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Assessing Disease Severity in COVID-19 Patients: Correlations with Laboratory, Radiological, Comorbidity, and Blood Gas Parameters

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ABSTRACT

Objective: To compare the lab investigations, blood gases analysis, and radiological findings to assess the severity of COVID disease in positive patients with comorbidities.

Study Design: Cross-Sectional Study.

Place and Duration of Study: Railway Hospital, Rawalpindi, and Services Hospital, Lahore, Pakistan, from Dec 21 to Apr 22.

Methodology: Data of 750 patients, admitted in Railway Hospital Rawalpindi and Services Hospital Lahore, were gathered, and WHO categories of COVID-19 disease severity were used, and correlated with TLC, HbA1c, CRP, LDH, pH, and oxygen requirement at baseline.

Results: Significant differences were observed among mild, moderate, severe, and very severe categories of COVID-19 patients concerning Total Leukocyte Count (TLC)(p=0.001), Hemoglobin A1c (HbA1c) (p=0.006), C -reactive protein (CRP) (p=0.001), Lactate Dehydrogenase (LDH) (p=0.010), oxygen saturation (SpO2) (p=0.001), pH(p=0.001), and oxygen requirement at baseline(p=0.034). Additionally, there was significant correlation between disease severity and HbA1c(r=0.244, p=0.003), TLC(r=0.458, p< 0.001), ferritin(r=0.260, p=0.001), C-reactive protein(r=0.443,p<0.001), LDH(r=0.211,p=0.01), and pH(r=0.653, p<0.001) and oxygen requirement at baseline(r=0.669, p<0.001). Significant associations with co-morbidities were seen in relation to severe and very severe COVID-19 disease (p-value ≤0.001)

Conclusion: Patients with severe and very severe disease were found to have raised levels of TLC, HbA1c, CRP, LDH, pH, and oxygen requirement at baseline; additionally, there is a strong association of comorbidities with severe and very severe disease.

Keywords: Covid severity, CRP, D-Dimer, HbA1c, LDH, Serum Ferritin.

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INTRODUCTION

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, became a global health crisis a while ago, significantly challenging healthcare systems worldwide.[1] To effectively manage such issues in future, it is essential to understand the diverse clinical manifestations and disease severity in COVID-19 patients.[2] Integrated assessment approaches that combine various diagnostic modalities can provide a comprehensive understanding of disease progression and aid in developing targeted therapeutic strategies.[3]

COVID-19 severity varies widely, from asymptomatic or mild cases to severe pneumonia, acute respiratory distress syndrome (ARDS), and potentially fatal outcomes. Identifying factors associated with severe disease is crucial for risk stratification, timely intervention, and optimal healthcare resource allocation.[4] Laboratory investigations, such as elevated inflammatory markers (e.g., CRP, IL-6, and procalcitonin) and abnormalities in complete blood counts (e.g., lymphopenia and increased neutrophil counts), play a pivotal role in assessing disease severity and guiding clinical management of COVID-19.[5] Moreover, coagulation profiles, including D-dimer levels, are critical in evaluating hypercoagulability and thrombotic complications in COVID-19 patients. Integrating these laboratory parameters into a comprehensive assessment framework allows for a nuanced understanding of COVID-19 severity.[6]

Chest imaging, including high-resolution computed tomography (HRCT) and chest X-rays, is vital for diagnosing and monitoring COVID-19-associated lung pathology, revealing features such as ground-glass opacities and consolidations common in

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severe cases. Understanding the correlations between radiological patterns and clinical parameters is essential for a holistic approach to disease severity assessment.[7] Additionally, underlying comorbidities, such as diabetes, cardiovascular diseases, hypertension, and respiratory disorders, significantly impact COVID-19 severity.[8]

Therefore, this study explores the integrated assessment of disease severity in COVID-19 patients, focusing on the correlations among laboratory parameters, radiological findings, comorbidities, and blood gas analyses. This comprehensive evaluation aims to improve risk stratification, guide therapeutic decisions, and enhance patient outcomes, if such encounters happen in future.

METHODOLOGY

This retrospective hospital-based cross-sectional study was conducted at Railway Hospital, Rawalpindi, and Services Hospital, Lahore, Pakistan, from Dec 21 to Apr 22. Ethical approval was obtained for the study from Islamic International Dental Hospital, Ref No: IIDC/IRC/2022/012/004. 750 admitted patients were selected for data collection using convenience sampling. Sample size was calculated using the WHO sample size calculator, taking a confidence level of 95% and a margin of error 5%. Based on the prevalence of Covid 19, which is 18.3%,[9] estimated sample size was 298.

Inclusion Criteria: Adults, both female and male, diagnosed Covid positive on RT- PCR between the ages of 24 - 66 years were enrolled in the study.

Exclusion Criteria: Smokers, patients with incomplete lab data and history, patients not willing to participate, and patients with active tumors or an autoimmune disease were excluded from the study.

Data for this study were retrospectively collected from hospital records of COVID-19 patients who presented with predominant symptoms such as fever, cough, loss of smell and taste, and diarrhea. The collection process was systematic and adhered to standardized protocols to ensure accuracy and reliability of the data. Upon admission, each patient's demographic information, including age, gender, and presence of any underlying comorbidities (e.g., diabetes, cardiovascular diseases, hypertension, and respiratory disorders), was recorded. This initial assessment also documented the primary symptoms reported by the patients.

Blood samples were analyzed to measure several laboratory parameters: White Blood Cell (WBC) count to assess the immune response and detect potential infections, Lymphocyte count as lymphopenia has been associated with severe COVID-19, D-dimer levels to evaluate the risk of thrombosis and coagulopathy, Ferritin levels as an indicator of inflammation and potential hyperferritinemia, C-reactive Protein (CRP) to measure the level of inflammation, Lactate Dehydrogenase (LDH) to assess tissue damage, HbA1c levels to determine glycemic control and identify undiagnosed diabetes, and blood pH to monitor acid-base balance, particularly important in patients with respiratory distress.

The severity of COVID-19 was assessed based on the patient's oxygen saturation (SpO_2) levels and respiratory rate, in line with WHO interim guidelines.[10] Patients were categorized into four groups: mild (RT-PCR positive without hypoxia), moderate (RT-PCR positive with signs of pneumonia but no hypoxia, SpO_2 >90%), severe (signs of pneumonia with respiratory rate > 30 breaths/min and/or SpO_2 ≤ 90%), and very severe/critical (presence of acute respiratory distress syndrome (ARDS) or septic shock). Chest imaging (HRCT and chest X-rays) was performed to identify radiological features such as ground-glass opacities and consolidations, which are common in severe cases.

The primary outcomes studied were recovery and mortality. Recovery was defined as discharge from the hospital with clinical resolution of symptoms, while mortality was recorded as death due to COVID-19 complications. All collected data were entered into a secure database for analysis. Statistical methods were applied to examine the correlations among laboratory parameters, radiological findings, comorbidities, and blood gas analyses with disease severity and patient outcomes. This integrated assessment aims to improve understanding of disease progression and guide therapeutic decisions for better patient management.

Data was entered in Statistical Package for Social Sciences (SPSS) version 22. Normality of the data was checked using Shapiro-Wilk test. Data was displayed as Mean+SD. Comparison of descriptive characteristics and lab parameters between the groups was done using One -way ANOVA. Correlation of disease severity with variables was checked using Pearson's correlation and Spearman's correlation for

normally and non-normally distributed data, respectively. D -Dimer was non-normally distributed. Association among comorbidity and severity was determined using Chi-square; the *p*-value ≤ 0.05 was considered significant.

RESULTS

Out of total 750 patients inducted in the study, 420(56%) were male, and 330(44%) were female. Mean age of the patients was 34.01±1.52 years, 44.61±3.52 years, 45.32±3.52 years, and 55.85±2.51 years in mild, moderate, severe, and very severe groups, respectively. Fever, body aches, loss of taste and smell, dyspnea, cough, tachypnea, diarrhea are the most come symptom frequency of each is mentioned in Table-I. Among the key findings of the study, no significant differences were observed between the patient groups in terms of age, gender, BMI, and symptoms (Table-I). However, there were significant differences in laboratory parameters across the four severity groups, particularly in total leukocyte count (TLC), HbA1c, C-reactive protein (CRP), and lactate dehydrogenase (LDH) levels. These values were markedly higher in very severe cases compared to the other categories (Table-II). Additionally, significant differences were found in SpO_2 levels, blood pH, and baseline oxygen requirements between the groups, with *p*-values of <0.001, <0.001, and 0.03, respectively. No significant differences were found in hemoglobin levels, lymphocyte counts, and D-dimer levels.

Correlation analysis showed that disease severity was significantly corelated with several laboratory parameters, including HbA1c (r=0.244, p=0.003), TLC (r=0.458, *p*<0.001), ferritin (r=0.260, *p*=0.001), CRP (r=0.443, *p*<0.001), LDH (r=0.211, *p*=0.01), pH (r=0.653, *p*<0.001), and baseline oxygen requirement (r=0.669, *p*<0.001). There was no significant correlation between disease severity and D-dimer levels (r=0.155, *p*=0.155) (Table-III).

Table I: Descriptive Characteristics of Covid Positive Patients (n=750)

Characteristics	Mild n= 190	Moderate n=210	Severe n=150	Very severe n=210	*p*-value
Age(years)	34.01±1.52	44.61±3.52	45.32±3.52	55.85±2.51	0.11
Gender	Male =100 Female =80	Male =110 Female =100	Male =100 Female =50	Male =110 Female=100	0.20
BMI(Kg/m2)	26.5±2.52	28.4±3.52	27.1±1.51	29.3±7.41	0.02
Symptoms					
Fever (0 C)	127(67%)	147(70%)	133(89)	205(98%)	0.23
Body aches	62 (33%)	69(33%)	49(33%)	205(98%)	0.34
Loss of taste	26(14%)	21(10%)	30(20%)	115(55%)	0.23
Loss of smell	4(23%)	21(10%)	57 (34%)	71 (34%)	0.18
Dyspnea	104(55%)	161 (77%)	133 (89%)	189(90%)	0.43
Cough	85(45%)	155(55%)	79 (53%)	186(89%)	0.34
Tachypnea	64(34%)	36(75%)	133 (88%)	210(100%)	0.25
Diarrhea	23(12%)	14(7%)	12(8%)	18(9%)	0.26

Table-II: Comparison of Blood Laboratory Parameters of COVID-19 Patients Based on Severity of the Disease (n=750)

Characteristics	Mild n=190	Moderate n=120	Severe n=150	Very Severe n=210	*p*-value
Hemoglobin (mg/dl)	12.03 ± 3.24	13.03 ± 3.14	13.06 ± 0.14	12.33 ± 2.14	0.06
TLC (/L)	11.21±2.76	9.88±2.68	12.89±4.80	17.03±5.84	<0.001*
Lymphocyte count	3.01±0.30	2.80±0.77	3.07±0.87	3.20±1.98	0.67
HbA1c(mmol/L)	5.56±0.43	6.10±1.09	6.32±1.41	7.09±2.12	0.001*
CRP (mg/l)	81.82±49.70	77.02±51.59	113.68±61.40	162.66± 74.16	<0.001*
Ferritin level (ng/mL)	733.85±251.0	746.83±304.46	893.53±379.72	1000.32±408.21	0.37
Lactate dehydrogenase (U/L)	277.92± 164.12	388.33± 290.62	530.48±300.66	555.54± 329.33	0.01*
d-dimer (ng/mL)	6.99± 3.95	3.80± 3.00	10.60± 44.72	21.11± 122.85	0.86
SpO_2(%)	94.71±9.10	91.50±1.10	85.6±2.50	73.06± 5.70	<0.001*
pH	7.36±0.04	7.37±.38	7.3±0.78	7.06±0.15	<0.001*
Oxygen requirement at baseline	2.40±0.75	3.16±0.71	4.04±0.99	5.60±6.40	0.03*

Table-III: Correlation of Disease Severity with Lab Parameters (n=750)

Parameter	r-Value	*p*-value
HbA1c	0.244	0.003
TLC	0.458	<0.001
Ferritin	0.260	0.001
D -Dimer	0.155	0.05
CRP	0.443	<0.001
LDH	0.211	0.01
pH	0.653	<0.001
Oxygen requirement at baseline	0.669	<0.001

** p-value significant, r-Value is Pearson's Correlation Coefficient*

Table-IV illustrates the significant association of disease severity and outcome with comorbidities (*p*≤0.001). whereas no significant correlation was

found between mild and moderate disease and comorbidities.

Table-IV: Association of Premorbidity with Disease Severity And Outcome (n=750)

Characteristics	Comorbidity Present (n=305)	Comorbidity Absent (n=445)	*p*-value
Disease severity categories			
Mild	34(11.1%)	356(80.0%)	<0.001*
Moderate	54(17.7%)	11(2.4%)	
Severe	109(35.7%)	8(1.8%)	
Very severe	108(35.5%)	70(15.7%)	
Outcome			
Cured	212(69.5%)	401(90.1%)	<.001*
Died	93(30.5%)	44(9.9%)	

** p-value significant*

DISCUSSION

The findings presented in this study provide significant insights into the relationship between laboratory parameters, disease severity, and comorbidities in patients diagnosed with COVID-19. Our analysis revealed notable differences in specific laboratory markers among different disease severity categories, suggesting their potential utility as prognostic indicators.[11] Furthermore, we observed significant correlations between disease severity and several laboratory parameters, highlighting their clinical relevance in predicting disease progression and outcomes.

The elevated values of total leukocyte count (TLC), glycated hemoglobin (HbA1c), C-reactive protein (CRP), and lactate dehydrogenase (LDH) in very severe cases compared to other severity categories underscore their potential as biomarkers of disease severity which were reported by Fathalla *et al*.[12] These findings align with existing literature indicating the association between these markers and inflammatory processes, cellular damage, and metabolic dysregulation commonly observed in severe disease states, as highlighted by Dwivedi *et al*., in their retrospective study exploring the role of laboratory parameters as disease severity and mortality predictors in COVID-19 patients.[13] Moreover, parameters such as oxygen saturation (SpO_2), pH, and oxygen requirement exhibited significant differences among severity groups, further emphasizing their role in assessing disease severity and guiding clinical management. These findings were similar to those of Satici *et al*., as exhibited in their study about how a noninvasive index such as 'SpO_2/Fio2'is helpful in predicting death rate in individuals afflicted with pneumonia caused by COVID-19.[14]

Our correlation analysis revealed significant associations between disease severity and TLC, ferritin, CRP, LDH, pH, and baseline oxygen requirement. These findings corroborate previous research done by Muhammad *et al*., suggesting the prognostic value of these parameters in predicting disease outcomes and guiding treatment decisions.[15] However, the lack of significant correlation between disease severity and hemoglobin, lymphocyte count, and D-dimers suggests their limited utility as independent predictors of disease severity in this context and these findings were contradicted by the study done by Poudel *et al*., which showed that, particularly, D-dimer levels upon admission are an effective biomarker for assessment of COVID-19 disease progression.[16]

Additionally, our study identified a significant correlation between severe and very severe disease and the presence of comorbidities, highlighting the impact of underlying health conditions on disease severity and outcomes. This finding underscores the importance of comprehensive patient evaluation, including the assessment of comorbidities, in guiding treatment decisions and optimizing patient care, and is corroborated by the study done by Honardoost *et al*.,[17]

The clinical implications of our findings are noteworthy. The identification of specific laboratory markers associated with disease severity in COVID-19 can facilitate risk stratification and guide the selection of appropriate treatment strategies.[18,19] Furthermore, our findings emphasize the need for multidisciplinary approaches to patient care, involving collaboration between healthcare professionals from various specialties.

LIMITATIONS OF STUDY

Several limitations in this study warrant consideration. The retrospective nature of our study introduces inherent biases. Additionally, our study focused on a specific patient population and disease condition, limiting the broader applicability of our results. The reliance on hospital records may have resulted in incomplete data capture or inaccuracies. Furthermore, the study did not account for potential confounding variables such as variations in treatment protocols, which could influence the outcomes. Future research should aim to validate our findings in larger, prospective studies encompassing diverse patient populations and disease conditions.

CONCLUSION

In conclusion, our study underscores the significance of specific laboratory parameters in assessing disease severity and predicting outcomes in patients with a certain condition. TLC, HbA1c, CRP, LDH, pH, and baseline oxygen requirement demonstrated significant associations with disease severity, while comorbidities significantly influenced disease outcomes. Integrating laboratory findings with clinical assessment and considering the presence of comorbidities can enhance prognostication and improve patient outcomes. These findings underscore the importance of comprehensive patient evaluation and highlight the potential of laboratory parameters in guiding clinical management and improving patient care.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

GJ & MI: Data acquisition, data analysis, critical review, approval of the final version to be published.

AFA & MA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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