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Research Article

A comparative study of treatment modalities in female androgenetic alopecia

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ABSTRACT

Background: Androgenetic alopecia (AGA) occurs in both men and women. It is characterized by progressive loss of hair from the scalp in a defined pattern. The aim of the study was to analyse and assess the efficacy of treatment modalities in female androgenetic alopecia (AGA) and assess the side effects, level of stress, associated family history and past history of any medical illness in these patients.
Methods: 60 female patients between 18-50 years of age were randomly divided into 2 groups, with 30 cases in each. The first group (Group A), received only topical 2% minoxidil, applied in the form of a 1 ml solution at an interval of 12 hours and the second group (Group B), received combination of 2% minoxidil and platelet rich plasma (PRP) therapy injections every 15 days for 2 months and then every monthly for 4 months. Patients were evaluated every 2 months for a period of 6 months based on patient and physician assessment of clinical improvement, photographic evidence and type of hair growth. Side effects during the treatment period were observed for.
Results: 70% (n=42) of patients were in the age group 18-30 years. 56.67% (n=34) had alopecia of Ludwig pattern type 2. Hypothyroidism was the major associated medical illness seen in 20% (n=20) of patients. Family history was seen in 46.66% (n=28). 73.33% (n=44) had stress in the range of 5-7 on a visual analogue scale (VAS) of 10. Excellent improvement was observed in 33.33% of patients of Group A (Minoxidil only), and in 60% (n=36) of patients of Group B (Minoxidil + PRP). Pruritis was the most common side effect seen in 13.33% (n=8) patients.
Conclusions: Non-invasive management for AGA is a safe, effective and promising tool for hair growth. It offers better patient compliance, less side effects and only topical anesthesia is required. Multimodality approach in the treatment of hair loss gives excellent response, which is seen in our study as combination therapy (2% minoxidil with PRP) is more effective than topical minoxidil alone.

Keywords: AGA, Minoxidil, PRP, Female, Hair loss

INTRODUCTION

Hair has a great social significance for human beings. In humans, the hair main purpose revolves around its profound role in social interactions. Loss of hair leads to significant psychological and emotional distress. Androgenetic alopecia (AGA) occurs in both men and women. It is characterized by progressive loss of hair from the scalp in a defined pattern.[1] Determining factors appear to be genetic predisposition coupled with the presence of sufficient circulating androgens. The prevalence is high (up to 50% of males are affected by 50 years of age). Although there are no serious health consequences, the loss of scalp hair can be very stressful to the patient.

AGA results from conversion of scalp terminal hair into miniaturised vellus hair in a defined pattern. Investigators

have found 5α-reductase activity and dihydrotestosterone (DHT) level is increased compared to non-balding scalp skin.[2] Testosterone is converted to DHT with the help of the enzyme 5α-reductase. Deficiency of this enzyme has been implicated in the development of AGA.[3]

Women can exhibit the "male" pattern; they also show a Ludwig pattern involving a progressive diffuse loss of hair from the crown while retaining the frontal hair line. Third type of pattern is Olsen Christmas tree pattern seen with central parting.

Minoxidil appears to prolong anagen growth phase by an unknown mechanism, leading to a decrease in hair shedding. Hence, once treatment is stopped, hair shedding rapidly resumes, with the loss of minoxidil stimulated hair growth.[4] Minoxidil, a vasodilator, causes increased expression of vascular endothelial growth factor (VEGF) mRNA in the dermal papillae, activation of cytoprotective prostaglandin synthase-1, an enzyme that stimulates hair growth and increased expression of hepatocyte growth factor (HGF) m-RNA which is another hair growth promoter.

Platelet-rich plasma (PRP) is a highly concentrated autologous solution of plasma prepared from patient's own blood. It contains tissue growth and regeneration factors such as platelet derived growth factor (PDGF), Fibroblast growth factor (FGF), Epidermal growth Factor (EGF), Vascular endothelial growth factor (VEGF), Transforming growth factor beta (TGF-β).[5,6] Activated PRP increases the proliferation of dermal papilla cells and stimulates extracellular signal-regulated kinase (ERK) and Akt signaling. Fibroblast growth factor 7 (FGF-7) and beta-catenin, which are potent stimuli for hair growth, are upregulated in dermal papilla cells.[7] The growth factors present in platelet rich plasma (PRP) induce follicular stem cells to shift from a dormant state to an active state that starts the process of hair production. VEGF-8 and PDGF-4 (platelet derived growth factor-4) found in PRP are known to facilitate angiogenesis around the hair follicle.[8]

METHODS

The study was carried out over a period of two year from November 2013 to October 2015.

Ethical clearance was obtained from Institutional Ethics Committee.

Inclusion criteria

- Female patients with clinically diagnosed Ludwig pattern grade I & grade II androgenetic alopecia.
- Age group 18-50 years.
- Patients who can come regularly for 6 months.

Exclusion Criteria

- Already taking treatment for hair loss from doctor.
- Any active skin lesion at local site such as Psoriasis, Herpes simplex infection, Bacterial infection, Fungal infection
- Bleeding abnormalities/Patient on anticoagulant therapy
- Hepatic, cardiovascular, renal disease, epilepsy or any major medical illness
- Patient with unrealistic expectations
- Patient not willing to give informed written consent

Study design

60 female patients were randomly divided in 2 groups, with 30 in each group.

Table 1: Treatment given to patients of each group.

Group A	2% minoxidil
Group B	2% minoxidil and platelet rich plasma (PRP)

Patients in Group A were only on topical 2% minoxidil therapy and were asked not to apply any other medication to scalp. Patients were instructed to apply minoxidil in form of solution, 1ml at an interval of 12 hours.

Patients in Group B were on combination of 2% minoxidil and PRP injection.

Platelet rich plasma

- Platelet rich plasma was prepared from 10 ml of patient's own blood by double spin centrifugation method. PRP is separated from whole blood by 'light spin' centrifugation. The platelets are then concentrated by 'heavy-spin' centrifugation.
- Calcium chloride was added to activate PRP.
- PRP was injected intra-dermally over the affected scalp using a 1ml insulin syringe at a distance of 1 cm in both horizontal and vertical direction.
- 8 such sittings were carried out at interval of 15 days for 2 months and then every monthly for 4 months. Total duration of treatment was 6 months. 2 % minoxidil solution was continued in every patient. Patient was instructed to stop minoxidil 3 days prior to PRP injection.

Evaluation procedure

Patient's self-assessment

The patients' perception of improvement in the degree of hair fall was evaluated from the baseline on a 3 point scale.

Table 2: Patient's self-assessment of improvement in hair fall.

-1	Worsening
0	No change
+1	Mild improvement
+2	Moderate improvement
+3	Excellent improvement

Physician's assessment

Patient was subjectively evaluated for the degree of hair growth from baseline on a 3 point scale.

Table 3: Physician's assessment of improvement in hair fall.

-1	Worsening
0	No change
+1	Mild improvement
+2	Moderate improvement
+3	Excellent improvement

Global photographic assessment

A standardized global pre-treatment and post-treatment photograph of the anterior and mid areas of the scalp was taken in each case.

Dermatological life quality index (DLQI)[9]

Fourteen patients randomly from each group were selected for assessing dermatological life quality index (DLQI). The DLQI was calculated by summing the scores of all questions. Patients were asked these questions at the baseline and then at the end of the therapy. DLQI was then calculated before and after the therapy.

Patients were evaluated every 2 months for a period of 6 months.

Statistical analysis was carried out using Pearson's Chi-Square test and the one-way analysis of variance (ANOVA).

Patients were examined for local as well as systemic side effects on each visit.

RESULTS

Table 4: Age wise distribution of patients.

Age group	Number
18-30	42
31-45	18
Total	60

70% (n=42) of females were in the age group 18-30 years.

Table 5: Marital status of patients.

Married	Unmarried	Total
40 (66.67%)	20 (33.33%)	60

66.67 % of females seeking advice were married.

Table 6: Employment of the patients.

Employed	Unemployed	Total
44 (73.33%)	16 (26.67%)	60

73.33% of patients were employed.

Table 7: Duration of hair loss.

Duration of hair loss	Number	Percentage %
5m	4	6.66
6m	4	6.66
1 Year	4	6.66
2 Year	8	13.33
3 Year	8	13.33
4 Year	10	16.66
5 Year	6	10
6 Year	6	10
7 Year	4	6.66
10 Year	6	10
15 Year	0	0

70.0% (n=42) of females had duration of hair loss between 2 to 7 years.

Maximum duration of hair loss was of 10 years.

Table 8: Pattern of alopecia.

Pattern of alopecia	Number	Percentage
Ludwig pattern 2	34	56.67%
Ludwig pattern 3	14	23.33%
Olsen christmas tree	12	20.00%

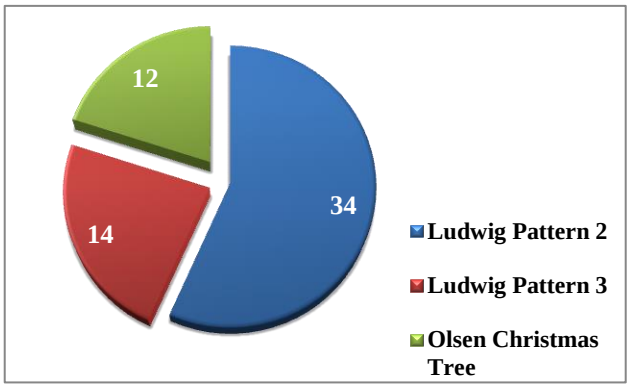

Figure 1: Pattern of alopecia.

Maximum number of patient (n=34) seeking advice were of type 2 Ludwig pattern.

14 patients were of Ludwig pattern type 3, and 12 of Olsen christmas tree pattern.

Table 9: Statistical analysis of grade of alopecia and age of patient.

ANOVA between grade of alopecia and age of female patients	P Value	Statistical significance
	0.393	Data is not statistically significant

Any age of patient can present with any grade of alopecia.

Table 10: Statistical analysis of grade of alopecia and hair loss.

ANOVA applied between grade of alopecia and duration of hair loss	P Value	Statistical Significance
	0.903	NOT

There was no statistical significant difference between different grade of alopecia and the duration of hair loss in females.

Table 11: Treatment history of patient.

Treatment History	Present	Absent
	24	36

Treatments in forms of local oil, ayurvedic treatment, hair spa etc. were undertaken by 40 % of patients.

Table 12: Past history of medical illness in patients.

Disease	Number	Percentage
Typhoid	4	6.66%
Diabetes	2	3.33%
Hypertension	2	3.33%
Hypothyroid	12	20%
Total	20	33.33%

Most common medical illness seen in 20% (n=12) patients was hypothyroidism, followed by typhoid.

On a visual analogue scale of 0-10 with 0 being no stress and 10 being severe stress.

73.33% (n=44) of patients scored within 5 and 7. On further questioning stress was due to marital disturbance, stress of children, work and career.

Table 13: History of stress in patients.

Visual analogue scale	0	1	2	3	4	5	6	7	8	9	10
Number	0	0	0	6	6	24	12	8	2	2	0

Table 14: DLQI in patients.

DLQI	Mean	Standard deviation
Pre treatment	16.71 (55.70%)	1.93
Post treatment	11.92 (39.73%)	2.49

As seen from above table there was 15.97 % decrease in the mean DLQI after treatment.

Table 15: Family history of hair loss.

Family History	Number	Percentage
Positive	28	46.67%
Negative	32	53.33%

Family history was positive in 46.67% (n=28) patients.

Table 16: Anemia and investigations.

	Pallor	↓ Hb	↓ S. Ferritin
Number	22	28	18
Percentage	36.67%	46.66%	30%

On general examination 22 patients showed pallor. Serum hemoglobin (Hb) and serum ferritin levels were estimated in these patients and found to be low in 28 and 18 of the patients respectively. These patients were treated for anemia in coordination with the medicine department.

Table 17: Special investigations.

	↑S. Testosterone	↑ S. DHEAS	↑LH	↑FSH	USG
Number	16	2	8	8	PCOD- 8

Hormonal profile was done in 24 patients who had signs of hyperandrogenism. Of these 24 patients, 16 had raised testosterone level and 8 had raised LH and FSH level. USG was performed in these entire patient and 8 patients were diagnosed as polycystic ovarian disease (PCOD). These patients were referred to obstetrics and gynaecology department for further management.

Excellent improvement was seen in 16.67% (n=10) patient of group B (minoxidil + PRP). Patient's assessment of group B (minoxidil + PRP) showed no improvement in 7 patients, and in group A it was 8 patients. Moderate improvement was more by 1 patient in Group B.

Table 18: Patients' self assessment at 3 months.

Groups	Improvement				Total
	None improvement	Mild improvement	Moderate improvement	Excellent improvement	
Group A –2% minoxidil	8	10	4	8	30
Group B –2% minoxidil + PRP	7	8	5	10	60
Total	15	18	9	18	30

Table 19: Physician's assessment of patients at 3 months.

Groups	Improvement				Total
	None improvement	Mild improvement	Moderate improvement	Excellent improvement	
Group A –2% minoxidil	5	12	5	8	30
Group B –2% minoxidil + PRP	4	7	7	12	30
Total	9	19	12	20	60

Table 20: Patients' self assessment at 6 months.

Groups	Improvement				Total
	None improvement	Mild improvement	Moderate improvement	Excellent improvement	
Group A –2% minoxidil	4	8	8	10	30
Group B –2% minoxidil + PRP	2	2	8	18	30
Total	6	10	16	28	60

Table 21: Physician's assessment of patients at 6 months.

Groups	Improvement				Total
	None improvement	Mild improvement	Moderate improvement	Excellent improvement	
Group A –2% minoxidil	2	8	8	12	30
Group B –2% minoxidil + PRP	0	2	10	18	30
Total	2	10	18	30	60

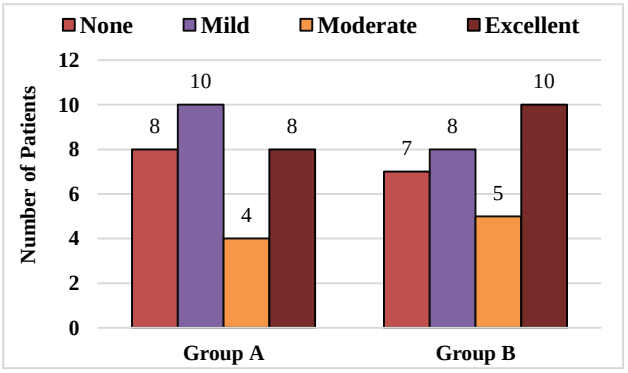

Figure 2: Patients assessment at 3 months.

Excellent improvement was seen in 12 patients in Group B (minoxidil + PRP) on physician's assessment and in 8 patients in group A (minoxidil only) which was comparable with the patient's assessment.

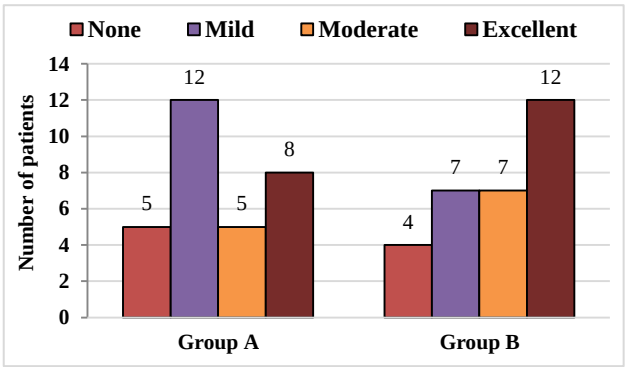

Figure 3: Physician assessment at 3 months.

Excellent improvement was seen in 60.00% (n=18) patients in Group B (minoxidil + PRP), while it was only 33.33% (n=10) patient in Group A (minoxidil only). No improvement was seen in 2 patient of Group B. Moderate improvement was seen in 8 patient of Group B (minoxidil + PRP) and was same as in Group A (minoxidil only).

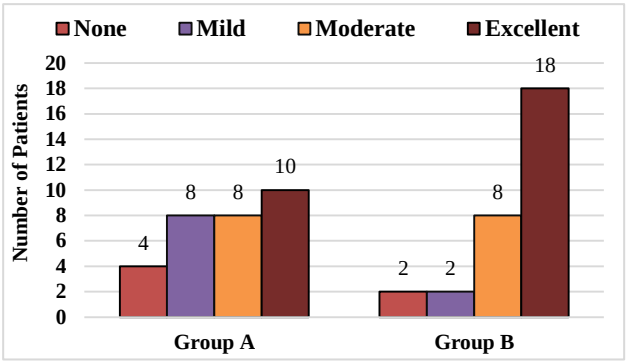

Figure 4: Patients assessment at 6 months.

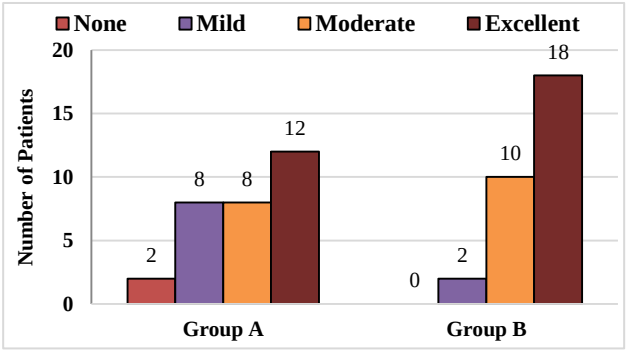

Figure 5: Physician assessment at 6 months.

Excellent improvement was seen in 18 patients in Group B (minoxidil + PRP) on physician's assessment and in 12 patients in Group A (minoxidil only) which was comparable with the patient's assessment.

8 (26.67%) patients in Group A (minoxidil only) showed moderate response at the end of 6 months. 6 more patient in Group B (minoxidil + PRP) showed excellent improvement compared to Group A (minoxidil only).

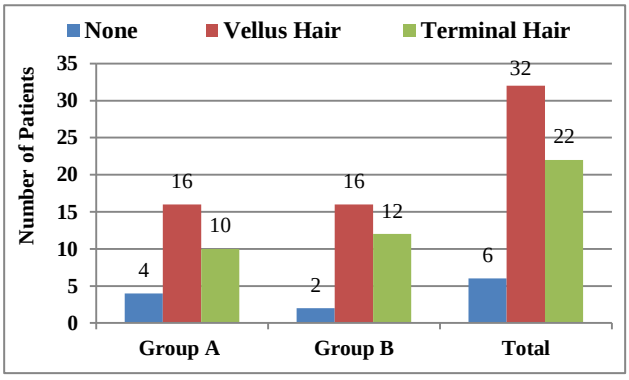

Figure 6: Type of hair growth in patients at 3 months.

Group A patients (Only minoxidil 2%), 4 patients showed no hair growth, 16 patients showed vellus hair growth and 10 patients showed terminal hair growth.

Group B patients (2% minoxidil + PRP), 2 patient showed no hair growth, 16 patients showed vellus hair while 12 patients showed terminal hair growth.

Overall, at the end of 3 months terminal hair growth was seen in 36.67% (n=22) patients and vellus hair growth in 53.33% (n=32) patients.

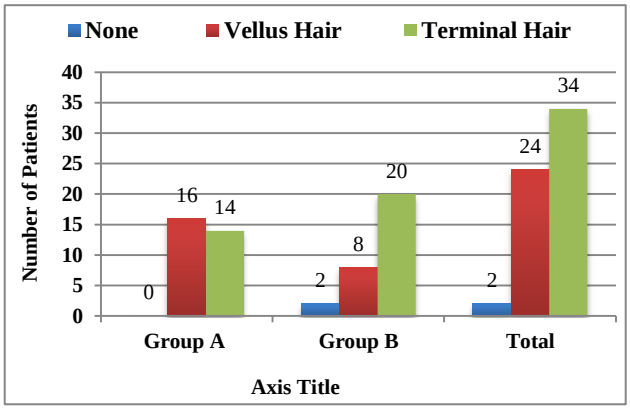

Figure 7: Type of hair growth in patients at 6 months.

Group A patients: Terminal hair growth was seen in 14 (23.33%) patients at the end of 6 months.

Group B patients: Vellus hair growth was seen in 8(13.33%) patients. Terminal hair growth was seen in 33.33% (n=20) patients.

34 patients in total had terminal hair growth along with 24 patients showing vellus hair growth.

Table 22: Side effects.

Side effects	Females	Percentage (%)
Headache	4	6.67
Pruritus	6	10
Seborrheic dermatitis	8	13.33
Irritation	4	6.67
Facial hypertrichosis	4	6.67
Total	26	43.33

43.33% (n=26) patients experienced side effects during the course of the treatment. Most common side effect in our study was seborrheic dermatitis in 8 patients followed by pruritus seen in 6 patients. Facial hypertrichosis was seen in 4 patients.

No other major medical events were observed during study period. Facial hypertrichosis improved in both patients after they were advised to apply minoxidil early in morning and late afternoon.

DISCUSSION

70% of female were in the age group 18-30 years which shows that younger females seek advice for hair loss more often. Ludwig pattern type 2 was the most common type of AGA seen in 56.66% (n=34) female patients. Patients of any age can present with any pattern of alopecia.

Average duration of hair loss seen in our study was between 2 to 7 years, showing AGA is a chronic problem. However, 33.33% (n=20) patients presented with hair loss of 1 year duration.

No statistical significant difference between grade of alopecia and the duration of hair loss was seen. This implies that patients with any grade of alopecia can present with any duration of hair loss.

History of treatment by household remedies was present in 40% (n=24) of the patients. Patients seek professional help not from the beginning of the problem. Hypothyroidism was the major abnormality seen among 20% (n=12) patients. 73.33% (n=44) of patients had stress levels between 5 to 7 on visual analogue scale of 0-10. In the present study there was 15.97 % decrease in the mean DLQI after treatment, indicating that AGA has a negative impact on a patient's quality of life.[10] According to Xiao-sheng, et al physicians need to offer relevant treatment not just for hair loss, but for their emotional distress.[11] Prevention of psychosocial complications such as depression, low self-esteem, an altered self-image and social withdrawal by supportive counselling and assurance is also essential.[12]

Family history for AGA was positive in 46.66% (n=28) patients which was comparable to Xingqi Zhang, et al study.[13] In the present study serum ferritin level was found to be decreased in 20% (n=12) of the patients. According to Zhang X, et al study serum ferritin level lower than required was seen in 25% of female patients.[14] Supplementing the diet with biotin is unlikely to harm a patient, and the importance of iron supplements in iron-deficient women with hair loss has been demonstrated.

An adverse event such as headache was seen in 6.67%, seborrheic dermatitis in 13.33% and pruritus in 10% of the patients. In Tsuboi R et al study headache was seen in 3 %, Pruritus seen in 1 % and Dermatitis seen in 2 % of patients.[15] Facial hypertrichosis was seen in 6.67% of patients. In the present study 20% of patients had signs of hyperandrogenism, of which 8 patients were diagnosed with polycystic ovarian disease. O'Driscoll, JB et al showed that women who present with androgenetic alopecia also often exhibit polycystic ovarian disease and hirsutism even if presenting with alopecia without menstrual abnormalities.[16]

8 (26.67%) patients showed moderate response at the end of 6 months. This was comparable with Richard L, et al study in which 20 % showed moderate response.[17] Patient's own assessment at 6 months showed excellent improvement in 60% (n=18) patients who were on Group B (minoxidil + PRP), while it was only 33.33% (n=10) patients of Group A (Only minoxidil). No improvement was seen in 2 patient of Group B (minoxidil + PRP) and moderate improvement was seen in 8 patients in group B which was same as in Group A (minoxidil only).

Physician assessment at 6 months of age showed excellent improvement in 30% (n=18) of Group B (minoxidil + PRP) and 60% (n=12) patients of group A (minoxidil only).

This shows that combination therapy of minoxidil with PRP is more effective than topical minoxidil alone. Evelyn - Evanthia Betsi, et al study finds that global pictures showed a significant improvement in hair volume and quality, which was confirmed by a high overall patient satisfaction in patients treated with platelet rich plasma for hair loss.[18]

16 patients of Group B (minoxidil + PRP) had vellus hair growth at 3 months which was 3 more than group A (minoxidil only). 20 patients of Group B (minoxidil + PRP) had terminal hair growth, as compared to 14 patients of Group A (minoxidil only).

CONCLUSION

The present study shows that non-invasive management for androgenetic alopecia is an effective and a promising tool for hair growth. It is done on the outpatient basis and has no downtime. Minoxidil and PRP therapy is very safe as no major adverse events were noted. Many factors may contribute to androgenetic alopecia, thus multimodality approach offers the best therapeutic option for hair growth. Hair growth by these non-invasive therapies may also reduce the number of hair follicles to be transplanted during hair transplant surgery.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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