EFFECT OF STRESS AND ANXIETY ON POLYCYSTIC OVARY SYNDROME AND RELATED HEALTH PROBLEMS IN CHHATTISGARH WOMEN

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Abstract:

Hormone status is affected by environment, as proved by many previous studies. Stress is now part of our environment. Mental Stress as Mental pollution has been drastically increased in last decade. Now it is significantly affecting the in vivo hormonal production, their chemistry and even their functioning. This stress as environmental pollutant precipitates significantly low levels of progesterone, extremely high levels of testosterone, hence Polycystic ovary syndrome..[PCOS] Between 1 in 10 women of childbearing age has PCOS. It can occur in girls as young as 11 years,. Polycystic Ovary Syndrome, or PCOS, is a metabolic disorder that affects the female reproductive system. The key characteristics in the studied group include irregular menstruation, obesity, infertility, acne and hair growth on the face, chest, and back (hirsutism) and ovarian cysts. Some have Type 2 diabetes. And most of them have effects of androgenic (masculinizing) hormones. Serum insulin levels are significantly higher in subjects having PCOs, androgens, specifically testosterone, and often less estrogen and progesterone than normal. Many other associated health problems are also seen –dyslipidemia, autoimmune thyroiditis , high blood pressure. But the most disastrous effect is stress via PCOs stimulates excessive production of Insulin, finally Insulin Resistance Diabetes [Type –II Diabetes] is developed. Stress driven or PCOs driven obesity is present in studied group. As High Testoesterone level is the single most diagnostic criterion. Hyper insulinaemia is related to hyper androgonism. Body weight was related to ovarian stroma and hirsutism. The study showed that stress has significantly adverse effect on hormonal profile of the subjects and this condition is strongly co-related with occurrence of PCOs and Diabetes in females.

Keywords: *hormones, mental pollution, environmental pollutants*

Introduction:

PCOS is a complex metabolic, endocrine and reproductive disorder affecting approximately 5-10% of the female population in developed countries. The prevalence of PCOs is on the rise in developing nations like India, which are undergoing rapid nutritional transitions due to westernized

diets and lifestyle. However, less appreciated in the literature are the developmental psychosocial impacts for women diagnosed with PCOS, especially in developing countries.

Everyone gets stressed from time to time. There's no way to avoid the condition all the time, but as a woman living with PCOS it's extremely important to recognize the signs to becoming stressed, and to know how the emotion impacts one's imbalance. Men and women report different reactions to stress, both physically and mentally. They attempt to manage stress in very different ways and also perceive their ability to do so — and the things that stand in their way — in markedly different ways. Findings suggest that while women are more likely to report physical symptoms associated with stress, they are doing a better job connecting with others in their lives and, at times, these connections are important to their stress management strategies but mostly stress is over-ruling their condition.

Though they report similar average stress levels, women are more likely than men to report that their stress levels are on the rise. They are also much more likely than men to report physical and emotional symptoms of stress. When comparing women with each other, there also appears to be differences in the ways that married and single women experience stress. (Eder, U.; Gibian, H.; Haffer, G.; Neef, G. N.; Sauer, G.; Wiechert, R. (2003)-

Symptoms of stress include feeling tense, depression, poor memory, poor concentration, increased alcohol consumption, anger/hostility, difficulty making decisions, frequent mood swings, negative thinking, distractibility, excess smoking or eating & feeling overwhelmed or helpless

Some experts feel that women are particularly susceptible to stress-

Women are socialized to be the caretakers of others. More women than men have both a career outside the home and continue to try to juggle traditional responsibilities after hours. Over 70% of married women with children under the age of 18 are employed outside the home. Sociologists describe women as struggling to achieve the "male standard" at work, while trying to maintain the perfect wife and mother standards at home.

Women are also less likely to be in as powerful positions as men to change their environment. Women find it harder to say no to others' requests and often feel guilty if they can't please everyone. They often spend less time nurturing their own emotional and physical needs, as that might be perceived as selfish. In addition, relationship alterations or the loss of loved ones can produce empty nest or other separation syndromes.

As women progress through life's stages, hormonal balance associated with premenstrual, post-partum and menopausal changes can affect chemical vulnerability to stress and depression.

Consequences of Long-Term Stress-

A little stress every now and then is not something to be concerned about. Ongoing, chronic stress, however, can cause or exacerbate many serious health problems, including:

- Mental health problems, such as depression, anxiety, and personality disorders

- Cardiovascular disease, including heart disease, high blood pressure, abnormal heart rhythms, heart attacks, and stroke

- Obesity and other eating disorders

- Menstrual problems

- Sexual dysfunction, such as impotence and premature ejaculation in men and loss of sexual desire in both men and women

- Skin and hair problems, such as acne, psoriasis, and eczema, and permanent hair loss

- Gastrointestinal problems, such as GERD, gastritis, ulcerative colitis, and irritable colon

Etio-pathology – Stress precipitates PCOs –

- Excess eating due to stress is common .Adipose tissue possesses aromatase, an enzyme that converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese patients creates the paradox of having both excess androgens (which are responsible for hirsutism and virilization) and estrogens (which inhibits FSH via negative feedback).

- Corticosteroids are secreted during stress and this hormone causes aromatization of estrogen at 19th carbon and stimulates production of Testosterone in place of estrogen. Thus female hormone reduces significantly with rise in Androgens –especially Testosterones.

- This changed hormone profile causes formation of cysts in the periphery of the ovaries,

- The frank symptoms of PCOs are developed .

- This condition stimulates testicular: enzymatic (5-alpha-reductase d· Also Androgen receptor are stimulated.(Androgen sensitivity syndrome)

- Polycystic ovaries are a sign of anovulation and are often associated with changes of obesity, hypertension, diabetes and excessive hair growth (hirsutism). On ultrasound, the ovaries of these women often show bead-like, little cysts along the periphery of the ovary. Experts remind us that this is not actually one disease but actually a sign of a cascade of disorders encompassing atherosclerosis, obesity, hyperlipidemia, hypertension and androgen excess.

- Women with PCOS have abnormalities in the metabolism of androgens and estrogen and in the control of androgen production. High serum concentrations of androgenic hormones, such as testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S) encountered in these patients. However, individual variation is considerable, and a particular patient might have normal androgen levels.

- PCOS is also associated with peripheral insulin resistance and hyperinsulinemia, and obesity amplifies the degree of both abnormalities. Insulin resistance in PCOS can be secondary to a post binding defect in insulin receptor signalling pathways, and elevated insulin levels may have gonadotropin-augmenting effects on ovarian function.

- In addition, insulin resistance in PCOS has been associated with adiponectin—a hormone secreted by adipocytes that regulates lipid metabolism and glucose levels; both lean and obese women with PCOS have lower adiponectin levels than women without PCOS.

- Raised luteinising hormone (LH) in the early part of the menstrual cycle.

- Disturbed thyroid function tests .

- lower amounts of the blood protein that carries all sex hormones (sex-hormone-binding globulin)

- A small increase in the amount of insulin and cellular resistance to its actions.(Insulin Resistance Syndrome with frank Type- II Diabetes)

- A raised levels of anti-Mullerian hormone, when compared with women with normal regular cycles (this may become a more useful and accurate test than checking LH or the LH to FSH ratio).

- A raised levels of prolactin and of thyroid stimulating hormone (TSH). Both these hormones are produced from a particular part of the brain, the anterior pituitary in response to the changes hormonal profile in stress , specially due to cortico-steroids.

- Raised Prolactin levels can occur together with headaches and some disturbances of vision, whereas raised TSH levels indicate low thyroid hormones (hypothyroidism). Both these conditions lead to suppressed ovulation and infertility.

- Increased hair and acne reflect an increase in male hormones (androgens) in the blood. Other conditions can cause such an increase.

- Rarely, Ovarian cysts driven adrenal disorders or tumors cause increased androgens. In these conditions: hirsutism usually develops quite rapidly, previously normal periods may also stop and, occasionally, muscle weakness occurs.

- Loss of, or changes in, female aspects of body shape and appearance (secondary sexual characteristics), especially reduction in breast size, may also occur.

- As the androgen excess progresses, the voice can deepen and the clitoris can increase in size (clitoromegaly).

- A proposed mechanism for anovulation and elevated androgen levels suggests that, under the increased stimulatory effect of luteinizing hormone (LH) secreted by the anterior pituitary, stimulation of the ovarian theca cells is increased. In turn, these cells increase the production of androgens (eg, testosterone, androstenedione).

- Because of a decreased level of follicle-stimulating hormone (FSH) relative to LH, the ovarian granulosa cells cannot aromatize the androgens to estrogens, which leads to decreased estrogen levels and consequent anovulation. Growth hormone (GH) and insulin-like growth factor–1 (IGF-1) may also augment the effect on ovarian function.

- Hyperinsulinemia is also responsible for dyslipidemia and for elevated levels of plasminogen activator inhibitor-1 (PAI-1) in patients with PCOS. Elevated PAI-1 levels are a risk factor for intravascular thrombosis.

- Polycystic ovaries are enlarged bilaterally and have a smooth thickened capsule that is avascular. On cut sections, subcapsular follicles in various stages of atresia are seen in the peripheral part of the ovary. The most striking ovarian feature of PCOS is hyperplasia of the theca stromal cells surrounding arrested follicles. On microscopic examination, luteinized theca cells are seen.

- Most women with PCOS will have the ultrasound findings, whereas the menstrual cycle abnormalities are found in around 66 per cent of women and obesity is found in 40 per cent. The increase in hair and acne are found in up to 70 per cent, whereas the hormone abnormalities are found in up to 89 per cent of women with PCOS.

The Magnitude of the problem-

- More than 50 percent of women with PCOS will have diabetes or pre-diabetes (impaired glucose tolerance) before the age of 40.

- The risk of heart attack is 4 to 7 times higher in women with PCOS than women of the same age without PCOS.

- Women with PCOS are at greater risk of having high blood pressure.

- Women with PCOS have high levels of LDL (bad) cholesterol and low levels of HDL (good) cholesterol.

- Women with PCOS can develop sleep apnea. This is when breathing stops for short periods of time during sleep.

- Women with PCOS may also develop anxiety and depression and vice versa. It is important to consult doctor about treatment for these mental health conditions.

Based on these findings we designed a study based on women with high stress level-

Study size- 30 (randomly selected on the basis on the jab pattern and family atmosphere with high stress by contacting in clinics and compared with mentally and physically healthy age matched controls.

Age range-33-57 years.

Economic status –lower to moderate.

The following estimations were made-

➢ Their stress level was first assessed by Eight State Questionnaire (8 SQ Scale) developed by (Curran & Cattell, 1976)

➢ The subjects who scored high score for stress and anxiety were picked as study subjects. (Above 6 score)

➢ Their physical examination was done for physical symptoms of PCOs . The visual symptoms of the hormonal imbalances as virilism, hirsutism, infertility, acne, oligomennorohea/ amneorrhoea, hypermenorrhea, central obesity were also considered for conclusion.

➢ Their body measurements were measured and BMI was calculated.

➢ Their biochemical profile was assessed for conforming the occurrence of PCOs

➢ Serum estrogenic level (Estradiol) was assessed by competitive ELISA using Estradiol Kit manufactured by Adaltis Italia (Italy) in Abhay's lab, Bilaspur.

➢ Progesterone was estimated by using Thermo Scientific Varioskan Flash Multimode Reader Using an Enzyme-Linked Immunosorbent Assay in Akash patho lab, Bilapsur.

➢ Serum Testosterone level was also assessed by Thermo Scientific Varioskan Flash Multimode Reader Using an Enzyme-Linked Immunosorbent Assay.

➢ Serum Glucose level was assessed by using HbA1c by using Nycocard.

➢ Serum C-Peptide level was assessed by using- serum C-peptide (ELISA)- kit made by HIPAA.

➢ SHBG level was assessed by Ranbaxy lab , only for five persons .

➢ The Androgen Index was calculated by the formula-

FA1 = 100 X Total Testosterone /SHBG

➢ Total Lipid Profile was estimated by using Auto-analyser-

➢ Kits for analysis were used –

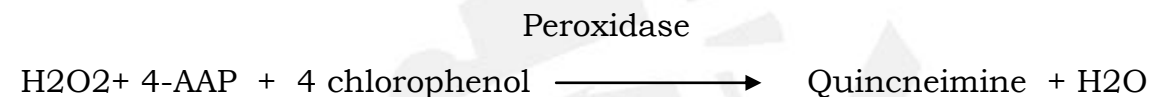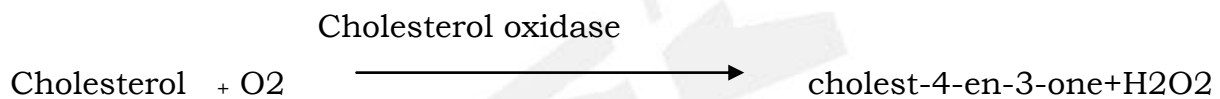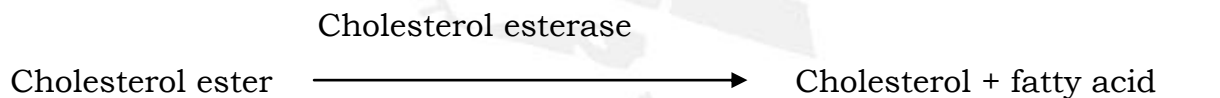(A) Cholesterol Estimation Kit (one step method of Wybenga and Plleggi) (Catalog No. – 25924)

(B) HDL Estimation Kit (One step method of Wybenga and Plleggi) (Catalog No.– 25924)

(C) Triglyceride Estimation Kit (Enzymatic colorimetric method GPO–PAP liquid stable single regent) (Catalog No. 77034 (6×250 ml)).

➢ HDL (High Density Lipoprotein) -The reagent used for it was 16% polyethylenglycol and the absorbance was read at 510nm against blank reagent and calculation was done by
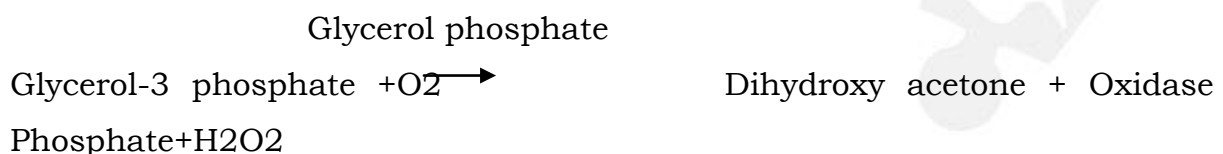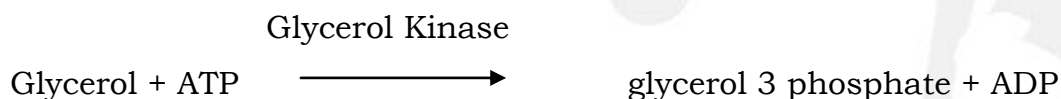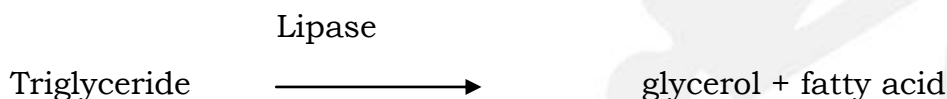
   $Ax/As \times 50 \times 2$ = mg/dl HDL cholesterol

➢ CHOLESTEROL : It was enzymatic calorimetrically measured at 510nm. The   reaction was as-

                  Cholesterol esterase

Cholesterol ester ⟶ Cholesterol + fatty acid

                  Cholesterol oxidase

Cholesterol $_+ O_2$ ⟶ cholest-4-en-3-one+H_2O_2

            Peroxidase

 H_2O_2+ 4-AAP + 4 chlorophenol ⟶ Quincneimine + H_2O

   The calculation was done by – $Ax/As \times 200$ = mg/dl cholesterol

➢ TEIGLYCERIDE : The Serum triglyceride levels were also also measured by enzymatic calorimetric method at 510 nm and expressed as $Ax/As \times 200$ = mg/dl triglycerides (x= sample, S= Standard)

               Lipase

Triglyceride ⟶ glycerol + fatty acid

         Glycerol Kinase

Glycerol + ATP ⟶ glycerol 3 phosphate + ADP

           Glycerol phosphate

Glycerol-3 phosphate +O_2⟶ Dihydroxy acetone + Oxidase Phosphate+H_2O_2

Peroxidase

$$H_2O_2 + 4\text{-}AAP + 4 \text{ chlorophenol} \longrightarrow \text{Quinoneimine (Red Coloured Dye)} + H_2O$$

The colour density of Quinoneimine is measured in colorimeter.

The LDL value was calculated by using – Fw formula.

➢ **Pelvic Exam was done by expert gynecologist-** to see if ovaries are enlarged or swollen by the increased number of small cysts.

➢ **Vaginal Ultrasound (sonogram) of the subjects was done on our request, we just collected the data.** To perform this test that uses sound waves to take pictures of the pelvic area. It is used to examine ovaries for cysts and to check the endometrium (lining of the womb). This lining may become thicker if periods are not regular.

➢ The thyroid is also affected due to this condition ,so we assessed T-3, T-4 and TSH levels of persons from each group. The estimation was done by Thyrocare lab, Bombay. Also visual symptoms of hypothyroidism as dry skin, constipation, fatigue, joint stiffness, swelling in face, hair loss were observed for conformation .

Mostly these estimations were done by the subjects and we collected the results. Some estimations were done by us.

Observations-

▸ Women are more likely than men (28 percent vs. 20 percent) to report having a great deal of stress (8, 9 or 10 on a 10-point scale).

▸ Almost more than half of all women (69 percent) surveyed said their stress has increased over the past five years, compared to four in 10 (39 percent) men.

▸ Women are more likely to report that money (79 percent compared with 73 percent of men) and the economy (68 percent compared with 61 percent of men) are sources of stress while men are far more likely to cite that work is a source of stress (76 percent compared with 65 percent of women).

▸ Women are more likely to report physical and emotional symptoms of stress than men, such as having had a headache (41 percent vs. 30 percent), having felt as though they could cry (44 percent vs. 15 percent),

or having had an upset stomach or indigestion (32 percent vs. 21 percent) .

▸ Married women report higher levels of stress than single women, with one-third (33 percent) reporting that they have experienced a great deal of stress in the past month (8, 9 or 10 on a 10-point scale) compared with one in five (22 percent) of single women. Similarly, significantly more married women report that their stress has increased over the past five years (56 percent vs. 41 percent of single women). Single women are also more likely than married women to say they feel they are doing enough to manage their stress (63 percent vs. 51 percent).

▸ Married women are more likely than single women to report they have experienced the following due to stress in the past month: feeling as though they could cry (54 percent vs. 33 percent), feeling irritable or angry (52 percent vs. 38 percent), having headaches (48 percent vs. 33 percent) and experiencing fatigue (47 percent vs. 35 percent).

▸ Men and women report wide gaps between determining what is important and how successful they are at achieving those behaviors.

▸ Women are much more likely than men to say that having a good relationship with their families is important to them (84 percent vs. 74 percent). While fewer women say they are doing a good job at succeeding in this area, they outpace men (67 percent vs. 53 percent).

▸ Women are also more likely than men to say that having a good relationship with their friends is important to them (69 percent vs. 62 percent), even though friendship is cited less often than family for both men and women.

▸ Even though nearly half of all women (49 percent) say they have lain awake at night in the past month because of stress, three-quarters of women rate getting enough sleep as extremely or very important (75 percent compared with 58 percent of men).

▸ Across the board, men's and women's perceptions of their ability to succeed in areas that are important to their well-being are far out of line with the importance they place on these behaviors. Even more so than women, men report less likelihood of success in these areas.

‣ Only 33 percent of women report being successful in their efforts to get enough sleep (compared with 75 percent who believe this is important); only 35 percent report success in their efforts to manage stress (compared with 69 percent who believe this is important); 36 percent report success in their efforts to eat healthy (compared with 64 percent who believe this is important); and only 29 percent are successful in their efforts to be physically active (compared with 54 percent who believe this is important).

BIOCHEMICAL OBSERVATION-

Mean, SD & 't' Values of parameters assessed-

parameters	(mean ± SD)		Change in percent-age value
	With high Stress & Anxiety (n=18)	With normal Stress & Anxiety (n=18)	
Serum Estrogen	92 pmol/L	233 pmol/L)	60.52 % down
Serum Progesterone	0.73 ng/mL	1.66 ng/mL.	56.03 % down
Serum testosterone	81 ng/dL	53 ng/dL	52.83 % up
Serum Cholesterol	281 mg/dl,	177 mg/dl,	58.75 % up
HDL (mg/ml)	32 mg/dl.	41 mg/dl ,	21.96 % down
Serum Triglyceride	314 mg/dl	183 mg/dl	71.58 % up
Cholesterol: HDL	6.1	4.9.	24.48 % up
LDL (mg/ml)	129 mg/dl,	78 mg/dl ,	65.38 % up
Waist/ hip ratio	0.83	0.62	33.87 % up
BMI	27.44 kg/m2	21.6 kg/m2	27.03 % up
Glucosylated Hb	8.3	5.2	59.61 % up
c-peptide	2. 3 ng/ mL	1.1 ng /mL	109.09 % up
Androgen Index	10.31	4.23	143.73% up

CONCLUSIONS:

1] The mean serum total estrogen level in the experimental group was observed [Follicular Phase-5 days] –92 pmol/L, it is 63% lower than the normal values. 92% ladies of the experimental group showed trend of lower serum estrogen levels. On the other hand 11% females who are matched in

demographic data, showed marginally low serum estrogen levels. Their mean estrogen level was 233 pmol/L when estimated on the matched phase.

2] The mean serum progesterone of experimental group [in pre ovulation phase] was observed-0.73 ng/mL, it is 57 % lower than the normal level. The 9 subjects of control group showed lower progesterone level , they have mean progesterone level 1.66 ng/mL.

3] The mean serum Testosterone level was quite higher in most of the experimental subjects-[74%] –the mean level was 81 ng/dL.The control group has mean serum Testosterone level 53 ng/dL.

4] The mean C-Peptide level of experimental group was observed significantly high. Approx 42% experimental subjects showed higher serum C-peptide levels. [mean 7.2 ng/ml] . This value is approx 49 % higher than the normal levels. The control group has mean 3.2 ng/ ml c-peptide level.So, 7 women of the experimental group have diagnosed type-II diabetes .

5] The level of Glucosylated Hb was-7.3 %   [HbA1c of 6% or less is normal. HbA1c above 6.1 % is a newly recommended criterion for diagnosing diabetes.]. 42 % subjects of experimental group have significantly higher c-peptide level. The control group showed mean level of 2. 3 ng/ mL.(Normal Range-1.1-4.4 ng /mL)[n= 6 each group]

6] Mean body mass index (BMI) was 21.6 kg/m2 in normal women, 27.44 kg/m2 in experimental subjects(n=44) and 31.86 kg/m2 in obese subjects from the experimental group.(n=11).

7] Mean waist: hip ratio (WHR) was 0.62 in normal controlwomen and 0.83 in subjects. Seventy percent subjects were overweight, among whom 46.93% had high testeron levels, 44.2% been hirsute, having significantly high BMI and total testosterone (TT).

8] 62.8% fulfilled sonographic criteria for diagnosing PCOS - 43.45% of them bilateral, 12.72% only left-sided and 6.81% only right sided. 59.3% were hirsute and 38.6% hyper insulinemic (BMI and TT were significantly high). Positive predictive value for TT was 64.44% .

9] The 6 subjects from each group have been tested for status of thyroid functioning, mean T3 level of experimental group was 0.83 nmol/L , mean T4 level was- 3.34 ugm/ dL, and TSH level was 6.12 ulU/ml . This profile

indicated marginal hypothyroidic status, but the results showed no significant difference with the control group. [Control group- T3- 1.03 nmol/L, T4-4.64 ugm/ dL, and TSH level was 5.32 ulU/ml.]

10] The Stress level is significantly correlated with high serum Glucose level. (r= 0.9055)

11] The stress and anxiety level is moderately correlated with obesity (r= 0.656), means the stress level drives the person to eat more.

12] Also a significant negative correlation is observed among stress and Estradiol level. (- 0.677)

13] Dislipidemia is prominent problem in androgenic hormonal profile, as expected the experimental group has prominent dislipidemia- with hypercholesterolemia, hyper-triglyceridemia, lower HDL serum levels.

  [mean Cholesterol- 281 mg/dl, Triglyceride-314 mg/dl and HDL – 32 mg/dl., LDL by Fw formula- 129 mg/dl, Cholesterol: HDL- 6.1.,where as the values of lipid profile of control group was within normal range- cholesterol- 177 mg/dl, triglyceride- 183 mg/dl and HDL-41 mg/dl , Cholesterol: HDL- 4.9. Thus a significant difference is observed among the groups –in respect of serum Cholesterol and triglyceride levels.]

14] The Androgen Index is 10.31, this is drastically high than normal index of 5-6 .

15] High to marginally high B.P. was observed in both the groups ,

16] The 82% experimental subjects have hirsutism and acne, 46% have hyper-menorrhoea , 23% have severe amenorrhoea, and 29% have oligo-menorrhea , 2% subjects are observed normal in this very aspect. 47% have central obesity.

The visual and biochemical examination of the experimental group showed strong univariate co-relation with the stress level and occurrence of PCO with disturbed hormonal profile in this particular respect. The development of type –II Diabetes is additional health problem significantly related with PCOs .The results are in coordination with some previous studies, but it is premature to conclude that the stress and anxiety are the root cause of the biochemical and hormonal imbalances of the experimental

subjects. A more wide and intense community based study is required to conform the correlation.

REFERENCES:

- Abbott, D. H., D. A. Dumesic, and S. Franks 2002 Developmental Origin of Polycystic Ovary Syndrome - A Hypothesis. Journal of Endocrinology 174(1):1-5.

- Abbott, D. H., D. A. Dumesic, J. R. Eisner, R. J. Colman, and J. W. Kemnitz 1998 Insights into the Development of Polycystic Ovary Syndrome (PCOS) from Studies of Prenatally Androgenized Female Rhesus Monkeys. Trends in Endocrinology and Metabolism 9(2):62-67.

- Abbott, D. H., D. K. Barnett, C. M. Bruns, and D. A. Dumesic 2005 Androgen Excess Fetal Programming of Female Reproduction: A Developmental Aetiology for Polycystic Ovary Syndrome? Human Reproduction Update 11(4):357-374.

- Adali, E., R. Yildizhan, M. Kurdoglu, A. Kolusari, T. Edirne, H. G. Sahin, B. Yildizhan,and M. Kamaci 2008 The Relationship between Clinico-Biochemical Characteristics and Psychiatric

- Allahbadia, G. N., and R. Merchant 2008 Polycystic Ovary Syndrome in the Indian Subcontinent. Seminars in Reproductive Medicine 26(1):22-34.

- Anderson, J. L., C. B. Crawford, J. Nadeau, and T. Lindberg 1992 Was the Duchess of Windsor Right? A Cross-Cultural Review of the 112 Socioecology of Ideals of Female Body Shape. Ethology and Sociobiology 13(3):197-227.

- Azziz, R. 2006 Diagnosis of Polycystic Ovarian Syndrome: The Rotterdam Criteria are Premature. Journal of Clinical Endocrinology and Metabolism 91(3):781-785.

- Balen, A., R. Homburg, and S. Franks 2009 Defining Polycystic Ovary Syndrome. BMJ (Clinical Research Ed.) 338.

- Barnard, L., A. H. Balen, D. Ferriday, B. Tiplady, and L. Dye Cognitive Functioning in Polycystic Ovary Syndrome. Psychoneuroendocrinology In Press, Corrected Proof.

- Bem, S. L. 1981 Bem Sex Role Inventory Professional Manual. Palo Alto, Calif.: Consulting Psychologists Press.

- Benson, S., O. E. Janssen, S. Hahn, S. Tan, T. Dietz, K. Mann, K. Pleger, M. Schedlowski, P. C. Arck, and S. Elsenbruch 113 2008 Obesity, Depression, and Chronic Low-Grade Inflammation in Women with Polycystic Ovary Syndrome. Brain, Behavior, and Immunity 22(2):177-184.

- Benson, S., P. C. Arck, S. Tan, S. Hahn, K. Mann, N. Rifaie, O. E. Janssen, M. Schedlowski, and S. Elsenbruch 2009 Disturbed Stress Responses in Women with Polycystic Ovary Syndrome. Psychoneuroendocrinology 34(5):727-735.

- Benson, S., S. Hahn, S. Tan, K. Mann, O. E. Janssen, M. Schedlowski, and S. Elsenbruch 2009. Prevalence and Implications of Anxiety in Polycystic Ovary Syndrome: Results of an Internet-Based Survey in Germany. Human Reproduction 24(6):1446-1451.

- Chugh, R., and S. Puri 2001 Affluent Adolescent Girls of Delhi: Eating and Weight Concerns. British Journal of Nutrition 86(4):535-542.

- Cohen-Bendahan, C. C. C., C. Van De Beek, and S. A. Berenbaum 2005 Prenatal Sex Hormone Effects on Child and Adult Sex-Typed Behavior: Methods and Findings. Neuroscience and Biobehavioral Reviews 29(2):353-384.

- Conn, J. J., H. S. Jacobs, and G. S. Conway 2000 The Prevalence of Polycystic Ovaries in Women with Type 2 Diabetes Mellitus. Clinical Endocrinology 52(1):81-86.

- Cronin, L., G. Guyatt, L. Griffith, E. Wong, R. Azziz, W. Futterweit, D. Cook, and A. Dunaif 1998 Development of a Health-Related Quality-of-Life Questionnaire (PCOSQ) for Women with Polycystic Ovary Syndrome (PCOS). Journal of Clinical Endocrinologyand Metabolism 83(6):1976-1987.115.

- Distress in Young Women with Polycystic Ovary Syndrome. Journal of International Medical Research 36(6):1188-1196.

- Ehrmann, D. A., D. R. Liljenquist, K. Kasza, R. Azziz, R. S. Legro, M. N. Ghazzi, S. Aronoff, R. Bernstein, D. Bodenner, S. Braithwaite, J. Cohen, D. DePaolo, D. Einhorn, J. Hone, A. Kenshole, C. Kilo, S. L. Kjos, M. Korytkowski, D. Koster, R. Lau, R. Lobo, J. Lucas, K. Martin, W. Meyer, S. Pek, S. Pfeifer, R. Rebar, G. Redmond, R. Rittmaster, P. Ross, S. Schwartz, R. Wild, and S. S. C. Yen 2006 Prevalence and Predictors of the Metabolic Syndrome in Women with Polycystic Ovary Syndrome. Journal of Clinical Endocrinology and Metabolism. 91(1):48-53.

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