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Clinical and Biochemical Profile of Women Presenting with Hirsutism and It's Treatment Outcome-A Prospective Study

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ABSTRACT

Background: *Hirsutism is the excessive growth of terminal hair in androgen dependent areas of a woman's body. It can be idiopathic or pathological. The treatment varies according to the cause of hirsutism.*

Objectives: This study was done to evaluate the various causes of hirsutism by clinical methods and biochemical investigations and their outcome noted after treatment for six months. The treatment was given depending upon the cause of hirsutism.

Materials and Methods: *We evaluated 73 subjects with hirsutism. The age group ranged from 15 to 51 years. The study was conducted at the department of Obstetrics and Gynecology, Kanyakumari Government Medical College, Asaripallam from January 2013to January 2016. Scoring of hirsutism was done using modified Ferriman-Gallwey scoring system. Scoring > 8 was considered as hirsutism. All the subjects were evaluated clinically and biochemically. OCP containing cyproterone acetate 2 mg and ethinyl estradiol 35 microgram was given for subjects with PCOD and idiopathic hirsutism and metformin was added if BMI was > 25 kg/m2.*

Results: *In this study, hirsutism was commonly seen between 20 and 31 years. The main cause of hirsutism was PCOD (63%). There were 4 subjects with androgen secreting ovarian tumours and one subject with late onset congenital adrenal hyperplasia. There existed a statistical significance between the PCOD and the non PCOD groups with respect to the complaints of infertility (p=0.012), menstrual irregularities (p=0.041) and weight gain (p=0.002). The outcome was evaluated in 64 subjects. There was a reduction in the scoring of hirsutism in both the PCOD (p=.000) and the non PCOD groups (p=0.001) after treatment for six months. The mean reduction in the scoring of hirsutism was 1 in the PCOD group and 1.18 in the non PCOD group. There was also a significant reduction in weight in both the groups after treatment (p=0.000).*

Conclusion: *Though hirsutism is a cosmetic problem, it also causes psychological insult to a woman. It can also be a manifestation of an underlying health problem. It can also be idiopathic. Hence women with hirsutism should be evaluated completely and given treatment based upon the cause.*

Keywords: *Hirsutism, modified Ferriman-Gallwey scoring, androgen, PCOD, non PCOD, tumours, virilization, free testosterone, infertility, Cyproterone acetate, Ethinyl Estradiol, Metformin.*

INTRODUCTION

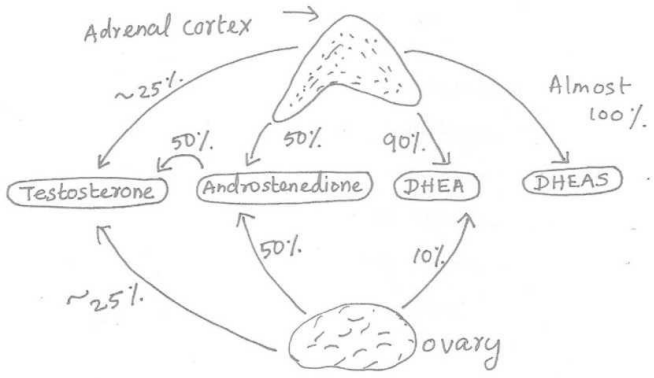
Hirsutism is a disorder which affects about 10 to 15 percent of women. Hirsutism is the most frequent androgen excess disorder in women[1].

Hirsutism is defined as the excessive growth of terminal hair in androgen dependent areas of a woman's body. Scoring is done by Ferriman-Gallwey scoring system.

Each of the nine areas is given a score of 0 to 4 depending upon the grade 1 –mild, 2-moderate, 3-complete light coverage and 4 for complete heavy coverage. A score of more than 15 is considered as severe hirsutism[2]. Occasionally, hirsutism may signal more serious pathology. Therefore, clinical evaluation should differentiate benign causes from tumours and other conditions that require specific treatment.

Hirsutism should be differentiated from hypertrichosis. Hypertrichosis is defined as a diffuse increase in vellus hair growth and is not androgen dependent. The causes of hypertrichosis include Hurlers syndrome, trisomy 18, fetal alcohol syndrome' hypothyroidism, anorexia nervosa, malnutrition, dermatomyositis, severe head injury and trauma.[3].

Picture No.1 Sources of Androgens In Adult Women



Approximately one-half of a woman's serum testosterone is derived from peripheral conversion of secreted androstenedione, and the other-half is derived from direct glandular secretion. The ovaries and adrenal glands contribute almost equally to the direct glandular testosterone production in women[1].

PATHOGENESIS OF HIRSUTISM

Hirsutism can result from an increase in androgen level or due to the oversensitivity of the hair follicles to androgen. Large quantities of circulating androgens are bound to sex hormone binding globulin (SHBG), cortisol- binding globulin and albumin. The free testosterone is the main bioactive component of plasma testosterone. The SHBG can decrease in the body in many conditions such as obesity, hyperinsulinemia or after administration of androgens, synthetic progestins, glucocorticoids and growth hormones. With the reduction in the SHBG levels in the body, the free testosterone level increases which can result in hirsutism. However the severity of hirsutism does not correlate well with the level of the androgen. This is because the sensitivity of hair follicles to androgen varies among individuals. The enzyme 5 alpha-reductase type 1 converts testosterone to the highly active dihydrotestosterone. Recent experimental evidence supports the hypothesis of intrauterine environment influencing hyperandrogenic phenotype in adult life.[5]

Both insulin and LH stimulate ovarian theca cell androgen production. As a result, affected ovaries secrete elevated levels of testosterone and androstenedione[6].

Insulin resistance independent of obesity has also been described as pathognomonic of PCOS[7]. Clinically, PCOS is characterized by menstrual irregularities, hyperandrogenism, hyperinsulinemia and long term metabolic disturbances such as diabetes mellitus, cardiovascular disease and dyslipidemias[8]. Insulin and body fat play an important role in regulating lipid levels[9].

Hirsutism is one sign of hyperandrogenism. Hirsutism can be familial, idiopathic, due to excess androgen secretion by the ovary and adrenal glands or from exogenous sources of androgens such as medications. Other causes include severe insulin resistance, anorexia nervosa, hyperprolactinemia, acromegaly, hypothyroidism and porphyria. Androgen secreting tumours of the ovary or adrenal gland usually present with virilization. Arrhenoblastoma, sertoli leydig cell tumour, theca cell tumour and some cases of granulosa cell tumour cause virilization. Androgen secreting tumours of the ovary or adrenal are usually heralded by virilization, rapid progression of hirsutism and cessation of menses. Androgen secreting adrenal tumours are less common[10].

REVIEW OF LITERATURE

The earliest reports of androgen excess, beginning 400 years BC focused on the appearance of male like hair growth and features in women often accompanied by menstrual cessation. The first of the etiologies identified were adrenal disorders, primarily adrenocortical neoplasms and adrenal hyperplasia.

Kozloviene et al , at Lithuania studied clinical and hormonal changes in women aged 18 – 35 years concluded that significantly higher levels of testosterone and dehydroepiandrosterone sulfate, higher levels of free androgen index and lower levels of sex hormone binding globulin ($p<0.01$) were found in females with hirsutism. The females with hirsutism complained more frequently of infertility, increased greasiness of skin, had higher body mass index, higher systolic and diastolic blood pressure, larger waist and hip circumference and higher WHR.[11]

Escobar and San Mill et al., concluded that basal serum 17(OH) progesterone measurement has an excellent diagnostic performance for congenital adrenal hyperplasia and CAH needs to be excluded in hyperandrogenic women.[12]

Carmina and Rosato et al ., concluded that classic PCOS is the most common androgen excess disorder and ovulatory PCOS and idiopathic hyperandrogenism are also common.[13]

The study by Azziz et al showed that hirsutism, menstrual dysfunction or acne improved in the majority of patients treated with a combination suppressive therapy.[14]

Pekhlivanov et al., concluded that in women with hirsutism, it is more appropriate to apply metformin as a monotherapy or in combination with body weight reduction. Hirsutism improved when metformin was given.[15]

Carmina et al., concluded that the addition of dexamethasone to antiandrogen therapy for hirsutism prolonged the duration of remission.[16]

In a study conducted by Marescalchi et al, at University of Bologna, Italy, it was concluded that despite different effects on androgen levels, flutamide, finasteride and EE-CPA constitute very satisfactory alternative therapeutic regimens in the treatment of hirsutism.[17]

Seaman and De Vries et al ., concluded that the risk of venous thromboembolism associated with EE-CPA does not differ significantly from that associated with the use of conventional COCs[18].

Cochrane data base analysis showed that OCP containing EE-CPA resulted in subjective improvement in hirsutism.[19]

Falsetti et al, showed the effect of long term treatment (60 cycles) with the EE-CPA Pill and the follow up after 6 months from cessation in PCOS. Mild to moderate hirsutism disappeared in 36 – 60 cycles, where as severe hirsutism decreased substantially but persisted after 6 months from the end of the therapy.[20]

According to Aesha sadaf Hameed et al, Metformin when added to OCP containing CPA has a better outcome in treating hirsutism, menstrual irregularity and BMI reduction[21].

Ancuta Gheorghisan – Geluteanu reported a Sertoli Leydig cell tumour in postmenopausal women with hirsutism. There was marked reduction in hirsutism after resection of tumour.[10]

V ATAY, C CAM, M MUHCU et al ., 2006 concluded that letrozole is associated with better ovulation induction 16.5% and higher pregnancy rate and as a first line treatment for anovulatory patients with PCOS.[22]

In a study conducted by 2 clinics in Berlin and Hamburg in 170 Oligomenorrheic patients, hyperandrogenemia was seen in 41.8%, hyperprolactinemia in 25.9%, abnormal thyroid function (TSH and / or TRH induced TSH) in 21.7% and hypergonadotropic FSH levels in 3.5% of all patients[23].

AIM OF THE STUDY

There are not many studies that look at the causes of hirsutism, their clinical profile and hormonal changes .Therefore, this study was undertaken to analyse the clinical profile, biochemical profile, various causes of hirsutism and the response to treatment.

MATERIALS AND METHODS

This is a prospective study. The period of study was from January 2013 to January 2016.Subjects were taken from Gynaecology outpatient department, Kanyakumari Govt Medical College Hospital, Asaripallam.Females with modified Ferriman-Gallwey scoring >8 were included in the study.After getting an informed consent from the subjects, they were subjected to clinical and biochemical evaluation after history taking. Women who were 60 years and above and pregnant women were excluded from the study.History of presenting complaints were enquired.Age of onset of hirsutism and duration were asked. This is because severe hirsutism can occur in a short duration in androgen secreting tumours. Longer duration of hirsutism is present in idiopathic hirsutism. Any history of irregular cycles or amenorrhoea were asked for. Menstrual complaints are common in PCOS, hypothyroidism, CAH and androgen secreting tumours. Amenorrhea is more common in CAH and androgen secreting tumours.History of infertility, weight gain and drug intake were noted. The patients in the study were subjected to clinical evaluation.

Hirsutism scoring was made according to modified Ferriman-Gallwey scoring system[24].

Height in cm and weight in kg were measured.

Blood pressure was recorded in the sitting position in the right arm.

Body Mass index was calculated by the formula, weight in kg/(height in metre)^2.Waist circumference (in cm) and hip circumference (cm) were measured for all subjects. Waist was measured at the level of belly button and hip was measured at the broadest level of the gluteal region. Waist hip ratio was calculated for all subjects. Normal WHR is 0.8. WHR > 0.8 is considered as a marker of insulin resistance.

The subjects were examined for signs of virilization and hyperandrogenism like acne, male pattern balding, increased muscle mass, deep voice, clitoromegaly, breast atrophy. Acanthosis nigricans was also looked for in each subject. Features of Cushing's syndrome like moon facies and buffalo hump were also looked for. Features of hyperprolactinemia like milk secretion were also looked for.

USG evidence of PCOS: Subjects who had 12 or more follicles in each ovary with size 2-9 mm and ovarian volume >10ml in one or both ovaries are considered as having polycystic ovaries[25]. Adnexal masses if any or any uterine abnormalities were also looked for.USG abdomen was taken in cases suspected of congenital adrenal hyperplasia or ovarian mass in addition to USG pelvis.CT abdomen was taken in cases of congenital adrenal hyperplasia and malignant ovarian tumours.

Biochemical Investigations

Free testosterone the unbound hormone and dehydroepiandrosterone sulphate levels from venous blood were measured in all individuals. Venous blood for free testosterone was taken from the subjects in the morning. DHEAS is a direct measure of adrenal androgen activity. 17 (OH) progesterone level was measured in cases suspected of CAH and adrenal tumours[30]. TSH is also measured in all cases since hypothyroidism also causes hirsutism. 24 hrs urinary cortisol has to be measured in cases suspected of Cushing's syndrome. Fasting blood sugar was measured from the venous blood for all subjects. Fasting blood sugar up to 125 mg/dl was considered as normal value and values between 126-200 mg/dl was considered as impaired glucose tolerance[32]. Values >200 mg/dl are considered as DM because insulin resistance can also cause hirsutism .100g OGTT is done in cases with fasting blood sugar > 125 mg/dl. PCOS is also associated with insulin resistance. Lipid profile was taken in all the subjects after 10 hrs fasting in the morning to rule out hyperlipidemia. These investigations were done to identify any co morbid illnesses like Diabetes mellitus and hyperlipidemia and to treat them at an early stage to prevent long term complications like atherosclerosis, stroke etc. Also PCOS is associated with metabolic syndrome.[26]

STANDARD LAB VALUES

- Free testosterone 0.4 - 2.0 pg/ml
- DHEAS 0.8-10.5 ng/ml
- TSH-0.5 to 5.5 mU/ml
- Lipid profile
- Total cholesterol <200 mg/dl

TGL < 150 mg/dl
HDL>55 mg/dl
LDL<130 mg/dl
Lipid profile and TSH are measured in the morning in empty stomach by enzymatic method.
Treatment
Subjects with idiopathic hirsutism and PCOS were given oral contraceptive pills containing cyproterone acetate 2mg with ethinyl estradiol 35mcg for 6months (6 cycles) and the outcome evaluated. The outcome evaluated were reduction in severity of hirsutism, regularization of cycles. In those with weight gain, metformin is added in a dosage of 500mg BD daily and looked for reduction in weight as well. Previous studies in women with documented PCOS have indicated that weight loss reduces insulin resistance and hyperandrogenism.[26,27,28]
In those with infertility, OCP containing cyproterone acetate 2mg and 35mcg ethinyl estradiol was given for 3 months along with metformin if BMI > 25 kg/m^2. Then letrozole was given for 3 cycles in a dosage of 2.5 mg OD for 5 days starting from the second day of the cycles. Metformin was also continued. Follicular study is done starting from 9th day of cycles and subjects were advised intercourse when the follicle reaches 18-20 mm. Subjects were asked to report to the hospital if there was a missed period or onset of menses. Pregnancy was confirmed by urine gravindex test and USG pelvis in the first trimester at 8 weeks.
In those with ovarian tumours, definitive surgery was done depending on the stage and followed by chemotherapy if needed. For late onset congenital adrenal hyperplasia, dexamethasone 0.5 mg OD is given and looked for response to treatment. This is given to suppress the excess androgen levels. They also show features of virilization. They may need procedures like clitoroplasty also.
Pharmacology of drugs used
Cyproterone acetate combined with ethinyl estradiol acts as a contraceptive agent. It is given for 21 days with a gap of 7 days in a cycle.
Cyproterone acetate has progestational activity which inhibits LH release augmenting the direct antiandrogenic action. It competes with dihydrotestosterone for the intra cellular androgen receptor and inhibits its binding.
In case of PCOD, it increases SHBG which binds the free testosterone thereby reducing hair growth, acne & dry skin and regularizes the menstrual cycle.
Metformin: It is a biguanide. It cause little or no hypoglycemia in non diabetic individuals and even in diabetics, hypoglycemia is rare. In addition to its action on blood sugar, it improves lipid profile in type 2 diabetes.
Letrozole:
It is an aromatase inhibitor, a orally active nonsteroidal compound. It reversibly inhibits aromatization all over the body, resulting in total oestrogen deprivation. It has 100% oral bioavailability.
Use: Ovulation induction.

RESULTS AND ANALYSIS
TEST STATISTICS USED WERE
• Chi – square test
• two sample ‘t’ test
• paired ‘t’ test
The subjects after clinical, biochemical analysis and ultrasonogram examination were grouped into PCOD and non PCOD. The treatment was given according to the cause of hirsutism. The outcome evaluated were weight reduction, regularity of menstrual cycles and reduction in the scoring of hirsutism. After treatment, 5 from the PCOD group and 3 from the non PCOD group conceived. There were 6 defaulters in the study. Two postmenopausal subjects were advised LASER treatment. They resorted to shaving the facial hair. One subject with malignant sertoli

leydig cell tumor had recurrence of the tumour and died due to metastasis. A p value<0.05 is significant

The mean age in the PCOD group is 24.11 years and in the non PCOD group, it is 30.15 years (p value < 0.05). It is statistically significant.

We infer that there exists a statistical significance between PCOD and non PCOD group with reference to age distribution

Table No.1 History of Subjects With Hirsutism

	PCOD	NON PCOD	Significance
Marital status Married unmarried	25(34.2%) 21(28.8%)	12(16.4%) 15(20.5%)	p=0.414
Family history of hirsutism	12(16.4%)	6(8.2%)	p=0.711
Drug intake	0	2	p=0.0296

There is no statistical significance between PCOD and NON PCOD group with reference to marital history, family history and drug intake in this study. There is a statistical significance between both the groups with regard to drug intake. (p=0.0296)

There exists a statistical significance in the BMI of subjects between the PCOD and the non PCOD group. p=0.000

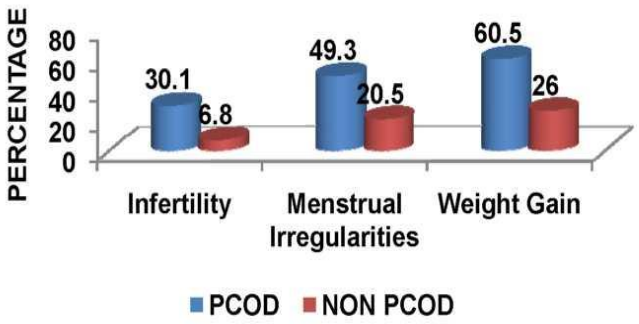
Mean waist hip ratio of subjects with PCOD and hirsutism is 0.83 and in the subjects in the non PCOD group, the mean waist hip ratio is 0.82. It is statistically insignificant. Here p value is 0.095

Table No.2 Primary Presenting Complaints of Subjects With Hirsutism.

Infertility	PCOD	NON PCOD	Total	Singificance
	22(30.1%)	5(6.8%)	27(37%)	P=0.012
Menstrual irregularities	36(49.3%)	15(20.5%)	51(69.9%)	P=0.041
Weight gain	44(60.3%)	19(26.0%)	63(86.3%)	P=0.002

There exists a statistical difference between PCOD and non PCOD groups with respect to the complaints of infertility, menstrual irregularities and weight gain.

Chart No.1 Primary Presenting Complaints of Subjects with Hirsutism



The mean duration of hirsutism in the PCOD group is 4.89 years and in the non PCOD, it is 5.52 years. It is statistically insignificant. (p=.569)

Table No.3 BMI of Subjects With Hirsutism In This Study

BMI	PCOD	NON PCOD	Total
18.5-24.9 % of total	1(1.4%)	9(12.3%)	10(13.7%)
25-29.9 % of total	20(27.4%)	12(16.4%)	32(43.8%)
>= 30 % of total	25(34.2%)	6(8.2%)	31(42.5%)

Chart No.2 Hirsutism Subjects with Elevated Dheas and Tsh

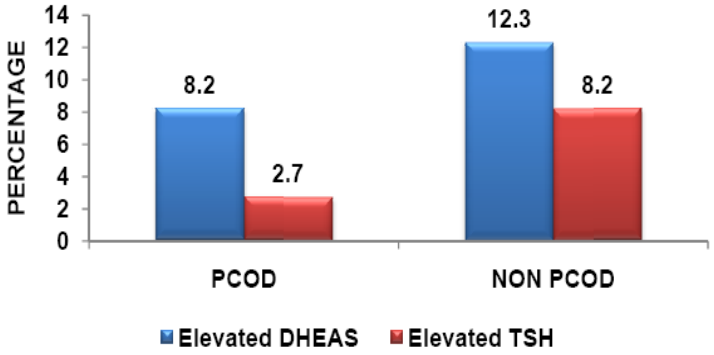
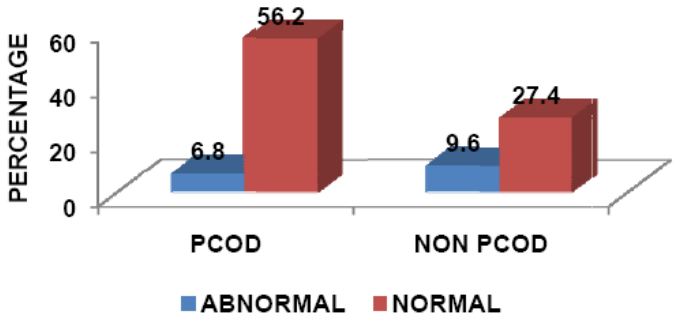


Chart No.3 Lipid Profile of Subjects with Hirsutism



There exists a statistical significance in the elevated TSH levels and elevated DHEAS levels

between the PCOD and the non PCOD groups. There is no statistical significance between the PCOD and non PCOD groups in elevated free testosterone levels and hyperlipidemia.

Table No.4 Group Statistics- Fasting Blood Sugar

	Total No:	Mean	Standard Deviation	Standard Error Mean
PCOD	46	88.98	15.937	2.350
NON PCOD	27	98.04	26.690	5.136

Here p value = 0.073
It is statistically not significant.

The mean free testosterone level in the PCOD group is 1.92 pg/ml and in the non PCOD group it is 2.18 pg/ml. Here p value is 0.494

Table No.5 Group Statistics - Dheas Levels

	Total No:	Mean	Standard Deviation	Standard Error Mean
PCOD	46	8.64	1.941	0.286
NON PCOD	27	8.76	2.114	0.407

Here p value = 0.806

TREATMENT OUTCOME OF SUBJECTS WITH HIRSUTISM

Table No.6 Pre Treatment Hirsutism Scoring of Subjects With Hirsutism

		Total No:	Mean	Standard Deviation	Standard Error Mean	Significant
Pre treatment hirsutism	PCOD	46	11.61	2.695	0.397	p=0.798
	NON PCOD	27	11.44	2.517	0.484	

Mean hirsutism score is 11.61 in the PCOD group and 11.44 in the non PCOD group. It is statistically insignificant.

Table No.7 Reduction of Hirsutism Scoring after Treatment In The Pcod Group Paired Samples Statistics

PCOD Group	Mean	No.	Standard deviation	Standard error
Hirsutism score Pre treatment	11.69	42	2.789	.430
Hirsutism Post treatment	10.69	42	3.272	.505

p=0.000

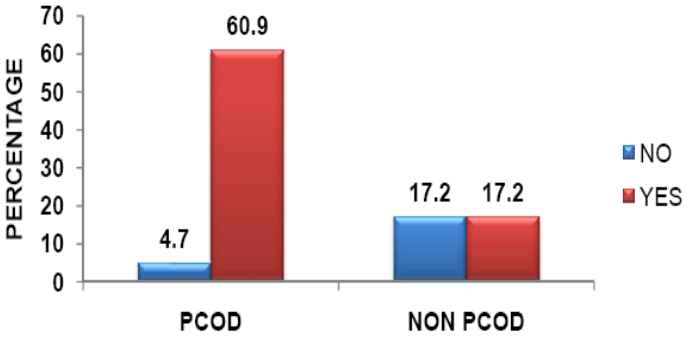
There is a statistically significant reduction in hirsutism score after treatment in the PCOD group. The mean reduction is 1.

Table No.8 Reduction in Hirsutism Scoring After Treatment In The Non Pcod Group

Non PCOD Group	Mean	No.	Standard deviation	Standard error
Hirsutism score Pre treatment	11.59	22	2.462	0.525
Hirsutism Post treatment	10.41	22	2.282	0.486

p=0.001
There exists a statistical significance between the hirsutism scores of the pre treatment and post treatment Non PCOD subjects. These is a mean reduction in score by 1.18

Chart No.4 Weight Reduction of Subjects with Hirsutism After Treatment

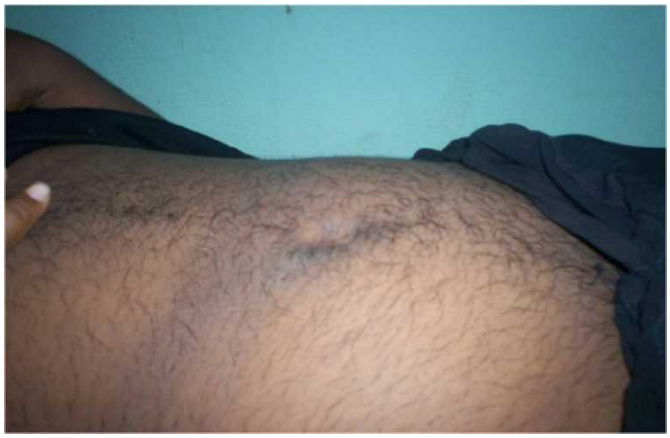


Chi-Square tests

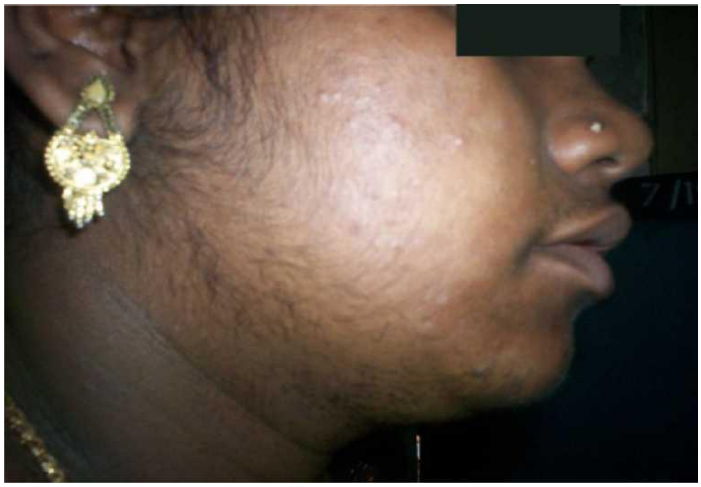
a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.81.
b. Computed only for a 2x2 table
p = 0.000
There is a statistically significant reduction in weight after treatment in hirsutism subjects in this study..
USG pictures of subjects with hirsutism

- Polycystic ovaries – 46.
- Hypoplastic uterus with adrenal hyperplasia-1
- Adnexal mass - 6.
- Dermoid cyst – 1
- Endometriotic cyst-1
- Ovarian mass-4
- Normal Study – 21

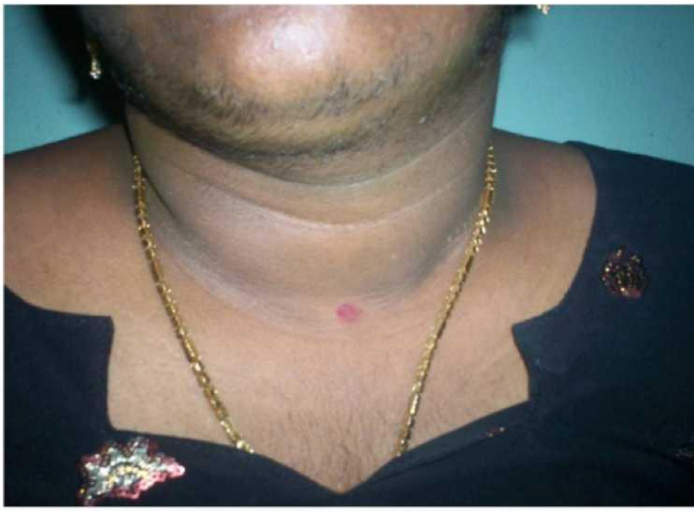
Picture No.2 Picture of A Subject with Excessive Hair in the Abdomen



Picture No.3 Picture of A Subject with Excessive Facial Hair



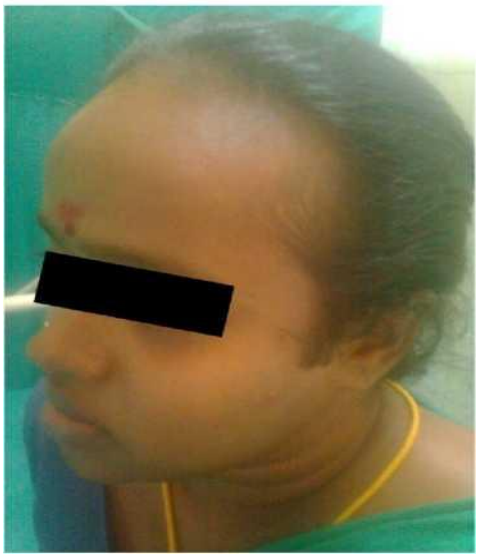
Picture No.4 Picture of A Subject with Excessive Chest Hair



Picture No.5 Picture of A Subject with Frontal Hair Loss
(She Was Diagnosed As Having Malignant Granulosa Cell Tumour)

Picture No.6 Picture of a Subject With Pcod with Frontal Hair Loss

Picture No.7 Picture of a Subject with Androgen Secreting Ovarian Tumour with Frontal Baldness



She underwent TAH with BSO. Histopathology report came as Juvenile Granulosa Cell Tumour.

DISCUSSION

A study by Aesha Sadaf et al., at Bahawalpur, Pakistan showed the age range of hirsutism was from 16 to 38 years. In our study the age range of hirsutism was from 15 to 51 years[23]. In our study 65% of PCOS subjects had onset of hirsutism between 10 and 20 years whereas 50% of non PCOS subjects had onset of hirsutism from 21 and 30 years.

In a study on 122 female residents by Kozloviene at al., at Lithuania aged 18-35 years in 2002-2003 ,the females with hirsutism complained more frequently of infertility (P<0.05), increased greasiness of skin (p<0.05), higher systolic and diastolic blood pressure, larger waist and hip ratio (P<0.001), higher levels of testosterone and dehydroepiandrosterone sulphate (P<0.05)[11]. In our study, the subjects complained of infertility (p=.012), irregular cycles (n=31) % oligomenorrhoea or amenorrhea (n=12). Increased waist hip ratio was seen in 14 subjects, increased free testosterone in 24 cases and increased DHEAS in 15 subjects(p=.038) in our study. Two subjects with hirsutism had premature ovarian failure . They had increased FSH and LH. They were given hormone replacement therapy.

In a study by Carmina et al., at Palermo, Italy between 1980 and 2004, the prevalence of androgen excess disorders was PCOS (72.1%), idiopathic hyperandrogenism (15.8%), idiopathic hirsutism (7.6%), 21-hydroxylase - deficient non classic congenital adrenal hyperplasia (4.3%), androgen secreting tumours (0.2%)[13]. In our study, the prevalence of PCOS was 63.01%, idiopathic hirsutism 0.44%, hypothyroidism 0.08% androgen secreting ovarian tumours 0.05%, premature ovarian failure (0.02%), drug induced hirsutism 0.02%, late onset congenital adrenal hyperplasia 0.014%[12]. A 15 years old girl who presented with features of virilization including hirsutism was diagnosed as congenital adrenal hyperplasia- late onset type.

In the study by Azziz et al., at Alabama between October 1987 and June 2002 in 873 subjects, a total of 257 patients were included in the assessment of the response to hormone therapy. The mean duration of follow up was 33.5 months (range 6-15.5). Hirsutism improved in 86%, menstrual dysfunction in 80%, and hair loss in 33% of patients[14].

In our study, free testosterone levels were elevated in 24 subjects (24/73=32.87%). DHEAS in 14/73=19.17%), abnormal lipid profile in 12/78=16.4%), elevated TSH in 8 subjects (10.95%). The response was assessed in 64 subjects after 6 months of treatment. Subjects who were post menopausal (n=2) were advised laser treatment. They did not go for laser treatment. They opted for shaving the excess hair in the face. They used to shave once in two weeks. 17 subjects in the PCOS group and 13 subjects in the non PCOS group showed reduction in the severity of hirsutism. Probably the others needed an increase in the dosage of cyproterone acetate or duration of treatment. However all of them need to be followed up after 1 year whether there is recurrence or not. 4 subjects were diagnosed as having diabetes mellitus in our study (1 in the PCOD group and 3 in the non PCOD group). 1 subject with PCOD was diagnosed as having impaired glucose tolerance.

In a study by Carmina et al., androgen levels remained low after 1 year of treatment with dexamethasone along with spironolactone[16]. In our study, we gave treatment for 6 months only but did not measure post treatment free testosterone levels. There was statistically significant reduction in the severity of hirsutism in both PCOS and non PCOS groups. We did not follow up the patient after 1 year in our study. In their study, those who were treated with spironolactone only, the hirsutism scores returned to baseline scores after 1 year.

A study by Marescalchi et al., Italy showed that OCP containing EE-CPA was most efficacious in treating hirsutism[17]. In their study, the hirsutism scoring was done after 6, 9 and 12 months. The decrease was -60±18%, -20±11%, 28±21% after 6,9 and 12 months respectively.

In our study the hirsutism scoring was done after 6 months of treatment. The cycles became regular in 46.57% PCOS subjects and 19.17% non PCOS subjects, remained irregular in 4.8% PCOS cases and 4.5% of non PCOS subjects. 4.7% PCOS subects were oligomenorrhoeic and 7.8% non PCOS subjects were amenorrhoeic in our study.

In a study by K Rautio et al., 35 women with PCOS (18 obese and 17 nonobese) were randomised to 6 months treatment with metformin or EE_2-CPA OCP[28]. Metformin treatment had beneficial effects on lipid profile and blood pressure[22]. In our study, metformin was used for subjects with BMI>25 kg/m^2, but follow up of the subjects with post treatment lipid profile was not done. 11 of the subjects in our study had abnormal lipid profile (ie, elevated total cholesterol and elevated low density lipoprotein).

There are not many studies in androgen secreting ovarian tumours. In our study, there were 4 cases of androgen secreting ovarian tumours. There was one malignant granulosa cell tumour, one juvenile granulosa cell tumour, two malignant sertoli leydig cell tumours. All the four had features of virilization. Of these, 3 showed marked reduction in severity of hirsutism, but the clitoromegaly, breast atrophy, hoarseness of voice did not change. One case of malignant sertoli leydig cell tumour stage 3 developed recurrence after 6 months and died due to lung metastasis.

There were 6 subjects with hypothyroidism in the non PCOD group. They were given EE-CPA along with thyroxine for six months. 5 subjects showed reduction in the severity of hirsutism by 1 to 3 scores. 1 subject showed no reduction in the severity of hirsutism.

One subject with PCOD showed frontal hair loss. She was obese with BMI of 30.01kg/m^2, had elevated LDL, cholesterol and TGL. She came with complaints of infertility and irregular cycles once in 3 to 6 months. She was given metformin along with EE-CPA for 3 months. She had a hirsutism score of 21. She showed reduction in weight and she had regular cycles after 3 months. She was started on letrozole from the second day of periods but she failed to conceive. She also showed no reduction in the severity of hirsutism.

Obesity has a negative impact on the efficacy of the treatment of hirsutism. Hence appropriate lifestyle advice is necessary for a successful treatment programme.[30]

Any disturbance in ovarian androgen metabolism will profoundly affect the reproductive state of a woman[35]. Significance of elevated serum LH, insulin resistance or polycystic appearing ovaries assessed by USG for the diagnosis of PCOS remains uncertain. Hyperandrogenism and chronic anovulation are mandatory for the diagnosis of PCOS[36]. Polycystic ovaries are common in normal women[37]. Women who are overweight can expect an improvement in their symptoms if they lose weight[38,39]. Pharmacologic and non pharmacological methods are used for hirsutism. Advances in laser hair removal methods and topical hair growth retardants offer new options[40].

Our study has shown that OCP containing EE-CPA along with metformin has been effective in reducing body weight and regularization of cycles and mild reduction in the severity of hirsutism.

SUMMARY

In this study, 52 had ovarian causes, (46 – PCOS, 4- ovarian tumour, 2- premature ovarian failure), one had adrenal cause (late onset CAH), systemic cause (hypothyroid -6) for hirsutism.

- Majority of cases of hirsutism in this study fall in the 21 – 30 years age group.
- In addition to hirsutism, menstrual irregularity is the chief complaint
- Majority had hirsutism scoring of 9 to 11. Severe hirsutism (Scoring more than > 15) was seen in androgen secreting ovarian tumour and PCOS (4 cases)
- Virilization features commonly were seen in all the 4 ovarian tumors and late onset CAH . Highly elevated free testosterone levels were seen in androgen secreting ovarian tumours and late onset congenital adrenal hyperplasia.

- Subjects with hirsutism were either overweight or obese except ovarian tumours and CAH.
- Co morbid conditions like hyperlipidemia, diabetes mellitus, hypertension were seen in few PCOS and few non PCOS subjects.
- Level of the testosterone did not correlate with the severity of hirsutism in the PCOS group.

CONCLUSION

This study evaluates the various causes of hirsutism, their clinical and biochemical profile and their outcome after treatment. Although PCOS is the most common cause for hirsutism, other causes should also be thought of. The treatment should be individualised depending upon the cause of hirsutism. We should have a high suspicion of virilizing tumours if features of virilization are present. Hirsutism has a response to OCP containing cyproterone acetate but the reduction in severity of hirsutism is mild. They might need increase in the duration of treatment and dosage of cyproterone acetate. Free testosterone and DHEAS may or may not be elevated in PCOS. Majority have normal levels. Free testosterone is highly elevated in androgen secreting ovarian tumours. This study has highlighted the importance of evaluating the other causes of hirsutism such as androgen secreting ovarian tumours and adrenal hyperplasia. Hirsutism causes cosmetic problem and psychological upset on a woman. It can also be a manifestation of an underlying health problem. Hence it should be properly treated so that a favourable outcome can be obtained.

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ABBREVIATIONS

PCOS	-	Polycystic Ovarian Syndrome
DHEA	-	Dehydroepiandrosterone
17(OH) Progesterone	-	17 hydroxy Progesterone
DHEAS	-	Dehydroepiandrosterone Sulphate
CAH	-	Congenital Adrenal Hyperplasia
BMI	-	Body Mass Index
CT	-	Computed tomography
USG	-	Ultrasonogram
TSH	-	Thyroid stimulating hormone
CHO	-	Cholesterol
TC	-	Total cholesterol
HDL	-	High density lipoprotein
LDL	-	Low density lipoprotein
VLDL	-	Very low density lipoprotein
EE-CPA		Oral contraceptive pill containing cyproterone acetate 2mg and Ethinyl estradiol 35 microogram
COCs	-	Combined oral contraceptive pills
OCP	-	Oral Contraceptive Pill
TRH	-	Thyrotropin releasing hormone
FSH	-	Follicle stimulating hormone
LH	-	Leutinizing hormone
SHBG	-	Sex hormone binding globulin