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Observational study on risk factors, complications and management of polycystic ovarian syndrome

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Abstract

Polycystic ovarian syndrome (PCOS) is a condition in women of reproductive age which is characterised by hormonal imbalance, chronic an ovulation, signs of multiple small ovarian cysts and excess androgen levels. A prospective observational study was conducted on 110 PCOS women of reproductive age (16-38 years) fulfilling the revised Rotterdam 2003 criteria were studied for a period of 6 months. The data was noted on a self-designed preform including patient demographics, symptoms, menstrual pattern, diagnostic test results and current medication related to management of PCOS. Self-report measures of both anxiety and depression were noted on two different inventories namely, Quick Inventory of Depressive Symptomatology (QIDS SR-16) and Beck anxiety inventory (BAI). The collected data was statistically analysed. In our study PCOS was observed more between the age group of 20 – 30 years (80.9%). Primary infertility (69.1%) was found to be higher than secondary infertility (31.9%). Most of them were overweight (34.5%) and obese (17.2%) with waist to hip ratio greater than 0.85 in 66.36% patients. Symptoms like Hirsutism (66.4%), acne (59.1%), hair loss (88.2%), and acanthosis nigricans (72.7%) were mostly monitored. Out of total population, a greater frequency of women was observed to have depression (52.7%) and also anxiety (52.7%). Metformin (45.5%) was the most prescribed drug. 87.27% of the patients showed medication compliance which showed a positive effect on the management of the symptoms. This study concludes that psychological wellbeing of the patient has to be taken care of by proper education regarding the condition to both the patient and the guardian as this may help deal with the emotional pressure aimed at the patient. Regular counselling alongside life style management and pharmacological therapy improves the overall disease prognosis.

Keywords: polycystic ovarian syndrome, acanthosis nigricans, oligomenorrhea, hyperandrogenism, hypersomnia

Introduction

Polycystic ovarian syndrome (PCOS) was first described in the USA by Stein and Leventhal in 1935. PCOS is a common and complex gynaecological endocrine disorder. The spectrum of clinical features includes ovulatory dysfunction (Oligomenorrhea/amenorrhoea) and hyperandrogenism leading to hirsutism, alopecia and acne. These symptoms can cause considerable patient distress and be difficult to manage. In addition, PCOS is associated with metabolic syndrome, reproductive difficulties, long-term cardiovascular issues and endometrial cancer.

Aim

- To assess the risk factors, complications, and the effect of therapy in women with PCOS.
- To observe the prevalence of mood and anxiety disorders in women with PCOS.
- To create general awareness regarding PCOS among women pertaining to sub-urban population, particularly the unlettered society.

Objectives

- To observe the risk factors associated with PCOS
- To assess the complications and comorbidities associated with PCOS
- To assess the variation among ethnic groups and genetic traits with PCOS
- To estimate the prevalence of mood and anxiety disorders in PCOS
- To check the prescription pattern of therapy in PCOS
- To assess the responsiveness to the medication upon follow-up
- To check the progression of PCOS

Methodology

Study protocol

It is a prospective observational study which is to be conducted for six months at Gandhi hospital, after the approval of Institutional Ethical Committee.

Study design

The study is a prospective observational study.

Study site

Site of work was Gandhi hospital, Musheerabad, Secunderabad, Telangana, India.

Study period

The study will be conducted for a period of 5-6 months.

Study population

The present study includes 110 patients.

Study criteria

Inclusion criteria

- Patients satisfying the age requirement of 15 – 50 years.
- Patients having metabolic syndrome.
- Patients having only cysts in the ovaries.
- Patient who are diagnosed with PCOS.
- Patients with secondary infertility.

Exclusion criteria

- Patients with ovarian tumours.
- Pregnant and lactating women.
- Post-menopausal patients.
- Patients who underwent laparoscopic ovarian drilling.
- Patients with complain of amenorrhea alone.

Outcome measurements

The study starts with a self-made questionnaire on patient details and their disease state comprising of 30 questions.

- **Rotterdam scale:** Explains the symptoms which state the severity of the syndrome. The Rotterdam Criteria require the presence of two of the following: oligo/anovulation, hyperandrogenism or polycystic ovaries on ultrasound.

Two of the following five criteria are required

- Oligo/anovulation
- Hyperandrogenism
- Clinical hirsutism or less commonly male pattern alopecia
- Raised FAI or free testosterone
- Polycystic ovaries on ultrasound

Method of analysis

- Chi-square test
- ANOVA (Analysis of Variance)
- Paired T-tests
- Pearson’s correlation coefficient

Scales used

One diagnostic criteria and two standard questionnaires were used for assessing depression and anxiety in general population are listed below

- **Quick Inventory Depression Scale-Self Report 16 (QIDS-SR16)** - This scale is a self-report measure of depression.
- **Scoring:** Questions in the QIDS – SR-116 correlate with the nine DSM-IV symptom criterion domains, Including: Sleep disturbance (initial, middle, and late insomnia or hypersomnia) (Q 1 - 4), Sad mood (Q 5), Decrease/increase in appetite/weight (Q 6 - 9), Concentration (Q 10), Self-criticism (Q 11), Suicidal ideation (Q 12), Interest (Q 13), Energy/fatigue (Q 14), Psychomotor agitation/retardation (Q 15 - 16).
- **Scoring Instructions:**
 1. Enter the highest score on any 1 of the 4 sleep items (1-4)
 2. Enter score on item 5
 3. Enter the highest score on any 1 of the appetite/weight items (6-9)
 4. Enter score on item 10
 5. Enter score on item 11
 6. Enter score on item 12
 7. Enter score on item 13
 8. Enter score on item 14
 9. Enter the highest score on either of the 2 psychomotor items (15 and 16)
 10. Sum the item scores for a total score. Total score range 0-27.
- **Becks Anxiety Inventory** - The Beck Anxiety Inventory (BAI) consists of 21 items and raw scores ranging from 0 to 63. The BAI scores are classified as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25), and severe anxiety (30 to 63).

Results

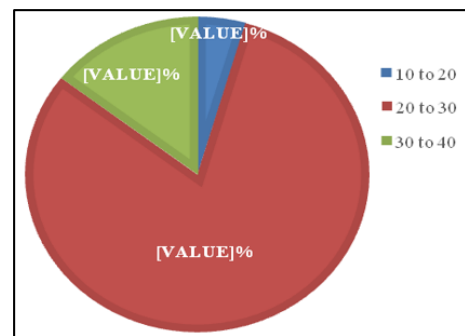


Fig 1: Age group distribution

The pie chart illustrates that maximum number of patients are between the age group of 20-30 years (80.9%).

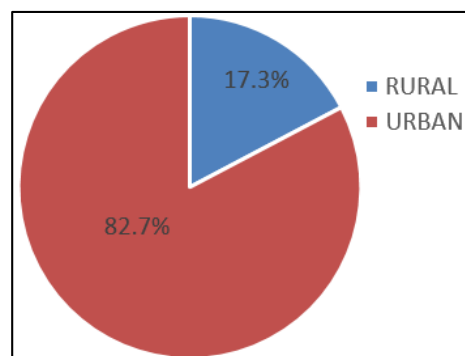


Fig 2: Area of residence

Patients reporting from urban residence are at 82.7% and rural are at 17.3%.

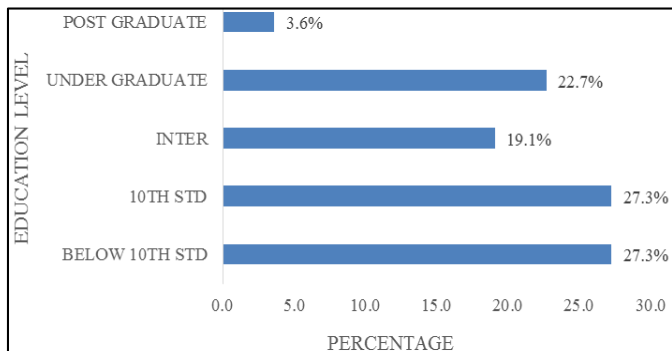


Fig 3: Education level

Patients with a 10th class degree and lower share the highest percentage with 27.3% each. 22.7% of the total patients were undergraduate.

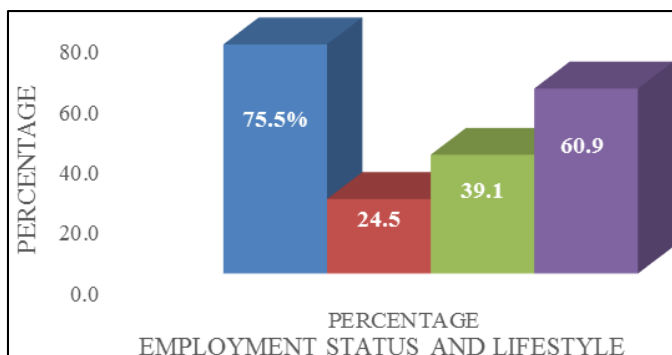


Fig 4: Employment status and life style

75.5% of the total patient pool was house wives. The patients who lead an active lifestyle are 60.9% followed by sedentary who are at 39.1%.

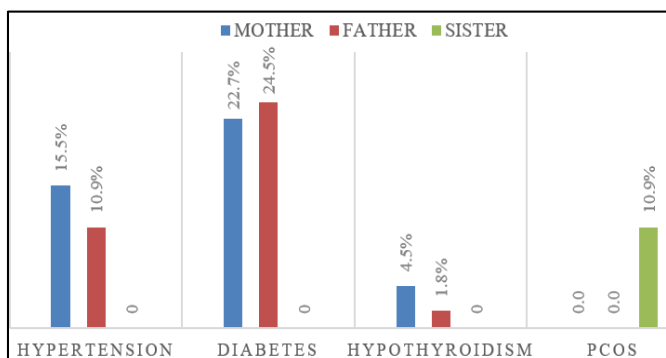


Fig 5: Family history chart

The bar graph shows the history of the comorbidities of the family who were related to the patient. We can observe that the most common comorbidity in the family was diabetes with the father occupying 24.5% and mother at 22.7%, followed by hypertension at 15.5% and 10.9% of the mother and father respectively. 10.9% of the patient's sister was found to be suffering with PCOS.

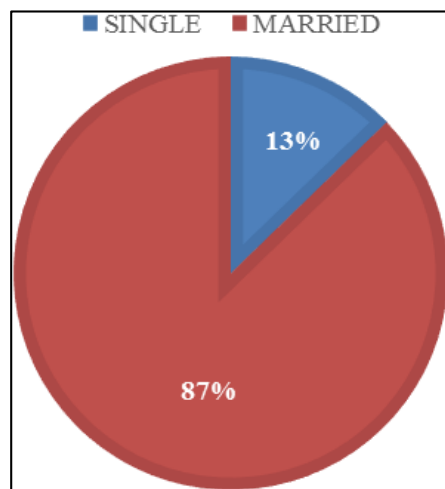


Fig 6: Marital status

Majority of the women diagnosed with PCOS were married (87.3%).

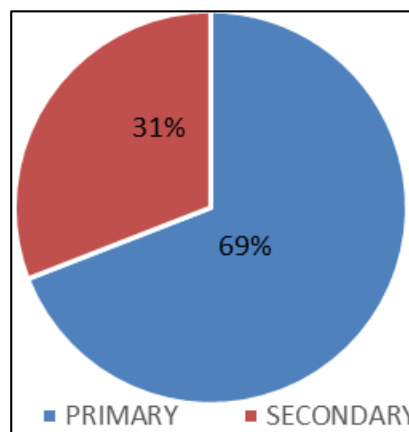


Fig 7: Types of Infertility

The pie chart gives information about distribution of patients with two types of infertility. It was observed that majority of them had primary infertility.

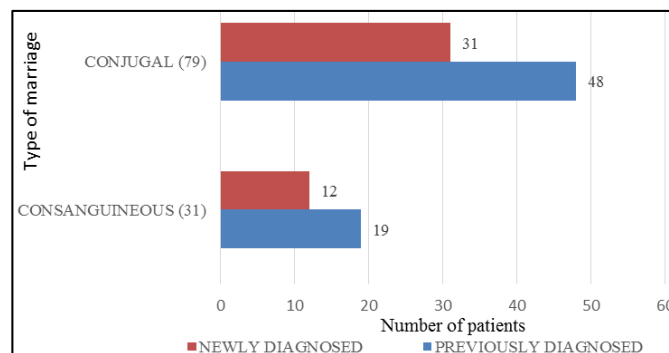


Fig 8: Coexistence of type of marriage and presence of PCOS

Patients who had PCOS and whose parents had a consanguineous marriage were 31 in number out of which 19 were previously diagnosed and 12 were newly diagnosed.

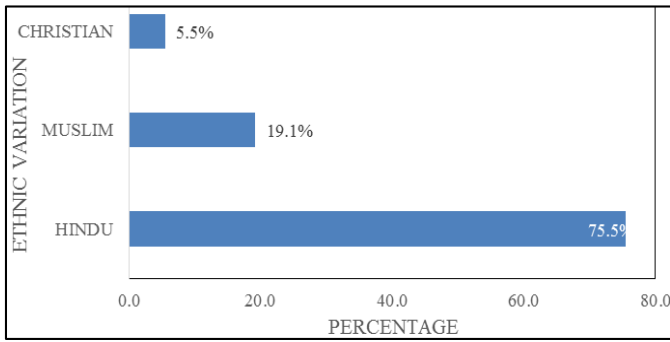


Fig 9: Ethnic variation

Hindus were the highest with a percentage of 75.5% followed by Muslims and Christians at 19.1% and 5.5% respectively.

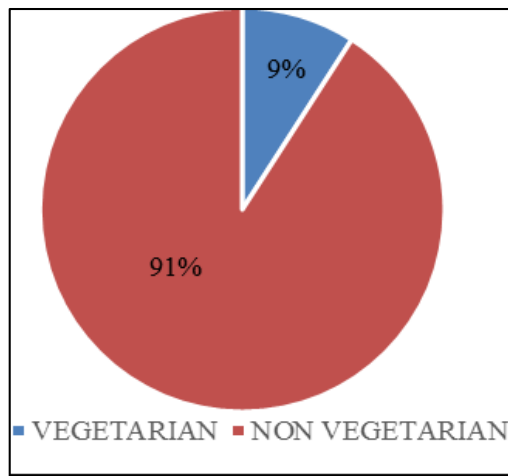


Fig 10: Dietary habits

The pie chart mentioned above shows non-vegetarians were dominating the patient pool with 90.9% and vegetarians at 9.1%

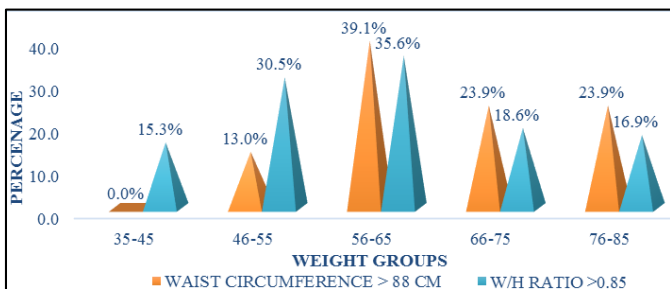


Fig 11: Waist circumference and waist/hip ratio across different weight groups

The graphical representation explains variation in waist circumference along with waist/hip ratio in relation to the weight. Patients within the weight group of 56-65 had the highest percentage of patients with waist circumference and waist/hip ratio at 39.1% and 35.6% respectively. Weight group of 66-75 showed the second most distribution of patients with the mentioned waist circumference and W/H ratio at 23.9 and 18.6 respectively.

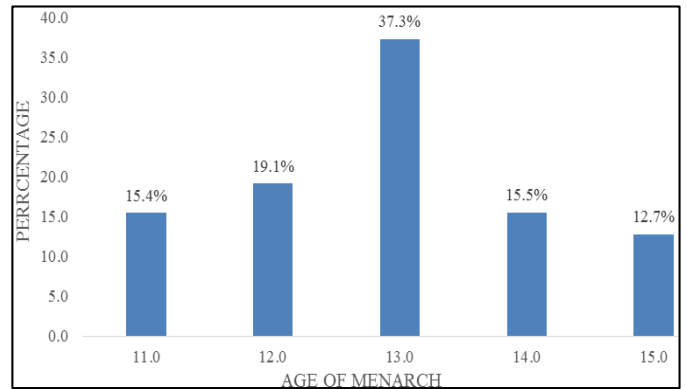


Fig 12: Age of menarche

The bar graph shows the percentage of the patients who reached menarche. The age 13 was the most common age to reach menarche at 37.7% followed by age 12 at 19.1% and age 14 at 15.5%

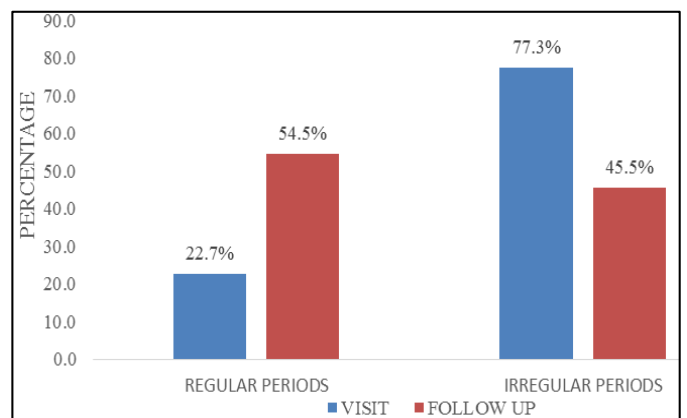


Fig 13: Regularity of periods

The bar graph shows the distribution of patients with regular periods and irregular in comparison with the follow up. During the first visit, the incidence of regular periods was at 22.7% and irregular periods were at 77.3%. In the follow up, there is an improvement in the regular periods at 54.5% and irregular at 45.5%

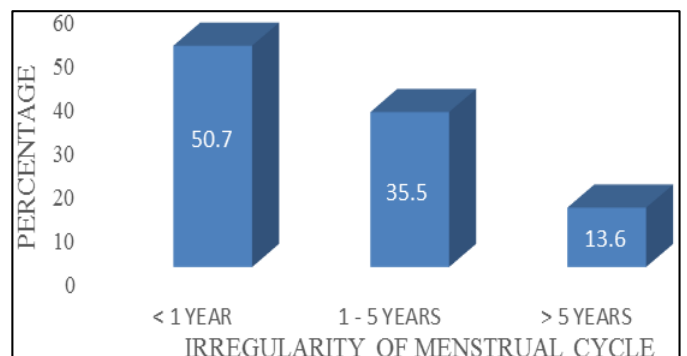


Fig 14: Irregularity of menstrual cycle

The graph shows the presence of irregularity in menstrual cycle compared to duration. Patients who were suffering with irregular menstrual cycle since less than a year are at 50.7%

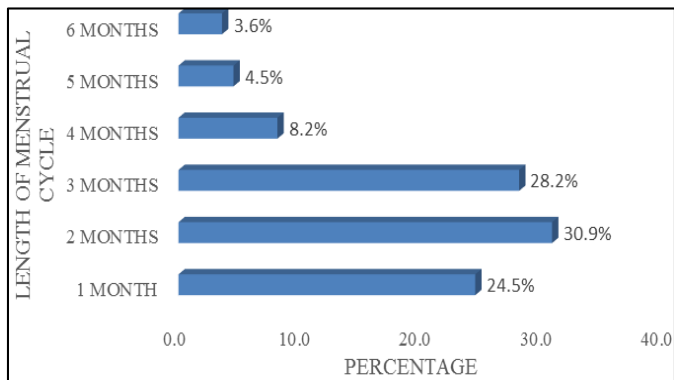


Fig 15: Length of Menstrual Cycle

This we can observe in the above graph, length of menstrual cycle with a gap of 2 months being most common with 30.9% followed by 3 months at 28.2% and 1 month at 24.5%.

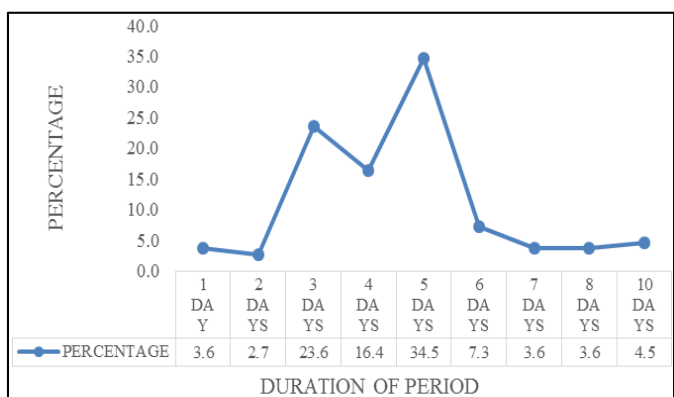


Fig 16: Duration of menstrual cycle

The following plot depicts the data which shows the number of days the period flow exists with 5 days being the common duration at 34.5%.

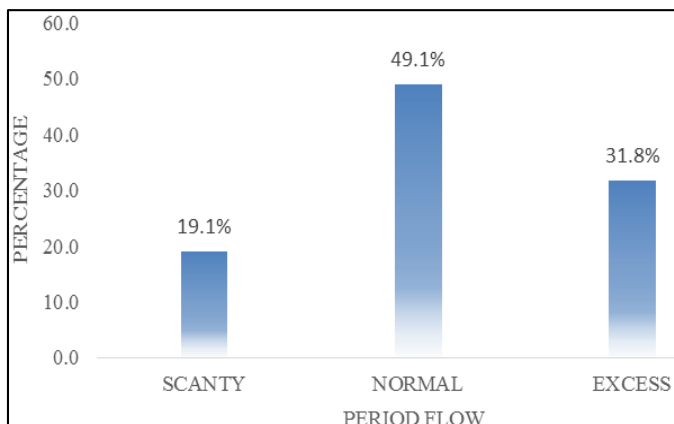


Fig 17: Period Flow

The bar graph described about the period flow during menstruation in patients suffering with PCOS. Describing the data in the given graph, we can depict that 49.1% of the patients had normal period flow when compared to 31.8% with excess flow and 19.1% with scanty flow.

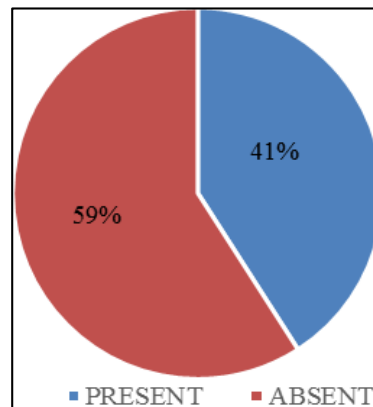


Fig 18: Pelvic Pain during Period

The pie chart mentioned above shows the distribution of patients among presence of pelvic pain and absence of pelvic pain during menstruation. 59.1% of the patients said they don't feel any pain compared to 40.9% of the patients who complained of pain.

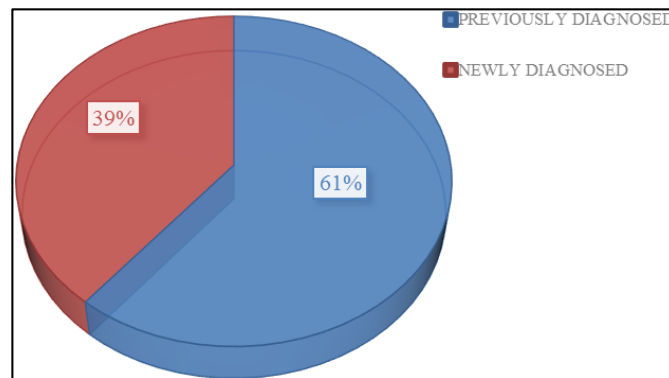


Fig 19: Presence of PCOS

The pie chart above shows when PCOS was diagnosed. Previously diagnosed patients were at 60.9% and newly diagnosed patients were at 39.1%.

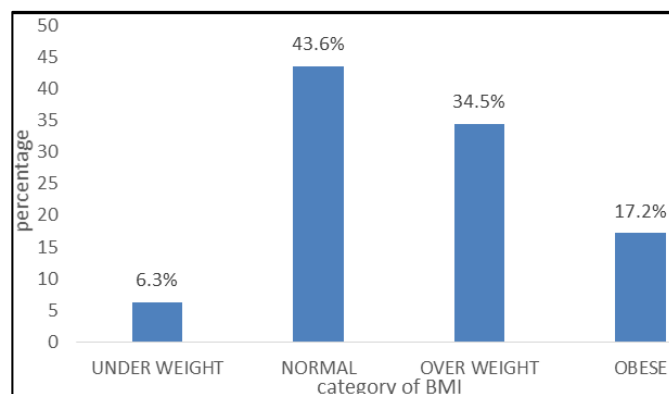


Fig 20: Distribution of BMI

In the study, the risk of PCOS is identical in patients falling in to the category of normal weight and overweight. It is observed that when percentage of overweight and obese are consolidated it exceeded the percentage of patients with normal weight increasing the risk of PCOS.

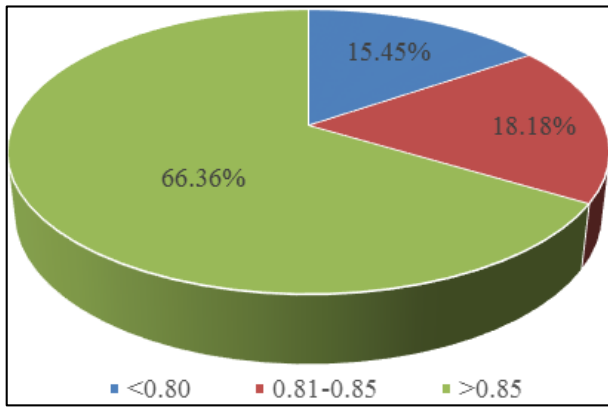


Fig 21: Distribution of Waist to Hip Ratio in Women

The graph depicts that 66.36% of women had a greater waist to hip ratio (above 0.85).

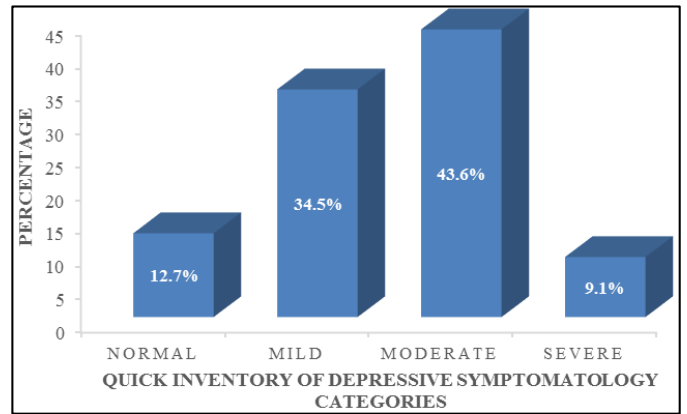


Fig 24: QIDS overall score

The bar graph depicts the distribution of the patients among the different classes of the QIDS-SR16 for the categorization of depression 43.6% of the patients were under the moderate category, 34.5% were in the mild category, 12.7% were in the normal range followed by 9.1% in severe classification

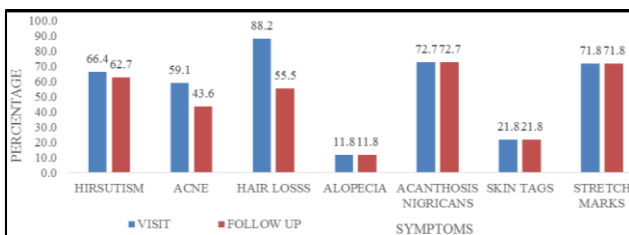


Fig 22: Symptoms of PCOS

The following bar graph shows the distribution of the symptoms in the patients when they first came with the condition in correlation to the follow up. We can observe that the most common complaint was hair loss at 88.2% followed by acanthosis nigricans at 72.7%, stretch marks at 71.8, hirsutism at 66.4% and acne at 59.1%. During the follow-up, patients who complained about hair loss were reduced to 55.5%, hirsutism at 62.7%, acne at 43.6% whereas alopecia, acanthosis nigricans, skin tags and stretch marks showed no improvement.

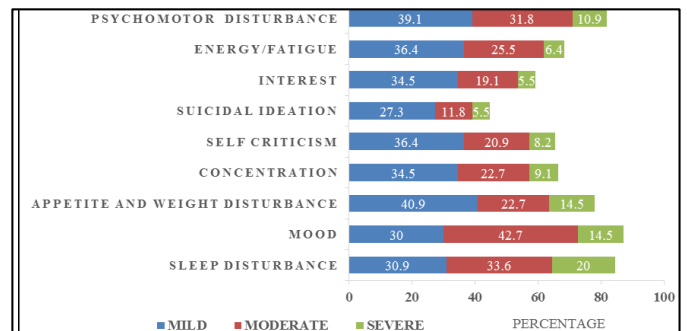


Fig 25: QIDS components

The bar graph depicts that among the considered QIDS components, appetite and weight disturbance was observed to be more common in mild category followed by mood swings in moderate category and sleep in severe category

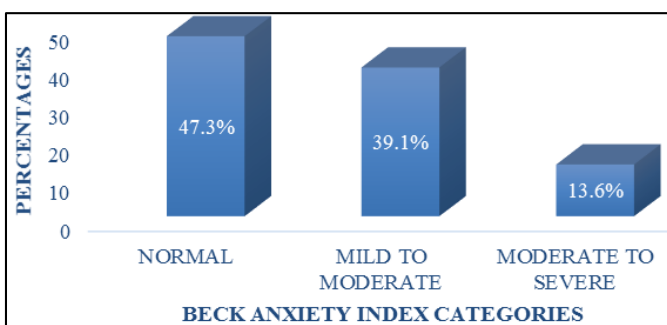


Fig 23: BAI overall score

The bar graph depicts the patients who are distributed in the BAI categories according to the score they acquired. 47.3% of the patients were in the normal category, 39.1% were in mild to moderate category and 13.6% were in moderate to severe category.

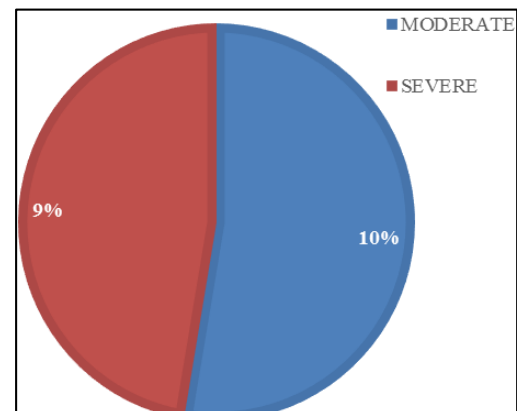


Fig 26: Coexistence of depression and anxiety in patient population

In the patients who are suffering with depression and anxiety, 10% of the patients suffer with both moderate depression and moderate anxiety whereas 9% suffer with severe anxiety and depression.

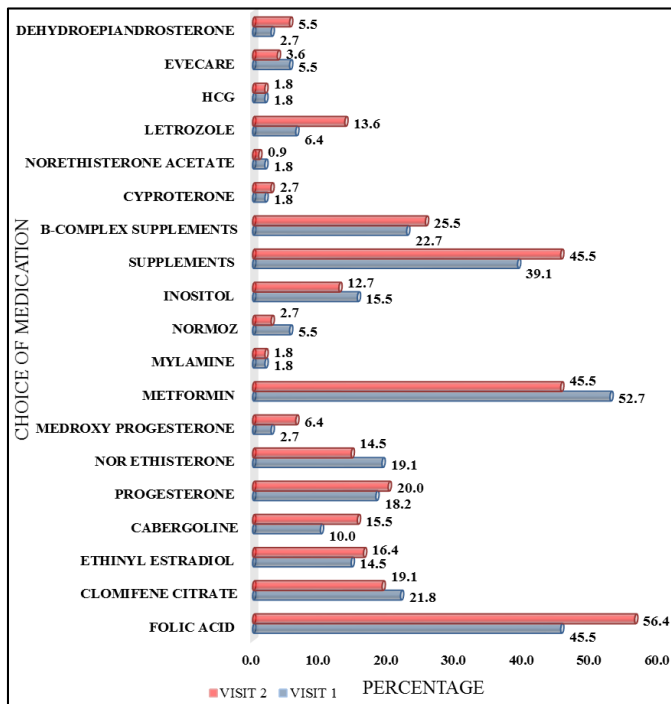


Fig 27: Pattern of prescribed drugs

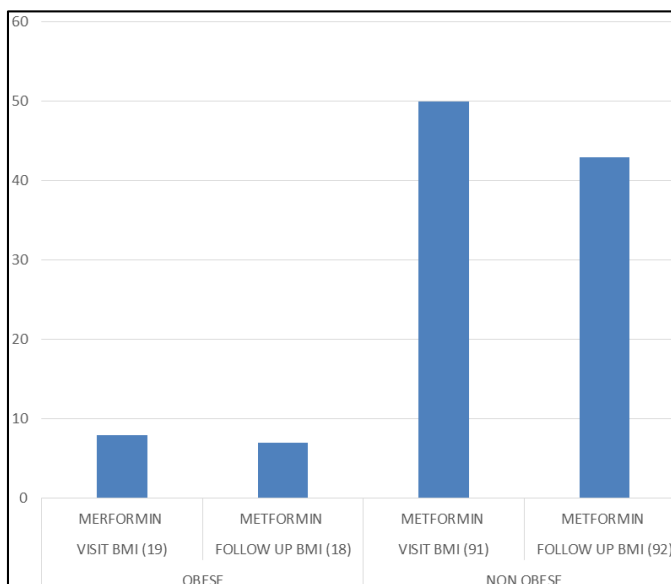


Fig 28: Prescription of metformin in obese and non-obese patients

The following chart shows the trend at which the drugs were prescribed. The drugs frequency was compared with follow up medication. From the following data, we can observe that metformin was prescribed the most number of times at 52.7% followed by folic acid at 45.5 and vitamin supplements at 39.1 during visit1. In visit 2, folic acid was prescribed to the highest number of patients at 56.4% followed by vitamin supplements and metformin at 45.5% each.

Discussion

The study population includes 110 women who were diagnosed with PCOS who met the modified Rotterdam criteria for the syndrome. Majority of the study population belongs to the age group 20 to 30 years (80.9%). Among those women (110), 87.3% were married and 12.7% women were single. Infertility was the primary concern of the

women who found out that PCOS was the underlying cause irrespective of their marital status. 60.9% of the women were already diagnosed with PCOS when the data was collected.

The prevalence of PCOS were found to be higher in urban areas (82.70%) than the rural counterpart (17.3%) because of their lifestyle changes including lack of exercise and low physical activity which play a role in prevalence of PCOS in most of the urban population than the rural counterpart. The reason behind this could be a sedentary lifestyle (39.1) and unhealthy diet especially junk food. On the contrary side, our study found out that among the study population (39.1%) were sedentary and housewives (75.5%). The study also reveals that 90.9% of the patient pool was on a non-veg diet. In our current literature 17.2%, women are obese, and 34.5% are overweight, i.e., more than 50% of the study population had high BMI ranges. In relation to the previous statement, the waist and hip circumferences were measured using standard measuring equipment, and it was observed that 28.1% of the overall population had a waist circumference over 88cms. The risk prediction based on waist and hip ratio is as follows: 15.4% women were at low risk (<0.80), 18.18% women were at moderate risk (0.81-0.85) and 66.36% women were at high risk (>0.85). After analysis, more correlations were observed in regards to waist circumference and waist and hip ratio. Women with a sedentary lifestyle (53.4%) had a waist circumference of 88 cm and above. In weight group from 56-65 kg 39.1% of the subjects had a high-risk waist circumference, and 35.6% subjects had a high-risk W/H ratio.

Out of 31 consanguineous history patients, 19 were newly diagnosed with PCOS and 12 with a past history of PCOS. Consanguinity was considered in our study because research shows that it has a close association with a risk of autosomal recessive diseases. Paternal history of DM was 24.5%, and HTN was 10.9%. Maternal history of DM was 22.7%, and HTN was 15.5%. Hypothyroidism was observed at 4.5% and 1.8% in maternal and paternal side respectively. 10.9% of the patient’s siblings were found to have PCOS.

Various symptoms of PCOS were investigated and reported. The profoundly observed symptoms among the study population that were observed are stretch marks, acne, acanthosis nigricans, hirsutism and hair loss. The moderately common ones were alopecia and skin tags. Frequencies of the symptoms mentioned above during the visit were acne (59.1%), hirsutism (66.4), hair loss (88.2%), AN (72.7%), stretch marks (71.8%), alopecia (11.8%) and skin tags (21.8%). Significant improvement was observed in the follow-up investigation. The frequencies observed were acne (43.6%), hirsutism (62.7) and hair loss (55.5%).

Menstrual history was interviewed, and the following observations were noted. 37.3% of the patients reached menarche at the age of 13 years. 77.3% of the overall population complained of irregular menstrual cycles of which 50.7% study population had a history of irregular menstrual cycles for a couple of months, 35.5% for 1-5 years and 13.6% for more than 5 years. 22.7% women had regular menstrual cycle. Upon follow up, a remarkable improvement was observed with 54.5% patients showing regularity in the menstrual cycle. Secondary amenorrhea was observed in 44.5% and oligomenorrhea was in 67.3% of the patients. Dysmenorrhea was observed in patients with the normal menstrual flow and excessive menstrual flow (44.6%). Menstrual flow lasted 5 days for significant part of the study

population (34.5%), and 23.6% has menstrual flow for only 3 days.

Diagnostic tests that are a proof of clinical findings include abdominal USG, which is a gold standard for ruling out PCOS. 77.3% of the patients exhibited a polycystic pattern in both the ovaries. 13.6% had cysts in the right ovary alone, and 9.1% had cysts in the left ovary. Insulin levels couldn't be hence, acanthosis nigricans (AN) was considered as a cutaneous marker for insulin. Based on BMI, 21.5% obese patients showed AN, and 37.5% of patients who were overweight showed AN. During follow-up, there was an improvement where 30% of the patients showed a while 20% of the patients reported abnormal TSH values. TSH levels with weight and DHEAS showed significant difference which means that there can be some underlying relation with the condition. 57.3% patients showed low levels of Hb. Prolactin in relation to Hb levels showed significant difference which means there can be some correlation with the condition. Overall, 9.1% patients reported low levels of LH. FSH levels were average in all of the patients. FSH with LH levels showed significant difference which means these may have an effect on the disease pathology. Weight, Waist circumference and hip circumference had significance on LH levels. High levels of testosterone were not observed in the study population but clinical evidence of hyperandrogenism like hirsutism and acne were reported by 66.4% and 55.1% respectively. RBS levels were found to be normal but RBS showed significance on waist circumference and hip circumference which means there can be some underlying relation. 16.4% patients showed prolactin levels greater than 25ng/ml which is usually a characteristic lab parameter for PCOS. Prolactin in relation to weight showed significance in statistical analysis.

In the study population, 52.7% exhibited anxiety and 87.3% exhibited depression. Coexistence of anxiety and depression was seen in 19% of the total population. The above-mentioned frequencies were obtained via personal interview which was carried out in a comfortable setting to ensure that the respondent's mood wasn't altered to avoid ambiguous statements.

In this regard two tools were used: Becks anxiety inventory (BAI) and Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR16). The observed population was categorised into normal, mild, moderate, severe. In the total study population, 9.1% were found to have 43.6% were moderate, and 34.5% were mild on the depression scale. Where as in terms of BAI, severe anxiety wasn't recorded but, 39.1% had mild anxiety and 13.6% had moderate anxiety. QIDS-SR16 correlates with nine DSM-V (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) symptom criteria domains of which, sleep disturbances were recorded in 84.5% of the subjects, psychomotor disturbances were recorded in 81.8% of the subjects, appetite/weight disturbances were recorded in 78.1% of the study population, depressed mood was observed in 87.2%, decreased interest was recorded in 59.1%, decreased energy/fatigue was observed in 68.3%, self-criticism was observed in 65.5%, concentration was impaired in 66.3%, suicidal ideation was reported in 44.6%. The significant difference existing between hair fall and stress, AN and mood changes, alopecia and appetite, weight changes and suicidal ideations, hirsutism and interest, acne and energy, nulligravida and psychomotor disturbances indicate that these symptoms are one of the main reason for

depression in patients with PCOS. Risk factor determination is difficult from the current depression interview.

Metformin is also recommended as a first-line therapy in obese patients. In our study, 17.2% of the total population were found to obese. In this class, out of 19 patients with obesity, 8 patients were prescribed metformin as a first line therapy since it can improve insulin resistance. In contrary, out of 91 patients who belong to the non-obese category, 50 were prescribed with metformin. Norethisterone was the most used drugs in this category which was prescribed to 21 patients (19.1%). During the follow up, there was a change in the prescribing trend with Progesterone being prescribed for 22 patients.

Inositol and Normos (combination of Inositol and chromium picolinate) were the two drugs which were prescribed in our department in which inositol was prescribed to 17 patients (5.5%) of which 9 patients were above the normal BMI. During the follow up, the number of patients who were prescribed inositol was decreased since there was a decrease in the frequency (from 51.7% to 47.2%) of the patients who were over the normal BMI value and hence 14 patients were prescribed inositol. Normos was prescribed for 8 patients.

Selective estrogen receptor modulator-Clomiphene citrate is the first line of treatment if PCOS woman is to be treated for infertility. 24 patients received this drug for infertility treatment during the visit. Ergot derivatives can improve the menstrual irregularity. Cabergoline was the drug of choice which was prescribed to 11 patients during the visit and 17 patients received this pill during the follow up.

Hypoglycaemic agents plays an important role in the treatment of PCOS since it can treat anovulation and infertility and it can also manage the insulin resistance of the patient. Metformin was approved by FDA for the treatment of Type 2 Diabetes Mellitus which means it the first line therapy to treat excess insulin levels and insulin resistance. 50 patients of all the BMI classes received the metformin therapy on the first visit, during the follow up, metformin was prescribed to less number of patients belonging the overweight and obese class which shows improvement in the patients with irregular menstrual cycle and/or insulin resistance.

In our study, 2 patients were given Cyproterone, whereas 3 patients were prescribed with the same drug at follow-up. In patients who were not responding to Clomiphene citrate were prescribed Letrozole, an aromatase inhibitor. In our study, the drug was prescribed to 7 people during the visit and 15 patients received the drug during the follow up. Evicare which is an herbal remedy to regulate menstrual cycle and relieves PMS, was rarely prescribed since 6 patients received during the visit and 4 patients received this at the follow up visit.

Conclusion

PCOS is a common endocrine disorder which affects women in the fertile age residing mainly in the sub-urban areas. Most of the patients in the study had poor education status and belong to the suburban population. Obesity was a common condition among women with PCOS which concludes that it is a major risk factor for the disorder. In the study, obesity, increased waist and hip ratio and comorbid conditions like hypothyroidism were found to be the major risk factors for PCOS. By current literature, more than 50% of women are overweight or obese. If the waist-hip ratio of women with PCOS increases, reproductive function and metabolic state of

the woman is altered more than in cases where no changes in parameters are seen. Various symptoms (hair loss, AN, acne and stretch marks) and diverse ethnic, cultural background was also observed. There is no much significant difference in the mood disorders with the treatment of PCOS and no specific medication for psychological impairment was observed. Most of the specific norms that are confined to PCOS affected women were not observed in the study population like excess testosterone levels, elevated blood glucose levels. The high prevalence rate of depression (52.7%) and anxiety (52.7%) was observed which suggests that initial evaluation should also include assessment of psychological health. Physicians need to pay proper attention especially in the view of factors that affect the psychological well-being since proper counselling and psychological care along with pharmacological treatment and lifestyle modification can contribute to better management of PCOS.

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