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Electronic Journal of Medical Research
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Research article

Clinicopathological presentation of COVID-19 patients presented at the rural healthcare center

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Article information:
Received: 23-07-2025
Revised: 21-08-2025
Accepted: 22-08-2025
Published: 27-08-2025

Academic Editor:
Dr. Anwar N. Y. Althubyani

Keywords:
SARS-CoV-2
Hematological anomalies
Critical patients
Hospitalized patients
Corona pandemic

Abstract: The current observational cross-sectional study was conducted to determine hematological anomalies in young (below 50 years old) and elderly (above 50 years old) patients that were suffering from coronavirus diseases-2019 (COVID-19) reported at an outpatient clinic in the rural healthcare center from 1st May 2021 to 31st August 2021. A total of 100 patients reported in the above-mentioned time frame were included in the current study, which were confirmed with diagnosis of COVID-19 infection by real time polymerase chain reaction (RT-PCR) using a nasopharyngeal swab (NPS). Data were collected on demographic factors, sign & symptoms, comorbidity status, and hematological parameters. A total of 100 COVID-19 positive patients were enrolled in this study with a mean age 49 years. The majority 66 (66%) of participants were male with a mean body mass index (BMI) of 26. In addition, the cough was the most prevailing symptom 74 (74%), followed by fever 68 (68%), shortness of breath 60 (60%), and absence of taste/smell 3 (3%), respectively. Also, diabetes was the most prevalent comorbidity 44 (44%), after that hypertension 33 (33%), ischemic heart disease 17 (17%), urinary tract infection 8 (8%), and chronic kidney disease 1 (1%), respectively. The bifurcations of hematological factors of COVID-19 positive patients with respect to age groups were also presented. This work determined that the hematological, coagulative, and inflammatory markers are the utmost important parameters in predicting the management, treatment, and prognostication of COVID-19 infection.

Article citation: Chaudhary, S.R.A., Singh, K.K.B., Rabaan, A.A. Clinicopathological presentation of COVID-19 patients presented at the rural healthcare center. Electron J Med Res. **2025**. 1(1): 54-60.

Introduction

In 2019, the COVID-19 infection was instigated by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (Ahmed et al., 2020). Firstly, the virus was identified in China in December-2019 (Ahmed et al., 2022). Internationally, including Pakistan is suffering from the COVID-19 outbreak (Ahmed et al., 2020). Globally on March 11, 2020, the World Health Organization (WHO) acknowledged the COVID-19 outbreak as a pandemic situation (Ahmed et al., 2020). As of September 19, 2021, a total of 229,415,774 positive cases have been reported worldwide, with 4,699,359 deaths. In the American continent, 88,561,500 cases have been reported positive, and counted deaths were 2,181,137. Also, three countries reporting most cases are the United States (42,287,762), Brazil (21,247,667), and Argentina (5,241,327) followed by the status of the death United States

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(676,075), Brazil (590,955) and Mexico (271,765) (Kalil et al., 2021). Likewise, in the Asian continent, the total of positive cases was 65,962,928, and the total number of counted deaths was 1,021,161. Moreover, three countries reporting the most detected cases are India (33,478,419), Iran (5,408,860), and Indonesia (4,192,695) subsequently the death counted numbers of the top three countries were India (445,133), Indonesia (140,634), and Iran (116,91), respectively (Kalil et al., 2021; Yusof et al., 2021).

In Pakistan 1,232,595 COVID-19, detected cases and 27,432 confirmed deaths have been reported(Anis et al., 2021). Furthermore, approximately 75,955,215 people have been vaccinated in Pakistan till September 22, 2021 (Anis et al., 2021). Additionally, data has shown that older patients with comorbidities are more vulnerable to the COVID-19 (Anis et al., 2021; Naveed et al., 2022). SARS CoV2 infection distresses the working of renal, hepatic, cardiac, gastrointestinal, and pancreatic systems (Rizvi et al., 2022; Sohail et al., 2023). Although, the virus has the capability to attack and cause neural disorders in the peripheral and central nervous systems (Pennisi et al., 2020; Tsatsakis et al., 2020).

The severity of COVID-19 disease shows up on a wide spectrum, with most people having no symptoms or a mild illness at one end of the spectrum and only a few going on to have moderate, severe, or critical disease (Kalil et al., 2021; Zeshan et al., 2021). The COVID-19 virus doesn't just affect the respiratory system; instead, it triggers systemic inflammatory reactions that manifest as a range of organ dysfunctions, including hematological issues (Franchini et al., 2020). Patients with COVID-19 have shown hematological abnormalities that include leukocytosis, lymphopenia, increased neutrophil to lymphocyte ratio (NLR), thrombocytopenia, and coagulopathy (Wang et al., 2020; Wj et al., 2020). Global literature surveys have identified the thromboembolic phenomenon (Bikdeli et al., 2020). The most common tests performed on patients who arrive at the hospital are complete blood counts and coagulation profiles, and it is vital that illness severity be determined as soon as possible in order to enhance prognosis. The main goal of our study is to find out which blood problems are most common in young (patients under fifty) and old (patients over fifty) COVID-19 patients in our area who went to an outpatient clinic at a rural health facility.

Materials and Methods

The observational cross-sectional study design included all males and females above 18 years of age or older reported at an outpatient clinic in the rural health center, Awan Dhai Wala, Lahore from 1st May 2021 to 31st August 2021. The study was approved by the under ethical number 514/21/RHC AD Wala. A total of 100 patients reported in the above-mentioned time frame were included in the study. The COVID-19 diagnosis was confirmed by RT-PCR of NPS.

Data about demographic characteristics like; age, sex, body mass index, travel history, and contact with the COVID-19 positive patients were collected. Also, symptoms (fever, cough, shortness of breath, and absence of taste/smell) and comorbidity status (ischemic heart disease, chronic kidney disease, hypertension, diabetes, and urinary tract infection) data were collected at the time of knowing the history of the patients. Pathology reports of all the patients diagnosed with COVID-19 were reviewed. Laboratory related data was collected on the following parameters; pathology lab tests (neutrophils, white blood cells, hemoglobin, creatinine, lactate dehydrogenase, alkaline phosphatase, alanine transaminase (ALT), ferritin, D-dimer, C-reactive protein, albumin, and aspartate transaminase (AST) were collected at the time reported at an outpatient clinic. All the above-mentioned data was collected on a structured questionnaire.

Statistical analysis

Statistical analysis was applied by using the SPSS software (version 20.0; SPSS, Chicago, IL, USA). Quantitative variables were stated as mean ± standard deviation and median (range: minimum and maximum) and frequencies and percentages were mentioned for qualitative. Chi-square test or fisher's exact test (when necessary) was applied to check the association between qualitative variables while for quantitative variables independent t-test was used to check the mean differences. Statistical significance was defined as a two-tailed p-value of 0.05.

Results

A total of 100 COVID-19 positive patients were enrolled in this study with a mean age and standard deviation of 49.25 ± 18.33 years. The majority 66 (66%) of participants were male with a mean body mass index and standard deviation of 26.01 ± 3.50. Furthermore, approximately 87 (87%) of the study population had negative travel history negative contact history with the COVID-19 positive patients. In addition, the cough was the most prevailing symptom 74 (74%), followed by fever 68 (68%), shortness of breath 60 (60%), and absence of taste/smell 3 (3%), respectively. Also, diabetes was the most prevalent comorbidity 44 (44%), after that hypertension 33 (33%), ischemic heart disease 17 (17%), urinary tract infection 8 (8%) and chronic kidney disease 1 (1%), respectively **(Table 1)**.

Table 1. Demographic characteristics, presenting symptoms and comorbidity status of COVID-19 positive patients.

Variables	Characteristics	N = 100
Demographic characteristics		
Age (years)	Mean ± standard deviation	49.25 ± 18.33
	Median (min-max)	51 (18-88)
Sex	Male	66 (66.0)
	Female	34 (34.0)
Body mass index	Mean ± standard deviation	26.01 ± 3.50
	Median (min-max)	26 (21-32)
Travel history	No	87 (87.0)
	Yes	13 (13.0)
Contact with COVID-19 positive patient	No	75 (75.0%)
	Yes	25 (25.0%)
Presenting symptoms		
Fever	No	32 (32.0%)
	Yes	68 (68.0%)
Cough	No	26 (26.0%)
	Yes	74 (74.0%)
Shortness of breadth	No	40 (40.0%)
	Yes	60 (60.0%)
Absence of taste/smell	No	97 (97.0%)
	Yes	3 (3.0%)
Comorbidity status at baseline		
Ischemic heart disease	No	83 (83.0%)
	Yes	17 (17.0%)
Chronic kidney disease	No	99 (99.0%)
	Yes	1 (1.0%)
Hypertension	No	67 (67.0%)
	Yes	33 (33.0%)
Diabetes	No	56 (56.0%)
	Yes	44 (44.0%)
Urinary tract infection	No	92 (92.0%)
	Yes	8 (8.0%)

Table 2 showed the mean and median descriptive statistics of hematological findings of COVID-19 positive patients.

Table 2. Baseline hematological findings of COVID-19 positive patients.

Variables	Mean ± SD*	Median (range: min-max)
Hemoglobin, g/dL	13.06 ± 1.93	13.20 (7.7-17.6)
White blood cells, × 10^3 cells/µl	10.75 ± 6.34	9 (2-32.70)
Hematocrit, L/L	39.32 ± 6.12	39 (23-58)
Neutrophils, × 10^3 cells/µl	71.76 ± 14.55	73 (42-97)
Lymphocytes, × 10^3 cells/µl	20.16 ± 12.83	17 (1.3-50.0)
Neutrophil-lymphocyte ratio, × 10^3 cells/µl	6.64 ± 7.76	4 (1-64)
Eosinophils, × 10^3 cells/µl	0.20 ± 0.46	0.01 (0-2.0)
Platelets, × 10^3 cells/µl	214.43 ± 109.32	196 (80-650)
D-dimer, mg/L	1496.64 ± 2681.62	600 (102-21353)
Ferritin, ng/mL ug/L	1142.64 ± 1204.13	857 (4.0-7254.0)
C-reactive protein, mg/L	137.97 ± 124.76	120 (1-490)
Lactate dehydrogenase, u/L	595.04 ± 452.54	523 (120-3477)
Alanine transaminase, U/L	127.69 ± 352-78	88 (9-3525)
Aspartate transaminase, U/L	138.56 ± 644.81	65 (14-6461)
Bilirubin, mg/dL	0.50 ± 0.53	0.40 (0.1-3.0)
Creatinine kinase, mg/dL	377.89 ± 729.49	150 (13-6432)
Sodium, mEq/L	133.60 ± 6.83	134 (166-157)
Potassium, mEq/L	3.89 ± 0.68	4.0 (2.6-6.7)

*Standard deviation.

Furthermore, body mass index and contacted history with COVID-19 positive patients showed statistical significance p-value <0.05. Furthermore, patients in having age group less than 50 years were had a more positive patient contact history of 19 (76%) as compared to above 50 years 6 (24%). Similarly, fever 36 (52.9%), cough 44 (59.5%), and shortness of breath 39 (65%) were the most prevalent symptoms in patients having age group above 50 years. Likewise, comorbidities were also commonly reported in patients above 50 years old as shown in **Table 3**.

Table 3. Bifurcation of demographic, presenting symptoms, and comorbidity status of COVID-19 positive patients with respect to age groups.

Variables	Characteristics	Up to 50 year 50 (100%)	Above 50 year 50 (100%)	*P*-value
Sex	Male	36 (72.0)	30 (60.0)	0.20
	Female	14 (28.0)	20 (40.0)	
Body mass index	Mean ± SD*	26.95 ± 3.63	25.06 ± 3.05	0.006
Travel history	Present	9 (69.2%)	4 (30.8%)	0.14
Contact with COVID-1 positive patients	Contacted	19 (76.0%)	6 (24.0%)	0.003
Fever	Yes	32 (47.1%)	36 (52.9%)	0.40
Cough	Present	30 (40.5%)	44 (59.5%)	0.001
Shortness of breath	Yes	21 (35.0%)	39 (65.0%)	0.001
Absence of taste/smell	Yes	3 (100.0%)	0 (0.0)	0.24
Ischemic heart disease	Present	1 (5.9%)	16 (94.1%)	0.001
Chronic kidney disease	Present	0 (0.0%)	1 (100.0%)	1.00
Hypertension	Present	5 (15.2%)	28 (84.8%)	0.001
Diabetes	Present	7 (15.9%)	37 (84.1%)	0.001
Urinary tract infection	Present	7 (87.5%)	1 (12.5%)	0.05

*Standard deviation.

Table 4 presented the bifurcation of hematological findings of COVID-19 positive patients with respect to age groups. Though, most of the high proportions of hematological findings were reported in patients above 50 years old. Therefore, Table 4 only presented the statistically significant hematological factors bifurcated with respect to age group p-value <0.05.

Table 4. Bifurcation of hematological findings of COVID-19 positive patients with respect to age groups.

Variables	Up to 50 years 50 *	Above 50 years 50 *	*P*-value
White blood cells, × 10^3 cells/µl	8.09 ± 4.26	13.30 ± 7.02	0.001
Hematocrit, L/L	40.47 ± 6.05	38.08 ± 5.98	0.05
Neutrophils, × 10^3 cells/µl	64.70 ± 14.11	78.72 ± 11.15	0.001
Lymphocytes, × 10^3 cells/µl	26.24 ± 12.71	14.10 ± 9.60	0.001
Neutrophil-lymphocyte ratio	3.90 ± 3.55	9.31 ± 9.66	0.001
Eosinophils, × 10^3 cells/µl	0.30 ± 0.54	0.10 ± 0.34	0.02
D-dimer, mg/L	927.78 ± 1431.12	2038.56 ± 3426.55	0.03
Ferritin, ng/mL ug/L	893.84 ± 1230.82	1371.92 ± 1135.81	0.04
C-reactive protein, mg/L	94.86 ± 114.15	178.32 ± 122.19	0.001
Lactate dehydrogenase, u/L	517.30 ± 537.33	667.66 ± 332.66	0.009
Alanine transaminase, U/L	83.78 ± 97.37	169.30 ± 485.76	0.04
Creatinine kinase, mg/dL	204.80 ± 213.98	546.42 ± 979.82	0.02

*Mean ± SD

Discussion

COVID-19 was first diagnosed in December 2019 in Wuhan, China. The occurrence of SARS-CoV-2 has since spread speedily and headed to a worldwide pandemic (Guan et al., 2020; Zhu et al., 2020). A total of 100 COVID-19 positive patients were enrolled in this study with a mean age and standard deviation of 49.25 ± 18.33 years. The majority 66 (66%) of participants were male with a mean body mass index and standard deviation of 26.01 ± 3.50. In addition, the cough was the most prevailing symptom 74 (74%), followed by fever 68 (68%), shortness of breath 60 (60%), and absence of taste/smell 3 (3%), respectively. Also, diabetes was the most prevalent comorbidity 44 (44%), after that hypertension 33 (33%), ischemic heart disease 17 (17%), urinary tract infection 8 (8%), and chronic kidney disease 1 (1%), respectively. The bifurcations of hematological factors of COVID-19 positive patients with respect to age groups were also presented. Though, most of the high proportions of hematological findings were reported in patients above 50 years old.

This study would help to check the comorbidity status, hematological parameters variations in below and above fifty years old patients. Cough (57.1%), fever (34.3%), and dyspnea (62.9%) were the prevalent symptoms as presented in the studies (Yang et al., 2020a; Zhou et al., 2020). In our study, the most common and prevalent symptoms were cough (74%), fever (68%), shortness of breath (60% and absence of taste/smell (3%), respectively. Liang et al. reported that old age (above 50 years old) and comorbidity status were the main risk factors of poor prognosis in COVID-19 patients (Liang et al., 2020). Likewise, in this work ischemic heart disease, chronic kidney disease, hypertension, and diabetes were reported in (94%), (100%), (84.8%) and (84.1%), respectively. These results also reflected a similar story as reported in the published data.

Additionally, patients with COVID-19 infection have subsequently benefitted from an understanding of the clinicopathological variations and laboratories features of the disease. Due to minimal awareness of the virus's pathology and epidemiology, the death rate was higher at the start of the outbreak. Successive treatment and management of COVID-19 patients have significantly improved regardless of the nonexistence of antiviral therapies (Liu et al., 2020b). COVID-19 is a multi-system condition that involves the hematopoietic, gastrointestinal, renal, pulmonary, and cardiovascular systems (Richardson et al., 2020). Hematological anomalies are repeatedly predicted in patients with COVID-19 infection and have prognostic and therapeutic importance (Terpos et al., 2020). Monitoring inflammatory indicators (CRP, ferritin, and LDH) and lymphocyte count variations might help to recognize the patients with poor prognosis and may need rapid treatment and management to improve outcomes (Fan, 2020; He et al., 2021).

In addition, published literature reported that white blood cells (*p*-0.001), neutrophil-lymphocyte ratio (*p*-0.001), eosinophil (*p*-0.02), ferritin (*p*-0.04), lactate dehydrogenase (*p*-009), alanine transaminase (*p*-0.04) and creatine kinase (*p*-0.02) were significantly lower in patients below fifty years old as compared to above fifty years old patients. Also, neutrophils, D-dimer, C-reactive protein, and lymphocytes were statistically significantly higher in patients presented with age above fifty years old (*p*-0.001, 0.03, 0.001, and 0.001, respectively). Therefore, more lymphocytes and D-dimer counts could be consumed or brutally reduced in the immune system. Many studies reported that D-dimer could be an important prognostic factor to predict the

severity of COVID-19 infection. These comparative results were comparable with the published data previously (Liu et al., 2020a; Qin et al., 2020; Yang et al., 2020b). It was a single center study. Sample size was limited as we selected all males and females above 18 years of age or older reported at an outpatient clinic in the rural health center, Awan Dhai Wala, Lahore from 1st May 2021 to 31st August 2021. Secondly, we have not been done any kind of follow-up of the patients to check the survival status and treatment modalities. Therefore, a multicenter prospective study should be done to check the efficacy of treatment survival status of the patients.

Conclusion

This study concluded that the hematological, coagulative, and inflammatory markers are the utmost important parameters in predicting the management, treatment, and prognostication of COVID-19 infection. These factors may provide convenient, reliable, and cost-effective techniques for envisaging complications rate and COVID-19 disease severity.

Author Contributions: Conceptualization, S.R.A.C.; methodology, S.R.A.C.; software, S.R.A.C.; validation, K.K.B.S., and A.A.R.; formal analysis, S.R.A.C.; investigation, S.R.A.C.; resources, K.K.B.S., and A.A.R.; data curation, K.K.B.S., and A.A.R.; writing—original draft preparation, S.R.A.C.; writing—review and editing, K.K.B.S., and A.A.R.; visualization, S.R.A.C.; supervision, S.R.A.C.; project administration, S.R.A.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Human Research Ethics Committee, Rural Health Centre, Awan Dhai Wala, Lahore, Pakistan, with code HREC Code: 5/4/21/RHC-AD-WALA approved on 25 August 2021.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: More data related to this research could be obtained upon a reasonable request to the corresponding author.

Acknowledgments: The authors would like to acknowledge Rural Health Center Awan Dhae Wala, Lahore for providing the research facilities.

Conflicts of Interest: The authors declare no conflict of interest.

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