ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 11, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

CLINICOPATHOLOGICAL STUDY OF NON-NEOPLASTIC LESIONS OF NASAL CAVITY AND PARANASAL SINUSES IN A TERTIARY CARE TEACHING HOSPITAL

SWATI SAINI[1], RAMA KUMARI BADYAL[1]*, HARPAL SINGH[1], SANJEEV BHAGAT[2]

[1]Department of Pathology, Government Medical College, Patiala, Punjab, India. [2]Department of Otolaryngology, Government Medical College, Patiala, Punjab, India.
*Corresponding author: Rama Kumari Badyal; Email: ramabadyal@gmail.com

Received: 02 May 2023, Revised and Accepted: 22 June 2023

ABSTRACT

Objective: A variety of non-neoplastic lesions involving the nasal cavity (NC) and paranasal sinuses (PNS) are encountered in clinical practice. The clinical features, symptoms, and advanced imaging technique help to reach a provisional diagnosis but histopathological examination remains the mainstay of final definitive diagnosis. There is a lack of studies that exclusively cover non-neoplastic lesions of sinonasal region. Hence, this study was done with the aim of examining the clinicopathological features of various non-neoplastic lesions of NC and PNS.

Methods: The formalin-fixed specimens of polypectomy/biopsy were received with complete clinical and radiological features in the department of pathology. Routine gross examination and required number of sections were taken and stained with hematoxylin and eosin stain. Periodic acid Schiff's was used wherever necessary.

Results: Histologically, maximum number of cases were of inflammatory polyp (IP) (57%), followed by Allergic polyp (AP) (18%) and Invasive Fungal Sinusitis-Mucormycosis (17%). Mucormycosis was found in patients who have recovered from COVID along with a steroid intake history or had diabetes mellitus or had multiple comorbidities along with COVID recovery and steroid intake.

Conclusion: Among the non-neoplastic lesion, IP is the most common lesion followed by AP. The significant number of mucormycosis cases was seen due to the ongoing COVID pandemic and liberal use of corticosteroids in the treatment.

Keywords: Nasal sinuses, Non-neoplastic, Polyps, Mucormycosis, COVID.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i11.48229. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODCTION

A variety of non-neoplastic lesions involving nasal cavity (NC) and paranasal sinuses (PNS) are encountered in clinical practice. The NC and paranasal sinuses – including the maxillary, ethmoid, sphenoid, and frontal sinuses are collectively referred to as the sinonasal tract [1]. Due to its prominent position anatomically, it becomes critical to diagnose and treat any scarring or ulceration as early as possible. Filtering and humidifying the temperature of inspired air are done by NC and the PNS [2]. Sinonasal area is exposed to various infective agents, chemicals, antigens, mechanical, and many other influences. These deleterious exposures lead to the formation of tumor-like and neoplastic conditions [3]. They can range from simple nasal polyps to infective polypoidal granulomatous lesions to malignant lesions [4]. Common presenting symptoms are nasal blockade, nasal discharge, epistaxis, facial swelling, and orbital and ear symptoms. The most common causes of these lesions are allergic, antigenic, and obstructive. Sinonasal area is exposed to various infective agents, chemicals, antigens, mechanical, and other influences [2]. The variation in the histopathological types and grades of the lesions, particularly malignancies has led to urgency in studying the clinical and pathological aspects. Understanding the exact nature of the lesion will help in strengthening the diagnosis and put an end to the confusions. The incidence of sinonasal masses is 1–4% in the total population [5]. Nasal polyps are a common cause of nasal obstruction (N Obs) in adults with 4% prevalence in the general population [6]. It is important to differentiate non-neoplastic from neoplastic lesions. The clinical features, symptoms, and advanced imaging technique help to reach a provisional diagnosis but histopathological examination remains the mainstay of the final definitive diagnosis [7]. There is a lack of studies that exclusively cover non-neoplastic lesions of sinonasal region. Hence, this study was done with the aim of examining the clinicopathological features of various non-neoplastic lesions of NC and PNS.

METHODS

A prospective and observational study was carried out in 100 patients of nasal masses coming to the department of otorhinolaryngology (ENT) and pathology of our institute. Ethical clearance was taken from the institutional ethical committee and informed consent was obtained from the patients. Nasal polyps were removed by endoscopic sinus surgery and subjected to biopsy. In suspected cases of fungal sinusitis (FSn), debridement followed by biopsy was taken. The formalin-fixed specimens of polypectomy/biopsy were received with complete clinical and radiological features in the department of pathology. Routine gross examination and required number of sections were taken and stained with hematoxylin and eosin stain. Periodic acid Schiff's was used wherever necessary. Brief clinical data were noted from the case records, which included the age and sex of the patient, relevant habits if any, presenting symptoms, radiological and endoscopic findings were noted. The sections from the specimen were fixed in 10% formalin. Then, Sections 4–6 microns in thickness were stained routinely with hematoxylin and eosin. Other special stains such as periodic acid schiff stain were done as and when required. The slides so obtained were then evaluated under microscope to describe the histopathological features and give a final diagnosis.

Statistical tests

Data so collected were analyzed using software statistical package student science version 23. Categorical variables were analyzed by Chi-square test. p value has been calculated and results are assessed accordingly.

RESULTS

Majority of the patients (24%) belonged to age group 41–50 years followed by 51–60 years and 21–30 years with 19% each, 31–40 years

Table 1: Distribution of patients according to location

Location	Bilateral		Right		Left		Total	
	n	%	n	%	n	%	n	%
Nasal Cavity (NC)	2	3.40	28	47.50	29	49.20	59	100.00
Maxillary sinus (MS)	0	0.00	11	40.70	16	59.30	27	100.00
Ethmoid sinus (ES)	1	25.00	0	0.00	3	75.00	4	100.00
ACPolyp (ACP)	0	0.00	0	0.00	3	100.00	3	100.00
Nasal cavity and maxillary sinus	0	0.00	2	66.70	1	33.30	3	100.00
Frontal sinus (FS)	0	0.00	1	100.00	0	0.00	1	100.00
Frontal, ethmoid sinus	0	0.00	0	0.00	1	100.00	1	100.00
Maxillary, Frontal sinus	0	0.00	1	100.00	0	0.00	1	100.00
Maxillary, ethmoid sinus	0	0.00	0	0.00	1	100.00	1	100.00
	3	3.00	43	43.00	54	54.00	100	100.00

Table 2: Distribution of patients according to clinical diagnosis

Clinical Diagnosis	Number	Percentage
Nasal Polyp	66	66
Rhinosinusitis	12	12
Fungal Sinusitis	6	6
Mass Sinus/Nasal Cavity	6	6
Rhino Orbital Mucormycosis	3	3
Nasal Obstruction	2	2
Antrochoanal Polyp	2	2
Facial Swelling	1	1
Deviated Nasal Septum (DNS)	1	1
Ethmoid Polyp	1	1
Total	100	100

with 18%, 11–20 years with 10%, 61–70 years with 5%, <10 with 3%, and >70 years with 2%. The mean value of age (in years) of patients was 39.16±13. It shows that a maximum number of cases fall within 3rd to 6th decade of life. After 6th decade, the frequency falls suddenly. There were 55% males and the rest 45% were females. It was observed that in maximum cases (29%), the duration of lesion was from 15 days (d) to 1 month (m) and of more than (>) 1 month to 6 months in similar number of cases (29%). Duration of more than 6 months to 1 year (y) was seen in 25% of cases. About 14% of cases showed duration of more than 2 years to 3 years. About 2% of cases presented with the duration of more than 1–2 years; and only 1% of case showed a duration of more than 3–4 years.

Maximum number of patients (70%) had a history of N Obs followed by hypomia/anosmia and nasal discharge (43% each), history of pain (42%), difficulty in breathing (41%), headache (40%), epistaxis (25%), and increase in size of lesion (22%). It was observed that the maximum patients (56%) presented with no medical history. Hypertension (HTN) was seen in 12% patients. About 11% of patients had previous history of COVID and corticosteroids intake during treatment. They presented with lesions after recovery. Eight patients gave a history of diabetes, 5% of patients had multiple comorbidities along with the previous history of COVID and steroid intake. About 3% of patients had a history of bronchial asthma, 1% each presented with HTN and bronchial asthma, HTN and diabetes mellitus, and dental extraction. One patient gave a history of nasal mass and had surgical removal of polyp. No patient had a positive family history. About 77% of patients gave no personal history, 13% of patients had a history of alcohol intake, and 9% of patients presented with a history of smoking. One patient had a history of both smoking and alcohol intake.

Location

Majority of the lesions were found to be unilateral (97%). Rests were unilateral. Maximum cases were seen in the NC (59%) followed by maxillary sinus (27%), ethmoid sinus (4%), and both in NC and maxillary sinus (3%). About 1% of case (1) each in frontal sinus and frontal with ethmoid sinus as shown in Table 1.

Table 3: Distribution of patients according to histopathological diagnosis

Clinical Diagnosis	Number	Percentage
Inflammatory Polyp (IP)	57	57
Allergic Polyp (AP)	18	18
Invasive Fungal Sinusitis-Mucormycosis (IFS-M)	17	17
Invasive Fungal Sinusitis-Aspergillosis (IFS-A)	2	2
Chronic non-specific inflammation (CNSI)	4	4
Epidermal Inclusion Cyst (EIC)	2	2
Total	100	100

Size

Maximum lesions (51%) had size between 2.1 and 4 cm followed by 25% of lesions which had size from 0 to 1 cm. In 20% patients, size was between 1.1 and 2 cm and lastly only 4% lesions had size >4 cm.

Clinical diagnosis (Table 2)

Maximum patients were given a clinical diagnosis of nasal polyp (66%) followed by rhinosinusitits (12%), FSn (6%), sinonasal mass was diagnosed in 6% patients, rhino-orbital mucormycosis (ROM) in 3%, N Obs in 2%, and antrochoanal polyp (AC P) in 2%. Rests of the patients (1% each) were diagnosed with facial swelling, DNS, or ethmoid polyp as shown in Table 2.

Histopathological diagnosis

Table 3 shows that the maximum cases presented with inflammatory polyp (IP) (57%), followed by allergic polyp (AP) (18%), invasive FSn-mucormycosis (IFS-M) (17%). About 4% of patients with chronic non-specific inflammation (CNSI) and 2% of cases each of invasive FSnaspergillosis (IFS-A) and epidermal inclusion cyst (EIC) were present.

Sex-wise distribution

In IP, 43.90% (25) patients were females and 56.10% (32) were males. AP comprised 33.30% (6) females and 66.7% (12) males.

In invasive IFS-M, 52.9% (9) patients were females and 47.10% (8) were males. In invasive IFS-A and EIC, 50% each were males and females. In CNSI, 75% (3) patients were females and 25% (1) male. No significant difference was observed in association with gender in various pathologies.

Chief complaints (Table 4)

Past medical history

It was observed that inflammatory and AP, CNSI, and EIC were more in cases with no medical history. Invasive FSn-M was found in patients who have recovered from COVID along with steroid intake history or have diabetes mellitus or have multiple comorbidities along with COVID recovery and steroid intake. Aspergillosis was more in patients who have DM or those who underwent dental extraction.

Personal history

It was found that the majority of cases of IP, AP, invasive IFS-M, and CNSI presented with no personal history of smoking or alcohol intake.

Table 4: Distribution of histopathological lesions according to chief complaints

Chief complaints	Inflammatory Polyp	Allergic Polyp	Invasive Fungal Sinusitis-Mucormycosis	Invasive Fungal Sinusitis-Aspergillo sis	Chronic non-specific inflammation	Epidermal inclusion cyst	Total	p-value
Increase in size	7 (12.30%)	5 (27.80%)	8 (47.10%)	2 (100.00%)	0 (0.00%)	0 (0.00%)	22 (22.00%)	0.002
Pain	19 (33.30%)	7 (38.90%)	9 (52.90%)	2 (100.00%)	3 (75.00%)	2 (100.00%)	42 (42.00%)	0.07
Epistaxis	9 (15.80%)	6 (33.30%)	11 (64.70%)	0 (0.00%)	1 (25.00%)	1 (50.00%)	28 (28.00%)	0.004
Nasal Discharge	18 (31.60%)	13 (72.20%)	6 (35.30%)	2 (100.00%)	4 (100.00%)	0 (0.00%)	43 (43.00%)	0.002
Nasal obstruction	42 (73.70%)	14 (77.80%)	7 (41.20%)	2 (100.00%)	4 (100.00%)	1 (50.00%)	70 (70.00%)	0.06
Headache	18 (31.60%)	7 (38.90%)	13 (76.50%)	2 (100.00%)	0 (0.00%)	0 (0.00%)	40 (40.00%)	0.003
Anosmia/hyposmia	20 (35.10%)	13 (72.20%)	7 (41.20%)	0 (0.00%)	3 (75.00%)	0 (0.00%)	43 (43.00%)	0.02
Difficulty in breathing	21 (36.80%)	9 (50.00%)	7 (41.20%)	0 (0.00%)	4 (100.00%)	0 (0.00%)	41 (41.00%)	0.08

Table 5: Distribution of lesion according to the location

Location	Inflammatory Polyp		Allergic Polyp		Invasive Fungal Sinusitis-Mucormycosis		Invasive Fungal Sinusitis-Aspergillosis		Chronicnon specificinflammation		EIC		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
AC Polyp	3	5.30	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	3	3.00
Ethmoidsinus	2	3.50	2	11.10	0	0.00	0	0.00	0	0.00	0	0.00	4	4.00
Frontal	1	1.80	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	1.00
Frontal and ethmoid sinus	0	0.00	1	5.60	0	0.00	0	0.00	0	0.00	0	0.00	1	1.00
Maxillary and Frontal sinus	0	0.00	1	5.60	0	0.00	0	0.00	0	0.00	0	0.00	1	1.00
Maxillary and ethmoid sinus	1	1.80	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	1.00
Maxillary sinus	13	22.80	1	5.60	9	52.90	2	100.00	2	50.00	0	0.00	27	27.00
Nasal Cavity	36	63.20	13	72.20	6	35.30	0	0.00	2	50.00	2	100.00	59	59.00
Nasal cavity and maxillary sinus	1	1.80	0	0.00	2	11.80	0	0.00	0	0.00	0	0.00	3	3.00
	57	100.00	18	100.00	17	100.00	2	100.00	4	100.00	2	100.00	100	100.00

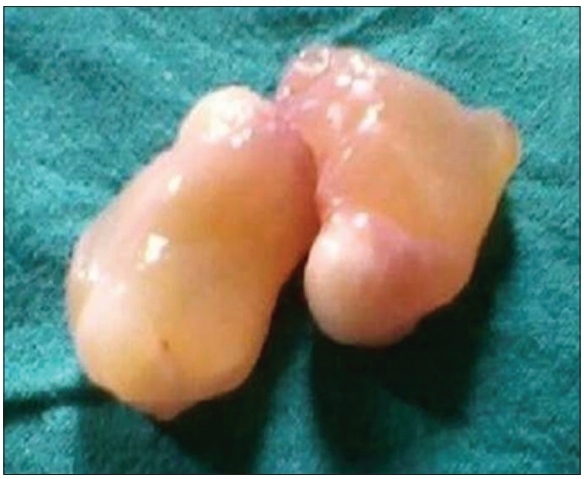

Fig. 1: Specimen of antrochoanal polypcreamish white polypoidal soft

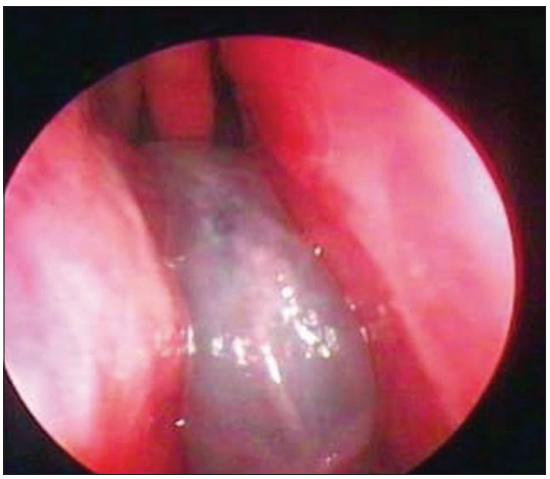

Fig. 2: Nasal endoscopic view of antrochoanal polyp

Among patients of chronic non-specific inflammation and EIC, 50% gave a history of alcohol intake in both conditions. About 50% of cases of invasive IFS-A gave a history of alcohol intake and the rest gave no history of such habits. No significant association was found between the personal history of the patients and the histopathological diagnosis.

Location (Table 5)

Majority of the lesions was found in NC (59%) followed by maxillary sinus (27%) and ethmoid sinus (4%). Inflammatory and APs were most commonly seen in NC. Both the cases of aspergillosis and majority of mucormycosis cases were located in maxillary sinus. CNSI was seen equally in both NC and maxillary sinus. Both the cases of EIC were located in NC.

DISCUSSION

In the present study, an analysis of 100 cases presenting as mass in NC and PNS was done for 2 years after approval from Institute's ethical committee. A detailed history, clinical examination, and investigations were carried out with aim to find out the frequency of non-neoplastic lesions among the masses in NC and PNS. The result of the present study is discussed below:

Age group

Majority of the patients (24%) in present study belonged to age group 41–50 years (5th decade) followed by 51–60 years (6th decade) and 21–30 years (3rd decade) with 19% each, 31–40 years (4th decade) with 18%, 11–20 years (2nd decade) with 10%, 61–70 years (7th decade) with

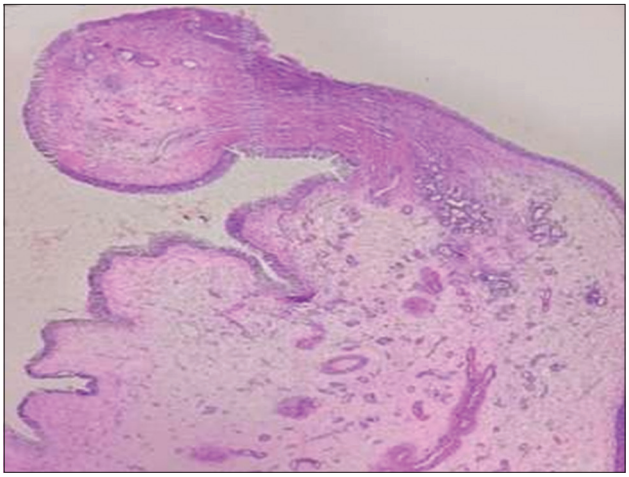

Fig. 3: Scanner view of allergic polyp displaying three-sided lining and submucosal edema along with inflammatory infiltrate. (H&E, 200×)

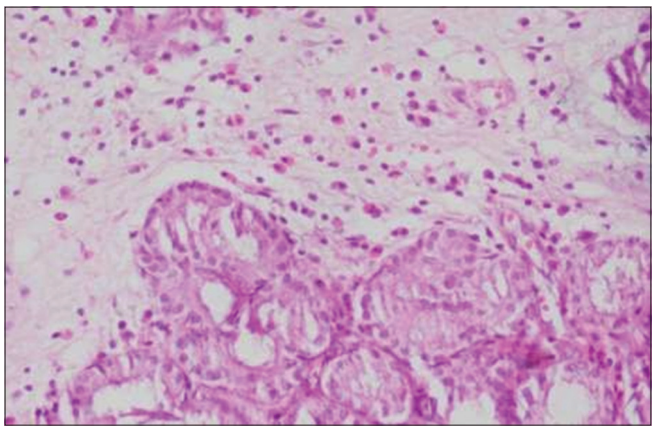

Fig. 4: High power view of allergic polyp showing inflammatory infiltrate comprising mainly eosinophils. (H&E, 400×)

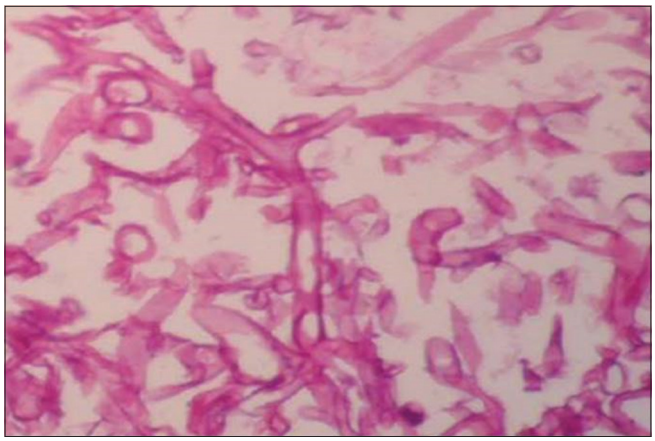

Fig. 5: High power view of mucor showing broad aseptate hyphae. (H&E, 400×)

5%, <10 years (1st decade) with 3% and >70 years with 2%. Mean value of age (in years) of patients was 39.16±13 years. It shows that a maximum number of cases fall within 3rd to 6th decade of life. After 6th decade, the frequency falls suddenly. It can be due to a lack of awareness among this age group in the study population. Kulkarni *et al*. (2020) observed that non-neoplastic lesions were commonly noted in 3rd and 4th decade [8]. This was in contrast to the present study. A study done by Kulkarni

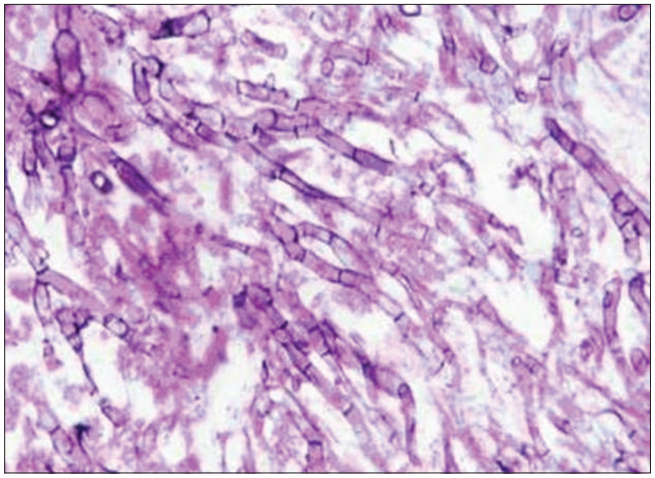

Fig. 6: High power view from paranasal sinus showing branched and septate hyphae of aspergillus (H&E, 400×)

et al. (2011) found that lesions of PNS and NC to be common in 2nd and 3 decades of life with the mean age of presentation being 22.5 years [9]. In a study by Zafar *et al*., the age of presentation ranged from 1st to 6th decade of life. The mean age of presentation was 22.5 years [10]. In both the above-mentioned studies, young adults were affected but in the present study, the mean age was 39.16 years which was greater than above-mentioned studies. This disparity can be attributed to the fact that elderly population with multiple comorbidities giving a history of COVID and steroid intake were more affected with FSn; thus increasing the mean age in the study population. Difference in the sample size can also contribute to the discordance.

Gender

In the present study, we found male predominance. There were 55% of males and 45% of females in the present study with male: female being 1.2:1. Similar results were shown by Zafar *et al*. and Shah *et al.* who showed male predominance in their study [10,11]. The study of Kumar *et al*. also had a predilection for males demonstrating a male-to-female ratio of 1.6:1 similar to a present study [12]. The study by Kulkarni *et al*. (2020) also revealed male preponderance in non-neoplastic lesions (62.25%) which was in accordance to the present study [8]. In another study conducted by Kulkarni *et al*. (2011), also male-to-female ratio for benign lesion of NC and PNS was 2.3:1 [9]. All these above-mentioned studies were in accordance to the present study and show male predominance.

Histopathological diagnosis

In the present study, it was observed that maximum cases presented with IP (57%), followed by AP (18%) (Figs. 3 and 4) and invasive IFS-M (17%). About 4% of patients with CNSI and 2% of cases each of Invasive IFS-A and EIC.

Sinonasal polyp

In a study by Kulkarni *et al*. (2020), also the most common non-neoplastic lesion was sinonasal polyp (85.72%) followed by fungal rhinosinusitis (Fig. 6) (5.10%), EIC (4.08%), rhinosporidiosis (2.04%), lepromatous leprosy (1.02%), chronic non-specific inflammation (1.02%), and arteriovenous malformation (1.02%) [8].

The study by Shah and Bhalodiya revealed that nasal polyps were the most common non-neoplastic lesions (91.67%). Among them, 64.93% were IP and 25.97% were AP [11].

In a study by Zafar *et al*., nasal polyp was the most common lesion observed in NC and PNS. It constituted 82.06% (119 cases) of non-neoplastic lesions [10].

In a study by Bakari *et al*., out of the histological result available, 45.9% were simple IP while 13.1% had allergic nasal polyp which was in accordance to the present study [7]. In the present study, inflammatory and APs showed male predominance. In IP, 56.10% were males while in AP 66.7% cases were males. Results obtained by Bakari *et al*. showed a higher preponderance among the females than males which were in contrast to the present study [7]. In a study by Zafar *et al*. [10], Parmar *et al*. [14], and Kulkarni *et al*. (2011), also male predominance was observed which was in accordance to the present study [9].

Regarding the age, 53% of patients were present within 4-6 decades of life and for APs, around 66.7% of patients were present in this age group. In a study by Zafar *et al*., the age range peak was seen in 2nd and 3rd decade of life [10]. These polyps were typically bilateral in 60% of cases and presented as mass in a single nostril in the rest. In the present study, the peak was 3–6 decade of life and mostly unilateral which was in contrast to their study. Parmar *et al*. also reported the most common age group for polyps 2–4 decade of life which was again dissimilar to the present study [14]. Regarding age group of nasal polyp, the study by Kulkarni *et al*. (2020) observed the peak incidence in 3rd decade which was in accordance with the present study [8]. In the study by Kulkarni *et al*. (2011), peak was seen in second and third decade of life with male predominance [9]. No significant correlation was observed among personal habits and inflammatory and AP.

Regarding the location of lesion, it was observed that a maximum number (63.20%) of IP s and APs (72.20%) were present in NC followed by maxillary sinus and rest all lesions were seen in other PNS. Hence, location of sinonasal polyps was in accordance to the study by Zafar *et al*. [10,14]. However, in the present study, most of lesions were unilateral (right side) which was in contrast to their study where the lesions were predominantly bilateral. In the present study among allergic lesions, most lesions were in NC followed by ethmoid sinus. Rokade *et al*. reported that Ethmoidal and AC Ps were generally allergic and inflammatory in nature, respectively. This trend was also similar to the two forms of the polyps in the present study [15].

In the present study, patients with IP most common presenting chief complaint were NObs (73.70%) followed by difficulty in breathing (36.80%), anosmia (35.10%), pain (33.30%), discharge and headache were observed in 31.60% each, least number of patients presented with nasal bleed and increase in size.

Among patients of AP, most commonly N Obs was seen (77.80%), followed by discharge and anosmia/hyposmia (72.20% each), difficulty breathing (50%), pain and headache observed in 38.90% each, epistaxis in 33.30%, and increase in size in 27.80% of patients.

In a study by Zafar *et al*., the patients presented with symptoms of nasal stuffiness, obstruction, and mass protruding from the nostril. Other symptoms were total and partial loss of smell, headache due to sinusitis, sneezing, and mucoid or watery discharge [10]. In the present study, also similar results were observed. A study by Kulkarni *et al*. [9] the patients presented with symptoms of nasal stuffiness and obstruction which was again in concordance with the present study.

Fungal rhinosinusitis

Acute fungal rhino sinusitis is mostly unilateral and may produce bone erosions with orbit and skull base invasion in advanced stages [9]. As it is highly fulminant with an increased risk of mortality, timely diagnosis and identification of fungus species are imperative for the appropriate treatment. The aspergillus hyphae are thin, uniform, and regularly septate, with dichotomous branching at 45° (Fig. 6). The mucor hyphae are broad and aseptate. The host response is minimal, with no inflammatory aspects of the tissue and no fungal invasion, although cases of invasive and extensive aspergillosis have been reported [16].

Invasive FSn-M

About 17% of patients were reported to have mucormycosis. Majority of the lesions were noted in NC, maxillary sinus or involved both NC and maxillary sinus. It was mostly present in 3–7 decade of life with peak incidence reported in 5th decade with male predominance. Maximum number of patients (64.70%) gave the history of recent recovery from COVID along with steroid intake. This was followed by diabetic patients who gave a history of recovery from COVID with steroid intake (23.50%); and patients of DM (11.80%). Three patients were clinically diagnosed with ROM which showed ocular involvement Significant number of mucormycosis cases can be attributed to the fact that the current COVID pandemic has greatly increased the hospitalization rates. The over-zealous use of steroids to control the viral infection and uncontrolled DM has been linked with the increased number [17,31]. In a study by Singh *et al*., male predominance was observed which was similar to the present study. Furthermore, the age range in their study was from 3 to 9 decade of life which was again in accordance to the present study [17]. Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million populations, while its prevalence is nearly 80 times higher (0.14/1000) in India compared to developed countries, in a recent estimate of year 2019–2020. In other words, India has the highest cases of the mucormycosis in the world. Notwithstanding, India is already having second largest population with diabetes mellitus and was the diabetes capital of the world, until recently. Importantly, DM has been the most common risk factor linked with mucormycosis in India [18-20].

In the present study, mucormycosis (Fig. 5) was found in patients who had recovered from COVID with a history of steroid intake during treatment or have diabetes mellitus or multiple comorbidities along with COVID recovery. Singh *et al*. in their study showed that mucormycosis was predominantly seen in males (78.9%), both in people who were active (59.4%) or recovered (40.6%) from COVID-19 [19].

COVID-19 recovered was defined as those who were either discharged from hospital or in-hospital but 2 weeks had passed post-detection, although there was evident overlap across the cases. In the study by Singh, hyperglycemia at presentation (due to pre-existing DM or new-onset hyperglycemia or new-onset diabetes or diabetic ketoacidosis [DKA] was the single most important risk factor observed in the majority of cases (83.3%) of mucormycosis in people with COVID-19, followed by cancer (3.0%) [19]. Pre-existing DM accounted for 80% of cases, while concomitant DKA was present in nearly 15% of people with mucormycosis and COVID-19. These results were similar to the result obtained in the present study.

In a 2019 nationwide multi-center study of 388 confirmed or suspected cases of mucormycosis in India before COVID-19, Prakash *et al*. found that 18% had DKA and 57% of patients had uncontrolled DM [22]. Similarly, in data of 465 cases of mucormycosis without COVID-19 in India, Patel *et al*. have shown that rhino-orbital presentation was the most common (67.7%), followed by pulmonary (13.3%) and cutaneous type (10.5%). The predisposing factors associated with mucormycosis among Indians include DM (73.5%), malignancy (9.0%), and organ transplantation (7.7%) [23]. The presence of DM significantly increases the odds of contracting rhino orbital cerebral mucormycosis by 7.5-fold (Odds ratio 7.55, p=0.001) as shown in a prospective Indian study, before COVID-19 pandemic [20-22].

The result of the present study was consistent with this study as all the patients who had mucomycosis were either COVID recovered, with a history of steroids intake, had diabetes, or presented with both. Regarding the signs and symptoms, patients with mucormycosis have diverse symptoms with the maximum patients having headache (76.50%), followed by epistaxis (64.70%), pain (52.90%), Increase in size (47.10%), nasal obstruction (41.20%), anosmia/hyposmia (41.20%), difficulty in breathing (41.20%), and discharge (35.30%).

Patel *et al.* in their review on mucormycosis reported that rhinocerebral mucormycosis is initiated with inhalation of spores into the PNS and the invasion of blood vessels. The infection starts with nasal congestion or discharge and it may progress to facial numbness, blurred vision, nasal discharge, nasofrontal headache, ocular pain, fever, diplopia, and irritation in eyes. Intranasal lesions characteristically have painless ulcerations with exudate and necrotic tissue, and usually progress rapidly over days. In the present study, patients presented with all above symptoms [23].

Sharma *et al.* in their review on rhinocerebral mucormycosis mentioned that clinical signs of rhinocerebral mucormycosis are non-specific, impeding early diagnosis. Symptoms are mostly associated with the involvement of the head region. One-sided headache behind the eyes and lethargy is the earlier presentation. Other general presentation includes nausea, fever, nasal congestion and rhinorrhea, epistaxis, nasal hypoesthesia, facial pain and numbness, history of black nasal discharge, and sinusitis [24]. Cerebral involvement was not found in the present study.

Chronic non-specific inflammation

In the present study, 4% of patients were diagnosed with chronic non-specific inflammation. 75% (3) patients were females and 25% (1) male. HPE revealed chronic inflammatory infiltrate comprising of lymphocytes, plasma cells, and few eosinophils with the absence of stromal edema or epithelial changes. About 50% of these cases were seen between 50 and 60 years of age. About 25% of cases were seen in 31–40 years of age and 25% of cases in 0–10 years. The study by Kulkarni *et al*. (2020) showed 1.02% of such cases of all non-neoplastic cases [8].

EIC

In the present study, 2% patients (2 cases) were diagnosed with EIC. One patient presented in 3rd decade and second in 6th decade of life. One patient was male and other female. One patient presented with NObs and one with epistaxis. Epistaxis can be explained by constant irritation and scratching of the lesions.

Dasgupta *et al*. presented with 0.5% of patients of non-neoplastic nasal polyps with EIC [25]. Zafar *et al*. studied 0.6% of cases of EIC [10]. These studies were dissimilar to the present study. Kulkarni *et al*. (2020) presented with 4.08% EIC of non-neoplastic lesions of sinonasal tract. This study was in accordance with the present study. These cysts are usually common in a young age due to their developmental origin. The presence of these cysts in adults in the present study can be due to their origin from the follicular epithelium of NC [25].

Invasive FSn-Aspergillosis

In the present study, 2 (2%) patients were diagnosed with Aspergillosis (one male and other female). They were seen in 21–40 years of age. All the patients presented with an increase in size of lesion, pain, nasal discharge, NObs, and headache. One patient was diabetic and one gave a history of dental extraction. HPE showed a dense accumulation of hyphae invading tissue. Vascular invasion is prominent with subsequent infarction and tissue necrosis.

Arora *et al*. in their study also showed the age range of patients with invasive aspergillosis to be 20–48 years which was similar to the present study [26]. In the present study, also 50% of patients were diabetic and 50% has underwent a dental extraction. In a study by Urs *et al*. in 2015, it was shown that in their case, patients with features of chronic sinusitis had a history of root canal treatment as well as surgical intervention to remove the broken root piece. Hence, both the intrusion of root-canal filling material as well as surgical exploration of an extraction socket under septic conditions could be the probable cause of aspergillus infection [27]. Martinez *et al*. also published a case report in apergilloma in maxillary sinus after a dental procedure [28]. Peral-Cagigal *et al*. studied a case of invasive maxillary sinus aspergillosis who similarly gave the history of dental extraction similar to our study [29,30].

Hence, from the present study, it is clear that the majority of the lesions was found in NC (59%) followed by maxillary sinus (27%) and ethmoid sinus (4%). Inflammatory and AP was most commonly seen in NC. Both the cases of aspergillosis and majority of mucormycosis cases were located in maxillary sinus. CNSI was seen equally in both NC and maxillary sinus. Both cases of EIC were located in NC.

CONCLUSION

It is important to recognize the range of non-neoplastic lesions in sinonasal region and to differentiate them from neoplastic lesions because of different treatment modalities and emotional burden on the patient. Among the non-neoplastic lesion, IP is the most common lesion followed by AP. A number of other non-neoplastic lesions were not seen in the study due to small number of patients and time of the study. The significant number of mucormycosis cases was seen due to the ongoing COVID pandemic and liberal use of corticosteroids in the treatment.

AUTHOR CONTRIBUTION

Dr. Swati Saini: Writing of manuscript and collection of data. Dr. Rama Kumari Badyal: Writing of manuscript, and analysis of data. Dr. Harpal Singh and SanjeevBhagat: Proof reading of manuscript.

CONFLICTS OF INTEREST

None.

AUTHORS FUNDING

None.

REFERENCES

1. Mane SA. Clinicopathological study of sinonasal masses. Ann Pathol Lab Med 2017;4:261-7.
2. Birare SD, Chaudhari AS. Clinicopathological study of lesions of nasal cavity and paranasal sinuses-a two year study. IP J Diagn Pathol Oncol 2021;6:259-66.
3. Lingen MW, Kumar V. Head and Neck. In: Kumar V, Abbas AK, Fausto N, editors. Robbin's and Cotran Pathologic Basis of Disease. 7th ed. Philadelphia: Elsevier Inc.; 2005. p. 783.
4. Kumar A. Lesions of nasal cavity, paranasal sinuses and nasopharynx: A clinicopathological study. Int J Res Rev 2022;4:1302-6.
5. Bateman ND, Fahy C, Woolford TJ. Nasal polyps: Still more questions than answers. J Laryngol Otol 2003;117:1-9. doi: 10.1258/002221503321046577, PMID 12590849
6. Parajuli S, Tuladhar A. Histomorphological spectrum of masses of the nasal cavity, paranasal sinuses and nasopharynx. J Pathol Nepal 2013;3:351-5. doi: 10.3126/jpn.v3i5.7857
7. Bakari A, Afolabi OA, Adoga AA, Kodiya AM, Ahmad BM. Clinico-pathological profile of sinonasal masses: An experience in national ear care center Kaduna, Nigeria. BMC Res Notes 2010;3:186. doi: 10.1186/1756-0500-3-186, PMID 20618972
8. Kulkarni A, Shetty A, Pathak P. Histopathological study of lesions of nasal cavity and paranasal sinuses. Indian J Pathol Oncol 2020;7:88-93.
9. Kulkarni AM, Mudholkar VG, Acharya AS, Ramteke RV. Histopathological study of lesions of nose and paranasal sinuses. Indian J Otolaryngol Head Neck Surg 2012;64:275-9.
10. Zafar U, Khan N, Afroz N, Hasan SA. Clinicopathological study of non-neoplastic lesions of nasal cavity and paranasal sinuses. Ind J Pathol Microbiol 2008;51:26-9. doi: 10.4103/0377-4929.40386, PMID 18417845
11. Shah H, Bhalodiya N. Scenario of fungal infection of nasal cavity and paranasal sinuses in Gujarat: A retrospective study. Gujarat Med J 2014;69:27-31.
12. Kumar A, Sood N, Gautam R, Ahlawat S, Nausaran K. Histopathological analysis of lesion of nasal cavity, paranasal sinus and nasopharynx-a clinical study. J Adv Med Dent Sci Res 2017;5:90-2.
13. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, *et al*. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology 2020;58:1-464. doi: 10.4193/Rhin20.600, PMID 32077450
14. Parmar NJ, Jethwani DP, Dhruva GA. Histopathological study of nasal lesions: 2 years study. Int J Res Med Sci 2018;6:1217-23. doi: 10.18203/2320-6012.ijrms20181271
15. Guarner J, Brandt ME. Histopathologic diagnosis of fungal infections

in the 21st century. Clin Microbiol Rev 2011;24:247-80. doi: 10.1128/CMR.00053-10, PMID 21482725
16. Rokade V, Shinde KJ, More GR. Clinicopathological profile of sinonasal masses-a tertiary care centre study in rural India. Int J Otorhinolaryngol Head Neck Surg 2020;6:1821-6. doi: 10.18203/issn.2454-5929.ijohns20204182
17. Singh V. Fungal rhinosinusitis: Unravelling the disease spectrum. J Maxillofac Oral Surg 2019;18:164-79. doi: 10.1007/s12663-018-01182-w, PMID 30996535.
18. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: A deadly addition to the pandemic spectrum. J Laryngol Otol 2021;135:442-7. doi: 10.1017/S0022215121000992, PMID 33827722
19. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr 2021;15:102146. doi: 10.1016/j.dsx.2021.05.019, PMID 34192610
20. Chander J, Kaur M, Singla N, Punia RP, Singhal SK, Attri AK, *et al*. Mucormycosis: Battle with the deadly enemy over a five-year period in India. J Fungi (Basel) 2018;4:46. doi: 10.3390/jof4020046, PMID 29642408
21. Laudien M. Orphan diseases of the nose and paranasal sinuses: Pathogenesis-clinic-therapy. GMS Curr Top Otorhinolaryngol Head Neck Surg 2015;14:Doc04. PMCID PMC4702053
22. Prakash H, Ghosh AK, Rudramurthy SM, Singh P, Xess I, Savio J, *et al*. A prospective multicenter study on mucormycosis in India: Epidemiology, diagnosis, and treatment. Med Mycol 2019;57:395-402. doi: 10.1093/mmy/myy060, PMID 30085158
23. Patel A, Kaur H, Xess I, Michael JS, Savio J, Rudramurthy S, *et al*. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India. Clin Microbiol Infect 2020;26:944.e9-15. doi: 10.1016/j.cmi.2019.11.021, PMID 31811914
24. Sharma AK, Nagarkar NM, Gandhoke CS, Sharma S, Juneja M, Kithan ZM *et al*. Rhinocerebral mucormycosis (RCM): To study the clinical spectrum and outcome of 61 cases of RCM managed at a tertiary care center in India. Surg Neurol Int 2023;14:15.
25. Dasgupta A, Ghosh RN, Mukherjee C. Nasal polyps-histopathologic spectrum. Indian J Otolaryngol Head Neck Surg 1997;49:32-7. doi: 10.1007/BF02991708, PMID 23119246
26. Arora V, Nagarkar NM, Dass A, Malhotra A. Invasive rhino-orbital aspergillosis. Indian J Otolaryngol Head Neck Surg 2011;63:325-9. doi: 10.1007/s12070-011-0240-8, PMID 23024936
27. Urs AB, Singh H, Nunia K, Mohanty S, Gupta S. Post endodontic aspergillosis in an immunocompetent individual. J Clin Exp Dent 2015;7:e535-9. doi: 10.4317/jced.52247, PMID 26535103
28. Martinez D, Burgueño M, Forteza G, Martin M, Sierra I. Invasive maxillary aspergillosis after dental extraction. Case report and review of the literature. Oral Surg Oral Med Oral Pathol 1992;74:466-8. doi: 10.1016/0030-4220(92)90297-4, PMID 1408022
29. Peral-Cagigal B, Redondo-González LM, Verrier-Hernández A. Invasive maxillary sinus aspergillosis: A case report successfully treated with voriconazole and surgical debridement. J Clin Exp Dent 2014;6:e448-51. doi: 10.4317/jced.51571, PMID 25593673
30. Banerji A, Piccirillo JF, Thawley SE, Levitt RG, Schechtman KB, Kramper MA, *et al*. Chronic rhinosinusitis patients with polyps or polypoid mucosa have a greater burden of illness. Am J Rhinol 2007;21:19-26. doi: 10.2500/ajr.2007.21.2979, PMID 17283555
31. Pal R, Singh B, Bhadada SK, Banerjee M, Bhogal RS, Hage N, *et al*. COVID-19-associated mucormycosis: An updated systematic review of literature. Mycoses 2021;64:1452-9. doi: 10.1111/myc.13338, PMID 34133798