STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS

Dissertation Submitted to

The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial

fulfilment of the regulations for the award of the degree of

M.S (Branch II)

OBSTETRICS AND GYNAECOLOGY

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

GOVERNMENT THENI MEDICAL COLLEGE

THENI 625531, TAMILNADU, INDIA

MAY 2019

CERTIFICATE

This is to certify that this dissertation titled **"STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS"** is a bonafide work done by **Dr.P.THANGAM**, at the Department of OBSTETRICS and GYNECOLOGY, Government Theni medical college, during her postgraduate study for MS Branch II OBSTETRICS and GYNECOLOGY (2016-2019) from October 2016 to September 2018. This dissertation is submitted to DR. MGR Medical University in partial fulfilment of the University rules and regulations for the award of MS degree in OBSTETRICS and GYNECOLOGY

Prof Dr.M.Thangamani, MD., DGO.,
Head of the Dept,
Dept of OG,
Govt Theni Med College,
Theni.

Prof Dr.C.Shanthadevi, MD.DGO.,
Chief,
Dept of OG,
Govt Theni Med college,
Theni.

PROF. DR.K. RAJENDRAN, MS., D.ORTHO.,
DEAN
Govt Theni medical college, Theni

CERTIFICATE BY GUIDE

This is to certify that this dissertation titled **"STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS"** is a bonafide work done by **Dr.P.THANGAM**, at the Department of OBSTETRICS and GYNECOLOGY, Government Theni medical college, during her postgraduate study for MS Branch II OBSTETRICS and GYNECOLOGY (2016-2019) from October 2016 to September 2018. This dissertation is submitted to DR. MGR Medical University in partial fulfilment of the University rules and regulations for the award of MS degree in OBSTETRICS and GYNECOLOGY

Prof Dr. A. SHANTHAVIBALA, M.D., OG.,

Assistant Professor & Guide,

Dept of OG

Govt Theni Med college

Theni

DECLARATION

I hereby declare that this dissertation entitled **"STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS"** was prepared by me under the direct guidance and supervision of **Prof. DR.M.THANGAMANI, MD.,DGO.,** The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfilment of the University regulations for the award of MD degree in Obstetrics and Gynaecology, Examination to be held in May 2019.

This record of work has not been submitted previously by me for the award of any degree or diploma from any other university.

Place: Theni **Dr. P. THANGAM**

Date:

ACKNOWLEDGEMENT

At the outset, it is with a sense of accomplishment and deep gratitude that I dedicate this dissertation to all those who have been instrumental in its completion.

First and foremost I express my heartful thanks to my esteemed and respected HOD, Department of Obstetrics and Gynaecology GTMCH, and my guide **Prof. Dr.M.Thangamani, MD, DGO, and Chief Professor, Dr. C. Shanthadevi, MD, DGO, DNB.,** had it not been for their whole hearted support throughout the period of this study, extending from their vast knowledge, invaluable advice and constant motivation, I truly would not have been able to complete this dissertation topic in its present form.

I sincerely thank my **Guide, Asst. Professor Dr. A. Shanthavibala, M.D., OG.,** for giving me practical suggestions and permitting me to carry out this study in their patients.

I sincerely thank my Asst. Professors **Dr. A.Mahalakshmi, M.D., OG., and Dr. K. Kameshwari, M.D., OG.,** for giving me practical suggestions and permitting me to carry out this study in their patients.

I am deeply indebted to all the teaching staff and my fellow postgraduates for their helpful attitude and valuable suggestions in every stage of my study.

Lastly, I thank the ethics committee for permitting me to do this study and more importantly

I thank all my patients involved for their kind help and cooperation.

CONTENTS

INTRODUCTION

Menstrual disorders is reported to occur in 9-14% of women between menarche and menopause. The prevalence of menstrual disturbances varies. In India, the reported prevalence of menstrual disturbances is about 17.9%.[22]

Thus menstrual disturbances is a common complaint among women of reproductive age group. It may be accompanied by pain and discomfort and causes significant social embrassement.

They have a substantial effect on health related quality of life.

It has been well known that thyroid dysfunctions are a common cause of AUB. Thyroid disorders have a profound effect on menstrual function and reproductive health. Thyroid disorders are more common in women than in men. Overt hypothyroidism is estimated to occur in 1% of female population.

Menstrual irregularities are occasionally the first sign of thyroid dysfunction (wilansky DL; Greisman 1992).

Therefore thyroid gland is the most vital organ which plays an important role in growth, metabolism and function of almost every organ of our body. Timely detection of thyroid dysfunction in women with menstrual irregularities and their proper management can prevent inappropriate diagnostic and therapeutic procedures.

AIM OF THE STUDY

The study is aimed at cross section of population presenting to the Department of Obstetrics and Gynaecology, Govt Theni Medical College and Hospital, Theni with complaints of menstrual irregularities. The study aims at

1. To study the association between thyroid disorders and menstrual abnormalities among women of reproductive age group(18-45 years).

2. To study the type of thyroid dysfunction among different types of menstrual irregularities.

3. To establish if screening for thyroid abnormalities is justified using fT3,fT4 and TSH.

REVIEW OF LITERATURE

1.Padmaleela et al, in 2011 found that most cases of menstrual irregularities occurred in age group of 25-34 years. The commonest complaint being menorrhagia in 50% of cases. Hypothyroidism was present in18.1% of cases and hyperthyroid in 8.4% of women[1].

2.Wilansky and Griesman et al in a study on early hypothyroidism in patients with menorrhagia showed that of 67 women presenting with menorrhagia 15 had evidence of primary hypothyroidism. The menorrhagia disappeared on treatment with thyroxine indicating that there is a cause and effect relationship between hypothyroidism and menstrual irregularities[2].

3. Kakuno et al in 2010 conducted a study in Japan concluded that patient with overt hypothyroidism had a higher prevalance of menstrual disturbances (34.8%) than mild to moderate cases(10.2%)[3].

4. Bjergved et al in 2014 conducted a random sampled study on 2102 persons participated for a 11 year follow up. The study concluded that change in TSH were significantly associated with a change in body weight. Weight increase was 0.3 kg in women and 0.8 kg in men for every one TSH (mu/L) Increase[4].

5.Koutras et al 1997 studied the association of menstrual disturbances in women with thyroid disorders found that 21.5% of 214 patients had

menstrual disturbances. Polymenorrhoea was the most common menstrual abnormality detected[5].

6. Andrew weeks in 1987 conducted a study at Jessop hospital 0n 650 patients with menstrual disturbances and stated that hypothyroidism is a under diagonsed cause of menorrhagia[6].

7. Croatian 1999 published an article about association between anaemia and hypothyroidism. It stated that the first sign of hypothyroidism may be anaemia. Hypothyroidism may be the etiology in certain cases of anaemia of uncertain etiology.20-60% women are anaemic in hypothyroidism[7].

Pernicious anaemia is also more common in hypothyroidism.

It also stated that thyroid hormones play an important role in in stimulation of growth of erythroid colonies directly and through erythropoietin.

8. Ravanbod M, et al in 2013 conducted a randomised double blind active controlled trial in 60 patients with subclinical hypothyroidism and iron deficiency anaemia. 20 patients received iron salts + placebo, another 20 patients received levothyroxine + placebo and the last 20 received iron salts + levothyroxine for 3 months. The increase in haemoglobin , ferritin and decrease in thyroid stimulating hormone was superior in the levothyroxine + iron salts group compared to the other groups[8].

9. Neelu et al 2012 stated that thyroid function tests must be evaluated in women presenting with menstrual irregularities to avoid unnecessary medical and surgical therapeutic interventions[9].

10. Jovitha et al 2017 showed a positive correlation between serum TSH levels and serum prolactin levels. That is as the S.TSH level increases S. Prolactin also increases. An increased serum prolactin inhibits follicular maturation and disturbs corpus luteal function there by leading to inhibition of normal pulsatile secretion of GnRH resulting in anovulation[10].

11. Javed ali et al 2015 showed that 53.5% cases of hypothyroid women had menorrhagia and in hyperthyroid women 58.6% had oligomenorrhoea stating that the commonest bleeding pattern in hypothyroid and hyperthyroid being menorrhagia and oligomenorrhoea[11].

12. Robuschi et al in 1987 found that the prevalance of hypothyroidism increases with age and it is more common in older woman .Nearly 45% of thyroid from older women show features of thyroiditis. The incidence of anti-thyroglobulin antibodies is 7.4% in women over 75 years and 16.9% in women over 60 years[12].

13. Rodoni et al 2010 found an association between increased risk of coronary heart disease and its related mortality in women higher TSH levels particularly those above 10mIU/ml[13].

14. Smith et al in 1987 showed that an advanced form of von willebrand's disease is noted in patients with untreated hypothyroidism. The hemostatic defects returned back to normal levels with thyroxine supplementation[14].

15. Blum and Blum in 1992 studied the possible relationship between occult hypothyroidism and menorrhagia in IUD-wearing women. They studied a group of 40 women with menorrhagia secondary to an intrauterine contraceptive device. They all had normal free thyroxine and TSH levels. The 10 patients who had highest TSH levels were given a TRH test and all proved to have early hypothyroidism. All patients showed a significant improvement with thyroxine treatment.

16. Hingham et al in 1992 reported that in case of hypothyroidism menstrual blood loss decreased from 480ml to 58 ml following treatment with thyroxine for 3 months[16].

17. Beckmann and habertte studied a cohort of 337 women suffering from PCOD and conclude women with TSH> 2mIU/ml were younger, had higher BMI and were insulin resistant than women with TSH< 2mIU/ml[17].

18. Knudsen et al studied a group of 4082 patients about the association between thyroid function and body mass index. It showed a positive association between BMI and TSH level, negative association between BMI and serum T4 and no association between BMI and serum T3 levels. It

concluded that there is a association between increased TSH levels and obesity[18].

19. Prentice et al in 2000 concluded that routine TFT (Thyroid function test) are of no help in menorrhagia and TRH should be tested for women with unexplained menorrhagia[19].

20. Chameron and Fraser in 1998 stated that thyroid disorders are the commonest endocrine abnormality associated with menstrual disturbances which is potentially amenable to treatment[20].

21. Danese MD et al in 1996 recommend highly sensitive TSH assay screening every 5 years beginning at the age of 35 years or every 2 years from the age of 60 or with appearance of symptoms of hypothyroidism[21].

From the above literature it is concluded that there is a strong association between thyroid disorders and menstrual disturbances.

PHYSIOLOGY OF MENSTRUATION

The menstrual cycle is at the same time one of the simplest and the most complex physiologic process. Normal menstruation is the periodic efflux of sloughed endometrium and blood out of the uterine cavity. Cyclical hormone production and parallel proliferation of endometrium prepares for the implantation of embryo[23].

For an adolescent menstruation signifies her passage into womanhood and capability of reproduction. Disorders of the menstrual cycle can lead to pathological conditions like abnormal uterine bleeding, infertility, recurrent miscarriage and even malignancy.

The menstrual cycle is due to synchronous interrelated events occurring in ovaries (oogenesis) as well as the uterine endometrium (endometrial preparation).

Menstrual cycle

Ovarian cycle uterine cycle

1.Follicular phase 1.Proliferative phase

2.Luteal phase 2.Secretory phase

The primordial germ cells arrive in the female gonad at about 9 weeks of gestation following which they differentiate into several clusters of

oogonia. They undergo rapid mitotic division and reaches 6-7 million by 16-20 weeks of gestation. At birth the no of oogonia is about 2 million as a result of prenatal oocyte depletion. At the onset of puberty the germ cell mass is further reduced to 3,00,000 to 5,00,000 units. Out of these only about 500 would actually ovulate. Each primordial follicle comprises of a primary oocyte arrested in prophase of meiosis. The mechanism for determining which follicles and how many of them will start growing during any one cycle is unknown. The number of follicles that will grow during each cycle appears to be dependent on the size of the residual pool of inactive primordial follicles.(e.g., unilateral oophorectomy)[24]

It causes the remaining follicles to redistribute their availability over time. It is said that the follicle which is singled out to play the leading role in a particular cycle is the one which is perhaps prepared by autocrine/paracrine actions and appropriate tropic hormone stimulation in its microenvironment. The first follicle able to respond to stimulation usually achieves the early lead that it never relinquishes. Thus, each cohort of follicles that begins growth is enrolled in a serious competition that ends with only one follicle succeeding.

Reproductive physiology is controlled by various hormones and is dependent on normal functioning of the hypothalamic pituitary ovarian hormones. The hypothalamus controls pituitary function through GnRH. The secretion of these is controlled by hormonal feedback and impulses from other parts of the brain[25].

The anterior pituitary secretes gonadotropins and prolactin whereas the posterior pituitary secretes oxytocin and vasopressin. Secretion of these hormones is controlled by hormonal feedback and the hypothalamus.

FOLLICULAR PHASE:

It spans from the first day of menses until ovulation. The primary goal of this phase is to develop a viable follicle capable undergoing ovulation. The follicle destined to ovulate is recruited in the first few days of the cycle. The early growth of follicles usually occurs over the time span of several menstrual cycles, but the ovulatory follicle is the one cohort of follicle which is recruited at the time of the luteal-follicular transition. The total duration of to achieve preovulatory status is approximately 85 days. Early follicular development is independent of hormonal control. However, this cohort of follicles reaches a stage where, unless recruited by follicle-stimulating hormone(FSH) the next step is atresia. Thus, follicles are continuously available (2–5 mm in size) for a response to FSH. An increase in FSH is the critical feature in rescuing a cohort of follicles from atresia, the usual fate of most follicles, eventually allowing a dominant follicle to emerge and pursue a path to ovulation. Maintenance of this increase in FSH for a critical duration of time is essential. Without the appearance and persistence of an increase in the circulating FSH level, the cohort is doomed to the process of apoptosis (

programmed physiologic cell death) to eliminate superfluous cells. Apoptosis is a Greek word meaning falling off, like leaves from a tree.

The first visible sign of follicular development is an increase in the size of the oocyte and the granulosa cells becoming cuboidal in shape rather than squamous.

These changes can be best viewed as a process of maturation rather than growth. At the same time, small gap junctions develop between the granulosa cells and the oocyte. Gap junctions are channels that when open permit the exchange of nutrients, ions, and regulatory molecules. Thus, it serves as the pathway for nutritional, metabolite, and signal interchange between the granulosa cells and the oocyte. The process of follicular growth is also influenced by factors derived from the oocyte. Mice which are genetically deficient in growth differentiation factor-9 (GDF-9), a peptide synthesized only in the oocyte after the primordial follicle becomes a preantral follicle, are infertile because follicular development cannot proceed beyond the primordial follicle stage. With multiplication of the cuboidal granulosa cells (to approximately 15 cells), the primordial follicle thus becomes a primary follicle. The granulosa layer is separated from the stromal cells by a basement membrane called the basal lamina. The surrounding stromal cells differentiate into concentric layers designated the theca interna (closest to the basal lamina) and the theca externa (the outer portion). The theca layers appear when granulosa proliferation produces 3–6 layers of

granulosa cells. Once growth is accelerated, the follicle progresses to the preantral stage as the oocyte enlarges and is surrounded by a membrane, the zona pellucida. The granulosa cells undergo a multilayer proliferation as the thecal layer continues to organize from the surrounding stroma. This growth is dependent upon gonadotropins and is correlated with increasing production of oestrogen. FSH causes aromatization of androgens present in the theca cells into oestrogen in the granulosa cell. Under the synergistic influence of oestrogen and FSH there is an increase in the production of follicular fluid that accumulates in the intercellular spaces of the granulosa, eventually coalescing to form a cavity, as the follicle makes its gradual transition to the antral stage. The accumulation of follicular fluid provides a means where by the oocyte and surrounding granulosa cells can be nurtured in a specific endocrine environment. The granulosa cells surrounding the oocyte are now designated the cumulus oophorus. The differentiation of the cumulus cells is believed to be a response to signals originating in the oocyte.

Oestrogen exerts a negative feedback effect on FSH as a result growth of all the follicles is inhibited except the one destined to become dominant follicle. Oestrogen also exerts a positive feedback effect on LH secretion. A Surge of LH occurs prior to ovulation. The positive action of oestrogen also includes modification of the gonadotropin molecule, increasing the quality (the bioactivity) as well as the quantity of FSH and LH at midcycle. LH levels

rise steadily during the late follicular phase, stimulating androgen production in the theca.

A unique responsiveness to FSH allows the dominant follicle to utilize the androgen as substrate thereby further accelerating oestrogen production. FSH also induces the appearance of LH receptors on granulosa cells. The follicular response to the gonadotropins is modulated by a variety of growth factors and autocrine/paracrine peptides. Inhibin B, secreted by the granulosa cells in response to FSH, directly suppresses pituitary FSH secretion. Activin, originating in both pituitary and granulosa cells, augments FSH secretion and action.

TWO CELLTWO GONADOTROPHIN THEORY[25]:

The synthesis of steroid hormones is compartmentalised into two different cells of the ovary(granulosa and theca cells) and is regulated by two gonadotrophins (FSH and LH).

The granulosa cells have FSH receptors and the theca cells have LH receptors.

The theca cells have the enzymes for androgen biosynthesis from cholesterol and the granulosa cells have aromatase which converts androgen to oestrogen

In response to LH stimulation, theca cells synthesise androgens which is transported to granulosa cells.

Under the effect of FSH, aromatization of androgen to oestrogen takes place in the granulosa cells.

The following changes in the endometrium takes place during the proliferative phase:

The functional and basal layers of the endometrium become well defined. The proliferation mainly occurs in the functional layer.The basal layer measures 1mm in thickness while the functional layer reaches a maximum thickness of about 3.5-5mm by 14^{th} day

The glands become elongated and slightly sinuous and the columnar epithelium lining them become taller. In the beginning , the glands are narrow and tubular, lined by low columnar epithelial cells. Mitosis becomes prominent and the areas of pseudostratification are observed.

There is an increase in ciliated and microvillous cells in the endometrial glands

Endometrial stroma becomes oedematous with wide separation of cells.

The stroma gets infiltrated with numerous cells including macrophages and leucocytes.

In the initial phase the spiral vessels are uncoiled and unbranched. However , soon the growth of the straight vessels occur so that they become more coiled and spiral.

Ovulation usually occurs within 36 hours (34-39 hrs) of onset of LH surge and within 12 hours of LH peak

OVULATION:

Ovulation is the process of release of an oocyte from the ovarian follicle. It usually occurs on the 14th day of menstrual cycle.It is triggered by midcycle LH surge. Initially, the first meiotic division of oocyte is completed and the first polar body is extruded. The ovum is now haploid. The second meiotic division usually occurs after fertilization, after which the second polar body is extruded. The LH surge initiates an inflammatory reaction in the part of the follicle close to the ovarian cortex. Prostagladins and cytokines are released. This causes weakening and lysis of the wall of the follicle at this point and the oocyte is extruded through this opening. The released oocyte moves from the ovary into fallopian tube (by the chemotactic effect of cytokines released during rupture) and may get fertilised by the spermatozoa in the ampulla of the fallopian tube. Once the oocytes has been extruded out , the empty ovarian follicle gets converted into corpus lueum which produces the hormone progesterone in the absence of fertilization.

LUTEAL PHASE:

Production of progesterone by the corpus lutuem induces secretory changes in the endometrium. The oestrogen decreases through the early luteal phase until through the mid luteal phase where it begins to rise as a result of corpus luteal secretion.The peak of secretory changes in the endometrium occurs 7-9 days after ovulation when the endometrium is most receptive to

implantation by free lying blastocyst. This time period is known as implantation window. It is considered as the optimum time for embryo transfer in the IVF cycles. The functionalis layer of the endometrium increases in thickness and the stroma becomes edematous.The glands become tortuous with dilated lumens and store glycogen. If pregnancy occurs,the placenta produces HCG to replace the progesterone and the endometrium and the accompanying pregnancy are maintained. If the pregnancy does not occur the corpus luteum degenerates the oestrogen and the progesterone levels cause a negative feedback at the hypothalamus resulting in fall in level of hormones FSH and LH. The spiral arteries becomes less coiled and have a decreased blood flow. At the end of this period they alternatively contract and relax causing disintegration of functionalis layer and menstruation occurs.The endometrial features include:

-The most characteristic feature of this phase is development of subnucleolar vacuolation in the glandular epithelial cells. In this glycogen filled vacuoles develop between the nuclei and the basement membrane (by the day17-18).

This is the first evidence that ovulation has taken place.

-The endometrium measures about 8-10mm in the secretory phase. The secretory phase reaches its peak activity by the 22nd day of cycle after which no growth occurs.

-The glands become crenated and tortuous to assume the cork-screw shaped appearance. The corkscrew pattern of the gland become saw toothed in the later part of the secretory phase.

-The stroma of the functional layer becomes oedematous further

-The functional layer of the endometrium can be divided into two layers

1.Superficial or compact layer

2.Deep spongy layer

-The spiral vessels becomes dense and deeply coiled

MENSTRUATION:

Menstruation is the end result of series of events occurring at the level of hypothalamo-pituitary-ovarian axis. Degeneration of corpus luteum leads to fall in hormones-both oestrogen and progesterone. Physiological withdrawal of hormone progesterone lead to molecular and cellular interactions, thereby resulting in menstrual bleeding. Progesterone withdrawal initiates synthesis of prostaglandins and COX-2 resulting in increased PGE2 and PGF2. Myometrial contractions and vasoconstriction brought about by PGF2 produces sloughing and degradation of endometrial tissue.

Oestrogen starts to stimulate regeneration of surface endometrial epithelium (through stimulation of vascular endothelial growth factor-

VEGF) within 2 days after menstruation. The repair is brought about by the glandular epithelium growing over the bare stroma.

THE NORMAL MENSTRUAL CYCLE

The duration of normal cycle usually last from 21-35 days with 2 to 6 days of flow. The average blood loss is about 20-60ml.(Vollman RF 1977 and Treloar AE,1967)[26].A Large number of studies have shown that only approximately two thirds of women have cycles lasting between 21-35 days(Friedman E,1977).The extremes of reproductive age have higher percentage of anovulatory or irregular timed cycles.

Abnormal uterine bleeding (AUB) is defined by ACOG (2013) as bleeding from uterine corpus which is abnormal in regularity , volume, duration or frequency occurring in the absence of pregnancy. AUB may be acute or chronic

Acute AUB refers to episode of acute bleeding of sufficient quantity requiring immediate clinical intervention to prevent further blood loss.

Chronic AUB refers to AUB present for the most of the previous 6 months.

The term menorrhagia has been replaced by the term heavy menstrual bleeding(HMB).

Heavy menstrual bleeding is defined as excessive menstrual blood loss which interferes with women's physical, emotional ,social and material quality of life.

DEFINITION OF MENSTRUAL CYCLE IRREGULARITIES[28]:

MENORRHAGIA:

Regularly timed episodes of bleeding that are excessive in amount or duration of flow

POLYMENORRHOEA:

Frequent but regularly timed episodes of bleeding that are occurring at a duration of 21 days or less

OLIGOMENORRHOEA:

Infrequent or irregularly timed episodes of bleeding occurring at an interval of more than 35 days

HYPOMENORRHOEA:

Regular timed episodes of bleeding that is decreased in amount

AMENORRHOEA:Absence of menstruation for a period of 6 months in a women with normal menstrual cycles or a period equal to duration of 3 cycles in irregular cycled woman

METORRHAGIA: Intermenstrual bleeding

MENOMETORRHAGIA:

Excessive prolonged bleeding that occurs at irregularly timed frequent intervals

THE THYROID GLAND

In 1656, Thomas Wharton an English Physician and anatomist gave the thyroid gland its modern name.It is derived from latin word glandula thyroidea.The gland was named thyroid as its shape resembled the shape that was commonly used in Greece.

Thyroid disorders are atmost nearly 10 times more common in women than in men (Medvei VC,1993)[29].

Thyroid gland is a butterfly shaped organ situated in front of the neck. It originates emryologically from an evagination of pharyngeal epithelium with contributions from lateral pharyngeal pouches.It weighs approximately about 25 grams.

The thyroid gland has two lobes each measuring about 5*3*2 cm connected together by an isthmus measuring 1.25 in height and width. The estimated bood flow ranges from 4-6 ml/min.

THYROID GLAND DEVELEPMENT:

During embryonic development , thyroid gland develops as an epithelial proliferation in the floor of pharynx at the base of the tongue between the tuberculum impar and the copula linguae at about 3-4 weeks gestational age. The thyroid gland then descends infront of the pharyngeal duct as a bilobed diverticulum through the the thyroglossal duct. Then it migrates to the base of neck over a few weeks. Throughout its migration the thyroid gland maintain its attachment to the tongue through the thyroglossal duct. At the end of 5 weeks the thyroglossal duct degenerates and the detached thyroid gland attains its final position over the next two weeks.

THYROID GLAND PHYSIOLOGY:

Thyroid hormone synthesis depends upon the availability of adequate iodide content in the diet. It is absorbed as iodide and enters the thyroid follicular cells (through sodium iodide sympoter) under the influence of TSH. Within the gland iodide is oxidized to elemental iodine in the follicular space*. It is then bound to tyrosine residues in the thyroglobulin molecules by the enzyme thyroid peroxidase. Thus mono and di –iodothyrosine –the precursors of thyroid hormones are formed. Mono and di-iodotyrosines combine to form thyroxine (T4) and triiodothyronine(T3) (Norman AW, Litwack G, 1987). These compounds are part of the thyroglobulin molecule which serves as a storage depot for the thyroid hormone. TSH induces a proteolytic enzyme that

result in the cleavage of iodinated thyrosine residues there by foming T4,T3,MIT,DIT and traces of reverse triiodothyronines. Thus T3 and T4 are released into the blood. Removal of one iodine from the phenolic ring of T4 yields T3.

About One – third of T4 Secreted is converted in the peripheral tissues, particularly in the liver and kidney to T3 and inactive Reverse T3 by the enzyme deiodinase . Though T4 (80%-90%) is secreted more than T3 (10-20%),T3 is responsible for most of the thyroid action in the body (Czarnocka B et al, 1985).

*Iodide entering the follicular cell travels from within the follicular cell to the follicular space by the action of pendrin , an iodide-chloride antiporter.

MECHANISM OF THYROID HORMONE ACTION

Thyroid hormone acts by binding to a specific nuclear DNA bound thyroid hormone receptor (TR).T3 has a 15 fold higher binding affinity for TRs than does T4(Brent GA)[30].The hormone –receptor binds to DNA and increases or decreases the expression of a variety of genes that in turn code for proteins that regulate cell function. There are 2 TR genes-alpha and beta. By alternative spilicing , each forms at least two mRNAs and therefore two different receptor proteins.

REGULATION OF THYROID FUNCTION

Thyroid function is regulated by two mechanisms-suprathyroidal(Short and long negative feed back loops)and intrathyroidal. The hypothalamus through the secretion of TRH(Thyrotrophin releasing hormone) acts on anterior pituitary stimulating Thyroid stimulating hormone (TSH) secretion. TSH binds to receptors on the follicular cells of the thyroid, activating adenylate cyclase and increasing cellular cyclic AMP (cAMP) leading to synthesis and secretion of thyroid hormones.

Increasing TSH secretion will exert a negative feed back effect on hypothalamus thereby inhibiting TRH secretion(short loop).Thyroid hormones both T3 and T4 exerts a negative feedback effect on anterior pituitary thereby inhibiting TSH secretion(long loop).Oestrogen increases the levels of TRH receptor in the anterior pituitary. Thus the TSH response to TRH is greater in women than in men and also greater in women taking combined oral contraceptives.

TRH not only causes an increase in TSH but also increase the prolactin levels thereby indicating a physiologic role for TRH in the control of prolactin secretion. Thus the measurement of T3,T4 and TSH provides an accurate assessment of thyroid function.

Intathyroidal mechanism –an autoregulatory mechanism based on the changes in glandular iodide content.

ROLE OF THYROID IN REPRODUCTIVE PHYSIOLOGY:

Even prior to the discovery of Long acting thyroid stimulators (LATS) in women with Graves disease in 1956, numerous investigators demonstrated a link between autoimmune thyroid disorders and reproductive physiology/pathology. The following facts suggests the role of thyroid hormone in the female reproductive physiology/pathology.

T3 and T4 are found in follicular fluid. It is found in large studies that T4 is found to enhance the action FSH and LH.

TSH receptors are found in granulosa cells.

The female hormonal environment and their potential effects on immune system play an important role in the increased risk (10 fold) of women to develop autoimmune thyroid disorder (Gaitan E et al, 1985 and Wenzel BE et al, 1987). The polygonal immunoglobulins produced against the thyroid create the clinical spectrum of autoimmune thyroid diseases that can adversely affect successful reproductive function.

Foetal and neonatal period:

Very few data are existing regarding the role of the thyroid hormones in the reproductive system of the foetus because there are no effective human studies available. Excessive Thyroid hormone levels in mice has been shown to cause early maturation of the reproductive tract and early opening of the vagina whereas hypothyroidism in mice causes small ovaries deficient in cholesterol. No change has been observed in human embryos.

THYROID HORMONE FUNCTION AND REPRODUCTIVE HEALTH:

A Normal thyroid function is essential to maintain normal reproduction via its several interaction pathways. In both gender changes in sex steroids and sex hormone binding globulin are associated with thyroid dysfunction. In males thyrotoxicosis causes abnormal sperm motility whereas hypothyroidism causes abnormal sperm morphology. Erectile dysfunction has also been reported.

Hyperthyroidism is usually associated with oligomenorrhoea and amenorrhoea. Hypothyroidism usually causes menorrhagia.

Menstrual irregularities caused by thyroid dysfunction can be attributed to a variety of mechanisms.

They are alteration in FSH and LH response, hyperprolactinemia.

Peripheral conversion to oestrogens, decrease in SHBG and alteration in coagulation factors(decrese in factor 7,8,9,11).

Hyperprolactinemia alters the GnRH pulsatile secretion thereby leading to defect or delay in LH secretion leading to luteal phase defect and anovulation.

Hyperthyroidism causes amenorrhoea/oligoamenorrhoea.

Because free T3/T4 increases SHBG secretion from the liver thereby decreasing the concentration of free oestradiol. Higher peak oestradiol are responsible for achieving LH peak .Thus in hyperthyroidism decreased free estradiol delay LH peak. Decreased menstrual flow is also attributed to effects on hemostatic factors particularly factor 7.

THYROID DISORDERS AND IRON DEFICIENCY ANAEMIA:

Anaemia and thyroid dysfunction often occurs simultaneously.Thyroid hormones stimulate the proliferation of erythroid precursors both directly as well as through erythropoietin production whereas iron deficiency anaemia negatively influences thyroid hormone levels. The cause-effect relationship usually remains ambiguous. Normocytic normocytic anaemia is the most common but microcytic and macrocytic anaemia can also occur.

Causes of anaemia in hypothyroidism include:

1. Bone marrow suppression thereby leading to impaired haemoglobin synthesis.

2. Decreased erythropoietin production.

3. Iron and folic acid deficiency(decreased intestinal absorption)

4. Incresed menstrual blood loss.

5. Lastly ,vitamin B12 deficiency leading to pernicious anaemia. Pernicious anaemia is common in autoimmune thyroid disorders(AITD) which is associated with autoantibody formation.

Diabetes mellitus and adrenal insufficiency are the two other condition associated with pernicious anaemia.

THYROID DYSFUNCTION AND OBESITY:

Obesity and hypothyroidism are the two common conditions that are linked together closely.

Thyroid hormones play an impotant role in regulating basal metabolism, thermogenesis, lipid and glucose metabolism.

Hypothyroidism is associated with decreased thermogenesis, decreased basal metabolic rate and obesity and vice versa i.e hyperthyroidism is associated with increased basal metabolic rate and lean patients. Mild

hyperthyrotropinemia could be secondary to obesity.At present there is no indication for using levothyroxine in inducing weight loss in obese patients except for those with hypothyroidism. Marzullo et al suggested that obesity is a risk factor for thyroid autoimmunity. Further large randomised control trials are necessary to study the association between leptin,thyroid autoimmunity and the subsequent development of hypothyroidism.

CLASSIFICATION OF THYROID DISORDERS:

FREE T3	FREE T4	TSH	DIAGNOSIS
NORMAL	NORMAL	NORMAL	EUTHYROID
ELEVATED	ELEVATED	LOW	HYPERTHYROID
LOW	LOW	ELEVATED	HYPOTHYROID
NORMAL	NORMAL	ELEVATED	SUBCLINICAL HYPOTHYROIDISM
NORMAL	NORMAL	LOW	SUBCLINICAL HYPERTHYROIDISM

HYPOTHYROIDISM:

Prepubertal /Pubertal:

In both sexes, thyroid hormones have an influence over sexual development and reproductive function. Infantile hypothyroidism if left untreated, leads to sexual immaturity whereas Juvenile hypothyroidism causes a delayed onset of puberty. Paradoxically, primary hypothyroidism can also cause precocious sexual development and galactorrhea. (Kleinberg DL, New England J.Med. 1977).

The McCune Albright syndrome is a disorder that affects bone,skin and several other hormone producing endocrine tissues that is characterized by hyperfunctioning endocrinopathies including hyper/hypothyroidism and sexual precocity, but the association may be considered coincidental (Albright F, Maine MJ, 1938)[34]. Precocious puberty with delayed bone age may suggests primary hypothyroidism. In cases of hyperprolactinemia, Serum TSH is increased, T4 is low and galactorrhea may be present.

HYPOTHYROIDISM AND ADULT WOMEN:

Grodstein F et al, 1993 have stated that severe form of hypothyroidism is associated with diminished libido, amenorrhoea or anovulation. In hypothyroidism, secretion of progesterone is inadequate (as a result of anovulation) and there is persistent endometrial proliferation resulting in

excessive and irregular breakthrough menstrual bleeding. There may also be deficient secretion of luteinizing hormone(LH). Rarely in certain cases of primary hypothyroidism, secondary depression of pituitary function may lead to ovarian atrophy and amenorrhoea. Severe hypothyroidism is usually associated with hyperprolactinemia which in turn is associated with anovulation. The mechanisms attributed to hyperprolactinemia in women with hypothyroidism include

1. There is decreased clearance of prolactin in women with hypothyroidism[33].

2. Patients with severe hypothyroidism have increased total and free oestradiol levels. This excess oestrogen increases prolactin secretion.

3. In patients with hypothyroidism the negative feedback effect of T3 on TRH is decreased.Thus the increase in hypothalamic TRH secretion and their action on lactotrophs causes hyperprolacinemia.

Hypothyroidism also appears to be associated with decreased fertility resulting form ovulatory dysfunction and spontaneous abortions may occur although many pregnancies are successful. (Lao TTH et al, 1988 and Morimotoc et al, 1990). There is usually a high incidence of early or potential hypothyroidism in women presenting with compaints of menorrhagia. Hypothyroidism can cause menorrhagia/ polymenoorrhea being present in 30-40% of the cases. (Koutras DA, 1997)[5]. Excess TSH leads to alteration in

GnRH pulsatality and anovulation occurs. Even slightest alteration in GnRH pulsatality can cause luteal phase defect.

Myxedematous infiltration can produce polycystic ovaries. (Kansen KA et al, 1997)

The values for plasma gonadotrophins (FSH and LH)are usually in the normal range in primary hypothyroidism. However, in postmenopausal women, levels are usually lower than in euthyroid women of the same age but within the menopausal range. This in turn provides a valuable means of differentiating between primary from secondary hypothyroidism (Melmed S,Hershman J,1982).

SUBCLINICAL HYPOTHYROIDISM:

It occurs in 4-10% of women. Women with subclinical hypothyroidism usually have normal free T3 and T4 Levels but with slightly elevated serum TSH levels usually between 5 and 15mu/L. Chronic autoimmune thyroiditis is the leading cause.

Other causes include antithyroid drugs, drugs such as amiodarone and lithium and radioactive iodine ablation of thyroid gland. It represents the early stage the disease and about 4%-18% will progress to overt hypothyroid every year.

Patients with elevated TSH and normal T4 levels progress to overt hypothyroidism usually at the rate of about 5% per year if associated with elevated thyroid auto antibody levels. If the serum TSH alone is elevated without positive antithyroid antibody titres, the annual risk of progression decreases to approximately 3% per year. Therefore most clinicians prefer to treat women with elevated serum TSH with positive antibody titres even in the absence of symptoms. (Vanderpump MPJ, Turnbridge WMG, 1996)[36].

There is good evidence to suggest that the treatment of patients with subclinical hypothyroidism prevents progression to overt hypothyroidism (Surks MI 2004)[37].Failed medical therapy of menstrual disturbances may be a under estimate of thyroid disorder.

HYPERTHYROIDISM:

The two most common causes of hyperthyroidism are Grave's disease (diffuse toxic goiter) and plummer's disease (toxic nodular goiter). Thyrotoxicosis in early age leads to delayed sexual maturation. There is an accelerated skeletal growth and physical development is usually normal. Menstrual changes in hyperthyroidism are usually unpredictable, ranging from normal cycles, oligomenorrhoea to amenorrhoea. Menstrual flow is initially diminished and later ceases and interval between cycles may be increased or decreased (McKenzie JM, 1979)[35]. Fertility is usually

diminished and miscarriage rates are increased. In most hyperthyroid women ovulation usually occurs as indicated by the secretory endometrium (Reid Rl, 1987)[38].However in some women anovulatory cycles with oligomenorrhoea can occur. Amenorrhoea usually occurs in women with severe forms of hyperthyroidism.

The mechanisms attributed incluude

1. Increased SHBG levels due to decrease peripheral clearance of testosterone and oestradiol.
2. Due to increase in peripheral blood flow there is peripheral aromatisation of oestrogen to progesterone
3. There is disruption in the amplitude and frequency in the GnRH Pulses (DeGroot N1979)[39].

SUBCLINCAL HYPERTHYROIDISM:

The incidence of subclinical hyperthyroidism is 0.9%.The risk of progression to overt hyperthyroidism is uncommon. In this there is a chronically decreased serum TSH level with free thyroid hormones in the normal range .The incidence increases in older women (Felicetta JU, 1987)

CLNICAL SYMPTOMS AND SIGNS OF THYROID DISORDERS

Hypothyroidism:

Symptoms:	signs:
Weight gain	hypertension
Constipation	coarse skin
Cold intolerance	bradycardia
Voice change	
Lethargy	
Palpitation	

HYPERTHYROIDISM:

Symptoms:	signs:
Weight loss	Proptosis
Diarrhoea	Lidlag
Heat intolerance	Tachycardia
Anxiety	Warm and moist skin
Fatigue	
Tremors	

THYROID DYSFUNCTION AND MENSTRUAL DISRODERS IN CERTAIN CONDITIONS:

ANOREXIA NERVOSA: Anorexia nervosa is an eating disorder characterised by abnormally low body weight, intense fear of gaining weight and distorted perception of bodyweight. The symptoms are due to dysregulation of hypothalamus mediated mechanisms. Anorexics are usually amenorrhoeic . There is a state of relative hypothyroidism. It occurs due to diversion from formation of active T3 to reverse T3 as a compensation for malnourishment.

TURNER'S SYNDROME: Women with turner syndrome characterized by 45XO karyotype-deletion of a long or short of a chromosome usually occurs.They usually have a short stature, primary amenorrhea, steak gonads, webbed neck, wide carrying angle, widely spaced nipples, shield chest and various other abnormalities of the heart and kidneys. A high prevalence of autoimmune thyroid disorders with about 50% of adult patients with Turners have antithyroglobulin (anti TG) antibody and anti-thyroid peroxidase (anti-TPO) . Approx. 30% will usually develop subclinical / clinical hypothyroidism (Barbesino G et al, 1998).

EXCERCISE AND SRESS :These patients usually amenorrhoeic there is an alteration in GnRH pulse frequency(olson BR,1989)[40].LH surge donot occur.Follicular development and ovulation usually does not occur. These

women are hypoestrogenic and menstrual dysfunction usually occurs.Athelets usually have a low T4 level but in amenorrhoeics usually have a overall decrease in all circulating thyroid hormones.

POSTPARTUM THYROIDITIS:

It is the occurrence of transient thyroid dysfunction during the first postpartum year in women who are euthyroid before pregnancy. It estimated to occur from 1.1%-16.7% .It may occur upto 25% in women with Type 1 diabetes. There occurs a transient hyperthyroidism followed by transient hypothyroidism returning to euthyroid state by the end of one year postpartum .It is an exacerbation of underlying autoimmune thyroiditis showing a strong association with antithyroperoxidase antibodies. Treatment is with beta blockers during the hyperthyroid state and thyroxine supplementation during the hypothyroid state. Antithyroid drugs are not indicated. The risk of recurrence in subsequent pregnancies is upto 70%.Monitoring must continue after every pregnancy and yearly thereafter.

LABORATORY EVALUATION OF THYROID FUNTION :

BMR measurement:

The Basal Metabolic Rate (BMR) is the amount of energy per unit time that a person to spend to keep the body functioning at rest. This test had poor sensitivity and specificity. Nowadays not used as thyroid function test.

Normal value is +/_ 20%.In hypothyroidism it is between _30% to_40% where as in hyperthyroidism it can go upto 100%

Protein bound iodine estimation:

It reflects the level T3 and T4 bound to plasma proteins. It has poor sensitivity and specificity. Normal value is upto 6g/ml. Elevated values are in hyperthyroidism and high altitudes. Decreased values are seen in pregnancy and hypothyroidism.

Radioactive iodine uptake:

It is a useful study for assessing thyroid dysfunction. It is performed by giving 4-10 micro curies of iodine131 orally in 100ml of water. The absorption of this tracer is studied after 4-6 hours by an x-ray counter over the neck. The normal uptake is between 15% and 25%.In hypothyroidism it is decreased to less than 15% whereas in hyperthyroidism it is elevated to 60%

Radionucleotide scan of thyroid gland:

It is an imaging performed by injecting iodine 131 or technicium 99 intravenously. A special camera is used to take image of the distribution of radioactive iodine in and around the thyroid gland.

Antithyroid antibodies:

It is used for evaluation of autoimmune thyroid disorders.The most commonly measured antibodies are

Thyroid peroxidise antibody, Thyroglobulin antibody, Thyroid stimulating immunoglobulin antibody, TSH receptor binding inhibitor immunoglobulin.

Free T3,T4,TSH ESTIMATION:

Although screening for TSH in a large number of patients is usually done in return for a only number of positive cases it is that in patient with menstrual disturbances with thyroid dysfunction , prompt return of menstrual cycles usually occurs when appropriate treatment is instituted(Caldwell G,1985) Various recommendations for thyroid screening include: American Thyroid Association(ATA)recommends routine screening for both men and women after 35 years and every 5 years.

American College Of Obstetrician and Gynaecologists (ACOG) recommends screening for asymptomatic women over the age of 40 years with TSH assay[27].

American association of clinical Endocrinologists (AACE)2002 recommened screening for older women[42]. Mild subclinical hypothyroidism is diagoned if TSH level is 4-10mIU/ml and severe if TSH level is more than 10mIU/ml and the management regarding subclinical hypothyroidism is

controversial. Treatment with thyroxine is warranted if mild subclinical hypothyroidism is symptomatic and in severe subclinical hypothyroid women follow up annually if TPO antibodies is positive and every 3-5 years TPO antibodies are negative.

National Academy of Clinical Biochemistry and National Health and Nutrition examination revealed that the target TSH values between 0.4 - 2.5mIU/ml.

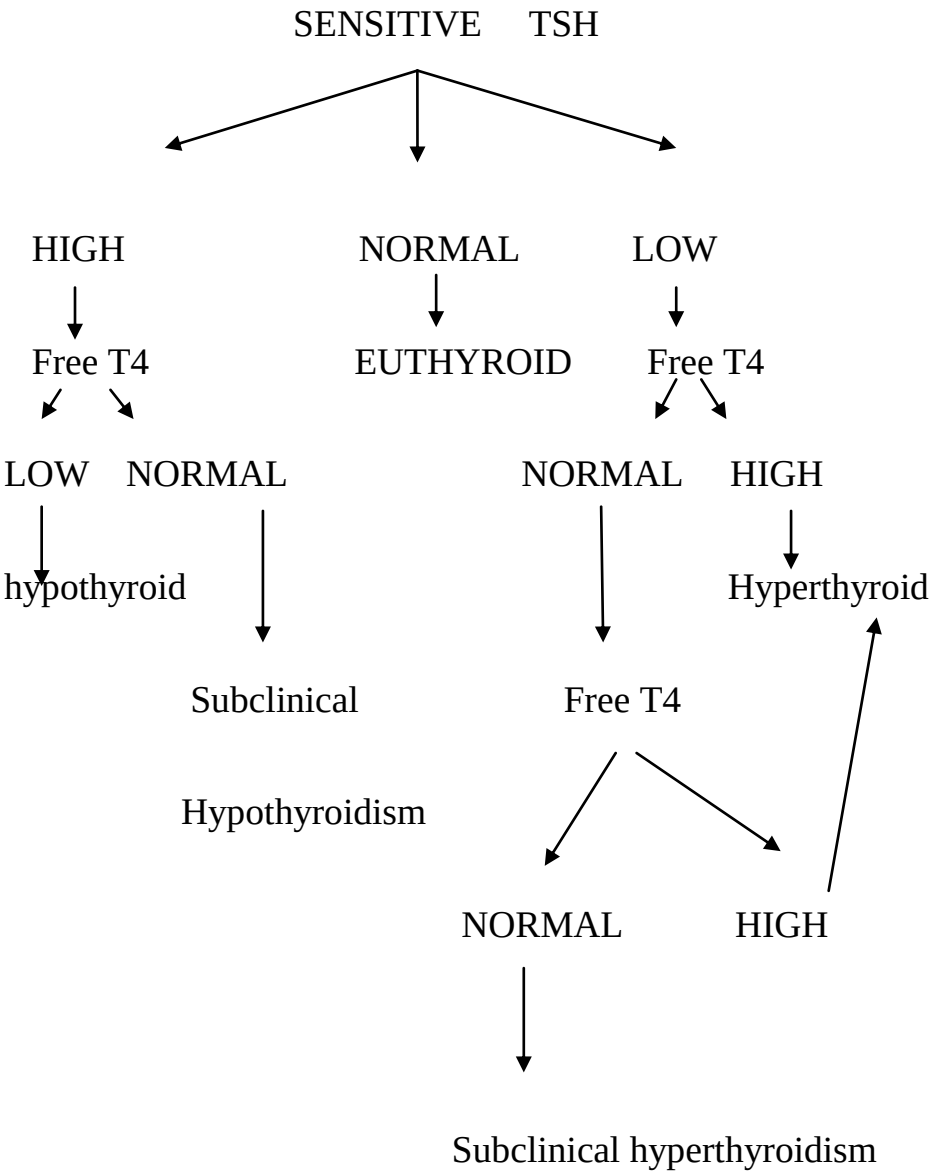
Measurement of free T3,T4 and TSH gives reflects accurate thyroid activity.

Total T3 and T4 measurement has its own disadvantages-

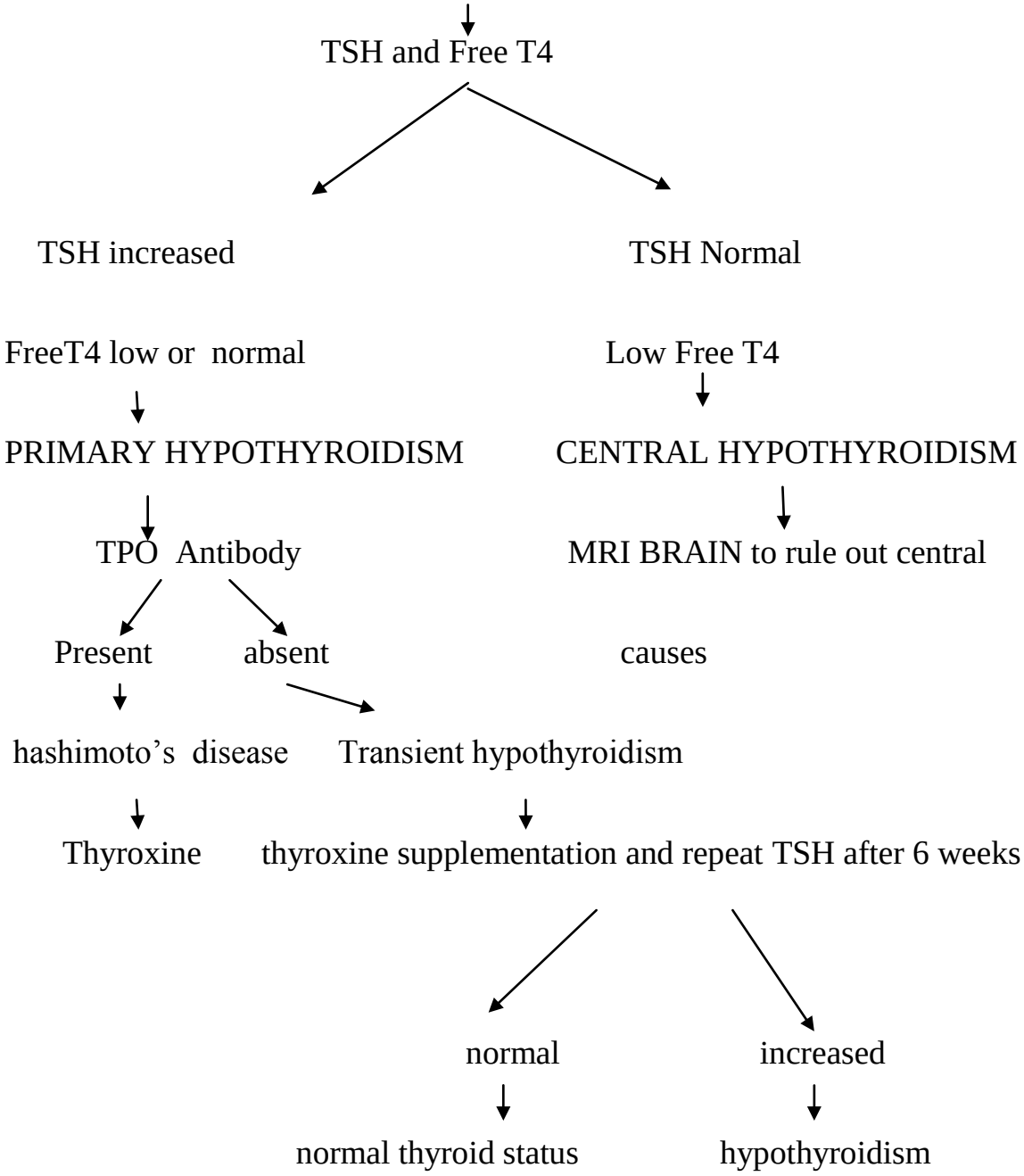
1. The major of it is bound to plasma protein does not take part in active metabolism

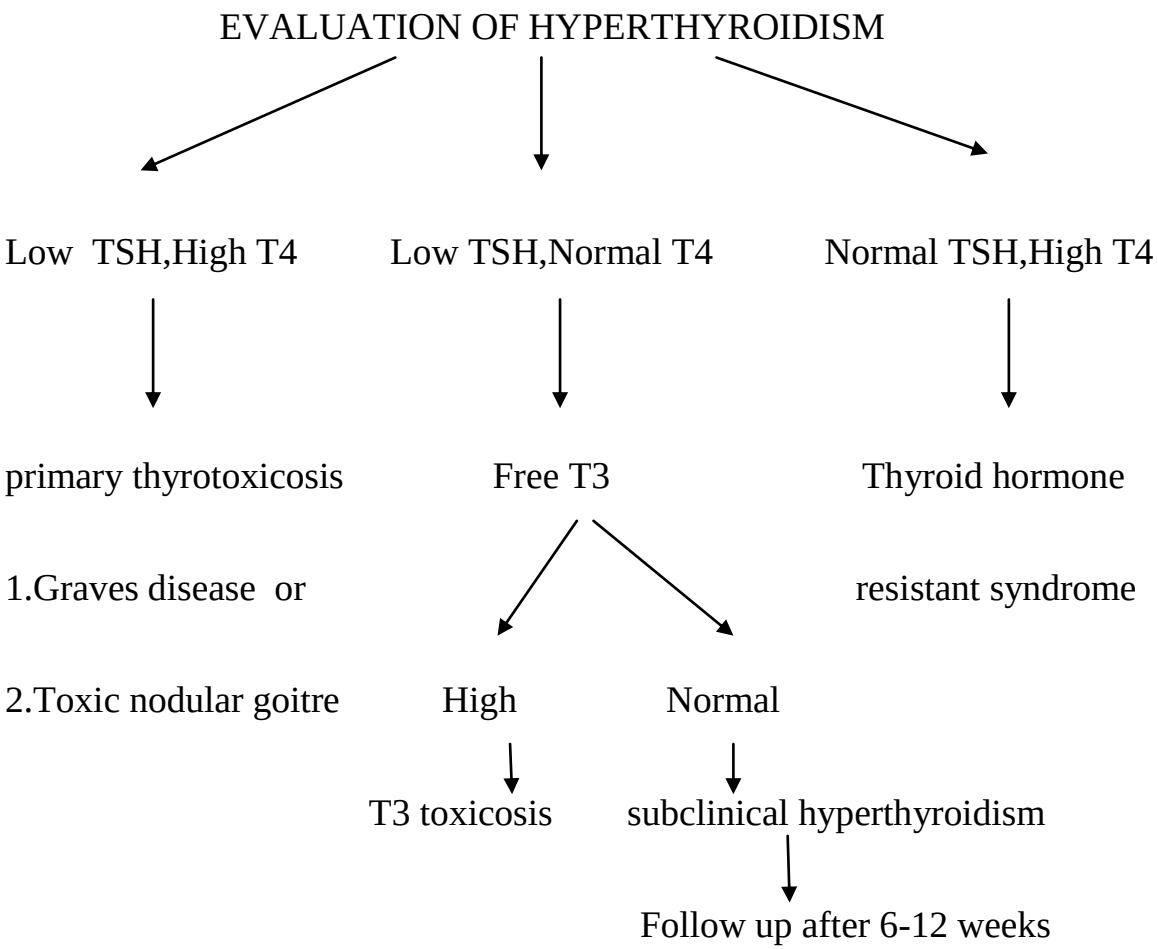
2. In certain conditions like pregnancy the increased thyroid binding globulin

TSH measurement plays an important role as it reflects the integrity of hypothalamo-pituitary-thyroid axis.


SENSITIVE TSH
HIGH
NORMAL
LOW
Free T4
EUTHYROID
Free T4
LOW
NORMAL
NORMAL
HIGH
hypothyroid
Hyperthyroid
Subclinical
Hypothyroidism
Free T4
NORMAL
HIGH
Subclinical hyperthyroidism

EVALUATION OF HYPOTHOTHYROIDISM




EVALUATION OF HYPERTHYROIDISM
Low TSH,High T4
Low TSH,Normal T4
Normal TSH,High T4
primary thyrotoxicosis
Free T3
Thyroid hormone
1.Graves disease or
resistant syndrome
2.Toxic nodular goitre
High
Normal
T3 toxicosis
subclinical hyperthyroidism
Follow up after 6-12 weeks

MATERIALS AND METHODS

The present study **"STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS"** was conducted at Gynaecology outpatient at Department of Obstetrics and Gynaecology, Govt Theni Medical College and Hospital , Theni. This is a cross sectional study based on the data collected from 200 women attending the gynaec opd with menstrual disturbances.

Study period: 2 year from Oct 2016 to Sep 2018

Ethical committee approval obtained.

The study group included the women with the following complaints:

MENORRHAGIA: regular cycles with excessive flow (80 ml or more) or duration.

OLIGOMENORRHOEA: Cycles lasting for more than 35 days.

POLYMENORRHOEA: Cycles lasting for less than 22 days.

POLYMENORRHAGIA: Frequent cycles with excessive flow.

HYPOMENORRHOEA: Bleeding for less than 2 days.

AMENORRHOEA: Absence of menstruation for 6 months (in women with regular cycles) or 3 cycles (in those with irregular cycles).

INCLUSION CRITERIA:

1. Women in the age group of 18-45 years

2. Women with any of the above menstrual disturbances

3. No demonstrable palpable pelvic pathology

4. Women with symptoms of hyperthyroidism/hypothyroidism

EXCLUSION CRITERIA:

1. Women less than 18 years or more than 45 years

2. Women with palpable pelvic pathology like fibroid/adenomyosis

3. Women with h/o bleeding disorders

4. Women on hormonal treatment/drugs which alter thyroid metabolism*/IUCD users

5. women with systemic hypertension/diabetes mellitus

Symptoms of hypothyroidism:

Weight gain (>10kg in 3months)

Constipation

Cold intolerance

Voice change

Lethargy

Palpitation

Symptoms of hyperthyroidism:

Weight loss(<10kg in 3 months)

Diarrhoea

Heat intolerance

Anxiety

Fatigue

Tremors

* Aspirin, Heparin, Sulpha drugs, Antithyroid medication, Eltroxin, Glucocorticoids, and Amiodarone.

PROCEDURE:

Patients were selected based on the above mentioned criteria History was

taken as per the proforma including a emphasis on detailed menstrual history and the signs and symptoms of hypothyroidism and hyperthyroidism. The following examinations were done.

A detailed general examination with a special note on the presence/ absence of anemia, thyroid swelling done. cardiovascular system, respiratory system and central nervous system system examination done. The height in centimeters and weight in kilograms were measured and the BMI calculated. A per abdominal, per speculum examination and Bimanual pelvic examination were done to rule out other causes of abnormal bleeding.The following investigations are done:

1.Hemoglobin estimation

2.bleeding and clotting time

3.Transabdominal Ultrasound

4.Thyroid function test

A morning fasting sample of 5 ml of venous blood without any anticoagulant was taken in a dry plain glass tube for free T3, free T4 and TSH

estimation and were assayed using Chemiluminescent assay.

REFERENCE VALUES:

- fT3:1.21-4.18pg/ml
- fT4:8.9-17.2pg/ml
- TSH:0.3-4.5mIU/ml

ANALYSIS OF THE STUDY

200 women with menstrual disorders without palpable pelvic

pathology were evaluated for thyroid dysfunction

STATISTICAL ANALYSIS:

The demographic variables in categories were given in frequencies along with their percentages.T3, T4 and TSH score were given in mean and standard deviation.

The association between demographic variables and Thyroid disorder score are analysed using pearson chisquare test .

$P<0.05$ was considered statistically significant. All statistical test are two tailed test.

The quantity of χ^2 is defined as:

$$\chi^2 = \Sigma (O-E)^2 / E$$

Σ (Observed frequency- expected frequency)^2/ Expected frequencies

Where O= observed frequencies

E = expected frequencies

$$\chi^2 = \Sigma \{(O-E) - 0.5\}^2 / E$$

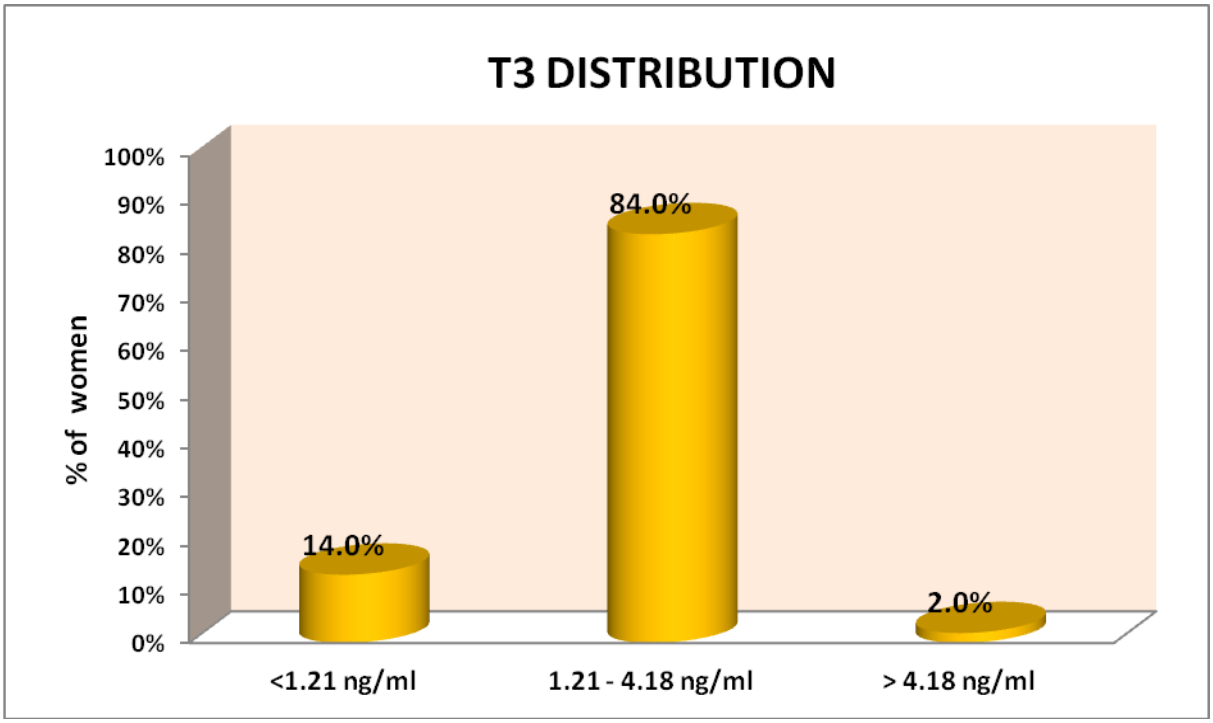
Table 1: LEVEL OF T3 DISTRIBUTION

T3	No. of women	%
<1.21ng/ml	28	14.0%
1.21 - 4.18ng/ml	168	84.0%
> 4.18ng/ml	4	2.0%
Total	200	100.0%

Table 2: LEVEL OF T4 DISTRIBUTION

T4	No. of women	%
<8.9 ng/ml	28	14.0%
8.9 - 17.2 ng/ml	168	84.0%
>17.2 ng/ml	4	2.0%
Total	200	100.0%

FIG 1


T3 DISTRIBUTION
% of women
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
14.0%
84.0%
2.0%
<1.21 ng/ml
1.21 - 4.18 ng/ml
> 4.18 ng/ml

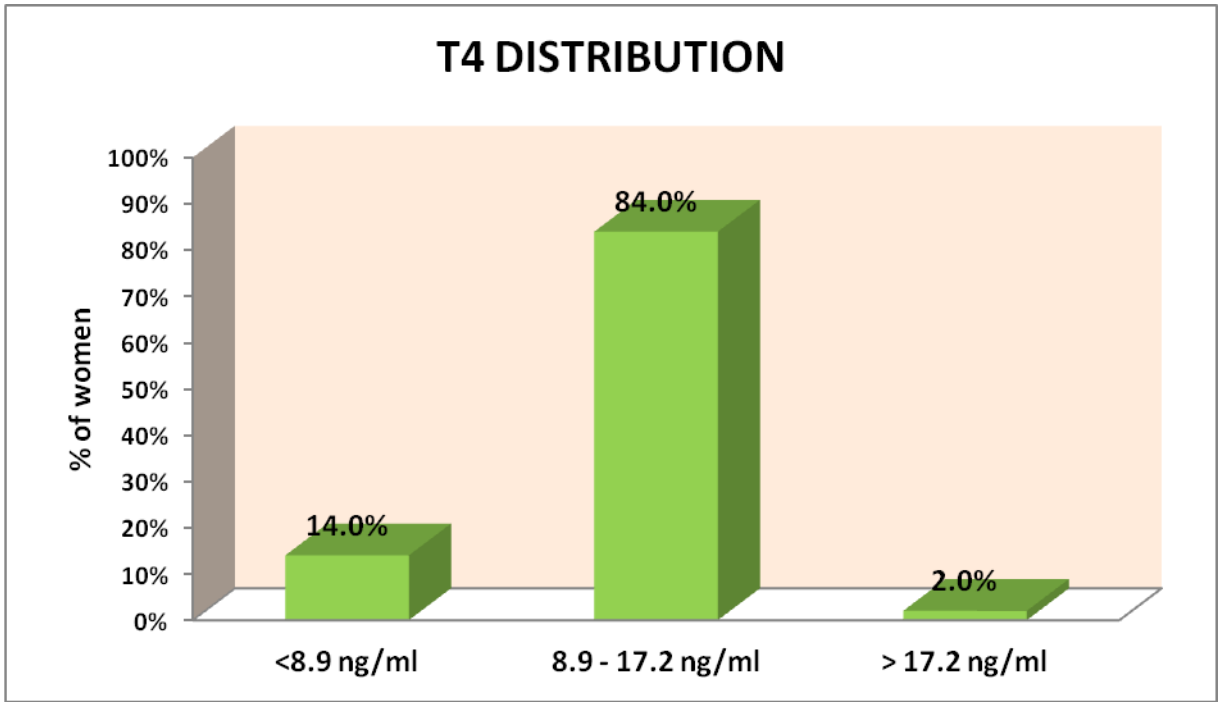
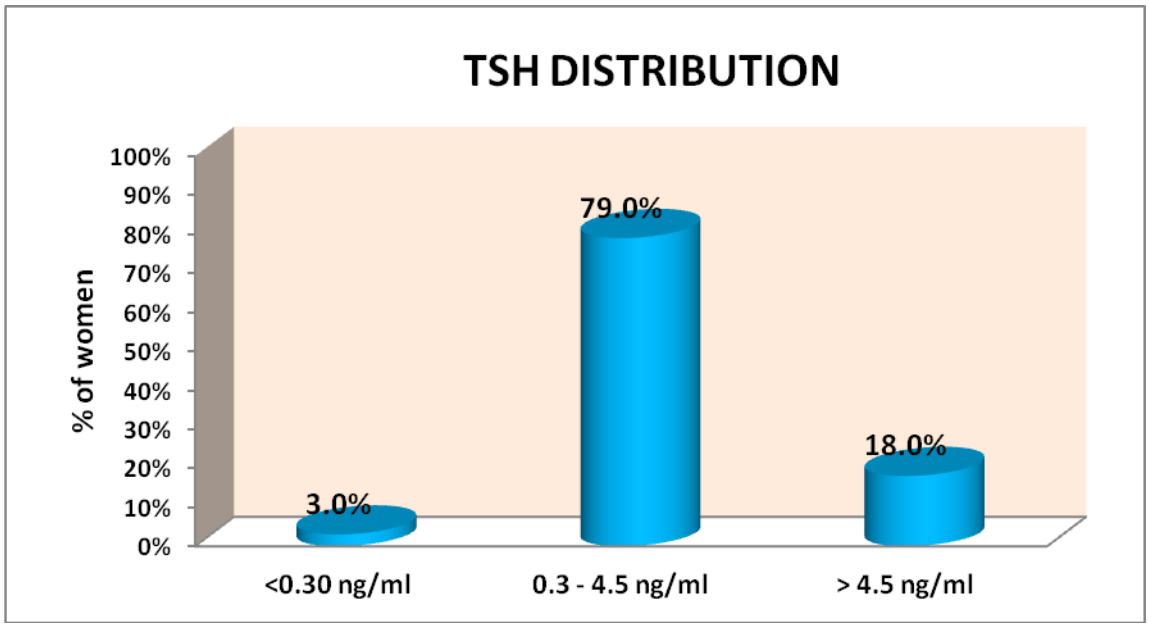

T4 DISTRIBUTION
% of women
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
14.0%
84.0%
2.0%
<8.9 ng/ml
8.9 - 17.2 ng/ml
> 17.2 ng/ml

FIG 2

Table 3: LEVEL OF TSH DISTRIBUTION

TSH	No. of women	%
<0.30 ng/ml	6	3.0%
0.3 - 4.5 ng/ml	158	79.0%
> 4.5 ng/ml	36	18.0%
Total	200	100.0%

Fig3



Among 200 women 158 had normal TSH values. Incidence of

Clinical hypothyroidism -18%

Subclinical hypothyroidism-4%

Clinical hyperthyroidism-3%

Subclinical hyperthyroidism-1%

Table 4: Prevalence of thyroid disorders in women with menstrual disorders(15-45years)

Total women	No, of Thyroid disorders	% of Thyroid disorders	95% CI
200	42	21.00%	18.12% – 23.88%

Table 5:Comparison of T3, T4 and TSH

Values	T3		T4		TSH	
	n	%	n	%	n	%
< Normal	28	14.0%	28	14.0%	6	3.0%
Normal	168	84.0%	168	84.0%	158	79.0%
>Normal	4	2.0%	4	2.0%	36	18.0%

AUB	NO OF WOMEN
MENORRHAGIA	79(39.5%)
POLYMENORRHOEA	20(10%)
POLYMENORRHAGIA	20(10%)
OLIGOMENORRHOEA	24(12%)
AMENORRHOEA	48(24%)
HYPOMENORRHOEA	9(4.5%)

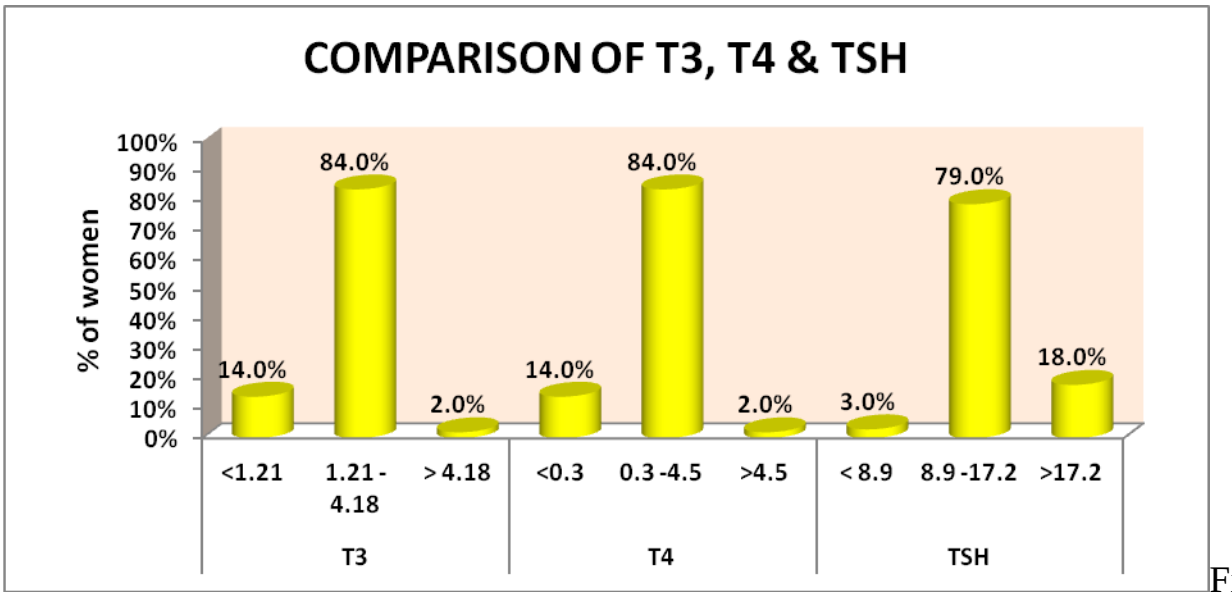
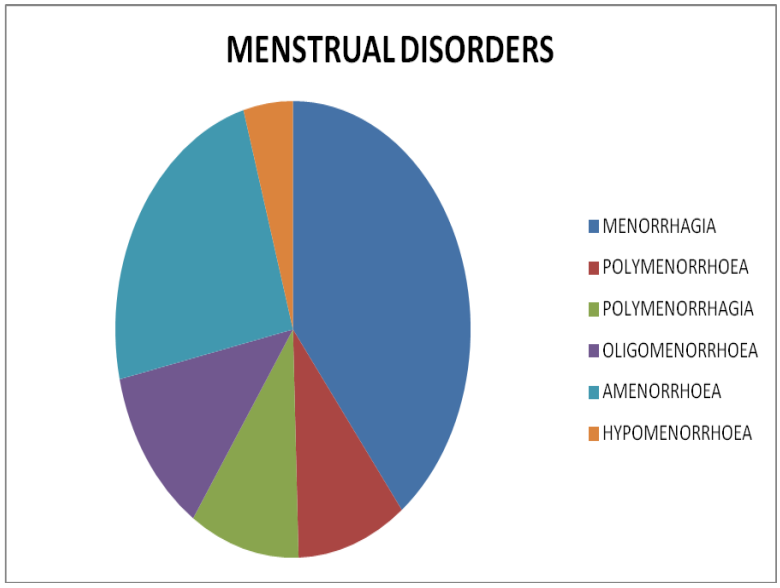


Fig 5 TABLE 6: TYPE OF MENSTRUAL DISORDERS:

FIG 6



Menorrhagia is most common menstrual disturbance occurring in about 39.5% of women followed by amenorrhoea (24%)

TABLE 7:MENSTRUAL DISORDERS AND DURATION:

DURATION	NUMBER OF WOMEN
1-3 MONTHS	78
4-6 MONTHS	66
7 MONTHS-1 YEAR	34
1-3 YEARS	16
>3 YEARS	2
SINCE MENARCHE	4

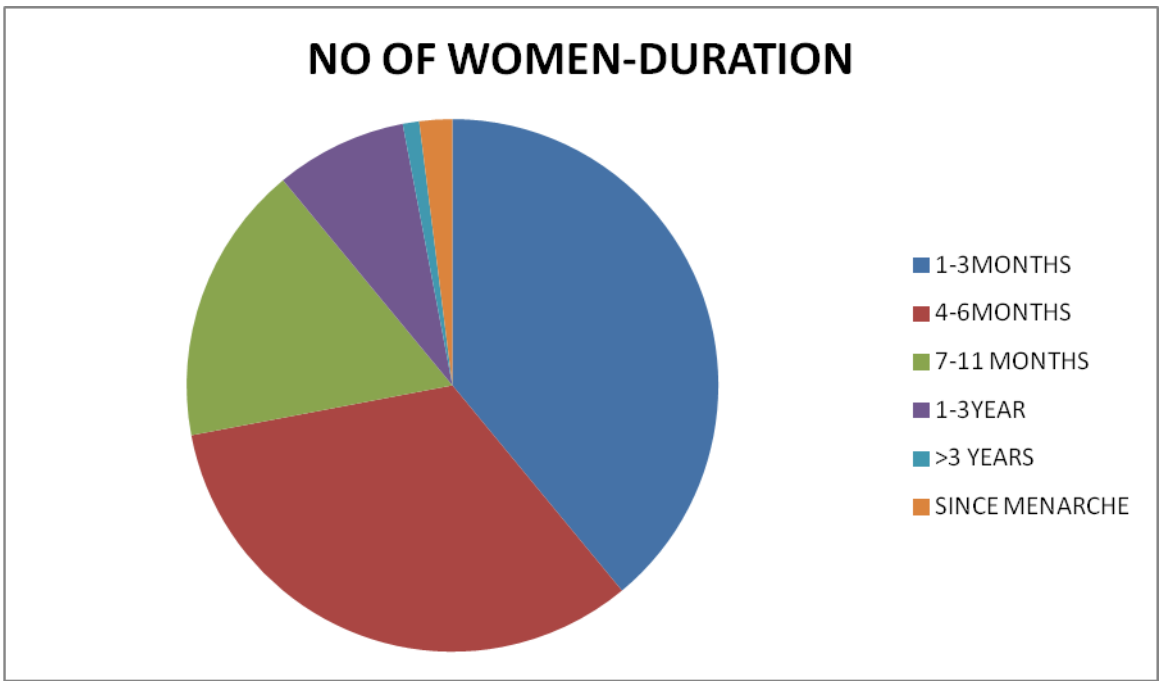


FIG 7

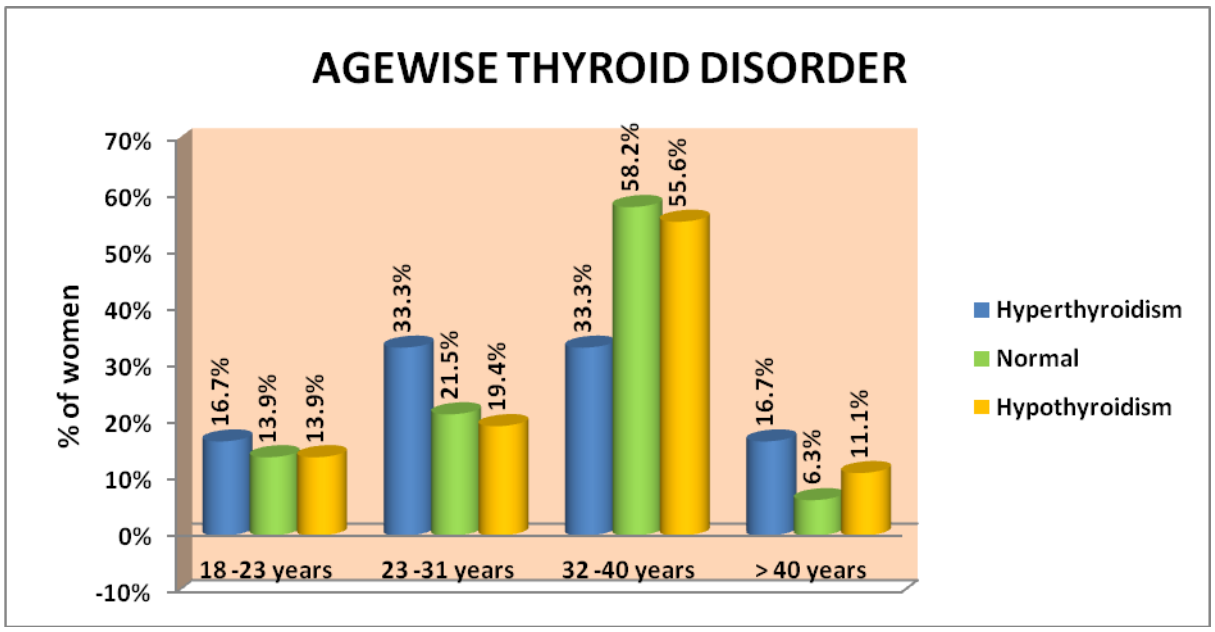
39% of women presented with complaints of 3 months duration.

Table 8: Age wise Thyroid Disorder

Age group	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	N	%	n	%	n	%	
18 -23 years	1	16.7%	22	13.9%	5	13.9%	χ=2.72 P=0.84 (NS)
24 -31 years	2	33.3%	34	21.5%	7	19.4%	
32 -40 years	2	33.3%	92	58.2%	20	55.6%	
> 40 years	1	16.7%	10	6.3%	4	11.1%	

Total	6	100.0%	158	100.0%	36	100.0%	

Fig8

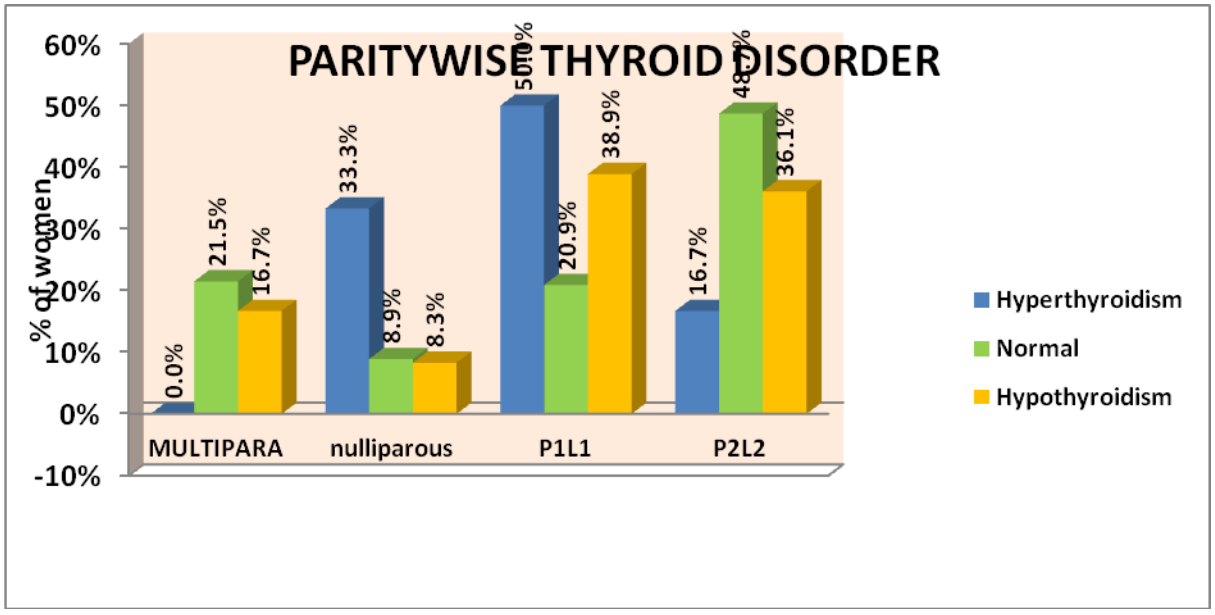


The thyroid disorders are more common in the age group of 32-40 years followed by the age group of 24-31 years.

Table 9: Paritywise Thyroid Disorder

Parity	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	N	%	n	%	
Multipara	0	0.0%	34	21.5%	6	16.7%	χ=12.76 P=0.05*(S)
Nullipara	2	33.3%	14	8.9%	3	8.3%	
P1L1	3	50.0%	33	20.9%	14	38.9%	
P2L2	1	16.7%	77	48.7%	13	36.1%	
Total	6	100.0%	158	100.0%	36	100.0%	

Fig9

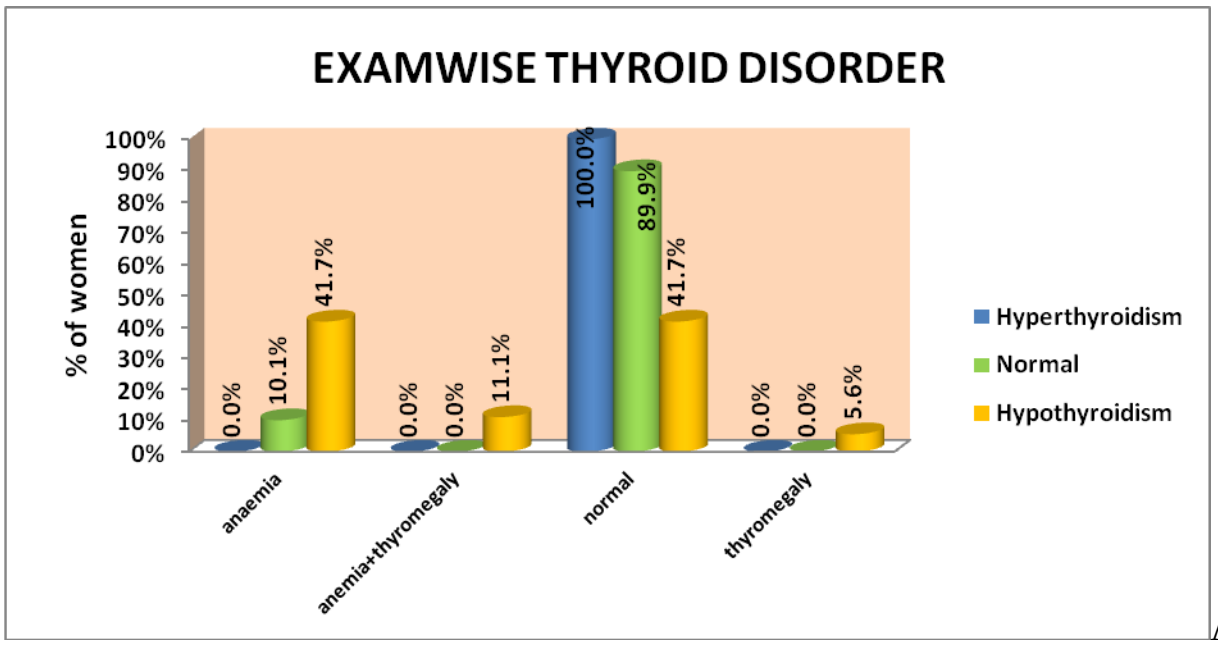


Out of the 200 women ,hyperthyroidism were more common in nulliparous and primiparous women

Table 10: Examination wise Thyroid Disorder

Examination	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	n	%	n	%	
anaemia	0	0.0%	16	10.1%	15	41.7%	χ=55.72 P=0.01** (S)
anemia+thyromegaly	0	0.0%	0	0.0%	4	11.1%	
Normal	6	100.0%	142	89.9%	15	41.7%	
thyromegaly	0	0.0%	0	0.0%	2	5.6%	
Total	6	100.0%	158	100.0%	36	100.0%	

FIG 10



A about 18.5% had abnormal findings on clinical examination.81.5% had normal findings.

Table 11: BMI wise Thyroid Disorder

BMI	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	n	%	n	%	
< 18	5	83.3%	2	1.3%	0	0.0%	χ=166.25 P=0.01**(S)
18 - 24	1	16.7%	131	82.9%	10	27.8%	
25 - 29	0	0.0%	21	13.3%	21	58.3%	
30 - 34	0	0.0%	3	1.9%	4	11.1%	
>35	0	0.0%	1	0.6%	1	2.8%	
Total	6	100.0%	158	100.0%	36	100.0%	

Fig11

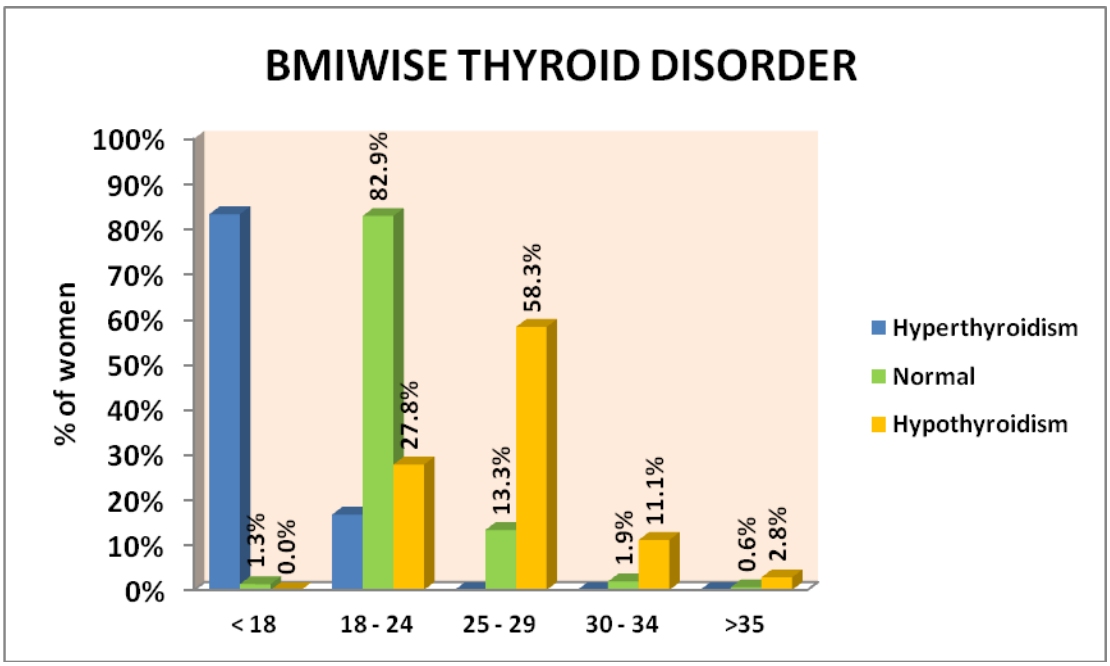
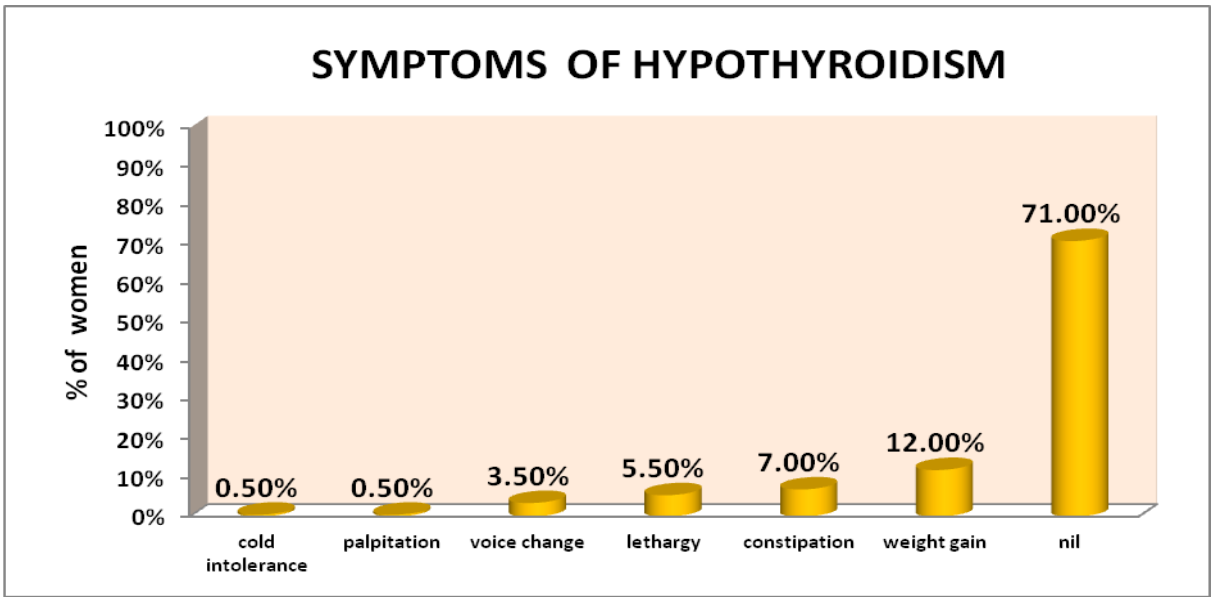


Table 12:SYMPTOMS OF HYPOTHYROIDISM

	n	%
cold intolerance	1	0.5%
palpitation	1	0.5%
voice change	7	3.5%
lethargy	11	5.5%
constipation	14	7.0%
weight gain	24	12.0%
Nil	142	71.0%
Total	200	100.0%

Fig12

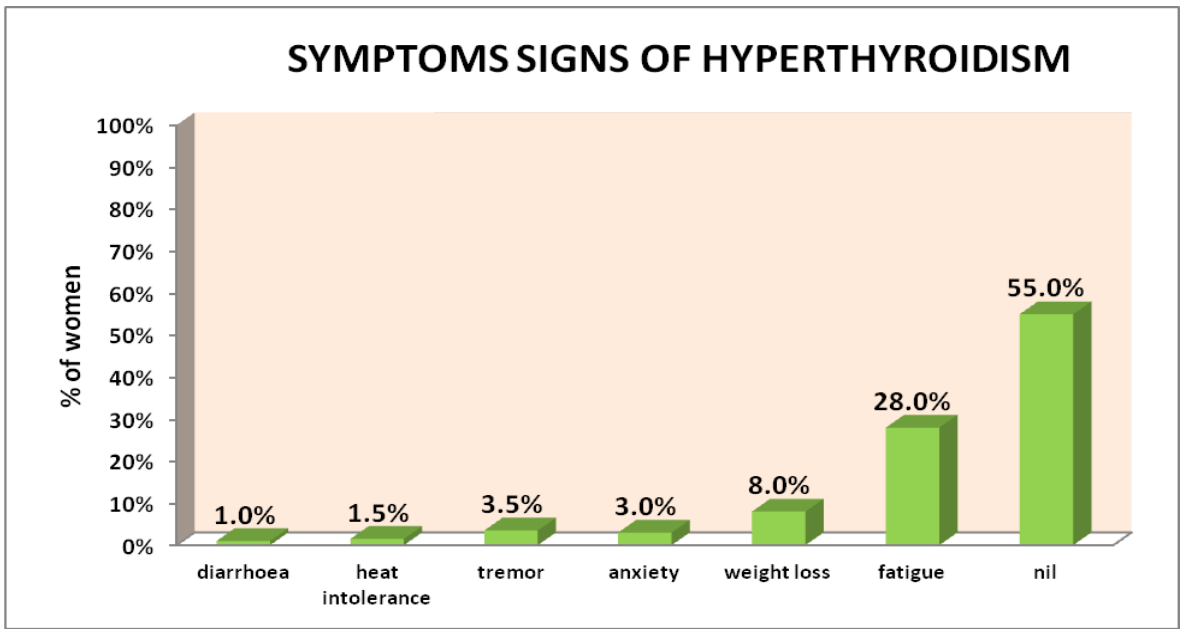


About 71% had no symptoms /signs of hypothyroidism. Weight gain was the most common complaint noted in about 12% of women.

Table 13:SYMPTOMS OF HYPERTHYROIDISM

	n	%
Diarrhoea	2	1.0%
heat intolerance	3	1.5%
tremor	7	3.5%
anxiety	6	3.0%
weight loss	16	8.0%
fatigue	56	28.0%
Nil	110	55.0%
Total	200	100.0%

Fig13

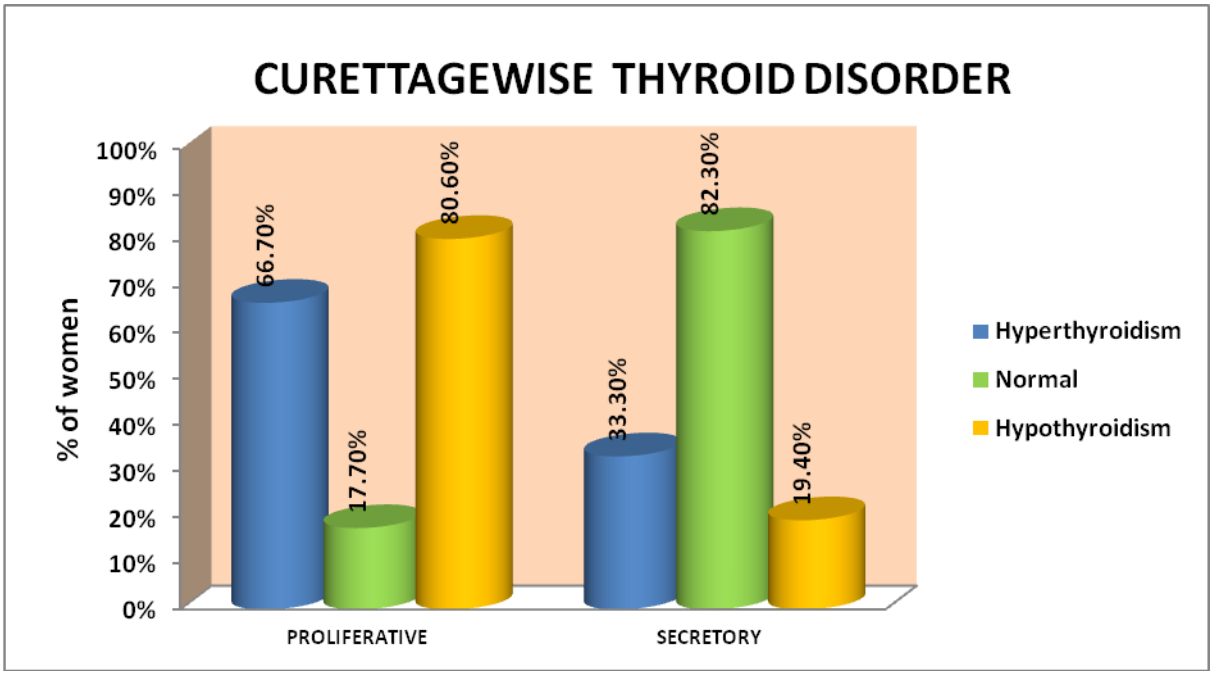


About 55% had no symptoms of hyperthyroidism. Fatigue was the most common complaint noted in 28% of women.

Table 14: Curettage wise Thyroid Disorder

# CURETTAGE	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	n	%	n	%	
PROLIFERATIVE	4	66.7%	28	17.7%	29	80.6%	χ=58.42 P=0.001*** (S)
SECRETORY	2	33.3%	130	82.3%	7	19.4%	
Total	6	100.0%	158	100.0%	36	100.0%	

Fig14



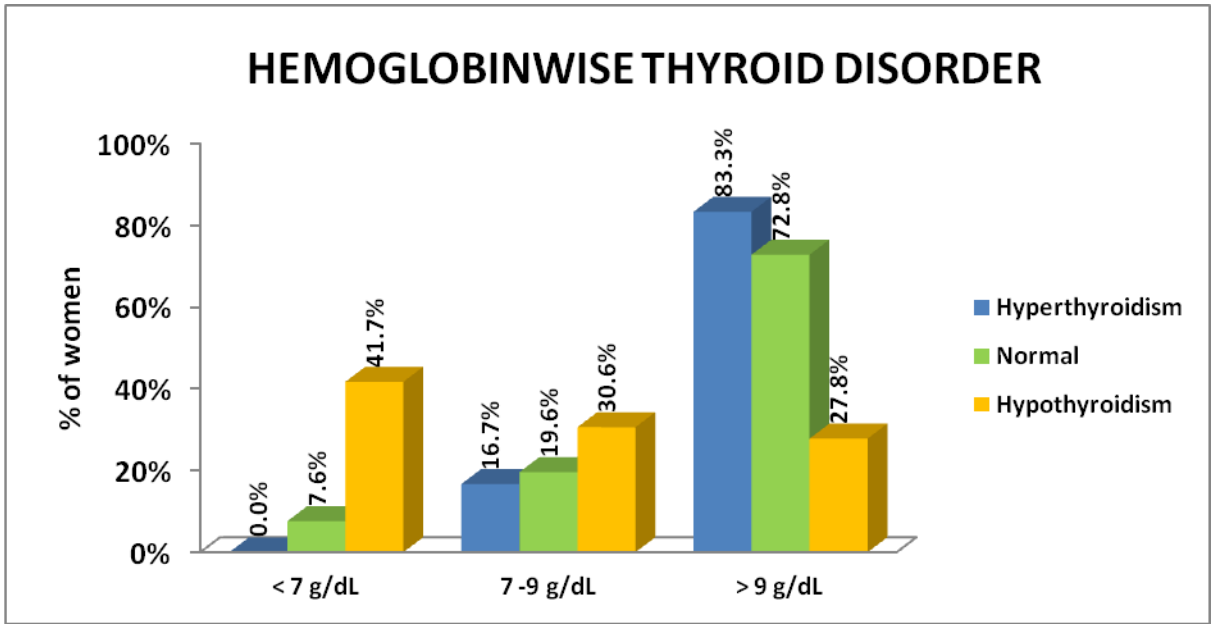
Majority of hypothyroid women 80.6% had proliferative endometrium due to associated anovulation. In hyperthyroid women both secretory and proliferative endometrium are seen.

Table 15: Level of Haemoglobin wise Thyroid Disorder

Hb	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	n	%	n	%	
< 7 g/dL	0	0.0%	12	7.6%	15	41.7%	$\chi 2=37.20$ P=0.001*** (S)
7 -9 g/dL	1	16.7%	31	19.6%	11	30.6%	

> 9 g/dL	5	83.3%	115	72.8%	10	27.8%	
Total	6	100.0%	158	100.0%	36	100.0%	

Fig 15



Most of the hypothyroid women are anaemic. hemoglobin level were normal in hyperthyroid women.

TABLE 16-1: AMENORRHOEA

Level	T3		T4		TSH	
	N	%	N	%	n	%
< Normal	1	2.08%	1	2.08%	4	8.3%
Normal	45	93.75%	45	93.75%	43	89.6%
>Normal	2	4.17%	2	4.17%	1	2.1%
Total	48	100.0%	48	100.0%	48	100.0%

Out of 48 amenorrheic patient in our study

2 women had clinical hyperthyroidism

2 women had subclinical hyperthyroidism

1 women had clinical hypothyroidism

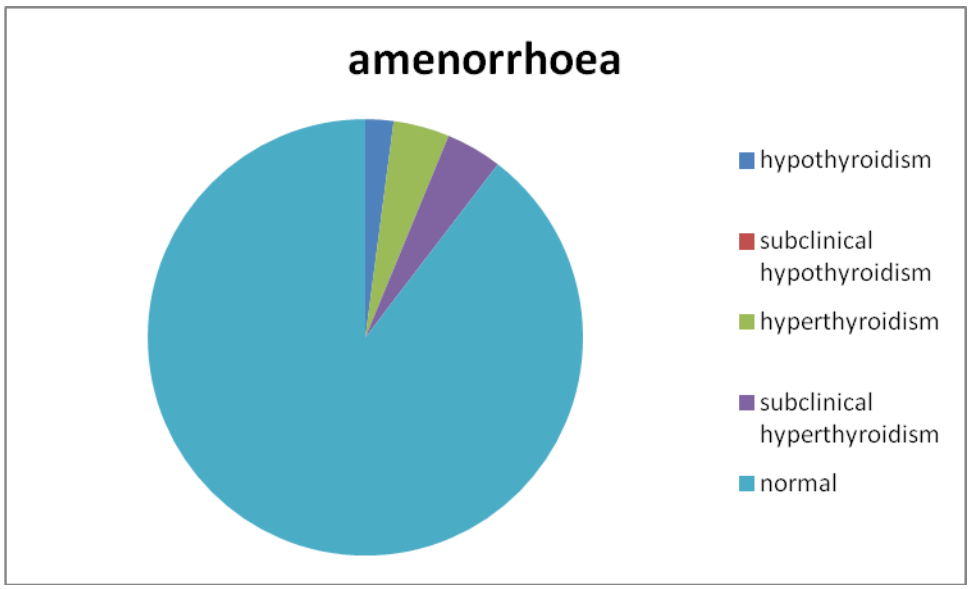


FIG 16-1

Thus Amenorrhoea is most commonly associated with hyperthyroidism

Table 16-2: HYPOMENORRHOEA

Level	T3		T4		TSH	
	n	%	N	%	n	%
< Normal	0	0.0%	0	0.0%	1	11.1%
Normal	8	88.9%	8	88.9%	8	88.9%
>Normal	1	11.1%	1	11.1%	0	0.0%
Total	9	100.0%	9	100.0%	9	100.0%

Out of 9 women with hypomenorrhoea,

1 women had clinical hyperthyroidism

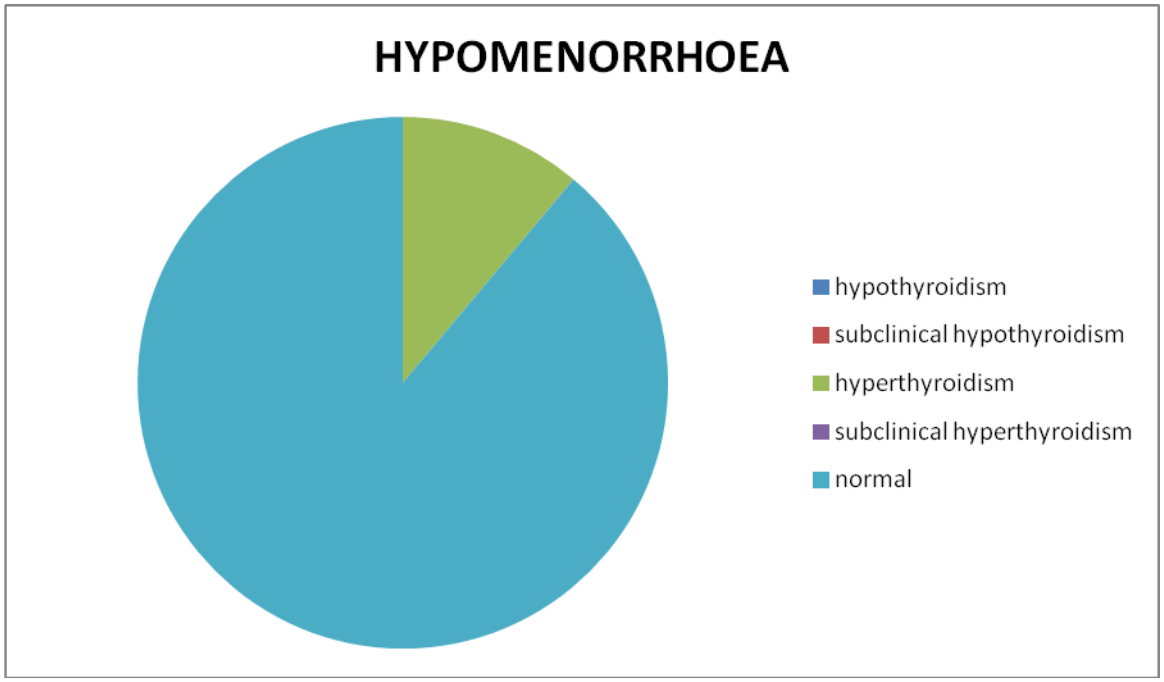


FIG 16-2

In hypomenorrhoea is found to be not significantly associated with any thyroid disorder.

Table 16-3: MENORRHAGIA

Level	T3		T4		TSH	
	n	%	n	%	n	%
< Normal	10	12.7%	10	12.7%	1	1.3%
Normal	68	86.1%	68	86.1%	60	75.9%
>Normal	1	1.3%	1	1.3%	18	22.8%
Total	79	100.0%	79	100.0%	79	100.0%

Out of 79 women with menorrhagia,

10 women had clinical hypothyroidism.

8 women had subclinical hypothyroidism.

1 women had clinical hyperthyroidism.

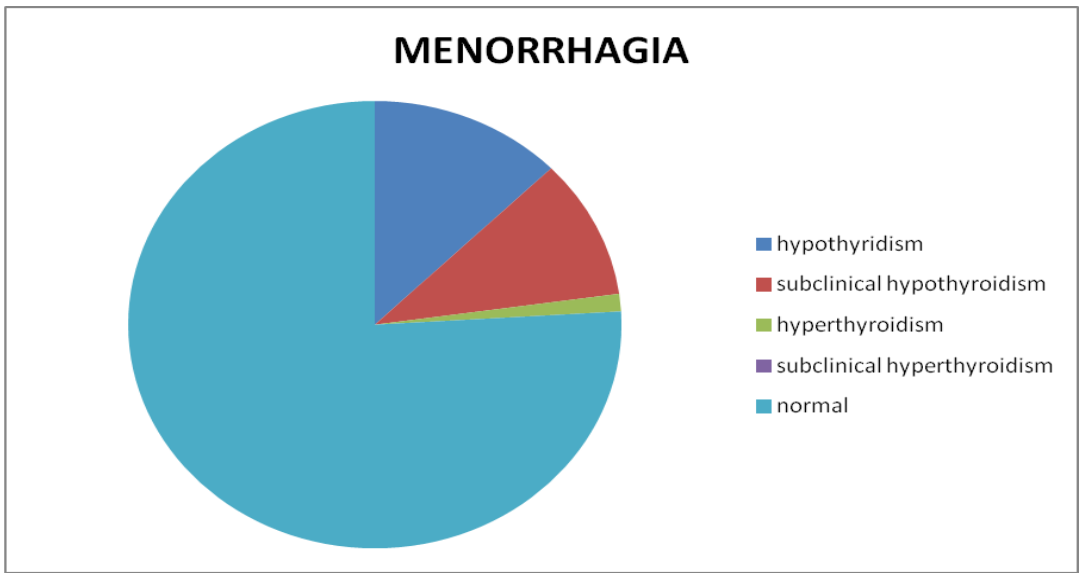


FIG16-4

Menorrhagia is found to have significant association with hypothyroidism

Table 16-5: OLIGOMENORRHOEA

Level	T3		T4		TSH	
	n	%	n	%	n	%
< Normal	3	12.5%	3	12.5%	0	0.0%
Normal	21	87.5%	21	87.5%	21	87.5%
>Normal	0	0.0%	0	0.0%	3	12.5%
Total	24	100.0%	24	100.0%	24	100.0%

Out of 24 women with oligomenorrhoea,

3 women had clinical hypothyroidism

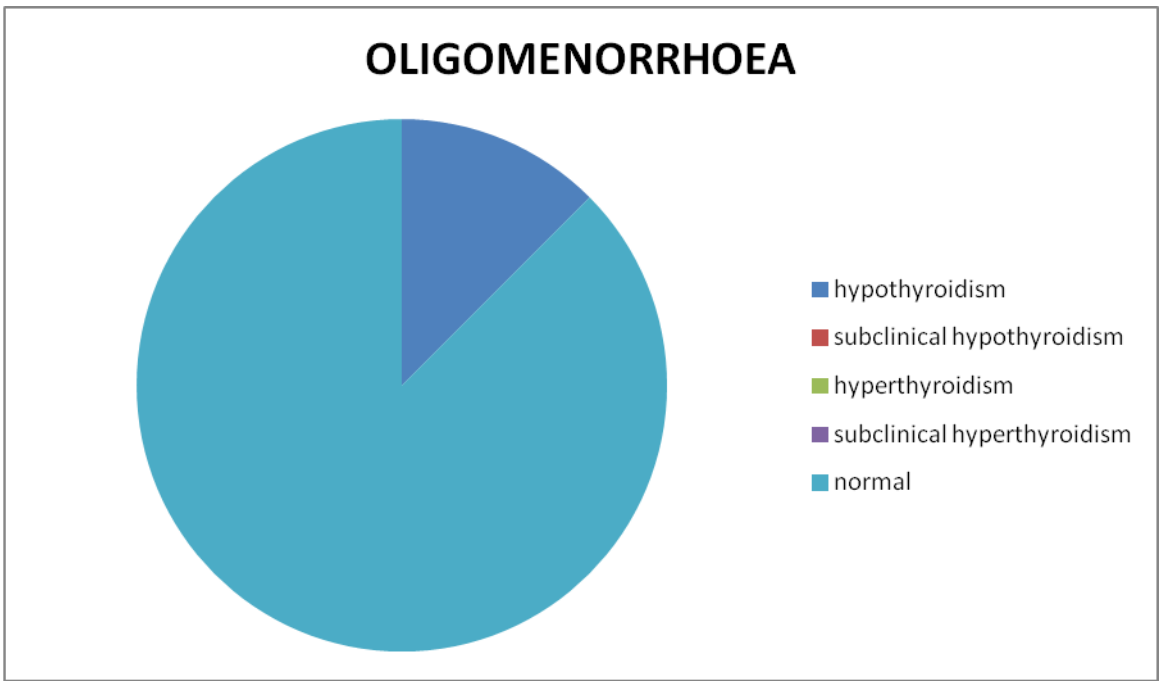


FIG 16-5

Oligomenorrhoea is associated with hypothyroidism in this study

Table 16-6: POLYMENORRHAGIA

Level	T3		T4		TSH	
	n	%	n	%	n	%
< Normal	10	50.0%	10	50.0%	0	0.0%
Normal	10	50.0%	10	50.0%	10	50.0%
>Normal	0	0.0%	0	0.0%	10	50.0%
Total	20	100.0%	20	100.0%	20	100.0%

Out of 20 women with polymenorrhagia,

10 women had clinical hypothyroidism.

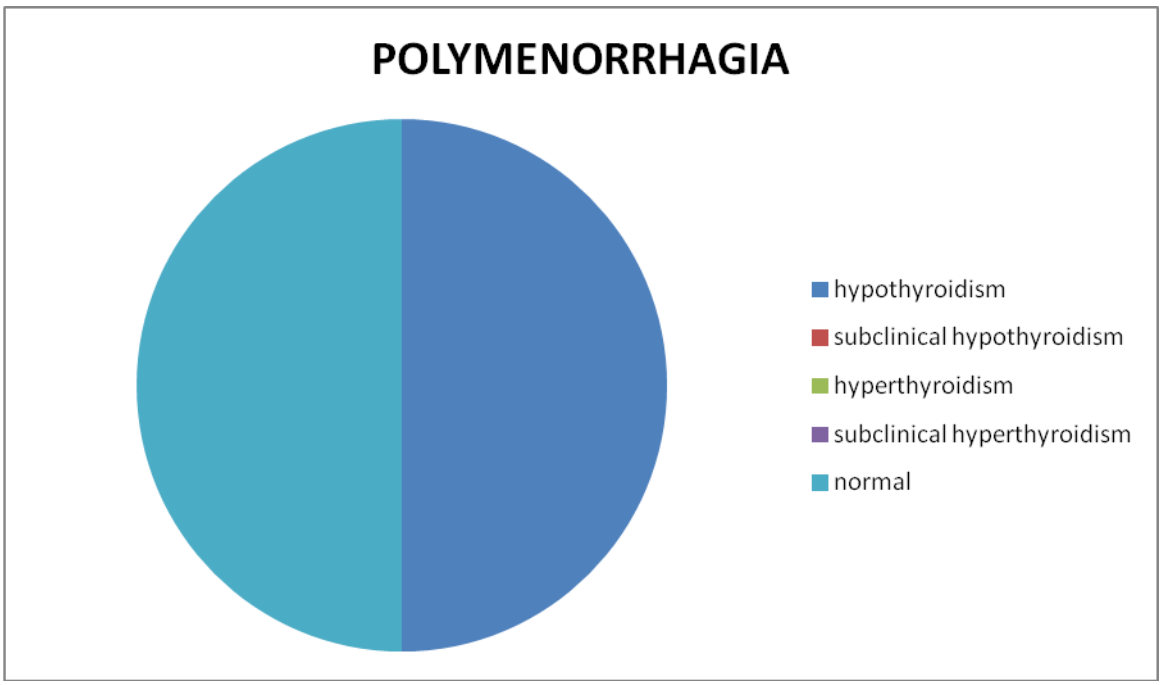


Fig 16-6

Table 16-7: POLYMENORRHOEA

Level	T3		T4		TSH	
	n	%	N	%	n	%
< Normal	4	20.0%	4	20.0%	0	0.0%
Normal	16	80.0%	16	80.0%	16	80.0%
>Normal	0	0.0%	0	0.0%	4	20.0%
Total	20	100.0%	20	100.0%	20	100.0%

Out of 20 women with polymenorrhoea, 4 had clinical hypothyroidism

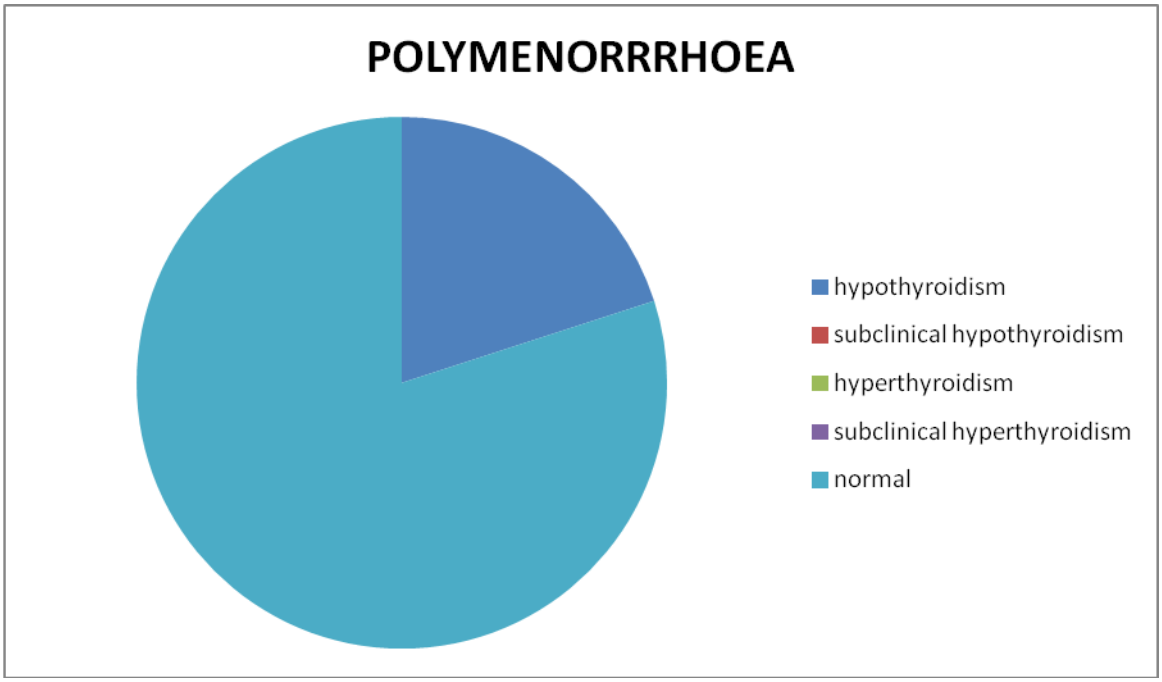


Fig 16-7

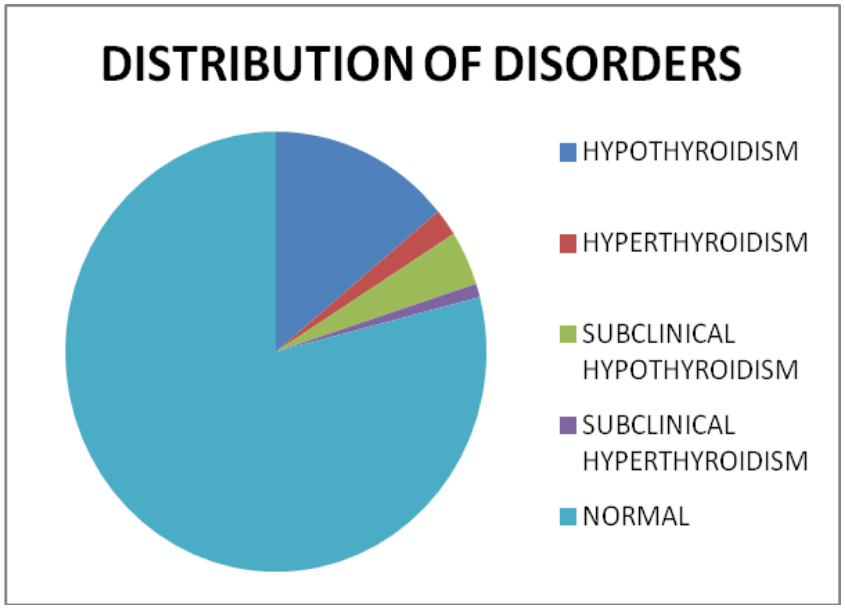


Fig 17

Table 17: DISTRIBUTION OF DISORDERS

	No. of women	%
Hypothyroidism	36	18.0%
Clinical	28	14%
SubClinical	8	4%
Hyperthyroidism	6	3.0%
Clinical	4	2.0%
SubClinical	2	1.0%
Normal	158	79.0%
Total	200	

TABLE 18:	N	Mean	Std.	Oneway

Symptomwise T3,T4,TSH values				Deviation	ANOVA F_Test
T3	AMENORRHOEA	48	2.90	1.25	
	HYPOMENORRHOEA	9	3.03	.53	
	MENORRHAGIA	79	2.18	.73	F=8.37
	OLIGOMENORRHOEA	24	2.57	.89	P=0.001*** (S)
	POLYMENORRHAGIA	20	1.58	.96	
	POLYMENORRHOEA	20	2.05	.81	
	Total	200	2.3700	1.00	
T4	AMENORRHOEA	48	13.47	2.11	
	HYPOMENORRHOEA	9	13.82	1.19	
	MENORRHAGIA	79	11.72	2.46	F=8.16
	OLIGOMENORRHOEA	24	12.09	2.32	P=0.001*** (S)
	POLYMENORRHAGIA	20	9.75	3.21	
	POLYMENORRHOEA	20	11.36	2.94	
	Total	200	12.05	2.67	
TSH	AMENORRHOEA	48	1.25	.73	
	HYPOMENORRHOEA	9	.91	.34	
	MENORRHAGIA	79	2.25	1.80	F=7.19
	OLIGOMENORRHOEA	24	1.83	1.84	P=0.001***(S)
	POLYMENORRHAGIA	20	3.77	2.61	
	POLYMENORRHOEA	20	2.45	2.30	
	Total	200	2.07	1.87	

TABLE 19:SYMPTOMWISE T3, T4,TSH values

	Disorder						Chi square test
	Hyperthyroidism		Normal		Hypothyroidism		
	n	%	n	%	n	%	
AMENORRHOEA	4	8.3%	43	89.6%	1	2.1%	$\chi 2=32.16$ P=0.001 *** (S)
HYPOMENORRHOEA	1	11.1%	8	88.9%	0	0.0%	
MENORRHAGIA	1	1.3%	60	75.9%	18	22.8%	
OLIGOMENORRHOEA	0	0.0%	20	87.0%	3	13.0%	
POLYMENORRHAGIA	0	0.0%	11	52.4%	10	47.6%	
POLYMENORRHOEA	0	0.0%	16	80.0%	4	20.0%	
TOTAL	6	100.0%	158	100.0%	36	100.0%	

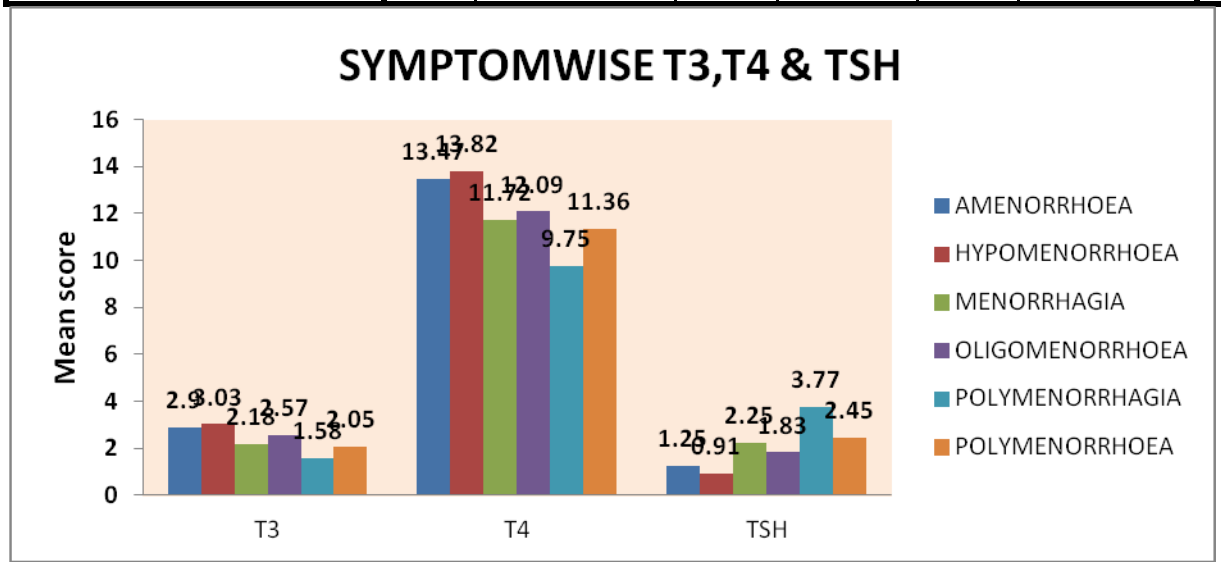


FIG 18

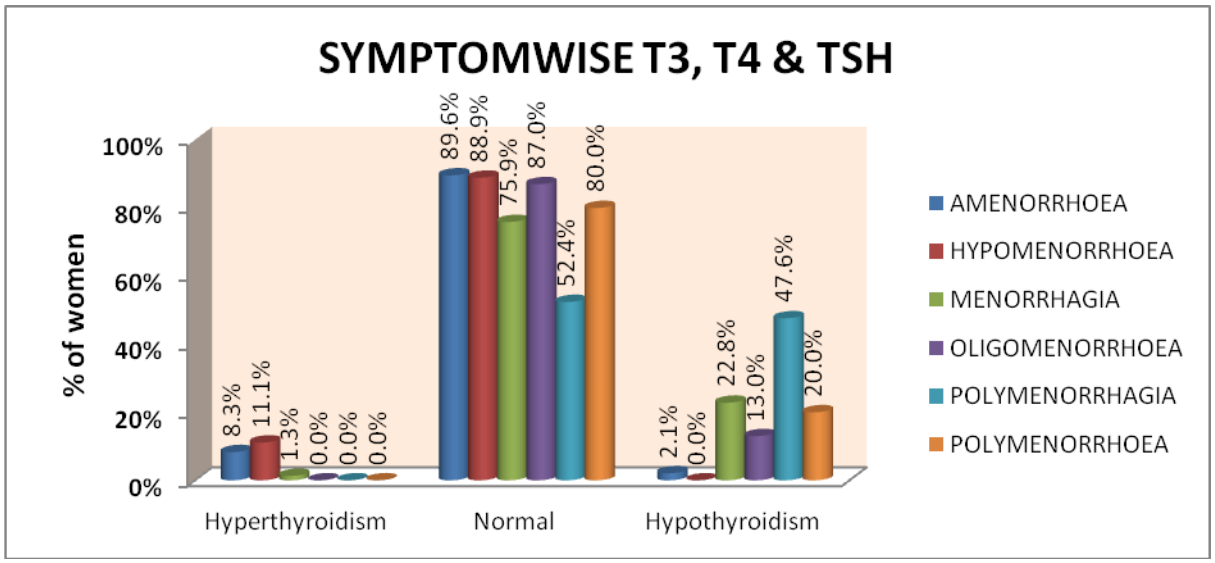


FIG 19

The type of thyroid dysfunction in different of menstrual disturbances are as follows:

	Hypothyroid	Subclinical hypothyroid	hyperthyroid	Subclinical hyperthyroid
Amenorrhoea	1(0.5%)	_	2(1%)	2(1%)
Hypomenorrhoea	_	_	1(0.5%)	_
Oligomenorrhoea	3(1.5%)	_	_	_
Menorrhagia	10(5%)	8(4%)	1(0.5%)	_
Polymenorrhoea	4(2%)	_	_	_
Polymenorrhagia	10(5%)	_	_	_

DISCUSSION

The study "STUDY ON ROLE OF THYROID DYSFUNCTION IN WOMEN WITH MENSTRUAL DISORDERS" was conducted in the Department of Obstetrics and Gynaecology ,Government Theni Medical College and Hospital.It comprises of 200 women with menstrual disturbances after excluding local pathology and systemic disease like diabetes mellitus, hypertension and known case of thyroid disorder.

The most common age group studied was between32-40years(57%)

Menstrual disorders have a significant association with thyroid dysfunction. This study was done to highlight the association of menstrual disorders with thyroid dysfunction by measuring free T3 and T4 in the fasting state.

Hypothyroidism (both clinical and subclinical) is observed in 9% of women with menorrhagia*.

Hyperthyroidism (both clinical and subclinical) is observed in 1% of women with amenorrhoea *.

*Out of 21% incidence in the study (hypothyroidism-18%,hyperthyroidism-3%)

THYROID DYSFUNCTION:

The overall incidence of thyroid dysfunction in the study is 21% .serum T3 and T4 are decreased in 14% of women , increased in 2% of women and within in normal limits in 84% of women .Serum TSH are increased in 18% of women ,decreased in 3% and within normal limits in 79% of women.

This correlates with the study of Wilansky et al,1992 in which th e incidence of thyroid dysfunction was 21%.

REFERENCE STUDY	INCIDENCE OF THYROID DISORDERS
Wilansky et al ,1992	21%
Menon et al,1995	26%
Koutras et al,1997	21.5%
Gomathi et al,2016	30%
Present study	21%

The incidence of subclinical hypothyroidism was 4%.Mark PG et al 1995 stated the prevalence of subclinical hypothyroidism was 4%-10%.

Hyperthyroidism was observed in 3% of women. This correlates with the study of Komathi et al 2016[31].

MENSTRUAL DISORDERS AND THYROID DYSFUNCTION:

Menorrhagia was the most commonest complaint observed in 39.5% of women followed by amenorrhoea which occurred in about 24% of women. This correlates with the study of Andrew D Weeks [6]2000 in which 56% women had menstrual disturbances and the most common complaint was menorrhagia (36%).

Another study by Col P Singh et al. 2007[42], showed that among hypothyroidism women menorrhagia was seen in nearly 32.4%.In our study hypothyoidism was found in nearly 27%(both clinical and subclinical) with menorrhagia and polymenorrhagia.

STUDY	TYPE OF AUB	PERCENTAGE
Wilansky et al,1992	Menorrhagia	21%
Prentice et al,1999	Menorrrhagia	36%
Kaur et al,1997	Menorrhagia	64.3%
Andrew weeks et al,2000	Menorrhagia	36%
Col P Singh et al,2007	Menorrhagia	32.4%

AGE :

In this study nearly 57% of women were in the age group of 32-40 years and 21.5% of women are in the age group of 23-31 years.In a study done by

sangeetha pahwa et al [43] about 42% of cases belonged to the age group of32-40 years.

Nearly 56.5% of women with hypothyroidism were in the age group of 32-40 years

GENERAL EXAMINATION:

Anaemia and thyromegaly(50%) were more common in the thyroid dysfunction cohort compared to other women in the study(10%).

BMI:

According to BMI ,71% of women had normal BMI,3.5% of women had decreased BMI and 25.5% of women had increased BMI. Of 3.5% of women with decreased BMI ,71.4% of wmen belonged to the hyperthyroid group. Of 25.5% of women with increased BMI 50.9% of women belonged to the hypothyroid group.Hence decreased BMI are associated with hyperthyroidism and increased BMI are associated with hypothyroidism.This correlates with the study of Jayakakshmi G Shenoy 2010.

COMPARSION OF BMI

Beckmann habertee et al	Positive association
Knudsen et al	Positive association
Present study	Positive association

Thus obesity has significant association with hypothyroidism.

HEMOGLOBIN:

Out of 200 women severe anaemia are observed in 13.5% of women,moderate anaemia is observed in 21.5% of women and Hb >9g/dl are observed in 65% of women.

Severe Anaemia (HB<7g/dl) are observed in 7.6% of euthyroid women and 41.67% of women with hypothyroidism. None were severely anaemic in hyperthyroid. Thus Anaemia is more commonly associated with hypothyroidism. This also correlated with the study of Jeyalakshmi G Shenoy 2010.

FRACTIONAL CURETTAGE:

Proliferative endometrium are more commonly observed in women with hypothyroidism (80.6%) due to associated anovulation whereas in hyperthyroidism both secretory and proliferative endometrium are observed.

SYMPTOMS OF HYPOTHYROID AND HYPERTHYROID:

Weight gain (24%) was the most commonest symptom of hypothyroidism in the study group. Nearly 50% of women with hypothyroid had symptom of weight gain.

Fatigue (28%) was the most commonest complaint of hyperthyroidism in the study Group. 50% of hyperthyroid women had hyperthyroid.

SUMMARY

The study population includes 200 women with menstrual disturbances .

The most common age group studied were between 32-40 years.

Hyperthyroidism were more common in Nulliparous and Primiparous women.(P value=o.o5)

The most common type of menstrual disturbance are

menorrhagia. (39.5%) Menorrhagia got significant association with thyroid dysfunction.

Majority of women with menstrual disturbances presented to the opd with menstrual disturbances of 1-3 months duration.

Hypothyroidism presents in 18%, subclinical hypothyroidism in 4% and hyperthyroidism in 2% and subclinical hyperthyroidism in 1% of the study population.

Prevalence of obesity in the study population is 4.5%.About 2.5% of obese women are hypothyroid.83.3% of hyperthyroid women are underweight(BMI<18).(P value=0.01)

52.7% of women with hypothyroidism had clinical findings of anaemia and or thyromegaly on clinical examination.(P value=0.01)

35% of women are anaemic in the study group.72.2% of hypothyroid women are anaemic.(P value=0.001)

Weight gain (24%) was the most commonest complaint of hypothyroidism in the study group. Fatigue (28%) was the most commonest

complaint in hyperthyroid.

BT and CT were within normal limits in study population.

Transabdominal ultrasound abdomen and thyroid dysfunction had no significant association in the study.

Majority of hypothyroid women had proliferative endometrium (80.6%).66.7% of women with hyperthyroid had proliferative endometrium.(P value=0.001).

The study showed a significant correlation between thyroid profile with different types of menstrual disturbances(P value=0.001).

CONCLUSION

From the above study it can be concluded that there is a significant association between thyroid dysfunction and menstrual disorders. The high prevalence of thyroid dysfunction (21%) in the study and the relative prevalence of subclinical hypothyroidism (4%) justifies the screening for thyroid dysfunction in women with menstrual disorders thereby preventing inappropriate therapeutic and diagnostic procedures.

PROFORMA

Name:

Age:

Parity:

Height: weight: BMI:

History: Menorrhagia ☐ Duration:

Polymennorhagia ☐

Oligomenorrhoea ☐

Polymenorrhoea ☐

Amenorrhoea ☐

Hypomenorrhoea ☐

Symptoms of hypothyroidism: weight gain ☐ lethargy ☐

constipation ☐ palpitation ☐

cold intolerance ☐ voice change ☐

none of the above ☐

symptoms of hyperthyroidism:weight loss ☐ anxiety ☐

diahorroea ☐ fatigue ☐

heating tolerance ☐ tremors ☐

none of the above ☐

General physical examination: normal ☐ anemia ☐ thyromegaly ☐

Systemic examination:

CVS:

RS:

CNS:

Abdominal examination:

Per speculum:

Bimanual pelvic examination:

HB : USG:

BT: TFT: free T3:

CT: free T4: #CURETTAGE:

TSH :

BIBILIOGRAPHY

1. K.Padmaleela et al,2013Thyroid disorders in Dysfunctional Uterine Bleeding among reproductive age group women –A cross-sectional study in a tertiary care hospital in Andhra Pradesh,India.IJMS,20134(1):41-46

2. Wilansky et al Menorrhagia association with hypothyroidism American journal of Obstetrics and Gynecology 1989 march 60 (3)673-7

3. Kakuno et al –menstrual disturbances in various thyroid diseases endocrinology journal 2010 57(12)1017-22.

4. Bjergved L et al 2014 Thyroid function and body weight:A Community based longitudinal study PLoS ONE 9(4):e93515

5. Koutras –Disturbances of menstruation in thyroid disease Ann NY Academic science1997 june 17,816 280-84

6 Andrew D Weeks. Correlating menstrual irregularities with levels of thyroid hormone deficiency. BMJ 2000;320(7235):649

7. Croatian article 1999 march-may 52(3-5)-Anaemia in hypothyroidism.

8. Rovaband et al 2013 Treatment of iron deficiency anaemia in patients with subclinical hypothyroidism Am J Med

9. Neelu Sharma and Anita Sharma- Thyroid profile in menstrual disorders –JK science .org vol 14 No 1 JAN-MAR 2012.

10. Jovitha et al ,2017 Assessment of thyroid and prolactin levels among the women with abnormal uterine bleeding-International Journal of Reproduction,Contraception,Obstetrics and Gynaecology6(6),2547-255

11. Javid ali et al 2015 Reasearch Article Study Of Relation of Thyroid Profile with Abnormal Uterine Bleeding

12. Roubushi et al a study on autoimmunity and age related thyroid dysfunction

13. Rodondi et al 2005 Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events and death. Archieves of internal medicine 165(21),2460-2466,2005

14. Smith SR,Auger MJ.Hypothyroidism and von willebrande's disease Lancet 1987;1:1314

15. Blum M. Blum G. The possible relationship between menorrhagia and occult hypothyroidism in IUD wearing women. Advance Contracep.1992; 8:313-317.

16. Hingham JM, Shaw RW. The effect of thyroxine replacement on menstrual blood loss in a hypothyroid patient, Br.J.Obstet, Gynaecol, 1992:99:695-696.

17. Beckmann and Haberette-TSH is associated with insulin resistance independently of body mass index and age in women with polycystic ovarian syndrome-oxford journal of reproductive medicine 2009 24(11)2924-30

18. Knudsen et al –small difference in thyroid function may be important for body mass index and the occurence of obesity in the population-Journal of clinical endocrinology and metabolism, July 2005 90(7)4019-24.

18. Prentice –Menorrhagia and hypothyroidism British Medical Journal 2000 320(735):649

19. Cameron IT (1992). Medical Management of menorrhagia .Curr obstet, Gynaecol 2,136-40.

20. Danese Md, powe NR, Sarvin CT, Landenson PW, screening for mild thyroid failure at the periodic health examination. A decision and cost effective analysis JAMA 276:285, 1996.

22. Management guidelines of Abnormal uterine bleeding in reproductive period (GCPR recommendations)

23. Text Book of Gynaecology: Shiela Balakrishnan

24. Leon Speroff, Robert H.Glass Nathan, G. Kase Clinical gynaecologic endocrinology and infertility sixth edition, 1999.

25. Essentials Of Gynaecology:Lakshmi Seshadri

26. Vollman RF. The Menstrual Cycle, In : Friedman E, Ed. Major problems in obstetrics and gynecology, W.B. Saunders Co., Philadelphia, 1977.

27. ACOG Committee on Practice Bulletins,Gynecology.American College of Obstetricians and Gynecologists. ACOG practice bulletin: management of anovulatory bleeding. Int J Gynaecol Obstet. 2001;72(3):263–271

28. Shaw's Text Book of Gynaecology 14th edition Editor Hawkins J.Bourne G.Churchill Livingstone Publication.

29. Medvei, VC. The history of Clinical Endocrinology The Pantheon Publishing group, New York, 1993.

30. Brent GA, The molecular basis of thyroid hormone action, New Eng. J. Med. 331:947, 1994.

31. A study of thyroid profile in abnormal uterine bleeding among reproductive age group women; komathi ISSN:2320-8147

32. Prevalance of subclinical hypothyroidism in reproductive age group women with abnormal uterine bleeding mohana dhanapal Jemds.com

33. Warfel W.Thyroid regulation pathways and its effect on human function 1992;32:145-150.

34. Lee PA, Van Dop C, Migeon CJ, Mc Cune Albright syndrome long term follow up JAMA 256:290,1986

35. Mackenzie JM, Zakariya M. Hyperthyroidism in Degroot LJ, Cahill GF,Martini L, eds. Endocrinology , New York :Greene and Stratton 1979:647

36. Vander pump MPJ Turnbridge VMG.The thyroid fundamental and clinical text,7th edition.1996;474-482.

37. Surks MI, Chopra IJ, Mariash CN, NiColoff JT, Solomon DH American Thyroid Association guidelines for use of laboratory tests in thyroid disorders JAMA 263:1529.1990

38. Thomas R, Reid RL. Thyroid disease and reproductive dysfunction Obstet. Gynaecol.1987;70:789-798

39. Mackenzie JM, Zakariya M. Hyperthyroidism in Degroot LJ, Cahill GF, Martini L, eds. Endocrinology , New York :Greene and Stratton 1979:647.

40. Olson BR. Exercise induced amenorrhea. Am. Fam. Physician 1989, 39:213-221

41. Berek and Novak's text book of gynaecology 24th edition

42. American association of clinical endocrinologist guidelines 2002

43. Col P Singh. Pattern of bleeding in hypothyroidism. MJAFI 2007;53:112-23.

44. Pahwa S, Gupta S, Kumar J; Thyroid dysfunction in Dysfunctional uterine bleeding. Journal of advanced research in biological science.5 (1) : 2013:78-83

45. Jayalakshmi G Shenoy 2010 A study on thyroid profile in abnormal uterine bleeding.

ABBREVIATIONS

AUB	-	Abnormal Uterine Bleeding
T4	-	Thyroxine
T3	-	Tri-iodothyronine
TSH	-	Thyroid Stimulating Hormone
TRH	-	Thyrotropin Releasing Hormone
LH	-	Luteinising Hormone
FSH	-	Follicular Stimulating Hormone
HCG	-	Human Chorionic Hormone
TR	-	Thyroid hormone Receptor
RT3	-	Reverse T3
TBG	-	Thyroid Binding Globulin
SHBG	-	Sex Hormone Binding Globulin
FT4	-	Free Thyroxine
TT4	-	Total Thyroxine
GnRH	-	Gonadotrophin Releasing Hormone
Anti TPO	-	Anti Thyroid Peroxidase
Anti TG	-	Anti Thyroglobulin
BMI	-	Body Mass Index
IUCD	-	Intra Uterine Contraceptive Device

S.NO	NAME	AGE	PARITY	c/o	DURATION	BMI	EXAMINATION	HB
1	kavitha	19	P1L1	MENORRHAGIA	since menarche	19.98	anaemia	6.2
2	sivagami	20	P1L1	POLYMENORRHOEA	1 1/2 year	20.45	anaemia	7.2
3	meena	21	nulliparous	POLYMENORRHOEA	9 months	20.55	anaemia+thyromegaly	8.3
4	sivalakshmi	18	P1L1	OLIGOMENORRHOEA	4 months	17.94	anaemia	8.2
5	meenatchi	19	P1L1	OLIGOMENORRHOEA	1 1/2 year	16.65	anaemia	8.2
6	sudhadevi	20	P2L2	HYPOMENORRHOEA	5 months	22.23	anaemia	8
7	krishnakumari	22	P2L2	HYPOMENORRHOEA	9 months	23.31	normal	10
8	madhumitha	23	P2L2	HYPOMENORRHOEA	4 months	24.65	normal	11
9	kavitha	19	P2L2	OLIGOMENORRHOEA	4 months	18.67	normal	11.1
10	kousalya	20	P2L2	OLIGOMENORRHOEA	9 months	18.67	normal	12.1
11	pandiselvi	21	P2L2	OLIGOMENORRHOEA	9months	19.98	normal	13
12	muthumari	22	P2L2	OLIGOMENORRHOEA	6 months	18.67	normal	10.1
13	ramuthai	23	P2L2	AMENORRHOEA	4 months	24.6	normal	9.1
14	mariyammal	18	P2L2	AMENORRHOEA	5 months	23.31	normal	9.2
15	pandiyammal	19	nulliparous	AMENORRHOEA	4 months	21.48	normal	9.4
16	swetha	22	P1L1	MENORRHAGIA	4 months	22.23	normal	9.6
17	maheswari	23	P1L1	POLYMENORRHOEA	10 months	23.47	thyromegaly	9
18	roja	26	P1L1	POLYMENORRHOEA	9 months	21.48	normal	9.1
19	sangeetha	20	nulliparous	AMENORRHOEA	4 months	24.14	normal	11
20	vimala	23	P2L2	AMENORRHOEA	5 months	23.31	normal	12
21	nirmala	20	P2L2	AMENORRHOEA	4 months	22.23	normal	11
229	lalitha	21	P2L2	HYPOMENORRHOEA	10 months	23.92	normal	14
23	shanthi	23	nulliparous	HYPOMENORRHOEA	5 months	24.14	normal	10.1
24	shantha	20	P2L2	HYPOMENORRHOEA	4 months	19.98	normal	10.2
25	lavanya	18	P2L2	HYPOMENORRHOEA	4 months	20.48	normal	11
26	sharanya	19	nulliparous	HYPOMENORRHOEA	4 months	21.48	normal	12
27	sarumathi	20	P2L2	AMENORRHOEA	4 months	23.47	normal	11
28	meera	18	P2L2	AMENORRHOEA	6 months	24.65	normal	12.3

29	priya	24	P2L2	AMENORRHOEA	5 months	23.47	normal	11.6
30	viji	26	P2L2	AMENORRHOEA	4 months	22.27	normal	12.2
31	subbulakshmi	26	P2L2	MENORRHAGIA	since menarche	20.55	anemia+thyromegaly	6.8
32	vasanthi	25	nulliparous	OLIGOMENORRHOEA	10 months	22.23	normal	10
33	vijaya	26	P2L2	OLIGOMENORRHOEA	6 months	36.1	normal	10.2
34	pavithra	25	P2L2	MENORRHAGIA	4 months	23.92	normal	9.1
35	radhika	26	P1L1	MENORRHAGIA	6 months	22.23	normal	12.1
36	eswari	30	P1L1	MENORRHAGIA	5 months	21.48	normal	11.3
37	priyanka	31	P1L1	MENORRHAGIA	4 months	20.55	normal	12.4
38	meenatchi	25	P1L1	MENORRHAGIA	10 months	23.31	normal	11.3
39	kaveri	26	P1L1	MENORRHAGIA	4 months	24.97	normal	10.6
40	latha	24	nulliparous	AMENORRHOEA	6 months	19.98	normal	9.6
41	suganya	25	MULTIPARA	AMENORRHOEA	6 months	20.55	normal	10.6
42	parameshwari	24	nulliparous	AMENORRHOEA	4 months	21.48	normal	10.2
43	rahamath	24	P2L2	AMENORRHOEA	2 1/2 months	22.23	normal	10.1
44	jancy	25	P2L2	AMENORRHOEA	1 1/2 months	23.31	normal	10.6
45	thiruselvi	26	P2L2	AMENORRHOEA	4 months	22.23	normal	10.2
46	veerayi	28	P2L2	MENORRHAGIA	6 months	31.2	anemia+thyromegaly	9.1
47	kalaiselvi	30	MULTIPARA	POLYMENORRHAGIA	1 1/2 year	32.3	anaemia	6.3
48	ganga	31	MULTIPARA	POLYMENORRHAGIA	5 months	30.8	anaemia	6.2
49	shillamari	26	nulliparous	MENORRHAGIA	2 1/2 months	22.23	normal	9.2
50	merlin	27	P1L1	MENORRHAGIA	4 months	23.31	normal	9.1
51	mumtaj	28	P1L1	MENORRHAGIA	1 1/2 months	22.1	normal	9.3
52	naveena	29	P1L1	MENORRHAGIA	4 months	23.31	normal	9.4
53	pandiyammal	30	MULTIPARA	MENORRHAGIA	1 1/2 months	24.97	normal	9.5
54	shahitha	26	nulliparous	AMENORRHOEA	5 months	19.98	normal	9.6
55	aishwariya	27	P2L2	AMENORRHOEA	6 months	20.55	normal	9.7
56	preethi	30	MULTIPARA	AMENORRHOEA	5 months	21.48	normal	9.8
57	kumari	31	MULTIPARA	AMENORRHOEA	1 1/2 months	22.23	normal	10
58	krishnaveni	24	nulliparous	AMENORRHOEA	5 months	24.65	normal	9.9

59	brindha	24	nulliparous	AMENORRHOEA	1 1/2 months	23.81	normal	11.2
60	sreeja	25	P2L2	AMENORRHOEA	6 months	22.23	normal	12.4
61	vijayalakshmi	42	P1L1	MENORRHAGIA	5 months	30.8	normal	11
62	vijaya	44	MULTIPARA	POLYMENORRHAGIA	1 1/2 year	26.22	anemia+thyromegaly	6.2
63	latha	34	P1L1	POLYMENORRHAGIA	2 1/2 months	25.3	normal	6
64	malliga	27	MULTIPARA	AMENORRHOEA	6 months	22.23	normal	11
65	sivalakshmi	28	MULTIPARA	AMENORRHOEA	9 months	22.23	normal	11.2
66	suruliyammal	26	P1L1	AMENORRHOEA	7 months	21.48	normal	12.1
67	mangammal	27	MULTIPARA	MENORRHAGIA	1 month	22.23	normal	13.3
68	vinothini	28	MULTIPARA	MENORRHAGIA	1 month	23.47	normal	12
69	ranjani	29	MULTIPARA	MENORRHAGIA	1 month	24.65	normal	11.1
70	shanthi	30	MULTIPARA	MENORRHAGIA	9 months	22.23	normal	10.3
71	kumari	31	P1L1	MENORRHAGIA	5 months	21.48	normal	9.1
72	lalitha	32	P1L1	MENORRHAGIA	2 1/2 months	34.1	normal	9.3
73	venmathi	33	P1L1	MENORRHAGIA	1 month	32.18	normal	10.2
74	amudha	43	MULTIPARA	MENORRHAGIA	7 months	36.1	normal	10.4
75	durga	44	MULTIPARA	MENORRHAGIA	1 month	24.65	normal	11.1
76	chandravathana	35	MULTIPARA	MENORRHAGIA	5 months	27.24	thyromegaly	11
77	selvi	36	MULTIPARA	POLYMENORRHAGIA	2 year	28.89	anaemia	6
78	rajathi	38	MULTIPARA	POLYMENORRHAGIA	2 year	26.22	anaemia	6.1
79	ayammal	42	MULTIPARA	POLYMENORRHAGIA	1 month	22.23	normal	12
80	ishwariya	44	MULTIPARA	POLYMENORRHAGIA	2 1/2 months	21.48	normal	12.1
81	karthiga	45	MULTIPARA	MENORRHAGIA	1 month	23.31	normal	13.1
82	subha	43	nulliparous	AMENORRHOEA	1 month	19.98	normal	10.6
83	jothi	44	MULTIPARA	MENORRHAGIA	3 months	20.55	normal	9.1
84	rameshwari	40	MULTIPARA	MENORRHAGIA	7 months	21.48	normal	9.2
85	yuvarani	41	MULTIPARA	MENORRHAGIA	1 month	18.67	normal	10.2
86	suganya	43	MULTIPARA	MENORRHAGIA	1 month	19.98	normal	11.1
87	subbu	40	MULTIPARA	POLYMENORRHAGIA	9 months	20.55	normal	12.1
88	suvalakshmi	41	MULTIPARA	POLYMENORRHAGIA	1 month	21.48	normal	10

89	vasanthi	33	MULTIPARA	MENORRHAGIA	1 month	22.23	normal	11
90	vijaya	34	P1L1	MENORRHAGIA	3 months	26.22	normal	9.2
91	pavithra	33	P1L1	MENORRHAGIA	1 month	27.2	normal	10.1
92	radhika	34	P1L1	POLYMENORRHAGIA	since menarche	28.89	anaemia	6.1
93	easwari	35	P1L1	POLYMENORRHAGIA	2 year	23.31	anaemia	6.2
94	maari	38	P1L1	POLYMENORRHAGIA	1 month	22.23	normal	9.2
95	vasantha	39	nulliparous	POLYMENORRHAGIA	8 months	20.55	normal	9.1
96	nandhini	33	MULTIPARA	AMENORRHOEA	8months	21.48	normal	11
97	krishnapriya	34	MULTIPARA	AMENORRHOEA	1 month	20.55	normal	12.1
98	uma	32	MULTIPARA	AMENORRHOEA	3 months	22.23	normal	13.2
99	kumari	33	MULTIPARA	POLYMENORRHOEA	3 months	23.31	normal	9.2
100	priya	39	MULTIPARA	POLYMENORRHAGIA	1 month	24.65	normal	9.1
101	sathya	40	P1L1	POLYMENORRHAGIA	3 months	20.55	normal	9.2
102	revathi	36	P1L1	POLYMENORRHAGIA	1 month	21.48	normal	9.3
103	bula	38	P1L1	POLYMENORRHAGIA	9 months	20.45	normal	10
104	gomathi	33	MULTIPARA	MENORRHAGIA	3 months	21.48	normal	9.2
105	kanjana	32	MULTIPARA	MENORRHAGIA	3 months	24.6	normal	9.3
106	shakthi	33	P2L2	MENORRHAGIA	1 month	25.78	normal	9.2
107	suganthi	34	P2L2	POLYMENORRHAGIA	3 months	26.22	anaemia	5.2
108	sathyabama	38	P2L2	POLYMENORRHAGIA	5 months	27.24	anaemia	4.9
109	ramadevi	33	P2L2	AMENORRHOEA	8 months	18.67	normal	9.2
110	devi	34	MULTIPARA	AMENORRHOEA	9 months	20.45	normal	9.3
111	ajitha	32	nulliparous	AMENORRHOEA	8 months	22.23	normal	9.1
112	archana	32	MULTIPARA	AMENORRHOEA	3 months	18.67	normal	9.2
113	anandhi	33	P2L2	AMENORRHOEA	1 month	20.55	normal	10.3
114	arulmani	36	MULTIPARA	MENORRHAGIA	7 months	24.65	normal	8.6
115	jeyanthi	35	MULTIPARA	AMENORRHOEA	2 month	21.48	normal	12
116	jeyakodi	40	MULTIPARA	AMENORRHOEA	1 month	22.32	normal	14.1
117	jeya	37	P1L1	MENORRHAGIA	2 month	23.81	normal	8.3
118	kodimalar	38	P1L1	MENORRHAGIA	3 months	24.65	normal	13

119	mala	36	P1L1	MENORRHAGIA	2 month	18.67	normal	11
120	deepa	34	P1L1	MENORRHAGIA	2 month	19.98	normal	12.2
121	sudhadevi	34	P1L1	MENORRHAGIA	2 month	26.22	normal	9.8
122	shanthini	39	P1L1	MENORRHAGIA	2 year	26.22	anaemia	6.9
123	saraswathi	41	P1L1	AMENORRHOEA	2 month	17.94	normal	10
124	vaishnavi	34	P2L2	AMENORRHOEA	2 month	18.67	normal	9.2
125	aarthy	33	P2L2	AMENORRHOEA	2 month	19.98	normal	11
126	karthiga	32	P1L1	AMENORRHOEA	7 months	20.45	normal	13.1
127	monisha	33	nulliparous	AMENORRHOEA	2 month	21.48	normal	14
128	manisha	34	P2L2	AMENORRHOEA	8 months	22.23	normal	13.1
129	malathy	36	P1L1	AMENORRHOEA	2 month	22.32	normal	12.4
130	anitha	35	P1L1	MENORRHAGIA	6 months	23.31	normal	8.6
131	angalaeshwari	37	P1L1	MENORRHAGIA	6 months	24.65	normal	8.7
132	sujitha	39	P1L1	MENORRHAGIA	6 months	24.65	normal	8.8
133	suji	38	P2L2	MENORRHAGIA	5 months	22.23	normal	9.8
134	keerthi	38	P1L1	MENORRHAGIA	2 month	21.48	normal	10.2
135	kathiriyammal	40	P1L1	MENORRHAGIA	2 month	30.02	normal	10.3
136	sathyadevi	40	P1L1	MENORRHAGIA	3 months	27.24	normal	8.1
137	pandeeswari	33	P1L1	MENORRHAGIA	2 1/2 year	28.89	anaemia	6.8
138	alagammal	34	P1L1	AMENORRHOEA	2 month	17.94	normal	11.2
139	indhrani	36	P1L1	MENORRHAGIA	3 months	21.42	normal	8.2
140	dhanalakshmi	35	P1L1	POLYMENORRHOEA	6 months	20.45	normal	8.4
141	anuradha	34	P1L1	POLYMENORRHOEA	6 months	21.32	normal	8.5
142	parvinbanu	33	P2L2	POLYMENORRHOEA	5 months	22.48	normal	8.6
143	mutheeswari	32	P2L2	POLYMENORRHOEA	3 months	23.31	normal	9
144	muthumari	34	P2L2	OLIGOMENORRHOEA	2 month	18.67	normal	11
145	nivetha	35	P2L2	OLIGOMENORRHOEA	2 month	19.98	normal	12.2
146	poorna	34	P2L2	POLYMENORRHOEA	6 months	20.55	normal	8.2
147	jeyanthi	35	P2L2	POLYMENORRHOEA	6 months	20.45	anaemia	8.3
148	vidhya	36	P2L2	OLIGOMENORRHOEA	2 month	18.67	normal	12.1

149	vaishnavi	38	P2L2	OLIGOMENORRHOEA	2 month	19.98	normal	10.2
150	meghana	40	P2L2	OLIGOMENORRHOEA	2 month	22.48	normal	10.3
151	jeya	34	P2L2	MENORRHAGIA	6 months	26.22	normal	8
152	parimalam	36	P2L2	AMENORRHOEA	3 months	27.24	normal	8.1
153	abirami	33	P2L2	AMENORRHOEA	2 month	16.65	normal	11.1
154	abinaya	36	P2L2	OLIGOMENORRHOEA	3 months	18.67	normal	10.1
155	thangammal	37	P2L2	OLIGOMENORRHOEA	10 months	20.45	normal	9.6
156	subashini	39	P2L2	POLYMENORRHAGIA	> 3 years	23.81	anaemia	6.7
157	sugirtha	38	P2L2	POLYMENORRHOEA	1 year	24.65	anaemia	6.2
158	suchitra	32	P2L2	POLYMENORRHOEA	10 months	20.55	anaemia	6.3
159	rasathi	33	P2L2	POLYMENORRHOEA	since menarche	22.23	anaemia	6.4
160	raji	34	P2L2	POLYMENORRHOEA	1 year	21.48	anaemia	6.2
161	rajeshwari	35	P2L2	POLYMENORRHOEA	>3 years	20.45	anaemia	6.3
162	ramya	36	P2L2	POLYMENORRHOEA	1 year	22.23	normal	8.1
163	saraswathi	37	P2L2	OLIGOMENORRHOEA	3 months	21.48	normal	10.2
164	seetha	39	P2L2	OLIGOMENORRHOEA	3 months	18.67	normal	11.1
165	sulochana	38	P2L2	OLIGOMENORRHOEA	3 months	19.98	normal	12.3
166	suseela	36	P2L2	MENORRHAGIA	6 months	26.22	anaemia	7.2
167	brindha	38	P2L2	MENORRHAGIA	1 year	27.24	anaemia	7.3
168	chitra	26	nulliparous	AMENORRHOEA	10 months	16.65	normal	11.2
169	durgadevi	39	P2L2	OLIGOMENORRHOEA	3 months	18.67	normal	12.3
170	gayathri	32	P2L2	OLIGOMENORRHOEA	3 months	20.45	normal	13.2
171	gowri	36	P2L2	OLIGOMENORRHOEA	3 months	21.48	normal	11.1
172	ayammal	34	P2L2	OLIGOMENORRHOEA	6 months	22.23	normal	11.2
173	haritha	35	P2L2	POLYMENORRHOEA	6 months	23.31	normal	10
174	kaleeswari	33	P2L2	MENORRHAGIA	10 months	24.65	normal	8
175	veerayi	33	P2L2	MENORRHAGIA	10 months	28.89	normal	8.2
176	veerammal	34	P2L2	POLYMENORRHOEA	3 months	27.24	normal	8.3
177	veeralakshmi	35	P2L2	POLYMENORRHOEA	10 months	26.22	normal	8.4
178	vanaja	37	P2L2	MENORRHAGIA	6 months	29.9	normal	8.5

179	akila	36	P2L2	MENORRHAGIA	3 months	28.89	normal	9
180	sangeetha	38	P2L2	MENORRHAGIA	6 months	26.22	normal	7.2
181	rajammal	34	P2L2	MENORRHAGIA	6 months	26	normal	8.8
182	seethalakshmi	37	P2L2	MENORRHAGIA	5 months	27.24	normal	8.6
183	adhilakshmi	24	nulliparous	HYPOMENORRHOEA	3 months	16.6	normal	10
184	arukayee	40	P2L2	MENORRHAGIA	2 1/2 year	26.22	anaemia	6.3
185	abinaya	38	P2L2	MENORRHAGIA	10 months	29.77	anaemia	6.4
186	janaki	39	P2L2	MENORRHAGIA	3 years	27.24	anaemia	6.5
187	jeyalakshmi	36	P2L2	MENORRHAGIA	3 years	28.89	anaemia	6.6
188	revathi	37	P2L2	MENORRHAGIA	10 months	26.22	normal	8.2
189	saranya	39	P2L2	MENORRHAGIA	6 months	27.24	normal	8.3
190	parvathy	38	P2L2	MENORRHAGIA	5 months	28.89	normal	8.3
191	sneha	37	P2L2	MENORRHAGIA	6 months	29.28	normal	8.4
192	tamilselvi	36	P2L2	MENORRHAGIA	10 months	26.22	normal	8.5
193	thangalakshmi	39	P2L2	MENORRHAGIA	5 months	27.2	normal	9
194	lingeshwari	38	P2L2	MENORRHAGIA	5 months	28.89	normal	8.6
195	tamilarasi	37	P2L2	MENORRHAGIA	2 month	29.1	normal	8.1
196	thangaselvi	42	P2L2	MENORRHAGIA	3 months	24.65	normal	9
197	geetha	41	nulliparous	OLIGOMENORRHOEA	10 months	25.78	anaemia	6.1
198	nirupa	18	P1L1	MENORRHAGIA	3 months	20.55	normal	9
199	vanitha	34	P2L2	MENORRHAGIA	3 months	26.2	anaemia	6.1
200	fathima	36	P2L2	MENORRHAGIA	3 months	27.24	anaemia	6.2

S.NO	# CURETTAGE	T3	T4	TSH	SYMPTOMS OF HYPOTHYROIDISM	SYMPTOMS OF HYPERTHYROIDISM	BT	CT	U/S
1	PROLIFERATIVE	1.8	10	5.6	weightgain	fatigue	1'45''	3'	NAD
2	PROLIFERATIVE	0.8	6	6.3	constipation	fatigue	2'	4'56''	NAD
3	PROLIFERATIVE	0.6	5	7.1	voice change	weight loss	3'14''	5'15''	NAD
4	SECRETORY	2.4	12.2	1.2	nil	weight loss	3'16''	4'45''	NAD
5	SECRETORY	2.3	14.2	1.3	nil	weight loss	3'34''	4'46''	NAD
6	SECRETORY	2.24	12.3	1.32	weight gain	anxiety	2'56''	5'15''	NAD
7	SECRETORY	3.34	14.3	0.91	nil	tremor	2'26''	4'56''	NAD
8	SECRETORY	3.47	15.2	0.82	nil	heat intolerance	3'16''	4'16''	NAD
9	SECRETORY	3.5	13.2	0.76	nil	weight loss	2'46''	4'46''	NAD
10	SECRETORY	2.32	12.6	1.26	nil	weight loss	3'03''	3'45''	NAD
11	SECRETORY	3.36	12.2	0.92	nil	weight loss	1'45''	4'35''	NAD
12	SECRETORY	3.36	12.1	0.98	nil	weight loss	2'30''	6'15''	NAD
13	SECRETORY	3.56	12.3	1.1	nil	nil	3'	6'	NAD
14	SECRETORY	2.52	12.3	1.2	nil	nil	1'37''	5'45''	NAD
15	SECRETORY	3.41	15.3	0.78	nil	nil	2'12''	4'46''	PCOD
16	PROLIFERATIVE	1.56	9.2	6	weight gain	nil	3'17''	4'47''	PCOD
17	PROLIFERATIVE	0.5	6	7.1	constipation	nil	1'12''	2'45''	NAD
18	PROLIFERATIVE	0.4	6.2	7.2	weight gain	nil	3'13''	5'30''	NAD
19	SECRETORY	2.21	12.3	1.32	nil	tremor	2'15''	4'30''	NAD
20	SECRETORY	2.32	12.3	1.1	weight gain	nil	3'15''	5'15''	NAD
21	SECRETORY	2.2	13.2	1.3	nil	nil	2'20''	4'45''	NAD
229	SECRETORY	2.3	12.2	1.2	nil	nil	3'10''	5'15''	NAD
23	SECRETORY	3.37	14.4	0.9	nil	nil	1'15''	3'15''	NAD
24	SECRETORY	3.32	14.6	0.96	nil	weight loss	2'19''	4'46''	NAD
25	SECRETORY	3.42	15	0.82	nil	nil	1'30''	4'47''	NAD
26	SECRETORY	2.46	12.4	1.16	nil	nil	1'45''	5'45''	NAD

27	SECRETORY	2.36	12.3	1.18	nil	nil	2'16''	4'48''	NAD
28	SECRETORY	2.44	12.2	1.2	constipation	nil	2'19''	3'	NAD
29	SECRETORY	2.54	12.6	1.3	nil	nil	2'40''	4'56''	PCOD
30	SECRETORY	2.42	14.2	1.42	nil	tremor	1'56''	5'45''	NAD
31	PROLIFERATIVE	1.3	9.2	5.2	constipation	fatigue	2'12''	4'46''	NAD
32	SECRETORY	0.6	6	6	voice change	nil	3'17''	4'47''	NAD
33	SECRETORY	0.4	7	6.5	weight gain	nil	1'12''	2'45''	NAD
34	SECRETORY	3.32	12.54	0.92	nil	nil	3'13''	5'30''	PCOD
35	SECRETORY	2.44	12.32	1.2	nil	nil	2'15''	4'30''	NAD
36	SECRETORY	2.42	12.4	1.32	nil	nil	1'12''	5'15''	NAD
37	SECRETORY	2.42	14.2	1.43	nil	nil	1'15''	4'45''	NAD
38	SECRETORY	2.43	14.1	1.52	weight gain	nil	2'15''	5'15''	NAD
39	SECRETORY	2.44	12.3	1.23	nil	nil	1'56''	3'15''	NAD
40	SECRETORY	2.52	12.5	1.32	nil	nil	3'15''	5'15''	NAD
41	SECRETORY	2.5	12.6	1.32	nil	nil	2'14''	4'34''	NAD
42	SECRETORY	2.43	14.3	1.43	nil	heat intolerance	1'15''	3'15''	NAD
43	SECRETORY	2.4	12.3	1.24	constipation	nil	2'14''	5'15''	NAD
44	SECRETORY	2.52	12.3	1.35	nil	nil	1'56''	4'45''	NAD
45	SECRETORY	3.66	15.6	0.69	nil	nil	1'35''	5'15''	NAD
46	PROLIFERATIVE	1.3	9.2	5.3	weight gain	anxiety	2'10'	3'15''	NAD
47	PROLIFERATIVE	0.3	7	8.1	cold intolerance	fatigue	2'12''	5'15''	NAD
48	PROLIFERATIVE	0.7	7.2	7.1	constipation	fatigue	3'17''	5'56''	NAD
49	SECRETORY	2.32	12	1.62	nil	nil	1'12''	4'45''	NAD
50	SECRETORY	2.32	13.1	1.53	nil	nil	3'13''	5'15''	PCOD
51	SECRETORY	3.36	12.4	0.86	weight gain	nil	2'15''	4'45''	NAD
52	SECRETORY	2.23	12.6	1.23	nil	nil	1'16''	5'22''	NAD
53	SECRETORY	2.32	12.84	1.46	nil	nil	2'14''	4'45''	NAD
54	SECRETORY	2.44	14.2	1.51	nil	heat intolerance	3'26''	6'	NAD
55	SECRETORY	2.56	12.8	1.34	constipation	nil	1'23''	4'46''	NAD
56	SECRETORY	2.39	12.6	1.36	nil	nil	2'17''	5'	NAD

57	SECRETORY	2.42	12.2	1.38	nil	nil	3'45''	5'18''	NAD
58	SECRETORY	2.42	13.3	1.41	nil	tremor	4'16''	5'56''	NAD
59	SECRETORY	2.53	13.2	1.42	nil	nil	3'36''	6'	NAD
60	SECRETORY	3.43	14.6	0.9	nil	nil	2'16''	4'46''	NAD
61	PROLIFERATIVE	1.32	9.2	5.2	weight gain	nil	1'15''	3'15''	NAD
62	PROLIFERATIVE	0.6	6	6	constipation	fatigue	1'23''	5'15''	NAD
63	PROLIFERATIVE	0.7	6.3	6.5	nil	fatigue	2'14''	5'16''	NAD
64	SECRETORY	3.43	14.7	0.92	nil	nil	3'23''	4'45''	PCOD
65	SECRETORY	3.34	14.6	0.85	voice change	nil	1'15''	5'23'	NAD
66	SECRETORY	2.23	12.6	1.2	weight gain	nil	2'25''	4'46''	NAD
67	SECRETORY	2.34	12.3	1.32	nil	nil	3'15''	5'15''	NAD
68	SECRETORY	2.42	13.2	1.41	nil	nil	2'15''	6'	NAD
69	SECRETORY	2.39	12.6	1.36	nil	tremor	3'16''	5'32''	NAD
70	SECRETORY	2.32	12.5	1.24	constipation	nil	2'48''	4'45''	NAD
71	SECRETORY	2.39	13.1	1.56	nil	nil	1'49''	4'45''	NAD
72	SECRETORY	2.4	12.7	1.36	nil	nil	3'23''	5'15''	NAD
73	SECRETORY	2.39	12.89	1.38	nil	anxiety	3'23''	4'45''	NAD
74	SECRETORY	2.42	12.9	1.32	nil	nil	3'32''	6'10'	NAD
75	SECRETORY	2.53	13.2	1.45	nil	nil	1'15''	3'15''	NAD
76	PROLIFERATIVE	1.26	9.3	5.5	weight gain	tremor	2'12''	5'56''	PCOD
77	PROLIFERATIVE	0.5	6	6.2	lethargy	fatigue	1'57''	4'46''	NAD
78	PROLIFERATIVE	1	7	5.6	weight gain	fatigue	3'12''	5'	NAD
79	SECRETORY	2.41	13.2	1.4	nil	nil	3'23''	4'16''	NAD
80	SECRETORY	2.1	11.2	1.72	nil	nil	3'32''	5'46''	NAD
81	SECRETORY	1.9	11.3	1.66	constipation	nil	1'15''	4'46''	NAD
82	SECRETORY	1.72	11.3	2.1	nil	nil	2'	5'15''	NAD
83	SECRETORY	2.42	13.2	1.32	nil	fatigue	2'16''	6'	NAD
84	SECRETORY	2.45	13.3	1.4	nil	fatigue	1'20''	5'32''	NAD
85	SECRETORY	2.43	12.7	1.12	constipation	nil	2'15''	4'45''	NAD
86	SECRETORY	3.35	14.6	0.87	nil	nil	3'16''	4'45''	PCOD

87	SECRETORY	3.41	14.3	0.98	nil	nil	2'48''	5'15''	NAD
88	SECRETORY	2.32	12.5	1.24	nil	nil	1'48''	5'45''	NAD
89	SECRETORY	2.41	13.2	1.4	nil	nil	1'15''	3'15''	NAD
90	SECRETORY	2.41	12.9	1.32	nil	nil	1'23''	4'45''	NAD
91	PROLIFERATIVE	1	7	5.2	weight gain	nil	2'15''	5'15''	NAD
92	PROLIFERATIVE	1.1	7.2	5	nil	fatigue	1'24''	4'45''	NAD
93	PROLIFERATIVE	0.6	6	5.3	nil	fatigue	1'23''	6'10'	NAD
94	SECRETORY	2.4	13.1	1.34	voice change	anxiety	1'34''	3'15''	NAD
95	SECRETORY	2.41	13.2	1.45	weight gain	nil	1'45''	5'56''	NAD
96	SECRETORY	2.34	12.9	1.7	nil	nil	1'50''	4'46''	NAD
97	SECRETORY	3.32	14.7	0.89	nil	nil	*2'15''*	5'	NAD
98	SECRETORY	2.42	12.7	1.2	nil	nil	3'16''	6'	NAD
99	SECRETORY	2.42	12.6	1.1	nil	nil	2'23''	5'	NAD
100	SECRETORY	2.46	12.9	1.32	nil	nil	2'36''	4'46''	NAD
101	SECRETORY	2.42	12.6	1.2	voice change	fatigue	1'25''	4'45''	NAD
102	SECRETORY	3.42	14.3	0.98	nil	fatigue	2'34''	5'25''	PCOD
103	SECRETORY	2.4	12.6	1.1	nil	nil	1'24''	5'46''	NAD
104	SECRETORY	2.36	12.4	1.23	nil	nil	1'16''	6'	NAD
105	SECRETORY	3.42	14.3	0.89	nil	nil	2'30''	6'15''	NAD
106	PROLIFERATIVE	0.9	6	5.7	weight gain	nil	3'	6'	NAD
107	PROLIFERATIVE	0.6	7	6.3	palpitation	fatigue	1'37''	5'45''	NAD
108	PROLIFERATIVE	0.8	7.2	6.4	lethargy	fatigue	1'12''	4'20''	NAD
109	SECRETORY	3.43	13.7	0.92	nil	weight loss	1'48''	5'45''	NAD
110	SECRETORY	3.34	14.6	0.85	nil	nil	1'13''	4'	NAD
111	SECRETORY	2.23	12.6	1.2	nil	nil	2'13''	4'34''	NAD
112	SECRETORY	2.34	12.3	1.32	nil	nil	1'24''	3'14''	NAD
113	SECRETORY	2.42	13.2	1.41	constipation	weight loss	2'12''	3'56''	NAD
114	SECRETORY	2.39	12.6	1.36	nil	fatigue	1'46''	4'	NAD
115	SECRETORY	2.32	12.5	1.24	nil	nil	2'16''	3'34''	NAD
116	SECRETORY	2.39	13.1	1.56	nil	nil	3'	5'45''	NAD

117	SECRETORY	2.4	12.7	1.36	nil	fatigue	2'	4'45''	NAD
118	SECRETORY	2.4	13.1	1.34	lethargy	nil	1'56''	5'15''	NAD
119	SECRETORY	2.41	13.2	1.45	nil	weight loss	2'10''	4'46''	NAD
120	SECRETORY	2.53	13.2	1.45	nil	weight loss	1'10''	5'15''	PCOD
121	PROLIFERATIVE	1.24	9.3	5.7	weight gain	nil	1'23''	5'	NAD
122	PROLIFERATIVE	0.9	6.2	5.5	nil	anxiety	1'20''	5'10''	NAD
123	PROLIFERATIVE	6	19.2	0.22	nil	anxiety	1'13''	5'56''	NAD
124	SECRETORY	1.7	11.3	2.1	nil	weight loss	1'40''	5'15''	NAD
125	SECRETORY	2.14	12.6	1.67	nil	nil	2'10''	4'46''	NAD
126	SECRETORY	2.2	12.7	1.2	weight gain	nil	2'	3'45''	NAD
127	SECRETORY	3.12	13.3	0.98	nil	nil	1'17''	3'40''	NAD
128	SECRETORY	3.3	14.2	0.86	nil	nil	1'30''	4'45''	NAD
129	SECRETORY	2.88	12.6	1.36	nil	nil	1'15''	5'15''	NAD
130	SECRETORY	2.42	13.2	1.42	nil	fatigue	1'10''	5'	NAD
131	SECRETORY	2.34	13.2	1.54	nil	fatigue	1'20''	4'10''	NAD
132	SECRETORY	2.42	12.7	1.2	nil	nil	2'10''	4'45''	NAD
133	SECRETORY	2.42	12.6	1.1	nil	nil	1'24''	3'25''	NAD
134	SECRETORY	2.46	12.9	1.32	nil	nil	1'23''	3'35'	NAD
135	SECRETORY	1.9	11.3	1.66	nil	nil	1'20''	4'46''	NAD
136	PROLIFERATIVE	0.6	7	5.6	weight gain	fatigue	1'13''	3'45''	NAD
137	PROLIFERATIVE	1.3	9.3	5.3	lethargy	diarrhoea	1'40''	3'40''	NAD
138	SECRETORY	7	19	0.12	nil	weight loss	2'10''	4'45''	NAD
139	SECRETORY	3.3	14.2	0.86	nil	nil	1'34''	4'20''	NAD
140	SECRETORY	2.88	12.6	1.36	nil	fatigue	1'35''	5'45''	PCOD
141	SECRETORY	2.34	13.2	1.54	nil	fatigue	1'46''	4'	NAD
142	SECRETORY	2.42	12.7	1.2	nil	fatigue	2'56''	4'34''	NAD
143	SECRETORY	2.32	12.5	1.24	nil	nil	3'	3'14''	NAD
144	SECRETORY	2.39	13.1	1.56	lethargy	weight loss	1'20''	4'45''	NAD
145	SECRETORY	2.4	12.7	1.36	weight gain	weight loss	1'13''	4'20''	NAD
146	SECRETORY	2.41	12.7	1.36	nil	fatigue	1'40''	5'45''	NAD

147	SECRETORY	2.42	13.1	1.34	nil	fatigue	1'23''	5'56''	NAD
148	SECRETORY	3.36	12.1	0.97	nil	nil	1'45''	4'	NAD
149	SECRETORY	3.56	12.3	1.12	nil	nil	1'10''	4'21''	NAD
150	SECRETORY	2.52	12.3	1.21	nil	nil	1'46''	5'10''	NAD
151	PROLIFERATIVE	0.8	6	5.3	lethargy	fatigue	1'34''	5'46''	NAD
152	PROLIFERATIVE	0.6	7.2	5.4	nil	fatigue	1'20''	4'46''	NAD
153	PROLIFERATIVE	7.2	19.3	0.21	nil	nil	1'46''	4'	NAD
154	SECRETORY	2.44	12.1	1.23	voice change	tremor	2'56''	4'34''	NAD
155	SECRETORY	2.52	12.4	1.32	lethargy	nil	1'34''	3'14''	NAD
156	PROLIFERATIVE	2.52	12.6	1.32	nil	fatigue	1'34''	3'35''	PCOD
157	PROLIFERATIVE	2.43	14.3	1.42	nil	fatigue	1'50''	4'16''	NAD
158	PROLIFERATIVE	2.2	12.2	1.26	nil	fatigue	1'45''	4'47''	NAD
159	PROLIFERATIVE	2.24	12.3	1.28	nil	fatigue	1'56''	4'50''	NAD
160	PROLIFERATIVE	2.35	13.4	1.56	nil	diarrhoea	1'24''	5'25''	NAD
161	PROLIFERATIVE	2.12	11.2	1.93	nil	fatigue	1'36''	4'	NAD
162	PROLIFERATIVE	3.42	14.3	0.96	weight gain	fatigue	2'25''	3'45''	NAD
163	SECRETORY	2.4	12.6	1.21	nil	nil	2'56''	5'54''	NAD
164	SECRETORY	2.36	12.4	1.32	nil	nil	1'17''	3'15''	NAD
165	SECRETORY	3.42	14.3	0.86	nil	nil	1'30''	4'23''	NAD
166	PROLIFERATIVE	0.4	6.2	5.2	constipation	fatigue	1'15''	5'15''	NAD
167	SECRETORY	1	6	5.3	lethargy	fatigue	1'10''	3'34''	NAD
168	SECRETORY	6	18.2	0.13	nil	fatigue	1'20''	5'45''	NAD
169	SECRETORY	2.1	10.6	2.1	nil	nil	2'10''	4'45''	NAD
170	SECRETORY	3.52	15.6	0.68	nil	nil	1'24''	5'15''	NAD
171	SECRETORY	3.3	14.2	0.8	nil	nil	1'23''	4'46''	PCOD
172	SECRETORY	2.88	12.6	1.32	nil	nil	1'20''	5'15''	NAD
173	SECRETORY	2.2	12	1.22	nil	nil	1'56''	3'35''	NAD
174	PROLIFERATIVE	2.24	12.3	1.3	weight gain	fatigue	2'10''	4'14''	NAD
175	PROLIFERATIVE	3.54	12.3	1.1	nil	fatigue	2'	4'20''	NAD
176	PROLIFERATIVE	2.23	12.6	1.21	nil	nil	1'15''	4'34''	NAD

177	PROLIFERATIVE	2.34	12.3	1.34	lethargy	fatigue	1'10''	5'15''	NAD
178	PROLIFERATIVE	2.42	13.2	1.4	nil	fatigue	2'10''	5'56''	PCOD
179	PROLIFERATIVE	2.34	12.3	1.34	nil	nil	1'34''	6'	NAD
180	PROLIFERATIVE	2.42	13.2	1.42	nil	fatigue	1'35''	5'56''	NAD
181	SECRETORY	0.6	6.2	5.2	nil	fatigue	1'46''	5'16''	NAD
182	SECRETORY	0.7	5.1	6.3	nil	nil	2'56''	4'45''	NAD
183	PROLIFERATIVE	3.4	14	0.12	nil	fatigue	3'14''	5'15''	NAD
184	PROLIFERATIVE	3.35	14.6	0.86	nil	fatigue	3'16''	4'45''	NAD
185	PROLIFERATIVE	3.41	14.3	0.96	voice change	fatigue	3'34''	4'46''	NAD
186	PROLIFERATIVE	2.4	13.1	1.32	nil	fatigue	2'56''	5'15''	NAD
187	PROLIFERATIVE	2.41	13.2	1.4	nil	nil	1'13''	4'47''	NAD
188	PROLIFERATIVE	2.3	12.1	1.2	lethargy	nil	1'34''	4'50''	NAD
189	PROLIFERATIVE	2.36	13	1.32	nil	fatigue	2'13''	5'25''	NAD
190	PROLIFERATIVE	2.42	13.4	1.45	nil	fatigue	2'45''	4'	NAD
191	PROLIFERATIVE	2.41	13.2	1.52	nil	fatigue	1'32''	4'	NAD
192	PROLIFERATIVE	2.4	12.6	1.1	constipation	nil	1'46''	4'15''	NAD
193	PROLIFERATIVE	2.36	12.4	1.23	nil	nil	2'56''	4'56''	PCOD
194	PROLIFERATIVE	2.4	13.1	1.34	nil	fatigue	3'14''	4'50''	NAD
195	PROLIFERATIVE	2.41	13.2	1.45	nil	fatigue	1'38''	5'25''	NAD
196	SECRETORY	0.7	6.3	6.2	lethargy	nil	2'34''	5'15''	NAD
197	SECRETORY	1	7.2	7.1	nil	nil	2'43''	5'23''	NAD
198	PROLIFERATIVE	3.6	14.2	0.13	nil	fatigue	2'45''	5'21''	NAD
199	PROLIFERATIVE	2.32	12	1.62	weight gain	fatigue	3'	4'47''	NAD
200	PROLIFERATIVE	2.32	13.1	1.53	weight gain	fatigue	2'36''	4'50''	PCOD

URKUND

Urkund Analysis Result

Analysed Document:	new thyroid final copy 2.docx (D42475965)
Submitted:	10/12/2018 1:45:00 PM
Submitted By:	dr.thangam1993@gmail.com
Significance:	1 %

Sources included in the report:

final thesis.docx (D42339748)

Instances where selected sources appear:

1