ASPERGILLOSIS IN NOSE AND PARANASAL SINUSES ALONG WITH NASAL POLYPOSIS. Arsalan Ahmed Shaikh¹, Muhammad Iqbal², Noman Ahmed³, Farhan Ahmed Shaikh⁴, Aamir Hussain⁵, Ghulam Mustafa Dahri⁶.

ABSTRACT:

Objective: To calculate the occurrence of aspergillosis in nose and sinuses in patients presenting along nasal polyps at tertiary care hospital. **Methods**: Cross sectional, descriptive Conducted at department of Otorhinolaryngology, Liaquat university hospital Hyderabad from January 2019 to June 2020 where 137 patients with nasal polyposis were studied. All relevant information was recorded in a proforma. The data recorded & analyzed on SPSS-20 version. **Results:** Out of 137 patient (81 males & 56 Females), 101 (73.72%) were positive fungal stain, Asprgillosis in 85 (84.15%) out of 101 cases, 53 (52.47%) were male and 48 (47.52%) were female while other 16 fungal stain had Rhizopus, Blastomyces, trichphytosis and mucor in four (4%) each. The mean age was 33.6 years \pm 13.47, youngest was 7 year old girl and oldest was 75 year old man in the patients presented with nasal polyposis. 16 (11.67%) patients had intra cranial and intra orbital extension and 04 (2.9%) patients had intra orbital extension alone. Commonly presenting complaints were Nasal obstruction, post nasal drip, hyposmia / anosmia, Facial pain and headache. **Conclusion**: Fungal rhinosinusitis is a.n usual entity in young individuals. Mostly patient having nasal obstruction and post nasal drip. Most common fungal organism in these patients is found aspergillosis. **KEY WORDS:** Aspergillosis, Nasal polyposis, Para-nasal sinus.

How to cite this article: Shaikh AA¹, Iqbal M², Ahmed N³, Shaikh FA⁴, Hussain A⁵, Dahri GM⁶. ASPERGILLOSIS IN NOSE AND PARANASAL SINUSES ALONG WITH NASAL POLYPOSIS. *JPUMHS*; 2021:11:01,100-104. http://doi.org/10.46536/jpumhs/2021/11.01.300

- 1. Associate Professor, Department of E.N.T, LUMHS, Jamshoro/Hyderabad.
- 2. Associate Professor, Department of E.N.T PUMHSW, SBA.
- 3. Assistant Professor, Instituate of Ophthalmology, LUMHS, Jamshoro/Hyderabad
- 4. Department of Pathology, LUMHS, Jamshoro/Hyderabad
- 5. Assistant Professor Department of Physiology, Bilawal Medical LUMHS, Jamshoro/Hyderabad
- 6. Prof. Department of Pharmacology PUMHSW, SBA.

For Correspondence: Dr. Arsalan Ahmed Shaikh Associate Professor Department of E.N.T Liaquat University of Medical & Health sciences, Jamshoro/Hyderabad Mobile: 0334-3322125 Email: <u>drarsalanshaikh@gmail.com</u>

Received on: Dec 4, 2020, Accepted On 15 March 2021, Published On 31 March 2021

INTRODUCTION

Greek word "polyp" undergone latinization, means [poly-pous] many footed. Nasal polyp is hypertrophic, edematous and pedunculated mucosa of nasal cavity & its sinuses. It is one of the commonest conditions responsible for loss of olfaction. Simple nasal polypi are common and easily recognizable clinical condition. They usually originate from ethmoid labyrinth and are associated with chronic sinusitis, nasal allergy and fungal sinusitis¹. The occurrence has stated to be 1% to 4% of the overall population. Polyp occur from narrow passage of the mucosal contact such as ostiomeatal complex, which undergo pathological changes results inflammation of ostiomeatal complex causing odema and finally obstruction of sinuses. The polyps usually lead to chronic rhinosinusitis with impaction and stasis of mucin. Inhalation and trapping of fungal spores can promote fungal growth.²

Fungal infection may occur in both individuals either immuno-compromised patients or immuno-competent patients. Allergic fungal rhino-sinusitis is a clinical condition with its recognized diagnostic criteria.³ The Aspergilli are one of the most common

fungi in environment which present in atmosphere. Katzenstein, Rager and Moutagne were the pioneers to identify aspergillus species. Human disease was first reported by Safirstein. Fresenius described aspergillus fumigatus. Aspergillus fumigatus infection can manifest as non invasive and invasive aspergillosis. Invasive aspergillosis is usually a disease of immunocompromised individuals particularly of those with defective granulocytes function.⁴ Aspergillus species are unique airborne infection. Majority of population constantly inspire numerous saprophytic fungi. These fungi were eliminated normally in the Healthy host by innate immune mechanisms so aspergillus was considered to be a weak pathogen for many years. Aspergillosis infection of the nose & paranasal sinuses were unusual but have been increasily recognized in recent years. Aspergillus species are considered the mostly fungal disease in both individual's i-e immunocompetent and immunocompromised⁵. Clinical examination i.e. rhinoscopy is an important part in both diagnostic and the therapeutic purposes. C-T Scan of the nasal cavity and paranasal sinuses particularly coronal view is an important component of the

evaluation of fungal disease which shows double density sign. Final diagnosis is based on the histopathology and fungal staining⁶. Tremendous research work has been done internationally and lot of published material is available on sinonasal pathologies associated with Aspergillosis but still our local (Pakistani) literature on this subject is scanty and we need a lot of research work in this regard.

PATIENTS AND METHOD:

This was the cross sectional descriptive study. This study was carried out at department of otorhinolaryngology, Liaquat university hospital Hyderabad from January 2019 to June 2020. 137 patient clinically diagnosed cases of sinonasal polyps were enrolled in this studied. Neoplastic conditions of nose and sinuses, immunocompromised patients or having immunosuppressant drugs and along comorbidity like chronic renal failure; chronic liver diseases, uncontrolled diabetes mellitus etc were excluded from study. Patients of any age and sex admitted in ENT department presenting with nasal polyposis through OPD were registered and those full fill the inclusion criteria were enrolled in the sample and informed written consent for inclusion of sample were taken from the patient. The basic demographic information including name, father/ husband name, age, sex, address was recorded. Clinical features like nasal obstruction, post nasal drip, nasal mass, hyposmia / anosmia, external deformity, headache, facial pain, proptosis, and hypertelorism were also recorded. Specific investigations i.e. C.T scan findings include double density sign, unilateral or bilateral involvement, orbital and skull base erosion was carried out. The specimen taken from nose was sent for tissue histopathology and staining for fungus. All relevant informations were recorded on especially design proforma. Data was entered and analyzed by using SPSS version 20 on computer. Relevant simple descriptive statistics with mean, SD of demographic variables (age, gender), Clinical features like nasal obstruction, post nasal drip and nasal mass. Special investigations of the patient like C.T. scan findings (double density sign, orbital and skull base erosion), histopathological and fungal staining findings were judged on results and Figure 01: Age Distribution of Patients

presented as positive and negative in proportion calculated. Frequency of aspergillosis was calculated from total data.

RESULTS

The mean age was 33.6 years \pm 13.47 (Figure 01). The youngest patient was 7 year old girl and oldest patient was 75 year old man includes in this study. A total 137 cases, out of which 80 (59.1%) were male and 56 (40.9%) were female (Figure 02). 137 cases of nasal polyposis were included, out of these 101 (73.72%) patients were found to have underlying fungus. Out of 101 cases, 85 (84%) were Aspergillosis, out of these 53 (52.47%) were male and 48 (47.52%) were female, while other sixteen fungal stains were Rhizopus, Blastomyces, Trichphytosis and Mucor in 04 (4%) each (Figure 03).12 year old girl was the youngest patient with underlying Aspergillosis was and 75 year old man was the oldest patient, with mean age was 28 year and \pm 14.51. 48 (35.03%) patients were unilateral nasal polyposis and 89 (64.96%) were bilateral nasal polyp. In 48 unilateral cases, 24 (50%) patients were Aspergillosis and in bilateral cases, 61 (68.53%) out of 89 patients were Aspergillosis. Among 137 patients, 16 (11.67%) patients had intra cranial and intra orbital extension on CT scan. 04 (2.9%) patients had intra orbital extension alone. All 20 patients were histopathologically proven fungus and on fungal staining the Aspergillosis species was detected post operatively. Nasal obstruction was the commonest presenting symptom and all patients had obstruction, out of which 85 (62.04%) patients were diagnosed as Aspergillosis (Table 01). 113 (82.4%) patients were complaining of headache, out of which 73 (64.60%) patients were later found to have Aspergillosis (Table 01). Hyposmia / Anosmia was noticed by 96 (70.07%) patients, out of which 68 (70.83%) were later found to have Aspergillosis (Table 01). 88 (64.23%) patients were complaining of Post Nasal drip, out of which 64 (72.72%) were later found to have Aspergillosis (Table 01). Facial pain was complained by 48 (35.03%) patients, and 36 (75%) patients had Aspergillosis (Table 01). CT scan has been performed in all 137 patients, 85 (62.04%) patients had later proved to have Aspergillosis. Double density sign was observed in 69 (81.17%) patients with underlying Aspergillosis.



Figure 02: Gender Distribution of Patients.





Figure 03: Distribution of Fungus In Nasal Polyps:

Table 01: Clinical Features in Relation Of Aspergillosis				
S.NO	CLINICAL FINDINGS	TOTAL	WITH ASPERGILLOSIS	
			n	%age
1	Nasal Obstruction	137	85	62.04%
2	Nasal Mass	137	85	62.04%
3	Headache	113	73	64.60%
4	Anosmia/Hyposmia	96	68	70.83%
5	Post Nasal Drip	88	64	72.72%
6	Facial pain	48	36	75%
7	Proptosis	16	12	75%
8	External deformity	10	05	50%
9	Hypertelorism	04	04	100%

DISCUSSION

Nasal polyps deserve attention, as it is distressing and disabling for the affected one. The geneses of sino-nasal polyps are until now debatable and many aspects contribute, in their formation and growth. This condition needs thorough workup, as it may be an marker of some co-existing pathology like granulomatous diseases or neoplasm, that further needs urgent, special attention⁷. This research was done to find the relationship of nasal polyposis with Aspergillosis. Frequency of fungal involvement in nasal cavity & its sinuses with nasal polyps is alot common. The pathology of the fungal connection in the nose and sinuses is unclear, that when fungi are present as pathogen or when as normal flora. Fungi can cause a spectrum of various diseases in the sinuses. They can appear in forms ranging from saprophytes to allergic sinusitis, fungal ball and in the most severe case in the form of invasive fungal rhinosinusitis⁸.

International literature also revealed the same findings but Deutsch E et al study showed Aspergillosis as less common causative fungal pathogen and being isolated in 4 - to - 7% cases⁹. While other international researchers showed fungus are the commonest pathogens 78 - to - 95% in nasal polyps ^{8, 10}. However, further international literature also showed that aspergillosis was the most common fungal species in immunocompetent individuals suffering from nasal polyps. The local researches. found 60% aspergillosis in

immunocompetent patients of nasal polyps.¹¹ while other showed $83.3\%^{12}$. In contrast, a large series of 200 cases of nasal polyposis of local researcher surprisingly found underlying fungus in only 14% of the patients¹³. In this study we have found the male preponderance and the ratio was 1.4:1. In 61% patients who were found to have Aspergillosis 52.37% were male and 47.62% were female with ratio of 1.2:1. This feature is comparable with the international study in which male and female ratio was 1.5:1¹⁴. Local researchers also showed the male preponderance in their study¹². While in contrast N et al showed slight female Suri preponderance¹⁵. Local literature also revealed the female preponderance in their research¹⁶. In this case series the mean age of all patients was 33.6 years with standard deviation of \pm 13.47and the range was 68 (7-75) years. The average age of patients with Aspergillosis was 32 years with a standard deviation of ± 14.51 and the range was 63 (12-75) years. All of the patients included in this study were immunocompetent and did not suffer in any metabolic, chronic illness or autoimmune disorders. These findings are comparable to international studies of which showed the mean age 31.1 years¹⁷. In another international study showed mean age 33.3 years & $\pm 13.1^7$. While in contrast to international study showed mean age was 45 years¹⁸. The finding of local researcher was also similar to the study of Haq et al where mean age was 31.56 years¹⁹. The average age of

the patient in the study of regional researcher was 20 years ± 6.32 indicating much lower age at presentation²⁰. Allergic sino-nasal polyp may be unilateral but mostly bilaterally. In this series 35% patients presented with unilaterally & 64% had bilateral disease. The Aspergillosis was discovered in 24 cases out of 48 in unilateral involvement while 61 cases out of 89 in bilateral involvement of nasal polyposis. This indicates that unpredictable attitude of this disease process and Aspergillosis can grow beside with polyps even in limited disease. The presenting complaints always act as the corner stone in the foundation of any diagnosis. In this study an especial emphasis was given towards the common clinical presentation which sets the index of suspicion for this specific disease. Nasal obstruction, nasal discharge, headache, presence of a nasal mass, anosmia / hyposmia and facial pain are the usual symptoms. All the researches and workers have a consensus over it. The findings in both local and international material are more or less same with insignificant difference in frequencies of the symptoms^{11, 12, 15,} ¹⁷. Nasal Obstruction was the prime symptom in all the subjects whether they had Aspergillosis or not. It was bilateral even in cases of unilateral polyps. This can be explained as the contralateral obstruction was usually complimentary to the ongoing inflammatory process. The osteo meatal complex of contralateral side may have some degree of edema.Nasal mass and headache were the second most frequent presenting complaints. Obstruction of the natural ostia, decreased ventilation of sinuses, sinonasal mucosal edema and pressure by expanding soft tissue mass and growing Aspergillosis all contributes to these complaints. Headache in the absence of other diagnostic criteria is not diagnostic for sinonasal disorder^{3, 7}.Chronic sinonasal disorder was a major cause of anosmia / hyposmia, but the initial concern in such patients was more about severe symptoms associated with the disease such as nasal obstruction, discharge and headache. In accordance to this observation, although 97 of our patients had loss of sense of smell, out of which 68(70.83%) patients were later found to have Aspergillosis but none of the patient presented with anosmia / hyposmia as their chief complaints. The smell loss was more severe in patient with nasal polyps than that seen in patient with chronic rhino-sinusitis. This was due to the fact that in addition to the inflammation of olfactory mucosa, they might contributed to some neuro-epithelial damage also¹.Typically the sinonasal disease causes episodes of pain over the sinus area, face or around the eyes, often associated with other symptoms. There was often feeling of heaviness and pressure rather than acute pain. Tenderness can be elicited over the facial areas corresponding with the sinuses. 48 patients had the complaint of facial pain and 37 of them had Extra sinus Aspergillosis involvement. extension in these cases was caused by some resorption of bone from pressure affect of expanding polypoidal or fungal ball and was not

reason by fungal invasion into mucosa, bone or other tissues of nose & sinuses. This may be because of the fact that aspergillus lacks keratolytic enzymes and cannot penetrate undamaged and intact mucus membrane in patients²¹.Extra immunocompetent sinus extension could be dangerous and worse for prognosis, when it might result into loss of some important function like vision or even turn into life threatening condition when extend intacranially. This series has 4 patients with intraorbital extensions through erosion of lamina papyracea. In all of them the lamina papyracea was breached. Although according to the international literature the risk of invasive of aspergillosis in tissue was very rare and may be in immunocompromised patients²². seen Hypertelorism in case of nasal polyposis is due to the expansion of ethmoids due to mass loading effect of the polyps. Bony erosion either because of pressure affects of expansible polyps or due to damage resulting in previous surgeries could also the reason for hypertelorism and external deformity. Bulging of the eye ball or proptosis is usually due to the erosion of lamina papyracea and entering of polypoidal or fungal mass into the orbit, pushing the eye ball usually in forward direction. CT scan proven intrawas present²¹. orbital extension As a pretreatment investigation, CT scan was performed in all patients. Hyperattenuation or double density along with soft tissue mass within the nose and PNS was observed. This reflects the good accuracy rate of diagnosing Aspergillosis on the basis of CT scan finding. This is in line with the published literature. This double density was because of accumulation of certain metals like Iron, Copper, Magnesium and Zinc, these element are known to be essential in fungal amino acid metabolism²¹.Keeping this study results in view, it is strongly recommended that every case of chronic should be thoroughly sinonasal disease scrutinized with a detailed history, clinical examination and specific investigations like CT scan, MRI (if intracranial / intraorbital involvement suspected), IgE level etc. and tissue removed surgically should always be subjected to histopathology, fungal staining and fungal culture to identify the fungal infection. This finding can change the whole line of management modality either medically or surgical technique for overcome the fetal complication and minimize chances of recurrence.

CONCLUSION

In young immunocompetent patients, with male preponderance, the frequency of Aspergillosis found significantly high in nasal polyps. Nasal obstruction was the chief presenting complaints present in all the patients followed by nasal mass, headache, anosmia/hyposmia and facial pain.In a temperate region with high humidity, which is a favorable condition for fungal growth, Aspergillus involvement in nose & sinuses is grave condition but often concealed aspect of nasal polyps. This fact highlight the significance of proper workup for underlying fungus (Aspergillosis) in such patients, this finding can change the whole line of management modality either medically or surgical technique for overcome the fetal complication and minimize chances of recurrence.

ETHICS APPROVAL: The ERC gave ethical review approval **CONSENT TO PARTICIPATE:** consent was taken from subjects and next of kin. **FUNDING:** Nil

ACKNOWLEDGEMENTS: We would like to thank the all contributors. AUTHORS' CONTRIBUTIONS: All authors read and approved the final manuscript. CONFLICT OF INTEREST: No

REFERENCES:

- Jankowski R, Rumeau C, Gallet P, Nguyen DT. Nasal polyposis (or chronic olfactory rhinitis). Eur Ann Otorhinolaryngol Head Neck Dis. 2018 Jun;135(3):191-196
- 2. Schleimer RP. Immunopathogenesis of Chronic Rhinosinusitis and Nasal Polyposis. Annu Rev Pathol. 2017 Jan 24; 12: 331-357.
- Qaisar Sajjad SM, Suhail Z, Ahmed R. Prevalence of fungal infection in nasal polyposis - A cross-sectional study, conducted at a tertiary care hospital in Karachi. J Pak Med Assoc. 2020 Jan;70(1):48-52.
- 4. Hirotsu M, Shiozawa A, Ono N, Miwa M, Kikuchi K, Ikeda K. Fungal extracts detected in eosinophilic chronic rhinosinusitis induced cytokines from the nasal polyp cells. Laryngoscope. 2014 Sep;124(9):347-53.
- Muñoz-Del-Castillo F, Jurado-Ramos A, Soler R, Fernández-Conde BL, Barasona MJ, Cantillo E, Moreno C, Guerra F. Fungal sensitization in nasal polyposis. J Investig Allergol Clin Immunol. 2009;19(1):6-12
- Rai G, Roy P, Gupta N, Sharma S, Dar SA, Ansari MA, Ramachandran VG, Das S. Computed Tomography Score an Excellent Marker: Differentiates Eosinophilic and Non-eosinophilic Variants of Chronic Rhinosinusitis with Nasal Polyp. Indian J Otolaryngol Head Neck Surg. 2019 Nov;71(Suppl 3):1787-1792.
- Stevens WW, Schleimer RP, Kern RC. Chronic Rhinosinusitis with Nasal Polyps. J Allergy Clin Immunol Pract. 2016 Jul-Aug;4(4):565-72.
- Hulse KE, Stevens WW, Tan BK, Schleimer RP. Pathogenesis of nasal polyposis. Clin Exp Allergy. 2015 Feb;45(2):328-46.
- 9. Deutsch E, Hevron I. Allergic Fungal Sinusitis: Diagnostic, therapeutic and

prognostic evaluation. Harefuah. 2004;143(6):394–397.464.

- Glass D, Amedee RG. Allergic fungal rhinosinusitis:a review. Ochsner J. 2011;11(3):271–275.
- Zakirullah Nawaz G, Sattar SF. Presentation and diagnosis of allergic fungal sinusitis. J Ayub Med Coll Abbottabad. 2010;22(1):53– 57.
- 12. Jawad A, Nisar YB. Frequency of fungal infection in the nasal polyposis patients undergoing polypectomy in a tertiary care unit. Rawal Med J. 2015; 40(4): 428–432.
- 13. Akhtar MR, ishaque M, saadat ullah Sh. Aetiology of nasal polyp – a study of 200 cases at combined military hospital rawalpindi. Pak J otolaryngol 2004; 20: 9-11.
- 14. Kaur R, Lavanya S, Khurana N, Gulati A, Dhakad MS. Allergic fungal rhinosinusitis: A study in a tertiary care hospital in India. J Allergy (Cairo) 2016;2016:7698173.
- 15. Suri N, Bhavya BM. Allergic fungal rhinosinusitis:an overview on pathogenesis, early diagnosis and management. Int J Otorhinolaryngol Head Neck Surg. 2018;4(3):694–700
- 16. Rashid D, Ahmed B, Muhammad SM, Hydri AS. Fungal sinusitis JCPSP 1999; 9:381-3.
- Chaitanya K, Kalavathi L. Evaluation of Diagnostic Criteria for AFRS: A Hospital Based Study. Bengal J Otolaryngol Head Neck Surg. 2017; 25(3):130–135.
- 18. Rains BM , Mineck CW. Treatment of allergic fungal sinusitis with high-dose itraconazole. Am J Rhinol. 2003; 17: 1-8.
- 19. Irshad-ul-Haq M, Farooq M, Qadri SH. Prevalence of allergic fungal sinusitis among patients with nasal polyps. J Sheikh Zayed Med Coll. 2014;5(4):690–692.
- 20. Thahim K, Jawaid MA, Marfani MS. Presentation and management of allergic fungal sinusitis. J Coll Physicians Surg Pak. 2007 Jan;17(1):23-7.
- 21. Marzouqi A Salamah, Mazin Alsarraj, Nawaf Alsolami, Kamal Hanbazazah, Abdulmajeed M Alharbi, Wael Khalifah, Sr. Clinical, Radiological, and Histopathological Patterns of Allergic Fungal Sinusitis: A Single-Center Retrospective Study. Cureus. 2020 Jul; 12(7): e9233.
- 22. Hassan Paknezhad, Nicole A. Borchard, Greg W. Charville, Noel F. Ayoub, Garret W. Choby, Andrew Thamboo, Jayakar V. Nayak. Evidence for a 'preinvasive' variant of fungal sinusitis: Tissue invasion without angioinvasion. World J Otorhinolaryngol Head Neck Surg. 2017 Mar; 3(1): 37–43.