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**Hiba Sattar Jabbar**  
College of Medicine, Al-  
Muthanna University, Iraq

**Safa Azhar Razzaq**  
College of Pharmacy, Al-  
Muthanna University, Iraq

## Effect of inositol and choline combination in females with polycystic ovary syndrome

**Hiba Sattar Jabbar and Safa Azhar Razzaq**

### Abstract

This metabolic-endocrine disorder is known as polycystic ovary syndrome (PCOS), Hyperandrogenism and anovulation are the most prominent symptoms. There is no known cause for PCOS, but insulin resistance has been associated with the condition, Reproductive and cardiovascular complications associated with glycemic changes. A precursor of phosphorinositides, myo-inositol (MYO) provides energy for cell function, A variety of functions are controlled by these proteins, including cell proliferation. Insulin resistance in PCOS patients is caused by altered inositol-phosphoglycan metabolism. Myo-inositol treatment is recommended based on available evidence together with folic acid, improves metabolic and reproductive outcomes for women with PCOS.

PCOS patients can benefit from the use of MYO based on current knowledge associated with insulin resistance with or without obesity, improving the quality and maturation of oocytes and pregnancy outcomes in this important group of women.

**Keywords:** Choline, inositol, polycystic ovary syndrome, pregnancy outcomes, insulin resistance

### Introduction

There are several types of PCOS, but one of the most common is polycystic ovary syndrome (PCOS). PCOS is characterized by hyperandrogenism and chronic anovulation in perimenopausal women<sup>[1-2]</sup>. An etiology is unknown. A specific population-based study has not yet been performed According to a conservative estimate, this disorder affects 5-10% of women in reproductive age. Based on studies investigating the prevalence of polycystic ovaries, this estimate is based on the upper limit. An ovarian ultrasound examination revealed polycystic ovarian morphology in 20% of self-selected normal Women<sup>[3]</sup>. The endocrine systems of many of these women were abnormal in subtle ways. It is estimated that 3% of women with secondary amenorrhea for 3 months or more have PCOS. This figure is calculated by taking into account that 75% of these women meet diagnostic criteria for PCOS<sup>[4]</sup>. A woman with PCOS may also experience less severe menstrual irregularities<sup>[1, 3, 5]</sup> The Burghen report has been released *et al.*<sup>[6]</sup> in 1980. There has been increasing evidence that PCOS is associated with metabolic and reproductive complications in addition to hyperinsulinemia. In addition to this association, extensive research has also been conducted on the relationship between insulin and gonadotropins<sup>[1, 7]</sup>. In turn, As a consequence of this association, insulin sensitizing agents such as inositol have been used to treat women with PCOS<sup>[7]</sup> Humans require choline as an essential nutrient, as it performs various functions in the body<sup>[8]</sup>. Patients with PCOS had significantly lower levels of choline in both plasma and follicular fluid<sup>[9-10]</sup>, Women with this disorder suffer from an imbalance of several metabolites in their blood, resulting in reduced fertility<sup>[9]</sup>. As a consequence, choline might become an important regulator of ovarian function in the long run. There is, however, no information about how dietary choline affects the ovarian system or ovulation. In this study, inositol and cholin were assessed for their effects on ovarian function in women with PCOS and oligomenorrhea. Improvement of endogenous gonadotropin response with insulin-sensitizing drugs, Decrease hyperandrogenemia and optimize menstrual cyclicality, The medication may be able to reverse PCOS-associated anovulation due to hyperinsulinemia<sup>[11]</sup>. To increase our understanding of PCOS' complex pathogenesis, this manuscript focuses on the latter concept.

### Patients and Methods

#### Patients

In PCOS, ovarian morphology is associated with menstrual disturbances as well as characteristic ultrasound features. High androgen levels and hyperandrogenism.

**Correspondence**  
**Hiba Sattar Jabbar**  
College of Medicine, Al-  
Muthanna University, Iraq

Amenorrhea and PCOS patients with oligomenorrhea (Cycle length 41 days; 8 cycles each year), Outpatient clinics offering gynecology, endocrine, and infertility services recruited patients less than 35 years of age. A hyperprolactinemia patient with an abnormal thyroid function test, and An adrenal hyperplasia congenital at birth was excluded. The ovarian appearance and follicle count were assessed during the transvaginal ultrasound at cycle day 2 and There was a diagnosis of polycystic ovaries among the patients, and they were taking medications that may affect the hormonal profile. The diagnosis was based on the assumption that most patients suffered from this condition. An individual who exhibits elevated androgen activity, signs of hyperandrogenism, or both would fall within this group [12]. Blood samples were aspirated about 8:00 and 11:00 a.m. In clear plastic tubes, about 10 ml are given to each patient on cycle day 2 Before centrifuging the serum sample for 10 minutes, let the samples sit for 15 minutes at room temperature, A clinical monitoring program that measures FSH, LH, E2 and prolactin levels.

### The role of Choline and inositol in PCOS

Lipotropic amine choline has a variety of functions in the body and has been called a human essential nutrient [8]. In most mammals, choline plays a critical role in normal physiological function which causes liver disorders if choline deficiency is present, Memory, growth, kidneys, and pancreas [13]. Choline is also essential for the synthesis of acetylcholine. Which neurotransmitter is primarily responsible for regulating smooth muscle contractions. Choline is also linked to fertility and fetal growth. As a result of a gradient in concentration, choline is pumped into the fetus while in utero, with choline levels in the amniotic fluid being ten times higher than those in the mother's blood, [14]. In addition, there is a fourfold higher mortality rate associated with abnormalities in neural tube development. Fetuses whose mothers are in the lowest choline intake quartile are ten times more likely to be exposed to choline in the amniotic fluid than those whose mothers are in the highest choline intake quartile [15]. Both plasma and follicular fluid choline levels were considerably lower in PCOS patients compared to controls [9, 10]. One of a group of metabolic diseases characterized by abnormalities in serum levels of metabolites, thus leading to a decline in fertility among affected women [9]. This provides more evidence that choline may play a general role in controlling ovarian activity. The role of dietary choline in ovarian maturation and ovulation is, however, not well understood. However, the function of dietary choline in ovarian development and ovulation is poorly understood [16, 17]. The role of dietary choline in ovarian maturation and ovulation, however, remains obscure. Function as mediators of insulin resistance in polycystic ovary syndrome [18]. Both basic research and clinical trials have described the physiological significance of inositol derivatives in gametogenesis and human reproduction, which has led to further exploration of their probable applicability in assisted reproduction techniques [19]. The pathophysiology of polycystic ovary syndrome (PCOS) has been connected to an increase in insulin resistance and hyperinsulinism, which in turn leads to various changes in MYO - inositol signaling pathways

that affect ovarian steroidogenesis. MYO- inositol has been shown to improve oocyte quality and regulate menstrual cycles in patients with PCOS, and both MYO- and regular inositol are insulin-sensitizing medications. It may have favourable impacts in reproductive terms via many pathways such as improved insulin sensitivity, increased ovulation, and decreased oxidative stress in follicular fluid. [19, 20]. Patients with polycystic ovary syndrome (PCOS) who took 2 grams of myo-inositol every day for three months showed statistically significant increases in the number of oocytes recovered during egg retrieval and the size of follicles identified by transvaginal ultrasound as being greater than 15 millimeters in diameter. In the same study, the average number of immature oocytes decreased significantly after being treated with MYO- inositol [21]. Similar improvements in ovarian function were observed in another randomized investigation, with the MYO- inositol group showing significantly improved frequency of ovulation and time to first ovulation and a greater and earlier effect on follicular development, which lined up with the elevation in estradiol levels that was seen in the blood during the first week of treatment. Positive metabolic alterations were also documented in MYO- inositol-treated patients, including an increase in high-density lipoproteins and considerable weight loss; however, no changes were reported in fasting blood glucose or insulin response to an oral glucose tolerance test [22]. MYO-inositol given prior to hormone stimulation improves oocyte and embryo quality in PCOS women undergoing assisted fertilization [19, 21, 23], rate of confirmed pregnancies [24]. In turn, follicular fluid of women with PCOS is characterized by a substantial fall in the concentration of MYO- inositol, in combination with greater insulin resistance [25], indicating oocytes may not be able to mature normally due to a lack of MYO- inositol in the immediate area. It has been theorized that MYO-inositol's positive effects on oocyte quality are at least in part attributable to its ability to promote cellular glucose uptake, which in turn meets the energy requirements of the ovary, also due to its role in calcium release stimulation and response to follicle stimulating hormone-mediated signaling. This process ensures that germ cells develop normally [19]. Genazzani *et al* findings provide substantial evidence for the concept that reduced epimerase expression/function is a hereditary propensity in people with diabetes and PCOS who have a family history of diabetes. It is hypothesized that the compensatory hyperinsulinism seen by these patients, especially the normal weight ones, is due to the decreased activity of a certain endocellular enzyme in these women. To keep metabolic balance and play a beneficial compensatory function, MYO- inositol administration is warranted in women with polycystic ovary syndrome and hyperinsulinemia [26, 27].

### Results

The results of this study show that there is decrease in the levels of LH, Total testosterone and prolactin in PCOS female after three months of treatment while there is increment FSH level. The patients follow the direction to decrease their body weight and there is reduction in their weight.

**Table 1:** Shows parameter, baseline value and after inositol and choline

Parameter	Baseline Value (Mean± SD)	After Inositol and Choline (Mean ±SD)
Age (years)	26.8±5.8	
Weight (KGs)	92.3±17.8	90.8±16.8
Total testosterone (nmol/L)	3.1±1.2	2.6±0.9
FSH (IU/L)	4.8±5.3	6.2±4.6
LH (IU/L)	9.6±6.8	8.6±7.2
Prolactin (ng/ml)	55±4.8	40±6.2

## Discussion

Polycystic ovarian syndrome is one of the endocrine disorders that most commonly occur in female in reproductive age and approximately affecting 5-20% of them. Oligo-ovulation or anovulation and hyperandrogenism are of PCOS signs. It also linked to high risk of occurrence of type 2 diabetes, cardiovascular disease and endometrial cancer. Most PCOS female have insulin resistance which represents the pathogenic link between metabolic and reproductive disorders in PCOS female both obese and female with normal weight [28]. This study was initiated to investigate the effect of inositol and choline combination in females with polycystic ovary syndrome. Inositol is an insulin second messenger, and its deficiency contributes to the various symptoms of PCOS [29]. The results of this study is in agreement with Luma *et al* (2015) who used cholin & inositol plus metformin in the treatment of patients with PCOS showing that there is significant decrease in BMI [30]. Also the result of this study in agreement with Papaleo *et al*. [31] which applied on 25 women with PCOS who have oligo or amenorrhea since childbearing age and show that there is decrease in menstrual cycle irregularity and decrease in serum free testosterone level after 6 months treatment with Myo-inositol + folic acid two times daily. Genazzani *et al*. [32] show that circulating LH, PRL and insulin level decreased in PCOS female after 12 weeks of treatment.

## Conclusions

The administration of MYO- inositol is indicated in women with polycystic ovarian syndrome and hyperinsulinemia in order to maintain metabolic balance and play a favorable compensatory role. Evidence suggests that MYO, a chemical produced from inositol, can improve oocyte quality and maturation, reproductive prognosis, and other metabolic hazards in women with polycystic ovary syndrome (PCOS) who are either overweight or obese and have insulin resistance and hyperinsulinemia. Continuing treatment also resulted in significant weight loss, suggesting that non-obese PCOS women with hyperinsulinemia may be an interesting group of patients for potential treatment with isomers of inositol like MYO. Inositol's positive benefits in PCOS women provide credence to the nutrient's potential therapeutic significance. It will take further large-scale randomized research to identify effective dosing and treatment duration. In conclusion, we show that choline supplementation aids in the maturation and ovulation of the female reproductive system. This is the first *in vivo* study to assess the effect of choline supplementation on ovarian maturation and function. Findings from the present study provide credence to the hypothesis that choline supplementation improves fertility and provide new perspectives on the potential utility of this nutrient for enhancing sexual performance.

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