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Original Research Article

COVID-19 Infection, Diabetes Mellitus, Old Age: A Deadly Trio for Mucormycosis in a Tertiary Care Hospital, South India

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Abstract:

Background: Coronavirus disease (COVID-19) causes an immunosuppressed state and increases risk of secondary infections like mucormycosis. The aim of this study is to report the spectrum of fungi, causing Mucormycosis in RT-PCR positive COVID-19 patients, by culture on SDA and study the role of other factors responsible for the disease.

Methodology: It is a prospective, observational study on mucormycosis in RT-PCR positive COVID-19 patients based on hospital records and fungal culture reports from 12th May 2021 to 21st July 2021. The study includes cultures conducted on Nasal debridement samples by 10% KOH (potassium hydroxide) mount, SDA (sabouraud dextrose agar) and LPCB (lactophenol cotton blue) mount from patients admitted in the hospital with RT- PCR confirmed COVID-19 and typical symptoms of Mucormycosis.

Results: In present study total of 114 patients fulfilling inclusion criteria, with mean age of 52.47±11.20yrs with male preponderance (77.2%) and female were 22.8%. among the included participants, 58.8% were with diabetes mellitus. The fungal culture was positive in 68.4% of the patients, among them 51.8% were positive for rhizopus, 6.1% for aspergillus niger, 2.6% for lichtheimia, 1.8% with aspergillus sp, aspergillus flavus, 1 patients each with aspergillus fumigates and rhizomucor. Steroid therapy was present in 20.2%.

Conclusion: Patients of Mean age 52 years with known diabetes status hospitalized for COVID-19 are at higher risk of developing Mucormycosis with the most common causative organism isolated being Rhizopus species.

Keyword: Mucomycosis, COVID-19, 10% KOH, SDA, LPCB Mount, Rhizopus, Aspergillus Fumigatus, Immunosupression.

Introduction

Coronavirus disease 2019 (COVID-19), caused by SARS coronavirus 2 (SARS-CoV- 2) was declared a worldwide pandemic by the World Health Organization (WHO) in March 2020. With over 162 million cases registered and over 3 million fatalities worldwide, the epidemic remains a public health threat. [1]With the increase in cases globally, possible COVID-19 consequences, such as increased sensitivity to secondary bacterial and fungal infections, are becoming more recognised. [2,3]

The immune dysregulation associated with COVID-19 is further aggravated by medical conditions such as diabetes mellitus, and the widespread use of immunosuppressive agents and broad-spectrum antibiotics. [4–6] The rate of hospital acquired secondary bacterial and fungal infection has been reported to be approximately 8%. It is observed that fungal infections were more likely to develop during the more advanced stages of COVID-19 infection, with higher mortality among patients with fungal co-infections. [3]

Mucormycosis is known to affect aged, immunocompromised patients especially those with diabetes mellitus, prolonged corticosteroid use, solid organ transplant recipients, neutropenia and haematological malignancies. [7–9] It is an opportunistic infection leading to invasion of blood vessels by fungal hyphae, causing infarction and necrosis of a variety of end-organ host tissues. Rhino-orbital infection with the mucorales species of fungus has a poor prognosis with a mortality rate reaching 50%, even with appropriate treatment. [4,6,10–14] In India there was a sudden increase in the number of mucormycosis cases in patients of COVID-19. At the time of this study large number

of cases of mucormycosis has been reported. [4,15–17] The present study aimed to report the spectrum of fungi, causing Mucormycosis in RT-PCR positive COVID-19 patients, and influence of old age and diabetes mellitus on the outcome of the patients.

Material & Method:

The study includes cultures conducted on Nasal debridement samples received from 12th May 2021 to 21st July 2021 from patients admitted in the hospital with RT-PCR confirmed COVID-19 and typical symptoms of Mucormycosis. This study was approved by the research and ethics committee. Data entry and analysis were performed using SPSS for windows version SPSS 14.0 software.

The diagnosis of COVID-19 was based on real-time polymerase chain reaction (RT-PCR) test from nasopharyngeal or oropharyngeal swabs. In clinically suspected patients, presence of fungal hyphae, by direct examination in 10% potassium hydroxide (KOH) from nasal debrided tissue was used for diagnosis. Mucormycosis was subsequently proven based on microbiological culture on SDA from debrided specimen. Apart from ascertaining COVID-19 status, blood investigations and computed tomography (CT) and/or magnetic resonance imaging (MRI) of the orbit, brain and/or paranasal sinuses were performed for all cases to assess the extent of involvement from mucormycosis.

Statistical Analysis: Data was collected and tabulated using Microsoft excel. Strata version 15 binominal regression model was used to derive incident rate ratios with 95% confidence interval for each outcome. The statistics of percentage was used

Result

In present study total of 114 patients fulfilling inclusion criteria, with mean age of 52.47±11.20yrs with male preponderance (77.2%) and female were 22.8%. among the included participants, 58.8% were with diabetes mellitus.(Table 1)

The fungal culture was positive in 68.4% of the patients, among them 51.8% were positive for Rhizopus, 6.1% for aspergillus niger, 2.6% for Lichtemia, 1.8% with aspergillus, aspergillus flavus, 1 patients each with aspergillus fumigates and rhizomucor. (Table 2)

Table 1: Demographic details of the study participants

		Frequency	Percent
Gender	Female	26	22.8
	Male	88	77.2
Diabetes mellitus	No	47	41.2
	Yes	67	58.8
Fungal Culture	Negative	36	31.6
	Positive	78	68.4
	Total	114	100.0

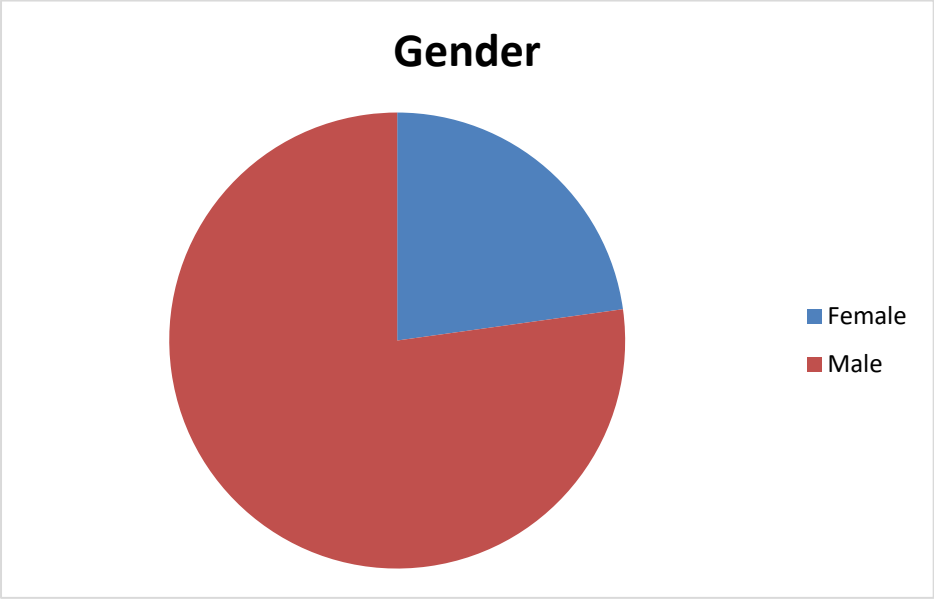

Figure 1: Gender distribution in present study

Table 2: Showing the frequency of fungal growth isolated from patients

		Frequency	Percent
Organism	Negative	37	32.5
	Aspergillus	2	1.8
	Aspergillus flavus	2	1.8
	Aspergillus fumigatus	1	.9
	Aspergillus niger	7	6.1
	Lichthemia	3	2.6
	Rhizomucor	1	.9
	Rhizopus	59	51.8
	Trichophyton	2	1.8
	Total	114	100.0

Table 3: In hospital stay details of the patients

		Frequency	Percent
Oxygen therapy	Yes	25	21.9
	No	89	78.1
Steroid therapy	Yes	23	20.2
	No	91	79.2
Acquired diabetes during hospital stay	Yes	24	21.1
	No	90	78.9
Underwent surgery	Yes	52	45.6
	No	62	54.4
Condition of patients	Healthy	42	36.8
	Disabled	5	4.4
	Death	5	4.4

In the present study, Steroid therapy was present in 20.2%, oxygen therapy in 21.9%, acquired diabetes mellitus during the hospital stay was seen in 21.1% patients, 45.6% underwent the surgical procedure and mortality was documented in 4.4% of patients. (Table 3)

Table 4: Showing the comparison of distribution of culture result with gender and diabetes mellitus

		Fungal culture				Chi-square test (p-value)
		Negative		Positive		
		Count	N %	Count	N %	
Sex	Female	8	22.2%	18	23.1%	0.01 (0.919)
	Male	28	77.8%	60	76.9%	
DM	No	17	47.2%	30	38.5%	0.780 (0.377)
	Yes	19	52.8%	48	61.5%	

Table 5: Comparison of mean age with presence of fungal infection and death of patient

		Age		p-value
		Mean	SD	
Death	No	52.0	11.2	0.01*
	Yes	62.4	5.1	
Fungal Culture	Negative	50.3	11.3	0.92
	Positive	53.5	11.1	

Table 6: Association of gender and diabetes mellitus with outcome of patients

		Sex				Chi-square (p-value)	DM				Chi-square (p-value)
		Female		Male			No		Yes		
		Count	N %	Count	N %		Count	N %	Count	N %	
Death	No	25	96.2%	84	95.5%	0.033	46	97.9%	63	94.0%	0.973
	Yes	1	3.8%	4	4.5%	(0.878)	1	2.1%	4	6.0%	(0.324)

There is significant association of the age with presence of fungal infection and the worst outcome as death.

However there was no significant difference with respect to the gender and presence of diabetes mellitus. However the incidence of the death and fungal infection was more common among the male and presence of diabetes mellitus.

Discussion

The epidemiology of mucormycosis has shifted dramatically in recent years. The global frequency of this extremely sick and deadly illness is rising, albeit it is more prevalent in Asian countries. [18] Extensive steroid use during COVID-19 therapy, poorly controlled diabetes mellitus (DM), haematological malignancy, solid organ transplant, immunosuppression, and other co-morbidities were the primary risk factors, followed by hypertension and other co-morbidities. [19] Mucormycosis, formerly known as zygomycosis, is a serious fungal illness caused by the mucoromycetes mould group. It is quite common in those suffering from or recovering from COVID-19 since it can harm the sinuses, brain, or lungs. Swelling on one side of the face, fever, headache, nasal or sinus congestion, and black lesions on the nasal bridge or upper inside of the mouth are all indications of mucormycosis. Many factors, including immune dysregulation (suppressed cell-mediated immunity), steroid-induced hyperglycemia, an acidotic environment (metabolic acidosis, diabetic ketoacidosis), hypoxia (pneumonia), hyper-ferritinemia, and complement-mediated thrombotic microangiopathy, may have contributed to the ideal environment for Mucorales fungus to thrive and propagate during Covid-19 illness. [2,3]

According to Nehara H et al research reported COVID-19 is generally associated with secondary infections, both bacterial and fungal, which may be caused by immunological dysregulation. Furthermore, the use of broad-spectrum antibiotics, steroids, or monoclonal antibodies in COVID-19 therapy may result in the development or aggravation of pre-existing fungal infections. They documented Rhizopus species as the common isolate across all patients included in the research in the case series. [14]

Rhinocerebral mucormycosis is treated by surgical draining of the PNS and debridement of orbital or cerebral illness, as well as intravenous antifungal medications. Intravenous liposomal amphotericin-B (5-10 mg/kg/day) is used as first-line antifungal treatment, while second-line antifungals such as intravenous or oral posaconazole can be used as salvage therapy, with a course of at least 6 weeks being necessary. Strict glycemic control is also an important component of therapy. Depending on the underlying diseases, the mortality rate for rhinocerebral mucormycosis ranges from 40 to 80%.20 prolonged hospitalisation, particularly in ICU patients receiving invasive or noninvasive ventilation and suffering from severe COVID-19, is more likely to predispose patients to the development of fungal coinfections. [21] According to Khatri et al., the presence of fungal spores in this sort of equipment might lead to the development of hospital-acquired mucormycosis. [22] similar to present study, Nehara H et al., documented that the patients with severe fungal infection and the mortality was seen in patients who were aged diabetic patients with COVID-19 infections. Showing the alarming influence of this trio in clinical outcome of patients. [14]

Present study is one among the few literature which is available from India, specially from the southern India documenting the mucormycosis.

Conclusion

Patients with known diabetes who are hospitalised for Covid-19 have a greater chance of getting Mucormycosis, with Rhizopus species being the most common causal organism isolated. There is significant influence of this trio of age, diabetes mellitus and COVID-19 infection on the clinical outcome of patients with mucormycosis. A multidisciplinary strategy that combines rapid diagnosis, treatment with intravenous and oral antifungals, surgical debridement, and medical care for underlying conditions is crucial in combating the mucormycosis epidemic in the COVID-19 pandemic.

Supplementary file: It included three figures of laboratory processing of nasal debridement samples by 10% koh (potassium hydroxide) mount, culture on SDA (sabouraud dextrose agar), and identification of fungi from the growth obtained on SDA by LPCB (lactophenol cotton blue) mount.

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