

## Comparative study of combined co-enzyme Q10 and Clomiphene Citrate vs Clomiphene Citrate alone for ovulation induction in patients with polycystic ovarian syndrome

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### Abstract

A total of 136 patients with PCOS were followed through the Department of the Obstetrics and Gynaecology, Unit-IV, Lady Aitchison Hospital, Lahore. Patients were randomly divided by lottery method into two groups i.e., Group-A (CoQ10 plus Clomiphene citrate) and Group-B (Clomiphene citrate alone). The selected patients in the study group (group-A) were given Clomiphene citrate 100mg/day from cycle days 2-6 for 45 days (2 cycles) and CoQ10 in a dose of 50mg soft gel capsules thrice per day starting at cycle day-2, until HCG administration. Patients in controlled group (group-B) received Clomiphene citrate 100mg/day twice a day cycle for 45 days. Data were analysed in SPSS v25.0.

In group-A (CoQ10 plus Clomiphene citrate), successful ovulation induction was noted in 16 (23.5%) patients, showing that with the addition of CoQ10, the chances of ovulation induction increased.

**Keywords:** Co-enzyme Q10, Clomiphene Citrate, Ovulation Induction, Polycystic Ovarian Syndrome.

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### Introduction

Polycystic ovarian syndrome (PCOS) is the most common heterogeneous endocrine disorder that affects women of reproductive years. Major clinical features of PCOS include menstrual cycle irregularities and clinical features of hyper-androgenism (alopecia, acne, and hirsutism) related with fertility problems, insulin resistance, and obesity. PCOS is related with increased risk of metabolic disorders which may be associated with hyper-androgenism, obesity, dyslipidaemia, insulin resistance, and impaired glucose tolerance. Antioxidant supplementation CoQ10 can neutralise free radicals and reduce oxidative stress. CoQ10 is an energy carrier, mainly involved in electron transport

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chain to produce Adenosine triphosphate and less concentrations of CoQ10 in plasma which is related to steroid hormones and hypogonadism. It undergoes the oxidising cycle in which it gets oxidised as electrons are produced, and decreases as electrons are accepted. When reduced, it is more readily able to provide electrons and acts as an antioxidant. In PCOS, CoQ10 is a fat-soluble coenzyme present in the mitochondrial inner membrane, and has been utilised as an antioxidant and oxidative stress reducer.<sup>1</sup>

In women with PCOS, Clomiphene citrate (CC) is the first-line therapy for ovulation induction. It has both antagonist and oestrogen agonist properties; it binds to the oestrogen receptors in hypothalamus resulting in falling oestrogen levels; increases gonadotrophin levels, promotes ovulation, and corrects menstrual irregularities.

The rationale of our study was to compare the effects of the CoQ10 and Clomiphene citrate vs Clomiphene citrate alone in induction of ovulation. Although Clomiphene citrate is the first-line medication for ovulation induction, the best results need meticulous monitoring even if ovulation induction with Clomiphene citrate is simple in principle.

No studies have been conducted to see the combined effect of CoQ10 and Clomiphene citrate in our population which is different from the Western population due to its unique genetic makeup. CoQ10 is rich in foods like soy oil, beef, avocado, olive oil, peanuts and organ meats such as heart, kidney, liver, chicken liver. Moreover, meat and fish are the richest sources of dietary CoQ10.<sup>2</sup> If its usefulness is proved in our population, it would be a great breakthrough as we would be able to treat the most common endocrinal disease prevalent in our population with a natural and cost-effective method.

### Patients/Methods and Results

Probability simple random sampling was done using the criteria of central limit theorem.<sup>3</sup> A sample of 136 patients (68 patients in each group) was estimated by use of 95% confidence level with 10% absolute precisions and the patients were included after obtaining informed consent. The patients included had expecting percentage of CoQ10 plus Clomiphene citrate of 95% and Clomiphene citrate as

85%. While all other patients were excluded.<sup>4</sup>

By using simple random sampling approach, a total 136 patients (68 each in each group i.e., group-A (CoQ10 plus chloroprene citrate) and group-B (Chloroprene citrate alone) were studied for a period of 12 months (February 2021 to January 2022) at the Department of the Obstetrics and Gynaecology, Unit-IV, Lady Aitchison Hospital, Lahore following the submission of the synopsis and reception of research grant. Patients were diagnosed with PCOS according to Rotterdam criteria<sup>5</sup> as those patients with: a) menstrual cycle irregularities (oligomenorrhoea or secondary amenorrhoea), b) Polycystic ovaries as determined by ultrasonography and may have signs of hyper-androgenism or acne, absence of any other endocrine disorder or any other cause of hyper-androgenism. The university administration and Department of the Obstetrics and Gynaecology Unit-IV, Lady Aitchison Hospital, Lahore, conducted this study and success will be computed through analysis and diagnosis of ultrasounds. Follow-up was done by representatives of Department of the Obstetrics and Gynaecology Unit-IV, Lady Aitchison Hospital, Lahore, and researchers through analysis of the test reports.

Data were analysed in SPSS v25.00. Quantitative variables like age, menstrual cycle, and score of hirsutisms is presented in terms of mean and SD. The Qualitative variables like gender and ovulation induction are presented as frequency and percentages.

The means of several variables for the two groups—one getting CoQ10+Clomiphene citrate and the other receiving Clomiphene citrate alone—are compared in Table 1. Age, menarche age, length of marriage, weight, height, BMI, SBP, DBP, cycle length, bleeding days, hirsutism score, cycle length after therapy, bleeding days after treatment, and bHCG are among the studied factors. Except for bHCG, where the mean was higher in the Clomiphene citrate alone group, all of the means were marginally higher in the CoQ10 plus Clomiphene citrate group.

As of Table-1, with mean ages of 26.40 years for the CoQ10 plus Clomiphene citrate group and 26.21 years for the Clomiphene citrate alone group, respectively, the participants' ages were comparable in both groups. The same similarity was shown for the menarcheal age and the length of marriage, where there was no statistically significant difference in averages between the two groups. Nevertheless, although the Clomiphene citrate alone group had a little higher mean bHCG level, the CoQ10 plus Clomiphene citrate group had a slightly lower mean weight, BMI, and shorter cycle length following therapy. These results together imply that adding CoQ10 to

**Table-1:** Comparison of means of different variables between groups.

Variables	Groups	
	CoQ10 plus Clomiphene citrate	Clomiphene citrate only
Mean Age (years)	26.40±4.545	26.21±4.991
Mean Age of menarche (years)	12.19±1.237	12.16±1.241
Duration of marriage (years)	3.12±2.079	3.04±1.874
Weight (kg)	66.6 ±4.659	67.09±4.971
Height (m)	1.56±0.148	1.86±0.215
BMI (kg/m <sup>2</sup> )	27.23±1.426	27.19±1.500
SBP (mmHg)	115.71±5.795	116.47±6.173
DBP (mmHg)	78.38±4.766	78.24 ±3.841
Duration of cycle (days)	36.47±10.208	35.82±10.421
Bleeding days	4.63±1.753	4.31±1.363
Hirsutism score	10.07±1.086	10.30±1.199
Duration of cycle after treatment (days)	33.19±8.223	32.04±6.724
Bleeding days after treatment	4.44±1.606	4.35±1.302
bHCG	305.62±259.116	350.25±166.078

**Table-2:** Comparison of ovulation induction between groups.

Ovulation induction	Groups		Total n (%)
	CoQ10 plus Clomiphene citrate n (%)	Clomiphene citrate only n (%)	
Positive	16 (23.5)	12 (17.6)	28 (20.6)
Negative	52 (76.5)	56 (82.4)	108 (79.4)
Total	68 (100)	68 (100)	136 (100)

clomiphene citrate therapy may result in modest benefits in several reproductive and cardiovascular health outcomes. The means of several variables for the two groups—one getting CoQ10+Clomiphene citrate and the other receiving Clomiphene citrate alone—are compared in Table 1. The findings show that the CoQ10+Clomiphene citrate group had marginally superior results in terms of weight, BMI, cycle length following treatment, and hirsutism score, but that other outcomes were not statistically different from the Clomiphene citrate alone group.

Table 2 compares the induction of ovulation in the CoQ10 +Clomiphene citrate and the Clomiphene citrate alone, groups. The table displays the total number and percentage of participants in each group as well as the number and percentage of participants with positive and negative ovulation induction findings. Each group contained 68 individuals in total, and the findings indicate that the CoQ10 + Clomiphene citrate group had somewhat more successful ovulation inductions (23.5%) than the Clomiphene citrate alone group (17.6%). The variation was insignificant, however. The majority of individuals in both groups—76.5% in the CoQ10 + Clomiphene citrate group and 82.4% in the Clomiphene citrate alone group—had negative ovulation induction outcomes. Overall, the results

indicate that ovulation induction outcomes may not be considerably enhanced by adding CoQ10 to Clomiphene citrate therapy.

Table 2, which analyses the outcomes of ovulation induction in the two groups, adding CoQ10 to the Clomiphene citrate therapy may not substantially increase ovulation induction results. Further study is required to validate these results and to establish the ideal CoQ10 supplements dose and duration for POC women, even if the data generally point to some good benefits of CoQ10 with Clomiphene citrate therapy.

These findings are in line with those of famous scholars<sup>6</sup> who observed that 85.65 percent of patients were overweight, and that weight gain and obesity occurs in approximately 61% to 76% of women with PCOS, most of them had abdominal or central obesity. Both tables provide light on the effects of CoQ10 combined with Clomiphene citrate therapy for polycystic ovarian syndrome in female patients.

Additionally, in patients with polycystic ovary syndrome obesity made their metabolic and reproductive issues worse. When compared to prevalence of PCOS in general population, research indicated a 5 to 6 times increase in prevalence of PCOS among first-degree female relatives of the afflicted individuals. Numerous studies have looked at how changing to a high-protein, low-carb diet affects a number of PCOS symptoms, such as hyperandrogenaemia and irregular periods.<sup>7</sup>

These findings matched those of the current research, which noted that CoQ10 with Clomiphene citrate in PCOS patients resulted in 23.5 percent positive ovulation. On the other hand, multiple prior studies have established the significance of CoQ10 supplementations in PCOS patients. The scholars discovered that ovulations occurred in 54/82 cycle (65.90%) in CoQ10 treated group compared to 15.5 percent in the control group.<sup>8</sup>

According to researchers, numbers of the follicles >14mm and > 18mm were significantly high in CoQ10 treated PCOS patients as compared to Clomiphene citrates only group<sup>9</sup> with ovulations occurring in 9 (45%) in CoQ10 treated group and 10 (50%) in control group, and clinical pregnancies occurred in 2/20 woman (10%) versus 1/20 woman (5%) into control group.<sup>10</sup>

According to pre-treatments baseline dataset, combined treatment improved ovulation stimulation in PCOS patients compared to Clomiphene citrate alone, with ovulation occurring in (17.6%) of PCOS patients who virtually all ovulate mature ova (the ova sizes 18 mm) in diameter.

As a result, CoQ10 appears to be promising adjuvant to the oral ovulatory agent like Clomiphene citrates, and their combination prove as safe, inexpensive as well as effective in stimulating follicular developments in PCOS patients, and may be tried successfully before more complicated treatments like laparoscopic or gonadotrophins ovarian drillings.

## Conclusion

In women with PCOS, combined treatment with the CoQ10 and Clomiphene citrates boosts ovulation rate much more than Clomiphene citrate alone. CoQ10 seems to be a potential adjuvant to Clomiphene citrate. For increasing follicular growth in PCOS, a combination of CoQ10 and the Clomiphene citrate has been shown as effective, affordable, and safer, and may be attempted effectively before a more difficult therapy like gonadotrophins or laparoscopic ovarian drilling.

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**Conflict of Interest:** None.

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