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Original Research Article

Inflammatory cell distribution accrediting Th2 inflammation in Sinonasal polyp in Indian Population

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ABSTRACT

Background: The pathophysiology of Chronic Rhino-Sinusitis with Nasal Polyposis (CRSwNP) showed distinct ethnic and geographic differences whereas the Western Caucasian population revealed Th2 eosinophilic inflammation in contrary to the Asian Mongolian population with Th1-Th17 non-eosinophilic inflammatory pattern.

Materials and Methods: Prospective Observational study was undertaken from December 2019 to December 2021 on 50 patients who were diagnosed to have sinonasal polyposis. The collected polyp tissue was sent to the histopathological department for further microscopic evaluation. The types of inflammatory cell infiltrate studied in the tissue specimens obtained during surgery included lymphocytes, eosinophils, neutrophils, mast cells, and plasma cells.

Results: The age of patients ranged from 11 to 70 years with a mean age of 31.80±17.69 years. The male to female ratio was 1.3:1. The 62% of patients showed the predominance of eosinophil which was of grade III and grade IV category, Lymphocyte infiltrate of grades III and IV was present in 46% of cases, Mast cell was 30% and 10% of grade III and Grade IV respectively, and the Neutrophils were found only in 22% and 105 of cases of grade III & Grade IV, respectively which was the least of all inflammatory cells found in polyp tissue.

Conclusion: The cellular predominance was shifted toward the Th2 type of inflammation with the predominance of Eosinophil, Lymphocytes, Plasma cells, and mast cells in the Asian Aryan sub origin population contrary to the Th17 type of inflammation as indicated by the least infiltration of Neutrophils as reported in Asian Mongolian Populations.

1. Introduction

Chronic rhinosinusitis is thought to be one of the most distressing diseases of humankind. Although the prevalence of the disease varies from 4 to 13% in different geographic and ethnic groups, which is presented as chronic rhinosinusitis without polyposis and chronic rhinosinusitis with polyposis. The exact incidence of chronic rhinosinusitis is still not clear. However, the Danish and Pennsylvania study claimed the 0.06 and 0.83 per thousand per year incidence which was contradicted by the Danish study of a single municipality that claims 2.7% prevalence of chronic rhinosinusitis with polyposis. In the United States, 1 to 4 per cent of the population are affected by this disease which is more prevalent in between 45 to 65 years of age group and males are twice more common sufferers than females.[1–3] The pathophysiology of CRSwNP showed distinct ethnic and

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geographic differences whereas the Western Caucasian population revealed Th 2 eosinophilic inflammation in contrary to the Asian Mongolian population with Th1-Th17 non-eosinophilic inflammatory pattern. Moreover, the study on the second-generation Asian Mongolian residing in the United States revealed a non-inflammatory Th1-Th17 pattern for CRSwNP.[4,5]

This type of study is lacking in Aryan or Indian sub origin including the population of Bangladesh, Pakistan, Afghanistan, Sri Lanka and other Arab countries. Hence, the present study, which is unique in its own type is designed to examine the Th1/ Th2/Th17 inflammatory pattern in the Indian sub origin population based on the study of inflammatory cellular distribution and cellular phenotypes in the tissue of Sino-nasal polyposis.

2. Materials and Methods

This is a Prospective Observational study undertaken from December 2019 to December 2021 for the evaluation of the distributions of inflammatory cells in the tissue of sinonasal polyposis. After approval from the institutional ethical committee with letter no: 1198/IEC/IGIMS/2019. Fifty diagnosed cases of sinonasal polyposis were selected from the patients presenting to ENT Outpatients Department and were included in this study. The diagnosis was made based on criteria advocated by the European Position Paper on Rhinosinusitis and Nasal polyps 2012.,[4] (Table 1)

Written informed consent was taken from each participant of the study. The inclusion and exclusion criteria of the study included-

2.1. Inclusion criteria

1. Diagnosed patients of sinonasal polyposis above the age of 10 years.
2. Willing to participate in this study.
3. Underwent for Functional Endoscopic Sinus Surgery.
4. Those polyp tissues underwent histopathological examination.

2.2. Exclusion criteria

1. Patients ≤ 10 years of age or pediatrics group.
2. Patients with pre-existing infections like HIV, T.B., Hepatitis.
3. Immunocompromised patients.
4. Patients with fungal rhinosinusitis, cystic fibrosis and sinonasal malignancies, acute rhinosinusitis, sinonasal trauma, inverted papilloma as excluded by the clinical, nasal endoscopic, nose and paranasal sinus contrast enhancement CT findings and finally with histopathological examinations.
5. Patients undergoing revision surgery.

The evaluation of the selected patients was done which included history, clinical examination including diagnostic nasal endoscopy, radiography including Computed Tomography (CT) of the paranasal sinuses. Clinical examination of the patients was done, which also included diagnostic nasal endoscopy.

After preoperative workup, the diagnosed cases of sinonasal polyposis underwent endoscopic sinus surgery. The collected polyp tissue was sent to the histopathological department for further microscopic evaluation. A histopathological examination of the specimen was done to assess the density of different inflammatory cell infiltration in the polyps and the diseased mucosa. The inflammatory cells studied in this study include lymphocytes, eosinophils, neutrophils, plasma cells & mast cells. Staining was done using Hematoxylin and eosin stain. Grading criteria of individual inflammatory cell infiltrate were as follows-

1. Eosinophil count (High power field magnification, 400X), ten high power fields were counted, and an average number of eosinophils per high power field (HPF) was calculated and, grading was done as, Grade I- 0-3 cells/HPF, Grade II- 4-10 cells/HPF, Grade III- 11-30 cells/HPF and Grade IV - >30 cells/HPF.
2. Lymphocyte count (High power field, 400X), ten high power fields were counted, and an average number of lymphocytes per High power field was calculated and, grading was done as, Grade I- 0-20 cells/HPF, Grade II- 21-50 cells/HPF, Grade III- 51-80 cells/HPF, Grade IV- >80 cells/HPF.
3. Neutrophil count (High power field, 400X), ten high power fields were counted, and an average number of neutrophils per high power field was calculated and, grading was done as, Grade I- 0-10 cells/HPF, Grade II- 11-15 cells/HPF, Grade III- 16-20 cells/HPF, Grade IV- >20 cells/HPF.
4. Mast cells (HPF, 400X), ten high power fields were counted, and an average number of mast cells per HPF was calculated, grading was done as, Grade I- 0-5 cells/HPF, Grade II- 6-10 cells/HPF, Grade III- 11-15 cells/HPF, Grade IV- >15 cells/HPF.
5. Plasma cells (high power field, 400X), ten high power fields were counted, and an average number of plasma cells per high power field was calculated, and grading was done as, Grade I- 0-30 cells/HPF, Grade II - 31-50 cells/HPF, Grade III - 51-80 cells/HPF, Grade IV - >80 cells/HPF.

The data analysis was done using the Microsoft Excel data analysis tool.

3. Results

A total of 50 patients who underwent FESS for sinonasal polyposis during the period from December 2019 to

Table 1: Chronicrhinosinusitis with nasal polyps (CRSwNP): European position paper on rhinosinusitis and nasal polyps 2012.[4]

Symptoms	Endoscopic	Nose and Paranasal sinus CT findings
Two or more symptoms, one of which should be either nasal: blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip) - ± facial pain/pressure ± reduction or loss of smell and either	Nasal polyps, and/or mucopurulent discharge primarily from the middle meatus and/or oedema/mucosal obstruction primarily in the middle meatus	mucosal changes within the ostiomeatal complex and/or sinuses Chronic rhinosinusitis with nasal polyps

December 2021 were included in this study.

Table 2: Age Distribution ofsubjects

Age	Frequency	Percentage
11-20	21	42%
21-30	6	12%
31-40	7	14%
41-50	8	16%
51-60	4	8%
61-70	4	8%
Total	50	100%
Mean±SD	31.80±17.69	

The age of patients ranged from 11 to 70 years with a mean age of 31.80±17.69 years. Maximum numbers of patients were in the age group 11-20 accounting for 42% of the total patients. (Table 2)

Table 3: Gender distribution

Gender	Frequency	Percentage
Male	29	58%
Female	21	42%
Total	50	100%

There were 29 males (58%) and 21 females (42%) in the study making the male-female ratio 1.3:1. (Table 3).

3.1. Distribution of inflammatory cells in the study population

The types of inflammatory cell infiltrate studied in the tissue specimens obtained during surgery included lymphocytes, eosinophils, neutrophils, mast cells, and plasma cells. (Table 4)

The above bar diagram shows grade wise distribution of different inflammatory cells in the study population. In the study population, 14 percent had grade I, 24 percent had grade II, 30 percent had grade III and 32 percent had grade IV of eosinophil. The distribution of lymphocytes was, 10 percent of the population under study had grade I, 44 percent had grade II, 36 percent had grade III and 10 percent had grade IV. The study population-based distribution of neutrophils included 32 percent had grade I, 36 percent had grade II, 22 percent had grade III and 10 percent had grade IV. The presence of mast cells in the study population was that 24 percent of the study population had grade I of mast cell, 34 percent had grade II, 30 percent had grade III and 12 percent had grade IV. The distribution of plasma cells in the study population was that 32 percent had grade I of the plasma cell, 34 percent had grade II, 20 percent had grade III and 14 percent had grade IV.

4. Discussion

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a complex inflammatory condition that affects a large proportion of the population worldwide and is associated with a high cost of management and significant morbidity. This study was done on fifty patients of sinonasal polyposis who fulfilled the inclusion and exclusion criteria. The mean age of the patients was 31.80 ± 17.69 years. Out of the fifty patients, twenty-nine were male and twenty-one were female, accounting for a male to female ratio of 1.3:1. Studies conducted on Danish and Pennsylvanian populations, also found a male predominance in CRSwNP and the male to female ratio ranged between 1.3 and 2.2.[1–3,6]

Nasal polyposis is considered to be grouped into eosinophilic and non-eosinophilic types, but among various attempts to further divide the nasal polyps based on inflammatory cells, in one of the subdivisions they can be clustered into five types depending on the presence and predominance of lymphocytes, plasma cells, eosinophils, neutrophils, and mixed inflammatory cells.[3,5,7] This pattern of results about the diverse distribution of type and population of the inflammatory cell can be explained as, sinonasal polyposis, commonly also known as Chronic Rhinosinusitis with Nasal Polyps, i.e., CRSwNP, is characteristically a heterogeneous disease with several etiologies and multiple predisposing factors. Nasal polyposis cases follow the pattern of inflammation that fluctuates considerably by geographical region and ethnicity and keeps evolving. The histologic pattern and clinical presentation of the cases of sinonasal polyposis vary enormously in different areas and among different clusters or groups of individuals. Histopathologic differences may also arise according to the status of polyp, history of radiation exposure, gender and odontogenic infections.[5–10]

There are three distinct patterns of inflammation seen in sinonasal tissue, with predominant eosinophilic infiltration in Th2 inflammation. Similarly, the abundance of Lymphocytes, Mast cells, and plasma cells is also

Table 4: Distribution of InflammatoryCells in the study population

Type of cells	Grades of cell count score							
	Grade I		Grade II		Grade III		Grade IV	
	Frequency		Frequency		Frequency		Frequency	
Eosinophils	7	14%	12	24%	15	30%	16	32%
Lymphocytes	5	10%	22	44%	18	36%	5	10%
Neutrophils	16	32%	18	36%	11	22%	5	10%
Mast cells	12	24%	17	34%	15	30%	6	12%
Plasma cells	16	32%	17	34%	10	20%	7	14%

strong evidence of Th2 determined inflammatory process. However, the Th17 inflammation is typically regulated by Neutrophils.[5,7–9]

4.1. Eosinophil

In the significant number of cases with CRSwNP showed markedly elevated eosinophil in NP tissue. This eosinophil is an important component of Th2 mediated inflammation. The toxic cationic protein liberated by eosinophil does the injury to the epithelial cells is responsible for the polyp. In our study, 62% of patients showed the predominance of eosinophil which was of grade III and grade IV category.[1,2,6,8]

4.2. Lymphocytes

The lymphocyte is another important marker of Th 2 inflammation. These activated T cells within NP can activate B cell response and produce pro-inflammatory cytokines such as IL-4 and IL-5. Hence, it has the potential to develop chronic inflammation and polyp formation. In the present study, the Lymphocyte infiltrate of grades III and IV was present in 46% of cases.[6,8]

4.3. Mast cells

The activated mast cells produce IL-5 which is a potent activator of eosinophil recruitment of eosinophils and other cells found within NPs. It also produces histamines that are responsible for vasodilatation and increase vascular permeability. Hence, the elevated mast cell in NP is also important evidence of Th2 inflammation. In our study, the Mast cell was 30 % and 10% of grade III and Grade IV respectively.[1–3,6]

4.4. Neutrophil

The Th17 played an important role in the requirement of a neutrophil by producing IL17. Hence its role in producing inflammatory responses and polyp formation is critical for Th17 mediated inflammation. This type of inflammation is predominant in the Asian population having CRS w Nasal polyposis.[2,3,9] However, the studied population is predominantly of the Mongolian race of Asian counties. In the Aryan race like the Indian population, the Th2 is more predominant than Th17. In our study, the Neutrophils were found only in 22% and 105 of cases of grade III & Grade IV, respectively which was the least of all inflammatory cells found in polyp tissue.

5. Conclusion

Since the cellular predominance was shifted toward the Th2 type of inflammation with the predominance of Eosinophil, Lymphocytes, Plasma cells, and mast cells in our study rather Th17 type of inflammation as indicated by the least infiltration of Neutrophils. Hence, in contrast to the study done predominantly on the Mongolian population of Asian countries and the Asian aborigines of Americans by previous researchers, our study indicates a predominantly Th2 type of inflammation in the Aryan sub-origin of the Asian population. To come to a final conclusion extensive genetic study is required to find out the genetic factors influencing such variations.

6. Ethical Clearance

Taken via letter no: 1198/IEC/IGIMS/2019.

7. Acknowledgement

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8. Source of Funding

None.

9. Conflict of Interest

None.

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