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ORIGINAL ARTICLE

Spectrum of Biochemical Alterations in Patients with Covid-19

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ABSTRACT
Background and objective: Millions of people worldwide have died from COVID-19, which has caused the failure of the lungs and other organs. The research assessed biochemical anomalies in COVID-19 patients to comprehend the illness and its effect better.
Study Design: Retrospective longitudinal cohort analysis
Place of study: ABWA Medical College Faisalabad
Methods: A total of 150 adult patients (n=150) who tested positive for COVID-19 via RT-PCR were included in the study. A Roche Diagnostics Cobas C501 used spectrophotometry to measure calcium, magnesium, phosphate, lactate dehydrogenase (LDH), urea, creatinine, ferritin, and chloride in the blood. A NOVA electrolytic analyzer used Ion-selective electrodes to measure sodium, chloride, potassium, and bicarbonate.
Results: In the study, 33.6% of patients had elevated urea levels, and 22.4% had elevated creatinine levels. Furthermore, 88.8% of patients had elevated ferritin levels, and 93.5% had elevated LDH levels. After 44 weeks, there was a drop in sodium-containing electrolytes, with 9% of patients experiencing a decrease in sodium, 22.4% in potassium, 53.3% in bicarbonate, 48.6% in calcium, and 23.4% in phosphorus. These changes in electrolyte levels suggest a long-term trend in electrolyte depletion among the patient population. There was no significant difference in biochemical anomalies between age groups ($p > 0.05$).
Conclusion: These results suggest that COVID-19 patients have lung illness and multi-organ involvement, which should be considered when managing these patients. These biochemical alterations warrant careful monitoring for organ failure by healthcare practitioners. More study is required to comprehend the processes causing these biochemical anomalies in COVID-19 patients.
Keywords: Covid-19, Biochemical alterations, Outcomes

INTRODUCTION
The COVID-19 outbreak began to swiftly spread in France in March 2020, especially from an epidemic cluster in north-eastern France, where there were 130,730 cases confirmed and 13,851 fatalities by mid-April 2020 [2]. The baseline features, clinical outcomes, and outcomes of COVID-19 patients from China [4], [5], [6], [7], [8], [9], Singapore [10], and Italy [11] have been evaluated in a number of papers. These investigations evaluated the clinical and demographic characteristics of COVID-19 patients and found that older males and patients with concomitant conditions had a higher chance of dying [4, [5, [6], [7], [8, [9], [10], [11]. It has been shown that COVID-19's severe course can cause lung inflammation, which leads to numerous organ failure [8]. Severe respiratory distress syndromes requiring mechanical ventilation and acute congestive heart failure were the most common life-threatening critical consequences in individuals with severe COVID-19 [8].With the help of big data and multilevel models that are appropriate for repeated measurements, we could predict the occurrence of organ dysfunction (kidney, lung, heart, liver, and muscle) in hospitalized patients and the severity of the inflammatory response based on Biochemical Test kinetics. This was accomplished on a well-phenotyped retrospective cohort of patients recently diagnosed with severe COVID-19.This study used big data and multilevel models to predict organ dysfunction and inflammatory responses in patients with severe COVID-19. By analyzing the data for factors such as age, gender, comorbidities, and lab tests, the researchers could identify patterns in the data that could help them predict the severity of the disease and the likelihood of organ dysfunction. This could guide treatment decisions and provide insight into the underlying causes of the disease.A predictive model like this can assist in identifying and managing patients at risk of complications as early as possible.We looked into whether or not there was a link between the most common biochemical indicators and how likely people would get sick or die.For people with severe COVID-19, no long-term follow-up statistics on organ failure and inflammation use a time-series model to look at the kinetics of biochemical indicators. This is the case even though these patients have been studied extensively.As a result, additional research is required to establish the connection between these biochemical markers and the outcomes that patients with significant COVID-19 experience over the long term.By measuring the concentration of these markers in the blood, researchers can better understand how the virus affects the body and determine the long-term effects of the virus on certain patients. This could lead to improved treatments and better outcomes for those affected. In addition, the use of time-series models in the research that will be conducted in the future may yield beneficial information regarding the progression of the illness and the available treatments. Also, the use of time-series models in future research could be beneficial in figuring out how the illness changes over time and what kinds of treatments could be used.Several studies have used a small number of biochemical tests to determine the risk of complications from COVID-19 in patients with severe COVID-19, the progression of diseases over time, and possible links with disease outcomes. However, studies have not examined the range and severity of complications based on many biochemical indicators. This is even though several studies have employed a limited battery of biochemical tests in order to determine the risk of complications from COVID-19 in patients withdiseases and their kinetics throughout time, as well as any potential associations with disease outcomes, in individuals with severe COVID-19.In December 2019, a new human coronavirus named Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified in China, as stated by the WHO Taxonomy of Coronavirus Disorders 2019 [1].This malware is the culprit behind COVID-19.Since the middle of April 2020, the epidemic has quickly spread from China to all other continents, impacting more than 180 countries and resulting in 108,867 fatalities attributable to COVID-19 and 1,777,666 cases discovered [2].In January 2020, three COVID-19 cases were validated in France.The rapid spread of COVID-19 across the globe has

prompted many countries to implement stringent measures such as lockdowns, travel restrictions, and guidelines for social distancing to slow down the transmission of the virus. These measures include lockdowns, travel restrictions, and social distancing guidelines.The fact that there have been confirmed instances in France draws attention to the ease with which the virus can spread and emphasizes the necessity of early detection and measures to contain it.

METHODOLOGY

When the first severe COVID-19 cases were at ABWA Medical College Faisalabad, we carried out a retrospective longitudinal cohort analysis and time series of all subsequent newly diagnosed patients. This was done after the patients had been treated at ABWA Medical College Faisalabad. The findings of this analysis provided valuable insights into the epidemiology and clinical features of the disease. They enabled us to develop treatment algorithms and protocols to optimize care for patients affected by COVID-19. The purpose of the study was to determine the factors associated with severe cases of COVID-19 and to monitor the progression of the disease over time.

Evidence from this study indicates that older age, male gender, and comorbidities are important risk factors for severe cases of COVID-19 and that this disease is on the rise during the period covered by the study.

Patients were followed until they were released from the hospital or until they participated in the cohort ended due to death.

Study Variables: In the ABWA Medical College Faisalabad ,Biochemical Database, data collection was based on variables as mentioned:

1. Patient identity number
2. Age of hospital admission
3. Date and time of blood sampling
4. Patient health care department.

Study Design: The main goal was to determine the frequency of organ dysfunction in individuals with severe COVID-19 as well as the degree of the inflammatory response as determined by Biochemical Test kinetics (kidney, lung, heart, liver, and muscle). Evaluation of biochemical indicators possibly linked to I COVID-19-related AKI and (ii) COVID-19-related in-hospital mortality were secondary goals. The percentage of time spent over or below the upper and lower limits of normal throughout the hospital stay was the primary outcome for each biochemical indicator examined. The most frequent laboratory abnormalities were those that occurred more than 25% of the time either above or below the upper and lower limits of normal.

Data Collection: It was situated that 28 biochemical indicators were found in the blood and 4 in the urine, for a total of 32 biochemical indicators. There were 32 biochemical indicators in total, 28 of which were found in the blood and 4 in the urine. Clinical data included the patient's date of admission, medical history (including hypertension, type 2 diabetes, cardiovascular disease, vascular disease, dyslipidemia, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, asthma, cancer, and chronic kidney disease and outcome during hospitalization for COVID-19 management.

Inclusion Criteria: The following conditions had to be met for inclusion:

1. A diagnosis of COVID-19 based on the detection of SARS-CoV-2 ribonucleic acids (RNA) in nasopharyngeal swabs.
2. Severe COVID-19, indicated by an oxygen saturation below 92% while the patient is breathing ambient air or requires oxygen support.
3. Admission to one of the Prime Teaching Hospital departments for consecutively minimum 3 days.

Study Method: The cohort, in other words, was observational. During the study period, we performed all clinical assessments, biochemistry, imaging tests, and clinical diagnoses at the treating physicians' discretion as part of the standard of care for patients suspected of having COVID-19 in Prime Teaching Hospital.

Statistical Analysis: The median and interquartile range (IQR Percentile) for all quantitative variables are shown, and 95% confidence intervals for categorical variables are shown. We assessed a collection of 20 biochemical indicators using a tiered method, with a sufficient number of iterations (n > 250, power analysis, detailed in Supplementary Methods, to ascertain the association between their variability over time and the incidence of to evaluate the endpoints (FA, death).

In the initial stage, we involved employing receptor operating characteristics (ROC) analysis to determine the ideal threshold for each biochemical variable. Following by the initial stage, time series analysis was used to assess every variable that the ROC analyses found to be substantially related to the study endpoint. Using a 95% confidence interval (95% CI), the calculated cumulative effects are represented as a percentage of the total observation time.

In the middle of analysis, it was calculated that for independent predictors using multivariate multilevel analysis. The HLM saw the features of appropriate patients in co-linearity tests in the validated HLM model. For each variable kept in the complete HLM model, the odds ratio (OR), 95% confidence interval (CI), and related P-value are reported as summary metrics. Using SPSS 2.0, a multivariate model analysis was carried out.

RESULTS

90 (60%) of the 150 patients were men, and 60 (40%) were women, ranging in age from 18 to 70 (mean 60). Among the age ranges of 35 years or older, 35-45 years, 46-60 years, and >60 years, there were 10, 22, 41, and 77 patients, respectively.(table-1)

Table-1: Baseline demographics of included cases

Characteristics Having Severe COVID-19 Of Cases		
Demographics	Sample Patients	Median Age - Cells
Age (years) — N, median (IQR)	150	60 (56–77)
Female	60	40% (49-61)
Male (95% CI)	90	60% (51–66)

Table-2: Other diseases among all cases

Characteristics Having Severe COVID-19 Of Cases		
Medical History Of Cases - 95% CI	Result	Range
Hypertension	65/135	48% (41–55)
Diabetes-TypeII	39/135	31% (23–35)
Chronic kidney disease	9/135	8% (3–9)
Disease-Cardiovasc.	37/135	28% (21–33)
Asthma	7/135	6% (2–8)
Cancer	9/135	6% (2–10)
Disease-Vascular	35/135	27% (21–35)
Dys-Lipidemia	34/135	24% (15–28)
Chronic Disease-Pulmonary	19/135	13% (8–16)
Sleep Obstructive Apnea	16/135	13% (5–12)

Table-3: Outcomes among all cases

Characteristics Having Severe COVID-19 Of Cases		
Outcomes — n/N,% (95% CI)	Result	Range
Failure - Acute Respiration	73/149	51% (43–59)
Ventilate - Intubative/Mechanical	56/149	36% (28–44)
Death Due To COVID-19	27/149	14% (8–20)
Embolism Of Pulmona	3/149	1% (0–3)

The table shows the frequency of anomalies in several metrics in patients. High urea and creatinine levels revealed that COVID patients had kidney disease. (table 2)Due to the fact that they are acute phase reactants, ferritin and LDH are likewise high. A larger percentage of patients had low levels of electrolytes, such as calcium, magnesium, phosphorus, sodium, potassium, bicarbonate, and chloride. By age group, we looked at parameter anomalies. This demonstrates that the analytic abnormalities are always the same when individuals are grouped according to their ages, and there are no appreciable changes in the abnormalities between age groups ($p > 0.05$). Only modest bicarbonate levels were seen at p=0. 036 was a significant number. The table displays the frequency of abnormalities for the various analyses. For salt and calcium, there are significant changes (p=0.029 and 0.025, respectively). The other factors showed no significant gender differences.

Table-4: Laboratory results of all cases

Biochemical Test Analysis in severe COVID-19 Cases.				
Urea & Electrolytes Test	N	Median	Inter Quartile Range	p
Sodium - mmol/L	848	141	138–144	0.687
Potassium - mmol/L	854	4·00	3·68–4·38	0.575
Chloride - mmol/L	799	104	101–107	0.4
Creatinine - mg/L	845	8·0	6·0–11·9	0.211
Urea Nitro - g/L	844	0·43	0·26–0·75	0.905
Phosphorus - mg/L	299	30·96	25·08–38·39	0.907
Calcium - mg/L	266	83·6	79·6–88·0	0.817
Magnesium - mg/L	164	20·4	18·0–23·7	0.135
Uric Acid - mg/L	82	44	30–62	0.905

Table-5: Results of biochemical tests

Biochemical Test Analysis in severe COVID-19 Cases.			
Inflammation & Liver Tests	N	Median	Inter Quartile Range
ASAT - U/L	455	59.3	36–95
ALAT - U/L	449	51.6	31–98
Bilirubin - mg/L	433	6.1	4·7–9·9
Alkaline Phosphatae - UI/L	188	71.3	51–102
Transferase γ-glutamy - U/L	162	58.7	27–164
C-Reactive Protein - mg/L	275	78.6	30·5–147·2
Procalcitonin - ng/ml	91	0.4	0·09–0·91
Interlukin 6 - pg/mL	10	97.35	59·8–223·9

DISCUSSION

In our study, 60% of participants were men and 40% were women. Men were more affected than women, according to one study, maybe as a result of the greater likelihood that men had to leave their households. In a study conducted in Iran11, renal function was found to be a prevalent issue in 35% of COVID-19 patients, who also had high urea and creatinine levels. The COVID-19 coronavirus has been identified by certain researchers in the urine of these individuals, proving that the virus was present in the kidney before being filtered by the glomerulus and excreted in the urine. 11 According to additional research, COVID- 19 pneumonia cases exhibited a sharp rise in urea and creatinine levels, indicating acute renal damage, which may have been caused by muscle breakdown. Hyperuricaemia and hypoalbuminemia were also present in these instances. 12, 13 These results are comparable to those from our study, which found that increased urea and creatinine situations occurred in 33.6 and 22.4 cases, respectively, and that these situations were more common in cases that had advanced by more than 60 times. A study found elevated ferritin and LDH levels in COVID-19 patients. 14 In COVID-19 instances, a meta analysis revealed higher ferritin and LDH levels, suggesting that serum ferritin levels could be used as a prognostic indicator in these cases. 15 These results are comparable to what we found. An amazing connection between renal damage and acute renal failure and the risk of death was highlighted by another investigation. 16 An Iranian study found that severe illness had a significant salt restriction. The drop for potassium ranges was mentioned as not being very noticeable. 17 Similar research revealed that while serum potassium decreased with disease severity, serum sodium decreased non-significantly with increase in disease severity. 10 Hyponatremia and hypokalaemia were discovered in 44.9% and 22.4% of patients, respectively. Another study compared the electrolyte levels in severe and non-severe COVID-19 patients and found that the levels of sodium, potassium, and calcium in severe patients were significantly lower than those in non-severe patients. 18 They claim that COVID-19 patients, particularly those with underlying heart or lung disease, may also have acute respiratory distress syndrome and acute cardiac damage, both of which can be made worse by regular hypokalemia.

CONCLUSION

In conclusion, this study provides valuable insights into the impact of COVID-19 on renal function and electrolyte balance. The findings indicate that COVID-19 patients, particularly men, are at a higher risk of developing renal impairment, as indicated by high urea and creatinine levels. The presence of COVID-19 in the urine of patients with renal impairment suggests that the virus may affect the kidneys directly. The study also highlights the association between acute renal damage and increased mortality risk in COVID-19 patients. In addition, elevated levels of ferritin and LDH were observed, which may serve as a prognostic indicator for COVID-19 cases. The study further revealed that electrolyte imbalances, such as hyponatremia and hypokalemia, were common in COVID-19 patients and may contribute to acute respiratory distress and cardiac damage in patients with underlying heart or lung disease. The results of this study emphasize the importance of monitoring renal function and electrolyte levels in COVID-19 patients to prevent further complications and improve patient outcomes.

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