Relation between Polycystic Ovary Syndrome and Infertility

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Abstract: Background: PCOS (Poly Cystic Ovary Syndrome) is the most common endocrine disorder in women of reproductive age with high prevalence. Poly Cystic Ovary Syndrome (PCOS) stands as one of the frequently occurring endocrinopathies in women of reproductive age with the incidence rate of 5-10% worldwide. PCOS is named as "Stein-Leventhal syndrome" after its earliest recognition by Dr. Stein and Leventhal. They described it as a syndrome of polycystic ovaries, with systemic reproductive, metabolic and psychological disturbances. The polycystic ovary syndrome (PCOS) is defined as a combination of hyperandrogenism (hirsutism and acne) and anovulation (oligomenorrhea, infertility, and dysfunctional uterine bleeding), with or without the presence of polycystic ovaries on ultrasound. It represents the main endocrinedisorder in the reproductive age, affecting 5% - 10% of women. It is the most common cause of infertility due to anovulation, and the main source of female infertility. When in the presence of a menstrual disorder, the diagnosis of PCOS is reached in 30% - 40% of patients with primary or secondary amenorrhoea and in 80% of patients with oligomenorrhea. PCOS should be diagnosed and treated early in adolescence due to reproductive, metabolic and oncological complications which may be associated with it. Treatment options include drugs, diet and lifestyle improvement. Methods& Materials: In this prospective observational study, Women who consulted in Obstetrics & Gynaecology Department were screened to identify the PCOS problems through clinical histories, PCOS questionnaire and ultrasonography over a period of 12 months at Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh. Patients diagnosed with PCOS were assessed for their clinical manifestations, severity, life style and treatment given, and were educated accordingly through patient counseling and awareness program. Results: We observed the prevalence of PCOS is 6.5 % out of 1000 women. Among the 65 PCOS women, 60respondents complains of irregular ministration which is about 92.30%, among 65 PCOS women, 24 did not yet have any child which is about 53.34%. Among the respondents 7 (33.33%) had the history of miscarriages or abortion and 21 (46.60%) had the child. Mostly received the advice of the lifestyle modification and treatment with metformin ethinyl estradiol, medroxy progesterone etc. Conclusions: PCOS is a complex condition with high prevalence of fertility problems, Obesity and others associated complications which need special attention with specific measures. It is the time needed demand to take initiatives for creating awareness towards this issue. Prompt diagnosis and appropriate treatment with lifestyle modifications may have good result.

Keywords: *Polycystic Ovarian Syndrome, Infertility, Clinical Manifestations, Fertility Problems, Therapeutic plan.*

Introduction

The polycystic ovary syndrome PCOS is conventionally defined as a combination of hyperandrogenism (hirsutismand acne) and anovulation (oligomenorrhea, infertility, and dysfunctional uterine bleeding) with polycysticovaries. At ultrasound, it is the main gynecological endocrinopathy of reproductive age, affecting 5% - 10%of women. It is the most common cause of infertility due to anovulation. In many countries, itrepresents the leading cause of female infertility. The specific pathophysiology of this syndrome has not yet been established, however it is associated with the presence of insulin resistance, obesity, diabetes mellitus type2, dyslipidemia, metabolic syndrome, hypertension, cardiovascular disease, hyperplasia and endometrial carcinoma.When it is considered in the presence of menstrual disorder, diagnosis of PCOS is obtained in 30%-40% of patients with primary or secondary amenorrhoea and in 80% of patients with oligomenorrhea.

Classification

The Rotterdam ESHRE/ASRM—Sponsored PCOS Consensus Workshop Group Fertilityand Sterility (2003)
Presence of 2 out of 3 criteria:
1) Oligo-ovulation or anovulation;
2) Clinical or biochemical signs of hyperandrogenism;
3) Polycystic ovaries on ultrasound.

The Thessaloniki ESHRE/ASRM—Sponsored PCOS (2006)
In 2006, The Androgen Excess and PCOS Society (AE-PCOS) published its positioning regarding the diagnosis of polycystic ovary syndrome. According to this association, the androgen excess needs to be present, either byclinical signs, or by biochemical hyperandrogenism. Thus, for diagnosing of the syndrome, two of the following criteria would be necessary:
1) Oligo and/or anovulation and polycystic ovaries on ultrasound;
2) Clinical or laboratory evidence of androgen excess.

The Amsterdam ESHRE/ASRM—Sponsored 3rd PCOS Consensus, 2012
Most recently defined presence of 2 out of 3 criteria:
• Menstrual dysfunction and/or polycystic ovary;
• Hyperandrogenia and/or hyperandrogenism;
• The ultrasound showing a polycystic ovary.

Infertility Treatment Options

Weight loss and exercise (first line of treatment): Losing weight through exercise and diet has been proven effective in restoring ovulatory cycles and achieving pregnancy for many of over-weight and obese PCOS patients. Weight loss of only5% to 10% of total body weight often leads to the return of ovulatory cycles. Life-style modifications are highly important for ovulation induction since the finding suggest that obese women are less likely to show good response without weight reduction and exercise.

Clomiphene citrate (CC) for ovulation induction (first-line of treatment): Ovulation induction can be accomplished in 60-80% of women with PCOS by the use of anti-estrogen, typically clomiphenecitrate. The starting dose of CC is 50 mg/per day for 5 days, starting between day 2 and 5 of current menstrual cycle.

Aromatase inhibitors for ovulation induction (second-line of treatment): Aromatase inhibitors such as letrozole block the conversion of testosterone and androstenedione to estradiol and estrone. In this way letrozole prevents the negative feedback at the hypothalamic-pituitaryaxis and leads to increased secretion of gonadotropins, which in turn leads to ovarian follicular growth and development.

Insulin sensitizing agents (Metformin) alone or in combination with CC (second-line of treatment): Risk of impairedglucose tolerance (IGT) and diabetes is highest in women who have both, menstrualdisorder (oligo-ovulation or anovulation) and hyperandrogenism, and the risk is further amplified by the obesity. Metformin treatment is indicated in those with IGT or in the case of frank diabetes. Metforminin combination with CC may increase the rate of ovulation andpregnancy.

Gonadotropins (second-line of treatment): Gonadotropins are treatment of choice in PCOS women who fail to ovulate or to conceive with oral ovulation induction drugs. Ovarian response should be monitored by the serial ultrasound measurement of follicular growth and endometrial development (endometrial thickness and lining).

In vitro fertilization (IVF) (third-line treatment): Studies have shown that the use of gonadotropin-releasing hormone (GnRH) agonist leads to higher rates of successful pregnancy and lower rates of abortion when compared with CC treatment. Pregnancy rates can approach 40% per cycle with IVF.

Surgical

Ovarian drilling (second-line treatment; indicated cases): Laparoscopic ovarian drilling may be as effective as low-dose FSH in inducing the ovulation, but additional therapy with CC and/or FSH is also required after surgery in 2/3 of cases. Laparoscopic ovarian drilling may be considered in women with clomiphene-resistant PCOS, particularly when there are other indications for laparoscopy, but surgical risks from procedure itself and postoperative adhesion formations remains a concern.

Objectives of the Study
The objectives of the study are as follows:
1. To estimate the prevalence of PCOS.
2. To find out the clinical characteristics of PCOS patients.
3. To identify the fertility problems of women with PCOS
4. To assess the available therapeutic plans for PCOS.

Methodology of the Study

Study area: The study was conducted at Shaheed Suhrawardy Medical College & Hospital, Dhaka, **Bangladesh.**

Study design: The study was prospective observational type.

Study duration: The study was conducted from January 2016 to December 2016.

Study population: This study consists of female patients attending the Gynecology Outpatient Department of Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh.

Sources of Data: Data were collected from primary and secondary sources.

Sources of Primary Data: Primary Data were collected from the respondents of the study area.
Sources of Secondary Data: Secondary Data were collected from Books, research report, journal, internet etc.

Sampling method: Purposive sampling method was used for the study.

Sample size: During this study period around 1000 women were consulted in Gynecology out Patient department, out of which 300 patients who have symptoms similar to PCOS were screened and only 65 patients were confirmed with PCOS through symptomology and USG abdomen.

Unit of analysis: All the necessary and relevant baseline information was collected. Prevalence of PCOS, clinical characteristics, fertility problems of women with PCOS and available therapeutic plans for PCOS were studied.

Informed Consent Forms: The informed consent forms were obtained from those who were willing to participate in study.

Inclusion Criteria: Women ≥18 years and the PCOS patients were included in the study.

Exclusion Criteria: Young women who had their menarche less than 3 years were excluded from the study.

Rotterdam criteria: The study followed the three Rotterdam criteria (i. Oligo-or anovulation, ii. Clinical (hirsutism, acne or androgenic alopecia) and iii. Polycystic ovaries on ultrasound examination.

Statistical analysis: The percentage method was used to analyze the patient distribution based on various parameters. The appropriate statistical parameters were used to calculate the prevalence of PCOS. The statistical parameters like frequency and percentage were considered to analyze the patient age & weight distribution. Collected data were analyzed by Computer Program SPSS version 20 (Statistical Package for the Social Sciences)

RESULTS
1000 women were consulted in Gynaecology Outpatient department of Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh. Out of which 300 patients who have symptoms similar to PCOS were screened and only 65 patients were confirmed with PCOS through symptomology and USG abdomen. The prevalence rate of this study is 6.5% (65 patients in 1000 women).

Table 1: Age of the Respondents

Age	Frequency	Percent
18-28 Years	43	66.15%
29-38 Years	20	30.77%
39-45 Years	2	3.08%
Total	**65**	**100%**

Age of the Respondents has shown in the above table. From the result, it was found that 66.15% respondents had age group 18-28 years which was maximum but 3.08% respondents had age group 39.45 years which was minimum and 30.77% respondents had age group 18-28 years.

Table 2: Marital Status of the Respondents

Status	Frequency	Percent
Married	45	69.23%
Unmarried	18	27.69%
Divorce	2	3.08%
Total	**65**	**100%**

Marital Status of the Respondents has shown in the above table. From the result, it was found that 69.23% respondents were married which was maximum and 27.69% respondents were unmarried. 3.08% respondents were divorcee which was minimum.

Table 3: Weight of the Respondents

Weight	Frequency	Percent
41-50 Kg	4	6.15%
51-60 Kg	21	32.31%
61-70 Kg	27	41.54%
71-80Kg	8	12.31%
81-90 Kg	5	7.69%
Total	**65**	**100%**

Weight of the Respondents has shown in the above table. From the result, it was found that 41.54% respondents had 61-70 Kg weight which was maximum but 6.15% respondents had 41-50 Kg weight which was minimum. On the other hand 32.31% respondents had 51-60 Kg weight, 12.31% respondents had 71-80 Kg weight and 7.69% respondents had 81-90 Kg weight.

Table 4: BMI of the women with PCOS

Characteristics	Mean
Height (cm)	159.6
Weight (Kg)	62.4
BMI (Kg/m^2)	23.52

BMI of the women with PCOS has shown in the above table. From the result, it was found that mean height of the respondents were 159.6 cm and mean weight were 62.4 Kg and mean BMI of the respondents were 23.52 Kg/m^2

**Table 5: Life Style habit (Physical exercise) of the Respondents**

Type	Frequency	Percent
Physical exercise	7	10.77%
No Physical exercise	58	89.23%
Total	65	100%

Life Style habit (Physical exercise) of the Respondents has shown in the above table. From the result, it was found that 89.23% respondents did not perform physical exercise leading to sedentary life and only 10.77% respondents performed physical exercise.

Table 6: Clinical manifestations of PCOS Patients

Item	Frequency	Percent
Acne	34	52.30%
Hirsutism	37	56.92%
Hair Loss	50	76.92%
Ovarian cyst	51	78.46%
Depression	35	53.85%
Acanthosisnigricans	43	66.15%
Skin tags	9	13.85%
Irregular menstruation	60	92.31%

Figure 1: Clinical manifestations of PCOS Patients
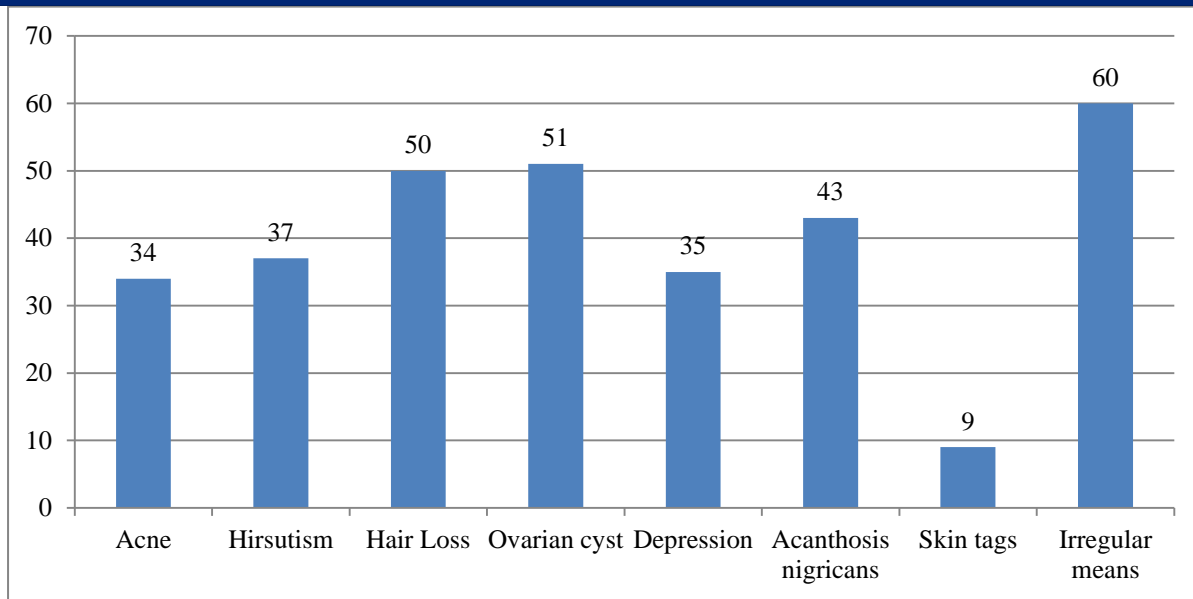
Clinical manifestations of PCOS Patients have shown in the above table and graph. From the result, it was found that 34 (52.30%) patients had acne, 37 (56.92%) patients had hirsutism, 50 (76.92%) patients had hair loss, 51 (78.46%) patients had ovarian cyst, 35 (53.85%) patients had depression, 43 (66.15%) patients had acanthosisnigricans, 9 (13.85%) patients had skin tags and 60 (92.31%) patients had irregular menstruation.

Fertility history of the Respondents

Table 7: Child History of the Respondents

Child History	Frequency	Percent
Having children	21	46.66%
Having no children	24	53.34%
Total	45	100%

Child History of the Respondents has shown in the above table. From the result, it was found that 46.66% respondents had children and 53.34% respondents had no children.

Table 8: Gestational History of the Respondents

Characteristics	Frequency	Percent
Live births	14	66.67
Miscarriages/Abortion	7	33.33
Total Gestations	21	100%

Gestational History of the Respondents has shown in the above table. From the result, it was found that 66.67% respondents delivered live births and 33.33% respondents had miscarriages/abortion.
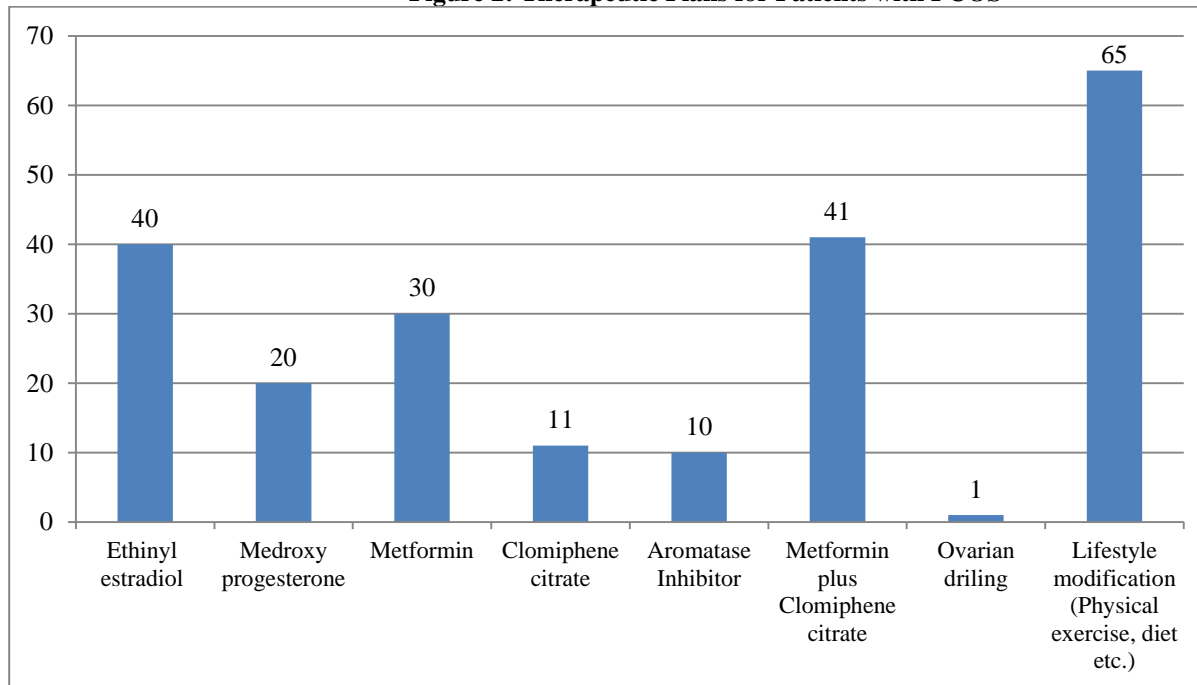
Therapeutic Plans for Patients with PCOS

Table 9: Therapeutic Plans for Patients with PCOS

Therapies	Frequency
Ethinyl estradiol	40
Medroxy progesterone	20
Metformin	30
Clomiphene citrate	11
Aromatase Inhibitor	10
Metformin plus Clomiphene citrate	41

Ovarian driling	1
Lifestyle modification (Physical exercise, diet etc.)	65

Figure 2: Therapeutic Plans for Patients with PCOS

Therapeutic Plans for Patients with PCOS has shown in the above table and graph. From the result, it was found that 40 (61.53%) patients were treated with ethinyl estradiol, 20 (30.76%) patients were treated with medroxy progesterone, 30 (46.15%) patients were treated with metformin, 11 (16.92%) patients were treated with clomiphene citrate, 10 (15.38%) patients were treated with aromatase inhibitor, 41 (63.07%) patients were treated with metformin plus clomiphene, 1 (1.53%) patient was treated with ovarian drilling and all the 65 (100%) patients were advised and counseled about lifestyle modification by diet, physical exercise etc.

Discussion

1000 women were consulted in Gynaecology Outpatient department of Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh. Out of which 300 patients who have symptoms similar to PCOS were screened and only 65 patients were confirmed with PCOS through symptomology and USG abdomen. The prevalence rate of this study is 6.5% (65 patients in 1000 women). which was very close to the study of Ligia G et al.[8] (8.5%), Samar M et al.[9] (7.3%), Fahimeh R et al.[10] (7.1%), Susan M et al. [11] (4-8%), Howard A et al.[12] (4%), Saghar S et al.[13] (3.42%), Wendy A et al.[14] (0.2 ± 2.2%) while Zahida B et al.[3] (40.9%) showed the highest percentage of prevalence.

In our study 66.15% of age group 18-28 years has shown the maximum PCOS and Generally, PCOS will occur only at reproductive age and the same was observed in our study, which is matched with other studies Samar M etal.[9] (20.2 ± 1.4), Zahida B et al.[3] (27 ± 8), Ligia G et al.[8] (30.7 ± 7.2), Fahimeh R et al.[10] (34.4).

From the result, it was found that 69.23% respondents were married which was maximum but 3.08% respondents were divorcee which was minimum and 27.69% respondents were unmarried.

From the result, it was found that 41.54% respondents had 61-70 Kg weight which was maximum. It was also found that means weight was 62.4 Kg, mean height of the respondents was 159.6 cm and mean BMI of the respondents was 23.52 Kg/m^2.The weight of the patients is the key point in PCOS. The mean weight of PCOS women included in our study is comparable with mean weight of the studies of Wendy Aet al. [14] (72.1), Ligia G et al.[8] (60.9), Samar M et al.[9] (60.19 ± 10.14).Increase in weight will cause some physiological changes in women by increasing in cholesterol level, which will increase androgen production which further produces male pattern characteristics, anovulation, miscarriages, or late pregnancy complications etc. Weight loss improves SHBG (sex hormone binding globulin) concentrations, decreases testosterone and improves menstrual function and conception rates. It will also improve insulin sensitivity.

From the result it was found that 89.23% respondents did not perform physical exercise leading sedentary life which is the most alarming issues in PCOS and only 10.77% respondents performed physical exercise.

Regarding Clinical manifestations of PCOS Patients, it was found that 34 (52%) patients had acne, 37 (56.92%) patients had hirsutism, 50 (76.92%) patients had hair loss, 51(78.46%) patients had ovarian cyst, 35 (53.84%) patients had depression, 43 (66.15%) patients had acanthosisnigricans, 9 (13.84%) patients had skin tags and 60 (92.30%) patients had irregular menstruation. Regarding clinical manifestations, it was found in the study that menstrual irregularity is one of the main symptom of PCOS and affects majority of the patients and same was observed in our study population and it correlates with the studies of Geetha K et al.16 (72%), Susan M et al.11 (85%-90%), Ligia G et al.8 (98.6).Mostly presented symptoms are irregular menses, acne, hirsutism, hair loss, depression, acanthosisnigricans, ovarian cyst, bleeding between cycles, skin tags. In the study of Geetha K et al.16 the occurrence of acne (20%), Hirsutism (28%), irregular menses (72%). In another study of Ligia G et al.8 the percentage of acne (5.5%), Hirsutism (79.5%) and irregular menses (96.3%).

Regarding fertility problems it was found that 46.66% respondents had children and 53.34% respondents had no children living with mental agony. About gestational issue, it was found that 66.67% respondents delivered live births and 33.33% respondents had miscarriages/ abortion. Our study is analogous to the study of Geetha K et al.

Therapeutic plans for PCOS include hormonal therapy, anti-androgen drugs; anti-diabetic drugs etc. Majority of patients were prescribed hormonal therapy which is a first line therapy for PCOS, followed by metformin. This indicates that the most of the patients are showing insulin resistance, which is the important sign of PCOS, others patients received therapy according to their clinical manifestations.

Regarding therapeutic issue, it was found that 40 (61.53%) patients were treated with ethinyl estradiol, 20 (30.76%) patients were treated with medroxy progesterone, 30 (46.15%) patients were treated with metformin, 11 (16.92%) patients were treated with clomiphene citrate, 10 (15.38%) patients were treated with aromatase inhibitor, 41 (63.07%) patients were treated with metformin plus clomiphene, 1 (1.53%) patient was treated with ovarian drilling and all the 65 (100%) patients were advised and counseled about lifestyle modification by diet, physical exercise etc.

These results are similar with the studies of Geetha K et al., 16 Metformin therapy (20%), ethinyl estradiol (10%), medroxy progesterone acetate (10%) and other treatments (13%). All the respondents were counseled and advise about their life style modification like physical exercise, diet along with medical treatment given to increase the likelihood ovulation and pregnancy.

CONCLUSION
PCOS is a combination of several endocrine disorders which is associated with mainly reproductive and cardiovascular complications. It is the main cause of anovulatory infertility with high risk of miscarriage or abortion. The prevalence rate of PCOS was 6.5% (65 patients in 1000 women). Among the married women, maximum 66.15% PCOS occur in age group 18-28 years. 41.54% women were 61-70 Kg weight. 53.34% had no child who had mental agony. 89.24% women had history of no physical exercise. 92.30% had the history of irregular menstruation, 33.33% had the history of miscarriage. Near about 100% had history of no physical exercise. Most of the women had the hormonal treatment or combination of hormonal and anti-diabetic drug even anti-androgen drug also. So, PCOS patients need special attention and interventions. It is the right time to take initiatives for creating awareness among PCOS patients. Prompt diagnosis and appropriate treatment will be able to relief their agony with a very good outcome.

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