



CORRELATION OF NEWLY-DIAGNOSED DIABETIC PATIENT AND PREVIOUSLY DIAGNOSED DIABETIC PATIENT WITH OTHER ETIOLOGIES IN SARS COV-2 ASSOCIATED MUCORMYCOSIS

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ABSTRACT **Background:** Covid associated mucormycosis is most commonly seen after impact of the 2nd wave of covid in India. It is seen that those who are immunocompromised i.e. most commonly diabetes and corticosteroid therapy they are more prevalent for fungal infection.

Methods and Material: a combined prospective and retrospective study conducted in Department of ENT and Head & Neck Surgery, M.L.B. Medical College, Jhansi, U.P. Two groups were created and their correlation with diabetes and other etiology were compared.

Aims: To correlate the newly-diagnosed diabetic patient and previously diagnosed diabetic patient with other etiologies in SARS COV-2 associated mucormycosis.

Results: The blood sugar level was more uncontrolled in patient with Previously diagnosed diabetic patient group with average HbA1c level of 10.5% in comparison to Newly-diagnosed diabetic patient. Steroid therapy was also seen in most of the patient during their covid treatment. Almost all the mucormycosis patients blood sugar were managed with insulin therapy. Combined surgical and medical treatment is the ultimate choice of treatment for better outcome. Vaccination role was not significant due to unavailability.

Conclusion: Covid associated mucormycosis is most commonly seen in diabetic patient. Blood sugar is more dearranged in case of previously diagnosed diabetic group than the newly diagnosed group. Insulin therapy is the main treatment choice for controlling blood sugar. Thus main focus should be given to the former group in terms of managing blood sugar level as well as treatment of mucormycosis.

KEYWORDS : Covid, Mucormycosis, Diabetes, HbA1C.

INTRODUCTION

Mucormycosis is a fungal infection caused by fungi belonging to the order Mucorales (*Rhizopus oryzae*) is the most common organism isolated from patients with mucormycosis and is responsible for 70% of all cases of mucormycosis^[1]. It is a serious disease spread by spores, most often via inhalation, contaminated food, or open wounds. The major risk factors for mucormycosis include uncontrolled diabetes mellitus, other forms of metabolic acidosis, treatment with corticosteroids, organ or bone marrow transplantation, neutropenia, malignancy, trauma and deferoxamine therapy in patients receiving hemodialysis.

In the present day scenario the incidence of covid-19 associated mucormycosis is increasing due to high glycemic index. As we know a diabetic patient has low immunity as a result of micro and macro vascular complications making our body susceptible to any type of viral, bacterial or fungal infections. As there is no known definitive treatment of covid we are dependent on steroids, monoclonal antibodies and many types of antiviral which ultimately decreases the immunity which leads to dreadfully opportunistic infections like mucormycosis, aspergillosis, candidiasis, pneumocystic jiroveci pneumonia, herpes, cryptococcal meningitis, etc. Even low-virulence bacterial may invade, proliferate, and cause disease in the immune deficient individual. Apart from the above infections we have encountered most of the cases were affected by fungus i.e. mucormycosis in the second wave of covid-19 in India.

Further, it has been noted that diabetic ketoacidosis and hyperosmolar hyperglycaemic state are unusually common in COVID-19 patients with diabetes. Most of the patient where having a history of previously diagnosed diabetes but due to covid many cases develop uncontrolled sugar level in their body which ultimately favours the growth of fungal infection.

People at risk for **Type 2** diabetes have an impaired relationship between insulin production and insulin resistance that's already

present at birth. The primary stressors that can upset that delicate balance are diet, weight and lack of physical exercise. Acute stressors such as pregnancy, steroids or inflammation from cytokine activation often seen in COVID-19 patients can bring out hyperglycemia in someone not known to have diabetes/prediabetes. We considered data on the number or proportion of COVID-19 patients (laboratory confirmed or clinically diagnosed) with newly diagnosed diabetes. Newly diagnosed diabetes was defined as new-onset diabetes (no prior history of diabetes with fasting plasma glucose [FPG] ≥ 7.0 mmol/L or random blood glucose [RBG] ≥ 11.1 mmol/L and HbA1c $< 6.5\%$) or previously undiagnosed diabetes (FPG ≥ 7.0 mmol/L or RBG ≥ 11.1 mmol/L and HbA1c $\geq 6.5\%$ or HbA1c $\geq 6.5\%$ only)^[2].

Previously diagnosed diabetic group are people with already history of diabetes. Glycosylated hemoglobin (HbA1c) is a predictor of incidence and progression of mucormycosis. Increased HbA1c level is the most important risk factor for the development of diabetic complications, including ketoacidosis.

Types of mucormycosis

1. Rhino-orbital mucormycosis
2. Rhino-orbital cerebral mucormycosis
3. Pulmonary mucormycosis
4. Cutaneous mucormycosis
5. Gastrointestinal mucormycosis

Rhino orbital cerebral mucormycosis is the most common type³ among others and gastrointestinal has a least incidence. Initial presentations of most of the patient were orbital symptoms then other symptoms develop gradually in the course of time.

AIMS AND OBJECTIVES

To correlate the newly-diagnosed diabetic patient and previously diagnosed diabetic patient with other etiologies in SARS COV-2 associated mucormycosis.

METHODS AND MATERIALS

This was a combined retrospective and prospective study of 50 mucormycosis patient who came to the ENT out patient department (OPD) and emergency in the month of April 2021 to July 2021 with the chief complaint of facial numbness and swelling, impaired vision, drooping of eye, diplopia, and nasal blockage. Diagnosis of mucormycosis was made on the basis of MRI, Nasal endoscopy and biopsy taken endoscopically. Again, according to their history of diabetes they were categorised into two groups, a Newly-diagnosed diabetic patient and Previously diagnosed diabetic patient. All the patient underwent covid testing and on the basis of result they were admitted in non-covid ward and covid ward respectively. Following this, a thorough history taking, local and general examination were carried out with proper precaution in case of covid patients. Random blood sugars was taken at the time of admission followed by fasting and post prandial blood sugar after admission. HbA1C were also measured and plotted in the table. Vaccination status were also taken into consideration. Important emphasis were given to those who took steroid therapy for covid treatment along with duration of treatment were also noted. Outcome of the result were compared with those underwent surgical debridement of fungus and anti-fungal drugs like inj. liposomal amphotericin-B or tab posaconazole. Daily monitoring of blood sugar were carried out and insulin therapy were also started on bed side after proper consultation from medicine department.

OBSERVATION AND RESULT

In our study we included 50 patients out of whom 35 (70%) were male and 15 (30%) were female. They were belonging to the age group from 16 to 75 years with maximum patient belonging to the age group of 31-40 years (35%). There were 20 (40%) patient belonging to newly diagnosed diabetes and 30 (60%) patient belongs to pre-diabetic group. Facial numbness were most commonly presented for about 66% followed by eye symptoms, facial swelling, and nasal obstruction in only 2%. At the time of admission 36 patients (72%) were covid negative and 14 patients (28%) were diagnosed positive for covid-19. About 45 (90%) cases were giving history of previously infected by covid-19 infection. Blood sugar status were plotted in the following tables:

Table 1: HbA1c values

Group	HbA1c values			Total
	Normal (4-5.6%)	Pre-Diabetic (5.7-6.4 %)	Diabetes (6.5% Or More)	
Newly-diagnosed diabetic patient	0	5	15	20
Previously diagnosed-diabetic patient	0	2	28	30
Total	0	7	43	50

Table 2: Treatment response with hypoglycemic agents.

Group	No. of patients responses with hypoglycemic agents		Total
	Controlled with OHA(oral hypoglycemic agents)	Controlled with insulin	
Newly-diagnosed diabetic patient	2	18	20
Previously diagnosed diabetic patient	0	30	30
Total	2	48	50

Table 3: Outcome of treatment

Treatment options		No. of responses		
		Cured	Death	Total
Medical	Unfit for anaesthesia	0	3	3
	Denied for surgery	1	2	3
Surgical		1	2	3
Combined medical and surgical		38	2	41
Total		40	9	50

Table 4: Steroid therapy

Group	Yes	No	Average Duration of treatment
Newly-diagnosed diabetic patient	11	9	5.5 days
Previously diagnosed diabetic patient	18	12	9 days
Total	29	21	

Table 5: Vaccination status

Vaccination status	Group		
	Newly-diagnosed diabetic patient	Previously diagnosed diabetic patient	Total
Yes	1 st dose	7	8
	2 nd dose	0	
No	18	24	42

DISCUSSION

In our study we found that about 43 patients (86%) were having HbA1c level more than 6.5%. In *Newly-diagnosed diabetic patient group*, about 75% of patient has >6.5% of HbA1c level in comparison to 93.3% in *Previously diagnosed diabetic patient group*. This shows that blood sugar level is more uncontrolled in patient with diabetic history. None of the patient were having blood sugar level under normal range. The average HbA1c level was 10.5% which was similar to the study conducted by John et al¹⁴.

We found that almost all the patients (96%) required insulin therapy to control their blood sugar level. Where as only 2 patients (4%) required oral hypoglycemic agents.

In the treatment outcome, maximum patients got benefitted from combined medical and surgical treatment in about 38 cases (92.6%) which is similar to study conducted by Dora E Corzo-León et al, 2018⁶¹ and Arunaloke Chakrabarti et al, 2006⁶¹. Only About 3 patient underwent for surgical treatment in which 1 patient died. Also, 3 patients who were unfit for anaesthesia, all of them eventually died (100%). From this observation we conclude that only 1 patient (16.6%) survive out of 6 patients which were treated with medication. Initially some patient was unable to get medical treatment because there was unavailability of drugs also we couldn't gave medication (anti-fungal) due to dearranged kidney function test (KFT) or serum electrolyte. Only option was to undergo surgery for those patients. Similarly some patients underwent treatment only through medication because they were unfit for anaesthesia and some denied for the surgery. Data showed that the mortality rate was low in patients treated with a combination of Amphotericin-B and surgical debridement of the infected tissue (19%–44%) compared with AmB monotherapy (50%–61%), these findings are in concordance with global data¹⁷.

We also observed that about 29 patient (58%) received steroid therapy, and out of 38 covid positive patient only 29 patient (76%) got steroid therapy during their course of treatment for covid-19. The average duration for steroid therapy was 5.5 days in *Newly-diagnosed diabetic patient* and 9 days in *Previously diagnosed diabetic patient*. As diabetes is one of the co-morbid condition which makes patients to receive steroid therapy for longer duration in comparison to non-diabetic patient.

We also found that only about 8 patient (16%) got vaccinated for covid-19. Out of which only 1 patient belongs to the *Newly-diagnosed diabetic patient group*. This is due to the fact that at the time of our study duration, vaccination was not running in full swing in our country and only 1st dose were available. Also, only those patient who were above 45 years got opportunity to get vaccination as per government guideline⁶¹. Thus very large number of patient fails to get vaccination.

CONCLUSION

Uncontrolled diabetes mellitus is the most common underlying disease associated with mucormycosis in India. According to our study we found that those who are Previously diagnosed diabetic patient their blood sugar level is more dearranged compared to those with newly diagnosed group. Thus these people are more likely candidate for fungal infection. Further they need more insulin dose to control their blood sugar instead of OHA. We also found that combined medical and surgical treatment is better choice for the overall management of covid associated mucormycosis. There was no significant role of vaccination in patient with mucormycosis due to insufficient vaccination in india.

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