

PRESCRIPTION PATTERN IN OBESE AND NON-OBESE INFERTILE WOMEN WITH POLYCYSTIC OVARY SYNDROME IN A TERTIARY CARE HOSPITALASHA AVIRAH MM^{1*}, ASWATHY ALIAS¹, MANJUSHA SAJITH¹, VANDANA NIMBARGI², SHIVHAR KUMDALE¹¹Department of Clinical Pharmacy, Bharati Vidyapeeth Deemed University, Poona College of Pharmacy, Pune, Maharashtra, India. ²Department of Obstetrics and Gynaecology, Bharati Hospital and Research Centre, Pune, Maharashtra, India.
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ABSTRACT

Objective: The objective of this study is to evaluate the treatment options for the management of obese and non-obese infertile women with polycystic ovary syndrome (PCOS).

Methods: A prospective observational study was conducted with 75 infertile PCOS women. The demographic details, body mass index, menstrual patterns, and current medication related to infertility were noted. The collected data were statistically represented in terms of range, frequency tables, and standard deviation wherever appropriate.

Results: A majority of the infertile PCOS women were aged 24–27 years with a mean age of 25.72±3.53 years, belonging to middle socioeconomic class (44%) and mostly found to be urban residents 68%. Most of the PCOS women were overweight (32%) and obese (21%) with irregular menstrual pattern (90.67%). In combination therapy, clomiphene citrate (CC) pre-treated with oral contraceptives (OC) (37.93%) was mostly given to obese PCOS patients followed by CC with metformin pre-administered with OC (31.03%), while on-obese PCOS patients were mostly administered CC with gonadotropins pre-treated with OC (44%). In single therapy, OC was mostly administered to both non-obese (90%) and obese PCOS patients (88.90%).

Conclusion: This study concluded that most of the infertile PCOS women were overweight and obese, a major risk factor causing hyperandrogenicity. CC pre-treated with OC and metformin with CC pre-treated with OC were mostly prescribed to obese PCOS patients. Lifestyle modifications along with treatment are strongly recommended, especially in obese PCOS patients.

Keywords: Polycystic ovary syndrome, Overweight, Obese, Oral contraceptives, Clomiphene citrate, Metformin.

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INTRODUCTION

Polycystic ovary syndrome (PCOS), one of the leading causes of infertility known today, is a as oligomenorrhea, amenorrhea, hirsutism, acne, alopecia, and obesity [1].

PCOS has a prevalence of 5–10% in women of childbearing age with variance among races, ethnicities, and geographical areas [2,3]. The highest reported a prevalence of 52% has been among the South Asian immigrants in Britain, of which 30–75% were obese [4]. Obesity is known to worsen the clinical, endocrine, and metabolic features of the syndrome by increasing insulin resistance and hyperinsulinemia and further causing hyperandrogenicity [5-7].

Management of PCOS in infertile women is mostly individualized and symptom oriented. The main objectives are to reinstate normal menstrual and ovulatory cycle along with fertility in terms of conception, to treat acne, hirsutism, and infertility, and to prevent weight gain and endometrial carcinoma. Currently, the commonly used regimens are clomiphene citrate (CC), metformin, oral contraceptives (OC), gonadotropins, and laparoscopic ovarian drilling (LOD); a minimally invasive surgery [8].

In today's era, infertility due to PCOS is becoming more common mainly because of their unhealthy lifestyle habits such as sedentary habits and junk food and many other unknown reasons. This study aimed at determining the treatment options in the management of PCOS in obese and non-obese women with infertility. Therefore, it is hoped that the findings from this study will enable us to determine the different

therapeutic options for PCOS in our locality since there is a paucity of knowledge in the provision of such care in our environment.

METHODS

A prospective case-control observational study was conducted in Bharati Hospital and Research Center Pune, Pune, over 9 months from August 2016 to April 2017 which included 75 infertile PCOS women.

The study was approved by the Institutional Ethics Committee, and before initiating the study, informed consent was taken from all patients participating in the study. Women of reproductive age (20–39 years) who are attending or admitted with complaints and symptoms suggesting PCOS leading to infertility were included in the study.

The details such as age, employment status, socioeconomic status, area of residence, body mass index (BMI), menstrual history, past medical history, past medication history, and current medication (number of medications, dose regimen, and frequency) related to infertility were noted from the fertility outpatient department (OPD) case paper sheets in the self-pre-designed patient profile form. Socioeconomic class and employment status were determined based on patient's education, husband's occupation, and monthly income. The BMI was calculated based on the height and weight revealed in the fertility OPD case sheets.

The collected data were analyzed for the various treatment options in obese and non-obese PCOS infertile women. The data were statistically represented in terms of range, mean, frequency tables, and standard deviation wherever appropriate.

RESULTS

Sociodemographic characteristics in infertile women with PCOS

Of 75 PCOS infertile women studied, most of the women were aged 24–27 years with a mean age of 25.72±3.53 years. Majority of the PCOS women were found to be housewives (61.33%), from a middle socioeconomic class (44%), and mostly residing in urban areas (68%) (Table 1).

Menstrual pattern, duration of infertility, and types of infertility in infertile women with PCOS

Table 2 presents that most of the infertile PCOS women were having irregular menstrual pattern (90.67%) with an average duration of infertility ≤2 years (77.33%). Primary infertility was most common type of infertility seen in PCOS women (22.67%).

BMI of infertile women with PCOS

Fig. 1 describes that most of the infertile PCOS women had obesity (53%) wherein 32% were overweight and 21% obese. 35% of the women had normal weight.

Frequencies of treatments used in the management of non-obese and obese infertile women with PCOS

Majority of the non-obese PCOS women were administered with OC (97%), followed by CC (65.71%) and gonadotropins (42.86%), whereas most of the obese PCOS women were given diet and exercise (100%), followed by OC (90.00%), CC (72.50%), metformin (27.50%), and LOD (10%) (Fig. 2).

Prescription pattern in non-obese and obese infertile women with PCOS

Table 3 describes that, of 75 PCOS patients in this study, 54 patients were given combination therapy (72.00%) while only 19 patients were

Table 1: Sociodemographic characteristics in infertile women with PCOS

Characteristics	Number of PCOS patients (n=75)
Age (years)	
20–23	20 (26.67)
24–27	33 (44.00)
28–31	15 (20.00)
32–35	7 (9.33)
36–39	0
Socioeconomic class	
Middle	33 (44.00)
Low	25 (33.33)
High	17 (22.67)
Employment status	
House wife	46 (61.33)
Employed	29 (38.67)
Area of residence	
Urban	51 (68.00)
Rural	24 (32.00)

PCOS: Polycystic ovary syndrome

Table 2: Menstrual pattern, duration of infertility, and types of infertility in non-obese and obese women with PCOS

Parameters	Number of PCOS patients (n=75)
Menstrual cycle	
Irregular	68 (90.67)
Regular	7 (9.33)
Duration of Infertility	
≤2 years	58 (77.33)
More than 2 years	17 (22.67)
Types of infertility	
Primary	51 (68.00)
Secondary	24 (32.00)

PCOS: Polycystic ovary syndrome

given single therapy (25.33%). In combination therapy, CC pre-treated with OC (37.93%) was mostly given to obese PCOS infertile patients followed by CC with metformin pre-administered with OC (31.03%). Non-obese PCOS infertile patients were mostly administered CC with gonadotropins pre-treated with OC (44%). In a single therapy, OC was mostly administered to both non-obese (90%) and obese PCOS infertile patients (88.90%).

DISCUSSION

In this study, most of the infertile PCOS women were aged 24–27 years (29.33%) with a mean age of 25.72±3.53 years. However, in India, this is not surprising as most of the women get married in their early or mid-twenties and hence shows an early need for conception. The result of the PCOS study group is similar when compared to Vrunda *et al.* [8] who reported that most of the infertile PCOS women were aged 21–26 years (58%) with a mean age of 25 years.

Many studies have revealed that lower and middle socioeconomic classes have increased PCOS rates due to stress related to financial hardships and treatment, poor nutritional diet, poor quality of life, and impaired health due to unhealthy lifestyle habits [8-10]. In this study, majority of the infertile PCOS women were from a middle socioeconomic class (44%). This study result is higher as compared to that reported by Dasgupta and Reddy, in Hyderabad, India [11], wherein most of the PCOS women were from low-middle socioeconomic class (38.4%). In this study, the prevalence PCOS women (65.71%) in urban areas were found to be higher than their rural counterparts. The reason behind this may be a sedentary lifestyle and unhealthy dietary habits mainly including junk foods. The study result is consistent with that the study reported by Sarkar *et al.* [12] in 2006 who revealed that lifestyle changes including lack of exercise and low physical activity play a role in the prevalence of PCOS to be more in urban than rural areas.

Primary infertility (68%) in infertile PCOS women was found to be higher than secondary infertility (32%) in this study. Similarly, a study conducted by Vrunda *et al.* [8] also reported a higher incidence of primary infertility (70%) than secondary infertility. Furthermore,

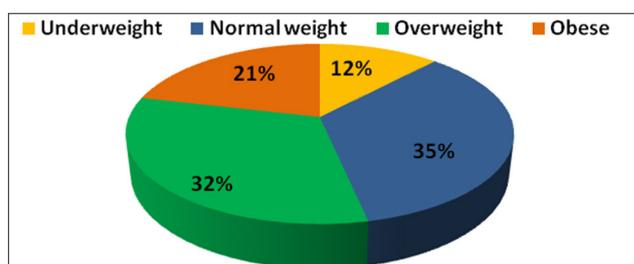


Fig. 1: Body mass index of infertile women with polycystic ovary syndrome

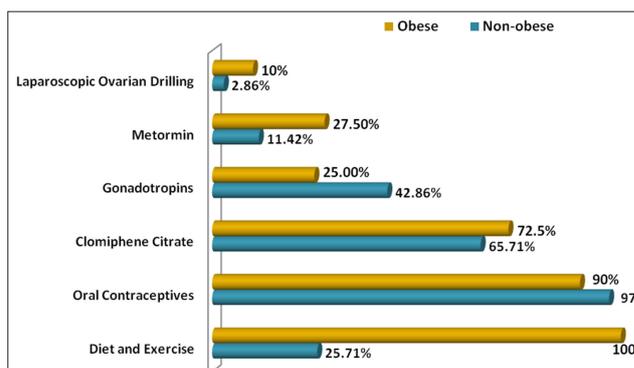


Fig. 2: Frequencies of treatments used in the management of non-obese and obese infertile women with polycystic ovary syndrome

Table 3: Prescription pattern in non-obese and obese infertile women with PCOS

Treatment options	Non-obese (n=35)	Obese (n=40)
Diet and exercise :	0 (0.00)	2 (5.00)
Single therapy:	10 (28.57)	9 (22.5)
OC	9 (90.00)	8 (88.90)
CC	0 (0.00)	1 (11.11)
Gonadotropins	1 (10.00)	0 (0.00)
Combination therapy:	25 (71.42)	29 (72.50)
OC/CC	7 (28.00)	11 (37.93)
OC/CC/gonadotropin	11 (44.00)	2 (6.90)
OC/CC/gonadotropin/ metformin	3 (12.00)	1 (3.45)
OC/CC/metformin	1 (4.00)	9 (31.03)
OC/CC/gonadotropin/ LOD	1 (4.00)	2 (6.90)
OC/gonadotropin	1 (4.00)	1 (3.45)
OC/metformin	0 (0.00)	1 (3.45)
CC/gonadotropin	0 (0.00)	1 (3.45)
OC/CC/LOD	1 (4.00)	0 (0.00)
OC/CC gonadotropin/ metformin/LOD	0 (0.00)	1 (3.45)

*(/) -Following. LOD: laparoscopic ovarian drilling, OC: Oral contraceptives, CC: Clomiphene citrate, PCOS: Polycystic ovary syndrome

the duration of infertility (71.67%) was mostly found ≤ 2 years in PCOS women. The apparent underlying reasons for infertility can be multifactorial such as persistent anovulation over a prolonged period, delay in seeking medical help, and expensive treatments.

Obese women are more prone to have irregularity in their menstrual cycles and anovulatory infertility than women with normal BMI. This study reports that 53% of PCOS patients had high BMI, wherein 32% were overweight and 21% were obese. The reason behind this can be the deranged metabolism, lack of exercise, unhealthy dietary habits, especially junk foods, impaired glucose tolerance, and a greater degree of insulin resistance in women with PCOS. This result is in good agreement with the study conducted in New Delhi [13] which showed that 58% of the patients had high BMI, wherein 38% were overweight and 20% obese.

Lifestyle modifications including diet and exercise are recommended as the first-line therapy of PCOS, especially in overweight and obese women as it improves ovulation as well as pregnancy rates and decreases testosterone levels [8,14]. In this study, 100% of the obese PCOS group was recommended diet and exercise, while only 25.71% of the non-obese PCOS group was recommended lifestyle modifications.

OCs are hormonal drugs prescribed as the first-line treatment by most infertility consultants as they are effective in regularizing menstrual cycle (downregulation) as well as in the treatment of hirsutism and acne [15]. OCs are also given as a pre-treatment pill for clomiphene-resistant patients as it improves ovulation induction as well as pregnancy rates [14]. CC is the recommended first-line treatment for ovulation induction [8]. The use of gonadotropin following CC was postulated by Kistner [16] in 1966 to improve ovulation as well as pregnancy rates as gonadotropin increases the number of pre-ovulatory follicles. Metformin plays a major role in improving ovulation induction in women with PCOS by decreasing the insulin levels or increasing insulin sensitivity and thus altering the effect of insulin on ovarian androgen biosynthesis, theca proliferation, and endometrial growth [17]. Therefore, it increases ovulation rate and pregnancy rate in patients resistant to CC alone. It is also recommended as first-line therapy in obese patients. Another treatment option for clomiphene-resistant anovulatory PCOS is LOD or diathermy and is a specific treatment option only for PCOS [8,14]. Letrozole, an aromatase inhibitor (for ovulation induction) that does not possess the adverse anti-estrogenic effects of CC, is used in the treatment of infertile PCOS patients [18].

Of 75 PCOS patients in this study, 54 patients were given combination therapy (72.00%), while only 19 patients were given single therapy (25.33%). In single therapy, OC was mostly administered to both non-obese (90%) and obese PCOS patients (88.90%). One of the reasons for the choice of OC is that it reduces ovarian hyperstimulation (downregulation treatment cycle). CC and gonadotropins alone were also given but less frequently. In combination therapy, CC pre-treated with OC (37.93%) was mostly given to obese PCOS patients followed by CC with metformin pre-administered with OC (31.03%). Non-obese patients were mostly administered CC with gonadotropins pre-treated with OC (44%). Other combinations such as metformin pre-treated with OC, gonadotropin pre-treated with OC, and CC with gonadotropin pre-administered with OC along with LOD (a minimal invasive surgery) were less frequently used.

Limitations of our study include a small sample size and short duration of the study. The short duration of the study (9 months) leads to lack of precise and accurate data as well as improper estimation of treatment outcomes. Further, this study was conducted in a tertiary care hospital, thus only focusing on a small population and lacking generalizability of other *in vitro* fertilization centres, fertility clinics or hospitals, and hence, lack of involvement of other possible infertile population was another limitation. Letrozole was not used in the current study as it was banned during the period of the study but licensed toward the end of the study as a better choice of ovulation induction drug in infertile PCOS patients.

CONCLUSION

PCOS is a common endocrine disorder within the age group of 24–27 years, from middle socioeconomic class and mostly residing in urban areas. Most of the infertile PCOS women had obesity concluding it as a major risk factor for this syndrome. Prescription pattern of obese PCOS women mostly involved combination therapy in which most women were given CC pre-treated with OC and CC with metformin pre-administered with OC, while in non-obese PCOS women, most of them were given CC with gonadotropins pre-treated with OC. Lifestyle modifications including diet and exercise are strongly recommended, especially for obese PCOS patients.

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CONFLICTS OF INTEREST

None of the authors have any conflicts of Interest.

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