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PCOS AND THYROID DYSFUNCTION - A STUDY

Obstetrics & Gynaecology

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ABSTRACT

Thyroid gland plays an important role in the metabolism of the body. Inadequate T3 causes menstrual disturbance affecting FSH/ LH secretion and Infertility A threefold increase in the prevalence of auto immune thyroiditis is reported in PCOS. This study aims to evaluate the effect of hypothyroidism on PCOS. 50 patients were studied over a duration of one year in this study. All patients were managed with the same protocol and tab. Thyroxine was given to the needful patients. Tablet Metformin was not used in this regimen. Patients were categorized by age, marital status, menstrual problems and reproductive performance.

26 women had TSH levels between 2-5. 10 women had TSH levels between 6-10. Another 10 women and TSH levels >10mIU/ml. Of the 38% women who had anti thyroid antibodies, 50% gave history of recurrent miscarriages and 46% showed reversal of FSH/ LH ratios. 88% had scan features of PCOS. 58% of these women had Primary infertility and 28% had secondary infertility.

All patients with menstrual problems responded well to treatment and had regular menstrual cycles. Corrected conception rate was 68.6%.

The group of patients with TSH <3mIU / ml had increased TRH response or partial hypopituitarism. This group was studied in detail.

PCOS is a metabolic disorder. Total health of PCOS women is exposed to risk of anovulatory infertility in addition to risk of Diabetes and Cardiovascular diseases. The mainstay of treatment in PCOS is Thyroxine supplementation since it corrects the Hormonal and metabolic dysfunction in addition to correcting ovum maturation. Improvement in screening techniques and early detection of thyroid dysfunction is an ideal tool in the management of PCOS.

KEYWORDS

Autoimmune thyroiditis, Hypothyroidism, Polycystic ovarian syndrome

INTRODUCTION:

Polycystic Ovarian Syndrome is a metabolic disorder where the patient presents with hyperandrogenism, obesity, hirsutism, menstrual irregularities, and impaired fertility.[1,3,6] Our aim should be to restore the health of the mother and her unborn child, for which the root cause need to be treated. Thyroid gland plays an important part in overall functions of our body [5]. Thyroxin regulates metabolism, hormonal production, and even maturation of ovum[3]. 1/3 of PCOS women were found to have anti thyroid antibodies[2]. Inadequate levels of T3 causes menstrual disturbances[3]. First 3 months, fetus depends on its mother for thyroxin. In view of all these, thyroid dysfunction has to be detected and treated early in PCOS women, so that after conception she goes through the pregnancy without complications and delivers a healthy baby.

AIM: To justify that use of thyroxin is the ideal one in PCOS management.

MATERIALS AND METHODS:

All women with menstrual problems, infertility, hirsutism, obesity and women with scan features of polycystic ovaries were grouped under PCOS case study. After clinical assessment they underwent blood tests for T3, T4, TSH, Free T4, S.Prolactin, Thyroid antibodies, FSH/LH and ultrasound scan for uterine and ovarian abnormality. All women and their husbands irrespective of their complaints received treatment for Chlamydia, bacteroids and fungal infections with Doxycycline, Tinidazole, and Fluconazole. Those women who had symptoms of pelvic infection (like whitish, curdy or blood stained vaginal discharge with itching feverish feeling especially during periods, heaviness in the legs, abdominal cramps continuous or congestive dysmenorrhoea, cervix hypertrophied and eroded, bulky uterus with tenderness in the fornices) received further treatment specifically.

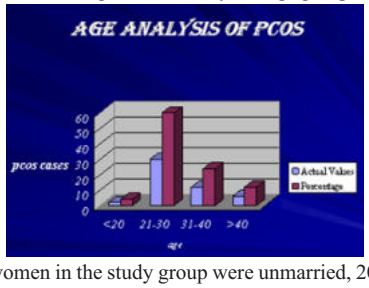
If thyroid deficiency is evidently seen with low T3, T4, FT3, FT4 and increased TSH >3miu/ml or presence of antithyroid antibodies, then these women were treated with Thyroxin. Those women having TSH less than 3 miu/ml were regarded as individualized cases with regard to thyroxin treatment.

To control excess vaginal bleeding Tranexamic acid used and if not controlled only then Progesterone tablet given to tie over the situation temporarily. Then, cyclical treatment, with Diane 35(ethinyl estradiol and cyproterone acetate), was given to regularize periods. Additionally, in PCOS, cyproterone acetate has the property of reducing insulin resistance and androgenecity.

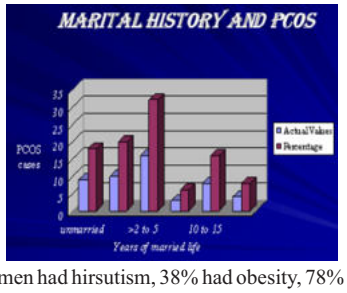
After 3 or 4 months of Thyroxin use and after confirming adequate replacement by testing FT4, TSH, ovulation was induced using clomiphene citrate /and 3 doses of HMG, HCG and luteal phase was supported with progesterone. If Prolactin value remained elevated in-spite of Thyroxin replacement, cabergolin administered. In patients having normal T3, T4, TSH values and no antithyroid antibodies, Thyroxin was withheld. Metformin was not given in our regime. 50 women thus treated were analyzed in this study.

RESULTS:

60% of the women belonged to 21 to 30 years age group. **[Table-1]**

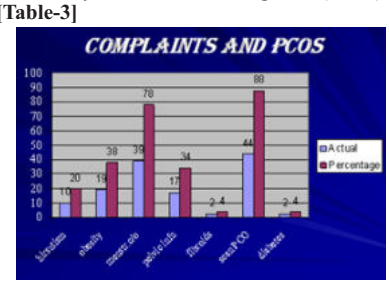


18% of the women in the study group were unmarried, 20% were of 1 to 2 years of marriage and 30% were of more than 5 years of marriage. **[Table-2]**

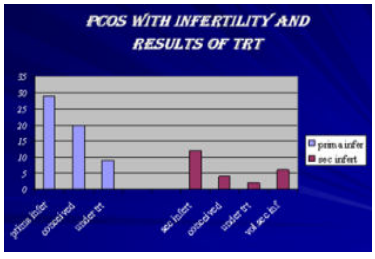


20% of the women had hirsutism, 38% had obesity, 78% had menstrual disturbances and continuous bleeding in 14%, oligomenorrhoea in

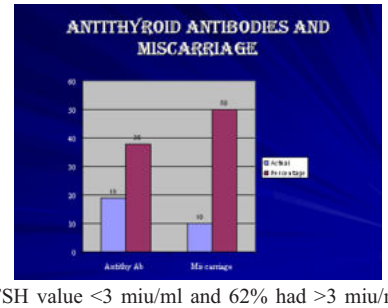
60%, and 4% had only withdrawal bleeding-79% (31/39) responded to treatment. **[Table-3]**



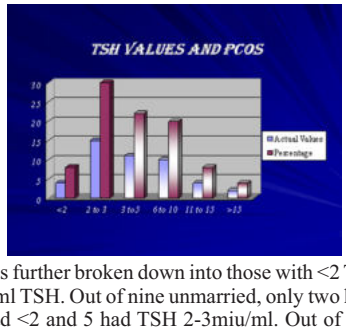
Out of 31 women, 16 conceived and out of 15 remaining, 9 were unmarried and 6 had voluntary infertility. They came for treatment of menstrual problems only. Rest 8 women are under treatment. Two women, who had vaginal bleeding, were planned for hysterectomy from another hospital, responded well to our regime and we could defer hysterectomy. 34% had pelvic infection, 4% had uterine fibroids. 88% had scan features suggestive of polycystic ovaries, 6% had diabetes. One had renal stone. 58% had primary infertility and 24% had secondary infertility. (18% unmarried) Corrected conception rate was (24/35) 68.6%. 20 women from primary infertility group and 4 from secondary infertility group conceived. Nine from primary infertility group and two from secondary infertility group are under treatment. Six women with voluntary secondary infertility came with bleeding problem**. [Table-4]**



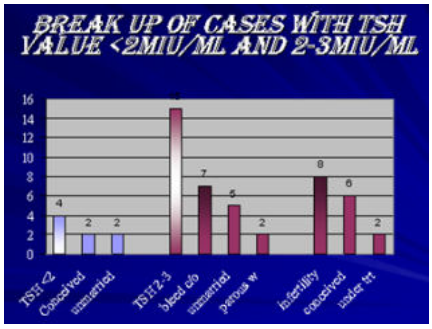
38% had antithyroid antibodies and 50% of these gave history of miscarriage. **[Table-5]**



39% had TSH value <3 miu/ml and 62% had >3 miu/ml i.e. overt hypothyroid according to new guideline. The group with <three miu/ml could include women with altered TRH response or cases of partial hypopituitarism. **[Table-6]**



This group was further broken down into those with <2 TSH and those with 2-3 miu/ml TSH. Out of nine unmarried, only two had >3 miu/ml TSH and 2 had <2 and 5 had TSH 2-3miu/ml. Out of 8 married and conceived women 6 had value of TSH between 2-3 and 2 had <2. These women did not receive thyroxin but after they conceived their TSH rose to 4.3 and 5, again showing their PCOS nature was predicting their underlying deficiency. Two women having primary infertility, with value of TSH 2-3 are under treatment. Two women with sec infertility had value with 2-3. They came with poly menorrhagia and responded to thyroxin and cyclical Diane 35(ethinyl estradiol and cyproterone acetate). **[Table-7]**



DISCUSSION:

Polycystic ovarian syndrome is a metabolic disorder, which leads to hyperandrogenism, hirsutism, alopecia-<10%, anovulatory infertility, obesity-50 to 65%,[1,3,6] menstrual disturbances like oligomenorrhoea, polymenorrhagia, insulin resistance leading to IDDM, and dyslipidemia causing atherogenesis and later cardiovascular disease. 40-50% women with PCOS showed bilaterally enlarged ovaries,[11]whereas in unselected population it was 23%. 15% of the PCOS women had dermoid cysts.[1] Dr Frank said; two phenotypes of PCOS women were recognized. 1. PCOS women with normal androgen, oligomenorrhoea, and no insulin resistance. 2. "Classic Syndrome" of anovulation with androgen excess, and more insulin resistance. Various reports establish the relation between insulin resistance and metabolic syndrome, with thyroxine. "Subclinical hypothyroidism is associated with insulin resistance" [14] "Low FT4 levels were significantly associated with Insulin resistance"[15] "Hypothyroidism is associated with metabolic syndrome and females are at increased risk" [16]

Thyroid gland plays a vital role in the overall functions of our body.[5] Thyroxin is important for the cellular metabolism in the mitochondria. It triggers protein synthesis. Thyroid dysfunction disrupts liver function leading to increase in cholesterol, [5,12] free fatty acids, triglycerides, homocysteine,[8] urates and decrease in folate.[8] Steroid biosynthesis is affected in Thyroid dysfunction. It regulates temperature. Thyroxine acts as a neurotransmitter [12]. It influences serotonin level which affects mood and behaviour. Thyroxine also plays a role in neuromodulation. "There is an interrelation of thyroxine with acetylcholine, nerve growth factor, and hippocampal function. Thus, a dysfunction in thyroid gland affects cognitive function of the individual."[11] Dr.Haddow has reported children born to mothers with untreated Thyroid disease have lower I.Qs [5]. Thyroxin is also important in the maturation of the ovum. Dr S.Cecconi, Dr N.Rucci etal in their study have mentioned, "Inhibitory activity of T3 on FSH induced aromatase activity, can be regarded as a part of the complex multihormonal regulation of mammalian follicle development and may contribute to explain the alteration in the female reproductive function after T3 hypo or hyper secretion"[3]. T3 also has been shown to modulate FSH/LH action on steroid biosynthesis as shown" by identification of multiple T3 receptors, mRNAs, T3 binding sites, in mammalian granulose cells, stromal cells and more recently in human cumulus cells and oocytes." Dr Janssen OU and colleagues have reported a 3-fold increase in the presence of autoimmune thyroiditis in PCOS women [2]. Inadequate T3 levels gave menstrual disturbances due to alteration in gonadotropin secretion and thus impaired fertility[3]. Study by Dr Joshi JV has shown in 45% menstrual disturbances preceded the appearance of symptoms of thyroid dysfunction by 2 months to 10 years [6]. Dr Haddow reported, "At the end of the study, women who did not know that they were hypothyroid during pregnancy were reviewed to determine whether their hypothyroidism was subsequently diagnosed. 64% of the undiagnosed case women had confirmed that hypothyroidism at the time of follow up. Average time to diagnose was five years [5]. Dr Haddow has said, "Thus early detection and treatment of hypothyroidism is emerging as an important health issue for the woman and her unborn child." Thyroid functional studies have revealed that in overt hypothyroidism, thyroid hormones are decreased with increase in thyroid stimulating hormone (TSH). In sub clinical hypothyroidism, thyroid hormones are normal with increase in TSH. Thyroid hormones can be decreased or normal with increased or normal TSH and antithyroid antibodies increased. It can also be like normal thyroid values with altered TRH response. In hypopituitarism, thyroid hormones can be low or normal with normal TSH value. Last ones are the tyrosine deficiency, Iodine absorption and incorporation defects, and de-iodinases enzyme defects. Metformin

was considered the cornerstone of PCOS treatment, since it decreases insulin resistance and thus hyperandrogenism and regularize menstruation. Conflicting reports are available about the drug. One report in fertility and sterility journal vol. 5 states it does regulate menstruation but no effect on 17 OH progesterone, SHBG, cholesterol, lipids and triglycerides. Even the effect on menstruation was not a longstanding one [4]. In our regime, we have not used metformin. Though we have used cyclical estrogen-progesterone combination earlier, now preferred one is cyclical estrogen with cyproterone acetate. Cyproterone is antiandrogenic and hence decreases hyperandrogenism, insulin resistance, and regularizes menstruation. Another method resorted is ovarian diathermy. It is said to be effective in women with large ovaries and increased ovarian stroma. There are reports of overenthusiastic treatment resulting in premature menopause[10]. The actual goal of PCOS treatment should be to correct the impairment in ovum maturation, so that a good mature ovum could result in a good progeny with minimum complications occurring during the course of pregnancy. Based on the above said rationale thyroid fitness of the patient was given more importance in our management protocol.

Dr Haddow had remarked, "It takes 5-10 years for the detection of hypothyroidism by traditional medical assessment and suggested early detection and treatment of hypothyroidism." [5] When Levothyroxine treatment was inadequate outcome of pregnancy was as follows-in overt group, abortion was 60%, preterm delivery 20%, and term delivery 20% while in sub clinical group, it was 71.4%, 7.2%, and 21.4% respectively. When replacement was adequate, effect was 100% to 90.5%. Thus, adequate treatment of hypothyroidism in pregnancy minimizes the risks and generally makes it possible for the pregnancy to be carried to term without complications.[13]It was seen in 10 patients with PCOS who conceived following conservative regimes from other hospitals, (not included in the presented 50 cases) two had abortions; three had PIH and preterm delivery in 4. These patients either were interpreted wrongly as normal, with TSH values around 5 or were inadequately treated and one discontinued voluntarily. PCOS women with antithyroid antibodies had increased chance of miscarriages-66 to 67%[7].

Dr Joshi in his study reported 1/3rd of patients with menstrual abnormalities had hypothyroidism. The cut off taken to diagnose hypothyroidism in this study was TSH->10 miu/ml. He also reported 44% of the euthyroid women (those having TSH <10 miu/ml with goitre) had menstrual abnormalities. Hence, it becomes imperative to find out closer values of TSH, which can identify thyroid dysfunction. The most near accurate TSH value taken as normal by American association of clinical endocrinologists is 0.3-3miu/ml. They also stated a TSH value of over 2miu/ml with normal T4 should be closely followed up. Thus, in our study >3miu/ml of TSH is taken as hypothyroid and women with TSH value <3miu/ml are subdivided into those with <2 miu/ml and those with TSH value between 2 and 3miu/ml. In patients with hypopituitarism and altered TRH response, TSH can be normal. Here FT3, FT4, T3, T4 values are given importance. Thus, TSH value of 2-3 was viewed with suspicion and less than 2miu/ml value was considered normal. 30 % were married for more than 5 years. These women have received treatment from other hospitals and did not conceive. 60% of the women were 21-30 years age group. (78%) 39 women had menstrual abnormalities out of which 31 responded well. 8 are undergoing treatment. These are recent recruits. Out of 31 women who responded, 16 conceived. From the remaining 15, 9 were unmarried, and six were the ones above 40 years who came only for menstrual complaints. There was an overlap in the number of women who had infertility, menstrual problem and pelvic infection. In Thyroid dysfunction, immunity is lowered and proneness for infection increased. 34% had pelvic infection that was treated completely. 58%(29) had primary infertility, out of which 20 conceived, and went through pregnancy without any complications. Nine are undergoing treatment. Out of 12 women with the secondary infertility, six had voluntary infertility and came for menstrual complaints. From the remaining six, four have conceived, and two are undergoing treatment. Our corrected conception rate was 68.6%. 38% had antithyroid antibodies, with 50% of this giving history of miscarriage. In other series, this is 34-36% with 66-67% miscarriage rate [7]. 38% had TSH <3 and 62% were hypothyroid (>three TSH) according to the new criteria and were undergoing treatment. Breaking down of these 9 women with TSH <3 showed 4 women had TSH <2 miu/ml. 2 of these were unmarried and came for menstrual problem. They were treated with usual protocol as mentioned above but without Thyroxin. Remaining two conceived following treatment for regularizing period and ovulation induction. These women had a TSH of 4.1 and 5 with onset of pregnancy and received Thyroxin.15 women with TSH 2-3 are the interesting cases. Seven had mainly menstrual complaints.5 were unmarried and received short course of thyroxin to control bleeding. 2 women had children and came for polymenorrhagia. They got usual treatment and underwent Dilatation and Curettage. Histopathology showed proliferative endometrium. One had cervical polyp removal also. They responded to treatment with Thyroxin and cyclical hormone. We could defer hysterectomy in three cases. Out of remaining eight women with TSH 2-3, 6 conceived and needed Thyroxin and ovulation induction. Two are under treatment. One important factor that is noticed in this type of management is that, the pregnancy is smooth without any complications, like abortion, preterm delivery, PIH, or congenital anomaly, which are usually seen in PCOS women who conceive. 30% of our women were of 30-40 years age and >5 years of marriage. They had conservative PCOS treatment using metformin, ovarian diathermy and ovulation induction, from other conception centres. Two women with high TSH values (with antithyroid antibodies) who conceived quickly when started on thyroxine had miscarriage but had normal conception later without any complications on Thyroxin. It was also seen obese PCOS women after correction with Thyroxin respond to ovulation induction quickly and had normal pregnancies. Lean PCOS women took time to respond and most of the time their TSH value remained 2-3 miu/ml. It is of extreme importance to mention here about five PCOS women who were not included in the study since they came after conception from other hospitals managed with conservative regime. One, who had abortion at 14 weeks, had a TSH value of five miu/ml. Following abortion, her TSH increased to 58 when she was started on thyroxin. Three women had PIH and one had preterm delivery. All of them had high TSH value postnatally.

CONCLUSION:

PCOS is a metabolic syndrome, where the root cause needs to be treated. Bert C, JM Fauser et al in endocrine abstracts says Gynaecologists should focus on the total health of the PCOS woman, instead of anovulatory infertility alone as total health of the PCOS woman is at stake due to diabetes, cardiovascular disease and other problems. Thyroxin is the mainstay of PCOS treatment, since it regulates all metabolic and hormonal processes and is important in ovum maturation. Importance should be given to early detection of hypothyroid nature, by improved screening values and adequate Thyroxin replacement, to ensure an uncomplicated pregnancy and a healthy child. Moreover, for a complete evaluation of hypothalamo pituitary thyroid axis, we have to study FT3, FT4, and TSH since as per Prof Paolo Falaschi from Italy "HPT axis is modified in clinical hypo/hyperthyroid patients with respect to the normal subjects"[17]. Dr Joshi J.V, Bhandarkar S.D. et al has rightly put-"Any type of menstrual disorder should be considered as a possible presenting symptom of Thyroid dysfunction and may indicate sub clinical abnormality."[6] "High level of suspicion index to be kept so that, the cause is easily treated to the tremendous advantage of mother and fetus." I strongly support this.

My acknowledgements are to my patients and my friends who supported me in my view.

REFERENCES:

1. **Walter Futterweit, MD,** Division of Endocrinology, Department of Medicine, "Polycystic Ovarian Syndrome: clinical perspectives and management" Obstetrics and Gynecological Survey; 1999; vol.54 (6) www.ncbi.nlm.nih.gov/pubmed/10358853
2. **Damian McNamara, "**An PCOS, Autoimmune Thyroiditis link studied: thyroiditis risk up threefold" OB/GYN News, Jan 1, 2004. http:// findarticles. com/p/ articles/mi m0CYD/is 1 39/ai 112542272/
3. **S.Cecconi, N.Rucci, M.L.Scaldaferri, M.P. Masciulli, G.Russi, C.Moretti** et al, Department of Experimental Medicine ,University of Aquilla, Italy. "Thyroid Hormone effect on Mouse Oocyte Maturation and Granulosa Cell Aromatase Activity" Endocrinology, 1999; vol 140 (4): 1783-1788. www.ncbi. nlm.nih.gov/ pubmed/ 10098516
4. **Laure C.Morin-Papunen MD, Riitta M. Koivunen MD, Aimo Ruokonen MD, Hannu K, Martikainen MD,** University Central Hospital of Oulu, Oulu , Finland. " Metformin Therapy improves the menstrual pattern with minimal endocrine and metabolic effects in women with Polycystic Ovarian Syndrome." Fertility and Sterility, April1998; Vol. 69(4).publisher-Elsevier Science Inc www.ncbi. nlm.nih.gov/ pubmed/ 9548159
5. **James E.Haddow,** MD. Head author, vice president and medical director, Foundation for Medical Research, Study done by Foundation for Medical Research, NIH, NICH, Published in NEJM, "Children born to mothers with untreated Thyroid Disease have lower I.Qs." http://www.kidsource.com/kidsource/content-5/ thyroid.baby.iq.html
6. **Joshi J.V., Bhandarkar S.D, Chadha M, Balaiah D, Shah R,** "Menstrual Irregularities and Lactation Failure may precede Thyroid dysfunction or Goitre" J.of Postgraduate medicine,1993;39: 137-141 www.ncbi.nlm.nih.gov/pubmed/8051643
7. **Samir F. Abdel Aziz MD, Azen A Moussa MD, Hisham O Kandil MD, Mohammed**

Y Shaheen MD, Mahmood M Abou Zeid, "Antithyroid antibodies in Unexplained Recurrent Abortion" Obstetric and Gynaecology Department AlAzhar University, Obst. and Gyn Department Cairo University, Clinical Pathology department AlAzhar university, Kelfr El-Zy at District Hospital. www. obgyn. net/pb/pb.asp? page=/pb/cotm/ 9905/Antithyrod1

8. **Mark Helfand MD, MPH." Screening** for Sub clinical Thyroid Dysfunction in Non-Pregnant Adults: A Summary of Evidence for the U.S. Preventive Services Task Force." Annals of Internal Medicine, Jan 2004; 140:128-141 www.ncbi.nlm.nih. gov/pubmed/ 14734337.
9. **Michiels J.J, Budde U,van der Planken M, van Wet H.H, Schroyens W, Brendan Z,** Department of Hematology, University Hospital, Antwerp, Belgium, "Acquired Von Willibrand Syndrome: clinical features, etiology, pathophysiology, classification and management," Best Practices Res. Clin. Hematology 2001, June; 14(2): 401-36.
10. **Halvard Gjounaess MD,** "Late Endocrine Effects of Ovarian Electrocautery in women with PCOS." Fertility and Sterility, April1998; vol 69(4). www.ncbi.nlm.nih.gov/ pubmed/ 9548160
11. **Smith J.V, Evans A.T, Costall B, Smythe J. W,** Postgraduate Studies of Neuropharmacology, school of Pharmacy, University of Bradford, U.K. "Thyroid hormones, Brain Function and Cognition- a brief review", www.ncbi.nlm.nih.gov/ pubmed/11835983
12. **Jennifer A. Philips,** "Thyroid Hormone Disorders" May 2001. www.csa.com/ discovery guides/ **thyroid**/overview.php
13. **M.Abalovich, S.Guturrez, G.Alcaraz, G.Maccallini, A.Garcia, O.Levalle.** "Overt and Sub clinical Hypothyroidism complicating pregnancy, Jan 2002; Thyroid vol 12(1):63-68.
14. **Dessein PH, Jeffe BI, Stanwix AE,** "Sub clinical Hypothyroidism is associated with Insulin Resistance in Rheumatoid Arthritis". Thyroid 2004 June; 14(6): 443-6.
15. **Roos A, Bakker S J, Links T P et al** "Thyroid Function is associated with components of metabolic syndrome in Euthyroid-subjects" J. of clinical endocrinology and metabolism, 2007;92(2):491-6 www.ncbi.nlm.nih.gov/pubmed/17090642
16. **Shantha GP, Kumar AA, Jayachandran V** et al dept of Gen. Medicine, Sri Ramachandra Univ., Chennai," Association between Primary Hypothyroidism and Metabolic Syndrome and Role of CRP A Cross sectional study from South India" Thyroid Res.2009; March 92(1)2
17. **Paolo Falaschi, Antonio Martocchia, Antonella Proietti, Rosario D'Urso** et al, The Hypothalamo-Pituitary-Thyroid Axis in subjects with sub clinical thyroid diseases: the impact of the negative feedback mechanism. Neuroendocrinology Letters 2004; 25(4): 292-296.