



## Original Article

# Assessment of Obese and Non-Obese Impacts on Fertility Treatments in Adolescence Women with Polycystic Ovary Syndrome

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### ABSTRACT

**Background:** Polycystic ovary syndrome (PCOS), which is considered as one of the important gynaecological endocrine disorders, usually affects 6-10% of the women population. The present work described the effect of obese and non-obese on fertility treatment practices in polycystic ovary syndrome affected women populations.

**Materials and Method:** About 105 PCOS affected women patients (18-41 years old) along with control who had regularly visited the hospital for fertility treatment were selected for the present study and clinical experiment was performed. The PCOS affected population was classified into two groups based on their Body Mass Index (BMI) as obese and non-obese PCOS affected groups and the clinical and biochemical aspects were studied.

**Results:** There was a significantly higher rate of BMI was noticed in obese PCOS patients ( $29.32 \pm 0.40$ ) than non-obese PCOS ( $21.75 \pm 0.36$ ) and control group ( $21.95 \pm 0.97$ ). The level of Luteinizing Hormone (LH) was found to be high in the non-obese PCOS group than the obese PCOS while a decreased rate of FSH noticed was more in obese PCOS group than non-obese group. The frequency of positive pregnancy was significantly high in obese groups (66.7%) than non-obese group with IVF treatment.

**Conclusion:** It is concluded that higher level of BMI and LH was noticed in PCOS groups compared to non-obese and a decreased rate of FSH was recorded in PCOS patients. The results of the present investigation confirm that the impact of obesity and non-obesity on PCOS women fertility treatment showed higher pregnancy rates in women compared with normal BMI. Of the two groups tested, a significantly higher per cent of pregnancy was recorded with obese PCOS than non-obese PCOS patients.



## Introduction

Polycystic ovary syndrome (PCOS) or Stein-Leventhal syndrome is considered to be the most important endocrine disorder in the reproductive age of women<sup>1,2</sup>. The incidence of PCOS affects teens metabolism that are having serious implications with health care<sup>3</sup>. The clinical manifestations of PCOS include menstrual irregularities, hyperandrogenism with hirsutism, acne, alopecia, truncal obesity and multiple ovarian follicular cysts<sup>4</sup>. The significant endocrine abnormalities caused by PCOS includes Leutinizing Hormone (LH) hyper secretion, decreased follicle stimulating hormone, alterations of the Gonadotropin-Releasing Hormone (GnRH) pulse generator and ovarian stromal-thecal hyperactivity that leads to major biochemical, reproductive and metabolic dysfunction<sup>5</sup>.

It has been reported that about 40-50% PCOS affected women are overweight or obese, presented with high insulin levels and reduced glucose-induced insulin metabolism<sup>6</sup>. Also both thin and obese women with PCOS, were found to be insulin resistant reflected by fasting glucose/insulin ratio<sup>7</sup>. The major consequences of obesity on health include infertility, menstrual problem and maternal defects in pregnancy<sup>8</sup>. It has been noticed that nearly 65% of PCOS patients are obese and pregnancy is severely affected by obesity, overweight or elevated body mass index among women population. Obese women are also associated with high chance of miscarriage after fertility treatment due to less number of oocytes release<sup>9</sup>. Therefore, a new worldwide threat to adolescence is obesity and its serious concern is onset of PCOS.

Many adolescent women with PCOS do not ovulate regularly and takes longer time for the women to conceive. The PCOS event has been increased recently and the age of onset of PCOS is getting early<sup>10</sup>. Regardless of PCOS incidence, earlier results indicated that pregnancy

achievements are affected much by obesity<sup>9</sup>. Most of the earlier studies suggested that obesity is the major cause for onset of PCOS in women population. However, few reports have demonstrated the relationship between PCOS and BMI. Wang and Zhu<sup>10</sup> reported that obesity is not the only criteria for onset of PCOS in Asian race. In addition there are few published reports that showed contradictory findings for PCOS in recent past. Earlier study suggested that modest weight loss of 5% (non-obese) has proved to result in increased percent of hyperandrogenism and ovulatory function in PCOS women patients. Further, it is suggested that adiposity is also playing an important role not only for the onset but also for the maintenance of PCOS in women population. It is hypothesized that adolescent women population with PCOS may partly depending on ever increasing prevalence of obesity worldwide. It is pointed out that though the obesity has prominent effects on regulation of reproductive cycles in women with PCOS, the exact mechanisms for onset of PCOS are not fully identified. The most recent study showed that metabolic and sex hormones levels were found to be high in obese PCOS women compared with non-obese PCOS women<sup>11</sup>. Although, there are reports on development and maintenance of PCOS, there is still a shortage of studies pertaining to obesity and non-obesity impacts on fertility treatments in PCOS women patients especially in our region. In view of the above, the present investigation was focused to find out the impacts of obese and non-obese on fertility treatment and to determine the rate of pregnancy apart from biochemical assessments in women patients with PCOS.

## Material and Method

This study was performed on adolescence women with PCOS who had visited the gynecological outpatient department of J. S. hospital, Salem. The study methodology was approved by the institutional review board of the hospital. About 105 adolescent women patients were tested for identification of PCOS incidence by ultrasonography. They were classified into two groups depending on their Body Mass Index (BMI): 62 obese (ward A) and 43 non-obese (ward B) women patients. Further, 30 healthy non-obese, normal women were included as control (ward C). The adolescence women patient for the diagnosis of PCOS was followed the revised Rotterdam criteria. The patients must have at least 2 out of the following 3 criteria: 1) hyperandrogenism, 2) oligomenorrhea /or amenorrhea, and 3) presence of polycystic ovary found in ultrasound. Any kinds of medications that will affect sex hormone levels or carbohydrate and lipid metabolism were terminated a month before the experiment. All women patients selected for the present PCOS diagnosis were in good health conditions.

The clinical parameters namely height and body weight were measured on the morning of testing. Blood pressure was also measured. The Body Mass Index (BMI) was calculated using the formula: Weight in Kilograms/Height in m<sup>2</sup>. Body mass index with body fat as Standard Consensus Statement for Indian population was considered, for obese : >25kg/m<sup>2</sup> and <25kg/m<sup>2</sup> for non-obese PCOS patients as cut off for BMI<sup>12</sup>.

The biochemical parameters for the study groups were performed in the hospital laboratory. Two PCOS groups (ward A and ward B) as well as the control women (ward C) were examined for the basal gonadotropic hormone levels such as Follicle Stimulating Hormone (FSH),

Luteinizing Hormone (LH) and Prolactin (PRL). The blood samples were collected on the day 2 or 3 of their menstrual cycles by venipuncture and stored in plain vacutainers. The clotted blood was centrifuged and the separated serum was analyzed using autoanalyser by the Immunofluorescent assay technique (Johnson & Johnson S.P. A-Ortho Clinical Inc.).

Both obese and non-obese PCOS women patients were placed on metformin tablets 500mg b.d. before the commencement of pituitary down regulation. Both IVF and IUI treatments were proceeded by down regulation from the mid-luteal phase of the previous menstrual cycle. Ovulation stimulation was performed by FSH using the standard protocol. When at least one or two follicle had reached a minimum diameter of >18mm, ovulation was achieved with HCG (10,000 IU). Oocytes were aspirated within 36-38 hour after induction of ovulation by guidance of transvaginal ultrasound. Patient weight and height data were taken in attention at the time of oocyte retrieval and BMI was calculated. The collected oocytes were fertilized *in vitro* by IVF. Gamete handling, fertilization and embryo culture were carried out according to the Standard IVF protocol. The collected fast moving sperms were then injected into the mother's womb by IUI method using standard procedure. An ultrasound scan was conducted 4-6 weeks later to test the viability of pregnancy. The pregnancy percent was compared between the two PCOS groups with IVF/ and IUI treatments. Main outcome measures that reflect IVF/IUI treatments were defined as positive pregnancy, negative pregnancy and miscarriage.

The result obtained for clinical as well as biochemical parameters and fertility treatments were used for statistical analysis. The mean, percentage and standard error of

the clinical and biochemical measurements were calculated for all the data obtained from both the PCOS affected patients (obese and non-obese) and the control group selected for the present study. The rate of pregnancy obtained in the fertility treatment among the obese PCOS and non-obese PCOS groups along with their percentage of miscarriage was expressed as percentage. Data were presented as mean  $\pm$  SE and Student 't' test was applied to identify the differences between two wards.

## Results

About 105 PCOS affected adolescent women patients (obese: 62 and non-obese:43) were selected for the present study. Clinical data for obese, non-obese PCOS women patients and healthy non-obese control women patients are depicted in Table 1. The present results revealed that the non-obese groups was similar in age while the mean age of obese PCOS women patients was significantly higher when compared to non-obese PCOS patients and non-obese healthy (control) women population. The BMI rate was found to be significantly higher in obese PCOS patients compared to the control group. It is interesting to note that the BMI was alike in both non-obese PCOS and non-obese control groups (Table 1).

The biochemical parameters are illustrated in Table 2. The BMI rate was negatively linked with basal FSH level in PCOS women patients than that of control population. Furthermore, obese PCOS women with a BMI of 29.3kg/m<sup>2</sup> had a significantly lower level of FSH (6.2mIU/ml) compared to non-obese women with a BMI of 21.7kg/m<sup>2</sup>. The rate of LH was found to be high in PCOS women patients. When compared with obese PCOS women patients, the LH level was more in non-obese PCOS women patients compared with the control (non-obese). In the case of

Prolactin (PRL), obese PCOS women had lower level of PRL compared with non-obese PCOS women patients.

Further, menstrual irregularities recorded were significantly elevated among PCOS women patients than control. However, there was a significant increase in the rate of menstrual irregularities in obese PCOS patients when compared with non-obese PCOS patients. Of the two PCOS groups, a significantly higher per cent of hirsutism (68.2%) was noticed in obese PCOS women but less in non-obese patients compared with control. The rate of oligomenorrhea was increased greatly in obese PCOS patients (87.77%) when compared to the non-obese PCOS patients.

The outcome of the fertility treatment on pregnancy and miscarriage rate in obese and non-obese PCOS women patients is depicted in Table 3. In the present study, three types of treatments namely 1) Medication mediated, 2) Intrauterine Insemination (IUI) and 3) *In vitro* Fertilization (IVF) were adopted. In the case of obese PCOS patients, the level of positive and negative pregnancy recorded was 17% and 64.4% respectively and the percent of miscarriage was 17.8% with medication treatment. After IUI treatment, about 36.4% obese PCOS women patients were achieved positive pregnancy, while the negative pregnancy rate recorded was 45.5% and nearly 18.1% patients had met miscarriage. Among the three treatments, a maximum percent of positive pregnancy (66.7%) was noticed with IVF treatment followed by similar rate of negative pregnancy (16.7%) as well as miscarriage (16.7%) in obese PCOS patients (Table 3). Maximum rate of positive pregnancy (50%) was observed in non-obese PCOS patients with IVF treatment followed by IUI and medication mediated treatments. Results clearly showed that highest percent of negative pregnancy obtained was 65.7 and

50% for medication and IUI as well as IVF respectively whereas about 14.7 and 16.7% of miscarriage was noticed with medication and IUI treatments respectively.

## Discussion

The current investigation was focussed to assess the impact of obesity and non-obesity on fertility treatments in adolescence women patients with PCOS and compared the results between PCOS patients (obese PCOS and non-PCOS) and normal non-obese without PCOS women (Control). Further, we compared the present results with earlier findings published. Although there are reports on obese and non-obese PCOS women patients, the current study has several advantages: 1) obese and non-obese PCOS subjects were compared along with non-obese without PCOS normal control for the influence of BMI on FSH, LH and Prolactin in both groups on fertility, 2) the major concern is that the percentage of pregnancy could have influenced in both obese PCOS and non-obese PCOS by adaptation of different fertility treatments. It is well understood that PCOS along with an adverse metabolic and reproductive disorder profile is a complicated disease with symptoms such as insulin resistance, oligo/anovulatory menstrual cycles, hyperandrogenism, hirsutism and obesity that leads to infertility, cardiovascular risk factors, type 2 diabetes and endometrial cancer<sup>13</sup>.

In the current study, the PCOS affected women populations were diagnosed using the Rotterdam norms for the characterization of oligoanovulation, biochemical, or clinical hyperandrogenism and polycystic ovarian ultrasound morphology. The study population was separated into two groups based on their BMI as obese PCOS (ward A) and non-obese PCOS (ward B) women patients along with the healthy non-obese without PCOS

control (ward C). When compared with the obese PCOS group, the non-obese PCOS and non-obese control group did not exhibit any significant difference by age. Similarly, Beydoun *et al*<sup>9</sup> had reported that PCOS patients and non-PCOS control were found to be almost same in the age group. With regard to BMI, both the control and non-obese PCOS groups had similar BMI, whereas the obese PCOS group had significantly higher level of BMI. Similar results were also reported in the previous study where the non-obese PCOS and control BMI was found to be the same when compared with the obese PCOS group<sup>10</sup>. It is reported that the development of hyperandrogenism was found to be high in obese with PCOS women populations<sup>14</sup>. It was observed that the obese women with PCOS had significantly increased proportion of hirsutism and oligomenorrhea when compared with non-obese PCOS women patients and the control in the present study. Gambineri *et al*<sup>15</sup> also reported that obese women with PCOS exhibited a higher proportion of hirsutism and menstrual irregularities than the normal weight women. Previous studies have reported that obesity not only plays an important role in the development of PCOS, but also it increases the rate of hyperandrogenism in PCOS patients<sup>16</sup>.

The present study analysed the level of gonadotropic hormone in both the obese and non-obese PCOS affected women populations along with the control non-obese healthy women. The results indicated that the level of FSH was found to be low in the PCOS affected women patients compared with the non-PCOS control. As expected the LH level was increased in PCOS patients than non-PCOS healthy control. Feuser *et al*<sup>17</sup> observed that an increased level of LH, LH:FSH ratio, PRL was recorded in PCOS patients compared to the non-PCOS groups. The most recent

report indicated that FSH level was found to be low in obese women patients when compared with non-obese women patients<sup>11</sup>. The present study strongly suggested that both the LH and prolactin sex hormones were found to be significantly increased in PCOS affected women group than non-PCOS control group, where as a decreased rate of FSH was recorded in PCOS affected women patients compared with healthy women population. Further it is interesting to note that the rate of FSH sex hormones was declined more in obese PCOS patients compared with non- obese PCOS groups. It has been found that FSH plays an important role in the regulation of oogenesis, follicle development and gametogenesis and their decreased rate can result in the failure of pregnancy<sup>18,19</sup>. It is known that higher rate of BMI in obese women leads to abnormalities/ changes in the level of various sex hormones especially FSH and LH. As expected the rate of FSH was found to be low in obese PCOS women patients in this study. These results together suggested that low level of FSH in PCOS affected women patients was ultimately resulted the loss of pregnancy. According to the earlier report, elevation of LH causes excess androgen production and ovarian cyst formation that affects the rate of pregnancy in PCOS women population. The present study reveals that the level of LH was found to be significantly higher in both obese and non-obese PCOS groups when compared to the FSH levels along with the control. Similar results were also reported by Rajitha *et al*<sup>20</sup> who observed higher rate of LH in the PCOS group compared with the control.

In order to achieve the pregnancy in PCOS affected women groups, different fertility treatments were adopted and the effect of obese and non-obese PCOS groups on pregnancy undergoing fertility treatment was also investigated. Initially, both obese PCOS and non-obese PCOS patients were

treated with medicine for pregnancy. After few cycles of medication mediated fertility treatment, pregnancy failure patients were continued with IUI methods followed by IVF treatments. With regard to the obese PCOS women patients, a higher rate of positive pregnancy was obtained from the IVF method than the IUI or medication methods. The results obtained from the present study have been supported with the evidence that obesity in PCOS has been connected to the delayed response or failure of ovulation drugs or gonadotropins<sup>21,22</sup>. However, when obese and non-obese PCOS groups were compared, there was a significant reduction in pregnancy levels in non-obese PCOS groups. Therefore the pregnancy rate was depending upon the effect of obese and non-obese PCOS women patients. It is reported that the high rate of hypertension was noticed to be greatly linked with the development of obesity among women populations<sup>23</sup>. However, Sneed *et al*<sup>24</sup> reported that BMI does not affect the IVF fertility treatment. Al-Azemi *et al*<sup>25</sup> also demonstrated that ovulation induction with drugs in PCOS patients was severely affected by obesity. Huang *et al*<sup>26</sup> demonstrated that lean PCOS groups had higher rate of pregnancy than obese PCOS phenotypes in Chinese women populations. Most recent study indicated that obese PCOS patients had less percent of infertility treatment compared with non-obese PCOS phenotypes<sup>27</sup>. The present study also confirmed that the level of miscarriage percentage was found to be more in obese PCOS group than non-obese PCOS group during the treatment.

## Conclusion

In summary, the present study demonstrated the effect of obese and non-obese PCOS on fertility treatment were correlated with BMI as well as sex hormones levels in pregnancy achievement

with PCOS affected women patients. Among the three fertility treatments, IVF method appeared to be the best one for achievement of increased rate of positive pregnancy in both obese and non-obese PCOS patients followed by IUI and medication method. Results strongly showed that BMI appeared to have a significant impact on IVF treatment in PCOS patients. The results of the present findings confirm that the impact of obesity and non-obesity on PCOS women fertility treatment that showed positive effect on clinical pregnancy rates in women with high compared with normal BMI.

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### Conflict of Interest

The authors declared no conflicts of interest in this experiment

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Nil

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**Table 1.** Comparison of the clinical characteristics of the PCOS affected two women populations along with Control

Variables	Obese PCOS (ward A)	Non-Obese PCOS (ward B)	Control (Non-obese) (ward C)
Age(years)	27.25±0.61* (18-41 years)	25.53±0.67 (18-41 years)	25.33±1.20 (18-41 years)
Height(m <sup>2</sup> )	155.25±0.74	155.25±0.90	156.33±0.33
Weight(kg)	69.79±1.13**	52.55±1.06**	53.66±2.33
BMI(kg/m <sup>2</sup> )	29.32±0.40**	21.75±0.36**	21.95±0.97
ML(years)	5.96±0.53	4.84±0.57	4.33±0.33
Oligomenorrhea	87.77 ± 1.03*	75.9 ± 1.27*	0
Hirsutism	68.20 ± 1.607*	48.13 ± 1.867*	0

Values represented as mean ± SE. Body Mass Index (BMI) expressed as <25kg/m<sup>2</sup> for non-obese PCOS and >25kg/m<sup>2</sup> for obese PCOS patients. ML = Married Life Duration.

\*P<0.05 compared with other two groups

\*Significant at p<0.05% level (Student's t' test)

\*\*Significant at p<0.01% level (Student's 't' test)



**Table 2.** Gonadotropic Hormone levels studied during follicular phase among three populations

Variables	Control (Non-obese)	Obese PCOS	Non-obese PCOS
FSH(mIU/ml)	7.17±1.77	6.22±0.28	6.66±0.30
LH(mIU/ml)	4.75 ±1.22	8.64±0.75**	9.36±0.85**
PRL(ng/ml)	21.01±4.28	23.47±1.80*	25.79±1.81*

FSH = Follicle Stimulating Hormone, LH = Leutinizing Hormone, PRL = Prolactin

\*Significant at p<0.05% level (Student's 't' test)

\*\*Significant at p<0.01% level (Student's 't' test)

**Table 3.** Fertility rate of the study group expressed in percentage by the mode of Ovulation Induction, IUI and IVF methods

Treatment Mode	Obese PCOS (%)			Non-obese PCOS (%)		
	Positive pregnancy	Negative pregnancy	Miscarriage	Positive pregnancy	Negative pregnancy	Miscarriage
Ovulation Induction by medication	17.8	64.4	17.8	20.0	65.7	14.7
Intra-Uterine Insemination (IUI)	36.4	45.5	18.1	33.3	50.0	16.7
<i>In vitro</i> Fertilization (IVF)	66.6	16.7	16.7	50.0	50.0	0.0