



Long term glyceic control in patients of diabetes with invasive fungal sinusitis

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Abstract

Invasive fungal sinusitis is a disease affecting the immunocompromised individuals. Diabetes being the major contributor for immunocompromised conditions worldwide is a close associate of the above-mentioned disease. Various studies over a period have shown that poor glycaemic controls had detrimental effect over the condition of the patients, and it was also proved that high sugar levels contributed to high mortality rate. But the studies aimed at analysing the effect of glycaemic control in diabetics with invasive fungal sinusitis are less. In this prospective observational study, we aim to study this association. A sample size of 25 diabetic patients were selected who were suffering with invasive fungal sinusitis. These patients were treated for the disease and their blood sugar levels were recorded on the day of admission, 1 month, 3 months, and 6 months. This close monitoring along with proper pharmacological management of diabetes with lifestyle modification was done for all 25 patients and their clinical condition were recorded and analysed. Our study proved fruitful when we found a positive relation between the improving patient condition along with lowered blood sugar levels.

Introduction

The term fungal rhinosinusitis refers to a group of disorders characterised by inflammation of mucosa of paranasal sinuses due to infection by pathogenic fungi. Based on the ability of the fungi to invade into the tissue, it is further divided into invasive fungal rhinosinusitis and non-invasive fungal rhinosinusitis. (1) The invasive fungal rhinosinusitis is further of three types, acute fulminant invasive fungal rhinosinusitis, granulomatous invasive fungal rhinosinusitis, chronic fungal rhinosinusitis.

Invasive fungal rhinosinusitis (IFRS) is associated with immunocompromised body condition except the chronic invasive variant. The immunocompromised body condition includes, diabetes mellitus, malignancy, solid organ transplantation, HIV, iatrogenic immunosuppression and the recently added covid 19 infection (2). In case of diabetes, the increased blood sugar levels are responsible for hampering the neutrophilic immune response causing immunodeficiency. (5) The glycaemic control thus becomes a critical prognostic factor in the patients of invasive fungal sinusitis. Many studies done on this topic have proven the detrimental effect of high blood sugar levels on the prognosis of invasive fungal sinusitis, but the data on whether the control of blood sugar level brings about any effect or even has a relation with the prognosis is scarce. In this article we aim to study the correlation between

the glycaemic control in patients of diabetes mellitus with invasive fungal rhinosinusitis and its prognosis.

AIMS

To study the effect of long-term glycaemic control in patients of diabetes with invasive fungal sinusitis.

OBJECTIVES

The objective of this study is to

- 1) To identify the patients of invasive fungal sinusitis
- 2) To give them appropriate treatment
- 3) To keep a record of their prognostic outcome and glycaemic control over a period of 6 months
- 4) To correlate between glycaemic control and prognostic outcome.

MATERIALS AND METHODS

Study Design: It is a prospective observational study. **Source of Data:** All patients coming to tertiary care centre in outpatient or emergency department during the period of October 2020 to October 2022. **Sample Size:** 25 patients who fulfilled the inclusion criteria were enrolled in this study. **Inclusion Criteria:** Patients from age group of 15-70yrs of age of both sex. Patients who are known case of Diabetes mellitus presenting with clinical features of invasive fungal rhinosinusitis. **Exclusion Criteria:** Age below 15 years. Nondiabetic patient with invasive fungal sinusitis.

Evaluation of Patients: Patients who satisfied the inclusion criteria were enrolled and examined in detail. Relevant history was taken and noted, all necessary investigations were done. All the complaints, clinical signs and diagnostic nasal endoscopic(DNE) findings were noted. Fasting blood sugars (FBS), post prandial blood sugar (PPBS) and glycosylated haemoglobin (HBA1C) were recorded at the time of admission and termed as baseline values. After routine blood investigations the patients were subjected to appropriate surgical/medical treatment modalities. The patients were followed up at 1 month, 3 months and 6 months. Upon each follow up the patient's complaints were evaluated; clinical and endoscopic findings were noted, and routine blood sugar investigations were done and recorded. The patients were graded as static improves or worsened based on their clinical features and overall condition. Additionally, there were remarks made on the glycaemic control of the patients like worse, better, and good. Good were those patients whose FBS was 80 to 130mg/dl, PPBS was 120 to 160mg/dl and HBA1C was <7mg/dl. Better were those patients whose FBS was 130 to 150mg/dl, PPBS was 151 to 200mg/dl and HBA1C was 7 to 8%. Poor were those patients whose FBS was 150 to 200mg/dl, PPBS was 201-300mg/dl and HBA1C was 8 to 10%. Worst were those patients whose FBS was >200mg/dl, PPBS was >350mg/dl and HBA1C was >10%. This collected data was analysed and the following results were obtained.

RESULTS AND OBSERVATIONS

Table 1: Frequency and Percent distribution of patients by Chief Complaints/ DNE findings

Chief Complaints/DNE/features	Clinical	Frequency	Percent
Headache	Yes	12	48.0
	No	13	52.0
Eye swelling or eye pain	Yes	11	44.0
	No	14	56.0

Facial swelling or facial pain	Yes	12	48.0
	No	13	52.0
Nasal obstruction	Yes	12	48.0
	No	13	52.0
Discharge	Yes	5	20.0
	No	20	80.0
Mucosal changes	Yes	13	52.0
	No	12	48.0
Crusting	Yes	21	84.0
	No	4	16.0
Palatal lesion	Yes	-	-
	No	25	100.0
Teeth tenderness /mobility	Yes	4	16.0
	No	21	84.0
Gum pustules	Yes	4	16.0
	No	21	84.0
Sinus Tenderness - Maxillary	Yes	19	76.0
	No	6	24.0
Sinus Tenderness - Ethmoids	Yes	11	44.0
	No	14	56.0
Sinus Tenderness - Frontal	Yes	9	36.0
	No	16	64.0
Health nasal mucosa with no crusting	Yes	-	-
	No	25	100.0
Dead necrotic bone /fungal debri	Yes	-	-
	No	25	100.0

The above table is a systematic representation of the various complaints, clinical features and DNE findings of 25 patients at the time of admission where “yes” affirms the presence of the complaint and” no” indicates its absence.

Table 2: Mean and standard deviation(SD) of patients on FBS, PPBS and HBA1C during Baseline

	Minimum	Maximum	Mean	Std. Deviation
FBS	92.00	434.00	240.36	102.219
PPBS	120	525	311.32	113.139
HBA1C	5.20	14.00	9.93	2.59

FBS- The mean±SD for FBS was observed to be 250.36±102.21. The minimum and maximum were seen to be 92 and 434 respectively.

PPBS- The mean±SD was found to be 311.32±113.13 while the minimum and maximum were seen to be 120 and 525 respectively.

HBA1C- We see that the mean±SD were observed to be 9.93±2.59. The minimum and maximum were observed to be 5.20 and 14.

Table 3: Mean and standard deviation of patients on FBS, PPBS, HBA1C by time period and Results of Repeated Measure ANOVA test

	Time period	Mean	SD	F-value
FBS	Baseline	240.36	102.21	F= 30.632 p= .001
	1st Month	150.68	42.80	
	3rd Month	127.52	24.45	
	6th Month	117.12	13.85	
	Time period	Mean	SD	F-value
PPBS	Baseline	311.32	113.13	F= 34.840 p= .001
	1st Month	210.40	51.11	
	3rd Month	179.60	31.64	
	6th Month	163.72	20.30	
	Time period	Mean	SD	F-value
HBA1C	Baseline	9.93	12.59	F= 45.131 p= .001
	1st Month	7.85	1.52	
	3rd Month	6.90	0.91	
	6th Month	6.14	0.66	

The mean±SD FBS in baseline was observed to be 240.36±102.21 while the mean±SD for the 1st month, 3rd month and 6th month were observed to be 150.68±42.80, 127.52±24.45 and 117.12±13.85 respectively. The repeated measure ANOVA revealed a significant difference (F= 30.632; p= .001) indicating a change in the mean scores from baseline to 6th month.

The mean±SD for PPBS baseline, 1st month, 3rd month and 6th month were observed to be 311.31±113.13, 210.40±51.11, 179.60±31.64 and 163.72±20.30 respectively. The repeated measure ANOVA test revealed a significant difference (F= 34.840; p= .001) which indicates a significant decrease in the mean scores from PPBS baseline to 6th month.

The mean±SD for HBA 1C baseline was found to be 9.93±2.59. The mean±SD for 1st month, 3rd month and 6th month were observed to be 7.85±1.52, 6.90±.91 and 6.14±.66 respectively. The repeated measure ANOVA revealed a significant difference (F= 45.131; p= .001) which indicates a significant change in the mean scores of HBA 1C from baseline to 6th month.



Graph 1: shows the Mean FBS of patients over six month



Graph 2: Shows the Mean PPBS of patients over six months



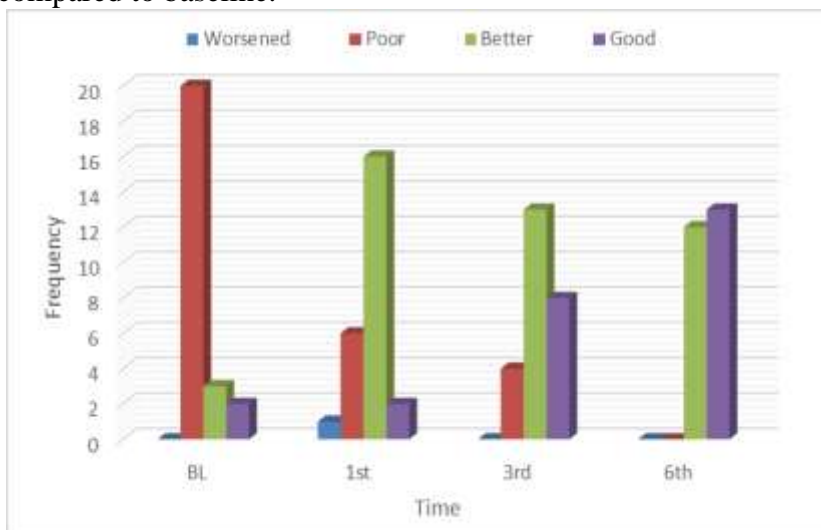
Graph 3: Shows the Mean HBA1C of patients over six months

Table 4: Frequency and Percent distribution of patients on Glycaemic by time period along with chi-square test results

Glycaemic		Time			
		BL	1st	3rd	6th
Worsened	F	0	1	0	0
	%	0.0%	4.0%	0.0%	0.0%
Poor	F	20	6	4	0
	%	80.0%	24.0%	16.0%	0.0%
Better	F	3	16	13	12
	%	12.0%	64.0%	52.0%	48.0%
Good	F	2	2	8	13
	%	8.0%	8.0%	32.0%	52.0%
Pearson Chi-square		$X^2 = 55.372$ $p = .001$			

At the baseline, 80% of the patients had poor glycaemic control while 12% of them had better glycaemic control and 8% of them had good glycaemic control. In the 1st month, 64% of the patients had better glycaemic control while 4% of them had worsened glycaemic control and 24% of them had poor glycaemic control. In the 3rd month, 52% of them had better glycaemic control while 16% of them had poor glycaemic control and 32% of them had good glycaemic control. In the 6th month, 52% of them had good glycaemic control while 48% of them had

better glycaemic control. The chi-square test revealed a significant association ($X^2= 55.372$; $p= .001$) indicating a significant increase in the patients with good glycaemic control during the 6th month compared to baseline.



Graph 4: Shows the frequency distribution of patients on Glycaemic by time period

Table 5: Chi- square test result of various complaints by calculating their frequency and percentage of distribution in patients at various time periods

Sr.no	complaints	X2	P value	Significance
1	Headache	15.152	0.002	Significant
2	Eye swelling	37.079	0.002	Significant
3	Facial pain and facial swelling	48.837	0.001	Significant
4	Tooth tenderness	10.292	0.016	Significant
5	Palatal lesion	6.122	0.106	Not Significant
6	Nasal obstruction	40.909	0.001	Significant
7	Discharge	12.500	0.006	Significant
8	Mucosal changes	48.837	0.001	Significant
9	Crusting	51.184	0.001	Significant
10	Gum pustules	7.801	0.050	Significant
11	Maxillary sinus tenderness	70.370	0.001	Significant
12	Ethmoid sinus tenderness	37.079	0.001	Significant
13	Frontal sinus tenderness	29.670	0.001	Significant
14	Healthy nasal mucosa	69.490	0.001	Significant

The above data shows that there was an improvement in the complaints of the patients over a period of six months follow up and almost all complaints have a significant correlation except for palatal lesions.

Table 6: Frequency and Percent distribution of patients on Prognosis by time period along with chi-square test results

Prognosis		Time			
		BL	1st	3rd	6th
Worsened	F	25	1	0	0
	%	100.0%	4.0%	0.0%	0.0%
Static	F	0	5	0	0
	%	0.0%	20.0%	0.0%	0.0%
Improved	F	0	19	25	25
	%	0.0%	76.0%	100.0%	100.0%
Pearson Chi-square		$X^2 = 109.699$ $p = .001$			

The chi-square test revealed a significant association ($X^2 = 109.699$; $p = .001$) indicating that a significant increase in the number of patients having an improved prognosis during the 6th month compared to baseline. In other words, none of the patients had improved prognosis during the baseline while all the patients during the 6th month had an improved prognosis.



Graph 5: Shows the frequency distribution of patients on Prognosis by time period.

DISCUSSION

IFRS is a highly pathogenic disease that is seen in Immuno-compromised individuals like patients suffering with diabetes mellitus. In The present study, there are 25 patients out of which 18 are male 7 are females. It is interesting to note that amongst the sample size, males are predominantly affected compared to women. It could be attributed to the fact that the males might be twice at a risk of developing Diabetes Mellitus than women. (6).

The patients of invasive fungal sinusitis present with a variety of symptoms. In our tertiary care centre, most common complaints was Headache, facial pain and Nasal obstruction (48%) while eye swelling, and eye pain (48%) were next most common complaints, Followed by Tooth tenderness, Tooth mobility, gum pustules which was a clear indication of maxillary involvement(20%) and patients who were Negligent or delayed presenting to the Hospital and had very fulminant course of Infection also presented with palatal Lesion which was 8%. After admission, the patients were examined Thoroughly, In Diagnostic Nasal Endoscopy we found that discharge (20%), mucosal colour and texture changes (52%) and Nasal crusting

(16%) were most commonly encountered. Maxillary sinus tenderness was elicited in 76% patients which makes this sinus most affected amongst all other sinuses followed by ethmoids and frontal sinus.

The patients underwent blood sugar examination like FBS, PPBS, and HBA1C at the time of admission. Over the course of treatment of invasive fungal sinusitis, In the hospital, these patients were on insulin therapy and there was strict sugar monitoring. On discharge, suitable antidiabetic medication was prescribed and on follow up, levels of blood sugars were checked. In our study we found that the minimum baseline fasting blood sugar noted was 92 and maximum was 434, and the minimum post prandial baseline blood sugar was 120 while maximum was 525. The mean baseline FBS and PPBS is 240 and 311 respectively which is very high. The HBA1C values were also deranged. With maximum being 14(mean= 9.9). The hba1c values represent the average blood sugar values of last 3 months. Hyperglycaemia leads to glycosylation of ferritin and transferrin and in turn reduces the iron binding by decreasing the ability of transferrin to chelate iron, acidosis presents an additive effect causing an overall increase in free iron levels, allowing the fungus to thrive.

Upon follow up, we found that the fasting blood sugar levels at 1st month, 3rd month and 6th month showed a significant drop in the levels of mean FBS being 240 at time of admission, slowly reduced to 150 at 1month and 127.52 at 3rd month and 117.2 at 6th month. This significant reducing trend was also seen in post prandial blood sugars. The PPBS mean was 311 at the time of admission, which reduced to 210.4 by 1 month, 179.6 by 3rd month and 163.7 by 6th month. Another parameter of HBA1C also showed a significant decrease from the mean value at the time of admission being 9.93 which reduced to 7.85, 6.9 and 6.14 in 1 month, 3 months and 6 months respectively.

Though the blood sugar parameter showed improvement over a period of 6 months in most of the patients, the curiosity was to know their clinical status and prognosis. For this, some of the clinical symptoms were compared for individual patients at the time of admission and at 6 months. It showed that complaints like headache which was widely prevalent at the time of admission in most of the patients significantly reduced by 6 months ($p = 0.002$, $\chi^2 = 15.152$). The chi square test revealed significant association. The similar kind of significant association was seen with other complaints like eye swelling, eye pain ($\chi^2 = 37.079$, $p = 0.001$) facial swelling, facial pain ($\chi^2 = 48.837$, $p = 0.001$) tooth tenderness, tooth mobility, gum pustules ($\chi^2 = 10.292$, $p = 0.016$) nasal obstruction ($\chi^2 = 40.909$, $p = 0.001$) and nasal discharge ($\chi^2 = 12.500$, $p = 0.006$). When diagnostic nasal endoscopies were done in these patients at the time of admission, 1st month follow up, 3rd month follow up and 6th month follow up revealed some significant changes. 20% patients showed presence of discharge at time of admission which was absent at 6 months ($\chi^2 = 14.394$ and $p = 0.002$). A similar kind of response was seen with other findings like mucosal changes in nose and para nasal sinuses. However, crusting was present at baseline (infective) in the first month (non-infective postoperative) and later decreased from 3rd month onwards. The maxillary sinus tenderness, ethmoidal sinus tenderness and frontal sinus tenderness all shows significant improvement and there is a rise in statistics of healthy nasal mucosa. Based on the clinical findings and examination, the patients were marked as worsened, static and improved. When this prognosis status was analysed for all 25 patients, it revealed that there was significant improvement in number of patients having improved status. The glycaemic control of all the patients were also marked as worsened, poor, better, good. 20 patients had poor glycaemic control, 3 had better glycaemic control while 2 had good glycaemic control at the time of admission. By the end of 6 months, 12 patients had better glycaemic control and 13 had good glycaemic control. The above findings were significant and indicated a strong positive relation between glycaemic control and improvement in the prognosis of invasive fungal sinusitis patients. In many studies dealings with invasive fungal sinusitis and diabetes

mellitus, poor glycaemic control is a predictor of mortality or poor prognosis (7, 8) none of them had any data that showed that effective sugar control could lead to a good prognosis in the patients. Due to lack of literature on this analysis we did not have any specific comparative study to analyse our outcome. Anyhow all the 25 patients who survived the test of time with apt and fine amalgamation of medical therapy, surgical intervention, family support and individual will power stood testimony to prove our part that effective blood sugar levels indeed lead to a good prognosis in patients suffering with invasive fungal sinusitis.

CONCLUSION

The above findings of blood sugar values over a period of 6 months along with the record of various clinical findings in patients of invasive fungal sinusitis with diabetes mellitus prove that glycaemic control in patients of diabetes with invasive fungal sinusitis has a significant relation with the prognosis of the disease. While most of the patients were in the category of poor or worse glycaemic control at the time of admission, due to strict sugar monitoring, drug therapy and lifestyle modification patients improved their blood sugar levels and came in good or better categories of glycaemic control over a period of 6 months. The clinical findings and complaints of patients were no exception to the improving trend. While the patients came to the hospital with a set of specific complaints most of the complaints alleviated by the end of 6 months. There was improvement in the healthy nasal mucosa and the overall patient's health. There was a positive correlation established between the improving condition of patients with good blood sugar control.

REFERENCES

1. DeShazo RD, Chapin K, Swain RE. Fungal sinusitis. *New England Journal of Medicine*. 1997 Jul 24;337(4):254-9.
2. Schubert MS. Allergic fungal sinusitis: pathophysiology, diagnosis and management. *Medical Mycology*. 2009 Jan 1;47(Supplement_1):S324-30.
3. Chakrabarti A, Sharma SC, Chander J. Epidemiology and pathogenesis of paranasal sinus mycoses. *Otolaryngology--Head and Neck Surgery*. 1992 Dec;107(6_part_1):745-50.
4. Veress B, Malik OA, El Tayeb AA, El Daoud S, Mahgoub ES, El Hassan AM. Further observations on the primary paranasal aspergillus granuloma in the Sudan. A morphological study of 46 cases. *American Journal of Tropical Medicine and Hygiene*. 1973;22(6):765-2.
5. Baynes JW, Thorpe SR. Role of oxidative stress in diabetic complications: a new perspective on an old paradigm. *Diabetes*. 1999 Jan 1;48(1):1-9.
6. Nordström A, Hadrévi J, Olsson T, Franks PW, Nordström P. Higher prevalence of type 2 diabetes in men than in women is associated with differences in visceral fat mass. *The Journal of Clinical Endocrinology & Metabolism*. 2016 Oct 1;101(10):3740-6.
7. Raizada N, Jyotsna VP, Kandasamy D, Xess I, Thakar A, Tandon N. Invasive fungal rhinosinusitis in patients with diabetes. *The Journal of Infection in Developing Countries*. 2018 Sep 30;12(09):787-93.
8. Baghel SS, Keshri AK, Mishra P, Marak R, Manogaran RS, Verma PK, Srivastava AK, Kumar R, Mathialagan A, Bhuskute G, Dubey AK. The Spectrum of Invasive Fungal Sinusitis in COVID-19 Patients: Experience from a Tertiary Care Referral Center in Northern India. *Journal of Fungi*. 2022 Feb 24;8(3):223.