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Comparison of Laboratory Factors in COVID-19 Patients with and Without Mucormycosis

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ABSTRACT

Background: There is increasing evidence that COVID-19 infection increases the patient's risk of secondary fungal infections. We aimed to compare the role of blood factors and inflammatory markers during COVID-19 infection in patients with and without mucormycosis.

Materials: The current research is cross-sectional and descriptive-analytical. The statistical population of this research included hospitalized patients with mucormycosis related to COVID-19 (as case group) and hospitalized patients with COVID-19 without mucormycosis (as control group) in Booali Sina and Velayat hospitals, Qazvin, Iran. Demographic information (age, gender) and laboratory findings were recorded in the prepared draft.

Results: We enrolled 69 patients as case group and 82 patients as control group. The mean age of the surveyed patients was 56.89 ± 16.06 years. Seventy-nine (52.3%) people from the patients, were male and 72 (47.7%) people were female. The mean of hemoglobin and WBC was higher in patients without mucormycosis and these differences were statistically significant (P<0.05). The trend of CRP changes in patients without mucormycosis decreased more than patients with mucormycosis (P<0.001).

Conclusion: Differences in hematologic and inflammatory markers between COVID-19 patients with and without mucormycosis suggest that routine monitoring of parameters such as WBC, hemoglobin, CRP, and blood glucose may help identify patients at higher risk for mucormycosis and enable earlier diagnosis and intervention.

Keywords: Mucormycosis, Laboratory Factors, COVID-19

Introduction

Coronavirus disease 2019 (COVID-19) infection caused by the novel coronavirus 2 (SARS-CoV-2) shows a broad and rapidly varying clinical picture, ranging from mild upper respiratory tract infection to fatal pneumonia. It has shown a broad and rapidly varying clinical picture, ranging from mild upper respiratory tract infection to fatal pneumonia (1).

It has also been known to be accompanied by various secondary bacterial and fungal infections either due to pre-existing comorbidities or as a result of aggressive treatment of life-threatening COVID-19 pneumonia. One such severe post-COVID-19 infection that emerged as an epidemic in various parts of India was COVID-associated mucormycosis (CAM), which manifested as rhino-orbito-cerebral mucormycosis (ROCM), which worsened complications among vulnerable populations (2).

Mucormycosis, commonly known as black fungus, is an acute, fulminant, invasive fungal sinusitis caused by fungi belonging to the order Mucorales. factors such as uncontrolled diabetes mellitus, organ transplantation, iron overload, renal failure, long-term steroid therapy, and immunotherapy. The second wave of COVID-19 has seen a very unusual and dramatic increase in mucormycosis in active and recovered patients compared to the first wave (3, 4). Several factors, such as quarantine conditions, travel restrictions, and limited access to medical care, uncontrolled blood sugar, use of systemic steroids and immunomodulators, oxygen therapy during hospitalization, and use of wet, contaminated masks, have contributed to this sudden increase (5). Extensive corticosteroid use and inflammation, along with dysregulated iron metabolism in COVID-19, as indicated by elevated ferritin levels, are potential risk factors (6). Addressing these issues could reduce morbidity and mortality among vulnerable populations. However, we found a significant group of patients with normal to mildly elevated blood sugar, a short duration of steroid use, and no history of hospitalization.

COVID-19 pneumonia can cause alveolar epithelial damage. Extracellular matrix proteins may be exposed, and Rhizopus spores have been shown to adhere to laminin and type IV collagen (7).

In prospective case-control studies, serum glucose regulator protein 78 (GRP78) levels have been shown to be increased during COVID-19 pneumonia compared with healthy subjects, which may reflect a stress response and endothelial dysfunction (8). Accordingly, there is a positive correlation between C-reactive protein levels and GRP78 levels. COVID-19 causes lymphopenia, associated with disease severity. Lymphopenia has been a risk factor for invasive fungal infections (9).

The inflammatory response to SARS-COV-2 infection is characterized by an increased cytokine response, particularly IL-6 secretion. This is thought to stimulate ferritin and hepcidin synthesis and may lead to iron sequestration in macrophages. Since excess intracellular iron is associated with an increased risk of mucormycosis, a hyperferritinemic state may increase the likelihood of an increased risk, although this has not been definitively proven. Furthermore, a hyperferritinemic state can maintain a pro-inflammatory loop and also modulate the lymphocytic response (10). Indeed, there have been reports of mucormycosis in hyperferritinemic syndromes such as hemophagocytic lymphohistiocytosis (11).

COVID-19 has led to delay or avoidance of care for non-COVID-19 health conditions, including those requiring urgent or emergency care. Accessibility problems due to state or local imposed quarantines, widespread hospital bed shortages, and disruption of support systems with multiple household infections may indirectly contribute to delays in identification and treatment (12).

Mucormycosis leads to clinical complications and mortality through thromboembolism, leading to irreversible tissue necrosis. The observed coagulation is from complement-mediated thrombotic microangiopathies, not sepsis (13). This leads to endothelial damage and microvascular thrombosis. D-Dimer and serum ferritin are two of the many inflammatory markers that are increased during COVID-19 infection. High serum ferritin levels have been shown to facilitate fungal growth. On the other hand, D-dimer is a fibrin degradation product, high levels of which reflect an active clotting process or thrombus formation.

We aimed to compare hematological and inflammatory factors in COVID-19 patients with and without mucormycosis.

Materials and Methods

The present study was cross-sectional and descriptive-analytical. The study was conducted in Bu-Ali and Velayat Qazvin hospitals, Qazvin University of Medical Sciences, Qazvin, Iran in 2021-2022.

The study was approved by the Dissertation Council of the Faculty of Medicine of Qazvin University of Medical Sciences (Ethics Code: IR.QUMS.REC.1400.444). Informed written consent was obtained from all participants prior to data collection, and the study was conducted in accordance with the ethical guidelines of the declaration of Helsinki (1964, revised 2000). Finally, in order to maintain confidentiality, the results of this study were reported without disclosing the names and identifiable characteristics of the patients.

For this purpose, the relevant data were collected retrospectively through file reading from COVID-19 patients with mucormycosis as the case group and COVID-19 patients without mucormycosis as the control group. The control group was selected consecutively from the same hospitals (Booali Sina and Velayat) and within the same study period as the mucormycosis cases. All control patients were hospitalized in similar wards and under comparable clinical management protocols, including corticosteroid and oxygen therapy practices.

The sample size was estimated based on the study by Bhanuprasad et al., in which the mean CRP level in COVID-19 patients with mucormycosis was 85.05 ± 72.70 mg/L and in those without mucormycosis was 80.71 ± 99.91 mg/L (2). Considering a type I error (α) of 0.05, a type II error (β) of 0.2 (power = 80%), and a minimum detectable difference (d) of 28 mg/L between the groups, the calculated sample size was 100 participants per group (total = 200).

However, during the study period (2021–2022), only 69 eligible mucormycosis cases and 82 controls fulfilling all inclusion criteria were available in the participating hospitals. Consequently, the final sample size was 151 participants. Based on the observed effect sizes, the post-hoc power of the study was recalculated as approximately 78%, considered adequate for detecting the significant differences observed in this analysis.

Patients hospitalized in Booali Sina Hospital in Qazvin and Velayat with COVID-19 infection and having an indication for hospitalization based on the diagnostic criteria of the national guidelines. The basis for diagnosing corona in the present study was typical evidence in a CT-Scan of the lung or a positive specific PCR test from oropharyngeal secretions. In addition, the patient was diagnosed with mucormycosis with positive potassium hydroxide (KOH) staining and clinical features consistent with a fungal infection.

Inclusion criteria for the study, in addition to COVID-19 infection, for the case group, was hospitalization with a diagnosis of mucormycosis in each of the two hospitals. The inclusion criterion for the control group was COVID-19 patients who were not infected with mucormycosis. Incomplete patient records were one of the exclusion criteria for this study.

Data were collected using a structured checklist that included two main sections. The first section covered demographic information (age and sex),

and the second section comprised laboratory parameters such as hematological indices (HB, PLT, WBC, lymphocyte, and neutrophil counts, as well as the neutrophil-to-lymphocyte ratio), inflammatory markers (CRP and ESR), liver and kidney function tests (AST, ALT, ALK, BUN, and creatinine), electrolyte levels (Na and K), mineral levels (Ca, Mg, and P), and blood glucose (BS). For each patient, laboratory data were recorded at three time points: upon diagnosis, at the midpoint of hospitalization, and at discharge. In addition to the laboratory data, information on diabetes status, corticosteroid therapy (dose and duration when available), oxygen therapy, ICU admission, and baseline disease severity was extracted from hospital medical records. However, certain variables such as HbA1c, serum ferritin, D-dimer, and detailed information on corticosteroid regimen (cumulative dose, duration, and route of administration), as well as oxygen source/type, were not consistently available in the hospital records and therefore were excluded from the analysis.

Data Analysis

Statistical analyses were performed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean ± standard deviation for quantitative variables and as frequency (percentage) for qualitative variables. Independent *t*-test and chi-square test were used to compare laboratory and demographic variables between groups.

Although group-level data on key clinical and laboratory variables (age, sex, diabetes, corticosteroid use, and disease severity) were available and analyzed, individual-level patient data were not accessible in this retrospective dataset. Therefore, multivariable logistic regression could not be performed to adjust for potential confounders.

Given the large number of laboratory parameters assessed, *P*-values were interpreted with caution to minimize the risk of type I error. Although formal multiple-comparison corrections (e.g., False Discovery Rate adjustment) were not feasible due to the group-level nature of the data, significant findings were interpreted considering their clinical plausibility and consistency with previous studies.

Results

Overall, 69 COVID-19 patients with mucormycosis were included as the case group and 82 COVID-19 patients without mucormycosis were included as the control group. The mean age of the patients was 56.89 ± 16.06 years (range: 18–92 years). Overall, 79 patients (52.3%) were male and 72 (47.7%) were female (Table 1).

Among the 69 patients with COVID-19–associated mucormycosis, the diagnosis was confirmed by KOH smear in all cases. In addition, histopathological confirmation was available in 37 (53.6%) patients, fungal culture in 21 (30.4%), and PCR-based confirmation in 9 (13.0%) patients. Overall, 49 patients (71.0%) had at least one confirmatory diagnostic test beyond KOH microscopy, while the remaining 20 (29.0%) were diagnosed based on consistent clinical and radiological features together with positive KOH findings.

Table 1: Demographic characteristics of COVID-19 patients with and without mucormycosis

Variable	*With mucormycosis (n = 69)*	*Without mucormycosis (n = 82)*	*P-value*
Age, mean ± SD (yr)	55.38 ± 15.53	58.19 ± 16.49	0.288†
Male sex, n (%)	40 (58.0)	39 (47.6)	0.252‡

† Independent-samples *t*-test; ‡ Chi-square test

According to the findings of the first experiment, the mean hemoglobin in patients with mucormycosis was lower, while the mean WBC in patients with mucormycosis was higher, and these differences were statistically significant (P<0.05). In addition, the mean AST in patients without mucormycosis was higher, and these differences were statistically significant (P<0.001).

Also, according to Table 2, in patients with mucormycosis, blood sugar levels were higher than in patients without mucormycosis, and this difference was significant (P<0.05). However, the mean fasting blood sugar level showed that there was no significant difference between patients with mucormycosis and those without mucormycosis. Other laboratory factors examined did not differ significantly between patients with mucormycosis and those without mucormycosis (Table 2).

Table 2: Laboratory parameters of COVID-19 patients with and without mucormycosis

Laboratory parameter	***With mucormycosis (n = 69) mean ± SD or median (IQR)***	***Without mucormycosis (n = 82) mean ± SD or median (IQR)***	***P-value†***
Hemoglobin (g/dL)	11.68 ± 2.54	12.92 ± 2.13	0.002
Platelet count (×10³/µL)	189.92 ± 89.15	185.39 ± 62.48	0.777
WBC (×10³/µL)	9.01 ± 5.91	6.79 ± 3.52	0.008
Lymphocyte (%)	21.16 ± 11.07	17.26 ± 9.97	0.086
Neutrophil (%)	73.80 ± 12.04	77.74 ± 10.33	0.139
Neutrophil-to-lymphocyte ratio	5.15 ± 3.88	6.63 ± 5.16	0.094
CRP (mg/L)	54.97 ± 39.57	58.41 ± 33.39	0.240
ESR (mm/hr)	62.05 ± 32.35	59.21 ± 34.25	0.623
LDH (U/L)	527.38 ± 201.73	639.41 ± 398.08	0.144
ALT (U/L), median (IQR)	29 (19–50)	22 (14–48)	0.057
AST (U/L), median (IQR)	23 (15–34)	38 (27–57)	<0.001
ALK (U/L)	238.5 (174–329)	217.5 (170.5–286)	0.249
BUN (mg/dL)	22.26 ± 13.16	23.17 ± 19.57	0.217
Creatinine (mg/dL), median (IQR)	1.20 (0.98–1.40)	1.10 (0.90–1.40)	0.102
Sodium (mmol/L)	137.5 ± 4.67	136.45 ± 4.51	0.291
Potassium (mmol/L)	4.06 ± 0.46	4.07 ± 0.46	0.850
Calcium (mg/dL)	8.30 ± 0.83	8.19 ± 1.30	0.690
Magnesium (mg/dL)	2.02 ± 0.34	2.13 ± 0.34	0.130
Phosphorus (mg/dL)	3.83 ± 1.05	3.66 ± 1.34	0.405
Blood sugar (mg/dL)	182.23 ± 100.88	154.16 ± 87.05	0.036

*Values are presented as mean ± standard deviation or median (interquartile range).

†Independent-samples t-test or Mann–Whitney U test, as appropriate.

As shown in Table 3, the trend of CRP changes in patients with mucormycosis and those without mucormycosis differed significantly, with a greater decline observed in the non-mucormycosis group (P < 0.001), as illustrated in Figure 1.

Table 3: Serving changes in laboratory factors in patients with and without mucormycosis

Laboratory factors	***Without Mucormycosis Number: 82 SD ± mean***	***Mucormycosis Number: 69 SD ± mean***	*P-value*[*]
CRP first test	58.33 ± 41.39	54.39 ± 97.57	<0.001
CRP middle test	43.31 ± 91.50	56.31 ± 94.0	
CRP last test	21.25 ± 68.52	51.34 ± 23.35	
Hb first test	12.2 ± 92.13	11.20 ± 68.54	0.414
Hb middle test	12.2 ± 12.07	10.2 ± 26.30	
Hb last test	11.2 ± 97.42	10.1 ± 32.94	
PLT first test	185.62 ± 39.48	189.89 ± 92.15	0.081
PLT middle test	213.81 ± 86.08	196.10 ± 78.43	
PLT last test	201.82 ± 86.08	185.72 ± 23.51	
WBC first test	6.3 ± 79.52	9.5 ± 1.91	0.190
WBC middle test	8.3 ± 11.72	9.5 ± 4.63	
WBC last test	9.5 ± 39.34	9.5 ± 81.80	
ALT first test	42.62 ± 87.54	34.34 ± 47.80	0.578
ALT middle test	51.79 ± 93.18	53.70 ± 73.31	
ALT last test	55.65 ± 86.67	40.44 ± 61.83	
AST first test	55.74 ± 8.43	34.36 ± 25.89	0.478
AST middle test	42.31 ± 3.65	50.59 ± 38.09	
AST last test	52.34 ± 81.33	41.33 ± 11.38	
BUN first test	23.19 ± 17.57	22.13 ± 26.16	0.807
BUN middle test	33.25 ± 50.63	27.14 ± 62.40	
BUN last test	36.29 ± 95.24	32.23 ± 3.86	
Cr first test	1.1 ± 52.71	1.1. ± 63.57	0.797
Cr middle test	2.2 ± 0.82	1.0 ± 89.89	
Cr last test	1.3 ± 92.54	2.1 ± 4.24	
Na first test	136.4 ± 45.51	137.4 ± 5.67	0.050
Na middle test	138.4 ± 23.27	137.4 ± 68.07	
Na last test	137.4 ± 73.04	138.4 ± 92.50	
K first test	4.0 ± 7.46	4.0 ± 6.58	0.107
K middle test	4.0 ± 17.52	3.0 ± 81.55	
K last test	4.0 ± 25.55	3.0 ± 98.73	

*Repeated Measures test

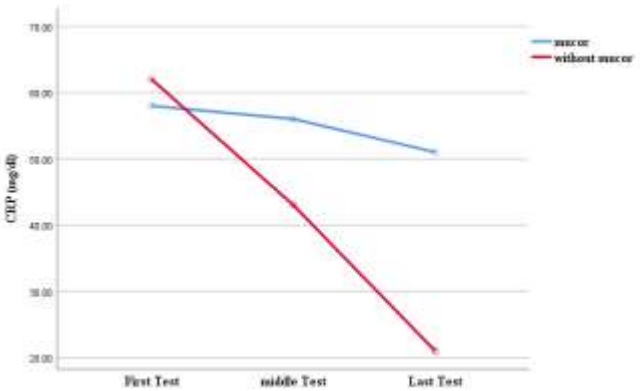

Figure 1: Mean trajectories of CRP (mg/dL) over time in COVID-19 patients with and without mucormycosis

Table 4 showed that there was no significant difference in mean blood glucose and fasting blood glucose levels between patients who experienced mortality and discharged patients with mucormycosis.

Table 4: Serving the relationship between blood sugar levels and mortality in patients with mucormycosis

Laboratory factors	***Mortality Number: 22 Mean ± SD***	***Without mortality Number: 47 Mean ± SD***	***P-value****
BS	184.61±106.76	181.10±99.43	0.826
FBS	152.75±69.92	127.18±74.30	0.409

* Mann-Whitney Test

Discussion

In this study, we compared the clinical and laboratory characteristics of COVID-19 patients with and without mucormycosis in two referral hospitals in Qazvin, Iran. A total of 69 COVID-19 patients with mucormycosis (case group) and 82 COVID-19 patients without mucormycosis (control group) were included from Booali Sina and Velayat hospitals. The main differences between the two groups were observed in hematological and inflammatory parameters. Patients with mucormycosis had significantly lower hemoglobin levels and higher WBC counts at admission, as well as lower AST levels, compared with patients without mucormycosis. In addition, the longitudinal trend of CRP showed a significantly slower decline in patients with mucormycosis, indicating a more persistent inflammatory response during hospitalization.

Some reviews have reported a surge in CAM during the second wave of the pandemic in India, highlighting an unprecedented rise in cases (14, 15). This increase has been attributed to multiple risk factors, including uncontrolled diabetes, corticosteroid therapy, and oxygen supplementation during COVID-19 management.

Recent reviews and studies have provided important insights into CAM. García-Carnero and Mora-Montes highlighted the high mortality and neglected nature of mucormycosis, emphasizing the need for early diagnosis and awareness among clinicians (16). Saberi-Hasanabadi et al. reviewed the emerging incidence of mucormycosis during the COVID-19 pandemic and underscored risk factors including diabetes, corticosteroid therapy, and prolonged hospitalization (17). In a regional study in Northwest Iran, Diba et al. reported that *Rhizopus arrhizus* was the predominant pathogen among COVID-19 patients with mucormycosis, and identified hyperglycemia, corticosteroid use, and ICU admission as key predisposing factors (18).

Together, these findings corroborate our observations regarding the association of uncontrolled diabetes, steroid therapy, and inflammatory dysregulation with CAM, highlighting the importance of vigilant monitoring and timely diagnosis in high-risk patients.

In the present study, the mean age of patients with COVID-19-associated mucormycosis was 55.38±15.53 years, which was slightly lower but statistically similar to the mean age of our non-mucormycosis COVID-19 patients (58.19±16.49 years). Therefore, we cannot conclude that younger individuals are more susceptible to mucormycosis. However, further research is needed on this issue, as we might have reached statistical significance if the cohorts had been larger.

The findings showed that most patients with mucormycosis were male (58%). Saadi et al. also evaluated data from 101 patients with COVID-19-associated mucormycosis, most of whom were male (78.9%) (19). The male predominance observed in our study is consistent with

previous studies, in which 78.9%–66% of COVID-19-associated mucormycosis cases to date have been male. This is likely related to a greater susceptibility to mucormycosis in men, which could be attributed to changes in their innate immunity and to a more severe and persistent COVID-19 infection.

COVID-19 infection causes a decrease in functional hemoglobin, which leads to respiratory distress and discomfort (20). The mean Hb level of patients with COVID-19-associated mucormycosis was lower than that of the control group, although this difference was not statistically significant ($P<0.05$). This observation may reflect an association rather than a direct causative relationship. Our findings were almost similar to those of Soni et al. , who reported a mean hemoglobin of 10.65±2.19 in patients with COVID-19-associated mucormycosis, lower than that of their control group ($P<0.05$) (21).

The mean lymphocyte count in patients with mucormycosis was 21.16±11.07, and there was no statistically significant difference between the case and control groups. Glucocorticoid use is a known risk factor for the development of mucormycosis (22). Glucocorticoids cause immunosuppression, hyperglycemia, and lymphopenia, all of which predispose to the development of mucormycosis. The widespread use of glucocorticoids in COVID-19 patients has contributed to the increase in cases of mucormycosis (23, 24). Therefore, virus-induced lymphopenia is another variable that may contribute to susceptibility COVID-19 patients to mucormycosis.

The mean neutrophil count was lower in patients with mucormycosis than in patients without mucormycosis; however, this difference was not statistically significant ($P>0.05$). Based on available evidence, individuals with impaired phagocytic function or reduced neutrophil activity may be more susceptible to mucormycosis. Neutrophils play a critical role in preventing the germination and spread of fungal spores (22). In a typical host, Mucorales are eliminated by mononuclear and polymorphonuclear phagocytes through the production of reactive oxygen species and cationic peptides, such as defensins (25).

Our COVID-19-associated mucormycosis patients also had higher ESR levels at the first test than the non-mycosis COVID-19 group, the significance of which is unknown. Consistent with our findings, in a study, patients with mucormycosis had significantly higher ESR and CRP levels than controls (19).

Patients with mucormycosis exhibited persistently higher CRP and ESR levels during hospitalization compared to controls, reflecting a more pronounced systemic inflammatory response. Elevated ferritin, commonly observed in severe COVID-19, may further enhance fungal growth by increasing iron availability and promoting inflammation, thereby contributing to susceptibility to mucormycosis (26, 27). Monitoring inflammatory and iron metabolism markers could help identify high-risk patients and guide timely interventions.

Mucormycosis is associated with diabetes mellitus, a significant risk factor. In the present study, patients with mucormycosis had higher blood glucose levels than patients without mucormycosis, and this difference was significant ($P<0.05$). It is important to note that several clinical and treatment-related factors, including diabetes mellitus, corticosteroid therapy, oxygen supplementation, ICU admission, and baseline disease severity, could influence both the development of mucormycosis and alterations in laboratory markers such as CRP, AST, and WBC. Although our study did not include a multivariable adjustment due to the group-level nature of the data, these potential confounding effects were considered during the interpretation of results. Future studies with larger and patient-level datasets are warranted to further clarify the independent impact of these factors.

Uncontrolled diabetes and systemic corticosteroid use are well-established risk factors for the development of mucormycosis. Patients with uncontrolled diabetes developed mucormycosis

2–3 weeks earlier after COVID-19 diagnosis than those without diabetes (28). Additionally, corticosteroid therapy could impair macrophage function, increasing susceptibility to fungal infections (29).

In agreement with our findings, in another study, the majority of COVID-19-associated mucormycosis patients had diabetes (63.6%) (30). However, our results are consistent with the study by Soni et al., which showed that there was no significant difference in mean fasting blood glucose levels between patients with and without mucormycosis (21).

Hyperglycemia is associated with impaired phagocyte function and may contribute to susceptibility to mucormycosis (31). In addition, based on studies, higher blood glucose in patients with severe COVID-19 and mucormycosis compared to patients with mild disease may also play a major role in increasing the prognosis of the disease and ultimately mortality. However, our findings showed that the mean blood glucose and fasting blood glucose levels in patients who died and discharged patients with mucormycosis were not significantly different, which could be due to the small number of samples in the present study. Therefore, this highlights the need for blood glucose monitoring to improve the prognosis in patients with COVID-19-associated mucormycosis.

In COVID-19 patients, elevated cytokine levels can exacerbate insulin resistance, a condition commonly induced by interleukin-6 (IL-6), which impairs insulin receptor signaling (32). Notably, one-third of individuals with mild COVID-19 exhibited elevated IL-6 levels, potentially contributing to glycemic dysregulation (33). In addition, certain COVID-19 treatments, including glucocorticoids, lopinavir-ritonavir, and remdesivir, may further impair glycemic control and increase the risk of developing mucormycosis (32).

Definitive diagnosis of mucormycosis requires histopathological confirmation, culture, or PCR-based identification of the pathogen (14, 15). In our cohort, all cases were initially diagnosed by KOH microscopy, and only a subset had additional confirmation through histopathology or culture, which may introduce diagnostic uncertainty and potential misclassification. PCR-based assays provide high diagnostic accuracy, with pooled sensitivities of up to 97.5% in bronchoalveolar lavage fluid and approximately 81.6% in blood samples (29). These findings support the inclusion of molecular diagnostics in the definition of CAM. Although PCR confirmation was not available for our patients, future studies incorporating comprehensive diagnostic testing—including histopathology, culture, and PCR—would enhance early detection, improve diagnostic precision, and facilitate timely management, particularly in high-risk COVID-19 patients.

Limitations

This study has several limitations. First, it was a retrospective chart review based on hospital records, which may be affected by documentation bias and missing data. Second, although all mucormycosis cases were confirmed by KOH microscopy, only a subset had additional confirmation by histopathology, culture, or PCR, raising the possibility of diagnostic misclassification. Third, key clinical and laboratory parameters such as HbA1c, serum ferritin, and D-dimer were not consistently available, limiting comprehensive analysis. Fourth, the control group was selected retrospectively, which may introduce selection bias. Fifth, the final sample size (n=151) was smaller than the originally calculated target (n=200), slightly reducing statistical power. Finally, because only group-level data were available, multivariable regression adjustment for confounders was not possible, and multiple-comparison correction could not be applied.

Despite these limitations, the study provides valuable insight into laboratory and inflammatory profiles among COVID-19 patients with and

without mucormycosis and underscores the need for larger prospective studies with complete datasets and confirmatory diagnostic testing.

Conclusion

This study highlights that COVID-19–associated mucormycosis is accompanied by a distinct pattern of hematologic and inflammatory alterations, suggesting a more persistent inflammatory state compared with COVID-19 patients without mucormycosis. Although no single laboratory marker can independently predict the development of mucormycosis, the combined assessment of routinely available parameters—particularly markers of systemic inflammation and immune response—may help clinicians identify patients at increased risk. Early recognition of these laboratory patterns, together with careful metabolic control and judicious use of corticosteroids, may facilitate timely diagnosis and intervention, potentially reducing morbidity and mortality associated with this severe opportunistic infection.

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Conflict of interest

The authors assert that there are no conflicts of interest.

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