



## MEAN PLATELET VOLUME (MPV), PLATELET DISTRIBUTION WIDTH (PDW), NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) AND EOSINOPHIL TO LYMPHOCYTE RATIO (ELR) AS MARKERS IN NASAL POLYPS AND AS PREDICTORS OF RECURRENCE.

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### Abstract

**Background:** Nasal polyps (NP) are benign protrusions of para-nasal sinus formed as a result of long standing mucosal changes due to allergy or infection. Treatment options include medically (oral or topical steroids) or surgically (Endoscopic sinus surgery). Novel inflammatory markers have been investigated in recent years for their levels in nasal polyps and as markers of recurrence.

**Methodology:** 37 patients (21 males and 15 females) with histopathologically confirmed nasal polyps (ethmoidal and antrochoanal), presenting in ENT OPD were taken up for surgery (Endoscopic polypectomy/ FESS). All patients had their Complete blood count (CBC) performed with an automated blood cell counter. Preoperative nasal endoscopy and computed tomography (CT) scans were conducted on each patient. The following values were directly derived and tabulated from the CBC reports: Absolute neutrophil count (N), Absolute eosinophil count (E), absolute lymphocyte count (L), Mean platelet volume (MPV), Platelet distribution width (PDW). The Neutrophil to lymphocyte ratio and eosinophil to lymphocyte ratio were calculated and tabulated. CBC was repeated at 6 months and 12 months post-operative.

**Results:** All the parameters had a significant decrease in the post-operative period when comparing Baseline vs 6 months and 1 year values of. comparing recurrent( 9/ 37) vs non recurrent( 28/37) cases, there was highly significant difference(decrease) in all parameters (MPV-p=0.000 ; PDW-p=0.002; NLR-p=0.000 ; ELR-p=0.000).

**Conclusion:** MPV, PDW, NLR and ELR are simple and reproducible parameters in predicting recurrence in nasal polyps. They can be used with clinical observation and follow up of nasal polyp cases after FESS and predicting response to surgery

**Keywords:** Nasal polyps, MPV, NLR, PDW, ELR

### INTRODUCTION

Nasal polyps (NP) are benign protrusions of para-nasal sinus (usually from the outflow tract of one or more) and nasal mucosa. It is a multifactorial disease with unclear etiology. They are usually freely movable, smooth and semi translucent.

They are formed as a result of long standing mucosal changes due to allergy or infection(chronic rhino-sinusitis). Frequency is usually 4%in generalpopulation [10]. They predominantly affect adults and are uncommon in children younger than 10years. There is a male preponderance of the disease. They cause significant morbidity with common symptoms of nasal obstruction, rhinorrhea, and olfactory disturbances. Treatment options include medically (oral or topical steroids) or surgically (Endoscopic sinus surgery). Recurrence rates have been estimated to be 15-25% [46].

Local allergic mechanisms with eosinophilic mediators are possible mechanisms in initiation. The most common histological type is the edematous, eosinophilic (so-called "allergic") nasal polyp, with other variants presenting as fibroinflammatory polyp, pronounced hyperplasia of seromucinous glands and with atypical stroma [11].

Interleukine-5 (IL-5) has found to be significantly raised in NP compared with healthy controls [12]. Other proinflammatory mediators implicated are interleukin (IL)-3, granulocyte-macrophage colony-stimulation factor (GM-CSF), tumor necrosis factor and interferons diagnosed using immunohistochemistry staining and Leukotrienes (LCT4) with radio immunoassay [47, 48, and 49]. Recent studies have focused on novel inflammatory and immunological markers for diagnosis of nasal polyps. Eosinophils have been primarily implicated to accumulate in nasal polyps through inflammation and also by stimulation of collagen synthesis[13]. Neutrophilic polyp is an identified phenotype with lower expression of IL 17 A, MUC5AC, and CD68 than eosinophilic types [14], with lesser response to corticosteroids [15].

Platelet distribution width (PDW) and mean platelet volume (MPV) are inflammatory markers, increasing in conditions of platelet destruction, investigated in recent times with nasal polyps. Studies have revealed that mediators released from mast cells, which had an important role in the etiopathogenesis of allergic rhinitis, asthma and NP, caused inflammation and fibrosis, subjecting these patients to stroke, dilated cardiomyopathy and atherosclerosis [16]. Neutrophil to lymphocyte ratio (NLR) has been the most studied of parameters with MPV.

We were not able to trace any single study concerning MPV, PDW, NLR and ELR in relation to NP, with their evaluation in post-operative period. Our study attempts to study the levels of these novel markers of inflammation in Indian subjects, after FESS and in recurrence cases in the same study group, so as to deduce their utility as predictors of recurrence.

## **MATERIALS AND METHODS**

37 patients (21 males and 15 females) with histopathologically confirmed nasal polyps (ethmoidal and antrochoanal), presenting in ENT OPD were taken up for surgery (Endoscopic polypectomy/FESS), . All patients had their Complete blood count (CBC) performed with an automated blood cell counter. Samples were run in duplicate.

Patients with informed consent were included in the study. Patients with associated cardiovascular diseases, smoking, chronic renal , liver or lungdiseases, on antiplatelet therapy, autoimmune diseases, bleeding diathesis , aged less than 18 years and more than 60 years ,hypothyroidism, malnutrition, neuromuscular diseases, chronic allergic rhinitis, cystic fibrosis, acute infection, parasitic infections, atopic conditions, family history of allergy, or with recent steroid use were excluded from the study. Cases lost to follow up were excluded from the study.

Preoperative nasal endoscopy and computed tomography (CT) scans were conducted on each patient. The following values were directly derived and tabulated from the CBC reports: Absolute neutrophil count (N), Absolute eosinophil count (E), absolute lymphocyte count (L), Mean platelet volume (MPV), Platelet distribution width (PDW). The Neutrophil to lymphocyte ratio and eosinophil to lymphocyte ratio were calculated and tabulated.CBC was repeated at 6 months and 12 months post-operative and the same data collection and tabulation protocol followed. Patients were reassessed with

nasal endoscopy and CT scan at 12 months and scored as per the LUND MACKAY scoring system (for polyps SCORE 0: NO POLYPS, SCORE 1: POLYP ONLY IN MIDDLE MEATUS, SCORE 2: POLYPS EXTENDING BEYOND MIDDLE MEATUS, SCORE 3: POLYPS FILLING THE NASAL CAVITY). Assessment of score and staging was not a part of final study results. Patients were followed up over a 2 year period and patients who followed up with recurrence were included in the final analysis. The earliest case of recurrence was at 1 year and the latest at 1 year 7 months.

All the data was statistically analyzed using SPSS program version 20. Descriptive statistics of parameters in study was carried out at different time intervals, comparison of the study parameters was done using ANOVA and TURKEY POST HOC test was applied to get the significant pairs at different time intervals. Comparison of study parameters at 12 months after surgery between the subjects with recurrence of polyp and those with non-recurrence was done using unpaired t-test.

## RESULTS

The mean age of the patients in the study was  $36.65 \pm 11.354$  yrs.

Males were 56.8% of the study group.

30 patients (81.1%) had ethmoid polyps and the rest antrochoanal type.

9 patients had recurrence after surgery (earliest at 1 year/ latest case at 1yr 7 months)

**TABLE 1**

MEAN ± SD OF STUDY PARAMETERS				
	MPV	PDW	NLR	ELR
<b>BASELINE</b>	10.697±	13.005±	3.7516±	.2212±
	1.8755	1.8195	1.5751	0.1449
<b>6 MNTHS</b>	8.96±	11.016±	2.6159±	.1174±
	1.5732	1.223	1.5776	0.8353
<b>12 MNTHS</b>	9.235±	11.254±	2.8954±	.1526±
	1.863	1.5267	2.015	0.1308

The mean value of neutrophil count at baseline (cases) was  $(5.3 \pm 1.38)$ , eosinophil  $(0.3143 \pm 0.168)$  and lymphocyte count  $(1.603 \pm 0.68)$  vs. the normal reference range of our institution (NEUTROPHILS:  $2 - 7 \times 10^3 / \mu\text{L}$  EOSINOPHILS:  $0.02 - 0.5 \times 10^3 / \mu\text{L}$  LYMPHOCYTES:  $1 - 3.0 \times 10^3 / \mu\text{L}$ ).

Table 1 shows the mean of all parameters of our study at baseline 6 months and at 1 year post op. There is a decrease in all values at 6 months and marginal increase at 1 year. The difference between 6 and 12 months was not statistically significant. But the difference was significant between cases when compared to both post-operative time periods as shown in Table 2 except the NLR ratio which had more than marginal increase at 1 year although it was less than pre-operative period. This of course is explained by the recurrence cases with NLR spiking the most of all parameters at 1 year. The difference of (N), (E) values were significant at both time periods but (L) values did not show a significant alteration in values.

**TABLE 2**

TURKEY HSD POST HOC TEST TO GET SIGNIFICANT PAIRS AT DIFFERENT TIME INTERVALS								
	MEAN DIFFERENCE AND p value							
	MPV	p value	PDW	p value	NLR	p value	ELR	p value
<b>BASELINE</b> vs 6 mnth	1.7297	<0.000	1.9892	<0.000	1.13571	<0.016	0.10377	<0.02851
<b>BASELINE</b> vs 1 year	1.4622	<0.002	1.7514	<0.000	0.85621	<0.090	0.6863	<0.02851

**TABLE 3**

RECURRENT CASES(REC) VS NON RECURRENT CASES(N-REC)								
MEAN ±SD AND P VALUE								
	MPV	p value	PDW	p value	NLR	p value	ELR	p value
REC	11.21 ±	<0.000	12.5889 ±	<0.002	5.922 ±	<0.000	0.3278 ±	<0.000
	1.53		1.34		1.54		0.12	
N-REC	8.60 ±		10.825 ±		1.9225 ±		0.097 ±	
	1.48		1.33		0.813		0.073	

Comparing recurrent cases( 9/ 37) with non-recurrent ones ( 28/37), there was highly significant difference between all parameters .Means of all parameters showed a decrease in non-recurrent cases suggesting that these parameters demonstrated a steady increase prior to recurrence in cases. There was also significant difference in N, E and L values between the two groups lower N and E values and higher L counts in non-recurrent cases (N:p<0.000; E:p<0.000; L:p<0.029)

## DISCUSSION

Differential diagnosis is important to rule out congenital anomalies, as well as benign or malignant tumors[17], as Hypertrophic turbinates ,blob of mucus, angiofibroma ,rhinosporidiosis, hamartoma, transitional cell carcinoma, squamous cell carcinoma, meningocele and other malignancies of nose. CBC is a widely used blood test that provides useful information about patient general health and inflammatory status. A high neutrophil count suggests acute infection or sometimes malignancy, high eosinophil count can denote a parasitic infection or allergic reaction and low lymphocyte count usually is a marker of viral infection or severe stress. NLR and ELR are simple and convenient ratios that can be calculated from CBC reports. MPV and PDW are directly observed from CBC.

The size and activity of platelets are correlated. Increased platelet activity, increased secretion of chemokines, is associated with increased platelet volume, which can be measured by larger mean platelet volume MPV and PDW. Large platelets are more adhesive and tend to aggregate more than smaller ones [45] MPV is increased in conditions of platelet destruction. Along with PDW, it is a marker for activation of platelets, although less specific [8]. MPV is increased in IBD, ITP, Myeloproliferative disease and Bernard soulier syndrome while low values occur in thrombocytopenia. Assessing whole blood count, MPV should not be undervalued, as its increase should suggest a careful assessment of cardiovascular risk [1]. MPV is increased in nasal septal deviation [2, 3] and adenoid hypertrophy [5] associated with severity of obstruction [3]. Thus these patients should be subjected to surgery as an increase in MPV and PDW values are related to increase in the risk of cardiopulmonary complications of nasal obstruction [4, 5].

There have been contrasting opinions in various studies regarding the levels of MPV in nasal polyps. Sharma et al[18], Sagit et al[19] ,Akil et al [20] and Eyibilin et al[6] found an increase in comparison to Tayfun et al[21], Atkas et al[22], Cengriz et al[23], Sayit et al[24] who found a decrease. Mean MPV at baseline in our study, at baseline, stood at (10.69±1.88) which was higher than the reference range of our institution, corroborating the former group and there was a decrease in MPV values in the post-operative period, further agreeing on the fact.

PDW was increased in nasal polyps in studies by Sharma et al [18] and Sayit et al [24] while it was normal as per Sagit et al [19] and Ferit et al [7]. Mean PDW in our study, at baseline (13.01± 1.82) was higher than reference range of our institution. This was further supported by the fact that the values significantly decreased after polypectomy. One study suggested that the sensitivity of PDW was superior to MPV in determining platelet activation [9], which remains a further area of study.

NLR is a marker of subclinical inflammation [25] and systemic stress. It has been applied in determining prognosis of CV diseases as well as Ca esophagus, gastrointestinal and breast [27, 28,

and 29]. Studies have proved NLR to be increased in Bell's palsy [30] and idiopathic sudden SNHL [31]. NLR co relates with clinical status in children with cystic fibrosis [32] and can be supportive evidence for tonsillectomy [33], and also with various systemic autoimmune and rheumatic disease [34, 35].

Studies by Tayfun et al [21] and Atan et al [36] found an increase in NLR in nasal polyps along with Alper yenigun [37] and Brescia G et al [38] who concluded higher NLR in recurrent cases. Our study findings, with a baseline mean NLR ( $3.75 \pm 1.58$ ) higher than normal values stated by few studies [39], reveal a significant decrease in NLR values post-surgery. Higher NLR values of recurrent cases (9/37) vs. non recurrent (28/37) revealed a statistically significant difference. Hence they can be considered as predictors of recurrence after polypectomy in endoscopic sinus surgery, also pointed out by Osman faith et al [40].

Studies relating tissue eosinophil count and nasal polyps, correlating with asthma and allergy [41, 42] and its relevance with skin prick test [43] have been apparent. ELR can be used in conjunction with skin prick test in pediatric patients with allergic rhinitis [44]. ELR is increased significantly in recurrent cases [37, 38] and also decreases post-surgery [38]. Our study agrees with the above findings as there is significant difference between recurrent and non-recurrent cases at/ after 1 year post op.

Other recent studies have focused on other blood parameters as PLT, RDW, PCT, CRP and more specifically basophil to lymphocyte ratio in predicting recurrence of nasal polyps after surgery. These certainly remain an area for further investigation on larger study groups.

## CONCLUSION

Our study is probably the first one in literature to combine multiple markers of inflammation in relation to nasal polyps.

It is safe to conclude, from our results, that MPV, PDW, NLR and ELR are simple and reproducible parameters in predicting recurrence in nasal polyps.

They can be used in conjunction with clinical observation and follow up of nasal polyp cases after FESS.

They can also be investigated on larger populations for their use in predicting response to surgery.

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## CONFLICT OF INTEREST

None declared

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