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COVID-19 impact on hematological and biochemical parameters on outcomes of admitted patients

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Abstract--COVID-19 an ongoing pandemic has high transmission and mortality rate gets the attention of researchers to focus on the disease. The burden of disease on the health care system focuses on the COVID-19 impacts on the hematological and biochemical parameters. This study aimed to focus on the laboratory indicators that fluctuate in COVID-19. The single-center cross-sectional study in the pathology department of POF hospital Wah Cantt from August

2021 to December 2021. Three hundred positive COVID-19 patients were included in the study. About 138 (46%) were males and 162 (54%) females and the mean age was 58 ± 15.06 (range 5 – 86). The biochemical indicator raised in COVID-19 included CPK (191.25 ± 507.39), CRP (68.81 ± 70.95), LDH (429.48 ± 246.96), and ALT (46.50 ± 43.23). In hematological parameters, only neutrophils elevated (70.00 ± 13.52) lymphocytes decreased. Laboratory parameters measured were similar values in recovered and death cases. The findings suggest the raised level of CRP, LDH, CPK, ALT, ferritin, D-Dimer, and neutrophils predict early diagnosis and prompt treatment.

Keywords---Hematological, Biochemical, COVID-19, Recovered, Death, Outcomes, Pathology.

Introduction

WHO defined COVID-19 as an infection caused by SARS-CoV-2 and the patient has a severe acute respiratory syndrome and presents on an epidemiological basis of high-risk transmission and confirmed rRT-PCR. SARS-CoV-2 is a new strain of the Coronoviridae family that is highly transmissible and infectious (Bogiel et al., 2021). The high transmission rate and dynamic infectivity patterns make coronavirus more pathogenic and mortal. On March 31, 2020, World Health Organization announced the public health emergency action plan and takes necessary measures to combat COVID-19. The positive cases may be symptomatic, non-symptomatic, or severely ill (Rutledge et al., 2021).

COVID-19 affects the respiratory tract along with other organs including the gastrointestinal system, liver, heart, etc. The hematological and biochemical indices show the altered values in COVID-19 patients. These biomarkers were helpful in a patient's prognosis and in managing critical illness (Fong et al., 2021).

These biomarker alterations indicate the coronavirus effect on the body. These biomarkers show the pathological characteristics and prognosis and lead to diagnosis if measured and manage with other co-morbidities (Siripanthong et al., 2020).

Patients having COVID-19 symptoms show a high concentration of inflammatory markers like C-reactive protein, creatinine phosphate kinase, lactate dehydrogenase and alanine aminotransferase showing an increase in value (Rutledge et al., 2021). C-receptive protein, lactate dehydrogenase and neutrophils were raised in critical patients, and lymphopenia than in negative cases (Fan, 2020) (Fan et al., 2020). Another study on 145 patients, showed CRP neutrophils and lymphocytes were significant indicators in critical patients (Ahnach et al., 2020). Impact of COVID-19 observed the high values of neutrophils, platelets, CRP and LDH (Javadi et al., 2022). Many studies have been published on epidemiological, demographical, and clinical factors but the laboratory parameters comparison between the recovery and death was limited.

This study focused on the impact of COVID-19 on biochemical and hematological indicators and compared them in recovered and death cases.

Material and methods

Ethical consideration

The study was approved by the University of Haripur ethical committee of. The hospital management team has been informed of the research data collection. Written or oral consent was not needed for the research design.

Study Design and Setting

The single-center hospital-based and clinical cross-sectional was conducted on positive patients of COVID-19 who were presented to pathology laboratory POF Hospital, Wah Cantt from august 2021 to December 2021. Patients were grouped into two categories, recovered and dead. These groups were compared for different pathological indicators that changed in COVID-19. SPSS evaluates the data by using chi-square and t-test. The ethical committee of the University of Haripur approved the study, KPK, Pakistan.

Data Collection

Patients confirmed by rRT-PCR for COVID-19 were selected. Demographic history and clinical presentation are noted. All age groups and both genders will be included. The COVID-19 positive patients were followed for the laboratory tests.

The blood samples were collected for the hematological and biochemical pathology parameters to measure variation and case prognosis multiple parameters are tested. Hematology parameters including hemoglobin, lymphocytes, neutrophil, and platelets were measured on SYSMEX X1000. The biochemical tests include Lactate dehydrogenase, C-reactive protein, Creatinine phosphate kinase, Alanine aminotransferase, and D-Dimer were analyzed by COBAS C 311.

Statistical Analysis

The IBM SPSS Ver. 23 statistical package programs and Microsoft excel 2016 for data analysis. Continuous variables mean, standard deviation and categorical variables were measured as frequency and percentage. We determined the comparison between multiple groups by using the chi-square and continuous variable by independent t-test. The 95% CI having a two-tailed tests and $p < 0.05$ considered statistically significant.

Case Definitions

WHO defined a COVID-19 as an infection caused by SARS-CoV-2 and the patient presented with the severe acute respiratory syndrome and present in an epidemiological area of high-risk transmission and confirmed detected by the nucleic acid amplification techniques. COVID-19 is a severe acute respiratory syndrome caused by coronavirus. The mortality rate defined as the death of an

admitted patient due to COVID-19. Recovery rate defined as the number of patients discharged after being admitted to the hospital due to COVID-19 and getting treated.

3. Results

In our study, three hundred patients were diagnosed with COVID-19 and admitted to the hospital. The descriptive study presents among 300 patients, **138 (46%) were males and 162 (54%) females. Among them, 43 % (117) males and 56 % (153) females recovered.** About thirty deaths were reported having 21 (70%) in males and 9 (30%) in females during hospitalization. Demographic profile shows in Figure 1.

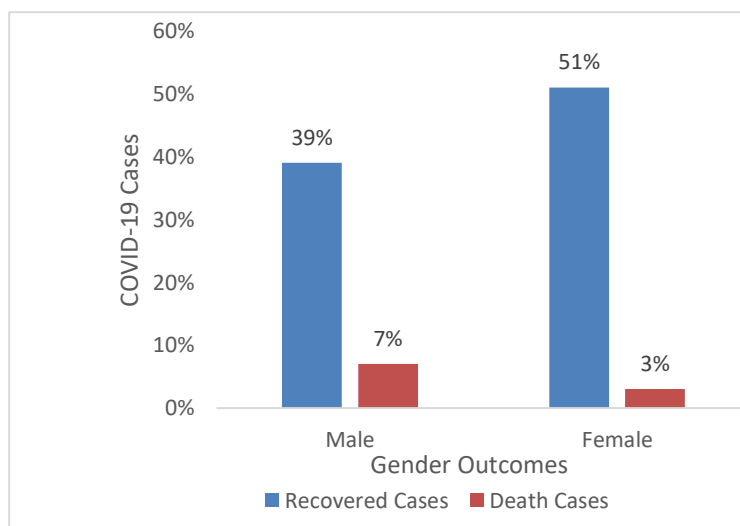


Figure 1 Demographic Profile

The mean age was 58 years (range 4- 84 years) the positivity rate was high in older patients. Males' mean age was 58 ± 13.15 and females' mean age was 58 ± 17.59 having a p-value of 0.00. The association between the age groups and gender shows a p-value of 0.00. the mean age in the recovered group was 57 ± 16.03 and in the death, group was 60 ± 12.12 . Males had a higher mortality rate 21 (15%) than females (5.5%) and $p > 0.002$. the Table 1 shows Age correlation with Outcomes in COVID-19 patients.

Table 1 Age correlation with Outcomes

Clinical characteristics	Outcome		P-Value	95 % CI	
	Recovered (n = 270)	Death (n = 30)		Lower	Upper
Age	57 ± 16.03	60 ± 12.12	0.039	-8.14	3.74

Creatinine phosphate kinase enzyme, an inflammatory indicator raised in COVID-19 infection raised to 191 u/L, C-Reactive protein raised to 68 u/L which is among the indicators. Lactate dehydrogenase, a muscle protein shows an increase in value with a mean of 429 u/L in infected patients. Alanine transferase shows a slight increase in changes.

The hematological parameters show the hemoglobin is in the normal range of 12.29 g/dL. neutrophil raised in COVID-19 and shows the mean of 70 % in positive patients. Lymphocytes in the below normal range show non-significance. Platelets remain in the normal range for COVID-19. Table 2 shows the statistical means of the laboratory indicators.

Table 2 Mean Statistics of Laboratory Parameters

Parameters	Normal Range	Mean ± S. D
CPK	46-171 u/L	191.25 ± 507.39
CRP	<5 u/L	68.81 ± 70.95
LDH	125-220 u/L	429.48 ± 246.96
ALT	<40 u/L	46.50 ± 43.23
HB	13-17 g/dL	12.29 ± 2.11
Neutrophil	40-75 %	70.00 ± 13.52
Lymphocytes	20-45%	20.60 ± 13.00
Platelets	150-400	225.29 ± 103.96
D-Dimer	<200	

The hematological profile of COVID-19 patients shows the lymphocytic count was decreased and neutrophils were raised. Platelets and hemoglobin levels were in the normal range. There is no significant difference in hemoglobin, neutrophils and lymphocytes count between the recovered and dead groups and p values were 0.764, 0.332 and 0.113 respectively. Only the p-value of platelets is 0.001, showing a significant difference. Table 3 shows the impact of hematological parameters.

Table 3 Comparison of Hematological Parameters among patients with COVID-19

Hematological indicators	Outcome		P-Value	95% CI	
	Recovered (n = 270)	Death (n = 30)		Lower	Upper
Hemoglobin	12.32 ± 2.11	12.06 ± 2.14	.764	-5.4	1.0
Neutrophils	69.66 ± 13.72	73.03 ± 11.28	.332	-8.4	1.7
Lymphocytes	20.48 ± 11.56	21.73 ± 22.35	.113	-6.1	2.6
Platelets	220.26 ± 94.75	270.2 ± 160.3	.001*	-88.97	-10.89

The biochemical indicators were compared between the two groups of recovered and death. The biochemical parameters CPK, CRP, LDH and ALT were showing p values of 0.928, 0.063, 0.193 and 0.071 respectively between death and recovered cases. Table 4 shows the impact of biochemical parameter.

Table 4 Comparison of Biochemical Parameters among patients with COVID-19

Biochemical Indicators	Outcome		P-Value	95% CI	
	Recovered (n = 270)	Death (n = 30)		Lower	Upper
CPK	188.8 ± 525.06	212 ± 314.86	0.928	-23.71	97.87
CRP	63.92 ± 69.69	112 ± 68.41	0.063	-48.2-	13.79
LDH	414.62 ± 244.64	561 ± 231.10	0.193	147.07	46.85
ALT	46.69 ± 44.75	44.80 ± 26.34	0.071	1.88	8.33

Discussion

The COVID-19 pandemic caused the world to open versatile fields and advancements in techniques to the world. The immediate spread of COVID-19

and its impact on human cells are still unknown to date. There were much more gaps and flaws in the COVID-19 in prediction and clinical correlation. The hidden information and lack of communication between different fields is a major drawback to exploring SARS-CoV-2. The enormous workload and tremendous efforts from the health staff managed the COVID-19 pandemic under control. The strategies developed to control the transmission, innovations in detecting SARS-CoV-2 and treatment procedures (Gennaro and Health, 2020).

The diagnostic technique for COVID-19 through the molecular technique for accurate and reliable results. The isolation of SARS-CoV-2 and its tracking for the epidemiological basis to break the chain of infections become enhanced and effective due to rapid detection methods (Carter LJ, 2020, May).

In the early phase of COVID-19 in Pakistan, most cases fell in young and adults group ranging age from 20 to 40 years, and very few cases in old, aged patients. About 71 % were males and 28 % were females at the start of the COVID-19 pandemic (Abid et al., 2020). Pakistan's population has an average age of about 22 years only and has only 4% of individuals above 65 years and an expected life of 67 years. These demographics show a low mortality rate and low CFR in COVID-19 (Waris et al., 2021). In my study males were 46% affected and females were 54%. Another study reported a high number of males affected than females due to social and cultural factors (Noreen et al., 2020).

Males were 223 (56.2%), and 174 (43.8%) were females and more deaths were reported in males (Sobhani et al., 2021).

The first death by COVID-19 in Pakistan was reported on 18th March 2020 and the ratio began to rise to 1.67% for 100 deaths (Chughtai and Malik, 2020).

Patients under 20 years of age were safe from the pandemic and adults from 20 years to 50 years of age were highly exposed by at minor risk with mild effects but the old age group shows a high-risk danger from COVID-19 and a high mortality rate (Chaudhry A et al., 2020).

The COVID-19 cause low deaths in young adults less than 40 years but more death in aged patients above 40 years (Wu and McGoogan, 2020). Researchers grouped the patients having confirmed COVID-19 cases. About 75% of cases were above 50 years of age (Saddique et al., 2021). Our study aligned with the previous reports and about 73.4 % of patients were older than 50 years of age. Age is considered a significant indicator of COVID-19 outcomes. As in my study mean age in recovered and dead patients were similar i.e., 57 ± 16.03 and 60 ± 12.12 having a p-value of 0.039. In a study by Pakistani researchers on 317 patients, about 198 (62.5%) were males and 111 (35.0%) were females. The mortality rate was 15.8% among admitted patients (Khalid et al., 2021).

Xavier and his fellows also enlighten the biochemical parameter to focus on prognoses like raised CRP, LDH, and ALT in patients. Hemoglobin shows a decline in value by about 40-50% (Xavier et al., 2020).

Our study shows a minor increase in levels of ALT levels up to 46.50 ± 43.23 . Zhang shares his findings of COVID-19 patients having liver dysfunction showing raised ALT levels in 14 to 53% of cases during the infection period (Zhang et al., 2020). Similar findings were reported in MERS-CoV having raised liver enzymes including LDH, ALT and AST. They also share that the recovery rate was enhanced if treated with special attention in mild COVID-19 cases (Zhang et al., 2020).

In our study, CRP raised to a mean of 68.81 ± 70.95 (<5 u/L). The CRP raised to 63.92 ± 69.69 in deceased patients and 112 ± 68.41 in recovered patients. Our study also reports the increase in CRP, a strong biomarker and indicator in death and recovered patients. The level of C-reactive protein elevates up to 49.73 ± 53.59 and a p-value less than 0.001, a highly an important indicator of COVID-19 (Khalid et al., 2021).

Our study also reported elevated levels of biochemical bioindicators. In the study by Chan and his fellow summarizing the elevated levels of CPK, CRP, LDH, and D-Dimer in COVID-19 patients. The study by Chen on 99 confirmed positive patients admitted to the hospital have raised LDH levels and a study by Huang in 2020 reported the significant levels of serum ferritin, C-reactive protein, and D-Dimer in COVID-19 prognosis (Najim, 2020). Our study conducted on 300 patients showed the level of LDH was extremely high 429.48 ± 246.96 u/L. LDH increase in COVID-19 and have a significant p-value of less than 0.001 between the critical and deceased group (Khalid et al., 2021).

CBC test was performed immediately and reported with distinguished factors giving more in-depth knowledge as a strong biomarker. These biomarkers include neutrophils, lymphocytes, platelets, and white blood cells. In our study hemoglobin remains in the normal range of 12.29 ± 2.11 g/dL with a standard deviation of ± 2.11 . The study revealed that admitted patients have normal hemoglobin levels and show no variations (Lei et al., 2020). Hemoglobin level shows no significant correlation ($p\text{-value} = 0.77$). between critical and non-critical patients (Waris et al., 2021).

WBC differential count represents the neutrophil raised to 70 %, CRP 16.16 mg/L, and D-dimer 580 ng/mL in an admitted 33-year-old lady (Lei et al., 2020).

Another study conducted on 32 confirmed patients, reported a decrease in lymphocytes and raised neutrophils. They were significant indicators in severe and critical patients (Katipoğlu et al., 2020). Our study supports the previous research and confirms that neutrophilia along with lymphocytopenia were an indicator of COVID-19. Neutrophilia was reported by Singapore on 148 admitted patients having critical illnesses. Gong et al. and Qin et al. and Li et al. also reported similar findings of neutrophilia in admitted patients (Khalid et al., 2021).

In another study, there was a significant correlation between critically ill and mild group patients having a p-value of 0.28 (Waris et al., 2021). In the present study, lymphocytes also show a minor decline, measured at $20.60 \pm 13.00\%$ (20.60 ± 13.00). Lymphocytopenia has been observed in the studies of Khalid, Atiqa, et al., CDC, and Huang et al in China among COVID-19 patients (Khalid et al., 2021).

Thrombocytopenia was observed in the COVID-19 patients and predicted the severity and prognosis. Our study showed the platelets counts were below in range (225.29 ± 103.96) and have a p-value of 0.001 between recovered and death groups. The mean platelets count decreased in critical patients to $165.0 \times 10^9/L$ (Waris et al., 2021). Thrombocytopenia in ventilated patients had a p-value of 0.049, indicating platelets were a major biomarker in COVID-19 (Khalid et al., 2021). Therefore, thrombocytopenia is a major biomarker for identifying coagulopathy.

Conclusion:

Elevated levels of LDH, CRP, CPK and ALT along with neutrophilia and lymphocytopenia help in predicting the COVID-19 without being evaluated for RT-PCR. The early detection helps in the productive prognosis of COVID-19 minimizes the patients' complications and reduces the risk of transmission. The monitoring and identifying of the hematological and biochemical parameters assist clinicians in prognosis and treatment. The raised values of inflammatory indicators help the careful monitoring of these parameters.

Limitations

These biomarkers and clinical investigations need further studies and should be used for risk stratification in patients with COVID-19. This study gives new knowledge into the significant job of other clinical attributes in patients with COVID-19. This will additionally assist with figuring out how to control and relieve the pandemic in general. Researchers need multiple center studies among COVID-19 patients on large scale to reach a single destination.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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Conflicts of interest

There are no conflicts of interest.

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