Research Article

# The Comparative Effect of Metformin and Grouping of Metformin Plus Myoinositol on Ovarian Reserve in Pcos Patients

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**Abstract:**

Polycystic ovarian condition (PCOS) is a typical endocrinopathy through numerous clinical signs. The consequences for ladies' lives start at adolescence and can endure all through her lifetime. Ladies every now and again experience unovulatory periods, fruitlessness, hirsutism, corpulence and expanded chance of lipid ,hypertension, diabetes mellitus, anomalies metabolic disorder. PCOS is a heterogenous problem a determination of rejection. By and large, ladies tormented will have feminine inconsistencies, ultrasound discoveries of strange ovarian size and morphology clinical or lab proof of hyperandrogenism. The clinical administration of PCOS is quick transforming from the mix hormonal pills/progesterone for cycle regularization, cosmetological management of skin inflammation and hirsutism to the board of heftiness and insulin obstruction. This training estimates the influences of the insulin sensitizers in increasing the medical and ovarian changes in belongings of PCOS and successful the reproductive results. To appraise the properties of combined metformin and myoinositol versus metformin alone on hormonal (LH, FSH, LH/FSH and testosterone) and ovarian reserve (ovarian size and Antral Follicular Count (AFC) This training comprised 90 sick with an age18<40 years. Those patient were analyzed with PCOS founded on Rotterdam principles. Patients stood categories into two groups: group 1: Is the M group and they received metformin 2: The MI+M group and they received the tablet of MI with metformin . Investigations stayed achieved at the standard and three months. Telephone meetings stood arranged after three months to best acquiescence and opposing properties. Comparison of mean body mass index(BMI),LH, FSH, LH/FSH ,testosterone, ovarian size and AFC between combination group and metformin group before and after treatment is shown at baseline, after treatment, combination resulted in more important decrease in mean ,BMI, LH, FSH, LH/FSH, ovarian size and AFC in comparison with metformin alone This training decisively evidences that myoinositol with metformin has a ultimate part in declining the ovarian reserve markers.

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## INTRODUCTION

Five to 15 % of reproductive-age women are suffered from (PCOS), creation it single of the greatest widespread endocrine illnesses[2]. Despite the influence of hereditary and environmental features, the precise origin of PCOS, the greatest mutual endocrine illness seen in females of reproductive age, continues to be unknown. PCOS is the syndrome that affects more women than any other conditions. A great number of trainings have been approved out to explore the distribution and composition of fat in females who have PCOS. PCOS has been linked to increased numbers of visceral adipose tissue as well as overall adiposity, which may boost the danger of fatness, cardiovascular illness, insulin fighting kind 2 diabetes in women with PCOS regardless of their weightiness status[3]. Insulin resistance appears to be more prevalent, occurring in about 30-40% of young females with PCOS. Furthermore, a malfunction in the pathway of insulin signaling appears to contribute to the development of insulin fighting. The precise mechanism underlying insulin fighting in females with PCOS remains unclear, nevertheless, a post-receptor fault affecting glucose transportation has stayed suggested[4]. The significance of insulin fighting in PCOS is underscored via the consideration of insulin-sensitizing medications for instance metformin, troglitazone, pioglitazone myoinositol (MI) as potential treatments to address dysfunction induced by hyperinsulinemia in the ovarian reaction to endogenous gonadotropins. Among these medications, metformin has been in use for the longest period, whereas MI represents a more recent development in insulin-sensitizing therapy. Our study primarily focuses on these dual insulin-sensitizing medicines, namely MI and metformin.

MI is lone of the nine stereo-isomeric types of a C6 sugar liquor that has a place with vitamin B-complex gathering[5]. Trainings have recommended that debilitation in pathway of insulin might be because of a deformity in inositol phosphoglycans (IPGs) another courier. In PCOS, imperfection in tissue accessibility or changed digestion of inositol or IPGs middle people might add to insulin obstruction[6]. Consequently, providing MI can speed up glucose removal and diminishing flowing serum testosterone , insulin improve ovulation. The usually utilized portion is 200-4,000 mg one time every day before mealtime in PCOS. Extremely great portions of MI can source gastrointestinal aftereffects similar queasiness, the runs, unsteadiness, sleep deprivation and conceivable deteriorating of bipolar problem. No instances of toxicity have been documented there is currently no evidence of drug interactions involving MI. Metformin is an oral anti-hyperglycemic medication classified as a biguanide. Its apparatus of achievement involves lowering blood glucose levels via hindering hepatic glucose creation (reducing gluconeogenesis), improving glucose approval via adipose tissue and skeletal muscles decreasing intestinal glucose concentration. Metformin also improves insulin compassion at the post-receptor flat and promotes insulin-mediated glucose disposal deprived of inducing hypo-glycemia in females with PCOS. It has stood utilized to manage an ovulatory sterility, insulin resistance hyper-androgenism in PCOS sick. However, metformin's efficacy is restricted owing to the little ranks of inositol in PCOS. Metformin dosage typically ranges as of 500-2,500 mg per day. Although metformin administration may lead to a notable rise in vomiting, nausea gastrointestinal discomfort in females with PCOS, there have been no printed intelligences of lactic acidosis associated with metformin treatment in this patient population.

## MATERIALS AND METHODS

**Study Design:** Initially, 95 patients were recruited, later, two sick stayed excepted (missing to follow-up). One patient in the metformin grouping developed pregnant two patients in the combination grouping withdrawn management owing to gastrointestinal difficulties, the remaining 90 sick completed the study. An entire of 90 sick were comprised in the investigation, 45 in each grouping, with an age of 18<40 years. Those patients were identified with PCOS founded on Rotterdam principles.

**Inclusion Criteria of Patients:** PCOS analyzed rendering to the Rotterdam principles. The age of women should be between 18-40 years.

**Exclusion Criteria:** Age 40 years or more, post-menopausal standards of FSH (>25 IE/L), kind 1 or 2 diabetes mellitus, liver and renal impairment, drug allergy and additional causes of oligo-menorrhea comprising irregular standards of thyroid stimulating hormone, prolactin, or 17-hydroxy- Pregnant women.

**Grouping of Patients:** Sick stayed categories into two groups: Group 1:Is the M group and they received metformin as 500mg orally twice daily .Group 2: The MI+M group and they received the tablet of MI contained 500mg MI and stood managed as one dosage double daily with metformin dosage. Investigations were

achieved at the standard and three months. Telephone meetings stood arranged three months later to document adherence and any opposing reactions.

All patients underwent pelvic trans-abdominal or transvaginal ultrasounds, depending on their sexual action, to assess ovarian morphology. A analysis of PCO morphology (PCOM) was established when ovarian size exceeded 12mm and the AFC (Antral Follicle Counts) surpassed 20 follicles per ovary.

**Ethical Consideration:** The training was accepted via principled agreement committee of Collage of Medicine/ University of al Al-Qadsiyah. All participants were informed to given an oral consent after full illustration of the aims and procedures of the current stydy.

**Time and Location of the Study:** The patients were recruited from the Maternity and Pediatrics Teaching Hospital in Adiwaniyah Province, Iraq. The training is outmoded rear to September the 22st 2023 and extend to March 28st 2024.

**Method of Statistics:** The data was collected, compiled, investigated accessible by means of the Statistical Program for Social Sciences (SPSS) style 23 and Microsoft Office Excel 2010. Qualitative (definite) variables stood stated using numerals and percentages, while the Kolmogorov-Smirnov examination stayed engaged to evaluate the standard dissemination of measureable (numeric) variables before using the mean (a quantity of central propensity) and standard deviation (a quantity of dispersal) to represent normally distributed numeric variables.

**The Next Statistical Examinations Stood Conducted:**

- - A chi-square examination was utilized to assess the correlation among two definite variables, providing that fewer than 20% of the cells had an projected amount of fewer than 5.
- -The independent testers t-test was engaged to parallel the means of two groups, assuming that the numeric variables followed a normal distribution.
- A importance flat of $p = 0.05$ stayed measured statistically important.

**RESULTS AND DISCUSSIONS**

(Table 1) displays the comparison of mean age between the combination grouping and the metformin grouping. There stayed no statistically important alteration in aging mean observed between the two groups.

Comparison of mean body mass index (BMI) between combination group and metformin group before and after treatment, after treatment, combination caused in further important decrease in mean BMI in comparison with metformin

Appraisal of mean serum LH between combination group and metformin group before and after treatment is shown in (Table 3) after treatment, combination resulted in more significant reduction in mean LH in comparison with metformin

Appraisal of mean serum FSH among combination grouping and metformin grouping before and after treatment is shown in (Table 4) after treatment, combination resulted in significant reduction in mean FSH ($p<0.001$), whereas, metformin resulted in a reduction that was not important ($p = 0.126$)

Appraisal of mean LH/FSH among combination group and metformin group before and after treatment is shown in (Table 5) after treatment, combination resulted in more significant reduction in mean LH/FSH ratio in comparison with metformin

Appraisal of mean serum testosterone among combination grouping and metformin grouping before and after treatment is shown in (Table 6) after treatment, both combination and metformin resulted in significant reduction in mean serum testosterone level, , comparison of the variance in mean level of mutually groups was significant ($p =0.015$)

Comparison of mean ova size between combination group and metformin group before and after treatment is shown in (Table 7) after treatment, combination caused in important decrease in mean size ($p<0.001$), whereas, metformin ensued in no important decrease ($p = 0.928$.

Comparison of mean antral follicle count (AFC) between combination group and metformin group before and after treatment is shown in (Table 8),after treatment, combination resulted in more significant reduction in mean AFC in comparison with metformin.

(PCOS) is a prevalent endocrinological condition affecting women, marked by excessive androgen levels, irregular or absent ovulation ovaries with a polycystic appearance (PCO). The diagnosis typically relies on three primary criteria: the 1992 National Institutes of Health (NIH) principles[7]. 2004 Rotterdam principles[8,9] and the 2006 Androgen Additional Society principles[10,11] Dependent on the analytic principles used, the occurrence can assortment from as little as 6% (NIH) to

as great as 20% (Rotterdam)[12]. Women diagnosed with PCOS typically exhibit ovaries characterized by heightened ovarian stroma, an augmented follicle count a thicker, hyper plastic theca cell layer when paralleled to those deprived of the condition[13]. Hyperinsulinemia animates the improvement of antral follicles, expanding the responsiveness of granulosa cells to FSH, accordingly expanding the quantities of follicles in addition to ovarian size[14,15]. The biguanide metformin has stood widely utilized for PCOS management, particularly in ladies with hyper-glycemia and insulin opposition. Regardless of the depicted advantageous impacts of metformin on ovarian functioning, the systems of activity of this biguanide in the ovary are as yet hazy. It is generally acknowledged that metformin applies helpful impacts in PCOS ladies other than its activity on glucose digestion. Various examinations have revealed an expansion in ovulation and pregnancy proportions next metformin management in PCOS sick going through Craftsmanship. Metformin has stayed the best option medication to reestablish ovulation in PCOS ladies and has an anti-hyper androgenic impact temporarily. To be sure, an insulin sensitizer follows up on various tissues, comprising the ovary lessens glycemia ranks, diminishing the ovarian creation of androgens and the centralization of circling androgens[16].

Inositols are synthetically recognized as cyclohexanes and incorporate a group of nine stereoisomers. Myo-inositol (MI) is the best broadly conveyed in environment. The really nutritional wellsprings of MI stay natural products, grains beans nuts. Day to day MI consumption doesn't surpass 500-700 mg/day for a regular Western eating regimen. MI can likewise be effectively blended (up-4 g/day) in the hominid body (particularly in the liver and cerebrum)[17] MI is many times the main line of protection in dealing with and forestalling problems like PCOS[18]. MI is a six-hydroxyl bunch cyclic carb that has numerous metabolic capabilities in the body[19].

In this study, metformin alone ensued in important weightiness decrease, nonetheless, adding of myoinositol triggered further important decrease in BMI . Similarly the training via Bahadur *et al.,* in which they renowned a additional important reduction in BMI in the MET+MI+DCI grouping[20]. The way by which these drugs affected the BMI ,metformin chiefs to a decrease in body weightiness and glucose creation by the liver, owing to its anoreptic effect and its interaction with AMP-activated protein kinase (AMPK)[21]. Furthermore, it

has been documented that inositol, whether in the form of DCI or MI, facilitates glucose approval via enhancing insulin compassion. The insulin-mimetic properties of MI or its isomers appear to stem from inositol Phosphoglycans (IPG), which incorporates MI or DCI[22].

In this study, it was observed that metformin was able to significantly reduce testosterone, LH and LHL, FSH ranks in females with PCOS, however, combination of this drug with myoinositol more to do soNabi S, in alignment with our study, affirmed that alterations in
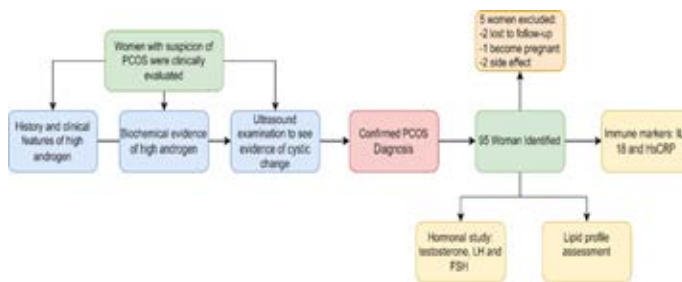


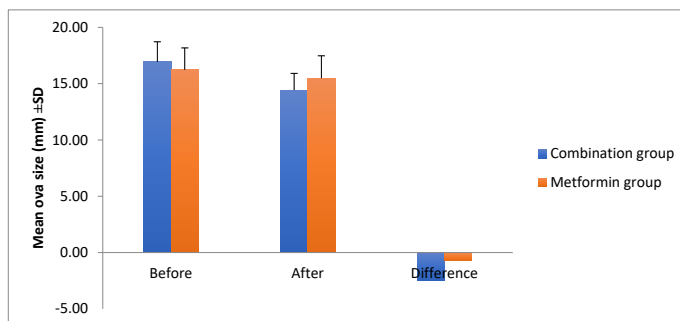Fig. 1: Flow chart of the study



Fig. 2: Comparison of mean ova size between combination group and metformin group before and after treatment
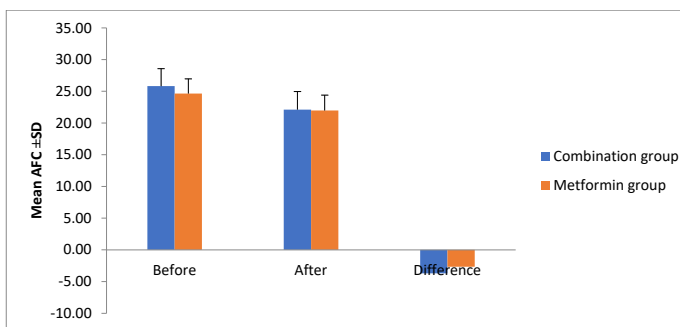


Fig. 3: Comparison of mean AFC between combination group and metformin group before and after treatment

**Table 1: Comparison of mean age between combination grouping and metformin group**

| Representative | Combination grouping n = 45 | Metformin grouping n = 45 | P |
|---|---|---|---|
| **Age (Years)** | | | |
| Mean±SD | 26.20±5.34 | 26.71±5.77 | 0.664 I |
| Range | 18-36 | 18-38 | NS |

**Table 2: Appraisal of (BMI) among combination group and metformin grouping before and after treatment**

| Characteristic | Combination grouping n = 45 | Metformin grouping n = 45 | p |
|---|---|---|---|
| **BMI1 (kg/m$^2$)** | | | |
| Mean±SD | 30.21±3.24 | 30.42±2.75 | 0.736 I |
| Range | 26.04-35.7 | 25.84-35.38 | NS |
| **BMI2 (kg/m$^2$)** | | | |
| Mean±SD | 27.28±3.22 | 28.64±3.00 | 0.042 I * |
| Range | 23.48-32.9 | 25-34.13 | |
| Difference in mean | -2.93 | -1.78 | |
| P | < 0.001 Pa *** | < 0.001 Pa *** | |

**Table 3: Comparison of mean serum LH ranks among combination grouping and metformin grouping earlier and next treatment**

| Characteristic | Combination group n = 45 | Metformin group n = 45 | p |
|---|---|---|---|
| **LH Before** | | | |
| Mean±SD | 17.64±6.47 | 17.35±6.91 | 0.349 I |
| Range | 6.78-29.44 | 8.6-32.83 | NS |
| **LH after** | | | |
| Mean±SD | 8.36±3.60 | 11.82±5.57 | 0.001 I *** |
| Range | 3.23-14.2 | 1.5-19.65 | |
| Difference in mean | -9.29 | -5.53 | |
| P | < 0.001 Pa *** | < 0.001 Pa *** | |

**Table 4: Comparison of mean serum FSH levels between combination group and metformin group before and after treatment**

| Characteristic | Combination group n = 45 | Metformin grouping n = 45 | p |
|---|---|---|---|
| **FSH Before** | | | |
| Mean±SD | 4.95±1.85 | 4.94 ±0.79 | 0.401 I |
| Range | 1.96-7.9 | 4.07-7.05 | NS |
| **FSH after** | | | |
| Mean±SD | 5.87±1.08 | 5.16±1.95 | 0.048 I |
| Range | 3.6-7.3 | 3.24-9.44 | NS |
| Difference in mean | 0.92 | 0.53 | |
| p | < 0.001 Pa *** | 0.126 Pa NS | |

**Table 5: Comparison of mean LH/FSH ratio between combination grouping and metformin group before and after treatment**

| Characteristic | Combination grouping n = 45 | Metformin group n = 45 | p |
|---|---|---|---|
| **LH/FSH Before** | | | |
| Mean±SD | 3.76±0.91 | 3.60 ±1.08 | 0.440 I |
| Range | 3.06-6.19 | 1.21-4.93 | NS |
| **LH/FSH after** | | | |
| Mean±SD | 1.43±0.65 | 1.77±0.64 | 0.013 I * |
| Range | 0.63-3 | 0.43-2.82 | |
| Difference in mean | -2.34 | -1.83 | |
| P | < 0.001 Pa *** | < 0.001 Pa *** | |

**Table 6: Appraisal of mean serum testosterone ranks among combination grouping and metformin grouping before and after treatment**

| Characteristic | Combination group n = 45 | Metformin group n = 45 | p |
|---|---|---|---|
| **Total testosterone Before** | | | |
| Mean±SD | 0.66 ±0.53 | 0.64±0.53 | 0.888 I Range |
| | 0.25-2.05 | 0.2-1.81 | NS |
| **Total testosterone after** | | | |
| Mean±SD | 0.22±0.12q | 0.28 ±0.11 | 0.015 I * |
| Range | 0.13-0.5 | 0.14-0.5 | |
| Mean difference | -0.44 | -0.40 | |
| p | < 0.001 Pa *** | < 0.001 Pa *** | |

**Table 7: Comparison of ultrasound characteristics of ovarian size between combination group and metformin group before and after treatment.**

| Characteristic | Combination grouping n = 45 | Metformin grouping n = 45 | P |
|---|---|---|---|
| **Ova size Before** | | | |
| Mean±SD | 16.93±1.79 | 16.23±1.94 | 0.078 I |
| Range | 13.5-19.6 | 13.5-19.7 | NS |
| **Ova size after** | | | |
| Mean±SD | 14.43±1.48 | 15.49±1.98 | 0.005 I ** |
| Range | 11.1-16.5 | 12.8-19.4 | |
| Difference in mean | -2.50 | -0.73 | |
| P | < 0.001 Pa *** | 0.928 Pa NS | |

**Table 8: Comparison of antral follicle count (AFC) between combination group and metformin group before and after treatment.**

| Characteristic | Combination group n = 45 | Metformin group n = 45 | P |
|---|---|---|---|
| **AFC Before** | | | |
| Mean±SD | 25.82±2.75 | 24.64±2.32 | 0.061 I |
| Range | 22-30 | 22-28 | NS |
| **AFC after** | | | |
| Mean±SD | 22.11±2.86 | 23.98±2.43 | 0.042 I * |
| Range | 18-27 | 19-26 | |
| Difference in mean | -3.71 | -2.67 | |
| P | < 0.001 Pa *** | 0.003 Pa ** | |

serum testosterone levels were more pronounced with MI compared to MET[23]. Metformin potentially exerts a straight inhibitory influence on the appearance of diverse enzymes engaged in thecal cell steroidogenesis and androgen construction[24]. Inositols are acknowledged as insulin sensitizers due to their regulation of components within insulin signaling pathways[25]. In a potential, randomized organized trial involving 72 sick, Anupama *et al.* (2021) observed a significant alteration in the ratio of (LH/FSH) between PCOS patients who established either metformin 1g/day alone or in combination with MI 550 mg twice daily orally[26].

In a potential, randomized organized trial involving 72 sick, Anupama *et al.* observed a significant alteration in the ratio of (LH/FSH) between PCOS patients who established either metformin 1g/day alone or in combination with MI 550 mg twice daily orally[26]. This effect primarily arises from a reduction in LH levels quite than an increase in FSH. The decline in LH might be attributed to a reduction in androgen levels, which in turn inhibits unsuitable androgen response on the pituitary and hypothalamus[27].

In the training via Angik[28], the amount of follicles reduced more in myoinositol group than in metformin group also ovarian size reduced more in myoinositol grouping which is similar to our study ,but our study there is not significant of metformin group in ovarian size may be the time is not sufficient to appeare reduction in this parameter ,the same to our study doing by Morin-Papunen *et al*. documented that the mean sizes of both the right and left ovaries remained unchanged following two months of metformin therapy similarly after four to six months of treatment[29].

In the training conducted via Nabi *et al.,* it stood noted that the decline in the numeral of follicles stayed significantly greater with MI compared to MET, although the reduction in ovarian size stood nearly identical in mutually groups[30]. Nevertheless, both interventions exhibited similar reductions in the number of follicles. Although ovarian size appeared to be inferior in the MET grouping compared to the MI grouping, this discrepancy was not statistically important based on findings from the research by Kutanaei [31]. MI appears to production a significant part in regulating ovarian morphology modern trainings propose it can be a critical feature in enhancing oocyte and embryo value.

## CONCLUSION

Combination of metformin and myoinositol improved ovarian volume, LH, FSH and LH/FSH ratio compared metformin alone and more improvement in AFC with this combination, so MI based management have more benefits in controlling of hormonal and ovarian reserve.

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