1
	Increased	634	61.9
2.S.Creatinine	Normal	694	67.8
	Increased	330	32.2

Table 3(b): Comparison of Renal Function Tests in COVID Positive Patients with Comorbidity

Comorbidities		**Absent**		**Present**		**P value**
		N	**%**	**N**	**%**	
1.Blood Urea	Normal	247	47.0	143	28.7	<0.001**
	Abnormal	279	53.0	355	71.3	
2.S. Creatinine	Normal	388	73.8	306	61.4	<0.001**
	Abnormal	138	26.2	192	38.6	

In 61.9% of covid positive patients blood urea levels were increased. In 32.2% of covid positive patients serum creatinine levels were increased. Blood urea and serum creatinine levels were increased in covid positive patients assosciated with comorbidities and were found statistically highly significant (p<0.001).

Table 4(a): Liver Function Tests in COVID Positive Patients.

		Number	**Percentage**
1.SGOT	Normal	450	43.9
	Increased	574	56.1
2.SGPT	Normal	705	68.8
	Increased	319	31.2
3.ALP	Normal	625	61.0
	Increased	399	39.0
4.BIT	Normal	924	90.2
	Increased	100	9.8
5.TSP	Normal	435	42.5
	Decreased	589	57.5
6.ALB	Normal	513	50.1

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	Decreased	511	49.9
7.GLOB	Normal	770	75.2
	Decreased	254	24.8

Table 4(b): Comparison of Liver Function Tests in COVID Positive Patients with Comorbidities.

Comorbidities		**Absent**		**Present**		
		N	**%**	**N**	**%**	
1.SGOT	Normal	238	45.2	212	42.6	0.388
	Increased	288	54.8	286	57.4	
2.SGPT	Normal	349	66.3	356	71.5	0.076
	Increased	177	33.7	142	28.5	
3.ALP	Normal	318	60.5	307	61.6	0.696
	Increased	208	39.5	191	38.4	
4.BIT	Normal	476	90.5	448	90.0	0.773
	Increased	50	9.5	50	10.0	
5.TSP	Normal	234	44.5	201	40.4	0.182
	Decreased	292	55.5	297	59.6	
6.ALB	Normal	288	54.8	225	45.2	0.002*
	Decreased	238	45.2	273	54.8	
7.GLOB	Normal	398	75.7	372	74.7	0.720
	Decreased	128	24.3	126	25.3	

In 56.1% of covid positive patients SGOT levels were increased. In 31.2% of covid positive patients SGPT levels were increased. In 39.0% of covid positive patients ALP levels were increased. In 9% of covid positive patients bilirubin levels were increased. In 57.5% of covid positive patients total proteins levels were decreased. In 49.9% of covid positive patients albumin levels were decreased. In 24.8% of covid positive patients globulins levels are increased. Serum albumin levels were decreased in covid positive patients assosciated with comorbidities and were to be found statistically highly significant ($p<0.001$).

Table 5(a): Serum Electrolytes in COVID Positive Patients

		Number	**Percentage**
1.Na+	Normal	734	71.7
	Increased	290	28.3
2.K+	Normal	739	72.2
	Increased	285	27.8

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Table 5(b): Comparison of Serum Electrolytes in COVID Positive Patients with Co-morbidities

Comorbidities		Absent		Present		P value
		N	%	N	%	
1.Na+	Normal	401	76.2	333	66.9	0.001*
	Increased	125	23.8	165	33.1	
2.K+	Normal	395	75.1	344	69.1	0.032*
	Increased	131	24.9	154	30.9	

In 28.3% of covid positive patients serum sodium levels were increased. In 27.8% of covid positive patients serum potassium levels were increased. Serum sodium levels and serum potassium levels were increased in covid positive patients assosciated with comorbidities and was found statistically highly significant ($p<0.001$).

DISCUSSION

The ongoing pandemic of COVID-19 is characterized by respiratory illness and diverse systemic clinical presentations, which in turn are reflected by routine laboratory abnormalities, based on the severity of disease presentation.[19] In this study, we have focused on the laboratory finding in COVID-19 patients with an aim, for a better understanding of the novel coronavirus disease. We have evaluated various biomarkers that include Organ function tests (RFTs, LFTs), blood sugar and serum electrolytes in this study markers in this study. Many laboratory parameters make it possible to assess the severity of the disease.

In present study most of the cases were in the age group of 51-60 years and median age was 53 years as in concordance with Wuhan study by Liu et al,[20] and Similarly in Maharashtra study by Shukla et al,[21] the median age of patients was 54 years.

In our study males were more affected (59.8%) as compared to females (40.2%) similar to Maharashtra study (21) where 58% patients were males. It may be because of more mobility and socialization of males as compared to females. As regards the urban/rural difference 78.8% cases were from urban areas. The reason could be that in the first wave of Covid pandemic urban areas were more involved and more health care facilities are located in the urban area.

In this study as in [Table 3(a)] Blood Urea and Serum Creatinine are increased in 61.9% and 32.2% covid positive patients respectively. Covid positive patients with comorbidities as in [Table 3(b)] have increase in urea 71.3% and creatinine 38.6% values which is highly significant. SARS-CoV-2 infects the host using the ACE-2, a membrane-bound peptidase, expressed more in the kidney than in other organs (lung, heart, intestine, and endothelial cells.[22,23] While ACE converts angiotensin I (Ang I) to angiotensin II (Ang II), ACE2 degrades Ang II to angiotensin 1–7 [Ang-(1–7)]. Ang II plays a role in vasoconstriction and adrenergic stimulation, binding type 1 Ang II receptors (AT1), while Ang-(1–7) opposes the Ang II-AT1 axis through vasodilatation, and anti- Direct Mechanisms of Renal Damage. SARS-CoV-2 can directly infect human kidney tubules and also induce cytoplasmic renal tubular inclusions. The indirect renal damage may be due to different mechanisms, such as renal hypo-perfusion, humoral response to

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viruses, thrombotic micro-angiopathy and activation of the complement system.[24]

In this study as in [Table 4(a)] SGOT,SGPT,ALP are increased in 56.1%, 31.2%, 39.0% covid positive patients respectively and TSP, albumin, globulin are increased in 57.5%, 49.9%, 24.8% in covid positive patients. The SARS-CoV-2 virus has been shown to use the angiotensin-2 converting enzyme (ACE2) as a means for cell entry. In healthy liver tissue, ACE2 is expressed mainly on cholangiocytes.[25] In addition, immune-mediated inflammation, such as a cytokine storm, might be a critical factor associated with disease severity and mortality.[26] Immune dysfunction, including lymphopenia or immune system overreaction, which accompanies disease progression, can also independently lead to liver derangement. Pneumonia-associated hypoxia and hypotension might also contribute to liver injury or even develop into liver failure in patients with COVID-19 who are critically ill.[27] This form of direct viral entry could possibly lead to the liver enzyme derangement seen in COVID-19 patients.[28] Patients with abnormal liver enzyme levels and liver injury had significantly decreased values of albumin and total proteins ($p<0.0001$) as compared to patients with normal liver enzyme levels. This could be attributed, possibly to the poor nutritional intake and the role of 'cytokine storm' with the release of major acute-phase cytokines, in down regulating the albumin synthesis in liver, after the onset of COVID-19.[29]

The liver has an important immune function and contains a large number of cells related to the immune response. After being infected with SARS-CoV-2, a large number of immune cells may be overactivated and secrete excessive cytokines, chemokines, etc, such as TNF-α, interferon-γ (IFN-γ), IL-6, IL-8, etc, leading to acute respiratory distress syndrome and SIRS as well as inducing ischemia and hypoxia, which result in further cell damage and necrosis. Such a vicious cycle not only leads to lung injury but also may develop into MODS, such as the liver, myocardium, and kidney. These results suggest that the SIRS and cytokine storms caused by SARS-CoV-2 infection may be one of the important mechanisms of liver injury.[30]

In this study [Table 6(a)] blood sugar is increased in 43.2% in covid positive patients and in [Table 6 (b)] 63.3% Covid positive patients with comorbidities have increase in blood sugar levels are significant. Muniyappa and Gubbi identified the following five mechanisms that may increase the ability of COVID-19 to impact patients with diabetes: higher affinity cellular binding and efficient virus entry, decreased viral clearance, diminished T-cell function and increased susceptibility to hyperinflammation and cytokine storm, and the presence of cardiovascular disease. The cytokine storm is more likely to occur in patients with diabetes because in these patients Inflammation induces the cytokine storm and increases risk for vascular hyperpermeability, multiorgan failure, and death as seen by high blood concentrations of inflammatory markers. The cytokine storm is more likely to occur in patients with diabetes because these patients at baseline carry a risk for low-grade chronic inflammation.[31]

In this study [Table 5(a)] Serum Sodium and Potassium is increased in 28.3%, 27.8% respectively in covid positive patients and in [Table 5(b)] Covid positive patients with Co-

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morbidities have increase in serum sodium and potassium levels are significant. A COVID-19 infection can cause dangerous kidney problems, which in turn may lead to hyperkalemia. Viral attacks on the kidneys that result in reduced kidney function may be one cause of hyperkalemia among people with COVID-19. Another may be a surge in hormones and inflammatory immune cells caused by the disease. Impaired renal function can lead to obstruction of excretion of metabolites and toxins in the body, which will adversely affect the maintenance of the electrolyte and acid-base balance of the human body.[32] People with COVID-19, who are taking drugs that inhibit the RAS, reduce the production of aldosterone, and this can cause fluid and electrolytes imbalances in the patient. Mineralocorticoid receptor (MR), which is of different types, is expressed in various tissues, including the kidneys, GI tract such as the colon, central nervous sys-tem (CNS), and heart, and is known as aldosterone receptor. Activation of MR leads to changes in the concentration of ions (such as sodium and potassium). These changes are necessary to maintain the balance of fluid and electrolytes in the body. Still, due to MR's presence in the large intestine, if the aldosterone pathway is disrupted, the absorption and secretion of ions in the colon are disrupted, and fluid and electrolyte imbalance occurs.[33]

CONCLUSIONS

In the above study the deranged Blood Urea, SGOT and TSP levels reflect Renal and liver dysfunction in Covid Positive patients. Those Covid patients who had Comorbidities had significantly increased Blood Sugar levels and Serum electrolytes levels also. These alterations in renal and liver biochemical parameters can be explained by the binding of the spike protein of SARS COV 2 with the ACE 2 receptors expressed in these organs.The critical serum potassium levels are affected as a consequence of the viral attack on kidneys The patients with comorbidities are more susceptible to the hyperinflammation and cytokine storm. Therefore this study concludes that Covid -19 disease being a potential cytokine storm can affect multiple organ functions and estimation of Biochemical Laboratory parameters is a very important tool in the management of Covid -19 patients to prevent them from going into multiple organ failure and hence to lower the morbidity and mortality.

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