CLINICAL, SOCIO-DEMOGRAPHIC AND BIOCHEMICAL VARIABLES IN PATIENTS WITH COVID-19: A CROSS SECTIONAL STUDY

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ABSTRACT

INTRODUCTION

Covid-19 is a debilitating disorder which affects the lungs with multiple organs involvement. The biochemical variables play important role in the management of the Covid-19 patients who are with different clinical profile, socio-demographic, and co-morbid conditions like diabetes and hypertension.

MATERIAL AND METHODS

This cross sectional study was conducted in the Covid-19 hospitalized cases at UCMS, Bhairahawa. Total of 150 patients were enrolled in the study period from May 2021 and October 2021 whose clinical profile, sociodemographic and biochemical variables were assessed.

RESULTS

The gender wise distribution shows the male dominancy with M:F ratio 1:0.85. The maximum age group vulnerable to Covid-19 in our study was found to be 41-60 years with median age of 47 years. There were constellations of symptom with shortness of breath 70% becoming first followed by cough 67.3% and fever 54%. The frequency of diabetes and hypertension was 19.3% and 24% showing co-morbidity associated changes in biochemical parameters. The male to female differences in biochemical changes have been associated with Covid-19 patients, however age wise distribution do not show any difference in biochemical parameters.

CONCLUSION

COVID 19 patients have a high prevalence of diabetes and hypertension, which is a common morbidity. A few biochemical indices (D-dimer, LDH, CRP, and ALT) change significantly between males and females. All biochemical parameters, on the other hand, are unaffected by age.

KEYWORDS

Biochemical, Clinical, Diabetes, Hypertension

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INTRODUCTION

COVID-19 instances has increased and spread all over the world since its first incidence in Wuhan, Hubei province, China, in December 2019.[1] Many of them are symptomatic, with the new virus directly affecting various organ systems.[2] More than 110 million cases have been confirmed world-wide, with 2.44 million deaths as of February 16, 2021, according to recent World Health Organization (WHO) data.[3]

COVID-19 complicates the clinical situation for persons with underlying illnesses such as diabetes, hypertension, and cardiac, renal, and respiratory diseases, leading to increased hospitalization and mortality rates.[4,5] Electrolyte and other indicators such as urea, uric acid, creatinine, D-dimer, C-Reactive Protein (CRP), Lactate Dehydrogenase (LDH), Aspartate Aminotransferase (AST), and Alanine Aminotransferase (ALT) may have a significant impact on the care of COVID patients. Sodium, potassium, calcium, urea, uric acid, creatinine, D-dimer, CRP, LDH, AST, and ALT levels in the blood may all have a role in disease progression.

This study will be the first of its kind in the south western region of Nepal, where COVID-19 patients with or without underlying co-morbid conditions are admitted to Universal College of Medical Sciences Teaching Hospital (UCMS-TH). If it could not be handled in a timely manner, it could place an additional stress on the patient and their family. As a result, the opportunity to investigate the socio-demographic associations of biochemical variables with age and sex was seized in our set-up.

MATERIAL AND METHODS

A cross-sectional study was conducted in confirmed COVID-19 cases admitted to UCMS-TH based on standard operating procedure (SOP) to determine biochemical parameters from May 2021 to July 2021 after receiving ethical clearance from the Institutional Review Committee (IRC No:UCMS/IRC/040/21).This study included 150 COVID-19 confirmed patients based on clinical history, RT-PCR report along with comorbid conditions like diabetes and high blood pressure. However, pregnancy, malignancy, chronic liver disease, deep vein thrombosis, surgery or trauma within 30 days, and individuals who did not give written consent was also excluded from the study.The D-dimer and CRP tests were performed using a GPP-100 Specific Protein Analyzer for quantitative measurement using Immunonephelometry in human plasma/serum. D-dimer > 200 ng/ml and CRP and > 6 mg/L was considered as elevated D-dimer and CRP level respectively. Serum Urea, Uric acid, Creatinine, LDH, AST, ALT were assessed in fully automated analyzer Humalyzer XL-600 by standard spectrophotometric UV kinetics method. Serum Na^+, K^+ and Ca^{++} were estimated by ion selective electrode analyzer. Data were entered and analyzed in Statistical Package for the Social Sciences version 22.0 (SPSS), IBM. Descriptive statistics like frequency, percentage, median IQR were obtained. The median were compared between groups by Man Whitney U test.

RESULTS

Table 1. General characteristics and clinical profile of COVID subjects based on gender

Variables			Gender		p-value
		Total (N=150)	Male (n=81)	Female (n=69)	
Age group (in years)	≤ 20	3(2%)	1(1.2%)	2(2.9%)	
	21-40	43 (28.7%)	25 (30.9%)	18 (26.1%)	
	41-60	83 (54.3%)	43 (53.1%)	40 (58%)	
	61-80	36(24%)	20(24.7%)	16(23.2%)	
	>80	2(1.3%)	2(2.5%)	0(0%)	0.769
Fever	Yes	76(54%)	41(50.6%)	35(50.7%)	0.99
	No	74(46%)	40(49.4%)	34(49.3%)	
Cough	Yes	101(67.3%)	58(71.6%)	43(62.3%)	
	No	49(32.7%)	23(28.4%)	26(37.7%)	0.227
Fatigue	Yes	44(29.3%)	19(23.5%)	25(96.2%)	
	No	106(70.7%)	62(76.5%)	44(63.8%)	0.087
Diarrhea	Yes	15(10%)	6(7.4%)	9(13%)	
	No	135(90%)	75(92.6%)	9(13%)	0.251
Vomiting	Yes	6(4%)	1(1.2%)	5(7.2%)	
	No	144(96%)	80(98.8%)	64(92.8%)	0.061
	Yes	25(16.7%)	15(18.5%)	10(14.5)	
ST	No	125(83.3%)	66(81.5%)	59(85.5%)	0.51
	Yes	20(13.3%)	9(11.1%)	11(15.9%)	
Loss of T/S	No	130(86.7%)	72(88.9%)	58(84.1%)	0.386
	Yes	105(70%)	56(69.1%)	49(71%)	
SOB	No	45(30%)	25(30.9%)	20(29%)	0.802
	Yes	22(14.7%)	13(16%)	9(13%)	
CP	No	128(85.3%)	68(84%)	60(87%)	0.604
	Yes	36(24%)	16(19.8%)	20(29%)	
HTN	No	114(76%)	65(80.2%)	49(71%)	0.187
	Yes	29(19.3%)	9(11.1%)	20(29%)	
DM	No	121(80.7%)	72(88.9%)	49(71%)	0.006

Abbreviations: ST: Shortness of breath, Loss of T/S: Loss of taste and smell, CP: Chest pain, HTN: Hypertension, DM: Diabetes mellitus

Table 1 shows that among the studied subjects, maximum number of the patients 83(54.3%) were between 41-60 years among which 43 (53.1%) were males and 40 (58%). Maximum number of patients presented with the symptom of shortness of breath 105 (70%) followed by cough (67.3%) and fever (54%) and least presented with vomiting (4%) and diarrhea (10%). There were 36 (24%) patients who were hypertensive among which 16 (19.8%) were males and 20 (29%) were females. Diabetes mellitus was present in 29 (19.3%) patients among which 9 (11.1%) were males and 20(29%) were females with statistical significant difference (p-value=0.006).

Table 2. Biochemical parameters of COVID subjects based on gender

Variables	Total Median (IQR)	Gender		p-value
		Male	Female	
Age (yrs)	48 (36.75-56)	47 (36.5-57.5)	49 (38-55)	0.84
Na^+	139.2 (136.35-141.2)	139.2 (136.15-141.2)	139.2 (136.9-141.25)	0.554
K^+	4.2 (3.775-4.525)	4.2 (3.75-4.7)	4.1 (3.75-4.5)	0.453
T. Ca^{++}	7 (1.975-8.7)	7.2 (2.05-8.7)	6.5 (1.6-8.7)	0.493
Crea	1 (0.9-1.2)	1 (0.9-1.2)	1 (0.9-1.3)	0.265
Blood Urea	33 (23.75-45)	34 (24-43.5)	29 (23-47)	0.864
UA	3.4 (2.8-4)	3.5 (3-4.1)	3.3 (2.6-40)	0.228
D- dimer	0.8(0.33-2.1)	0.5 (0.25-1.75)	1 (0.65-2.65)	<0.001
CRP	68.75 (25.375-110.775)	50.9 (20.3-101.7)	85 (42.3-116.85)	0.015
LDH	978 (708-1314)	922 (659-1166.5)	987 (798-1523)	0.037
AST	75 (45-112.25)	78 (47-106.5)	64 (44-116)	0.671
ALT	69.5 (38.75-118)	81 (51-126)	51 (31-103)	0.005

Table 3. Biochemical characterization of COVID subjects based on age group

	Median (IQR)	Age group (in years) ≤20	21-40	41-60	61-80	>80	*p*-value
Na$^+$	139.2 (136.5-141.2)	142 (132.8-142)	139.2 (137.8-142)	139.6 (136.9-140.9)	141.2 (128.2-144)	140.95 (104.9-126)	0.714
K$^+$	4.2 (3.7-4.5)	3.5 (3.5-4.5)	4.25 (3.8-5.2)	4.2 (3.7-4.8)	4 (3.7-4.3)	4.55 (2.8-23.5)	0.449
T. Ca^{++}	7 (1.9-8.7)	1 (1-8.2)	6.4 (2-8.3)	7.55 (1.9-8.7)	7.3 (1.3-8.7)	1.9 (1.35-21)	0.398
Crea	1 (0.9-1.2)	1.4 (0.8-1.7)	0.9 (0.9-1.1)	1 (0.9-1.2)	1.2 (0.9-1.5)	3.85 (10.9-24.3)	0.135
Blood Urea	33 (23.7-45)	50 (16-58)	33.5 (20.2-42.7)	34.7 (26-47)	36 (28.2-55.2)	20.5 (11.2-39)	0.138
UA	3.4 (2.8-4)	2.8 (2.8-4.2)	3.5 (2.6-40	3.5 (2.8-4)	3.65 (3.2-4.1)	1.7 (0.4-21.7)	0.709
D- dimer	0.8 (0.3-2.1)	0.8 (0.8-1.6)	0.8 (0.5-1.6)	0.8 (0.31-3.1)	1.41 (0.3-2.7)	3.6 (1.8-23.1)	0.571
CRP	68.7 (25.4-110.8)	122 (10.4-123)	79.3 (18.5-132.6)	63.7 (25.3-116.7)	79.7 (27.2-122.1)	100.6 (71.1-99.4)	0.884
LDH	978 (708-1314)	1024 (622-1157)	954 (566-1133.5)	986 (714-1512)	922.5 (564.2-1274)	1104 (672.7-1002.7)	0.606
AST	75 (45-112.25)	78 (32-329)	76 (52-107)	70 (47-97)	49.5 (34.7-106.2)	86 (60-88.5)	0.191
ALT	69.5 (38.7-118)	70 (16-129)	84 (40-136)	82 (52-144.5)	53 (31.15-82.5)	68 (41.2-80.2)	0.287

Variation in different biochemical parameters on the basis of age group was described in table 3. There is no significant difference in biochemical parameters in subjects among various age groups.

significance difference between age and diabetes. Man Whitney U test shows statistically significant difference in serum CRP (p=0.026), serum LDH (p =0.010), and ALT (p =0.034) in subjects with and without DM.

Table 4. Biochemical characterization of COVID subjects based on history of DM

Variables	History of DM Yes(n=29)	No (n=121)	*p*-value
Age	49 (43.5-55.5)	48 (36-56)	0.497
Na$^+$	139.2(136.75-141.7)	139(136-141)	0.582
K$^+$	4.2(3.75-4.5)	4.1(3.7-4.6)	0.551
T. Ca^{++}	7.7(1.2-8.45)	6.5(2.1-8.7)	0.459
Crea	1(0.9-1.4)	1(0.9-1.2)	0.201
B U	29(24.5-44)	34(23.5-45)	0.766
UA	3.2(2.7-3.7)	3.5(2.8-4.1)	0.200
D- dimer	0.74(0.3-2.15)	0.8(0.4-2.0)	0.636
CRP	92.4(59.1-118.35)	55.9(21.9-104.8)	**0.026**
LDH	1100(956-1156)	941(664-1235)	**0.010**
AST	60(44.56-98)	76(46-114.5)	0.531
ALT	43(30-85)	72(41-120)	**0.034**

Abbreviation: Na+-Sodium (mmol/L), K+-Potassium (mmol/L), T.Ca++-Total Calcium (mg/dl), Crea- Creatinine (mg/dl), BU- Blood Urea, UA-Uric Acid (mg/dl), D-dimer- D-dimer mg/L, CRP-C-Reactive protein, LDH-Lactate Dehydrogenase (U/L), AST-Aspartate aminotransferase (U/L), ALT-Alanine aminotransferase (U/L). Results obtained from Man Whitney U test. P-value <0.05 considered statistically significant, and indicated bold

Table 4 illustrates comparison of different biochemical characteristics on the basis of presence of History of Diabetes mellitus in COVID subjects. The median age group of the patients with diabetes mellitus was 49 years with an inter quartile range of 43.5-55.5 years and there is no statistical

Table 5. Biochemical characterization of COVID subjects based on history of hypertension

Variables	History of Hypertension Yes(n=36)	No (n=114)	*p*-value
Age	52 (46.5-59)	46 (35-54.25)	**0.002**
Na$^+$	139.5 (136.4-141.4)	139.2 (136.3-140.8)	0.391
K$^+$	4 (3.5-4.3)	4.2 (3.8-4.7)	**0.034**
T. Ca^{++}	7.75 (3.3-8.8)	6.45 (1.8-8.7)	0.516
Crea	1.05 (0.9-1.4)	1 (0.9-1.2)	0.392
Blood Urea	34.5 (27-59.7)	31.5 (22.75-42)	**0.044**
UA	3.45(0.4-1.9)	3.4 (2.8-4.02)	0.996
D- dimer	0.7(0.4-1.9)	0.8(0.3-2.1)	0.879
CRP	87.2(40.7-121.05)	62.4(24.7-105.3)	0.140
LDH	997(772-1609)	978(664-1233.2)	0.153
AST	68.5(47.2-151.2)	77(44.78-109.2)	0.982
ALT	56(32.2-106.2)	70(39.75-118)	0.477

Abbreviation: Na+-Sodium (mmol/L), K+-Potassium (mmol/L), T.Ca++-Total Calcium (mg/dl), Crea- Creatinine (mg/dl), BU- Blood Urea, UA-Uric Acid (mg/dl), D-dimer-mg/L, CRP-C-Reactive protein, LDH-Lactate Dehydrogenase (U/L), AST-Aspartate aminotransferase (U/L), ALT-Alanine aminotransferase (U/L). Results obtained from Man Whitney U test. P-value <0.05 considered statistically significant, and indicated bold

Table 5 illustrates comparison of different biochemical characteristics on the basis of presence of History of hypertension in COVID subjects. Man Whitney U test shows statistically significant difference in age (*p*=0.002), serum K+ (*p*=0.034), and serum Urea (*p*=0.044) in subjects with and without HTN.

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DISCUSSION

Despite the fact that the clinical aspects of COVID-19 infection have been extensively characterized, the overview of alterations in the most common biochemical markers observed in COVID-19 infected patients is still unclear. As a result, the purpose of this report is to investigate the changes in key biochemical markers seen in COVID-19 patients.

Shortness of breath (70 %), cough (67.3 %), fever (54 %), fatigue (29.3%), loss of smell sensation (16.7 %), chest pain (14.7 %), loss of taste sensation (13.3 %), diarrhoea (10 %), and vomiting (4 %) were the most common symptoms in adults infected with COVID-19, which contradicts the findings of Hadi Zare-Zardin et al. Fever (80–98%), dry cough (80%), and weariness (40–60%) are the most common symptoms in people infected with COVID-19.[6] The major reason behind contradictory findings can be due to delayed presentation of the cases, being partially treated outside in their febrile phase and admitted to our center with complications like shortness of breath (ARDS).

Diabetes and hypertension were found to be prevalent in patients with COVID-19 in previous systematic reviews, ranging from 9.7% to 11.9 percent and 17.1% to 20%, respectively. In our investigation, diabetes and hypertension were found to be 19.3 % and 24 %, respectively.[7-10] A study conducted by Francisco J Barrera et al observed a prevalence of diabetes (12%) and hypertension (26%).[11] In our investigation, the mean sodium and potassium concentrations were 139.2 mmol/l and 4.2 mmol/l, respectively, whereas Hugo De Carvalho et al found that the mean serum sodium and potassium concentrations were 139 mmol/l and 4.0 mmol/l, respectively.[12]

During the hospitalization of COVID-19, all of the patients without CKD showed no evident abnormalities in renal function, and none of the patients developed acute kidney injury (AKI), despite non-CKD patients normally do not have AKI in our clinical set-up.[13] Poudel et al. found a link between COVID 19 infections and d-dimer in both males and females; similarly, our investigation found a link that is highly significant.[14] Comparing to non-severe cases, severe cases had a higher level of serum LDH (321.85±186.24 vs 647.35±424.26, $p<.001$).[15] Alanine transaminase and gamma-glutamyl transferase, CRP, and ferritin levels all increased significantly ($p= 0.0001$).[16] The diabetes group had greater LDH levels as well as higher CRP concentrations than the secondary hyperglycemia and euglycemia groups with p value <0.05.[17] CRP, Ferritin, LDH, and D-dimer levels in the blood were all found to have substantial positive relationships with newly diagnosed DM. Furthermore, newly diagnosed DM had substantial positive relationships with age, BMI, severe COVID-19, and positive chest CT findings (p 0.001, for all).[18] Potassium levels and blood pressure levels were identified to have a negative relationship.[19] Patients with a history of hypertension have a larger proportion of patients with increased blood urea nitrogen (55 percent vs. 37.4%, p.05).[20] Since Diabetes and Hypertension groups were higher risk population in COVID-19 infection and the raised biochemical markers were also significantly raised in those groups that are to be focused while managing the patients.

CONCLUSION

The prevalent morbidity associated with COVID 19 patients is of diabetes and hypertension. In both males and females, a few biochemical parameters (d-dimer, LDH, CRP, ALT) are significantly differs. On the other hand, all biochemical parameters remained similar among different age groups.

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CONFLICT OF INTEREST

None

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