**ORIGINAL ARTICLE** 

# Malaysian Nasal Polyps: Eosinophil or Neutrophil-Predominant

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#### ABSTRAK

Polip hidung jenis eosinofil biasa terjadi dalam populasi Barat. Tujuan utama kajian ini adalah untuk menentukan jenis histologi polip hidung dalam kalangan kumpulan etnik di Malaysia. Data demografi 122 pesakit yang mengidap kronik rinosinusitis dan mempunyai polip di dalam hidung mereka telah dikenalpasti dan direkod. Kepingan histologi untuk sampel polyp hidung telah dikumpulkan. Bilangan eosinofil dan bukan eosinofil serta purata sel-sel inflamasi yang terlibat dikira. Kecenderungan sel eosinofil didapati sebanyak 32.8% dan bukan eosinofil adalah sebanyak 67.2%. Jenis histologi polip hidung menunjukkan sangat signifikan di antara kaum (x = 8.322; p < 0.05). Sebanyak 78.9% polip hidung dari kaum Cina adalah bukan eosinofil, sementara peratusan bagi kaum Melayu dan India masingmasing adalah 71.9% dan 40.7%. Kajian ini menunjukkan kecenderungan polip hidung di dalam populasi Malaysia adalah jenis bukan eosinofil dan ianya sangat signifikan bagi kaum Cina.

Kata kunci: eosinofil, polip, histology

#### ABSTRACT

Eosinophil-type nasal polyp (NP) is common in Western population. This aim of this study was to determine the histology type of NP among different Malaysian ethnic groups. A total of 122 chronic rhinosinusitis with nasal polyposis (CRSwNP) patients were retrospectively enrolled and demographic data was recorded. The histological slides were retrieved. The number of eosinophils and non-eosinophils were counted and average number of inflammatory cells for each high power field was calculated. Eosinophil-predominant was seen in 32.8% of patients and 67.2% was non-eosinophil-predominant. Phenotypes of NP significantly showed

Address for correspondence and reprint requests: Salina Husain, Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +60391456045 Fax: +60391456675 Email: drsalina\_h@yahoo.com an association with ethnicity (x = 8.322; p < 0.05). A total of 78.9% of Chinese nasal polyps showed non-eosinophil predominant, while Malay and Indian nasal polyps revealed 71.9% and 40.7% of non-eosinophilic phenotype, respectively. Our study showed that Malaysian population had a non-eosinophilic phenotype of nasal polyps. There was a significant association in Malaysian ethnicity with the highest percentage in Chinese population.

Keywords: eosinophil, polyps, histology

## INTRODUCTION

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a chronic, nonneoplastic inflammatory disease of the paranasal sinuses, and mostly originates in the nasal mucosa of the middle meatus. The estimated incidence in the general population is 1-4% (Couto et al. 2008).

Research studies conducted on Caucasian population showed that eosinophil-predominant was the most common feature of NP and ranged between 73-92.5% of their sample size (Armengot et al. 2010; Garin et al. 2008; Snidvongs et al. 2012; Couto et al. 2008). However, research studies conducted in India and Asian countries. showed that about 48-69% of NP was neutrophil predominant and had lower cases of eosinophil-predominant NP compared to the Caucasian studies (Dafale et al. 2012; Hao et al. 2006; Ba et al. 2011). A study showed 17% of the sample were in combination of eosinophil and neutrophil, and 27% of NP had high level of mast cell, suggesting that the pathogenic mechanism of NP involved a complex inflammation included other inflammatory cells (Hao et al. 2006). A study about the comparison of histological aspects

of nasal polyps among Chinese, Caucasians and Africans patients different geographical and from background ethnological showed that African patients had more severe types of NP (92% are stage 3 nasal polyps) compared to others and the numbers of eosinophilic infiltration in the African patients was the highest among all. However, there was no major histological difference in the NP obtained from African, Chinese and Caucasian patients and they suggested that nasal polyposis could be the same disease entity in this three groups studied (Lacroix et al. 2002). The aim of the present study was to view the NP specimen and to identify the phenotype of NP among Malaysians.

## MATERIALS AND METHODS

This was a retrospective study done on patients who were diagnosed with nasal polyps (NP) from January till August 2013 in Universiti Kebangsaan Malaysia Medical Centre (UKMMC). NP tissues were obtained from 122 CRSwNP patients during routine endonasal sinus surgery, at Department of Otorhinolaryngology, UKMMC. The diagnosis of NP was based on each patient's medical history and on the results of nasal endoscopy and computed tomography (CT).

All patients diagnosed with bilateral NP were included in this study. The ethic and research committee board approved the study.

Endoscopic physical findings were scored. The degree of nasal polyps was classified in relation to fixed anatomical landmarks in four steps: 0 = "no polyposis", 1 = "polyps in middle meatus only", 2 = "polyps beyond middle meatus but not blocking the nose completely", 3 = "polyps completely obstructing the nose" (Fokkens et al. 2012).

Findings on CT scans were graded according to the Lund- Mackay scoring system. The mucosal abnormalities were graded as 0 (no abnormality), 1 (partial opacification), or 2 (total opacification) of the frontal, maxillary, anterior ethmoid, posterior ethmoid and sphenoid sinus, bilaterally. The ostiomeatal complexes were scored bilaterally as 0 (not occluded) or 2 (occluded). Those with CT grading more than 1 were considered positive and the maximal CT grading score is 24 (Lund & Kennedy 1997).

The histological slides for all cases of NP were retrieved from Pathology Department UKMMC. These of samples were fixated in a formalin solution (10% formaldehyde), included in paraffin; 5 m sections were made, which were hematoxylin/eosin stained. All slides were examined under light microscope with 400x magnification and a total of 10 high power fields were chosen for inflammatory cell counting. The number of neutrophils and/or eosinophils was counted, and average

number of inflammatory cells for each high power field was calculated (Wen et al. 2012).

All statistical analyses were completed using SPSS v21.0 statistical software (SPSS, Inc, Chicago, IL). Descriptive data was presented as percentages and means +/- standard deviation (SD). Chi square analyses were used for relationships of nominal variables.

## RESULTS

Out of total of 122 patients included in this study, 85 were males and 37 were females. The age ranged between 14-87 years (mean = 55.3 years). In the NP group, the ethnic classes were 57 Malays, 38 Chinese, and 27 Indians. Eosinophil-predominant was seen in 32.8% of patients and 67.2% were non-eosinophil predominant (Figure 1). Phenotype of NP was significantly associated with ethnicity (x = 11.536; p < 0.05) (Table 1).

## DISCUSSION

The pathogenesis of CRSwNP involves complex inflammation regulated by various chemical mediators and

Table 1: Statistical significance (p value) of clinical measurement

	м	SD	r	x2	Р
Race					
Malay	-	-	-	11.536	0.030
Chinese					
Indian					

M, Mean; SD, Standard Deviation; n, number; CT, Computed tomography P value ≤ 0.05 statistically significant



Figure 1: Percentage of cell phenotypes

cytokines produced by inflammatory cells in nasal mucosa (Bernstein et al. 1997). Clinically, it presents as a mass with round, smooth, translucent, glistening appearance, soft. pale, non-tender and moves with probing, and it is attached to the nasal sinus mucosa (Irfan & Shamim 2009). Clinical manifestations include nasal obstruction. rhinorrhea. anosmia hyposmia, and/or headaches and general malaise (Couto et al. 2008). On histological observation of nasal polyps (NP), generally it is lined by ciliated pseudostratified epithelium, the layer itself is thickened by oedema and infiltrated with inflammatory cells, mostly eosinophils (Garín et al. 2008).

The general histopathological classification is eosinophil-predominant or neutrophil-predominant. Most histological studies of nasal polyp have been performed in Caucasian patients and data from Asian population is still lacking. The majority was found to be eosinophil-predominant, comprising 73-92.5% (Armengot et al. 2010;

Garin et al. 2008; Snidvongs et al. 2012; Couto et al. 2008) whereas neutrophil-predominant was only 48-69%. A study done with 145 patients with NP in Sriraj Hospital, Thailand (Jareoncharsri et al. 2002) showed that 81.9% of NP was neutrophilpredominant, supported by study done in China (Ba et al. 2011). This suggested that Asian population might have different pathological mechanism from Caucasian population. Our study also showed that in Malaysian population, non-eosinophilic predominant polyps accounted for 67.5% thus differing from Caucasian populations.

The treatment modalities for eosinophilic or neutrophilic infiltration of NP differ from each other. Studies showed corticosteroid is effective to eosinophilic CRS by improving patients' symptom scores and polyp size scores, reducing numbers of eosinophil in NP but not numbers of neutrophils or levels of their mediators (Sakuma et al. 2011; Wen et al. 2012). On the other hand, macrolides effectively reduced interleukin-8, which is an important chemo-attractant of neutrophil, and size of nasal polyps (Wen et al. 2012; Majima 2004), while it showed poor therapeutic efficacy and worse clinical response in eosinophilic NP (Haruna et al. 2009; Peric et al. 2011). By understanding the histological types of the NP, it would provide us certain prognostic information and allow specific tailored treatments.

There are certain limitations to consider in our study. As this study was conducted in a tertiary centre, it may not represent the entire population. Thus, a larger community based study may be necessary to validate the results. Besides, due to the retrospective nature of this study, errors such as inadequate samples and missing data were inevitable.

#### CONCLUSION

Non-eosinophilic predominant NPs among patients in UKMMC and this result supports the finding from other Asian countries. There was a significant association in Malaysian ethnicity with the highest percentage in Chinese population.

### REFERENCES

- Armengot, M., Garin, L., de Lamo, M., Krause, F., Carda, C. 2010. Cytological and tissue eosinophilia correlations in nasal polyposis. *Am J Rhinol Allergy* 24(6): 413-5.
- Ba, L., Zhang, N., Meng, J., Zhang, J., Lin, P., Zhou, P., Liu S, Bachert C. 2011. The association between bacterial colonization and inflammatory pattern in Chinese chronic rhinosinusitis patients with nasal polyps. *Allergy* 66(10): 1296-303.
- Bernstein, J.M., Gorfien, J., Noble, B., Yankaskas, J.R. 1997. Nasal Polyposis: immunohistochemistry and bioelectrical findings (a hypothesis for the

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development of nasal polyps). J Allergy Clin Immunol **99**(2): 165-75.

- Couto, L.G., Fernades, A.M., Brandao, D.F., Santi Neto, D.D., Valera, F.C., Anselmo-Lima, W.T. 2008. Histological aspects of rhinosinusal polyps. *Braz J Otorhinolaryngol* 74(2): 207-12.
- Dafale, S.R., Yenni, V.V., Bannur, H.B., Malur, P.R., Hundgund, B.R., Patil, S.Y. 2012. Histopathological Study of Polypoidal Lesions of The Nasal Cavity-A Cross Sectional Study. Al Ameen J Med Sci 5(4): 403-6.
- Fokkens, W.J., Lund, V.J., Mullol, J., Bachert, C., Alobid, I., Baroody, F., Cohen, N., Cervin, A., Douglas, R., Gevaert, P., Georgalas, C., Goossens, H., Harvey, R., Hellings, P., Hopkins, C., Jones, N., Joos, G., Kalogjera, L., Kern, B., Kowalski, M., Price, D., Riechelmann, H., Schlosser, R., Senior, B., Thomas, M., Toskala, E., Voegels, R., Wang de, Y., Wormald, P.J. 2012. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl* (23):3 p preceding table of contents, 1-298.
- Garín, L., Armengot, M., Alba, J.R., Carda, C. 2008. Correlations between clinical and histological aspects in nasal polyposis. *Acta Otorrinolaringol Esp* **59**(7): 315-20.
- Hao, J., Pang, Y.T., Wang, D.Y. 2006. Diffuse mucosal inflammation in nasal polyps and adjacent middle turbinate. *Otolaryngol Head Neck Surg* 134(2): 267-75.
- Haruna, S., Shimada, C., Ozawa, M., Fukami, S., Moriyama, H. 2009. A study of poor responders for long-term, low-dose macrolide administration for chronic sinusitis. *Rhinology* 47(1): 66-71.
- Irfan, M., Shamim, A.K. 2009. Routine histological examination for nasal polyp specimens: is it necessary? *Med J Malaysia* **64**(1): 59-60.
- Jareoncharsri, P., Bunnag, C., Muangsomboon, S., Tunsuriyawong, P., Assanasen, P. 2002. Clinical and Histopathological classification of nasal polyps in Thais. *Siriraj Hosp Gaz* **54**(11): 689-97.
- Lacroix, J.S., Zheng, C.G., Goytom, S.H., Landis, B.N., Szalay-Quinodoz, I., Malis, D.D. 2002. Histological comparison of nasal polyposis in black African, Chinese and Caucasian patients. *Rhinology* **40**(3): 118-21.
- Lund, V.J., Kennedy, D.W. 1997. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg* 117(3 Pt 2): S35-40.
- Majima, Y. 2004. Clinical implications of the immunomodulatory effects of macrolides on sinusitis. *Am J Med* **117**(Suppl 9A): 20S-25S.
- Peric, A., Vojvodic, D., Radulovic, V., Vukomanovicurdevic, B., Miljanovic, O. 2011. Correlation between cytokine levels in nasal fluid and eosinophil counts in nasal polyp tissue in

asthmatic and non-asthmatic patients. *Allergol Immunopathol (Madr)* **39**(3): 133-9.

- Sakuma, Y., Ishitoya, J., Komatsu, M., Shiono, O., Hirama, M., Yamashita, Y., Kaneko, T., Morita, S., Tsukuda, M. 2011. New clinical diagnostic criteria for eosinophilic chronic rhinosinusitis. *Auris Nasus Larynx* 38(5): 583-8.
- Snidvongs, K., Lam, M., Sacks, R., Earls, P., Kalish, L., Phillips, P.S., Pratt, E., Harvey, R.J. 2012.

Structured histopathology profiling of chronic rhinosinusitis in routine practice. *Int Forum Allergy Rhinol* **2**(5): 376-85.

Wen, W., Liu, W., Zhang, L., Bai, J., Fan, Y., Xia, W., Luo, Q., Zheng, J., Wan,g H., Li, Z., Xia, J., Jiang, H., Liu, Z., Shi, J., Li, H., Xu, G. 2012. Increased neutrophilia in nasal polyps reduces the responseto oral corticosteroid therapy. J Allergy Clin Immunol 129(6): 1522-8.