



## “EFFECT OF COENZYME Q10 SUPPLEMENTATION ON OVARIAN RESPONSE AND IVF OUTCOMES IN WOMEN WITH POOR OVARIAN RESERVE: A RANDOMIZED CONTROLLED TRIAL IN A IVF CENTER”

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### ABSTRACT

**Background:** Diminished ovarian reserve (DOR) is a significant contributor to infertility and low response to in vitro fertilization (IVF) stimulation that may result in inadequate pregnancy outcomes. Coenzyme Q10 (CoQ10) is an antioxidant and cofactor in the mitochondrion that has demonstrated the potential to enhance the quality and energy metabolism of the oocytes.

**Objective:** To identify the effect of Coenzyme Q10 supplementation on the ovarian response and the IVF outcome of women with poor ovarian reserve.

**Methods:** The study was a randomized controlled trial, which was carried out at the Khaula Hospital, IVF Center, Muscat. April 2024 June 2024. Eighty women with low ovarian reserve were randomly placed under CoQ10 (200mg/day) and placebo for eight weeks before IVF stimulation. All the subjects had undergone a standard gonadotropin-releasing hormone (GnRH) antagonist therapy.

**Results:** CoQ10 supplementation significantly improved ovarian response parameters, including mean oocytes retrieved ( $6.2 \pm 1.8$  vs.  $3.9 \pm 1.5$ ;  $p < 0.001$ ), mature oocytes ( $4.8 \pm 1.6$  vs.  $2.9 \pm 1.3$ ;  $p < 0.001$ ), and fertilization rate (68.4% vs. 52.3%;  $p < 0.001$ ). The proportion of Grade I embryos and clinical pregnancy rates were also higher in the CoQ10 group (65% and 35%, respectively) compared with controls (42% and 17.5%;  $p < 0.05$ ).

**Conclusion:** Coenzyme Q10 supplementation enhances ovarian function, oocyte quality, and IVF outcomes in women with poor ovarian reserve. It represents a promising, non-invasive adjunct to standard ovarian stimulation protocols in assisted reproduction.

**Keywords:** *Coenzyme Q10; Diminished ovarian reserve; In vitro fertilization; Oocyte quality; Antioxidants; Mitochondrial function.*

## INTRODUCTION

Infertility remains a global reproductive health concern, affecting approximately 10-15% of couples of childbearing age, with female factors accounting for nearly half of cases. Among the various female factors, diminished ovarian reserve (DOR) has been identified as a major cause of infertility, which is manifested by the combination of diminished quantity and quality of oocytes, and consequently, the poor results obtained from the use of assisted reproductive technologies (A.R.T.). Recent studies have also identified the possible effect of Coenzyme Q10 (CoQ10) supplementation on the DORs of women, which may lead to better response of fertility and quality of embryos. Lin et al.'s (1) research findings were supported in a systematic review and meta-analysis that CoQ10 pretreatment may result in a better ovarian response and more retrieved oocytes and quality embryos in women undergoing IVF/ICSI, thereby identifying its therapeutic role in patients with limited ovarian reserve.

Dawoud et al. (2) studied the effect of CoQ10 in combination with dehydroepiandrosterone sulfate (DHEA-S) in young, poor responder women undergoing IVF/ICSI cycles. However, the use of CoQ10 has been mainly explored because of its antioxidant character, but the part it plays in the enhancement of mitochondrial function and the gain of oocyte competence is still a growing research area. Moreover, the comparative trials with L-carnitine have shown its beneficial effect on fertility outcomes as well. Abu-Zaid et al. (3) published a meta-analysis reporting that L-carnitine supplementation improved ovulation and increased clinical pregnancies among patients with polycystic ovary syndrome (PCOS), underscoring the importance of mitochondrial energy modulators in fertility treatments. Women identified with reduced ovarian reserve may benefit most from early interventions such as oocyte cryopreservation or hormonal therapy. Bhide (4) discussed anti-Müllerian hormone (AMH), antral follicle count (AFC), and follicle-stimulating hormone (FSH) levels as the main parameters that determine fertility and are required in clinics for assessment and management.

Poor ovarian reserve patients still have poor results regardless of the improvement in ART protocols. Han et al. (5) examined the effectiveness of estrogen pretreatment in women of POSEIDON groups 3 and 4 and reported the enhanced outcomes in follicular synchronization and the oocyte yield. In the same vein, Tang et al. (6) suggested the use of electro-acupuncture as a possible treatment of DOR in a randomized placebo-controlled trial, which is indicative of the increasing interest in non-pharmacological and pharmacological methods of improving ovarian response. Meanwhile, Potiris et al. (7) addressed the role of metabolomics in the discovery of biomarkers of poor ovarian response in a manner that gives fresh insights into the biochemical basis of DOR. These innovations highlight the complexity of ovarian dysfunction and the necessity of personalized treatment.

The co-treatment with growth hormone (GH) has also been tested with regard to its potential to improve the results of ovarian stimulation. According to Tuelek and Kahraman (8), GH co-treatment has the potential to enhance fertilization and clinical pregnancy rates in women with anticipated normal ovarian response, but the advantageous effect on poor responders is still under study. Han et al. (9) proposed another Chinese traditional medicine intervention, Erzhi Tiangui formula, that demonstrated better oocyte yield and fertilization in poor responders, which further expands the therapeutic picture. Moreover, Erdoğan et al. (10) emphasized that the level of oxidative stress markers, in particular thiol/disulfide homeostasis, is a key factor in ovarian reserve status, and redox imbalance is associated with poor quality oocytes. Since CoQ10 is a powerful antioxidant in the mitochondria, its supplementation is likely to stabilize the oxidative state and enhance the activity of the ovaries by altering the cellular energy metabolism.

Ovarian health has also been attributed to lifestyle and dietary factors. According to Ziaei et al. (11), low quality of diets in the form of low Diet Quality Index-International (DQI-I) scores correlated with an increased risk of reduced ovarian reserve. These results help to substantiate the idea that diet-based interventions, such as the use of antioxidant supplements, can enhance reproductive performance. Han

et al. (12) also explained the molecular action of growth hormone in ART and how it may alter folliculogenesis via PI3K/AKT and JAK/STAT signaling pathways. These mechanistic observations are in line with the mitochondrial bioenergetic impact of CoQ10 on the maturation and fertilization capacity of oocytes. Chen et al. (13) compared GnRH antagonist and progestin-primed ovarian stimulation (PPOS) algorithms and had no difference in their cumulative live birth rates, which implied that protocol optimization might not be enough to surpass the biological constraints of poor ovarian reserve. In this respect, new treatment methods, including mechanical force modulation, are suggested.

Chang (14) proposed the idea of mechanical stimulation of the ovary to increase the follicular growth, and this offered new possibilities of promoting fertility in women with impaired ovaries. Additionally, Chen et al. (15) showed that even in low-prognosis women, cumulative live birth rates were still less than optimal in several embryo transfer cycles, which underlines the urgency of the need to implement the interventions that would enhance intrinsic oocyte quality instead of the intensity of stimulation exposure. Prevention measures of ovarian reserve disorders are emerging due to the accelerating rate of reproductive aging worldwide. Man et al. (16) reported the need to use several preventative strategies, such as lifestyle change, antioxidant supplementation, and early fertility preservation, to prevent the deterioration of ovarian function. Liu et al. (17) also reported that follicular output was improved with letrozole co-treatment, especially in PCOS women with high BMI, which indicates its possible use as an adjunct in improving ovarian response. Moreover, when fixed dosing and degressive dosing schemes of medroxyprogesterone acetate with letrozole were compared and found to have similar effects of OSE on the ovaries, the necessity of individualized approaches to ART treatment was strengthened.

**Objective:** To evaluate the effect of Coenzyme Q10 supplementation on ovarian response, oocyte quality, and in vitro fertilization (IVF) outcomes among women with poor ovarian reserve at Khaula Hospital, IVF Center, Muscat.

## MATERIALS AND METHODS

**Study Design:** Randomized Controlled Trial.

**Study Setting:** Department of Obstetrics and Gynecology, Khaula Hospital, IVF Center, Muscat.

**Study Duration:**

April 2024 June 2024

**Inclusion Criteria:** Women aged 25-40 years were considered with a diagnosis of poor ovarian reserve based on at least two of the following criteria; anti-Mullerian hormone (AMH) levels of less than 1.1 ng/mL, antral follicle count (AFC) of less than 5 or a history of poor ovarian response during an IVF cycle (retrieval of 3 or less oocytes with conventional stimulation). Women with a normal cavity of the uterus during transvaginal ultrasound and ovaries intact were also eligible. All the participants were interviewed and signed informed consent forms before enrollment and agreed to comply with the supplementation and treatment regimen.

**Exclusion Criteria:** Women who had endocrine or metabolic syndromes like polycystic ovary syndrome (PCOS), thyroid dysfunction, or uncontrolled diabetes mellitus were not included. However, patients with severe male factor infertility, abnormalities of the uterus, ovarian surgery history, endometriosis grade III–IV, or previous use of antioxidant or hormonal supplements within three months of recruitment were excluded. Participants who did not want to undergo an IVF cycle or follow the medication schedules were also locked out to guarantee protocol adherence.

## Methods

Participants who qualified were randomly allocated into two groups by utilizing a computer-based sequence. The intervention group was provided with oral Coenzyme Q10 (200 mg/day) for eight weeks before beginning controlled ovarian stimulation, and the control group was given the same placebo capsules. The two groups had a normal gonadotropin-releasing-hormone (GnRH) antagonist IVF procedure. Recombinant hCG was used to induce ovulation in the presence of leading follicles

18 mm or greater, and then oocytes were retrieved 36 hours later. The findings included the number of retrieved oocytes, mature oocytes (MII), fertilization rate, embryo quality, and clinical pregnancy rates. The entire processes were carried out by the same fertility experts to reduce inter-observer differences and evenness of the stimulation and laboratory procedures.

## Results

A total of 80 women with poor ovarian reserve were enrolled in the study. After randomization, 40 participants received Coenzyme Q10 supplementation (CoQ10 group) and 40 received placebo (control group).

**Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 80)**

| Variable                                | CoQ10 Group (n=40) | Control Group (n=40) | p-value |
|-----------------------------------------|--------------------|----------------------|---------|
| Age (years, Mean $\pm$ SD)              | 34.2 $\pm$ 3.8     | 33.9 $\pm$ 4.0       | 0.71    |
| BMI (kg/m <sup>2</sup> , Mean $\pm$ SD) | 25.6 $\pm$ 2.9     | 25.2 $\pm$ 3.1       | 0.64    |
| Duration of infertility (years)         | 5.1 $\pm$ 2.3      | 5.4 $\pm$ 2.0        | 0.58    |
| AMH (ng/mL)                             | 0.85 $\pm$ 0.22    | 0.83 $\pm$ 0.20      | 0.79    |
| AFC (count)                             | 4.3 $\pm$ 0.9      | 4.1 $\pm$ 1.0        | 0.42    |

Eight weeks of CoQ10 supplementation showed a considerable improvement in ovarian response parameters between the CoQ10 group and the control group. There were significant differences in the mean number of oocytes retrieved (6.2  $\pm$  1.8 vs. 3.9  $\pm$  1.5;  $p < 0.001$ ).

**Table 2: Comparison of Ovarian Response Parameters Between CoQ10 and Control Groups**

| Parameter                    | CoQ10 Group (Mean $\pm$ SD) | Control Group (Mean $\pm$ SD) | p-value |
|------------------------------|-----------------------------|-------------------------------|---------|
| Total gonadotropin dose (IU) | 2570 $\pm$ 410              | 2780 $\pm$ 450                | 0.048   |
| Oocytes retrieved            | 6.2 $\pm$ 1.8               | 3.9 $\pm$ 1.5                 | <0.001  |
| Mature (MII) oocytes         | 4.8 $\pm$ 1.6               | 2.9 $\pm$ 1.3                 | <0.001  |
| Fertilization rate (%)       | 68.4 $\pm$ 8.5              | 52.3 $\pm$ 9.2                | <0.001  |

The analysis of embryo quality showed that the CoQ10 group had a higher percentage of Grade I embryos (good-quality embryos) than controls had (65% vs. 42%,  $p=0.01$ ). Furthermore, the percentage of clinical pregnancy following embryo transfer was significantly higher in the CoQ10 group (35%) as compared to the control group (17.5%), and this represents the positive effects of antioxidant therapy on the capability of implantation.

**Table 3: Comparison of Embryo Quality and Pregnancy Outcomes Between Study Groups**

| Outcome                     | CoQ10 Group (n=40) | Control Group (n=40) | p-value |
|-----------------------------|--------------------|----------------------|---------|
| Grade I embryos (%)         | 65.0               | 42.0                 | 0.01    |
| Grade II embryos (%)        | 25.0               | 33.0                 | 0.27    |
| Grade III embryos (%)       | 10.0               | 25.0                 | 0.04    |
| Clinical pregnancy rate (%) | 35.0               | 17.5                 | 0.04    |

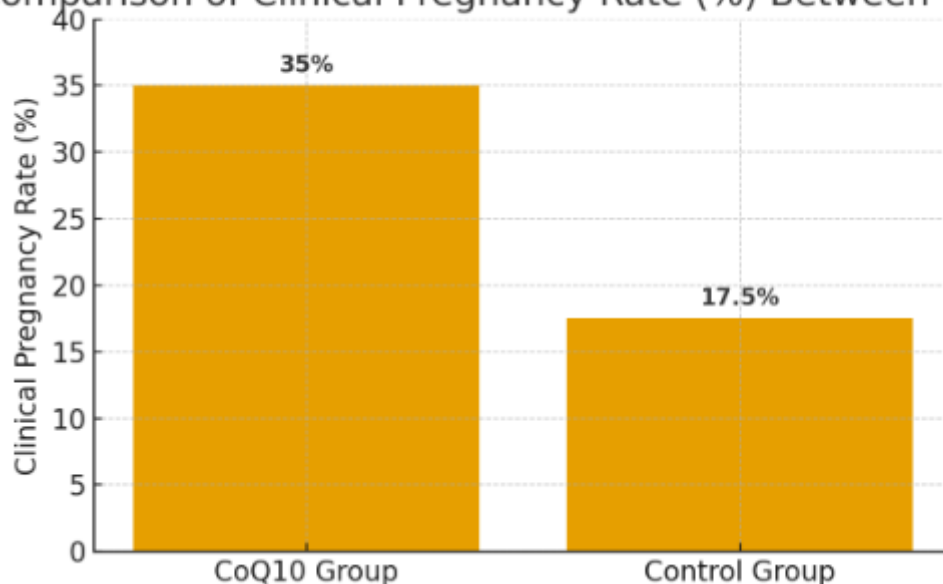
Under laboratory parameters, the CoQ10 group recorded a significant change in serum estradiol (E2) levels on the day of hCG trigger (1890  $\pm$  320 pg/mL) than the control group (1450  $\pm$  290 pg/mL,  $p<0.001$ ). Moreover, the CoQ10 group had more endometrial thickness, which promotes better follicular and endometrial growth.

**Table 4** outlines these hormonal and endometrial findings.  
*Hormonal and Endometrial Parameters on Day of Trigger*

| Parameter                  | CoQ10 Group (Mean $\pm$ SD) | Control Group (Mean $\pm$ SD) | p-value |
|----------------------------|-----------------------------|-------------------------------|---------|
| Serum Estradiol (pg/mL)    | 1890 $\pm$ 320              | 1450 $\pm$ 290                | <0.001  |
| Endometrial Thickness (mm) | 10.8 $\pm$ 1.3              | 9.1 $\pm$ 1.5                 | 0.002   |
| Progesterone (ng/mL)       | 0.85 $\pm$ 0.19             | 0.80 $\pm$ 0.21               | 0.41    |

The graphical representation of the distribution of clinical pregnancy rates between the CoQ10 and control group is given below and indicates a significant change in pregnancy rates of women receiving CoQ10 supplementation.

**Graph 1:** *Comparison of Clinical Pregnancy Rate (%) Between Groups*  
**Comparison of Clinical Pregnancy Rate (%) Between Groups**



(Bar graph depicting higher clinical pregnancy rate in CoQ10 group compared to control)

## Discussion

The findings of this study in terms of improved ovarian response in CoQ10 supplementation are consistent with the meta-analysis by Lin et al. (1) that established CoQ10 pretreatment as having a beneficial effect in terms of increased quality and quantity of retrieved oocytes among women with reduced ovarian reserve undergoing IVF/ICSI. CoQ10 mitochondrial-supported condition might be at the heart of this enhancement since oocytes rely heavily on mitochondrial ATP generation to enhance maturation and fertilization. In addition, the dysfunction of mitochondria has been identified as one of the characteristics of reproductive aging, which is a sign of poor oocyte competence. CoQ10 increases cellular bioenergetic and decreases oxidative stress by refilling mitochondrial coenzyme stores, eventually restoring follicular response. Similar benefits have been recorded when CoQ10 is used together with other fertility-enhancing supplements.

According to Dawoud et al. (2), CoQ10 supplementation in combination with dehydroepiandrosterone sulfate (DHEA-S) has a significant positive effect on fertilization rates and embryo quality in poor responders, which supports a potential synergistic antioxidant and endocrine effect. Likewise, other mitochondrial cofactors, i.e., L-carnitine, have been indicated to have positive effects on ovulatory

and reproductive outcomes as indicated by Abu-Zaid et al. (3). Collectively, these results lend to the potential of mitochondrial function modulators in the restoration of oocyte energy balance and optimum IVF success in women with poor ovarian performance. The importance of early identification and management of women with low ovarian reserve is also strengthened by the current study. As pointed out by Bhide (4), AMH and AFC are two key markers of ovarian reserve that can help clinicians to predict the results of treatment and customize the use of stimulation protocols.

Women with AMH <1.1 ng/mL and AFC <5 in our trial, who received CoQ10 supplementation, demonstrated significant improvements, which might indicate that specific antioxidant treatment can regulate ovarian activity even in the advanced age groups of reproductive age. Although a range of pharmacological and non-pharmacological remedies has been suggested to treat POR, such as estrogen pretreatment (5) and electro-acupuncture (6), the treatment success rate is rather low. The metabolomic observations reported by Potiris et al. (7) also indicate that poor ovarian response is rooted in oxidative stress and metabolic maladaptation. Thus, antioxidant treatments such as CoQ10, which reverse oxidative injury, directly address one of the fundamental pathophysiological processes underlying reduced ovarian reserve. Co-treatment with growth hormone (GH) has been evaluated for its potential to improve ovarian stimulation outcomes. According to Tulkel and Kahraman (8), GH stimulates follicular development and oocyte production, findings similar to those observed in this study with CoQ10 supplementation.

Han et al. (9) established those herbal preparations like the Erzhi Tiangui formula enhanced the response and pregnancy rates of poor responders. The overall outcome of these findings is the rationale to use metabolic and endocrine modulators to enhance outcomes of ART. Besides, Erdoğan et al. (10) discovered that oxidative imbalance, determined by thiol/disulfide ratios, is one of the most important predictors of depleted ovarian reserve. This biochemical data supports the antioxidative effect of CoQ10 to restore reproductive activity. The dietary contribution to the ovarian reserve is also worth considering. According to Ziaei et al. (11), a low-quality diet had a significant relationship with increased risk of reduced ovarian reserve, which implies that oxidative stress caused by nutrient deficiency can hasten follicular depletion. Likewise, Han et al. (12) explained that GH works through overlapping CoQ10 mitochondrial enhancement mechanisms, and this strengthened the correlation between bioenergetic support and better ovarian outcomes.

Although ovarian stimulation protocols, including the GnRH antagonist and the progestin-primed ovarian stimulation (PPOS) regimens, were flexible, Chen et al. (13) found that the results of these approaches were similar, and remaining levels of the intrinsic quality of oocytes were the primary determinant of IVF success. CoQ10 was found to be a key in enhancing the quality of embryos and clinical pregnancy in our study, without any significant change in the dosage of gonadotropin, an observation that could be important in highlighting its effectiveness in enhancing intrinsic oocyte competence. On the same note, the emergent research carried out by Chang (14) suggests the possibility of improving the follicular responsiveness through mechanical ovarian stimulation, but the less invasive and biologically realistic approach is provided by pharmacological antioxidants such as CoQ10. Cumulative live birth rates among women with compromised ovarian reserve have been revealed to be suboptimal after multiple ART cycles (15), whereas using stimulation alone is of limited use in this population.

Interventions that enhance mitochondrial and oxidative activity, e.g., CoQ10, are therefore promising in improving long-term reproductive outcomes. Moreover, the article by Liu et al. (17) revealed that the co-treatment with letrozole increased the follicular output in PCOS women, which is conceptually compatible with treatment options that are designed to stimulate oocyte maturation by optimizing metabolic state. Likewise, Zhang et al. (18) observed no significant difference between fixed and degressive progestin regimens, indicating that the adjunct treatment options, instead of protocol variations, may cause meaningful improvements in outcomes. Generally, our results are aligned with the world literature that underlines the contribution of oxidative stress and mitochondrial dysfunction in reproductive aging and infertility. The oocyte energy metabolism and developmental potential seem

to be improved by CoQ10 as an indispensable part of the electron transport chain and a powerful antioxidant (16).

The high success rates in oocyte retrieval, fertilization rate, embryo quality, and clinical pregnancy experienced in the study indicate that CoQ10 supplementation can be used as a useful, non-invasive, and affordable add-on to IVF protocols in women with low ovarian reserves. Future research needs to be based on bigger multicentric randomized controlled trials to substantiate these results and evaluate the best dosage, length, and timing of CoQ10 administration (18). Furthermore, CoQ10 may be used in combination with other antioxidants or endocrine modulators (DHEA or GH), which may also promote better reproductive health. Introducing lifestyle change, such as improvement of diet and reduction of stress, could also be synergistic with pharmacological antioxidant treatment to enhance fertility rates.

## Conclusion

This was a randomized controlled trial that was carried out at Khaula Hospital, IVF Center, Muscat, and proved that Coenzyme Q10 supplementation showed significant benefits in ovarian response, oocyte maturation, embryo quality, and clinical pregnancy rates in women with poor ovarian reserve undergoing IVF treatment. CoQ10 improves mitochondrial bioenergetics and oxidative stress, which positively influences follicular development and oocyte competence, leading to better reproductive outcomes. The results are in line with the emerging international evidence that mitochondrial-targeted antioxidants can be used as an adjuvant therapy in assisted reproductive technologies. CoQ10 supplementation is a promising adjunct to the traditional stimulation protocols of poor responders due to its good safety record, accessibility, and non-invasiveness. The use of multicenter studies with large populations in the future should be justified to verify these findings, perfect the treatment duration and dosage, and determine possible synergies with other adjuvant treatment methods. The use of CoQ10 in IVF regimens can increase the success rates and provide new hope to women with low ovarian reserve.

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