

CLINICAL OUTCOME AND SAFETY PROFILE OF COMBINATION THERAPY WITH LOW DOSE SEMAGLUTIDE AND METFORMIN VS. METFORMIN ALONE IN POLYCYSTIC OVARY SYNDROME WITH OBESITY

MD. RAFAYEL ISLAM¹, HURJAHAN BANU², MD. SHAHED MORSHED³, MA HASANAT⁴

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder where obesity exacerbates metabolic and androgenic features. The combination of low-dose semaglutide and metformin in South Asian women with PCOS and obesity may be an effective and safe treatment modality. The aim of the study was compare the effectiveness and safety of a combined low-dose semaglutide and metformin with metformin alone in women with PCOS and obesity. **Methods:** This Phase II randomized controlled trial was conducted at the Department of Endocrinology in Bangladesh Medical University from 11th January to 16th October, 2025. A total of 31 reproductive-aged Bangladeshi women with PCOS and obesity (BMI ≥ 27.5 kg/m²) were randomly assigned to two groups. The metformin group (n=16) received 1000 mg of daily metformin. The combination group (n=15) received identical metformin dosing plus subcutaneous semaglutide, starting at 0.25 mg weekly for 4 weeks, then increasing to 0.5 mg weekly for 12 weeks. Both groups received similar standardized lifestyle modification. Clinical and metabolic data were obtained at baseline and after 16 weeks, with interim clinical evaluations at weeks 4, 8, and 12. Data analysis employed paired and independent t-tests, Mann-Whitney U test, Chi-square test, and Fisher's Exact test with a significance level established at $p < 0.05$. **Results:** The combination therapy group achieved greater reduction in body weight (mean difference, MD = "4.6%, $p = 0.001$), waist circumference (MD = "5.7%, $p < 0.001$), hip circumference (MD = "3.2%, $p < 0.001$), waist-to-hip ratio (MD = "2.9%, $p = 0.028$) and diastolic blood pressure (MD = "6.8%, $p = 0.023$) compared to the metformin group. Changes in the modified Ferriman–Gallwey score and systolic blood pressure did not differ significantly between groups. Notably, 93.3% of combination-treated participants achieved clinically meaningful weight loss ($\geq 5\%$ from baseline), compared with only 43.8% receiving monotherapy ($p = 0.006$). Adverse events were primarily gastrointestinal, predominantly in the initial treatment weeks, and resolved completely. **Conclusion:** Combining low-dose semaglutide with metformin substantially outperforms metformin monotherapy in managing obesity and associated clinical metabolic derangements in women with PCOS and obesity. The superior weight loss, enhanced mobilization of abdominal fat, reduced diastolic blood pressure, combined with a favorable safety profile, establish this combination as a valuable therapeutic option for PCOS cases with obesity in Bangladesh.

Keywords: Polycystic ovary syndrome (PCOS), Semaglutide, Metformin

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Affiliations:

1. FCPS part 2 trainee, Bangladesh Medical University,, Dhaka, Bangladesh. E-mail: rafayel06@gmail.com
2. Associate Professor, Dept of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh.
3. PhD candidate, Dept of Endocrinology, Bangladesh Medical University,, Dhaka, Bangladesh.
4. Professor, Dept of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh.