e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(3); 655-663

Original Research Article

Role of Platelet-Rich Plasma in Treatment of Primary Atrophic Rhinitis

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Received: 01-12-2025 / Revised: 15-01-2026 / Accepted: 21-02-2026

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Conflict of interest: Nil

Abstract

Introduction: Atrophic rhinitis (AR) is a chronic condition characterized by progressive atrophy of the nasal mucosa and underlying bone. AR can be classified as either primary or secondary to a predisposing factor or an event. Platelet-Rich Plasma (PRP) is a platelet-rich concentrate of plasma proteins and growth factors that aids in regeneration of nasal mucosa.

Aim and Objectives of the study: Evaluation of efficacy of PRP injection in Primary Atrophic Rhinitis (PAR).

Objectives: (1). To analyse Sino-Nasal Outcome Test-25(SNOT-25) scores before & after PRP therapy in patients with PAR. (2). To study any local side effects following PRP injection.

Methodology: The Hospital based prospective cohort study was conducted in Department of Otorhinolaryngology, Deen Dayal Upadhyay Hospital, and New Delhi from May 2022 to May 2023. Autologous PRP was given intranasally at 0, 2 and 4 weeks interval. Outcome measures - Primary- Improvement in SNOT-25 scores. Secondary- Improvement in nasal symptoms like nasal crusting and nasal obstruction.

Results: In this study, The SNOT-25 scores showed improvement over 6 months follow-up period, suggesting tissue regeneration and wound healing. The mean ± SD SNOT-25 score at 0, 1 and 6 months was found to be 44.08±4.12, 25.18±8.42 and 10.48±4.61 respectively. Nasal symptoms like nasal crusting and nasal obstruction also improved.

Conclusions: In the present study autologous PRP was given in patients of PAR intranasally with good results without any complications. SNOT-25 score and nasal symptoms showed significant improvement after PRP injection in 6 months follow-up period.

Keywords: Atrophic Rhinitis, Platelet-Rich Plasma, Primary Atrophic Rhinitis, Secondary Atrophic Rhinitis, Sino-Nasal Outcome Test-25.

DOI: 10.25258/ijcpr.18.3.104

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Introduction

Atrophic rhinitis (AR) is a chronic condition characterized by progressive atrophy of the nasal mucosa and underlying bone. It leads to the formation of nasal crusts, fetor, nasal obstruction, epistaxis, olfactory disturbances, secondary infection and nasal deformity. [1,2]

AR can be classified as either primary or secondary to a predisposing factor or an event. AR, as the name suggests, is characterized by atrophy of nasal mucosa, affecting both the mucous glands and nerves.[3] Various treatment modalities are being used like local, systemic (medical), or surgical. PRP is a neoteric material that is being used increasingly in many surgical specialties. Its various advantages include safety (because it is an autologous material), the increased recruitment of platelets and growth factors (GF) in the healing area, and a short preparation time.

PRP in Otorhinolaryngology has shown potential benefits in terms of improved tissue healing, reduced post-operative pain and bleeding, and tissue regeneration.

Recently, the use of PRP has been introduced to support regeneration of nasal mucosa in patients

with PAR. Therefore, in this study, we evaluated the efficacy of PRP injection in PAR.

Material and Methods

A prospective cohort study was done for a period of 12 months from May 2022 to May 2023 in Department of Otorhinolaryngology, Deen Dayal Upadhyay hospital, New Delhi. After obtaining written and informed consent from the patients, detailed medical history was taken & clinical examination was done. Clinical diagnosis was made on the basis of presence of characteristic feature like nasal crusting, nasal obstruction, fetor, anosmia and epistaxis, wide roomy nasal cavities.

STUDY POPULATION: Patients of age 18 to 65 years visiting ENT outpatient department were selected according to inclusion and exclusion criteria.

SAMPLE SIZE - At 95% confidence level and taking improvement in nasal crust symptoms after Platelet rich plasma injections as 69.23% cases in primary atrophic rhinitis cases (Mostafa HS et al) [3] and with relative error of 20%, the sample size estimated was 50 using the formula.

$n = Z\alpha 2\ p\ q / L2$,

Inclusion Criteria

Clinically diagnosed patients of PAR of either sex between 18 to 65 years of age with nasal symptoms of-

1. Nasal crusting
2. Nasal obstruction
3. Fetor
4. Anosmia
5. Epistaxis

Exclusion Criteria: Patients with any of the following-

1. Any patient of Secondary Atrophic Rhinitis (SAR) (history of previous surgery, nasal trauma, sarcoidosis, tuberculosis, syphilis, leprosy etc.).
2. Patients with hematological disorders such as hemolytic anemia, iron deficiency anemia.
3. Any known case of uncontrolled diabetes mellitus and hypertension.
4. Patients on anticoagulants.
5. Pregnant and lactating mothers.
6. Any known case of immuno-compromised condition.

Preparation of PRP: Under all aseptic precautions, around 10 ml of venous blood was withdrawn in a tube containing 3.2% sodium citrate). It was centrifuged using table top centrifugation machine (REMI R-8C BL) for 3 minutes at 3000 rpm and again for 3 minutes at 3300 rpm at Blood Bank, Deen Dayal Upadhyay Hospital. Obtained PRP (around 2.5 ml) was then taken in 5 ml syringe. This PRP was agglutinated using 0.5 ml of Calcium Chloride making the volume 3 ml.

Prepared PRP (volume 3 ml) was divided into equal parts each of 1.5 ml, in two 2 ml syringes. Approximately 0.5 ml of prepared autologous PRP was then injected bilaterally each into Inferior turbinate (submucosally 1 cm behind the anterior end), Nasal septum (submucosally 1 cm behind the mucocutaneous junction) and Nasal floor (submucosally 1 cm behind the mucocutaneous junction under endoscopic control (0˚ 4 mm endoscope) using 2 ml syringe with 26G needle).

These patients were evaluated using SNOT-25 score and analysing improvement in nasal symptoms over 6-month follow-up period.

Ethical Clearance: The research procedure followed was in accordance with the approved ethical standards of Institutional Ethics Committee-Deen Dayal Upadhyay Hospital, New Delhi, India.

Results

In our study, the mean age of the study participants was 35.98 years. The youngest patient was 19 years old while oldest was 62 years old. The median of the age (years) of the study group was 34.5. The maximum incidence was found in third and fourth decade

Out of 50 subjects in the study group, there were 33 female and 17 male subjects. Female to male ratio of the study group was found to be 1.94: 1.

The present study shows that the SNOT-25 scores improved over 6 month's follow-up period, suggesting tissue regeneration and wound healing. The mean ± SD SNOT-25 score at 0, 1 and 6 months was found to be 44.08±4.12, 25.18±8.42 and 10.48±4.61 respectively.

We also observed that nasal symptoms like nasal crusting and nasal obstruction were improved. Fetor, anosmia and epistaxis were found to be reduced over 6 months follow-up period.

In the present study, after 6 months of follow up after PRP administration, none of the patients had any complications.

Discussion

AR is a progressive chronic nasal disease characterized by atrophy of nasal mucosa and underlying bone. AR was first described by Frankel in 1876, as a triad of crust formation, foul odour and nasal mucosal atrophy. [4,5]

As suggested by the name, AR is characterized by atrophy of the nerves and mucous glands of nose. Non-ciliated squamous epithelium replaces the normal ciliated respiratory epithelium causing a

reduction in mucociliary clearance. Both olfaction and sensation are diminished, and neuro-regulation is lost. Patients generally exhibit crusting, fetor, epistaxis and have wide nasal cavities. Ozena, a Greek term denoting stench, is often used interchangeably in the literature with "atrophic rhinitis" to describe this chronic nasal disease.[6]

There are two types of AR: primary and secondary. PAR is most commonly caused by K. ozaenae infection.[7]. AR or ozaena (from the Greek word "ozaena" meaning "stench") may be connected to environmental conditions and malnutrition. It affects both sides of the nose, occurs after puberty and is more common in women. Due to this, an endocrine imbalance has been proposed as the probable cause of the disease. It is also thought to have an autoimmune origin, particularly by a virus; or vitamin, and iron deficiency. This needs to be distinguished from SAR which, unlike PAR, is more commonly a complication of extensive surgery, radiation, trauma, cocaine usage, and granulomatous or infectious diseases, such as syphilis or rhinoscleroma.[8]

PAR is largely a diagnosis of exclusion focused on evaluation for the causes of SAR. Symptoms including chronic nasal blockage, nasal crusting, anosmia and recurrent epistaxis in the patient's history point towards a diagnosis of AR. Patients of AR can be managed medically or surgically. The mainstay of treatment of AR is conservative. Medications can be administered locally or systematically like nasal drops, douching, antibiotics and PRP.

Surgical management includes decreasing the size of the nasal cavities and promoting regeneration of normal nasal mucosa

Platelet-Rich Plasma: PRP is an autologous blood product prepared by centrifugation of whole blood. The term PRP originated in the 1970s by hematologists describing plasma with a platelet count higher than peripheral blood, which at the time was being used as a transfusion product in thrombocytopenic patients. [9,10]

PRP is a neoteric material that is being used more and more frequently in many surgical specialties. Its various advantages include safety, the increased recruitment of platelets and GFs in the healing area, and it is easy to obtain. PRP was first used in 1987 in cardiac surgery and is now considered beneficial in wound healing and tissue regeneration. PRP promotes tissue regeneration and healing, hence it has been used in various surgical specialties, like cardiothoracic surgery, orthopedic surgery, neurosurgery, plastic surgery, dentistry, and oral and maxillofacial surgery. [11,12]

PRP contains a number of GFs that are useful for wound healing and tissue regeneration such as platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor alpha (TGF-α), transforming growth factor beta (TGF-β), fibroblast growth factor (FGF), insulin-like growth factor and platelet-derived angiogenesis factors, along with white blood cells, phagocytic cells, fibrinogen, and vasoactive and chemotactic agents. [11,13]

Classification of PRP: PRP has been widely used during the past decade, therefore multiple formulations are available. Ehrenfest et al [10,14] (Table 1) classified PRP on the basis of presence of cell content and fibrin architecture.

The PAW classification (Platelets, Activation, White blood cells (WBC)) (Table 2) is based on platelet concentration, activation and WBC count, including the neutrophil subgroup. [10,15]

Table 1: Ehrenfest Classification [10,14]

TYPE	CONTENT
Pure platelet-rich plasma (P-PRP)	Leukocyte-poor, low-density fibrin network
Leukocyte and platelet-rich plasma (L-PRP)	Contains Leukocytes and low-density fibrin network
Pure platelet-rich fibrin (P-PRF)	Without Leukocytes and high-density fibrin network
Leukocyte and platelet-rich fibrin (L-PRF)	Contains Leukocytes high-density fibrin network

Table 2: PAW Classification [10]

Parameter	Sub-Parameter	Condition	Category
Platelets	Concentration (/μL)	≤ baseline	P1
		> baseline – 750,000	P2
		> 750,000 – 1,250,000	P3
		> 1,250,000	P4
Activation	Exogenous	—	X
White Blood Cells (WBCs)	Total WBCs	Above baseline	A
		≤ baseline	B
	Neutrophils	Above baseline	α
		≤ baseline	β

Table 3: PLRA Classification [10]

	Criteria	Final Score
	P	**M**
P Platelet count	Volume Injected	M Cells/µL
L Leucocyte content*	> 1%	+
	< 1%	–
R Red blood cell content	> 1%	+
	< 1%	–
A Activation **	Yes	+
	No	–
*If white blood cells are present (+), percentage of neutrophils should be reported. **The method of exogenous activation should be reported.		

PRP promotes mitogenesis, angiogenesis and endothelial cell proliferation resulting in tissue regeneration and wound healing. In our study, we evaluated SNOT-25 questionnaire after PRP injection at 0, 1 and 6 months interval. The mean ± SD SNOT-25 score at 0, 1 and 6 months was found to be 44.08±4.12, 25.18±8.42 and 10.48±4.61 respectively.

Mostafa et al [3] in his study divided patients with PAR into two groups: group A receiving PRP and group B receiving PPP. In group A, SNOT-25 scores were averaged 40 initially, with improvement to 11 at 1 month and to 9 at 6 months after PRP. Whereas in group B, SNOT-25 scores were averaged 38 initially, to 37 at 1 month, and 39 at 6 months after PPP (p value<0.005), similar to our study.

Kim et al [1] in his study evaluated effect of PRP (group A) and saline spray (group B) in patients with SAR. In group A, SNOT-22 scores were averaged 42 initially to 31 at 1 month and to 32 at 6 months. In group B, SNOT-22 scores were averaged 38 initially, to 34 at 1 month and 32 at 6 months resembling the present study.

Friji MT et al [12] used concurrent autologous lipoaspirate transfer and PRP in five patients of PAR. SNOT-20 scores, like present study, were averaged 36 before administration with improvement to 8 at 6 months after autologous lipoaspirate transfer and PRP. So, SNOT-25 questionnaire in follow-up after PRP injections proves beneficial in PAR

In our study, nasal symptoms improved over the follow-up period. Nasal crusting was present in 90% of the cases at 0 month, 80% of the cases at 1 month and 36% of the cases at 6 months (p value < 0.001). Nasal obstruction was present in 84% of the cases at 0 months, 70% of the cases at 1 month and 30% of cases at 6 months (p value < 0.001).

Mostafa et al [4] reported improvement in nasal symptoms. In Group A, the incidence of Nasal crusting was seen in 92.30% of the cases at 0 month, 53.84% at 1 month and 23.07% at 6 months. Nasal obstruction was seen in 76.92% of the cases at 0 month, 53.84% at 1 month and 23.07% at 6 months. In group B only minimal changes were seen.

This shows after PRP injection there was significant improvement in nasal crusting and nasal obstruction. Also, PRP was found beneficial in reduction of fetor, anosmia and epistaxis in subjects.

Ahmed MA (2023) [16] et al published a review article investigating use of PRP in treatment of atrophic rhinitis including multiple articles. Based on their review it was found that PRP contains a very high platelet content, chemotactic factors, cytokines and growth factors that help in tissue healing and regeneration making PRP a good treatment for treating atrophic rhinitis supporting the findings of the present study.

As on date very few studies have been published using PRP in PAR patients. Longer follow up periods and small sample size were drawbacks of the study.

Limitations of the study include repeated blood withdrawals, although none of the patients complained about the procedure.

In our study, during 6 month follow-period no complications or side effects were encountered in subjects related to PRP injection.

Table 4: Comparison of subjects in Distribution of age groups

Distribution of age groups	Total subjects	Percentage
18-20 years	7	14%
21-30 years	12	24%
31-40 years	14	28%
41-50 years	10	20%
51-60 years	5	10%
61-65 years	2	4%

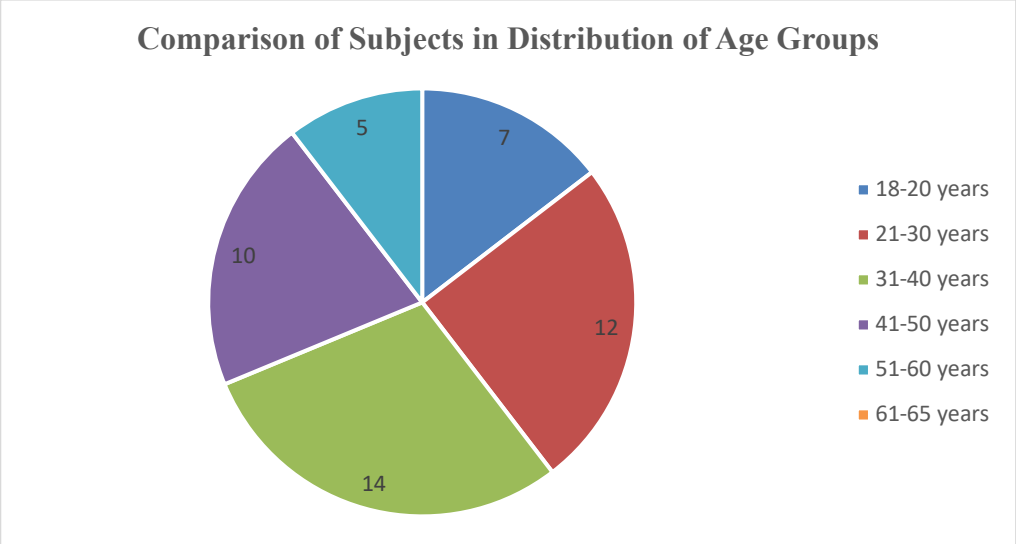

Figure 1: Comparison of subjects in Distribution of age groups

The mean of the age of the study group was 35.98 years. Distribution of age (years) was as follows: 18 to 20 (years)- 7 (14%), 21 to 30 (years)- 12 (24%), 31 to 40 (years)- 14 (28%), 41 to 50 (years)- 10 (20%), 51 to 60 (years)- 5 (10%), 61 to 65 (years)- 2 (4%) as shown in table 4 and figure 1. The median of the age (years) of the study group was 34.5.

Table 5: Gender Distribution in study group

		Subjects	Percentage
Gender	Female	33	34%
	Male	17	66%
	Total	50	100.0

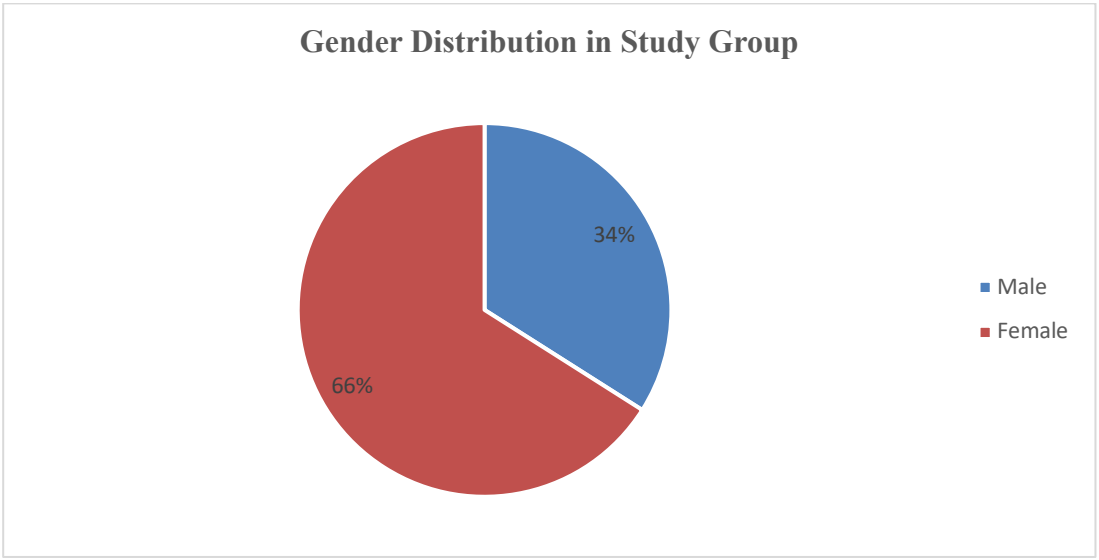

Figure 2: Gender Distribution in study group

Out of 50 subjects in study group, there were 33 female and 17 male subjects as shown in table 5 and figure 2. Female to male ratio of the study group was found to be 1.94:1, findings similar to other studies.

Table 6: Distribution of Males and Females in various age groups

Distribution of age groups	Male Subjects (Percentage)	Female Subjects (Percentage)
18-20 years	2 (4%)	5 (10%)
21-30 years	5 (10%)	2 (4%)
31-40 years	2 (4%)	12 (24%)
41-50 years	4 (8%)	6 (12%)
51-60 years	4 (8%)	1 (2%)
61-65 years	NIL	2 (4%)

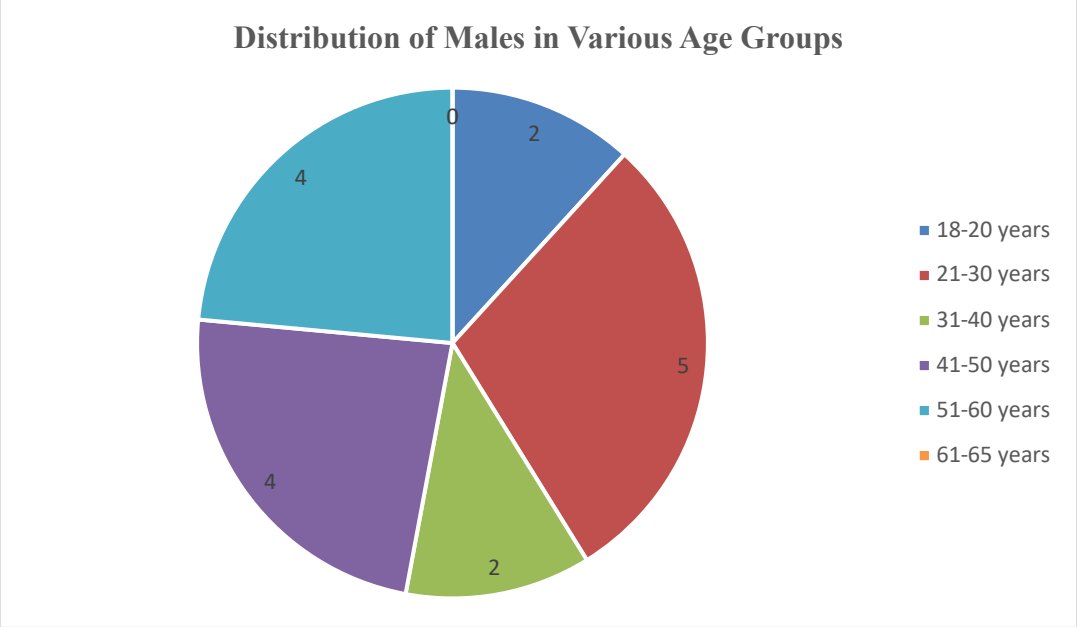

Figure 3: Distribution of Males in various age groups

Total number of males in comparison to females in each distribution age group were as follows: 18 to 20 (years)- 2 (28.57%), 21 to 30 (years)- 5 (41.66%), 31 to 40 (years)- 2 (14.28%), 41 to 50 (years)- 4 (40%), 51 to 60 (years)- 4 (80%), 61 to 65 (years)- NIL as shown in table 6 and figure 3.

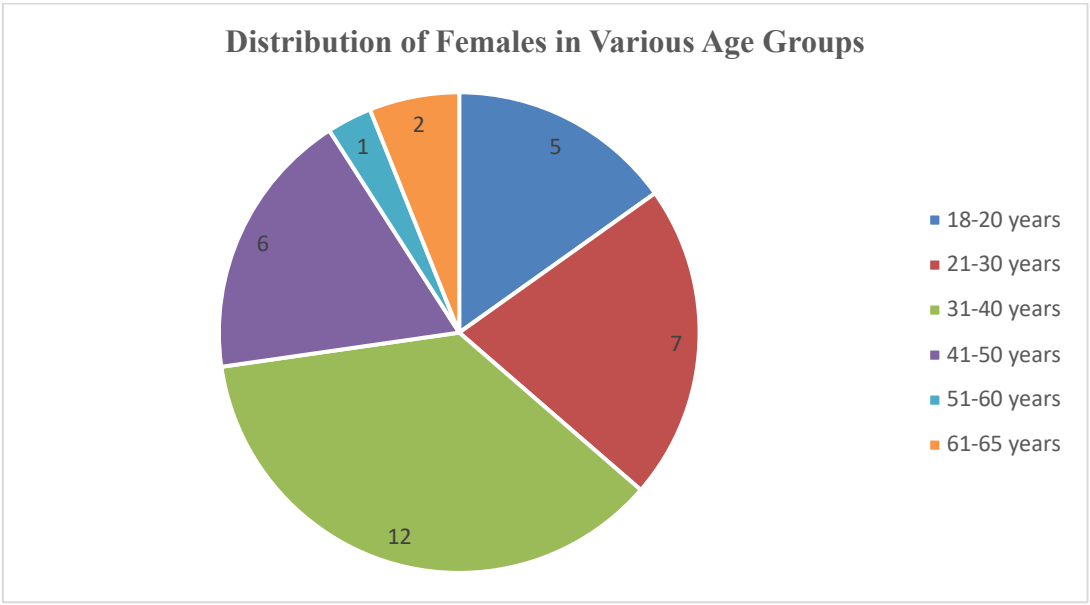

Figure 4: Distribution of Females in various age groups

Total number of females in comparison to males in each distribution age group were as follows: 18 to 20 (years)- 5 (71.42%), 21 to 30 (years)- 7 (58.33%), 31 to 40 (years)- 12 (85.71%), 41 to 50 (years)- 6 (60%), 51 to 60 (years)- 1 (20%), 61 to 65 (years)- 2 (100%) as shown in table 6 and figure 4.

Table 7: Comparison of SNOT-25 score at 0, 1 and 6 months using Paired T- Test.

PAIRS	SNOT-25 score	N	Mean ± SD	Mean difference ± SD	t value	p value
Pair 1	SNOT-25 (0m)	50	44.08±4.12	18.9±7.18	18.61	<0.001
	SNOT-25 (1m)	50	25.18±8.42			
Pair 2	SNOT-25 (0m)	50	44.08±4.12	33.6±6.55	36.29	<0.001
	SNOT-25 (6m)	50	10.48±4.61			
Pair 3	SNOT-25 (1m)	50	25.18±8.42	14.7±8.67	11.99	<0.001
	SNOT-25 (6m)	50	10.48±4.61			

The mean ± SD SNOT-25 score at 0 month was found to be 44.08±4.12 % as shown in table 7 and figure 5. The mean ± SD SNOT-25 score at one month was found to be 25.18±8.42 as shown in table 7 and figure 5. The mean ± SD SNOT-25 score at six months was found to be 10.48±4.61 as shown in table 7 and figure 5.

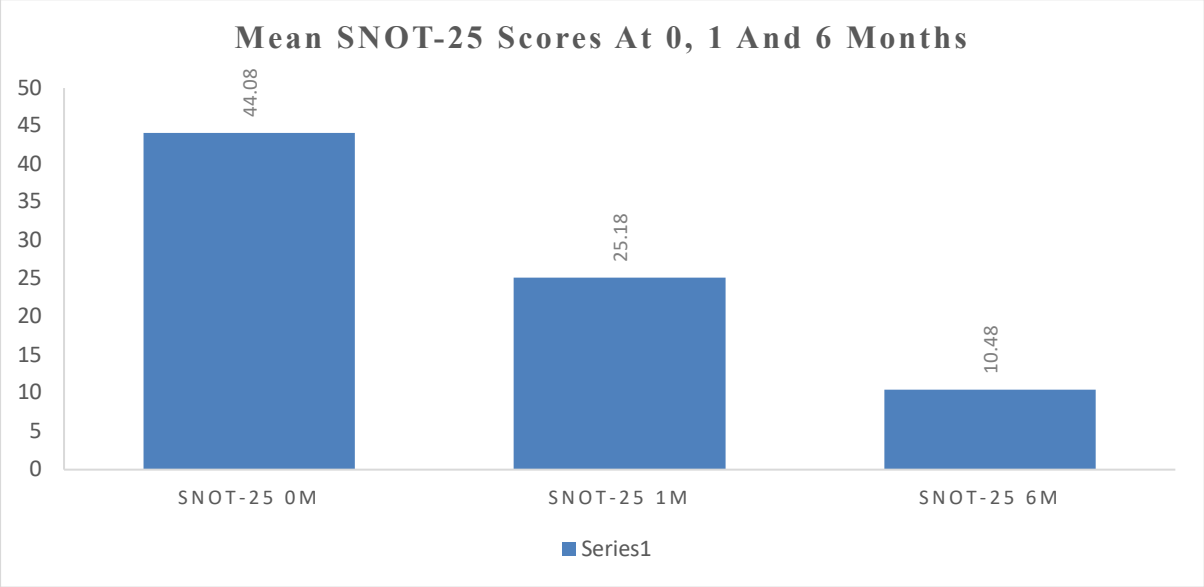

Figure 5: Mean SNOT-25 scores at 0, 1 and 6 months.

Interpretation of the variables using Paired T-Test-

On comparison of the mean ± SD values of SNOT-25 score at 0 month and at 1 month, the mean ± SD values of SNOT-25 at 0 month is higher with a difference of 18.9 which is statistically significant with the p value of < 0.001 as shown in table 7 and figure 5.

On comparison of the mean ± SD values of SNOT-25 score at 0 month and at 6 months, the mean ± SD values of SNOT-25 at 0 month is higher with the difference of 33.6 which is statistically significant with a p value of < 0.001 as shown in table 7 and figure 5.

On comparison of the mean ± SD values of SNOT-25 score at 1 month and at 6 months, the mean ± SD values of SNOT-25 score at 1 month is higher with the difference of 14.7 which is statistically significant with a p value of < 0.001 as shown in table 7 and figure 5.

Table 8: Comparison of improvement of nasal crusting at 0, 1 and 6 months using Mc Nemar chi square Test

		Total	Percentage	p value
NC 0m	Absent	5	10.00%	Reference
	Present	45	90.00%	
NC 1m	Absent	10	20.00%	0.063
	Present	40	80.00%	
NC 6m	Absent	32	64.00%	<0.001
	Present	18	36.00%	

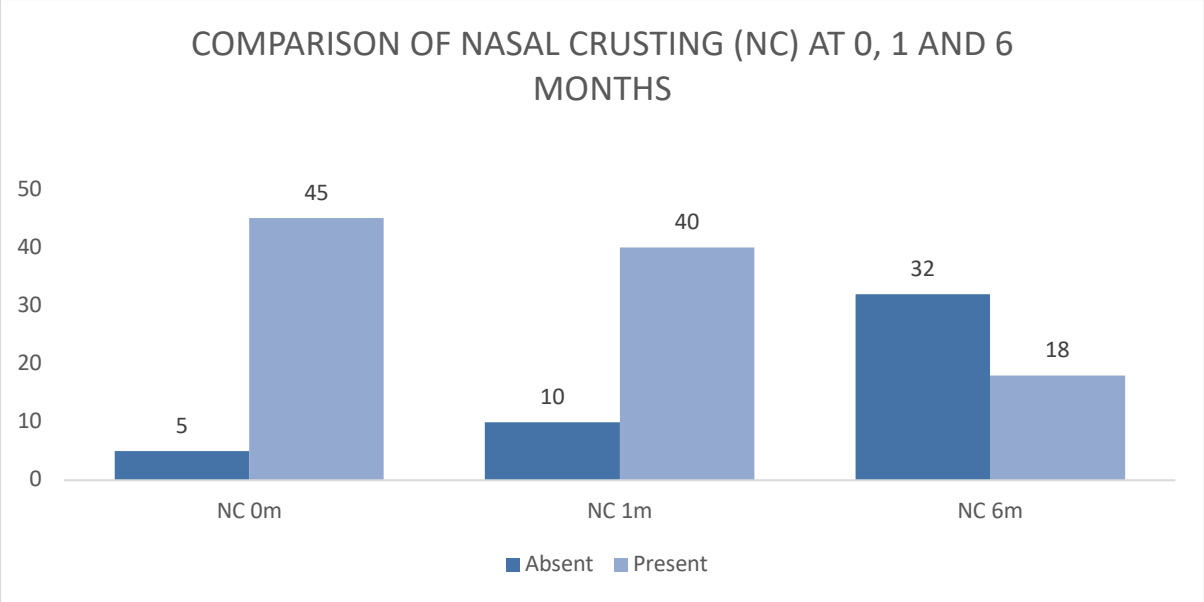

Figure 6: Comparison of improvement of nasal crusting at 0, 1 and 6 months using Mc Nemar chi square Test

Symptoms of the subjects were compared at zero months one month and six months using Mc Nemar Chi Square test. Nasal crusting was present in 90% of the cases at 0 month, 80% of the cases at 1 month and 36% of the cases at 6 months which is statistically significant with a p value < 0.001 as shown in table 8 and figure 6.

Table 9: Comparison of improvement of nasal obstruction at 0, 1 and 6 months using Mc Nemar chi square Test

		Total	Percentage	p value
NO 0m	Absent	8	16.00%	Reference
	Present	42	84.00%	
NO 1m	Absent	15	30.00%	0.016
	Present	35	70.00%	
NO 6m	Absent	35	70.00%	<0.001
	Present	15	30.00%	

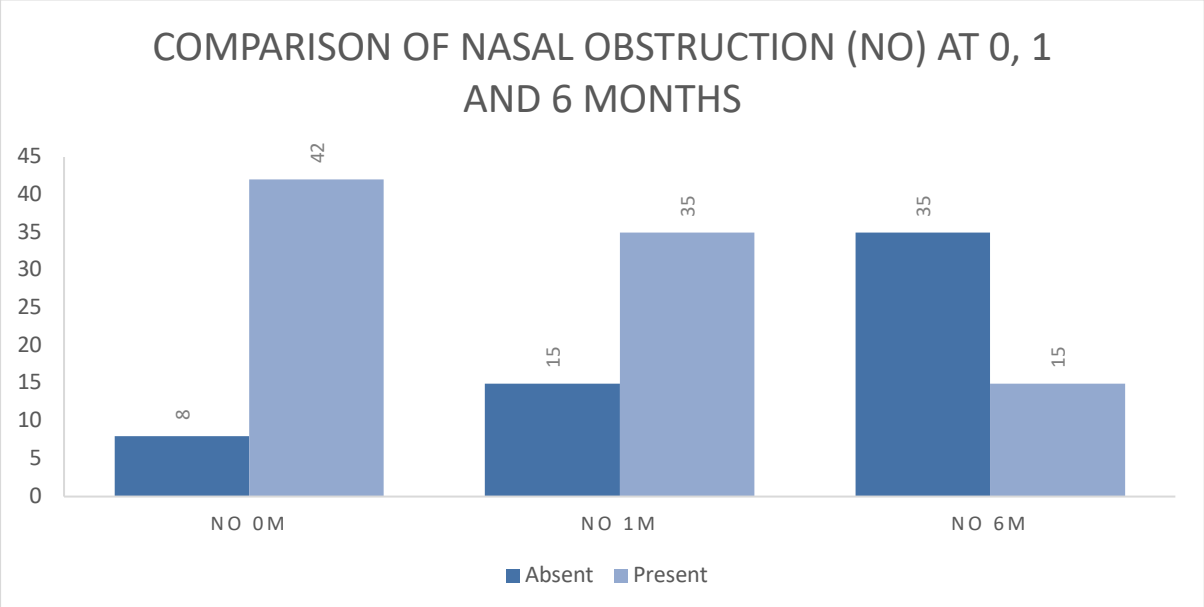

Figure 7: Comparison of improvement of nasal obstruction at 0, 1 and 6 months using Mc Nemar chi square Test

Nasal obstruction was present in 84% of the cases at 0 months, 70% of the cases at 1 month and in 30% of cases at 6 months which is statistically significant with a p value < 0.001 as shown in table 9 and figure 7.

Conclusions

Atrophic rhinitis is a progressive chronic nasal disease characterized by atrophy of nasal mucosa and the underlying bone. Patients generally exhibit distressing symptoms like nasal crusting, nasal obstruction, fetor, anosmia and epistaxis. Various treatment modalities are available- medical and/or surgical with varying results.

In the present study autologous PRP was given in patients of PAR intranasally with good results without any complications. SNOT-25 score and nasal symptoms showed significant improvement after PRP injection in 6 months follow-up period. Symptoms like nasal crusting and nasal obstruction were markedly improved at 6-month follow-up in the patients.

Thus, this treatment regime is a safe, simple and cost effective OPD procedure with no adverse effects or complications and is strongly recommended for the treatment of PAR patients.

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