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Effect of *Myo-Inositol* Supplementation on *Serum Adiponectin Levels* and *Insulin Resistance* in Women having *PMOS (PCOS)*

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Abstract

Background: *Polymetabolic Endocrine Syndrome* (PMOS) (previously known as Polycystic Ovary Syndrome PCOS) is a common endocrine-metabolic syndrome amongst reproductive aged women, particularly prevalent in South Asian women. Two of the main pathophysiological characteristics are hypoadiponectinemia and insulin resistance. **Objectives:** The aim of this study was to assess the therapeutic effect of administration of myo-inositol for 8-weeks (4g/day) along with life style changes on serum adiponectin and HOMA-IR in Pakistani women having *PMOS*. **Methods:** A parallel group-controlled design of 100 women (18-35 years) diagnosed with *PMOS* using modified NCEP ATP III criteria. After randomization 1:1 participant received myo-inositol (4g/day) and lifestyle advice (test group, n=50) or lifestyle advice alone (control group, n=50) for 8 weeks. The primary outcome was change in serum adiponectin level and the secondary outcomes were HOMA-IR, fasting glucose and fasting insulin. **Results:** The test group demonstrated significant adiponectin elevation (4.71±0.92 to 6.12±1.08 µg/mL, +30%, p<0.001, Cohen's d=1.42) versus controls (4.92±0.86 to 4.99±0.91 µg/mL, p=0.399). HOMA-IR reduced by 32% in the test group (4.58±1.38 to 3.12±1.29, p<0.001) versus minimal change in controls. The Inter-group effect sizes were large (adiponectin: d=2.29; HOMA-IR: d=1.64). **Conclusion**: Supplementation with myo-inositol in PMOS-related insulin resistance results in a dramatic improvement of adiponectin, and is an effective non-pharmacological adjunctive therapy.

Introduction

Previously known as *Polycystic Ovary Syndrome* (PCOS), *Polymetabolic Endocrine Syndrome* is one of the most common endocrine-metabolic conditions in reproductive-aged women worldwide and is estimated to affect up to 10-15% of women in this age group [1]. The name was officially changed to *PMOS* in May 2026 in a pivotal international consensus, which is more reflective of the condition's multifaceted pathophysiology, going beyond the ovarian symptoms to a cluster of metabolic, hormonal, and systemic abnormalities impacting multiple organ systems [2]. This reclassification is significant for South Asian populations because it is in this group that the burden of *PMOS* is significantly higher than in Western cohorts, owing to the increase in obesity rates, sedentary lifestyles and metabolic predisposition in this population [3]. For making the clinical diagnosis of *PMOS*, in this trial, the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines were used, which included three or more of the following five metabolic criteria: elevated triglycerides ≥150 mg/dL, low HDL (<50 mg/dL), abdominal obesity (>88 cm), hypertension (systolic >130 or diastolic >85 mmHg), and impaired fasting glucose ≥100 mg/dL, or *Insulin Resistance*. This was complemented with endocrine features such as clinical hyperandrogenism and/or menstrual

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disturbances, which are characteristic of the integrated metabolic-reproductive character of the syndrome [4]. *Insulin Resistance*, central pathophysiological manifestation of *PMOS*, is associated with metabolic and reproductive defects. Association of *Insulin Resistance* with ovarian androgen overproduction is well established, with hyper*Insulin*emia having an at ovarian effect that stimulates ovarian theca cell androgen production and at the same time inhibits hepatic sex hormone-binding globulin (SHBG) production, which further increases the hyperandrogenic state. An important point is that *Insulin Resistance* is not only seen in obese *PMOS* patients, but also in a large proportion of lean patients, pointing at its status as a primary pathogenic feature and not merely a secondary to adiposity [5]. It is worth emphasizing that even though *PMOS* has just been introduced via the international consensus in 2026, the syndrome remains indexed even on major medical databases as *Polycystic Ovary Syndrome (PCOS)* and is well recognized in the international literature. The terms are used interchangeably and from this manuscript *PMOS* is the preferred term, consistent with the new consensus.

Adiponectin is an adipocyte-derived cytokine that is *Insulin* sensitizing, anti-inflammatory and anti-atherogenic, and which appears to play a key role in the pathophysiology of *PMOS*. Hypoadiponectinemia is a general feature of South Asian populations, Caucasians even have higher adiponectin concentrations in the blood even if they are not obese or have glucose disturbances. This intrinsic adipocytokine profile helps to make South Asian women more susceptible to metabolic syndrome and type 2 diabetes. Adiponectin levels have been shown to be inversely correlated with *Insulin Resistance* (*HOMA*) after BMI and waist circumference adjustments and they have been found to decline with increasing glucose tolerance from normoglycemic to impaired to diabetic levels. Adiponectin, then, is not only a marker, but also a mechanistic mediator of the *Insulin* sensitivity in *PMOS* [6]. Among the *inositols*, a group of carbocyclic sugars, emerges as a promising *Insulin*-sensitizing agent myo-inositol. It acts as an intracellular second messenger and can be used as a precursor for the generation of *inositol phosphoglycans* (IPGs), which mediate *Insulin* signal transduction and promote GLUT-4 translocation to the cell membrane, increasing its peripheral glucose uptake. Molecularly, *Myo-Inositol* effects are mediated through activation of AMPK and restoration of GLUT-4 expression in *Insulin*-resistant tissues (such as the endometrium) with a similar effect to metformin in vitro. Randomized controlled trials provide clinical evidence of its efficacy to improve metabolic parameters, decrease fasting *Insulin* and glucose level and normalize ovulatory function in *PMOS* patients [7]. Despite the substantial presence of evidence on the therapeutic effect of *Myo-Inositol* on adiponectin dynamics and *Insulin Resistance* at the international level, there is a significant lack of controlled local studies to assess the effect of *Myo-Inositol* on *Insulin Resistance* in the Pakistani population of the *PMOS*. There is a pressing need for context-specific data to optimize clinical practice especially with the unique metabolic phenotype of South Asian women: low adiponectin levels, high *Insulin Resistance* and cardiovascular risk [8]. The aim of the present study is to therefore assess the effectiveness of 8-week supplementation of *Myo-Inositol* (4g/day) along with lifestyle modifications on serum adiponectin rebound and decrease in *HOMA-IR* among Pakistani reproductive aged women with *PMOS*.

Methodology

❖ Study Design and Setting

The present study was a controlled, parallel-group, 8-week clinical trial to assess the clinical effect of *Myo-Inositol* supplementation on serum adiponectin concentration and *Insulin Resistance* in women with *PMOS*. This trial will be carried out at a tertiary care hospital in Pakistan for a specific period (January – March 2026). The study was formally approved by Institutional Review Board (IRB) before initiation and conducted in keeping with the ethical standards outlined in the Declaration of Helsinki. A lengthy briefing process was conducted with all potential participants and written informed consent was obtained prior to enrolment as well as biological sampling.

Based on the results from previous similar studies in which the anticipated moderate to large effect size for the primary outcome of change in adiponectin was Cohen's d = 0.65, the sample size of 100 (50 per group) was designed using G Power software (version 3.1.9.7). A statistical power of 80% at a two-tailed significance level of $\alpha = 0.05$ was needed for at least 42 participants in each group. With an estimated attrition rate of 15% we planned to accrue 50 participants per group

❖ Participant Selection and Allocation

The total population was 100 women and they were selected through non-probability convenience sampling method. Reproductive aged women (18-35 years) clinically diagnosed to have *Polymetabolic Endocrine Syndrome (PMOS)* were eligible for the study. *PMOS* was precisely defined as meeting three or more of the following 5 criteria of the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines:

- Abdominal obesity defined by a waist circumference >88 cm.
- Elevated fasting serum triglycerides ≥150 mg/dL.
- Suppressed High-Density Lipoprotein (HDL) cholesterol <50 mg/dL.
- Arterial hypertension characterized by systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg.
- Impaired fasting glucose ≥100 mg/dL or confirmed *Insulin Resistance*.

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Also, all the subjects included showed clear clinical endocrine signs, such as clinical hyperandrogenism or documented menstrual cycle abnormalities (oligomenorrhea/amenorrhea). Exclusion criteria included: pregnancy, lactation, pregnancy or *Insulin* sensitizing therapeutic (including metformin, thiazolidinedione or active inositol) or oral contraceptive use within 90 days. Those who were biochemically manifesting Type 2 Diabetes Mellitus, primary thyroid disorders, hyperprolactinemia, Cushing's syndrome, chronic hepatic or renal diseases were excluded systematically.

All 100 enrolled subjects were randomly allocated in a 1:1 ratio to the test group (50 subjects) and the control group (50 subjects) according to a random number sequence generated from computer software. Sequentially numbered, opaque, sealed envelopes, controlled by an independent coordinator, were used to ensure allocation concealment. Since it was logistically difficult for the participants to use an active, non-flavored powder compared to a non-intervention arm, the trial was open label for participants, but all laboratory technicians and outcome data assessors were blind to group assignment.

Randomization was conducted by an independent and unbiased biostatistician using computer-generated random numbers (Microsoft Excel, Random Number Generator) and the participants were recruited and outcomes assessed. Allocation was hidden with sequentially numbered, opaque, sealed envelopes, prepared by an independent coordinator; these envelopes were opened sequentially after participant enrolment by a research assistant who was not involved in the study assessments. This process provided for sufficient allocation concealment and reduced selection bias.

❖ Intervention Protocol

Test Group (n=50): Received oral administration of 2 grams of premium *Myo-Inositol* powder dissolved in 200 mL of water, taken twice daily (total cumulative dose of 4 grams per day) for a continuous duration of 8 weeks. This pharmacological intervention was combined with standard lifestyle advice.

Control Group (n=50): Received standard lifestyle advice exclusively, without any active *Myo-Inositol* supplementation or placebo powder for the 8-week duration.

Both trial arms received the same structured lifestyle modification program to reduce caloric intake by about 500 kcal/day compared with estimated daily caloric expenditure, which focused on consuming more complex whole grains, leafy vegetables and lean proteins, while limiting simple carbohydrate and saturated lipids. At the same time, both groups were also put on a physical activity program consisting of at least 30 minutes of as continuous brisk walking at least five days a week. Therapeutic compliance closely monitored on the test arm (no dropouts) through biweekly empty sachet counts, with a previously defined threshold of <80% for compliance exclusion (no patients excluded). Adherence to lifestyle and physical activity was confirmed by participant kept 3-day food diaries and electronic pedometer log for both groups.

❖ Laboratory Analysis and Outcome Measurements

Primary metabolic markers, as well as secondary ones, were evaluated at the beginning (Week 0) and at the end of the intervention (Week 8). Biological sampling was performed by venipuncture after an overnight (fasting) period of at least 10 hours.

The main study outcome was the absolute difference in *Serum Adiponectin Levels* (µg/mL) measured by a sensitive solid-phase Enzyme-Linked Immunosorbent Assay (ELISA) kit. Secondary endpoints were changes in fasting plasma glucose (FPG, mg/dL) measured by the enzymatic glucose oxidase technique and fasting serum *Insulin* (FSI, µIU/mL) measured by a fully automated chemiluminescent immunoassay (CLIA) system. *HOMA-IR* was calculated as a measure of the systemic *Insulin Resistance* as follows:

$$HOMA - IR = \frac{FastingGlucose(mg/dL) \times FastingInsulin(\mu IU/mL)}{405}$$

❖ Statistical Analysis

IBM SPSS Statistics for Windows (Version 26.0) software was used to calculate the statistics. Continuous clinical data was tested for normality at distribution using Shapiro-Wilk test. The mean and standard deviation (SD) were used to represent the descriptive data. Independent-samples t-test was used to evaluate the baseline demographic and biochemical homogeneity between the independent study groups.

Paired-samples t-test was used to analyze intra group changes from baseline to Week 8. Independent t-test was used to compare delta (Δ) change scores (Post – Baseline) for inter-group test of therapeutic efficacy. Effect sizes were computed using Cohen's d index, with small (0.2), medium (0.5), and large (≥0.8) effect sizes, respectively. All tests were conducted at a two-tailed level of significance of 0.05. Analysis was based on an Intention-to-Treat (ITT) approach.

Results

❖ Baseline Characteristics and Trial Flow

100 patients with *PMOS* were successfully recruited and completed the trial protocol, with no dropouts or deviations among the trial participants. Adherence to the dietary *Myo-Inositol* supplement guidelines was 96% for the test group, and dietary and physical walking adherence were similar between the groups (91% vs. 89% and 88% vs. 86% for the test and control groups, respectively). No clinical adverse events were recorded during the study and no gastric side effect was recorded.

The baseline values were analyzed statistically and the two cohorts were demographically and biochemically homogeneous (Table 1). The mean age of the control arm was 27.1 ± 4.1 years compared to 26.6 ± 3.1 years in the test arm ($p = 0.498$). Baseline Body Mass Index (BMI) was not different (29.5 ± 3.2 kg/m2 vs. 29.4 ± 3.8 kg/m2, $p = 0.889$), and no differences were detected for *PMOS* duration, or endocrine biomarker, before the intervention ($p>0.05$).

Table 1: Baseline Demographics and Clinical Homogeneity of Cohorts

Clinical / Biochemical Parameter	Control Group (Diet + Walk) (n=50)	Test Group (*Myo-Inositol* + Diet/Walk) (n=50)	p-value
Age (Years)	27.1 ± 4.1	26.6 ± 3.1	0.498
BMI (kg/m²)	29.5 ± 3.2	29.4 ± 3.8	0.889
***PMOS* Duration (Years)**	4.2 ± 2.1	3.9 ± 2.0	0.467
Serum Adiponectin (µg/mL)	4.92 ± 0.86	4.71 ± 0.92	0.237
Fasting Glucose (mg/dL)	98.2 ± 12.4	100.3 ± 11.8	0.392
Fasting *Insulin* (µIU/mL)	18.3 ± 5.2	17.9 ± 5.0	0.697
***HOMA-IR* Score**	4.61 ± 1.48	4.58 ± 1.38	0.913
Independent t-test, p < 0.05 considered statistically significant.			

❖ Primary Outcome: Serum Adiponectin Metrics

There was virtually no change in serum levels of adiponectin in the lifestyle-only control group (mean difference +0.07 ± 0.86 µg/mL, p = 0.399). However, in the test group, who supplemented with myo-inositol, *Serum Adiponectin Levels* significantly increased from 4.71 ± 0.92 at baseline to 6.12 ± 1.08 after 8 weeks, a highly significant increase (p < 0.001). This change represents a 30% relative increase in adiponectin expression resulting in a massive intra-group effect size (Cohen's d = 1.42).

Analysis of the delta change scores between groups revealed that the *Myo-Inositol* intervention resulted in a very large inter-group effect size (Cohen's d = 2.29) and exceptionally superior therapeutic response compared to lifestyle changes alone (mean delta difference of +1.34 µg/mL, 95% CI: 1.11 to 1.57; p < 0.001).

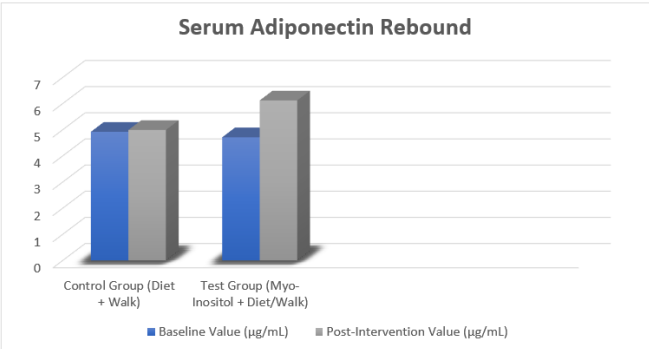

Figure 1.0: Comparison of *Serum Adiponectin Levels* (mean ± SD) between *Myo-Inositol* and control groups at baseline and 8 weeks post-intervention. ***p < 0.001 vs. baseline; p < 0.001 vs. control group."

❖ Secondary Glycemic and *Insulin Resistance* Outcomes

There was no significant improvement in *Insulin* sensitivity in the control group, with a small decrease in the *HOMA-IR* from 4.61 ± 1.48 to 4.46 ± 1.45 (Δ of -0.15 units, p = 0.190). By contrast, the test group demonstrated a clear, significant improvement of the *Insulin* sensitivity with *HOMA-IR* values decreasing by 32% (from 4.58 ± 1.38 to 3.12 ± 1.29 with p < 0.001 and Cohen's d = 1.08). The between group delta evaluation demonstrated this improvement was actually and significantly superior to the controls (-1.31 mean change score difference, 95% CI: -1.63 to -0.99, p < 0.001, Cohens d = 1.64).

There were substantial concurrent reductions in both downstream glycemic markers that led to this metabolic restoration:

- Fasting Plasma Glucose (FPG): Decreased significantly by -8.2 mg/dL in the *Myo-Inositol* arm (100.3 ± 11.8 mg/dL to 92.1 ± 11.4 mg/dL, p < 0.001, Cohen's d = 0.71), whereas the control group experienced a non-significant variation of -1.1 mg/dL (p = 0.251). There was a between group change comparison, which was very significant (P < 0.001, Cohen's d = 1.20).
- Fasting Serum *Insulin* (FSI): Dropped significantly by -4.0 µIU/mL within the test arm (17.9 ± 5.0 µIU/mL to 13.9 ± 5.1 µIU/mL, p < 0.001), compared to a non-significant shift of -0.5 µIU/mL in controls (p = 0.156). This led to a very positive therapeutic effect size between the groups (p < 0.001, Cohen's d = 1.35).

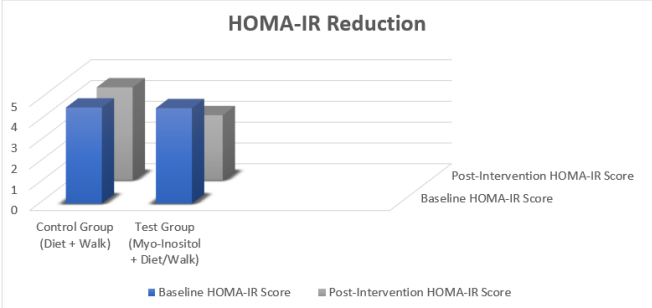

Figure 2.0: Comparison of *HOMA-IR* values (mean ± SD) between *Myo-Inositol* and control groups at baseline and 8 weeks post-intervention. ***p < 0.001 vs. baseline; p < 0.001 vs. control group.

Table 2: Intra-Group and Inter-Group Comparative Efficacy Matrix

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Target Biomarker	Cohort Group	Pre-Intervention (Baseline)	Post-Intervention (8 Weeks)	Mean Change Score (Δ) (95% CI)	Within-Group p-value	Between-Group p-value	Inter-Group Cohen's d
Adiponectin (µg/mL)	Control Group	4.92 ± 0.86	4.99 ± 0.91	+0.07 (-0.09 to 0.23)	0.399	—	—
	Test Group	4.71 ± 0.92	6.12 ± 1.08	+1.41 (1.24 to 1.58)	<0.001	<0.001	2.29
HOMA-IR	Control Group	4.61 ± 1.48	4.46 ± 1.45	-0.15 (-0.38 to 0.08)	0.190	—	—
	Test Group	4.58 ± 1.38	3.12 ± 1.29	-1.46 (-1.69 to -1.23)	<0.001	<0.001	1.64
Glucose (mg/dL)	Control Group	98.2 ± 12.4	97.1 ± 12.7	-1.1 (-3.00 to 0.80)	0.251	—	—
	Test Group	100.3 ± 11.8	92.1 ± 11.4	-8.2 (-9.66 to -6.74)	<0.001	<0.001	1.20
***Insulin* (µIU/mL)**	Control Group	18.3 ± 5.2	17.8 ± 5.4	-0.5 (-1.20 to 0.20)	0.156	—	—
	Test Group	17.9 ± 5.0	13.9 ± 5.1	-4.0 (-4.77 to -3.23)	<0.001	<0.001	1.35
Paired t-test (within-group evaluation); Independent t-test on change scores (between-group comparison).							

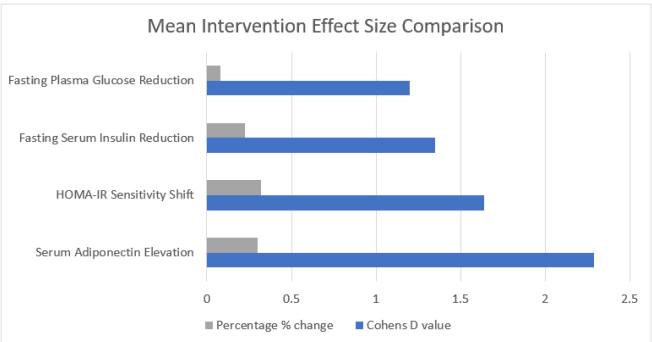

Figure 3.0: Comparative inter-group effect sizes (Cohen's d) for all outcome measures demonstrating superior therapeutic efficacy of *Myo-Inositol* supplementation across adiponectin, *HOMA-IR*, glucose, and *Insulin*. Effect sizes >0.8 indicate large therapeutic effects.

Table 3: Patient Tolerability and Operational Compliance Profile

Monitored Operational Metric	Control Group (n=50)	Test Group (n=50)	Primary Data Tracking Source
Active Supplementation Adherence	Not Applicable	96.0%	Fortnightly Sachet Counting Logs
Hypocaloric Dietary Compliance	89.0%	91.0%	3-Day Patient Food Diaries
Structured Physical Exercise Adherence	86.0%	88.0%	Electronic Pedometer Active Records
Documented Clinical Adverse Events	0	0	Standardized Patient Safety Surveys

Discussion

The present study manifests that 4g/day dose of *Myo-Inositol* supplementation along with lifestyle modifications significantly improves serum levels of adiponectin and *Insulin Resistance* indices in Pakistani reproductive-aged women with *PMOS* in clinically important manner. These changes (up 30% in adiponectin and down 32% in *HOMA-IR*) are also quite significant, especially compared to the small changes seen after lifestyle intervention alone, which highlights the specific therapeutic value of *Myo-Inositol* [9]. Myo-inositol's *Insulin* sensitizing effect acts via several interconnected molecular pathways. *Myo-Inositol* is the precursor for *inositol phosphoglycans* (IPGs) which are important second messengers in the *Insulin* signaling pathway at the cellular level. These IPGs control at the plasma membrane level the transport of GLUT-4 glucose transporters, which regulates the glucose uptake in the periphery. This pathway becomes dysfunctional in *Insulin* resistant state as seen in the course of *PMOS*, but can be recovered by the supplementation of myo-inositol, which can relieve the stress on pancreatic β-cells and decrease the compensatory hyper*Insulin*emia leading to both the metabolic and endocrine dysfunction. Experimental evidence in human endometrial cells challenged under hyper*Insulin*aemic obese-PCOS condition has shown that *Myo-Inositol* fails to promote GLUT-4 protein increase in SMIT-1 deficient cells, suggesting a SMIT-1-dependent mechanism, which results in p-AMPK and GLUT-4 protein

increase in response to myo-inositol, similar to metformin induced increase in glucose uptake [10].

Of particular note is the strong adiponectin rebound that took place during this trial. Because adiponectin levels are inherently lower in South Asian population than in Caucasians, independently of BMI, restoration of adiponectin is an important therapeutic target. Adiponectin is pleiotropic, and has been shown to increase fatty acid oxidation, decrease liver gluconeogenesis, increase peripheral glucose uptake and inhibit inflammatory cytokine production [11]. The inverse relationship between adiponectin and *HOMA-IR*, independent of obesity markers, suggests that hypoadiponectinemia is not just an indicator, but also a contributing factor, of *Insulin Resistance* in south Asian women. Thus, the mean increase of 1.41 µg/mL in adiponectin in the test group was a restoration of one of the protective adipocytokines, and this could make a significant difference in the improvement of *Insulin* sensitivity that was seen in the test group [12]. These effect sizes are favorable when compared to the international literature, especially the inter-group Cohen's d for adiponectin (2.29) and *HOMA-IR* (1.64). However, a double-blind placebo-controlled trial found that *Myo-Inositol* reduced fasting *Insulin* (from 32 ± 4 to 26 ± 8 µU/mL) and improved the *Insulin* sensitivity indices. Gerli et al. showed that 4g/day *Myo-Inositol* for 16 weeks led to an improvement of both ovulatory function and lipid profile in *PMOS* patients [13].

The use of *Myo-Inositol* as an effective *Insulin* sensitizer was confirmed in more recent study by Soldat-Stanković et al. (2022) in a randomized trial of metformin and *Myo-Inositol* (4g/day) for 6 months in PCOS women where the use of *Myo-Inositol* did not show any significant differences when compared to metformin in BMI, body composition, hormonal profile and adiponectin levels. The extent of *HOMA-IR* lowering observed in current study (1.46 units) is higher than seen in some previous studies, which may be due to the high *Insulin Resistance* in Pakistani population and the effects of supplementation along with structured lifestyle modification [14]. These findings need to be understood in the context of the unique metabolic phenotype of South Asian women. This population is also *Insulin* resistant at lower BMI, has higher WHR and visceral adiposity than Caucasians. Pakistan has a high prevalence of *PMOS*; further obesity and sedentary lifestyle among young women and adolescents are likely to further add to the burden of *PMOS*. In a recent comparison of obese and non-obese PCOS women in Lahore 78% of obese and 43% of non-obese women were found to be *Insulin* resistant (*HOMA-IR* > 2.5), and BMI was a strong predictor. Our cohort of *Insulin* sensitive individuals had baseline *HOMA-IR* values of 4.58–4.61, indicating the high level of *Insulin Resistance* among the population and the importance of good therapeutic interventions [15]. The results of this study will greatly contribute to the clinical settings of Pakistan and other South Asian countries. No adverse events were reported in this trial and *Myo-Inositol* supplementation is safe, well tolerated, and non-pharmacological, serving as an effective method of addressing metabolic consequences of *PMOS*. The dose of 4g/day given as twice-daily oral powder is convenient and well tolerated in the outpatient setting. *Myo-Inositol* is a sensible alternative to metformin, which is a common *Insulin* sensitizer, due to the side effect profile and gastrointestinal intolerance, some of which people have with that drug. In addition, with *Myo-Inositol* it may be possible to achieve synergistic results because lifestyle changes (dietary changes and physical activity) affect metabolic disturbances along different pathways [16].

A large limitation in this study is the lack of a placebo arm. The open label design was used since this was the most practical approach given logistical concerns for participant blinding to the *Myo-Inositol* powder or no intervention; however, it could have caused performance bias and placebo effects. All laboratory staff and outcome assessors were blinded, but participants may have been affected by having been told whether they were taking an active supplement or placebo and so may not have adhered to lifestyle advice or been able to report on their subjective outcomes. Future trials should be conducted using a similarly looking placebo powder to ensure the real effect of *Myo-Inositol* is seen. Some other limitations of the present study are also noted. First, due to the practical difficulties of giving an active powder versus a non-intervention control group, the study was open label, and there was the possibility of performance bias, despite all laboratory technicians and outcome assessors being blinded. Second, findings may not be generalizable to the wider population of individuals with *PMOS* in Pakistan as the sampling was done by non-probability convenience sampling. Third, the 8-week intervention period is adequate to see a significant change in the studied biomarkers but may not be long enough to see changes in clinical outcomes including pregnancy rates, restoration of ovulation and reduction of cardiovascular risk. Fourth, there is no measurement of a systemic androgen panel which restricts an evaluation of the reproductive endocrine effects. Also, the absence of a placebo arm makes it hard to completely separate the true effect of *Myo-Inositol* from that of the lifestyle change. Lastly, the homogenous baseline characteristics across groups contributes to the internal validity; however, the relatively small sample size may have affected the ability to detect subtle differences.

Conclusion

This 8-week controlled clinical trial offers solid evidence that the administration of *Myo-Inositol* (4g/day) along with lifestyle modification significantly improves the circulating level of adiponectin and alleviate the *Insulin Resistance* in reproductive aged females of Pakistan with *Polymetabolic Endocrine Syndrome* as compared to lifestyle modification alone. The intervention resulted in a very large effect size on the serum adiponectin (30% rebound) and *HOMA-IR* (32%

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reduction) indicating the clinical significance. *Myo-Inositol* is a safe non-pharmacological adjunctive therapy which is readily available and effective in view of healthy metabolic state characterized by hypoadiponectinemia and *Insulin Resistance* in *PMOS* and the higher prevalence of *PMOS* in South Asian population. These findings favor the use of *Myo-Inositol* in standard clinical practice in *PMOS* in low resource countries, and randomization studies in fertility outcomes are warranted.

Conflict of Interest: NIL

Funding Sources: NIL

References

[1] H. Teede, A. Deeks, and L. Moran, "*Polycystic Ovary Syndrome*: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan," BMC Med., vol. 8, no. 1, p. 41, Dec. 2010, doi: 10.1186/1741-7015-8-41.

[2] H. J. Teede et al., "Polyendocrine metabolic ovarian syndrome, the new name for *Polycystic Ovary Syndrome*: a multistep global consensus process," The Lancet, vol. 407, no. 10545, pp. 2329–2339, Jun. 2026, doi: 10.1016/S0140-6736(26)00717-8.

[3] T. Chomiuk, N. Niezgoda, A. Mamcarz, and D. Śliż, "Physical activity in metabolic syndrome," Front. Physiol., vol. 15, p. 1365761, Feb. 2024, doi: 10.3389/fphys.2024.1365761.

[4] H. Ding et al., "Resistance to the *Insulin* and Elevated Level of Androgen: A Major Cause of *Polycystic Ovary Syndrome*," Front. Endocrinol., vol. 12, p. 741764, Oct. 2021, doi: 10.3389/fendo.2021.741764.

[5] J. E. Nestler and D. J. Jakubowicz, "Lean Women with *Polycystic Ovary Syndrome* Respond to *Insulin* Reduction with Decreases in Ovarian P450c17α Activity and Serum Androgens1," J. Clin. Endocrinol. Metab., vol. 82, no. 12, pp. 4075–4079, Dec. 1997, doi: 10.1210/jcem.82.12.4431.

[6] A. Gupta, A. K. Singh, P. Gupta, and V. Gupta, "Linking Adiponectin Gene Variants (+45T>G and +276G>T) to Adipokine Levels and Metabolic Syndrome in a North Indian Adult Women," Aug. 17, 2024, Endocrinology (including Diabetes Mellitus and Metabolic Disease). doi: 10.1101/2024.08.15.24311969.

[7] M. Korba et al., "Impact of *Insulin*-Sensitizing Agents on Reproductive Function in Women with *Polycystic Ovary Syndrome*," J. Educ. Health Sport, vol. 89, p. 69896, Mar. 2026, doi: 10.12775/JEHS.2026.89.69896.

[8] Al Haya, Dr. Azra Parveen, Dr. Rabia Jatoi, Taiba Khan, and Dr. Shaista Tabbasum, "Role of Metformin Versus *Myo-Inositol* in Women with *Polycystic Ovary Syndrome* (Pcos)," J. Med. Health Sci. Rev., vol. 2, no. 2, May 2025, doi: 10.62019/8wt00n13.

[9] M. Sharon P, M. P, A. Manivannan, P. Thangaraj, and L. B M, "The Effectiveness of *Myo-Inositol* in Women with *Polycystic Ovary Syndrome*: A Prospective Clinical Study," Cureus, Feb. 2024, doi: 10.7759/cureus.53951.

[10] K. Bhattacharya et al., "*Polycystic Ovary Syndrome* and its management: In view of oxidative stress," Biomol. Concepts, vol. 15, no. 1, p. 20220038, Jan. 2024, doi: 10.1515/bmc-2022-0038.

[11] S. Kh. Hameed, R. F. Jawad, and H. A. Shamran, "The role of adiponectin in diabetic retinopathy and *Insulin Resistance*," Ital. J. Med., vol. 19, no. 4, Oct. 2025, doi: 10.4081/itjm.2025.2049.

[12] H. N. Lam et al., "Integrative Roles of Functional Foods, Microbiotics, Nutrigenetics, and Nutrigenomics in Managing Type 2 Diabetes and Obesity," Nutrients, vol. 17, no. 4, p. 608, Feb. 2025, doi: 10.3390/nu17040608.

[13] M. Shariff et al., "Unraveling the Therapeutic Role of Myoinositol in *Polycystic Ovary Syndrome*," Int. J. Res. Sci. Innov., vol. XII, no. IV, pp. 1360–1373, 2025, doi: 10.51244/IJRSI.2025.12040112.

[14] P. Ravn, F. Gram, M. S. Andersen, and D. Glintborg, "Myoinositol vs. Metformin in Women with *Polycystic Ovary Syndrome*: A Randomized Controlled Clinical Trial," Metabolites, vol. 12, no. 12, p. 1183, Nov. 2022, doi: 10.3390/metabo12121183.

[15] M. Zhu et al., "The waist-to-height ratio is a good predictor for *Insulin Resistance* in women with *Polycystic Ovary Syndrome*," Front. Endocrinol., vol. 15, p. 1502321, Dec. 2024, doi: 10.3389/fendo.2024.1502321.

[16] K.-J. Chang, J.-H. Chen, and K.-H. Chen, "The Pathophysiological Mechanism and Clinical Treatment of *Polycystic Ovary Syndrome*: A Molecular and Cellular Review of the Literature," Int. J. Mol. Sci., vol. 25, no. 16, p. 9037, Aug. 2024, doi: 10.3390/ijms25169037.

Declarations:

Authors' Contribution:

- All Authors Conceptualization, data collection, interpretation, drafting of the manuscript and intellectual revisions
- The authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed
- **Ethical Approval**: This study was conducted in accordance with the Declaration of Helsinki and received formal ethical clearance from the Institutional Review Board (IRB) of the tertiary care hospital where the trial was conducted prior to initiation of any study-related procedures. Although this trial was not registered in a clinical trial registry, the study protocol was approved by the Institutional Review Board prior to commencement
- **Informed Consent**: All participants provided written informed consent after receiving comprehensive information regarding the study objectives, procedures, potential risks, and benefits. Participants were informed of their right to withdraw from the study at any time without consequence.
- **Data Availability**: The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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