INTRODUCTION

A variety of non-neoplastic lesions involving 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.
with 19%, 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 hypomyia/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 (14%), 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 1: Distribution of patients according to location

<table>
<thead>
<tr>
<th>Location</th>
<th>Bilateral</th>
<th>Right</th>
<th>Left</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Nasal Cavity (NC)</td>
<td>2</td>
<td>28</td>
<td>29</td>
<td>59</td>
</tr>
<tr>
<td>Maxillary sinus (MS)</td>
<td>0</td>
<td>11</td>
<td>16</td>
<td>27</td>
</tr>
<tr>
<td>Ethmoid sinus (ES)</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
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<tr>
<td>ACPolyp (ACP)</td>
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<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Nasal cavity and maxillary sinus</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Frontal sinus (FS)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Frontal, ethmoid sinus</td>
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<td>0</td>
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<td>1</td>
</tr>
<tr>
<td>Maxillary, Frontal sinus</td>
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<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>Maxillary, ethmoid sinus</td>
<td>0</td>
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</table>

### Table 2: Distribution of patients according to clinical diagnosis

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

### Table 3: Distribution of patients according to histopathological diagnosis

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

### Clinical diagnosis (Table 2)

Maximum patients were given a clinical diagnosis of nasal polyp (66%) followed by rhinosinusitis (12%), FSn (6%), sinonasal mass was diagnosed in 6% patients, rhino-orbital mucormycosis (ROM) in 3%, N Obs in 2%, and antrochoanal polyp (ACP) 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 Fnsaspergillosis (IFS-A) and epidermal inclusion cyst (EIC) were present.

### 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)

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.
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%, 21–30 years (3rd decade) with 10%, 61–70 years (7th decade) with 10%.
5%, <10 years (1<sub>st</sub> decade) with 3% and >70 years with 2%. Mean value of age (in years) of patients was 39.1±13 years. It shows that a maximum number of cases fall within 3<sup>rd</sup> to 6<sup>th</sup> decade of life. After 6<sup>th</sup> 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 3<sup>rd</sup> and 4<sup>th</sup> decade [8]. This was in contrast to the present study. A study done by Kulkarni et al. (2011) found that lesions of PNS and NC to be common in 2<sup>nd</sup> 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 1<sup>st</sup> to 6<sup>th</sup> 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 39.1 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 FS; 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.

**Sinoonasal 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), 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 APs.

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 Ohs 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 osseous 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 pre-dominant 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 mucormycosis 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 (47.40%), 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 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 the 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 undergone 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 aspergillosis infection [27]. Martinez et al. also published a case report in apergilloma in maxillary sinus after a dental procedure [29]. Peral-Caggil 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 Sanjeev Bhagat: Proof reading of manuscript.

**CONFLICTS OF INTEREST**

None.

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