

Role of Glycosylated hemoglobin (HbA1c) as a predictive marker for Mucormycosis in post COVID-19 patients.

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Abstract

Introduction: Mucormycosis has been increasingly portrayed in patients with COVID-19, which is a severe and quickly spreading type of fungal infection that typically starts in the nose and paranasal sinuses after inhaling fungal spores. Uncontrolled diabetes can be taken as a predisposing factor for Mucormycosis, therefore, HbA_{1c} can predict the severity of Mucormycosis in post COVID-19 infection.

Objectives: To study the role of Glycosylated hemoglobin (HbA_{1c}) as a predictive marker for the development of Mucormycosis in post COVID-19 patients.

Methods: It’s an observational, comparative study of 3 months, conducted at Kamineni Academy Medical Sciences and Research Centre, LB Nagar. 35 subjects with post covid complaints of age between 20-70 years were divided into, 2 study groups. Group A – Controls

(n=16)- Post COVID-19 Mucormycosis negative patients and Group B- Cases (n=19)- Post COVID-19 Mucormycosis Positive patients, respectively. Glycosylated hemoglobin (HbA_{1c}) was taken as a predictive marker for Mucormycosis and study subjects were divided based on their HbA_{1c} values into Diabetic (>6.5), Prediabetic (5.7-6.4) and non-Diabetic (< 5.7), respectively. The data was analyzed using SPSS software.

Results: The study showed a majority of the subjects in the 41 to 60 years of age group (n=17, 48.6%). In Group A (Controls) female predominance (n=9, 56.2%) and in Group B (Cases) male predominance (n=16, 84.2%) was noticed. When the study population was distributed based on HbA_{1c} values, in Group A (Controls) majority were non-diabetic (n=8, 50%) and in Group B (Cases) majority were Diabetic (n=16, 84.2%), respectively. In the mean comparison of HbA_{1c} levels among study groups, Group A (Controls) showed 5.96 and Group B (Cases) depicted 8.91 mean values with a statistical significance (p<0.05*).

Conclusion: High HbA_{1c} levels were found to be associated with higher risk of developing Mucormycosis in post COVID-19 infections and can be used as a possible predictive marker.

Keywords: COVID-19, Mucormycosis, Glycosylated hemoglobin (HbA_{1c}), Predictive marker

Introduction

The World Health Organization (WHO) declared a pandemic on March 12th, in the year 2020 [1] for the coronavirus disease 2019 (COVID-19), which is brought on by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A wide range of clinical symptoms are displayed by COVID-19, from asymptomatic to pneumonia followed by systemic failure, which

ultimately leads to morbidity and mortality.[2] Low immunity in the patients suffering from COVID-19, made them susceptible to invasive fungal infections. [3] These immunocompromised patients were exposed to one such fatal fungal infection seen secondary to COVID-19 infection called Mucormycosis. Mucormycosis development is primarily through the inhalation of sporangiospores in immunocompromised hosts. It is a fungal infection caused by fungi of the order of Mucorales belonging to the class of zygomycetes. [4] Uncontrolled diabetes mellitus was one of the chief risk factors affecting the outcome in patients during the COVID-19 pandemic. Patients with diabetes had mortality rates four times greater than COVID-19 patients without diabetes, which made its monitoring compulsory in the hyperglycemic COVID-19 patients. [5] Glycosylated hemoglobin (HbA_{1c}) gives a better idea of the patient's glycemic control and is an important indicator of long-term glycemic control. [6]

In diabetic COVID-19 patients, compromised immune response to viral infection was the leading cause of mortality, which also gave way to many aggressive fungal infections like Mucormycosis. Covid-19 infection worsens the glycemic status and increases the risk of development of Mucormycosis in COVID-19 patients.

The present study has been taken up with the intent to study the role of HbA_{1c} as a predictive marker for the development of Mucormycosis in post COVID-19 patients.

Materials & Methods

Study design and population

It is an observational, comparative study of 3 months (April 2021 to June 2021) conducted at Kamineni Academy Medical Sciences and Research Centre, LB Nagar. In the present study, a total of 35 subjects with

post COVID-19 complaints (facial pain, sinusitis, fever, headache) of age between 20-70 years were enrolled. Ethical committee approval was taken before the initiation of the study. The informed consent form was distributed before the commencement of the study and the patients were explained about the study, the procedure, and the informed consent form was collected from all participating patients before the commencement of the study.

Group allocation

- **Group A – Controls** (n=16)- Mucormycosis negative patients
- **Group B – Cases** (n=19)- Mucormycosis positive patients

Inclusion criteria

- 20 to 70 years of age
- Patients of either gender
- Patients with post COVID-19 complaints
- Clinically and microbiologically confirmed Mucormycosis cases
- Having obtained his/her informed consent

Exclusion criteria

- <20 to > 70 years of age
- Patients without post COVID-19 complaints
- Pregnant women and lactating mother
- Non-Compliant patients
- Those who didn't give informed consent

Study procedure

Patients with post COVID-19 complaints were screened for Mucormycosis. The Clinically and microbiologically confirmed Mucormycosis cases were included. Glycosylated hemoglobin (HbA_{1c}) has been taken as a predictive marker for Mucormycosis and study subjects were divided based on their HbA_{1c} values into Diabetic

(>6.5), Prediabetic (5.7-6.4) and non-Diabetic (< 5.7), respectively.

Statistical analysis

The demographic data obtained were subjected to descriptive statistical analysis by using SPSS software, the data is stated as Frequencies (n), percentages (%) and Mean±SD in tabulated and graphs form. Paired t-test was performed to test the significance of the difference between the means of study groups In all the cases p value ≤0.05* is considered statistically significant.

Results

In the present study, the majority of the study subjects belonged to the age group of 41 to 60 years (n=17, 48.6%), followed by 20 to 40 years (n=10,28.6%), and the least were in the age group of 61 to 70 years (n=8, 22.9%), respectively.

Among the study population, Gender-wise distribution revealed that in Group A (Controls) most of the subjects were females (n=9, 56.2%) and the least were males (n=7, 43.8%). In Group B (Cases) the majority were males (n=16, 84.2%), and the least were females (n=3, 15.8%), respectively.

When the study population was distributed based on HbA_{1c} values, in Group A (Controls) high percentage (n=8, 50%) was of non-diabetic subjects, followed by Diabetic (n=4, 25%) and prediabetic (n=4, 25%), respectively. In Group B (Cases) most of the study population were Diabetic (n=16, 84.2%), followed by prediabetic (n=3, 15.8%), and none were non-diabetic.

In the present study, when the mean comparison of HbA_{1c} levels was done between the study groups, a mean value of 5.96 was noted in Group A (Controls) and comparatively a high mean value of 8.91 was noted in Group B (Cases), with a respective statistical significance (p<0.05*).

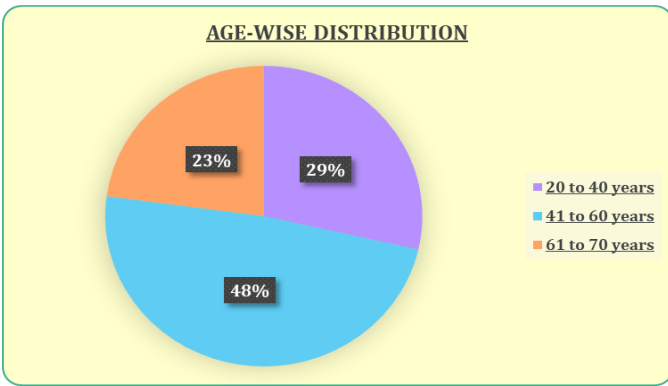


Figure 1: Age-wise distribution of study population

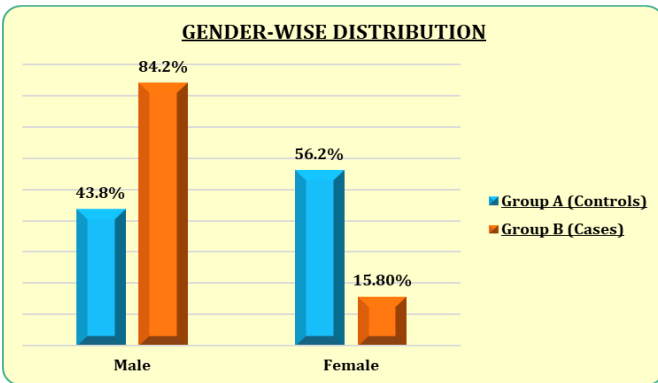


Figure 2: Gender-wise distribution of study population

Table 1: Distribution of study population based on HbA_{1c} values

Study Subjects (n=35)	Group A (Controls) (n=16)		Group B (Cases) (n=19)	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Diabetic Subjects	04	25%	16	84.2%
Prediabetic Subjects	04	25%	03	15.8%
Non-diabetic Subjects	08	50%	0	0%
Total	16/35	100%	19/35	100%

Table 2: Mean comparison of HbA_{1c} values among study population

Study Groups (n=35)	Mean±SD	p Value
Group A (Controls) (n=16)	5.96±0.95	<0.05*
Group B (Cases) (n=19)	8.91±2.13	<0.05*

Discussion

The present study aimed to determine the role of Glycosylated Hemoglobin (HbA_{1c}) as a predictive marker for the development of Mucormycosis in post COVID-19 patients. 35 patients with post COVID-19 complaints were taken and were studied for a period of 3 months. The HbA_{1c} levels were monitored in Mucormycosis positive and negative patients, respectively.

The current study has found that the majority of the subjects belonged to the age group of 41 to 60 years (n=17, 48.6%). In a study done by Iqbal N et al, in the year 2017, [7] the age of the diabetic patient with Mucormycosis fungal infection was 60 years which is in similarity to our study results. In another study done by Mishra Y et al, in the year 2021, [8] the mean age of the diabetic patients who were found to be suffering from Mucormycosis were recorded as 58 years, which was in accordance with the present study results where the majority of the subjects were from the age group between 41 to 60 years. [Figure 1]

In the present study, it was found that the majority were males (n=16, 84.2%), and the least were females (n=3, 15.8%), respectively. It can be clearly observed that a male predominance was revealed in the Mucormycosis patients. It is in similarity to a study conducted by Singh AK et al, in the year 2021, [9] where Mucormycosis was predominantly seen in males (78.9%), which is in similarity to the current study outcomes where male predominance was witnessed. [Figure 2]

In the existing study, the study population was distributed based on HbA_{1c} values. Most of the study population were Diabetic (n=16, 84.2%), followed by prediabetic (n=3, 15.8%), and none were non-diabetic. It was noted evidently in the present study that the

majority of the Mucormycosis positive patients were diabetic (84.2%), which is in exact similarity to a study done by Khanna M et al, in the year 2021, [10] where they studied the Risk of Mucormycosis in Diabetes Mellitus, in which the result of the study showed the increased risk of Mucormycosis in a diabetic patient. In another study done for studying Diabetes mellitus as the major risk factor for Mucormycosis by Corzo-León DE et al, in the year 2018, [11], they stated that diabetes mellitus was the most common risk factor for Mucormycosis. [Table 1]

In the present study, when the mean comparison of HbA_{1c} levels was done between the study groups, comparatively a high mean value of 8.91 was noted in Mucormycosis positive patients when compared to the Mucormycosis negative patients (5.96). Similar results were depicted in a study done by Paidisetty P et al, in the year 2022, [12] where more than half of the study population (52.94%) had uncontrolled diabetes with high HbA_{1c} levels (>8). [Table 2]

Conclusion

Elevated levels of Glycosylated hemoglobin (HbA_{1c}) have been found to be a major factor in the pathogenesis of Mucormycosis disease. Our study confirmed a significant increase in Glycosylated hemoglobin (HbA_{1c}) in patients with post COVID-19 complaints.

Furthermore, we found that uncontrolled Diabetes Mellitus was found to be associated with a higher risk of developing Mucormycosis in post covid infections, indicating its relevance as an early marker for assessing the risk of Mucormycosis.

Monitoring uncontrolled Diabetes Mellitus with elevated levels of Glycosylated hemoglobin (HbA_{1c}) can aid in better management of the disease.

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