



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>

Research Article

**ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE
IN POLY CYSTIC OVARIAN SYNDROME PATIENTS AND
FACTORS AFFECTING OVARIAN FOLLICULAR SIZE****S.Prathyusha¹, Syed Umar Farooq¹, Dr.A.Narsimha Reddy², Dr.D.Sudheer kumar³,
Dr.P.Kishore^{1*}**¹Department of Pharmacy Practice, Care college of Pharmacy²Gynaecologist, WISE (Warangal Infertility Sonography Center) Hospital, Warangal³Department of Pharmaceutics, Care college of Pharmacy**Abstract:**

Polycystic ovarian syndrome (PCOS) is defined as the presence of hyperandrogenism (clinically and/or biochemically) chronic anovulation in the absence of specific adrenal pituitary gland abnormality. The clinical features of PCOS are Hyperandrogens, Hirsutism, Acne, Obesity, Insulin resistance. The impact of these symptoms on a woman quality of life may be profound and can results in psychological distress that threatens her feminine identity. The study shows factors impacting quality of life in women. It has been measured by using chi-PCOSQ (Chinese PCOS Questionnaire) Likert scale. PCOS quality of life assessment is demonstrated by 1-7 point likert scale. Amongst all domains impairment was seen in infertility domain followed by menstrual irregularity, acne, and hair loss. Spontaneous abortions were found to be frequent in PCOS patients whose BMI range is above normal. In present study of assessing Quality of life, treatment with metformin shows effective results in overweight and obese patients. Clomiphene citrate and inositol are highly effective in non-obese and underweight patients.

Keywords: *Quality of life, HRQoL (Health related quality of life), PCOS (Polycystic Ovarian Syndrome), Clomiphene citrate, Metformin.*

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Please cite this article in press as P.Kishore et al, *Assessment of Health Related Quality Of Life in Poly Cystic Ovarian Syndrome Patients and Factors Affecting Ovarian Follicular Size*, Indo Am. J. P. Sci, 2017; 4(10).

INTRODUCTION:

Polycystic ovarian syndrome is the most common endocrine disorder in the women of reproductive age with a prevalence of approximately 7-10 % worldwide [1]. Studies of PCOS in India reported a prevalence of 3.7 % to 22.5 % [2,3], with 9.13% to 36% prevalence in adolescents only[4,5]. The Constitution of the World Health Organization (WHO) defines health as 'A state of complete physical, mental and social well-being not merely the absence of disease'. It follows that the measurement of health and the affects of health care must include not only an indication of changes in the frequency and severity of diseases but also an estimation of wellbeing and this can be assessed by measuring the improvement in the quality of life related to health care [6,7]. The impact of these symptoms on a woman's quality of life may be profound and it indirectly results in psychological distress that threatens her feminine identity. The condition may therefore result in altered self-perception, a dysfunctional family dynamics and problems at work. The therapy of PCOS is usually focused on ameliorating its symptoms. Effective treatments in PCOS reduce the burden of these symptoms as well as the associated psychological distress and thus improve health-related quality of life [8-10]. Assessing HRQoL helps healthcare provider understand whether patients are satisfied with their health and associated treatments. HRQoL is important to consider while evaluating various symptom management plans and disease treatment [11,12], especially when they provide similar effects on life expectancy. According to U.S. Food and Drug Administration's guidance for industry, assessment of HRQoL improves the clinical outcome and efficiency of treatment [13].

PCOS is a most common endocrine disorder affecting women of reproductive age. The symptoms typically associated with polycystic ovary syndrome (PCOS) are Acne, Hirsutism, Irregular menses, Amenorrhoea, Obesity and Infertility, a major source of Psychological morbidity and it shows negative impact on QoL [14]. Clinical features in PCOS are Reproductive features such as Hyperandrogenism, Hirsutism, Ovulatory and Menstrual dysfunction, Infertility, Complications in Pregnancy, Miscarriage, Pregnancy-Induced Diabetes (Gestational diabetes), Pregnancy-induced Hypertensive disorders and Neonatal complications and increased endometrial hyperplasia. Metabolic features such as Insulin resistance, metabolic syndrome, Dyslipidemia, High rates of premature impaired glucose tolerance, type 2 diabetes and increased cardiovascular risk factors. Psychological features such as anxiety, depression, poor self-esteem, reduced quality of life and negative body image are observed [15].

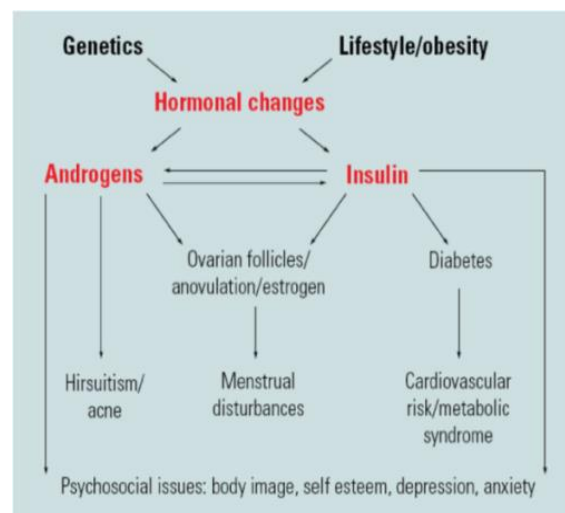


Fig:1 Schematic Representation of Etiology and Clinical features of PCOS [16]

The Hyperinsulinemia appears to be an important factor in maintaining hyperandrogenemia, acting directly to induce excess androgen production by theca cells leading to anovulation[17]. Obesity does in fact have profound effects on both pathophysiology and the clinical manifestation of PCOS by different mechanisms leading to androgen excess and increased free androgen availability affects the alterations of granulosa cell function and follicle development [18].

Clomiphene citrate remains the treatment of first choice for induction of ovulation in anovulatory women with PCOS. The starting dose of Clomiphene citrate is 50 mg/day (for 5 days) and the recommended maximum dose is 150 mg/day[19]. Clomiphene citrate act as an anti-oestrogen, inhibits the binding of estradiol to its receptors in the hypothalamus and pituitary which inturn blocks the negative feedback effect of endogenous estrogens including estradiol [20] . Metformin is taken in a dose that the woman can tolerate. The most effective dose for PCOS is generally 500 mg 3 times daily. Metformin reduces the insulin response by decreasing hepatic gluconeogenesis and reducing androgen levels [21]. Inositol molecule also reduces insulin resistance, improve ovarian function, and reduce androgen levels in women with PCOS [22]. Polycystic ovarian syndrome questionnaire is a disease specific HRQOL questionnaire that contains six domains. The questionnaire was taken from chi-PCOSQ.

DOMAINS: Each domain has its related questions such as emotional (7), Weight (6), Body hair (5), Infertility problems (3), Acne and hair loss (5), Menstrual problems (5). The first domain has a question which helps to assess the psychometric properties of the patients. It is calculated by 7 point scale (1: indicates maximum impairment and 7 indicates no impairment of HRQOL).

1-7 Point likert scale scoring :

Options are explained below based on this criteria scoring has been given.

1- All of the time, 2-Most of the time, 3-A Good Bit of the time, 4-Some of the time, 5- A little of the time, 6-Hardly any of the time, 7- None of the time.

The average (mean) of domain shows the impact of each domain in the patient.

EMOTIONAL DOMAIN - The importance of this domain is to estimate the condition of the patient based on their emotions (depression, anxiety and low esteem) which consists of questions regarding low self-esteem, mood swings, and lack of control over the situation with PCOS. The average of the domain indicates the patient's emotional status.

WEIGHT DOMAIN - Obesity plays a major role in PCOS. Obesity is a symptom and a risk factor for poly cystic ovarian syndrome. It also shows affect on insulin and it leads to insulin resistance. The domain indicates questions like the experience with difficulties staying at ideal weight, concern about being over-weight, frustration in trying to lose weight, trouble in managing weight. The domain average shows the impact of weight changes in patient's life.

BODY HAIR - Hirsutism is one of the clinical features in PCOS. It may not occur in all the patients but it affects the patients who are with increased androgen level in the body. The domain implies the patients who are suffering with embarrassment about excessive body hair, growth of visible body hair, hair on face, hair on upper lip and chin. These symptoms may affect the patient psychologically which indirectly affects the quality of life.

INFERTILITY PROBLEMS - Anovulation is common in PCOS patients which results in the concern about infertility problems. The domain average indicates impact on QoL.

ACNE AND HAIR LOSS - Patient may experience acne and may have excess hair loss due to hyperandrogenism. This affects the patients physiologically and psychologically. The domain average indicates impact of acne and hair loss in patient's quality of life.

MENSTRUAL PROBLEMS - Menstrual irregularity is a major clinical feature in PCOS. The domain average indicates the patients suffering during menstruation like abdominal bloating, menstrual cramps, last menstruation period and irregular menstrual periods.

MATERIALS AND METHODS:

STUDY SITE:

A prospective observational study was conducted at a Infertility center in Warangal. Patients were selected based on inclusion criteria and filled questionnaires were collected from patients.

STUDY DESIGN: It is a Prospective observational study.

STUDY PERIOD: This study has been carried out for 6 months period.

STUDY CRITERIA: All participants were provided written informed consent regarding their willingness to participate in the study. Patients who signed informed consent were included in the study.

INCLUSION CRITERIA:

Patients diagnosed with PCOS [Outpatients]

Patients of reproductive age group.

Patients able to respond to the questionnaire.

Patients who are regularly visiting to the clinic.

EXCLUSION CRITERIA:

Patients who are not diagnosed with PCOS.

Patients diagnosed with similar clinical presentation including congenital adrenal hyperplasia, androgen secreting tumors, Cushing's syndrome, thyroid dysfunction and hyperprolactinaemia.

Patients who are not willing to participate in the study and patients who have other infertility problems.

SOURCE OF THE DATA: Direct communication with patients and care takers and review of patient records. Demographics and other pertinent clinical data was collected from the patients along with filled questionnaires.

All our the study patients filled questionnaire but follow up was taken from 42 patients and their ovulation data, medication regimen (Metformin 500mg; Myo-inositol 550mg; Clomiphene citrate 50mg to 100mg) was analyzed based on ovulatory cycles and number of ovulations.

CHINESE POLYCYSTIC OVARIAN SYNDROME QUESTIONNAIRE PRODUCED WITH PERMISSION [Huang *et al*] [23].

DOMAINS

EMOTIONS:

- Q11 Low self-esteem as a result of PCOS
- Q18 Self-conscious as a result of having PCOS
- Q6 Moody as a result of having PCOS
- Q2 Depressed as a result of having PCOS
- Q17 Worried about having PCOS
- Q14 Afraid of getting cancer
- Q23 Lack of control over the situation with PCOS

WEIGHT

- Q24 Difficulties staying at your ideal weight
- Q3 Concerned about being over weight
- Q12 Frustration in trying to lose weight
- Q10 Trouble dealing with weight
- Q22 Feel unsexy because overweight
- Q14 Afraid of getting diabetes

BODY HAIR:

- Q16 Embarrassment about excessive body hair
- Q26 Growth of visible body hair
- Q15 Growth of visible hair on your face
- Q9 Growth of visible hair on upper lip
- Q1 Growth of visible hair on chin

INFERTILITY

- Q5 Concerned about infertility problems
- Q25 Sad because of infertility problems
- Q13 Afraid of not being able to have children

ACNE AND HAIR LOSS

- Q29 Growth of visible acne
- Q30 Feel acne is a problem
- Q27 Excess hair loss
- Q28 Feel excess hair loss is a problem
- Q4 Tired easily

MENSTRUAL

- Q19 Abdominal bloating
- Q21 Menstrual cramps
- Q20 Last menstruation period
- Q8 Irregular menstrual periods
- Q7 Headaches

RESULTS AND DISCUSSION:

Present study measures the psychological and emotional status of the patients. The each domain in PCOS indicates the patient's quality of life. As successful treatment of PCOS reduce the burden of the symptoms and as associated psychosocial stress [24] has an important impact on woman's HRQOL, assessment of HRQOL plays a vital role to evaluate

the effectiveness in PCOS [25].The symptoms typically associated with PCOS are Amenorrhea, oligomenorrhea, hirsutism, obesity, infertility, anovulation and acne these lead to reduction of HRQoL which shows impact on emotional wellbeing.

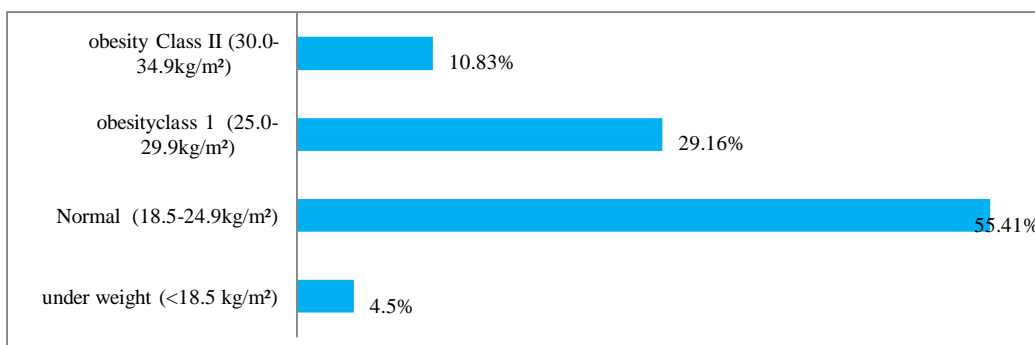


Fig 2: Percentage of distribution of patients according to their BMI

In the present study 240 patient data was assessed. The average BMI in the study group is 60.18 ± 11.84 more than half of the women (n=133; 55.41%) had normal body weight [BMI: 19-25], and 30% [n=70] of the patients were in class I (BMI: 30-34.9); 11% [n=26] of the patients were class-II obese (BMI-35.0-39.9) followed by 4.5% [n=11] with underweight. Similarly a study conducted by *stadnicka et al* [28] reveals that the average BMI (body mass index) of 24.68 ± 4.52 and over half [n=46, 59%] of the examined women had

normal BMI, 1 in 4 respondents (21; 26.92%) had overweight (BMI 26-30), and 1 in 10 (14.11%) were obese (BMI>30) [28]. Due to obesity and increased androgens levels, decreased Sex hormone binding globulin levels were seen. This is one of the causes for PCOS. Majority of the patients in our study had normal Body Mass Index which is similar to the study of *stadnicka et al* [28] Counseling had positive impact on the patients leading to significant weight reduction and follicular improvement.

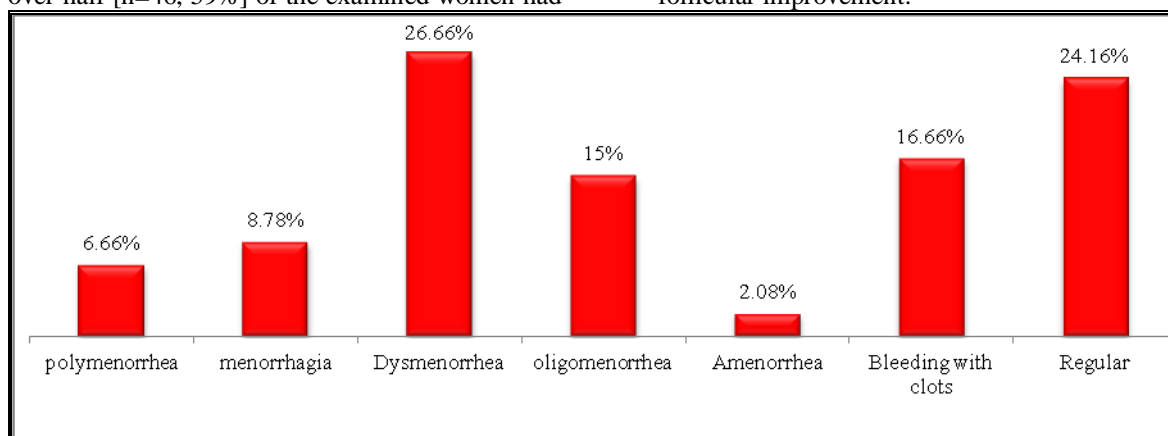
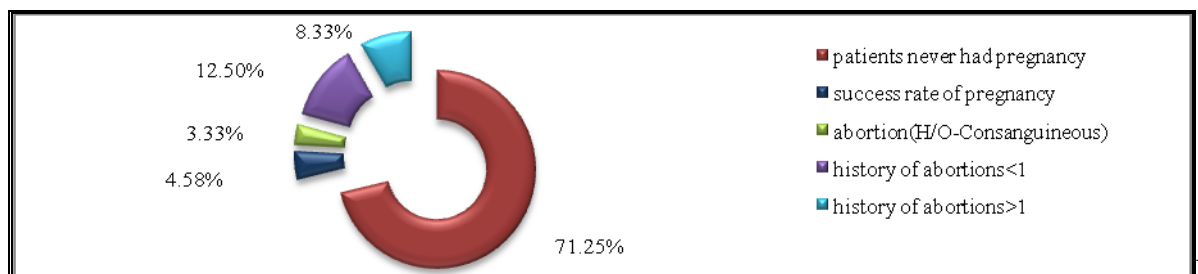


Fig 3: Percentage of patients with menstrual irregularities

In present study, 26.66 % patients were suffering with Dysmenorrhea followed by Oligomenorrhea (15%) (n-38), Menorrhagia 9% (n-21), Polymenorrhea 7% (n-16), Amenorrhea 3% (n-5), Bleeding with clots 17% (n-40) and 24.16 % of patients are regular menstruation with the use of medication.



ig 4: Gravida history in PCOS patients

In present study out of 240 patients 71.25 % (n-171) patients never had pregnancy, 29 % (n-69) of patients had history of terminations.

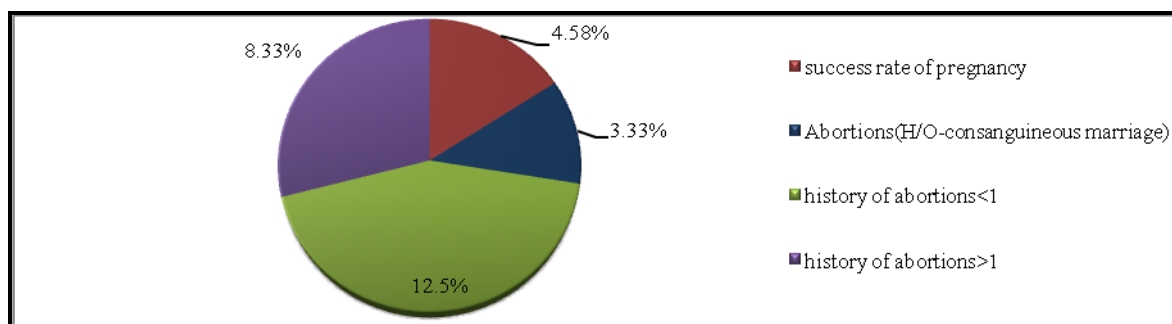


Fig 5: History of abortions in PCOS patients

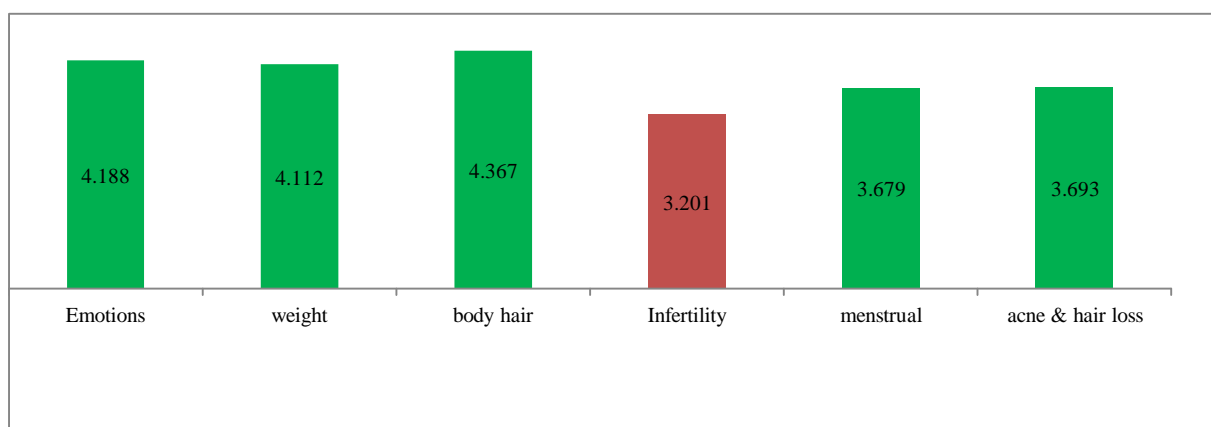


Fig 6: Average score of all domains in the questionnaire

In present study fig 5 shows 29 % (n-69) of subjects had history of pregnancy and in which 4.58 % (n-11) success rate of pregnancy was observed, 3.33% (n-8) had termination history (Due to consanguineous marriage), 12.5 % (n-30) of them <1 termination and 8.33% (n-20) of subjects with >1 which is similarly to the study *Fatemeh Bazarganipour et al* [26]. A spontaneous termination in patients with BMI above 30.0-34.9kg/m² was observed which is similar to study *Jim X.Wang et al* [26]. The concentration of estradiol at oocyte retrieval was also positively associated with the risk of miscarriage similar to the study *Jim X.Wang et al* [27].

In figure 6 shows the maximum impairment was seen in infertility domain 3.201 followed remaining domains. Mean scores of chi PCOSQ's sub scales in PCOS patients 1: indicates maximum impairment and 7: indicates no impairment.

In our study, the maximum impairment was seen in infertility domain among all the domains. The mean of infertility domain is 3.20. It shows negative impact on patient's quality of life. Similar study by *Stadnika G et al* [28] shows that infertility domain mean score was 4.33 which is second highest concern on the PCOSQ. No regular cycle and sometimes even no menstrual bleeding without the use of medication are strongly related with infertility and because of this the patients rated

their infertility as a bigger problem. However, some socio cultural generalizations are possible. The social pressure to have a child shortly after marriage is strong. Similar to the study *Joshi B et al* [3] social pressure for infertility shows a negative impact Quality of life of patients.

Menstrual irregularities are the major clinical feature in PCOS. The mean of the menstrual domain is 3.679; it shows major impact on the quality of life of PCOS patients. Mean value indicates the 'moderate problem' towards menstrual cycle and some of them had regular menstrual cycle with the use of medications. This may be the reason for the decrease in clinical presentation [amenorrhea, menorrhagia, oligomenorrhea, and dysmenorrhea] in the PCOS patients using medications. The physical stress results in hormonal imbalance which leads to anovulation in the PCOS women. Similarly a study reported that the menstrual domain had most negative influence on HRQoL, because the majority of participants had oligomenorrhea, amenorrhea similar to the conducted by *Stadnika G et al* [28].

Acne and hair loss is a clinical representation for increased testosterone levels and hormonal imbalance. Majority of the patients were suffering with acne and hair loss. The mean of acne and hair loss domain is 3.69. This domain stands as the third most effecting domain in Chi-PCOSQ. The

physical appearance of the patients [acne and hair loss] is significantly affecting the patient's quality of life.

In the weight domain, the mean score is 4.112 Similar to the study of *Stadnika et al*[28]. Obesity shows negative impact on HRQoL in PCOS women. An increased cholesterol level in obese women affects the Sex hormone binding globulin significantly which leads to hormonal imbalance.

In present study mean value of body hair domain 4.367 which shows the majority of the patients

were suffering with hirsutism. Comparing with the study of *Fatemeh Bazarganipour et al* [26] shows similar significant values of emotional 4.188 and body hair domain 4.367 were found. Women with PCOS have lower self-esteem, more negative self-image, higher levels of depression and psychological distress owing to the increased levels of androgens similar to the study of *Fatemeh Bazarganipour et al* [26].

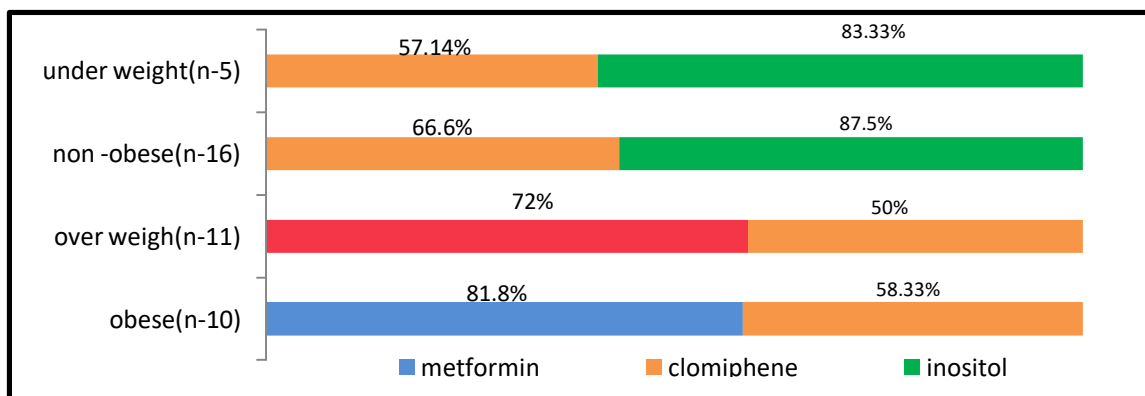


Fig 7: BMI vs drugs used in the treatment of PCOS

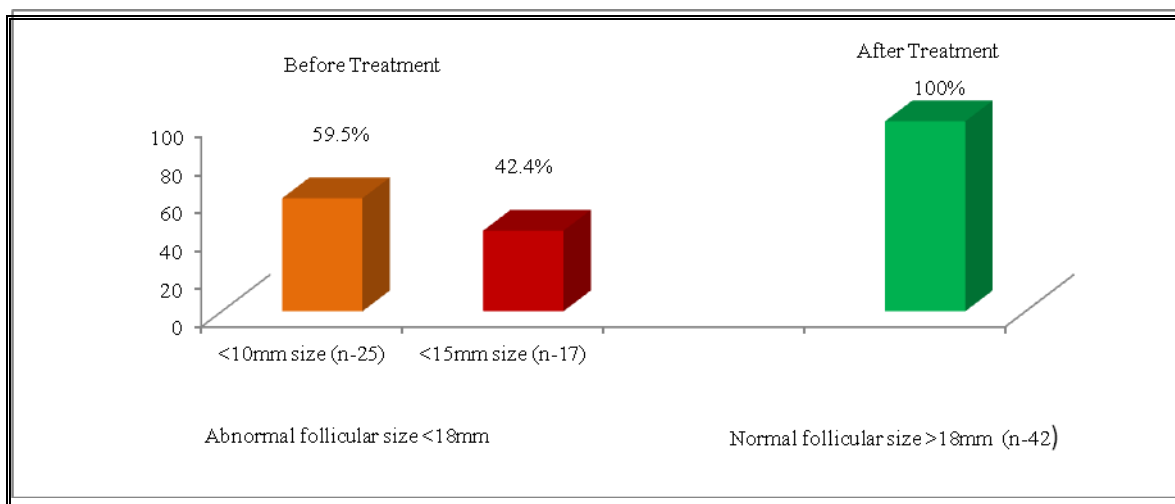


Fig 8: Comparison of follicular size before treatment and after treatment

Metformin showed in fig 7 effective results in the overweight and obese patients. Clomiphene citrate, inositol are highly effective in non-obese as well as in underweight patients. Drug efficacy and number of ovulations were differentiated based on their BMI ranges similarly to the study of *Mahnaz Ashrafi et al*[29].

In figure 8, Increase in follicular size (>18mm) was clearly observed in 42 patients after treatment and counseling, compared to before treatment (<15mm in 17 patients, <10mm in 25 patients). Counseling sessions helped patient reduce significant amount

of weight, develop self-confidence, impart positive attitude, all leading to normal physiological follicular function.

CONCLUSION:

PCOS quality of life assessment was demonstrated by 1-7 point Likert scale. Arranging all domains, impairment was seen in infertility domain followed by menstrual irregularity, acne, hair loss domain, weight, Body hair, Emotions. The complaints of menstrual irregularities like oligomenorrhea, amenorrhea, polymenorrhea, and menorrhagia were subsided by medication adherence. The quality of

life was seen to be affected by severe acne, hair loss and hirsutism in patients leading to low emotional quotient. Metformin showed effective results in the overweight and obese patients. Clomiphene citrate, inositol are highly effective in non-obese as well as in underweight patients. Counseling sessions help to improve the patient's psychological and physiological health status. Spontaneous abortions were found to be frequent in PCOS patients whose BMI range is above normal.

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