"A STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING"

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Dr. ASHRITHA REBALA

LIST OF ABBREVATIONS USED

AUB	Abnormal uterine bleeding
DUB	Dysfunctional Uterine Bleeding
OPD	Out Patient Department
T3	Triiodothyronine
T4	Thyroxine
TSH	Thyroid Stimulating Hormone
TBG	Thyroxine binding globulin
Tg	Thyroglobulin
MIT	Monoiodothyronine
DIT	Diiodothyronin
TRH	Thyrotrophin Releasing Hormone
RIA	Radio Immuno Assay
LMP	Last Menstrual Period
Inter	Interval
Dura	Duration
Quant	Quantity
MPH	Metropathia Hemorrhagica
TFT	Thyroid Function Tests
TDF	Thyroid Dysfunction
MBL	Menstrual blood loss
LH	Luteinising hormone

FSH	Follicle- stimulating hormone
GnRH	Gonadotrophin releasing hormone

ABSTRACT

Title: "STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING"

Background and objectives:

Abnormal uterine bleeding (AUB) is any uterine bleeding outside the normal volume, duration, regularity or frequency. Thyroid dysfunction is marked by large number of menstrual deviations. This study aimed at detecting thyroid dysfunction in patients with a provisional diagnosis of AUB and refer positive cases to physician for further evaluation.

Methods:

In this study, 151 cases of clinically diagnosed AUB were taken from gynaecology OPD and in Patients of R.L Jalappa Hospital and Research centre, constituent of Sri Devaraj Urs Medical College, Tamaka, Kolar. All patients from puberty to premenopausal age groups presenting as menorrhagia, acyclical metropathia, polymenorrhagia, metrorrhagia, oligomenorrhoea, polymenorrhoea and hypomenorrhoea were tested for their thyroid function by T3, T4, TSH estimations in their serum. Patients who had clinical symptoms and signs of thyroid disease, was on hormonal treatment, IUCD users, or had bleeding disorders were excluded from the study.

Results:

Among 151 patients studied, 23.17% of patients had thyroid dysfunction of which 13.25% of patients had subclinical hypothyroidism, 7.28% of patients had

hypothyroidism and only 2.64% of patients had hyperthyroidism. The commonest bleeding abnormality in subclinical hypothyroid patients were polymenorrhoea and menorrhagia. All hyperthyroid cases were oligomenorrhoeic.

Interpretation and Conclusion:

In our study thyroid dysfunction was noted in 23.17% of women with abnormal uterine bleeding, of which most common was subclinical hypothyroidism in 13.25%, followed by hypothyroidism (7.28%) and hyperthyroidism (2.64 %). Oligomenorrhoea (34.48%), followed by polymenorrhoea (33.3%) and acyclical bleeding (27.2%) were commonest menstrual abnormalities seen in thyroid dysfunction. Thus biochemical evaluation of T3, T4 and TSH estimations should be made obligatory in abnormal uterine bleeding cases, to detect thyroid dysfunction. Treatment of thyroid dysfunction in women with abnormal uterine bleeding will avoid unnecessary surgery and hormonal treatment.

Key words :

Abnormal Uterine Bleeding (AUB)

Thyroid dysfunction

Hypothyroidism

Subclinical hypothyroidism

Hyperthyroidism

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INTRODUCTION

Abnormal uterine bleeding (AUB) is any uterine bleeding outside the normal volume, duration, regularity or frequency. AUB accounts for 30% of the gynaecology related complaints. A number of menstrual aberrations are associated with thyroid dysfunction[1.]

Hypothyroidism as well as hyperthyroidism is equally associated with a mixture of changes in reproductive function including delayed onset of puberty, anovulatory cycles and during pregnancy an abnormally high fetal wastage. Clinical experiences show increased menstrual flow to be the most frequent menstrual problem of hypothyroidism[2.]

Even though the high incidence of menstrual disorders in hypothyroid woman has been documented, the number of hypothyroid patients initially requiring treatment for menorrhagia has not been carefully elicitated[3]. Moreover, majority of the cases have subclinical hypothyroidism and easily go by unrecognized. Hypothyroidism is frequent enough to deserve consideration in most older woman, justifying screening even in asymptomatic older women[4].

The introduction of serum thyroxine (T3) and serum thyroid stimulating hormone (TSH) radioimmunoassays has increased the sensitivity and specificity of thyroid function testing. The serum TSH assay has revealed to be a sensitive indicator of diminished thyroid functional reserve, since TSH levels become elevated before circulating serum thyroxine levels drop below the reference range[5].

Hence this study is to evaluate and detect thyroid dysfunction in patients with abnormal uterine bleeding. Positive cases are those patients showing thyroid dysfunction who can be treated. This may avoid unnecessary hormonal treatment like progesterone and surgical intervention like hysterectomy. Studies on thyroid dysfunction and AUB conducted in rural population are neither conclusive nor clear. This made us to take up a study with an objective to find if any.

OBJECTIVES

1. To study thyroid hormone levels in patients with abnormal uterine bleeding.
2. To correlate different menstrual patterns with varieties of thyroid dysfunction.

REVIEW OF LITERATURE

ABNORMAL UTERINE BLEEDING AND ITS CLASSIFICATION:

Abnormal uterine bleeding is defined by various authors in many ways leading to confusion as to, which are the exact entities, which come under this heading. It is a symptom and not a disease, which occurs in various forms. A rational approach and accurate diagnosis depends on recognizing the following types [6].

- Oligomenorrhoea: Infrequent irregular episodes of bleeding, usually occurring at interval of more than 35 days.
- Polymenorrhoea: Frequent but regular episodes of uterine bleeding usually occurring at intervals of 21 days or less.
- Menorrhagia: Uterine bleeding usually excessive and prolonged occurring at regular intervals.
- Menometrorhagia: Uterine bleeding usually excessive and prolonged occurring at frequent irregular intervals.
- Hypomenorrhoea: Uterine bleeding that is regular but decreased in amount.
- Intermenstrual bleeding: Uterine bleeding usually not excessive, occurring between regular menstrual periods.
- Metrorrhagia – Irregularly timed bleeding

Abnormal uterine bleeding may be categorized into two broad categories: the first is due to organic causes; the second is the so- called dysfunctional uterine bleeding (DUB), caused usually by anovulation or oligo- ovulation[7]. DUB is one of the most common causes of abnormal uterine bleeding. It is a diagnosis of exclusion.

Novak defines it as "bleeding without a causative uterine lesion such as tumour, infection or complications of pregnancy, although frequently there may be associated cysts of the ovary".

Sutherland defines DUB as "Abnormal uterine bleeding which is not explained by any palpable lesions of the reproductive organs" [8].

Taylor restricts the term DUB to be applied only when all possible causes for irregular, excessive or prolonged bleeding have been excluded. Such as exclusive approach would tend to eliminate from consideration any uterine bleeding for which an aetiology has been uncovered[9].

Telinde defines DUB as abnormal uterine bleeding occurring in the absence of identifiable pathology [10].

Speroff describes DUB as a variety of bleeding manifestations of anovulatory cycles (in absence of pathology or medical illness) [11].

Jeffcoates defines it as "excessive, prolonged, unpatterned bleeding from the endometrium unrelated to structural or systemic disease and thus other diagnosis must be excluded[7].

Dewhurst defines DUB as "abnormal bleeding from the uterus in the absence of organic disease of the genital tract"[1].

Classification of DUB-It is classified into ovular and anovular types[7.]

A. Ovular haemorrhages

1. Functional epimenorrhagia and epimenorrhoea
2. Functional menorrhagia
    - Irregular ripening of the endometrium
    - Prolonged or irregular ripening of the endometrium

B. Anovular haemorrhage

1. Threshold bleeding
2. Metropathia haemorrhagica

New Classification System Categorizes Causes of Abnormal Uterine Bleeding from FIGO (Medscape Education Clinical Briefs) **[12].** After a thorough 5-year review process beginning with workshops in 2005, a group of clinician-investigators from 17

countries on 6 continents who had substantial experience in AUB research developed and revised a draft system that was distributed for comments.

The PALM-COEIN classification system was then discussed at a meeting held in association with the 2009 FIGO World Congress in Cape Town, South Africa, and subsequently approved by the FIGO Executive Board as a FIGO classification system.

• June 7, 2011 — The International Federation of Gynaecology and Obstetrics (FIGO) has approved a new classification system (PALM-COEIN) for causes of abnormal uterine bleeding (AUB) in non gravid women of reproductive age.

. • Out of the 9 categories in the new FIGO classification system (PALM-COEIN), the first 4 were defined as visually objective structural criteria (PALM: polyp, adenomyosis, leiomyoma, and malignancy and hyperplasia). The second 4 are unrelated to structural abnormalities (COEI: coagulopathy, ovulatory dysfunction, endometrial, and iatrogenic), and the final category is for entities that are not yet classified (N).

Abnormal uterine bleeding: Palm Coein Classification

PALM

• P: Endometrial polyp
• A: Adenomyosis
• L: Leiomyoma
• M: Malignancy and hyperplasia

COEIN:

• C: Coagulopathy, Clotting factor deficiency or defect
• O: Ovulatory
• E: Endometrial
• I: Iatrogenic Conditions
• N: Not Classified

Causes of abnormal uterine bleeding by Age Group:

Reproductive age:

1. Anovulation
2. Pregnancy
3. Endocrine Disorder
4. Polyps/ fibroids/ Adenomyosis
5. Medication related (oral contraceptives)
6. Infection
7. Sarcoma, ovarian
8. Coagulation disorder

Perimenopausal:

1. Anovulation leading to unopposed estrogen and Hyperplasia
2. Polyp/ Fibroid/ Adenomyosis
3. Cancer

Postmenopausal:

1. Atrophy
2. Cancer/polyp
3. Estrogen therapy
4. Selective Estrogen Receptor Modulators

PHYSIOLOGY OF MENSTRUATION

As abnormal uterine bleeding is a hormonal disorder, knowledge of the normal hormonal control of menstruation is useful. Menstruation may be defined as a "periodical and cyclical shedding of progestational endometrium accompanied by loss of blood". It takes place at approximately 28 day intervals with a range of 21-35 days between the menarche (onset of menstruation) and menopause (cessation of menstruation) [2].

Under the influence of monthly cyclical production of estrogen and progesterone by ovaries, endometrium undergoes cyclic changes through the following phases[2].

- Proliferative phase
- Secretory phase
- Menstrual phase

The first 3-5 days are occupied with menstruation when two thirds of the endometrium is shed. The remaining 23-25 days are divided into the follicular and luteal phases or proliferative and secretary phases respectively. The follicular phase is characterized by maturation of the Graffian Follicle and the subsequent production of estrogen hormone which brings about proliferation of the endometrium. The luteal phase which occurs following ovulation is characterized by the formation of the corpus luteum and the production of both estrogen and progesterone which brings about secretory changes in the endometrium[13].

Ovulation is tuned in relation to the next menstrual period which is preceded by 14±2 days; this means that the luteal phase in the ovary is relatively constant in duration, whereas the length of the follicular phase differs with the total length of the cycle.

The onset and duration of these phases are determined by a cyclical and sequential discharge of gonadotrophins by the hypothalamopituitary system such as follicle stimulating hormone (FSH) and luteinizing hormone (LH) which are secreted by the anterior pituitary. Their release is mediated by a hypothalamic releasing factor – LH/FSH-RH (GnRH).

The action of matured Graffian follicle is predominant in the first half of the cycle which is stimulated by FSH – the follicular phase. The granulosa and the theca intima cells of the follicle produce increasing amounts of estrogen which reaches a peak just before ovulation.

The high levels of estrogen in the circulation, condition the pitutary to respond to the GnRH by secreting LH instead of FSH. A high level of LH induces ovulation and corpus luteum formation with a subsequent increase in the secretion of progesterone. The output of LH/FSH-RH (GnRH) then decreases. It is not known whether progesterone inhibits its release or whether the output of LH/FSH-RH (GnRH) is self-limiting. Whatever the mechanism, the production of the releasing hormone falls or stops. This leads to a drop in LH and degeneration of the corpus luteum. The resulting fall in the level of both estrogen and progesterone leads to menstruation and stimulates the hypothalamus to release GnRH to start the next cycle.

Estrogen which predominates during the proliferative phase, is secreted by the follicular cells and it is a very potent steroid, capable of producing rapid and significant changes in target tissue (uterus, vagina, breast) which depends on their activity to produce a special cytoplastic protein known as "estrogen receptor". Estrogen causes growth and proliferative of the cells (stromal and glandular) in the endometrium. Experimentally intravenous administration of estrogen causes prompt hyperemia and rapid uptake of water.

Progesterone whose effect prevails in the secretory phase, is secreted by the corpus luteal cells. Specific receptors for progesterone have also been detected in the endometrium. Progesterone helps in differentiation of stromal cells either into large predecidual cells or into small endometrial granulocytes. It also causes growth of spiral arterioles[13].

Criteria for normal menstrual cycle:

Menstrual cycle is judged by three clinical parameters

Cycle length:

It is the interval between the first day of one period and the first day of the next. During the active reproductive years, menstruation occurs at approximately 28 +/- 7 days. Every woman has her own rhythm which may alter after child birth[13].

Treloar et al in his prospective study over 30 years in Caucasian women, reported that the cycle length usually varies by 1 to 2 days each month and only 50 % women have cycles within 26-30 days range. Median cycle length declines from 28.87 (+/-2.75) days at age of 20 years to median of 26.8(+/-2) days by 40 years of age.

In reference to this study, in general cycles with length less than 24 days are considered polymenorrhoea and those with more than 35 days are consideredoligomenorrhoea[14].

Regularity of cycle length depends upon HPO axis. The immediate post menarche cycles are irregular and long due to immaturity of hypothalamus and pituitary, as a result of which regular ovulation is yet to be established. Again in perimenopausal period cycles become irregular and mostly longer due to diminished number of follicles with increased resistance to gonadotrophin stimulation [1].

Duration of menstrual blood loss:

As per Gullibaud and Bonner , normal range of duration of bleeding is 2 to 7 days with an average of 5 days. Shorter (hypomenorrhea) or longer (hypermenorrhea) than this is taken as abnormal [15].

Menstrual blood loss (MBL):

Average blood loss per cycle is considered to be 35-40 cc. This is equivalent to daily loss of 0.6 mg to 0.7 mg of iron throughout each month[16].

According to Rybo et al parity has a small effect on MBL, multiparas have a slightly higher average loss than nulliparas. WHO report mentions that in western European populations, the average blood loss during menstruation varies from 31-39 ml while Chinese and Japanese populations it is 47-54 ml and 52-56 ml respectively[17,18]. In Swedish population, Hallberg et al observed significant increase in the incidence of iron deficiency anaemia when the MBL was 80 ml or more[19].

ANOVULATORY BLEEDING

Anovulation or oligo-ovulation is the commonest cause of abnormal uterine bleeding when no organic cause has been found. The characteristic feature is the absence of active corpus luteum tissue in the ovary. A follicle ripens but fails to rupture, the ovum dies and follicle may go onto cyst formation whether it forms a cyst or not, it produces oestrogen for some time and this acts on the uterus without being opposed by progesterone. The production may be continuous at a moderate level, or intermittently high and low. In either case the uterus responds by hypertrophy of its myometrium and endometrium, and the latter may become polypoidal. On section the endometrium shows the picture of hyperplasia, usually of cystic type (SWISS CHEESE) but occasionally adenomatous.

Bleeding is acyclical it is continuous for 2-8 weeks and can be so heavy as to threaten life. In about half the cases it is preceded by a short period of amenorrhoea which coincides with a continuously high production of estrogen by the follicle and this type of clinical picture was earlier often labelled as metropathia haemorrhagica. When the granulosa cells becomes less active or when the endometrium grows so thick that the supply of estrogen becomes relatively inadequate, estrogen withdrawal bleeding takes place. The bleeding is always painless. On examination the uterus feels slightly enlarged and its sometimes possible to palpate cystic ovaries. A definitive

diagnosis is only by histological examination of curettings. The underlying cause is the failure in ovulation, and reflects an abnormal gonadotrophin stimulus. Behind this there is often a hypothalamic and cortical basis, as in the case of other forms of dysfunctional bleeding, being mostly seen in nervously tense and emotional subjects. It recurs most commonly during the few years preceding the menopause, but is occasionally seen in girls aged 12-20 years. In the latter it shows a strong tendency to spontaneous cure [20, 21].

INVESTIGATIONS

There is no, one clear sequence for use of endometrial biopsy, TVS, SIS, and hysteroscopy to evaluate abnormal uterine bleeding. None of these would distinguish all anatomic lesions with high sensitivity and specificity. USG, for several reasons is a logical first step. It is well-tolerated, cost-effective, and requires relatively minimal technical skill.

Additionally, it has the advantage of consistently determining whether a lesion is diffuse or focal. Once anatomic lesions have been identified, subsequent evaluation requires individualization. If endometrial hyperplasia or cancer is suspected, then endometrial biopsy may offer advantages. Alternatively, possible focal lesions may be best investigated with either hysteroscopy or SIS. Ultimately, the selection of appropriate tests depends on their accuracy to characterize the most likely anatomic lesions.

Embryology of thyroid gland

The tissue bud that eventually becomes the thyroid gland which arises initially as a midline diverticulum in the floor of the pharynx. This tissue originates from the primitive alimentary tract and consists of cells of endodermal origin. The main portion of this cellular structure descends into the neck and develops into a bilobar solid organ. A normally developed adult thyroid is a bilobed structure that lies next to the thyroid cartilage in a position, anterior and lateral to the junction of the larynx and trachea. In this position the thyroid encircles about 75% of the diameter of the junction of the larynx and the upper part of the trachea. The two lateral lobes are joined at the midline by an isthmus, whose superior edge is situated at, or just below the cricoid cartilage. The pyramidal lobe represents the most distal portion of the thyroglossal duct and in an adult it may be a prominent structure that can extend from the midline of the isthmus as far cephalad as the hyoid bone [22].

Blood Supply and Lymphatics

The arterial supply to the thyroid gland consists of four main arteries, two superior and two inferior thyroidal arteries. It has three pairs of venous systems which drain through thyroidal veins into external jugular vein. Lymphatics drain into internal jugular lymph node.

Physiology of thyroid gland

The thyroid gland weighs 10 to 20 g in normal adults and 1.5g in newborn. It is responsible inthe production of two families of metabolic hormones: the thyroid hormonesthyroxine (T4) and triiodothyronine (T3) and the calcium-regulating hormonecalcitonin. The spherical thyroid follicular unit is the important site of thyroid hormone production..

The thyroid follicle is made up of a single layer of cuboidal follicular cells that include a central depository of colloid filled mostly with thyroglobulin (Tg), the protein within which T4 and T3 are synthesized and stored. Each follicle is surrounded by a rich network of capillaries that interdigitate among the multiple follicular units contained within normal thyroid matrix. Iodine is essential for normal

thyroid function. It can be efficiently absorbed from the gastrointestinal tract in the form of inorganic iodide and can rapidly enter the extracellular iodide pool. The thyroid gland is responsible for storing 90% of total body iodide at any given time, with less than10% existing in the extracellular pool. The extracellular pool consists of freshly absorbed iodide, which is derived from the breakdown of previously formed thyroid hormone. Within the thyroid, iodide is stored either as preformed thyroid hormone or as iodinated amino acids. Iodide is transported from the extracellular space into the follicular cells against a chemical and electrical gradient. The transporter is an intrinsic transmembrane protein located in the basolateral membrane of the thyroid follicular cells. Once inside the cells, iodide rapidly diffuses to the apical surface, where it is quickly moved to exocytic vesicles. Here it is rapidly oxidized and bound to Tg. Transport of iodide into follicular cells is regulated by thyroid-stimulating hormone (TSH) from the pituitary gland, as well as by the follicular content of iodide. C cells, derived from the neural crest migrate into the thyroid during embryologic development. These cells rests in a parafollicular position, predominantly in the upper lobe of each thyroid. C cells are responsible for production of the hormone calcitonin, which has important role on regulation of calcium metabolism[23].

Thyroid Hormone Synthesis

Once organic iodide is efficiently oxidized and bound, it couples with tyrosine moieties to Tg and forms iodotyrosines in either a single confirmation (monoiodotyrosine [MIT]) or a coupled confirmation (diiodotyrosine [DIT]). The formation of DIT and MIT is dependent on an important intracellular catalytic agent, thyroid peroxidise which has been well characterized and is an integral part of the initial process of organification and storage of inorganic iodide. This enzyme is localized to the apical portion of the follicular cell, where it reacts on the cell colloid interface.

MIT and DIT are biologically inert. Coupling of these two residues give rise to the two biologically active thyroid hormones T4 and T3. T4 is formed by coupling of two molecules of DIT, whereas T3 is formed by coupling of a molecule of MIT with a molecule of DIT. In normal circumstances, formation of T4 is the major pathway. Both T3 and T4 are bound to Tg and stored within the colloid in the centre of the

follicular unit, which allows quicker secretion of the hormones than if they had to be synthesized. This rapid and metabolically active process results in the storage of about two weeks' worth of thyroid hormone within the organism under normal circumstances [24].The majority of thyroid hormone released from the thyroid gland is T4, which is deiodinated in peripheral extra thyroidal tissues and converted to T3.Release of T4 and T3 are regulated by the apical membrane of the follicular cell via lysosomal hydrolysis of the colloid that contains the Tg-bound hormones. The apical membrane of the thyroid cell form multiple pseudopodia and incorporates Tg into small vesicles, which are then brought within the cell apparatus. Within the vesicles, lysosomal hydrolysis results in reduction of the disulfide bonds, and both T3 and T4 are then free to pass through the basement membrane and be absorbed into the circulation, where more than 99% of each of the hormones is bound to serum proteins.

Fig: 1 Regulation of Thyroid Hormone Synthesis

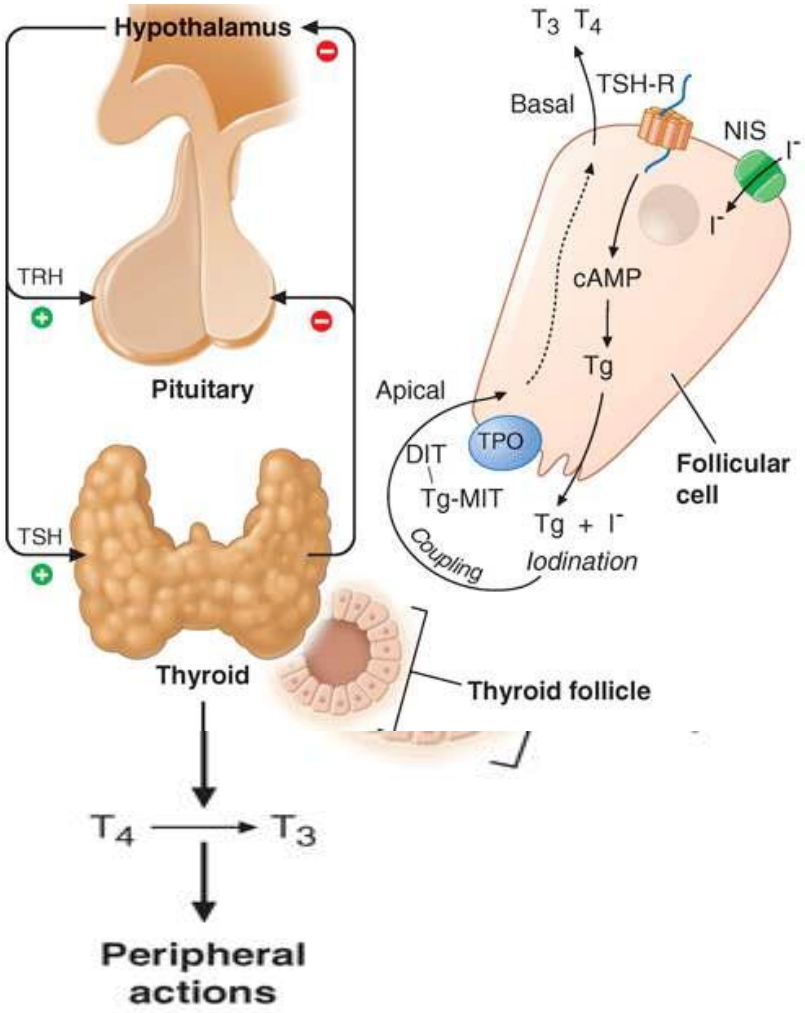
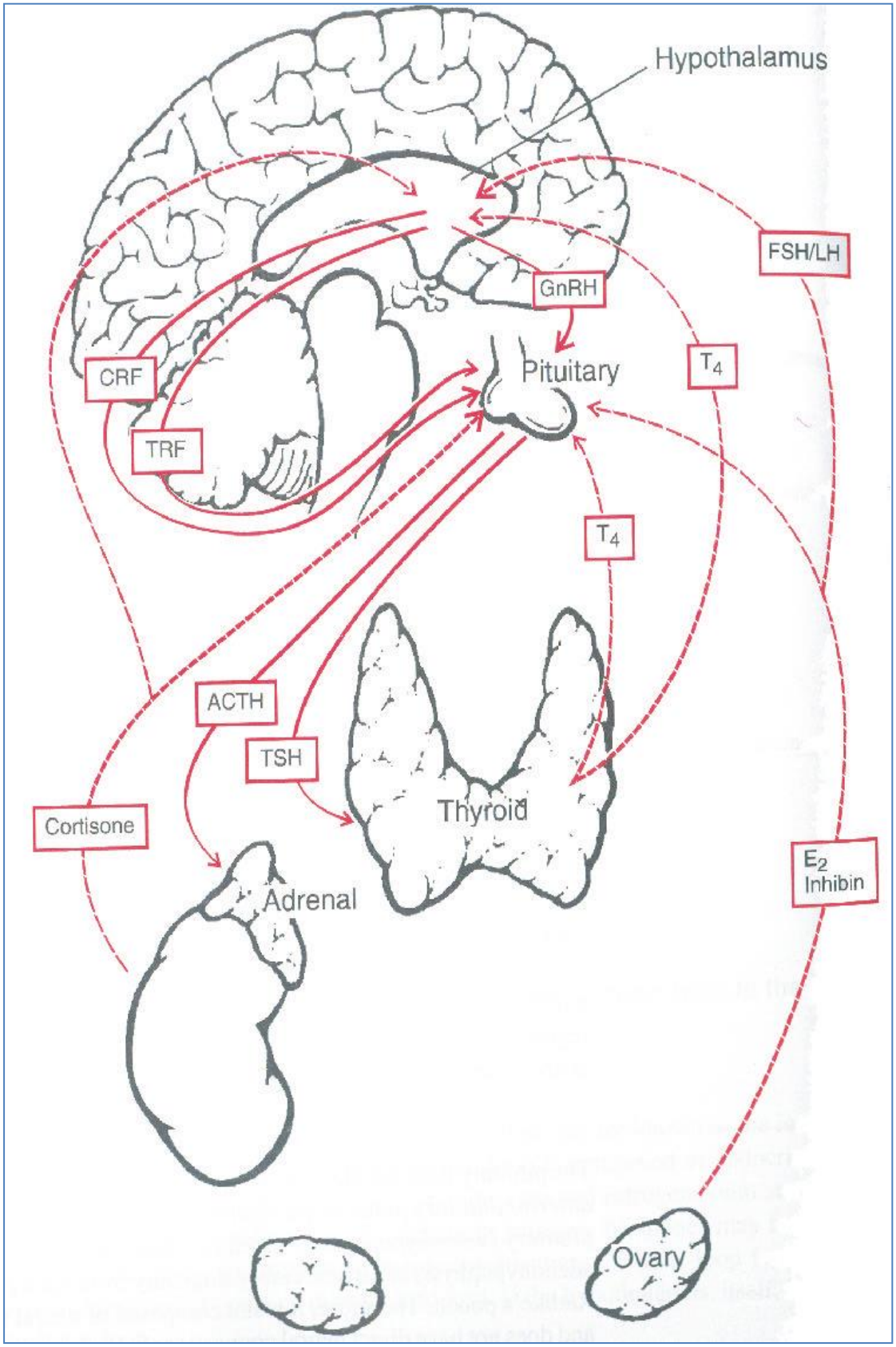


Fig: 2 Control of endocrine function of ovaries, thyroid , adrenal glands by Hypothalamus and pituitary

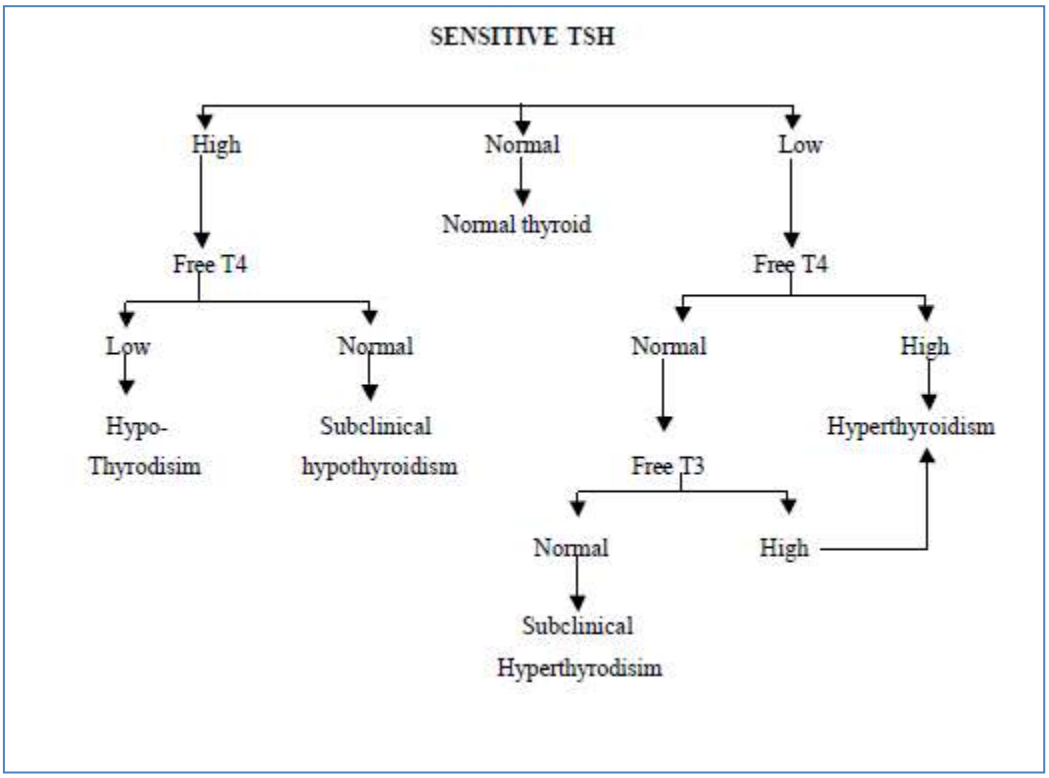


Regulation of Thyroid Hormone Secretion

Triiodothyronine and Thyroxine

The hypothalamic-pituitary-thyroid axis regulates thyroid hormone production and releases a classic endocrine feedback system. The major regulator of thyroid gland activity is the glycoprotein TSH, which is a major growth factor for the thyroid. TSH stimulates thyroid cell growth and its differentiation, as well as iodine uptake and organification and release of T3 and T4 from Tg. TSH is a 28-kd glycoprotein that is secreted in a pulsatile fashion by the anterior pituitary gland. It has two components. The α subunit is common to other anterior pituitary hormones. However, the β subunit is unique to TSH and determines the hormone's biologic specificity. TSH has specific activity through a receptor on the surface of the thyroid cell. Once the receptor is activated, it interacts with a guanine nucleotide– binding protein (G protein). This interaction stimulates the production of cyclic adenosine monophosphate (AMP). The synthesis of thyroid hormones is mediated through this cyclic AMP pathway. Negative feedback through increased peripheral levels of T3 and T4 can affect TSH secretion. Peripheral T4 is locally deiodinated in the pituitary and converted to T3, which then directly inhibits the release and synthesis of TSH. Excessively large doses of iodide has interesting and complex effects, including an initial increase in organification followed by suppressive effects, a syndrome known as the Wolff-Chaikoff effect [22].

Fig: 3 Variations of TSH, T3, T4



THYROID FUNCTION TESTS

The determination of circulating levels of thyroid hormones is essential for an accurate assessment of the functional status of patients. Serum thyroxine (T4) concentration was for many years the most useful first line test. Serum T4 is determined almost exclusively by RIA, values in euthyroid patients ranges 5-12 μg/dl.

In general (except T3 thyrotoxicosis etc.,) the value of T3 (serum triodothyronine) is parallel to T4 level and ranges in healthy subject being 80-200 ng/dl. Reverse T3 (rT3) varies from 10-60 ng/dl. rT3 values are often elevated in nonthyroidal illness [25, 26].

To assess the patients true metabolic status estimation of the concentration of free T4 or free T3 – the "active " hormones is advisable by equilibrium dialysis, the most precise method, (which may not be available in all centers)[27]. Serum thyrotropin (thyroid stimulating hormone, TSH) has been a reliable indicator of primary

hypothyroidism with levels rising even when thyroid deficiency is mild and T4 level still normal. Although RIAs were developed that could detect TSH concentrations of 0.1 to 0.3 μg/ml, it was achieved by extensive purification. Commercially available RIAs have not provided quantitative values below 1 μU/ml many second – generation assays detect TSH in the range of 0.1 to 0.5 μU/ml and third generation assay have an even 10 fold greater functional sensitivity [28, 29, 30, 31].

Extremely sensitive (fourth generation) assays can detect TSH levels = 0.004 mU/l but for practical purposes, assay sensitive to = 0.1 mU/l are sufficient. The widespread availability of TSH immuno chemiluminometric assays (ICMAs) has rendered the TRH stimulation test virtually absolute[32].The finding of an abnormal TSH level must be followed by measurements of circulating thyroid hormone levels to confirm the diagnosis of hyperthyroidism (suppressed TSH) or hypothyroidism (elevated TSH). Radioimmunoassays are widely available for serum total T4 and total T3.

Total thyroid hormone levels are elevated when TBG is increased due to estrogens (pregnancy, oral contraceptives, hormone therapy, tamoxifen), and decreased when TBG binding is reduced (androgens, nephrotic syndrome). Genetic disorders and acute illness can also cause abnormalities in thyroid hormone binding proteins, and various drugs [phenytoin, carbamazepine, salicylates, and nonsteroidal anti-inflammatory drugs (NSAIDs)] can interfere with thyroid hormone binding.

Tests for the end-organ effects of thyroid hormone excess or depletion, such as estimation of basal metabolic rate, tendon reflex relaxation rates, or serum cholesterol, are not useful as clinical determinants of thyroid function.

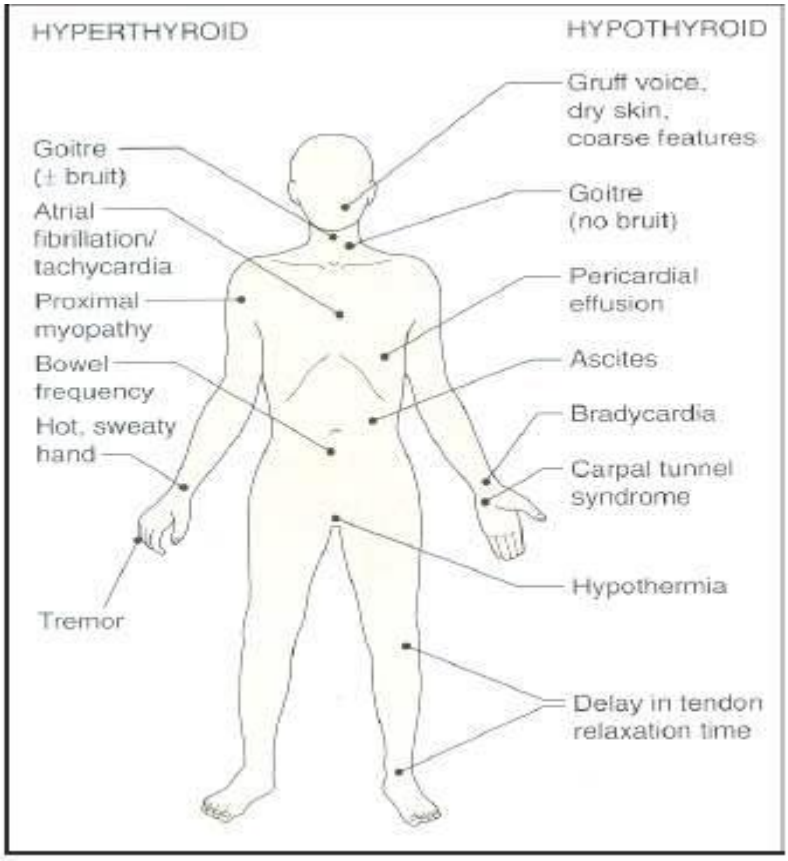
Disorders of the Thyroid Gland

Acting through thyroid hormone receptors and, hormones thyroxine (T4) and triiodothyronine (T3) plays a critical role in cell differentiation during development and helps to maintain thermogenic and metabolic homeostasis in the adults. Autoimmune disorders of the thyroid gland can stimulate overproduction of thyroid hormones (thyrotoxicosis) or cause glandular destruction and hormone deficiency (hypothyroidism).

Table A:-Patterns of thyroid function test results in patients with thyroid disease [33].

Type of disease	T4	T3	TSH
Conventional hyperthyroidism (95% of cases)	Raised	Raised	Undetectable
T3 hyperthyroidism (5% of cases)	Normal	Raised	Undetectable
Subclinical hyperthyroidism	Normal	Normal	Undetectable
Primary hypothyroidism	Low	Not Indicated	Raised (usually >20m U/L)
Subclinical hypothyroidism	Normal	Not Indicated	Raised
Secondary hypothyroidism i.e. pituitary or hypothalamic disease	Low	Not Indicated	Usually undetectable
Non thyroidal illness	Raised	Low, normal or raised	Usually undetectable

Fig: 4 Features of hyperthyroidism and hypothyroidism



Pathophysiology of abnormal uterine bleeding in Hypothyroidism

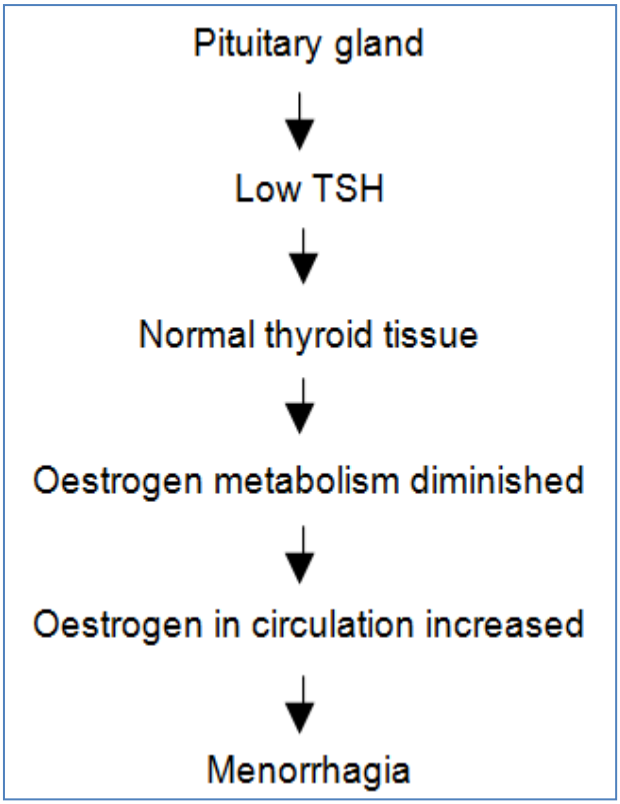
Abnormality of menstruation is primarily a disorder of hypothalamo-pituitary-ovarian axis either through direct effect or indirectly by their effect on target organ. Endocrinological disturbances other than the reproductive hormones form a small but significant sub-group in the aetiopathogenesis of abnormal uterine bleeding. Amongst the endocrinological causes, after the pituitary, thyroid is probably the most important endocrine organ which exerts a broad range of effects on the development, growth, metabolism and function of virtually every organ system in the human body. Alterations in production and activity of the thyroid hormones thyroxine (T4) and tri-iodothyronine (T3) may result in menstrual abnormality. Both hyperthyroidism and hypothyroidism may result in menstrual disturbances.

Hypothyroidism may result in excessive menstrual bleeding and severe blood loss. The mechanism of menorrhagia in hypothyroidism is incompletely understood. It is postulated that infrequent or absent ovulation leads to deficient secretion of

luteinizing hormone which may result in relative estrogen excess thereby causing menorrhagia. There may be episodes of amenorrhea interspersed with periods of heavy vaginal bleeding also.

Various studies have reported that there are changes in cycle length, amount and duration of bleeding associated with thyroid disorders. Sometimes they may also present with infertility, recurrent pregnancy losses and galactorrhoea [51].

Fig 5 Menorrhagia patients who had Hypothyroidism



Study conducted by Ajmani et al at a tertiary care hospital in 100 women aged between 15 and 45 years with menstrual disorders has shown, 44 % had thyroid disorders in which subclinical hypothyroidism was prevalent in 20 %, overt hypothyroidism in 14 %, and overt hyperthyroidism in 8 % of the women which was confirmed clinically and biochemically[34].

In a study conducted by Bhavani et al among 200 women, 38 cases have thyroid dysfunction (19%), 76.3% (29 out of 38) of thyroid dysfunction was seen

among nonstructural causes of AUB and 23.6% (9 out of 38) of thyroid dysfunction was seen in structural causes of AUB and menorrhagia is seen in 54% of cases, acyclical bleeding in 20.5% of cases and polymenorrhagia in 8.5% cases [35].

Deshmukh et al in their study noticed that subclinical hypothyroid and overt hypothyroid or profoundly hypothyroid cases together were the commonest thyroid dysfunction and menorrhagia was their commonest menstrual irregularity. These authors concluded that biochemical evaluation of thyroid function should be mandatory in all cases of AUB [36].

Gowri et al conducted a study on Role of thyroid function tests in women with abnormal uterine bleeding and found relationship between the thyroid gland and gonads which has more frequent occurrence of thyroid disorders in women than in men and by common appearance of goiter during puberty, pregnancy and menopause. Both hypothyroidism and hyperthyroidism may result in menstrual disturbances. They suggested that there is 17% incidence of thyroid diseases in India. Hence women with abnormal uterine bleeding are to be screened for thyroid dysfunction [37].

In a study conducted by Sangeetha et al on Thyroid dysfunction in dysfunctional uterine bleeding, the majority of patients were in the age group of 31-40years(42%). The most common complaint in hypothyroidism was menorrhagia (78.6%) followed by polymenorrhoea (10.52%), menometrorrhagia and metropathia haemorrhagica (5.26%). Hence normalization of thyroid status may correct the menstrural disturbances. So it is important to evaluate for thyroid dysfunction in all the women with menstrual irregularities[38].

Thyroid function test must be done in women presenting with abnormal uterine bleeding and also in those presenting with fatigue, obesity, lethargy in addition to infertility, luteal phase defects, delayed puberty and recurrent abortions. Also those presenting with thyroid dysfunction must be screened for menstrual disorders.

As there is 17% incidence of thyroid diseases in India, as per Neelu et al in their study on thyroid profile in menstrual disorders, it is important to screen for thyroid dysfunction and treat thyroid problems. This avoids unnecessary hormonal treatment with progestogens and surgery such as hysterectomy[39].

Studies conducted by Sruthi et al to find prevalence of hypothyroidism in patients with provisional diagnosis of dysfunctional uterine bleeding, had reported that subclinical hypothyroidism has a 11% prevalence in the population. It is necessary to evaluate thyroid function in cases with dysfunctional uterine bleeding in all age groups[40].

It has been documented that both hypothyroidism and hyperthyroidism can be associated with abnormal bleeding. In women with hypothyroidism, menstrual abnormalities, including menorrhagia is common. Hyperthyroidism can result in oligomenorrhoea and amenorrhoea and it can also lead to elevated levels of plasma estrogen [6].It was stated that hypothyroidism and hyperthyroidism can both depress ovarian and menstrual function. Altered pituitary functions, thyrotrophin releasing hormone and prolactin level causes menstrual irregularities[7].

Rosalind Pitt Rivers and WR Trotter in their earlier publication 'The thyroid Gland' stated that the effect on ovarian function is most commonly observed in the rhythm of the estrus cycle in thyroid deficiency which leads to lengthening or irregularity. 'Chu' conducted a study on ovaries of rabbits from which thyroid was removed surgically and found a marked increase in the number of unruptured follicle and a decrease in the number of ovulations. He attributed these changes to an increase in the secretion of FSH and a decrease in that of LH by the pituitary[41].

Scott and Mussey, in their study on myxoedema patients have reported incidence of subjective menorrhagia varies from 32 to 80% and it is a frequent complaint which is presented to physicians. Hyperthyroidism in contrast is associated with oligomenorrhoea and amenorrhoea which are in proportion with the severity of the thyrotoxicosis. Menorrhagia associated with hypothyroidism responds promptly to thyroid replacement, often the doses are insufficient to correct the other manifestations of the condition, so it was suggested that thyroxine have a direct effect on the spiral arterioles and on haemostasis during menstruation[42].

Ivor M.D. Jackson, stated that thyrotropin releasing hormone was equally effective in stimulating prolactin secretion from the normal pituitary gland but the importance of this hypothalamic releasing factor in the regulation of the pituitary thyroid axis in human beings has to be studied further, for understanding physiologic importance[43].

Study conducted by Wallance et al has observed the incidence of hypothyroidism around 44.44%in cases with menstrual irregularities. Authors in their study, also documented 18 cases of menstrual irregularities, out of which 8 cases presented with menorrhagia. Among them 5 pateints are diagnosed to have hypothyroidism. Hypothyroidismin these patients was due to low TSH levels so symptomatology i.e., menorrhagia can be due to low thyroid hormone resulting in less metabolism of estrogen and hence relatively high estrogen in circulation which causes menorrhagia[44].

In Wallance et al study among 10 oligomenorrhoea patients 8 had hypothyroidism. Hence in spite of increased TSH output, thyroid hormone production is less. When the thyroid hormone production is less it provokes more TSH release. This high TSH level increases, prolactin secretion which is responsible for oligomenorrhoea[44].

Jayadey Mukherjee and NN Roy Chowdhary conducted a study in 70 cases of puberty menorrhagia, it was reported that 5 cases had hypothyroidism (7.15%) and 3 out of 5 hypothyroid patients had no other disturbance clinically suggestive of hypothyroidism. Hypothyroidism was the second common cause of excessive bleeding in puberty. Adolescents with hypothyroidism are likely to have milder symptoms than older patients. The cause of excessive bleeding in hypothyroidism remains in the area of assumption [45].

Study conducted on early hypothyroidism in patients with menorrhagia by Douglas et al estimated 67 apparently euthyroid menorrhagic women with a thyrotropin releasing hormone test, 15 (22%) out of 67 showed “mild primary hypothyroidism” characterised by an elevation of basal TSH level (5.9 MU/L), lowering of serum thyroxine levels (85 nmol/l) and exaggerated response of serum TSH and thyroxine to administration of thyrotrophin releasing hormone. The terms “early” and “potential” hypothyroidism describe the preliminary phase of hypothyroidism. During the follow up, menorrhagia disappeared within 3 to 6 months and did not recur in 1 to 3 years in all patients with early hypothyroidism to whom L-

thyroxine was given along with improvement in thyroid profile without change in triiodothyroxine levels[46]

Dutta et al carried out a study on the hormonal profile of oligomenorrhoeic women. Radioimmunoassay of TSH, LH and prolactin were done at serial intervals and T3, T4, TSH were done randomly. This study showed that prolactin and T3play most significant role in deciding the FSH, LH levels and sometimes anovulation associated with amenorrhoea. The cause of oligomenorrhoea is mostly associated with anovulation which is related to either elevated prolactin or T3 levels or due to hypothyrodisim. Gonadotrophin level is being regulated by these hormones[47].

In a study conducted by Lakshmi Singh et al showed that 33.3% patients with hypothyroidism had menorrhagia because of poor progesterone production which is associated with persistent endometrial proliferation and may be accountable for massive bleeding. Another mechanism for this may be failure of LH secretion. Majority of patients with hypothyroidism had oligomenorrhoea due to galactorrhoea – amenorrhoea syndrome in longstanding hypothyroid patients[2]. Hypothyroidism can also be associated with acquired Von Willebrand's Disease leading to menorrhagia which will resolve following treatment of hypothyroidism[48].

William J. Butler involved 189 hypothyroid women in his study to find out their menstrual pattern and fertility status. Majority of them i.e, 91 patients (71.09%) had subclinical hypothyroidism, 46.87% had normal menstrual pattern. Oligomenorrhoea was the commonest menstrual abnormality found mainly in younger age group women. Menorrhagia was common in older age group. In this study author has commented that majority of cases are subclinical, and it is essential to evaluate thyroid function in all women with intractable menstrual disorders, infertility and recurrent pregnancy loss[10].

Charusheela et al in their study conducted on 213 patients with DUB, observed that, menorrhagia was the most common menstrual disturbance. Hypothyroidism was detected in 28.17% of the cases with proliferative endometrium. Majority of patients (78%) responded to medical treatment thereby avoiding hormones or surgical intervention. It was also noted that 45% patients were clinically

euthyroid but their biochemical levels are altered, while 55% patients had symptoms/ signs/ both. Easy fatiguability was the commonest symptom[49].

Table B: Menstrual pattern among hypothyroid patients

S.NO	Type	No. of patients	% (out of 60)
1.	Menorrhagia	38	63.33
2.	Polymenorrhagia	14	23.33
3.	Metropathia	4	6.66
4.	Metrorrhagia	4	6.66

Menstrual irregularities and bleeding problems are common in hypothyroid women. Amenorrhoea can be a result of hypothyroidism either with normal prolactin levels or with TRH induced increase in prolactin. Sex hormone binding globulin (SHBG) is a glycoprotein synthesised in liver which contains a single binding site for androgens and estrogens. Estrogen and thyroxine are stimulatory for its production.
Free oestrodiol levels are increased because of significant decrease in SHBG. The total binding capacity of SHBG will thus influence the amount that is free and unbound. High levels of estrogen and sustained availability leads to prolonged period of amenorrhoea followed by acute, often profuse bleeding with excessive blood loss[11].Among structural causes, leiomyoma is associated with 9% of thyroid dysfunction, of which 5.19% of patients have subclinical hypothyroidism. Among non structural causes of AUB subclinical hypothyroidism is the commonest (15.38%) followed by overt hypothyroidism (14.2%). Hyperthyroidism was seen in 2.19% of cases[35].

Material and methods

Source of Data: Women in reproductive age group with abnormal uterine bleeding who have visited to R.L. Jalappa Hospital and Research Centre constituent of Sri Devaraj Urs Medical College, Tamaka, Kolar, from November 2014 to June 2016 were included in this study. Institutional ethical clearance certificate was obtained before start of study.

STUDY DESIGN: A prospective, observational study.

STUDY PEROID: 20 months.

SAMPLE SIZE: 151

STATISTICAL ANALYSIS: Data was entered into Microsoft excel data sheet and statistical analysis was done using EPI INFO 7 VERSION software. Descriptive statistics such as frequency, proportion, mean, standard deviation was computed depending upon qualitative and quantitative data. Confidence interval of 95% was considered. Depending on review of literature, 11% frequency was used in assessing sample size. Five percent was taken as confidence limits. Chi-square test was the test of significance for qualitative data. $p \leq 0.05$ was considered as statistically significant.

Sample size was calculated using

$n= [DEFF \times Np(1-p)]/ [d2 /Z2\ 1-\alpha/2 \times(N-1)+ p \times(1-p)]$

Method of collection of data : (including sampling procedure, if any)

Data regarding socio demographic profile, medical and surgical history was collected.

Inclusion Criteria :

Women in reproductive age group who were provisionally diagnosed to have abnormal uterine bleeding.

All patients who had major complaint of menstrual disturbances such as menorrhagia, polymenorrhagia, polymenorrhoea, metropathia hemorrhagica, metrorrhagia, oligomenorrhoea and hypomenorrhoea.

Exclusion Criteria :

Patients who were on
Hormones (estrogens, progestrogens)
IUCD users
Genital malignancies
Known cases of coagulopathy or who were diagnosed during work up
Endometrial polyps,
Fibroids
History of bleeding disorders
Patients with previous known thyroid disorder.

Methodology:

Detailed history with special relevance to age, bleeding pattern was collected. Onset, duration, amount of bleeding, complaints related to thyroid dysfunction are noted in detail. Detailed physical examination, neck examination, systemic and per speculum and bimanual pelvic examination are done in cases included for study.
Informed consent obtained from all subjects.
Investigations such as:

Complete blood count was done using 5 part analyser
Bleeding time
Clotting time
Prothrombin time
Activated partial thromboplastin time, and other tests of coagulation where ever clinically indicated were done. Blood group and Rh typing, Complete urine analysis, Fasting and postprandial blood glucose was done using VITROS 250 dry chemistry analyzer which works on reflectance photometry HIV, HBSAg by using chemiluminescene, VDRL by slide method.

All patients are subjected to T3, T4 and TSH- (2ml of venous blood collected in fasting status, assayed by competitive chemiluminescence immunoassay using VITROS ECI machine).

Women with abnormal levels of thyroid hormones are subjected to further investigations such as free T3 and free T4 (as and when required). Abdominal and pelvic ultrasonography was done to rule out abdominal and/ or pelvic pathology. Hysteroscopy, dilatation and curettage (D&C) was performed as and when required.

OBSERVATION AND RESULTS

Abnormal uterine bleeding is one of the most commonly encountered condition in gynaecological practice. This study included 151 women with abnormal uterine bleeding, who attended to RL Jalappa hospital and research centre from December 2014 to June 2016.

The following are the tables which will give a descriptive analysis of the age distribution, the parity distribution, symptomatic distribution of abnormal uterine bleeding and its association with thyroid dysfunction.

TABLE 1: DISTRIBUTION OF PATIENTS ACCORDING TO AGE (n=151)

Age group (years)	No. of cases	Percentage
≤20	35	23.17
21-30	45	29.84
31-40	**55**	**36.40**
>40	16	10.59
TOTAL	151	100%

According to above table highest number of patients in the study group belong to the age group of 31-40 years –55 (36.40%) followed by age group 21- 30 years and 23.17% in age group ≤20 years. Least number of patients were seen in age group >40 years- 16 (10.59%).

CHART 1: DISTRIBUTION OF PATIENTS ACCORDING TO AGE

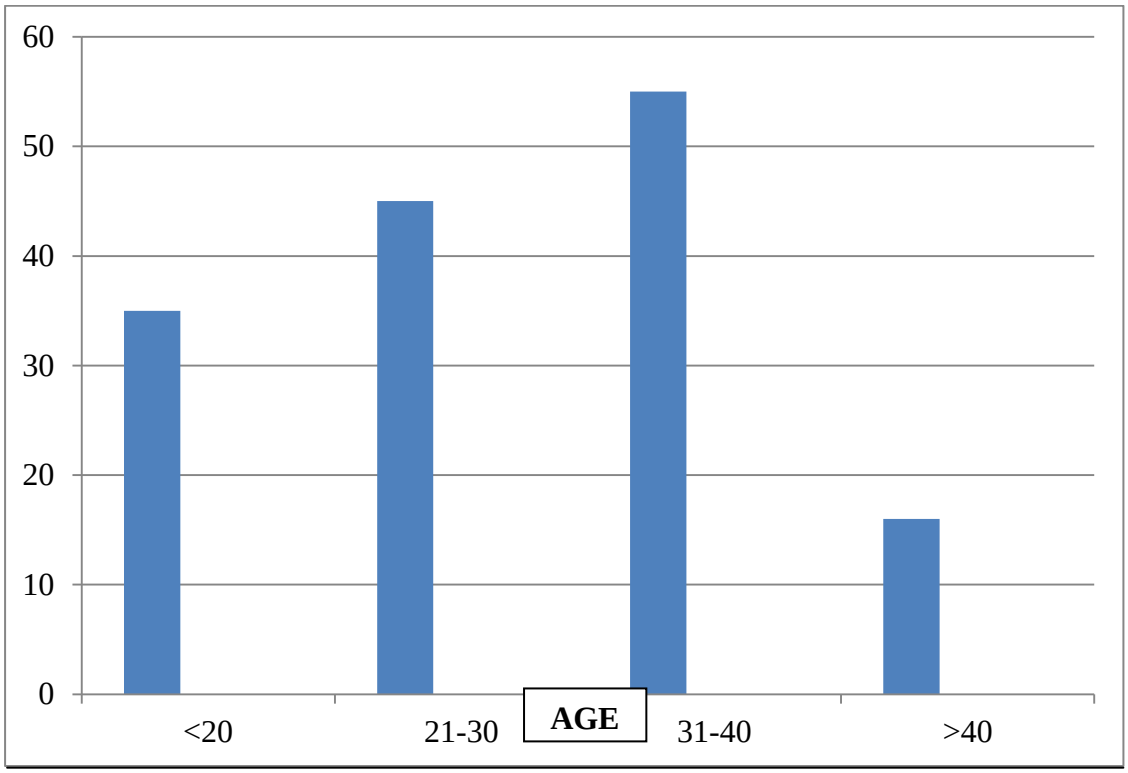


TABLE 2: DISTRIBUTION OF PATIENTS ACCORDING TO PARITY

PARITY	NO. OF PATIENTS	PERCENTAGE
Unmarried	**38**	**25.17%**
0	9	5.96%
1	13	8.60%
2	34	22.52%
3	32	21.20%
4	15	9.93%
5	10	6.62%
TOTAL	151	100%

The above column shows relationship of AUB with parity. Among 151 cases of AUB 38 (25.17%) patients were unmarried, nulliparas were 9 (5.96%) , 13 (8.60%) patients were para 1, 34 (22.52%) patients were para 2, 32 (21.20%) patients were para 3, 15 (9.93%) patients were para 4 and 10 (6.62%) patients were para 5. In this study maximum number of patients were unmarried (25.17%) and minimum number of patient presenting as clinical AUB cases were of nullipara (5.96%).

CHART 2: DISTRIBUTION OF PATEINTS ACCORDING TO PARITY

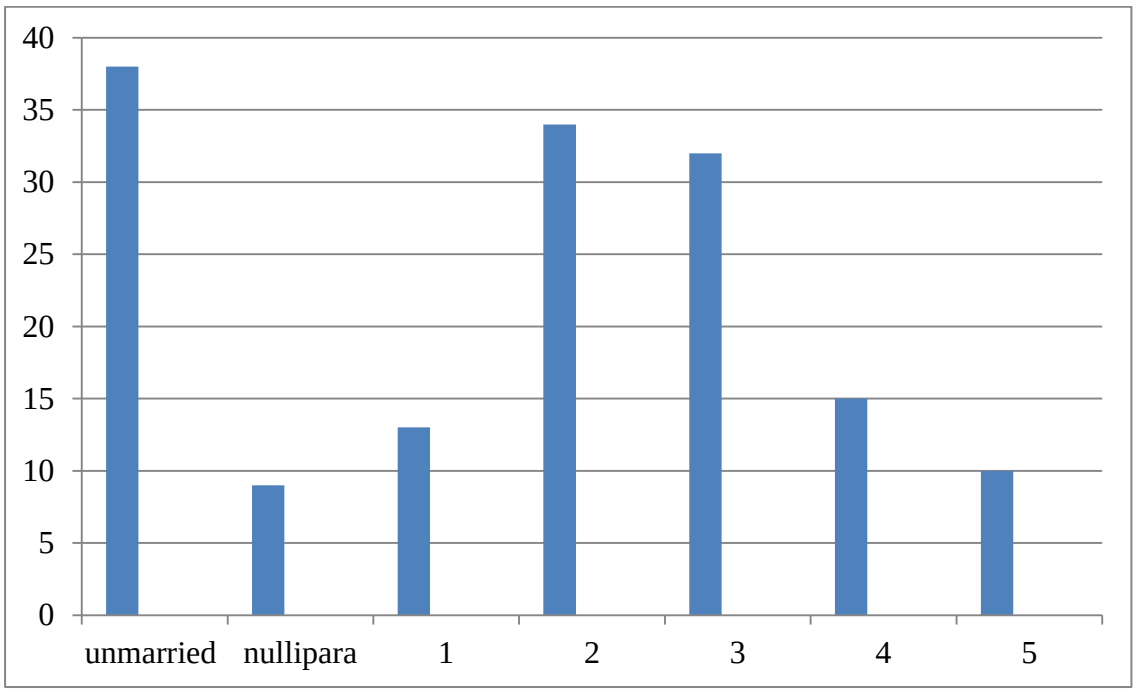


TABLE 3: DISTRIBUTION OF PATIENTS ACCORDING TO SYMPTOMS

Type of bleeding	No. of cases	Percentage
Acyclical	22	14.56%
Hypomenorrhoea	7	4.63%
Menorrhagia	**49**	**32.45%**
Metrorrhagia	4	2.65%
Oligomenorrhoea	29	19.21%
Polymenorrhagia	28	18.55%
Polymenorrhoea	12	7.95%
TOTAL	151	100%

The above column shows 151 patients who came with the complaints of different bleeding patterns. Commonest was menorrhagia 49 (32.45%), Among others 14.56% of cases presented with acyclical bleeding (MPH), 19.21% with Oligomenorrhoea, 18.55% had polymenorrhagia, 7.95% had polymenorrhoea, 4.63% had hypomenorrhoea, 2.65% had metrorrhagia. Maximum patients were seen with complaint of menorrhagia, following which oligomenorrhoea was seen.

CHART 3: DISTRIBUTION OF PATIENTS ACCORDING TO BLEEDING PATTERN

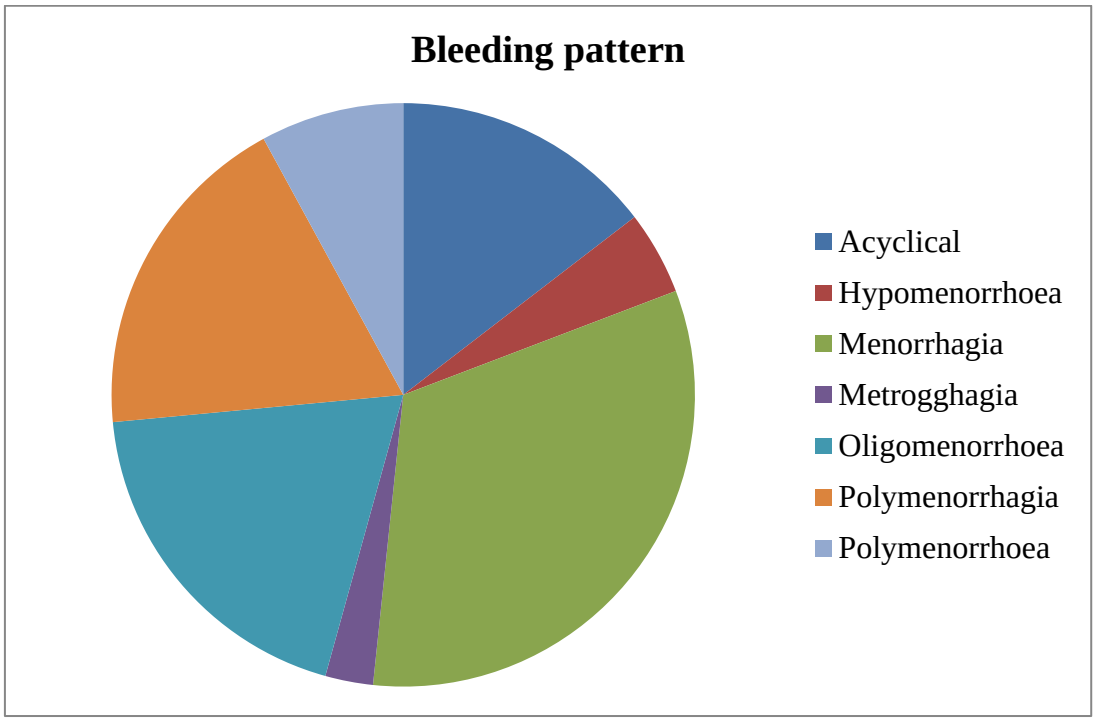


TABLE 4: DISTRIBUTION OF PATIENTS ACCORDING TO AGE GROUPS AND BLEEDINGPATTERN

Age in years	No.of cases	Acyclical		Hypomenorrhoea		Menorrhagia		Metrorrhagia		Oligomenorrhoea		Polymenorrhagia		Polymenorrhoea	
<20	35	8	22.85%	1	2.85 %	14	**40%**	1	2.85 %	6	17.4 %	0	0	5	14.28 %
21-30	45	4	8.88 %	4	8.88 %	17	**37.77 %**	0	0	11	24.44 %	8	17.77 %	1	2.22 %
31-40	55	8	14.54%	1	1.81 %	15	**27.27 %**	3	5.45 %	11	20%	12	21.81 %	5	9.09 %
>40	16	2	12.57%	1	6.25 %	3	18.75 %	0	0	1	6.25 %	8	**50%**	1	6.25 %
Total	151	22		7		49		4		29		28		12	

Patients with age less than and equal to 20 years, most frequent bleeding pattern was menorrhagia (40%). Followed by acyclical bleeding (22.85%), Oligomenorrhoea was present in 17.14% of the cases. Similarly in age groups- 21-30 years and 31 -40 years the commonest bleeding pattern was menorrhagia. Women with age>40 had polymenorrhagia (50%) as their commonest abnormal bleeding pattern.

CHART 4: DISTRIBUTION OF PATIENTS ACCORDING TO AGE GROUPS AND BLEEDINGPATTERN

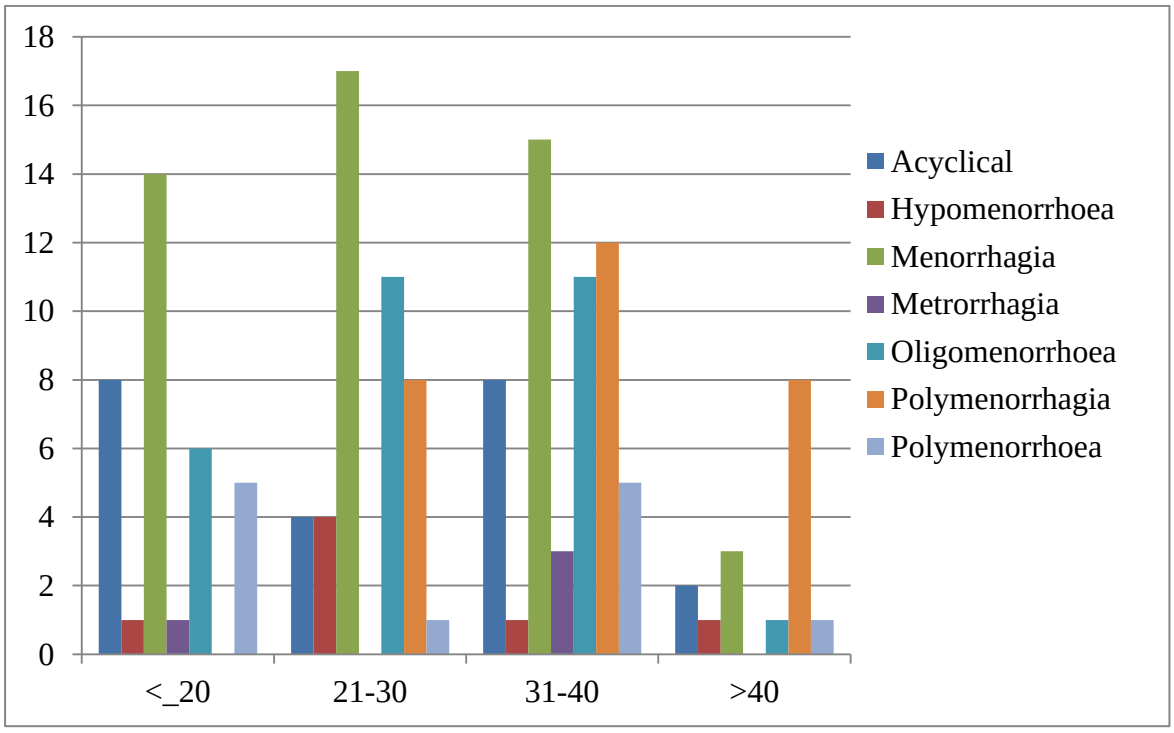


TABLE 5: DISTRIBUTION OF PATIENTS ACCORDING TO THYROID FUNCTION.

Thyroid disorder	No. of cases	Percentage
Euthyroid	**116**	**76.83%**
Hypothyroid	11	7.28%
Subclinical Hypothyroid	20	13.25%
Hyper thyroid	4	2.64%
Total	151	100%

According to this table utmost number of apparently normal patients with AUB belong to the category of Euthyroid (76.83%%), followed by subclinical hypothyroidism (13.25%). Hormonal levels revealing profound hypothyroidism in patients without any symptoms of thyroid dysfunction was present in only 7.28 % of cases. 2.64% of cases had hyperthyroidism though they were clinically normal.

CHART-5: THYROID FUNCTION

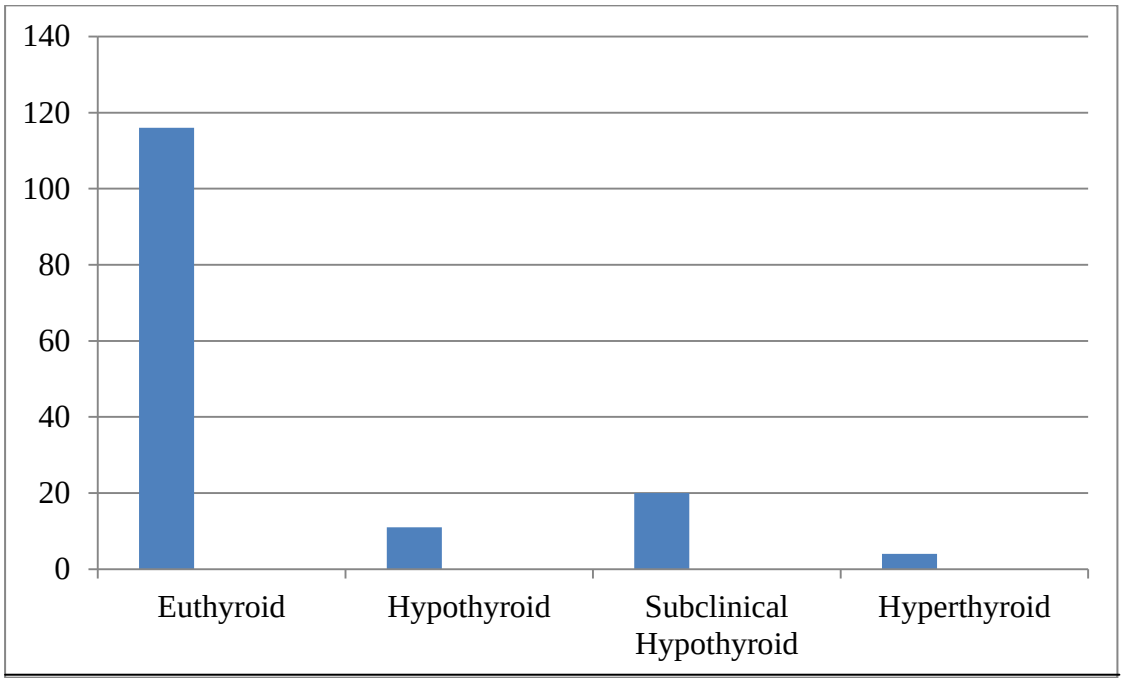


TABLE 6: THYROID DYSFUNCTION IN RELATION TO PARITY

Parity	No. of cases	Euthyroid	Thyroid dysfunction			Total Thyroid Dysfunction	Percentage
			Hypo	Sub	Hyper		
Unmarried	38	29	4	4	1	9/38	23.68%
0	9	6	1	2	0	3/9	**33.33%**
1	13	12	0	1	0	1/13	7.69%
2	34	26	2	5	1	8/34	23.52%
3	32	24	3	4	1	8/32	25%
4	15	11	0	3	1	4/15	26.6%
5	10	8	1	1	0	2/10	20%
Total	151	116	11	20	4	35	

This table shows the relationship of parity to thyroid dysfunction in patients with provisionally diagnosed AUB. Thyroid dysfunction was commonest among nulliparous patients about 33% and next common among patients who were para 4, i.e, 26.6%. Out of 38 patients among unmarried group, 9 (23.68%) of them had thyroid dysfunction. Thyroid dysfunction was least common in patients who were primipara only (7.69%). This shows that thyroid dysfunction can lead to infertility (nulliparous state) The difference in thyroid functioning in individual type of parity is not statistically significant. Chisquare = 13.34, P= 0.001 (NS).

CHART 6: THYROID DYSFUNCTION IN RELATION TO PARITY

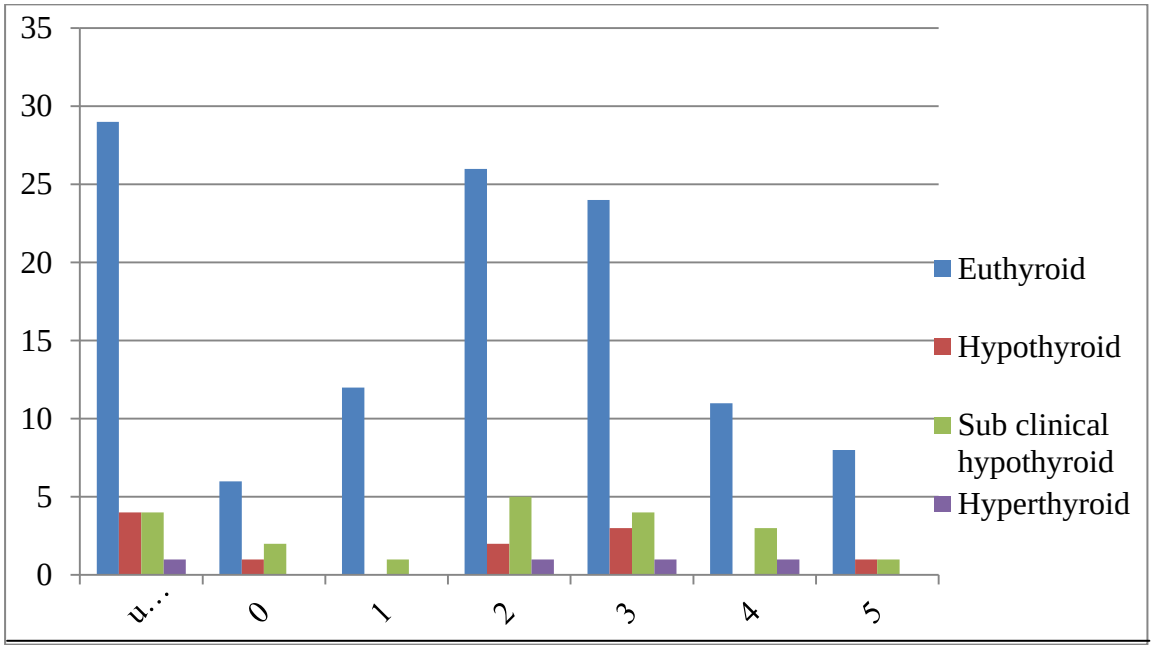


TABLE 7: THYROID DYSFUNCTION IN DIFFERENT AGE GROUPS

AGE	NO.OF CASES	EUTH-YROID	HYPO	SUBC-LINI	HYPER	TDF	PERCEN-TAGE
≤ 20	35	26	5	4	0	9/35	25.71%
21-30	45	39	1	4	1	6/45	13.33%
31-40	55	39	2	11	3	16/55	**29.09% (p<0.001)**
>40	16	12	3	1	0	4/16	25%
Total	151	116	11	20	4	35	23.17%

This table shows the relationship of thyroid dysfunction to different age groups. Among women with abnormal uterine bleeding, thyroid dysfunction was commonest in the age group between 31-40 years –29.07%. This was followed by 25.71% among patients of age group less than or equal to 20 years and 25% of patients more than 40 years. Thyroid dysfunction was least common in patients between 21-30 years-13.33%. This shows that thyroid dysfunction becomes common as patients age advances and in this study it is commonly seen in patients more than 31 years. Thyroid dysfunction is least common in patients between 21-30 years of age. The difference in thyroid functioning in individual age groups is statistically significant. Chisquare = 157.70 **p< 0.001**, **Statistically significant.**

CHART 7: THYROID DYSFUNCTION IN DIFFERENT AGE GROUPS

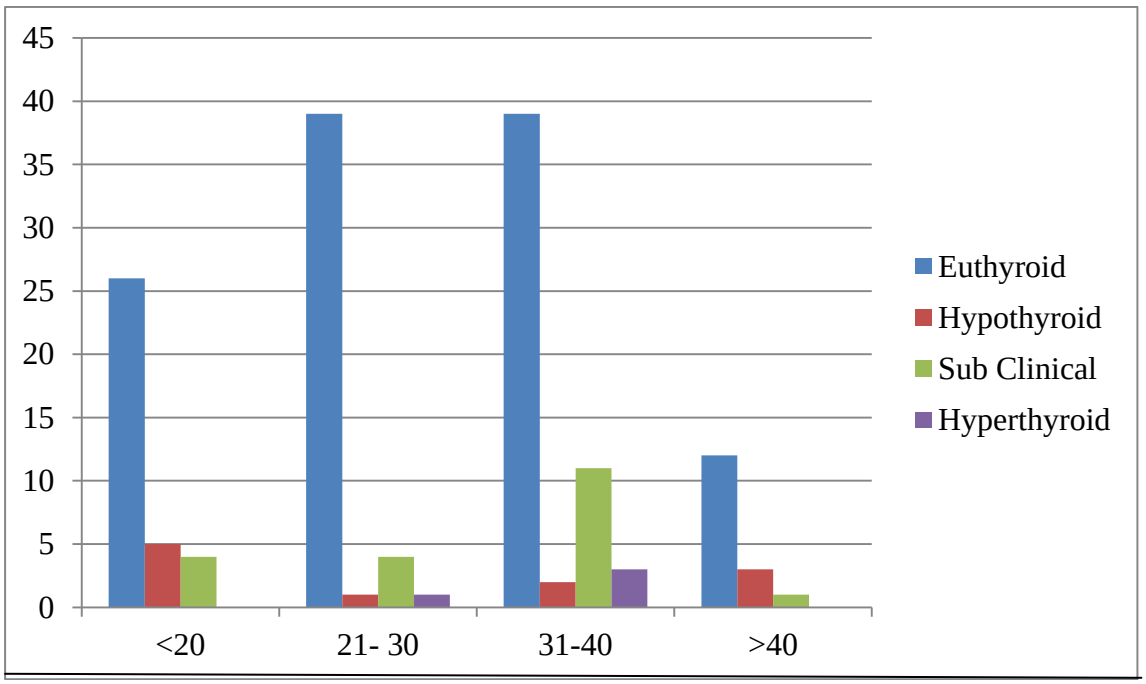


TABLE 8: BLEEDING PATTERN AND THYROID DYSFUNCTION

Types of Bleeding	No. of cases	Euth-yroid	Hypot-hyroid	Subcli-nical	Hyper-thyroid	TDF	Percent age
Acyclical (MPH)	22	16	3	3	-	6/22	27.2%
Hypomenorr-hoea	7	7	0	-	-	0	0%
Menorrhagia	49	36	3	10	-	13/49	26.53%
Metrorrhagia	4	4	0	-	-	0	0%
Oligomenorr-hoea	29	19	4	2	4	10/29	**34.48%**
Polymenorr-hagia	28	26	1	1	-	2/28	7.14%
Polymenorr-hoea	12	8	0	4	-	4/12	33.3%
Total	151	116	11	20	4	35	23.17%

This table shows how thyroid dysfunction which can be hypothyroidism, subclinical hypothyroidism or hyperthyroidism is related to various types of bleeding abnormalities. Thyroid dysfunction was commonest in patients with oligomenorrhoea – 34.48 %, next common in patients with polymenorrhoea– 33.3 % followed by patients with acyclical bleeding– 27.2 %. Patients with menorrhagia had thyroid dysfunction only in 26.53% of cases. Thyroid dysfunction was least common in patients with polymenorrhagia. (7.14%) and absent in patients with metrorrhagia and hypomenorrhoea. The difference in thyroid functioning in individual type of bleeding pattern is not statistically significant. Chisquare value= 10.65, P= 0.001(NS).

CHART 8 : BLEEDING PATTERN AND THYROID DYSFUNCTION

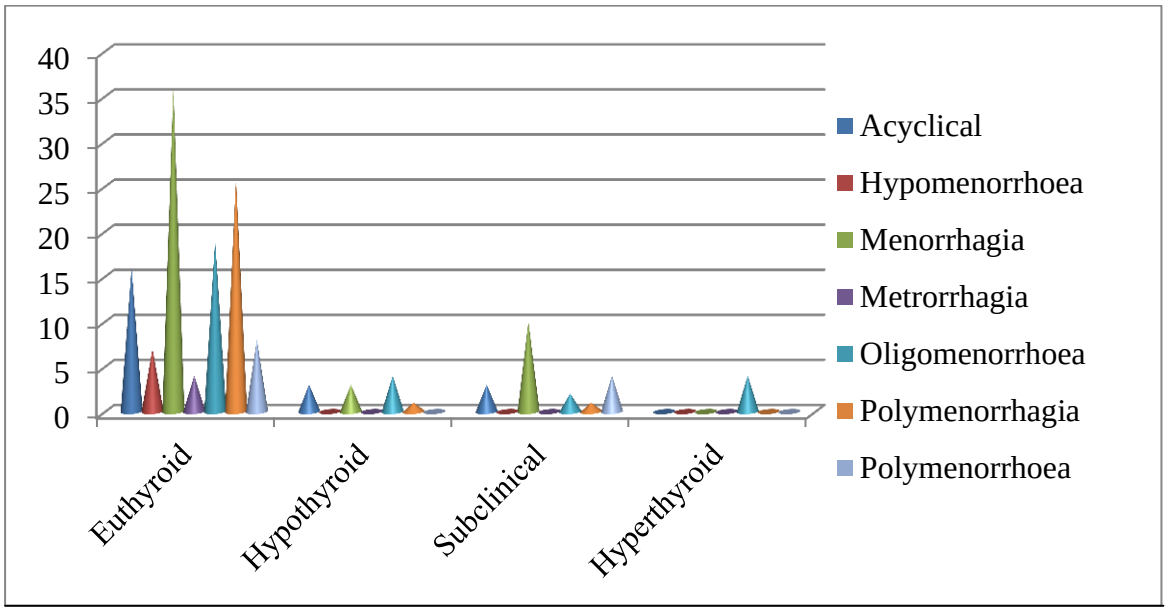


TABLE 9: TSH LEVELS AND DIFFERENT BLEEDING PATTERNS

TSH mcIU/ml	No.of cases	Acyclical	Hypomenorrhoea	Menorrhagia	Metrorrhagia	Oligomenorrhoea	Polymenorrhagia	Polymenorrhoea
≤0.39	4	-	-	-	-	4(100%)	-	-
0.4- 4.2 N	116	16 (13.79%)	7 (6.03%)	**36 (31.0%)**	4(3.44%)	19 (16.37%)	26 (22.41%)	8(6.89%)
4.3- 50 Sub	20	3 (15%)	-	**10 (50%)**	-	2(10%)	1(5%)	4(20%)
> 50	11	3 (27.27%)	-	3 (27.27%)	-	**4 (36.36%)**	1(9.09%)	0

This table shows the relation of TSH levels to different types of bleeding patterns. Among patients with TSH levels ≤0.39 mcIU/ml all of them presented with symptoms of oligomenorrhoea. Patients with TSH levels moderately elevated 4.3-50mcIU/ml as seen in subclinical hypothyroidism, 50% of patients presented with menorrhagia, 20 % of patients presented with polymenorrhoea and 15% presented with acyclical bleeding. In this group maximum number of patients presented with menorrhagia. Patients with TSH levels profoundly elevated i.e, >50mcIU/ml had Oligomenorrhoea in 36.36% of cases, menorrhagia and acyclical bleeding in 27.27% of cases. **So in this table it is seen that oligomenorrhoea was seen in patients with TSH value ≤ 0.39 mcIU/ml or when profoundly high i.e, >50mcIU/ml . On the other hand menorrhagia was mostly seen in patients with TSH value moderately elevated (4.3 - <50 mcIU/ml).**

CHART- 9: TSH LEVELS AND DIFFERENT BLEEDING PATTERNS

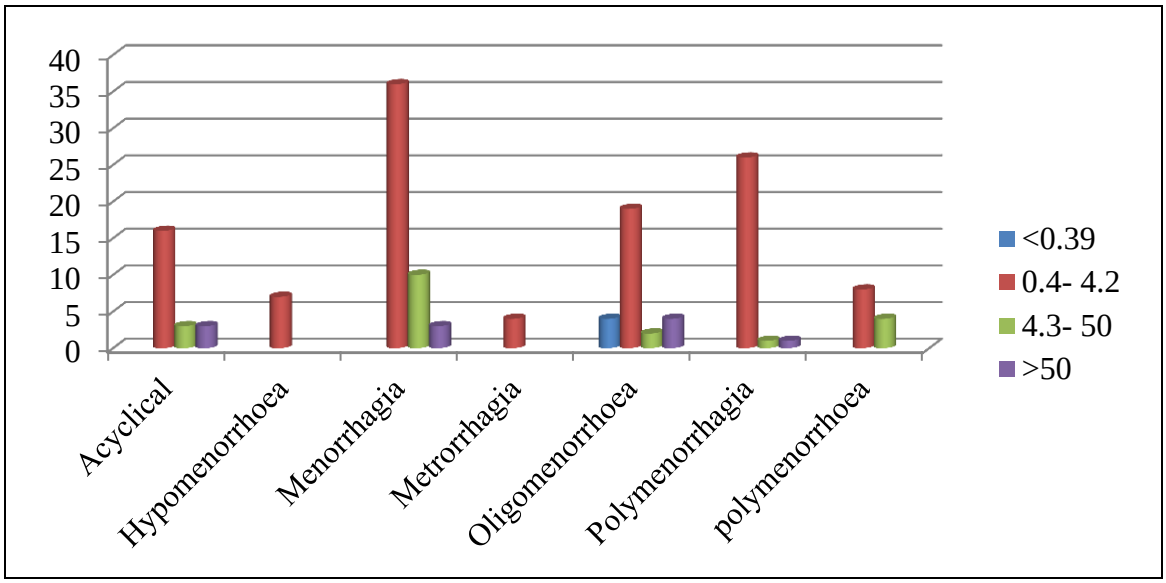


TABLE – 10: T3 LEVELS AND DIFFERENT BLEEDING PATTERNS

T3 ng/ml	No.of cases	MPH	Hypomen orrhoea	Menor rhagia	Metror rhagia	Oligomen orrhoea	Polymen orrhagia	Polymen orrhoea
≤0.71	11	3 (27.2%)	-	3 (27.2%)	-	**4 (36.36%)**	1 (9.09%)	-
0.71-2	136	19 (13.9%)	7 (5.14%)	**46 (33.82%)**	4 (2.94%)	21 (15.44%)	27 (19.85%)	12 (8.82%)
>2	4	-	-	-	-	**4 (100%)**	-	-

Normal range of T3 is 0.71- 2.0 ng/ml. This table shows the relationship of T3 levels to different types of bleeding pattern. Patients with T3 levels ≤ 0.71 had oligomenorrhoea in 36.36% of the patients, 27.2% of patients had acyclical bleeding and menorrhagia. When the T3 levels were >2 all patients had oligomenorrhoea. Only 42.85% of the total no. of patients showed abnormal T3 levels compared to 100% of patients who showed abnormal TSH levels.

CHART- 10: T3 LEVELS AND DIFFERENT BLEEDING PATTERNS

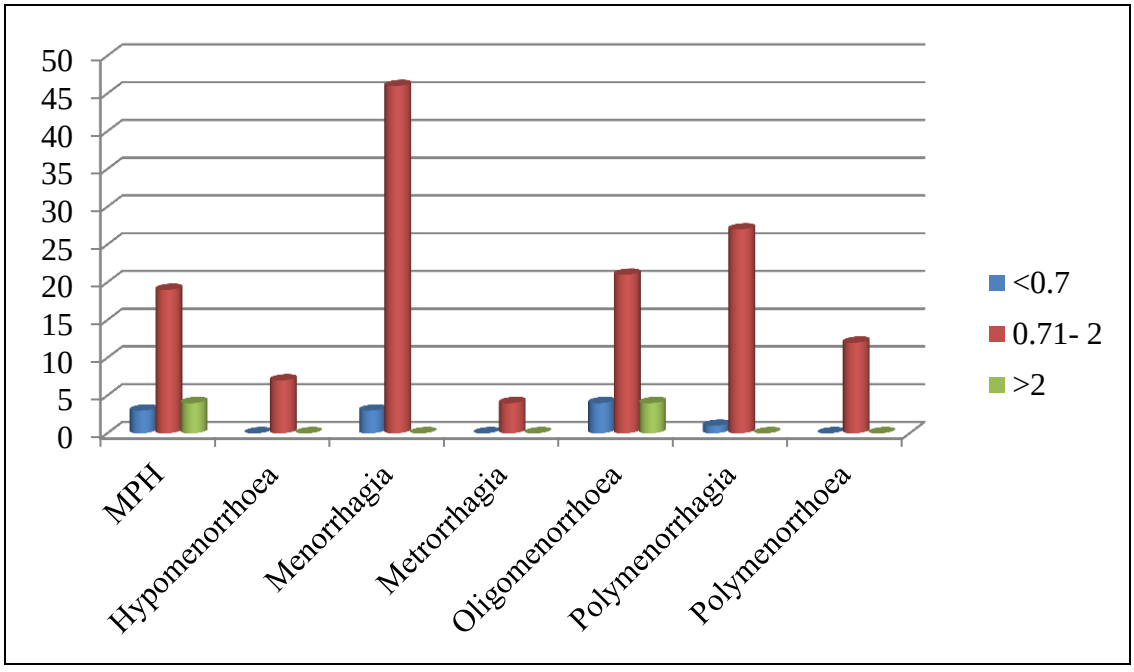


TABLE 11: T4 LEVELS AND DIFFERENT TYPES OF BLEEDING PATTERNS

T4 mcg/dl	No.of cases	MPH	Hypo Menor rhoea	Menor-rhagia	Metror-rhagia	Oligo Menor rhoea	Poly Menorr heagia	Poly Menor rhoea
≤4.5	11	3	-	3	-	**4**	1	0
4.6- 12	136	19	7	**46**	4	21	27	12
>12	4	-	-	-	-	**4**	-	-

This table shows relationship of T4 levels to different types of bleeding pattern. Patients with T4 level ≤ 4.5 had oligomenorrhoea 36.36% of the patients, 27.2% of patients had acyclical bleeding and menorrhagia. Where the T4 levels >12 all patients had oligomenorrhoea. Only 42.85% of the total No. of patients showed abnormal T4 levels compared to 100% of patients who showed abnormal TSH levels.

CHART- 11: T4 LEVELS AND DIFFERENT TYPES OF BLEEDING PATTERNS

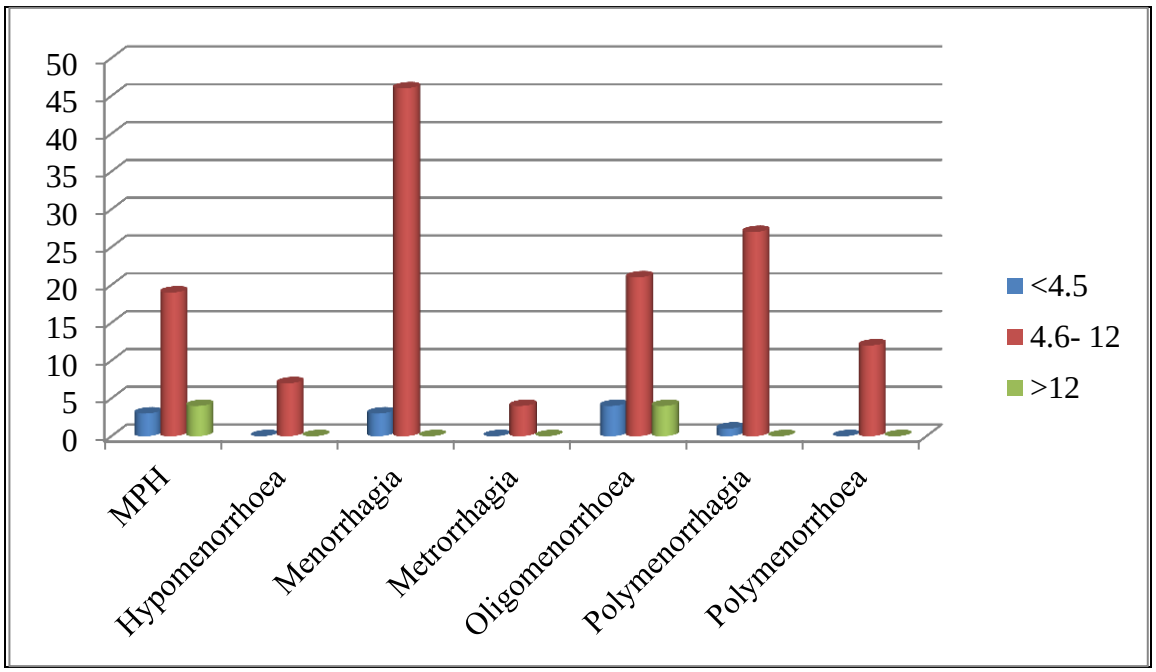


TABLE -12: SHOWING THE RANGE, MEAN, AND SD OF THE THYROID FUNCTION TESTS FOR EACH ABNORMAL UTERINE BLEEDING PATTERN

	AUB pattern	Acyclical	Hypo Meno-rrhoea	Meno-rrhagia	Metro-rrhagia	Oligo Menor-rhoea	Poly Meno-rrhaiga	Poly Menorrh-oea
TSH mcIU/ml	Mean	14.78	1.85	9.39	2.98	12.5	5.08	5.64
	SD	25.87	0.59	18.87	0.37	25.77	12.81	6.86
	Range	78.01	1.64	91.79	0.79	86.67	67.84	16.72
T3ng/ml	Mean	1.24	1.35	1.39	1.40	1.47	1.44	1.30
	SD	0.45	0.42	0.35	0.41	0.69	0.36	0.37
	Range	1.57	1.15	1.36	0.97	2.92	1.43	1.09
T4mcg/dl	Mean	7.69	8.30	8.31	10.10	8.54	7.73	8.53
	SD	2.44	1.42	2.26	1.74	4.18	1.84	1.41
	Range	8.50	4.70	8.80	4.20	16.06	8.30	4.20

The high mean TSH values are seen in women with acyclical bleeding (14.78) and followed by oligomenorrhoea (12.5).

DISCUSSION

Thyroid dysfunction is manifested by large number of menstrual aberrations. In our study patients were taken from reproductive age group which included less than 20 years, 21-30 years, 31-40 years and more than 40 years and Maximum number of patients belonged to the age group of 31-40 years. In a similar study conducted by Doifode CD et al at Bhopal as well, maximum number of patients belonged in age group 31-40 years. In our study patients with clinical signs and symptoms of thyroid dysfunction were excluded, but in their study all patients with menstrual aberrations irrespective of the presence of signs and symptoms of thyroid dysfunction were included [49].

In our study 23.68% of unmarried patients had thyroid dysfunction but in their study 15% of unmarried patients had thyroid dysfunction. In our study thyroid dysfunction was 33.33% among nulliparous women as compared to author's study which showed 6.67%. In our study patients who were para1, only 7.69% of them had thyroid dysfunction but in author's study (C.D Doifode et al) thyroid dysfunction was present in 33.33% of patients with para 1. Maximum numbers of patients with thyroid dysfunction were unmarried in our study (23.68%) as compared to Neelu S et al (9.09%) and Rani SA et al (0%), where multipara with hypothyroidism are more common in their studies. Our study shows maximum higher rate of thyroid dysfunction in nulliparous women (33.33%) as compared to Neelu S et al (9.09%) study, which was conducted in Jammu. This probably reflects geographical variation in thyroid dysfunction with younger age group being affected in our area. Higher frequency in nulliparous women probably may contribute to infertility [39, 51].

TABLE 13: AGE PATTERN IN AUB WITH THYROID DYSFUNCTION

Age in years	No. of patients with thyroid dysfunction			
	C.D. Doifode et al n= 213	Deshmukh PY et al n =100	Malini et al n= 250	**Present study** n= 151
≤ 20 years	7 (11.67%)	7 (31.8%)	**4 (44.44%)**	9 (25.71%)
21-30 years	10 (16.6%)	6 (22.2%)	14 (15.9%)	6 (13.33%)
31- 40 years	**29 (48.33%)**	14 (31.8%)	21 (19.2%)	**16 (29.09%)**
> 40 years	14 (23.33%)	**3 (42.8%)**	12 (40%)	4 (25%)
Total	60	30	54	35

This table compares the relationship of age patterns with thyroid dysfunction among patients with AUB in the present study and in various studies conducted in different parts of India. From this table it is noted that thyroid dysfunction was commonest in the age group 31-40 years, both in the present study and also in the study by C.D. Doifode et al. But in Deshmukh PY et al study, thyroid dysfunction is commonly seen in age group more than 40 years and in study by Malini et al, it is commonly seen in less than 20 years of age followed by more than 40 years of age group. Thyroid dysfunction was least common in the reproductive age group, 21- 30 years in rest of the studies, except in C.D. Doifode et al where it was in less than 20 years of age [49, 50, 53].

In our study 151 cases were included with the complaint of abnormal menstruation. Cases of metropathia haemorrhagica (MPH), menorrhagia, polymenorrhagia, polymenorrhoea, metrorrhagia, oligomenorrhoea, hypomenorrhoea were included.

In the Doifode et al study 213 cases of clinically diagnosed DUB were taken and women with oligomenorrhoea, hypomenorrhoea, and polymenorrhoea were excluded.

In both the studies the commonest complaint was menorrhagia. In the author's study (C.D.Doifode et al) 60 patients out of 213 patients showed their thyroid

dysfunction as hypothyroidism(either subclinical or profound) author's study had no case of hyperthyroidism.

In our study, all women with complaints of menorrhagia, metropathia, polymenorrhoea, polymenorrhagia and metrorrhagia showed their thyroid dysfunction to be hypothyroidism either subclinical or hypothyroidism.

TABLE 14: MENSTRUAL PATTERN IN HYPOTHYROIDISM

Bleeding Pattern	Kakuno Y et al	Deshmukh PY et al	C.D.Doifode et al	**Present Study**
Acyclical	**7 (6.3%)**	4 (8.32%)	4 (6.66%)	3 (27.2%)
Menorrhagia	-	13 (27%)	**38 (63.33%)**	3 (27.2%)
Polymenorrhagia	-	**17 (35.36%)**	14 (23.33%)	1(9.09%)
Metrorrhagia	2 (1.8%)	-	4 (6.66%)	-
Oligomenorrhoea	6 (5.4%)	10 (20.8%)	-	**4 (36.3%)**
Polymenorrhoea	2 (1.8%)	4 (8.32%)	-	-
Hypomenorrhoea	-	-	-	-
Total Hypothyroid Patients	17	48	60	11

The menstrual abnormality commonly seen in hypothyroidism was menorrhagia, in a study conducted by C.D. Doifode et al (63.33%) at Bhopal. In present study, oligomenorrhoea was the commonest menstrual abnormality (36.3%) [49].

In a study conducted by Kakuno Y et al in Japan, acyclical bleeding (6.3%) was commonest followed by oligomenorrhoea (5.4%) [52].

Polymenorrhagia is the commonest menstrual abnormality (35.36%) in the study by Deshmukh PY et al conducted at Maharashtra. Acyclical bleeding is the least common menstrual disorder in studies conducted by Deshmukh PY et al and C.D. Doifode et al. But in our study, oligomenorrhoea was the most common bleeding pattern and acyclical bleeding was the second most common menstrual disorder.

Polymenorrhagia (9.09%) is the least common disorder in hypothyroidism in our study [50].

TABLE 15: MENORRHAGIA IN SUBCLINICAL HYPOTHYROIDISM

Studies and total no.of women with menorrhagia	Subclinical Hypothyroidism in Menorrhagic Patients	Percentage
Douglas L et al (n = 67)	15	22.3%
Malini et al (n= 155)	28	18.06%
Deshmukh PY (n= 40)	5	12%
Bhavani et al (n= 108)	13	10.8%
Present Study (n = 49)	10	20.4%

Subclinical hypothyroidism is diagnosed in cases with normal levels of T3 and T4 [low normal levels] and raised TSH levels i.e., (Slightly raised). In this table cases with menorrhagia who were having subclinical hypothyroidism in the present study were compared with different studies.

Douglas L et al reported highest frequency of subclinical hypothyroidism of22.3% in women with menorrhagia in their study conducted in Canada, which was almost similar to our present study (20.40%).However studies by Deshmukh et al, Bhavani et al, showed lower incidence of 12%, 10.8% respectively.

TABLE16: OLIGOMENORRHOEA AND THYROID DYSFUNCTION

Study	No. of Cases	Hypo-Thyroid	Perce-ntage	Hyper-Thyroid	Perce-ntage	Total
Deshmukh PY et al	15	9/15	60%	2/15	13.33%	73.33%
Malini et al	18	2/18	11.11%	4/18	22.22%	33.33%
Ajmani et al	10	2/10	20%	4/10	40%	60%
Javed Ali et al	26	9/26	34.6%	17/26	65.3%	99.9%
Present Study	29	6/29	20.68%	4/29	13.79%	34.47%

In our present study 20.68% oligomenorrhoeic patients were showing hypothyroidism, 13.79% were having hyperthyroidism. Total patients showing thyroid dysfunction with oligomenorrhoea in present study is 34.47%.

However in contrast in a study conducted by Deshmukh PY et al most of the patients with oligomenorrhoea had hypothyroidism (60%).

In studies by different authors mentioned in this table, most of the oligomenorrhoeic patients had hyperthyroidism ranging from 65.3% to 22.22%.

In a study conducted by Javed Ali et al, 99.9% oligomenorrhoric patients had thyroid dysfunction. From these studies we can conclude that oligomenorrhoea can be a manifestation in both hypothyroid and hyperthyroid women.

In our study, oligomenorrhoea was seen with TSH $\leq$ 0.39mcIU/ml or >50mcIU/ml.

TABLE 17: OLIGOMENORRHOEA IN HYPERTHYROIDISM

Study	Oligomenorrhoea patients
Lakshmi Singh et al	64%
Javed Ali et al	58.6%
Wills G et al	36.36%
Bhavani et al	0%
Ajmani et al	80%
Present study	**100%**

This table clearly depicts that in almost all patients with hyperthyroidism, the most commonly seen menstrual disorder is oligomenorrhoea. However in a stark contrast, in Bhavani et al study there were no oligomenorrhoea patients with hyperthyroidism, instead they had menorrhagia, hypomenorrhoea and polymenorrhoea. In present study all 4 patients with hyperthyroidism had oligomenorrhoea. This shows that all patients with oligomenorrhoea should be compulsorily evaluated for thyroid dysfunction.

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CONCLUSION

- In our study thyroid dysfunction was noted in 23.17% of women with abnormal uterine bleeding, of which most common was subclinical hypothyroidism in 13.25%, followed by hypothyroidism (7.28%) and hyperthyroidism (2.64 %).

- Oligomenorrhoea (34.48%), followed by polymenorrhoea (33.3%) and acyclical bleeding (27.2%) were commonest menstrual abnormalities seen in thyroid dysfunction.

- In both hypothyroidism and hyperthyroidism oligomenorrhoea was the commonest menstrual abnormality.

- In subclinical hypothyroidism, menorrhagia was the commonest menstrual abnormality.

- Thus biochemical evaluation of T3, T4 and TSH estimations should be made obligatory in abnormal uterine bleeding cases, to detect thyroid dysfunction.

- Treatment of thyroid dysfunction in women with abnormal uterine bleeding will avoid unnecessary surgery and hormonal treatment.

SUMMARY

A total of 151 women, clinically diagnosed as abnormal uterine bleeding, from R L Jalappa Hospital and Research institute, over a period of 20 months were studied. Study was aimed to evaluate and detect thyroid dysfunction in patients with provisional diagnosis of AUB and positive cases i.e., patients showing thyroid dysfunction were referred to physician for further management.

1. In present study the patients belonged to various age groups ranging from below 20 years to 45 years. Maximum number of cases belonged to 31-40 years- 36.40%.
2. Parity of patients ranged from unmarried, 0-5, maximum number of patients with AUB belonged to unmarried group – 25.17%.
3. Commonest bleeding pattern was menorrhagia (32.45%).
4. Thyroid dysfunction was noted in 23.17% of cases (Subclinical hypothyroidism in 13.25% Hypothyroidism in 7.28% and hyperthyroidism in 2.64 % of cases).
5. Thyroid dysfunction was commonest in cases with oligomenorrhoea (34.48%) followed by polymenorrhoea (33.3%), acyclical bleeding (27.2%), menorrhagia (26.53%), polymenorrhagia (7.14%).
6. Thyroid dysfunction was commonest in nulliparous women (33.33%).
7. Predominant thyroid dysfunction was Subclinical hypothyroidism (13.25%) followed by Hypothyroidism (7.28%). Only 2.64% of cases who were hyperthyroid.
8. All 2.64% cases of Hyperthyroidism were oligomenorrhoeic.
9. Subclinical hypothyroidism was maximum among polymenorrhoeic patients (33.33%) and followed in menorrhagic patients(20.40%).
10. Oligomenorrhoea was seen in patients with TSH value $\leq$ 0.39 mcIU/ml or when profoundly high i.e, >50 mcIU/ml.
11. Out of 35 cases of thyroid dysfunction 100% cases showed abnormal TSH levels and 42.85% cases showed abnormal T3 and T4 levels. Thus TSH level has maximum sensitivity compared to T3 and T4 levels, in detecting thyroid gland dysfunction.

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ANNEXURES

CONSENT FORM

TITLE: STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING.

NAME OF PATIENT:

ADDRESS:

PHONE NUMBER:

PROCEDURE:

I the patient/ we the patient attenders have been explained about the need for thyroid function tests, the method of collection of data in detail in the language best understood by us and had the opportunity to ask questions regarding the study and abide by the study.

I have understood that my participation in this study is voluntary and I am free to withdraw anytime, without giving any reason.

I agree not to restrict the use of this data or results that arise from this study provided such a use is only scientific purposes.

I agree to take part in this study for scientific purposes.

NAME OF PATIENT:

SIGNATURE OF PATIENT:

DATE AND TIME:

INVESTIGATOR DECLERATION

Before obtaining the consent, I have explained the purpose of the study in depth. I/we have informed that there are no risk/side effects of this study. I have answered the questions regarding the study to the best of my ability.

NAME OF INVESTIGATOR: Dr. ASHRITHA REBALA

ADDRESS:

PHONE NUMBER:

SIGNATURE:

DATE AND TIME:

NAME OF IMPARTIAL WITNESS:

ADDRESS

PHONE NUMBER

SIGNATURE

DATE AND TIME

ತಿಳುವಳಿಕೆಯ ಒಪ್ಪಿಗೆ ಪತ್ರ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ:– "A STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING"

ಶ್ರೀ/ಶ್ರೀಮತಿ ಆದ ನಾನು ಈ ಮೇಲಿನ ಸಂಶೋಧನ ವಿಷಯದ ಬಗ್ಗೆ ನನಗೆ ಅರ್ಥವಾಗುವರೀತಿಯಲ್ಲಿ ನನ್ನದೇ ಭಾಷೆಯಲ್ಲಿ ತಿಳಿಸಿರುತ್ತಾರೆ.**ಈ ಸಂಶೋದನೆಯಲ್ಲಿ ಥೈರಾಯ್ಡ ಪರೀಕ್ಷೆಯ ಮಖ್ಯತ್ವವನ್ನು ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ** ಈ ಸಂಶೋಧನಾ ವಿಷಯದಲ್ಲಿ ನಾನು ಒಬ್ಬ ವಿಷಯಿಯಾಗಿ ಭಾಗವಹಿಸಲು ನನ್ನ ಸಂಪೂರ್ಣವಾಗಿಒಪ್ಪಿಗೆಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನಾಉದ್ದೇಶವನ್ನು ಪೂರ್ಣವಾಗಿಅರಿತಿರುತ್ತೇನೆ. ಈ ಸಂಶೋಧನೆಗೆ ನನ್ನಿಂದಯಾವುದೇಆರ್ಥಿಕತೆಯಅವಶ್ಯಕತೆಇರುವುದಿಲ್ಲ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಸಹಕಾರವನ್ನು ಹಿಂಪಡೆದು ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಹೋಗುವ ಹಕ್ಕನ್ನು ಹೊಂದಿರುತ್ತೇನೆ. ಇದರಿಂದ ನನ್ನಚಿಕಿತ್ಸೆಗೆಯಾವುದೇರೀತಿಯತೊಂದರೆಯಾಗುವುದಿಲ್ಲ. ಮುಖ್ಯವಾಗಿ ನನ್ನಿಂದ ಪಡೆದ ಈ ಮಾಹಿತಿಯು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಸೀಮಿತವಾಗಿರುತ್ತದೆ. ಮತ್ತು ಈ ಮಾಹಿತಿಯುಎಲ್ಲೂ ಸೋರಿಕೆಯಾಗದಂತೆಎಚ್ಚರಿಕೆವಹಿಸುವುದಾಗಿ ತಿಳಿವಳಿಕೆ ನೀಡಿರುತ್ತಾರೆಂದು ನಾನು ದೃದಪಡಿಸಿಕೊಂಡು ಒಪ್ಪಿಗೆ ನೀಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ/ ಸಾಕ್ಷಿ ಸಹಿ. ಸಂಶೋದಕನ ಸಹಿ

ಬೆರಳಚ್ಚು.

PROFORMA

A STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH ABNORMAL UTERINE BLEEDING

SERIAL NO: HOSPITAL NO. :

NAME : OCCUPATION :

AGE:

ADDRESS:

SOCIO- ECONOMIC STATUS :

1. **CHIEF COMPLAINTS** :
2. **HISTORY OF PRESENTING COMPLAINTS :**
   a. Bleeding per Vagina :
      i. Duration :
      ii. Interval :
      iii. Quantity : Scanty / Moderate /Excessive
      iv. H/o Dysmenorrhoea : Yes /No
   b. Other complaints :
3. **MENSTRUAL HISTORY** :
      i. Acyclical (MPH) : Yes /No
      ii. Hypomenorrhoea : Yes /No
      iii. Menorrhagia : Yes/No
      iv. Metrorrhagia : Yes/No
      v. Oligomenorrhoea : Yes/No
      vi. Polymenorrhagia : Yes/ No
      vii. Polymenorrhoea : Yes/No
      viii. Age of attainment of menarche:
      ix. Previous Menstrual cycles-
         1. □ Duration of Cycles :
         2. □ Amount of flow :
         3. □ Duration of flow :
         4. □ Associated dysmenorrhoea :

x. Date of last menstrual period :

4. **OBSTETRIC HISTORY** :

a. Married Life: Para: Living :

b. Abortion: Last Delivery:

c. Type of Deliveries: Tubectomy : Yes / No

5. PAST HISTORY:

a. TB / Bronchial asthma/ RHD/Blood transfusion / Any operations

6. **FAMILY HISTORY**:

a. TB / Bronchial Asthma / Diabetes mellitus / Hypertension / Any cancer / Bleeding disorders / Thyroid disorders

7. **PERSONAL HISTORY**:

a. Diet :

b. Appetite :

c. Bowels :

d. Micturition :

e. Sleep :

8. EXAMINATION OF PATIENT:

1. General Condition
2. Head to toe
    a. Distribution of hair
    b. Thickening of skin : Dryness / scaling
    c. Edema
    d. Hoarseness of voice
3. Nutritional Status
4. Anaemia
5. CVS
6. Respiratory System
7. Pulse rate
8. Blood Pressure

9. **PER ABDOMEN**:

a. Operative scar : Present / Absent

b. Engorged vein : Present / Absent

c. Ascites : Present / Absent

d. Any enlargement of Liver / Spleen : Palpable / Non Palpable

10. **VULVO VAGINA EXAMINATION** : Healthy / Non Healthy

11. **PER SPECULUM EXAMINATION :**

a. Vagina :

b. Cervix :

c. Bleeding : Present / Absent

12. PER VAGINAL EXAMINATION:

a. Cervix	:	Normal	Flushed with vault
b. Uterus	:	Anteverted	Retroverted
c. Normal size	:	Bulky	Smaller
d. Soft	:	Firm	Hard
e. Mobile	:	Fixed	
f. Tender	:	Non Tender	
g. Tenderness in fornix	:	Present	Absent
h. Uterocervical length	:		

13. Per rectal Examination :

14. **INVESTIGATIONS:**

a. □ Hb % Platelet count TC, DC

b. □ Urine : Albumin: Sugar: Microscopy:

c. □ BT, CT, PT,APTT

d. □ USG abdomen pelvis

e. □ Hysteroscopy

15. **COMPULSORY:**

i. Thyroid Function Test:

a. T3

b. T4

c. TSH

16. **OPTIONAL**:

i. Pap smear

ii. Histopathology of endometrium

KEY TO MASTER CHART

Sl. No	Serial number
Op/ Ip	Out patient / In patient
UM	Unmarried
MPH	Metropathia Hemorrhagica
T3	Triiodothyronine
T4	Tyroxine
TSH	Thyroid stimulating hormone
TDF	Thyroid dysfunction
EU	Euthyroid
SUB	Subclinical hypothyroidism
HYPO	Hypothyroidism
HYPER	Hyperthyroidism

SL. No.	OP/IP No.	Age in years	Parity	Duration	Cycle length in days	Type of Bleeding	T3 ng/ml	T_4 mcg/dl	TSH mcIU/ml	TDF
1	91115	19	0	2	45	Oligomenorrhoea	1.16	10.2	2.65	EU
2	110954	42	3	7	30	Menorrhagia	0.64	3.6	76.8	HYPO
3	117971	33	2	8	20	Polymenorrhagia	1.43	6.8	1.88	EU
4	121613	17	UM	10	60	MPH(Acyclical)	1.76	11.4	1.57	EU
5	156545	22	1	1	40	Oligomenorrhoea	0.94	7.9	1.33	EU
6	160696	18	UM	5	20	Polymenorrhoea	0.87	8.6	14.6	SUB
7	164959	36	5	10	90	MPH(Acyclical)	1.43	6.2	2.8	EU
8	169359	27	3	7	30	Menorrhagia	1.86	9.8	3.08	EU
9	164995	21	UM	6	20	Polymenorrhagia	0.53	2.8	68.7	HYPO
10	168953	32	4	1	40	Oligomenorrhoea	1.67	7.2	2.15	EU
11	190590	19	UM	1	30	Hypomenorrhoea	1.24	8.4	1.86	EU
12	233034	38	3	6	28	Menorrhagia	1.02	9.1	2.68	EU
13	237114	28	2	2	45	Oligomenorrhoea	1.92	7.9	3.3	EU
14	243438	34	4	8	30	Menorrhagia	0.96	10.4	21.26	SUB
15	245703	16	UM	10	60	MPH(Acyclical)	1.18	9.2	3.73	EU
16	247076	26	2	7	30	Menorrhagia	1.49	5.5	2.8	EU
17	257153	32	3	8	30	Menorrhagia	1.78	6.2	11.78	SUB
18	261129	41	2	2	30	Oligomenorrhoea	0.24	1.9	82.4	HYPO
19	261091	37	5	6	20	Polymenorrhagia	1.86	5.8	2.54	EU
20	275922	15	UM	1	Irregular	Metrorrhagia	0.89	7.7	3.08	EU
21	207976	29	3	7	30	Menorrhagia	1.29	6.8	3.68	EU
22	207434	34	1	1	36	Oligomenorrhoea	1.36	9.6	2.52	EU
23	208242	19	0	6	20	Polymenorrhoea	1.19	10.4	16.26	SUB
24	208810	21	UM	7	30	Menorrhagia	1.52	9.1	13.71	SUB
25	131570	45	4	5	20	Polymenorrhagia	1.64	8.6	1.7	EU
26	130229	18	UM	8	30	Menorrhagia	1.28	7.9	2.7	EU
27	136651	22	UM	2	45	Oligomenorrhoea	1.19	7.2	2.43	EU

28	150607	31	3	6	20	Polymenorrhoea	0.78	8.9	1.14	EU
29	1021582	16	UM	7	30	Menorrhagia	1.89	10.4	1.24	EU
30	1021699	48	5	6	20	Polymenorrhagia	1.96	9.5	2.96	EU
31	1021823	27	1	2	30	Hypomenorrhoea	1.38	8.1	2.39	EU
32	160760	18	UM	10	60	MPH(Acyclical)	1.44	9.3	1.69	EU
33	163821	34	4	6	20	Polymenorrhagia	1.18	7.7	17.26	SUB
34	165601	19	UM	7	30	Menorrhagia	0.58	2.9	64.8	HYPO
35	169148	29	2	5	20	Polymenorrhagia	1.22	8.5	2.1	EU
36	171309	43	3	8	30	Menorrhagia	1.46	10.3	1.14	EU
37	168346	37	4	2	45	Oligomenorrhoea	1.26	9.9	3.9	EU
38	76744	20	0	6	20	Polymenorrhoea	1.87	8.4	2.24	EU
39	23088	32	1	7	30	Menorrhagia	1.94	7.3	9.84	SUB
40	177178	39	3	10	90	MPH(Acyclical)	0.84	9.5	1.74	EU
41	181980	30	2	8	30	Menorrhagia	1.26	10.7	2.31	EU
42	181923	17	UM	2	40	Oligomenorrhoea	1.14	5.5	1.98	EU
43	53298	35	3	2	30	Hypomenorrhoea	1.43	7.4	1.27	EU
44	180272	15	UM	7	30	Menorrhagia	1.87	8.9	3.3	EU
45	191303	24	2	10	60	MPH(Acyclical)	1.67	10.8	0.6	EU
46	201380	37	3	7	20	Polymenorrhagia	1.28	7.5	1.2	EU
47	195313	20	0	1	30	Menorrhagia	0.61	3.4	92.7	HYPO
48	215702	31	1	2	40	Oligomenorrhoea	0.52	1.6	56.4	HYPO
49	213427	41	5	6	20	Polymenorrhagia	0.99	8.5	2.87	EU
50	225451	19	UM	8	30	Menorrhagia	1.08	9.4	1.49	EU
51	210563	23	UM	7	30	Menorrhagia	1.21	10.3	3.3	EU
52	231984	38	4	6	20	Polymenorrhoea	1.36	11.2	12.24	SUB
53	235450	16	UM	10	90	MPH(Acyclical)	0.47	3.1	78.6	HYPO
54	242602	36	3	2	45	Oligomenorrhoea	2.26	14.62	0.24	HYPER
55	196917	39	2	6	20	Polymenorrhagia	1.54	7.8	1.19	EU
56	241080	24	1	1	45	Oligomenorrhoea	1.44	9.6	0.8	EU
57	250770	34	4	7	30	Menorrhagia	1.53	10.4	2.3	EU

58	259951	17	UM	6	30	Menorrhagia	0.99	11.3	1.33	EU
59	264373	31	2	7	20	Polymenorrhagia	1.26	5.7	3.73	EU
60	222853	39	3	2	45	Oligomenorrhoea	3.16	16.48	0.12	HYPER
61	256429	20	0	10	70	MPH(Acyclical)	1.45	6.8	2.54	EU
62	268702	26	2	2	40	Oligomenorrhoea	1.86	7.9	1.75	EU
63	269031	29	3	6	20	Polymenorrhagia	1.78	8.9	2.47	EU
64	271556	44	5	9	30	Menorrhagia	1.69	9.2	1.33	EU
65	180767	35	4	2	Irregular	Metrorrhagia	1.58	10.4	2.43	EU
66	222401	30	2	8	30	Menorrhagia	1.36	11.5	2.8	EU
67	244269	34	3	10	60	MPH(Acyclical)	1.41	6.5	1.22	EU
68	150453	19	UM	7	20	Polymenorrhoea	1.52	7.4	2.47	EU
69	159988	22	UM	1	45	Oligomenorrhoea	1.64	8.3	0.91	EU
70	160219	32	3	6	30	Menorrhagia	1.78	9.2	3.58	EU
71	158786	23	UM	2	45	Oligomenorrhoea	1.87	10.9	0.84	EU
72	154363	37	2	7	20	Polymenorrhoea	1.64	6.4	1.65	EU
73	173055	43	3	10	90	MPH(Acyclical)	0.65	2.9	69.6	HYPO
74	178347	18	UM	8	30	Menorrhagia	1.72	5.3	1.45	EU
75	182131	32	2	6	20	Polymenorrhagia	0.92	7.4	2.6	EU
76	182410	27	1	1	30	Hypomenorrhoea	0.87	8.6	1.96	EU
77	182480	28	0	10	60	MPH(Acyclical)	1.72	9.8	1.86	EU
78	187910	15	UM	8	30	Menorrhagia	1.65	11.6	14.64	SUB
79	214099	37	5	2	45	Oligomenorrhoea	1.46	10.5	3.24	EU
80	217130	27	2	6	20	Polymenorrhagia	1.51	9.4	2.51	EU
81	242690	35	3	7	20	Polymenorrhoea	1.64	8.3	17.86	SUB
82	252120	36	4	8	30	Menorrhagia	1.46	7.2	2.13	EU
83	256492	17	UM	2	45	Oligomenorrhoea	1.39	6.1	1.29	EU
84	267049	41	3	7	20	Polymenorrhagia	1.09	5.9	1.62	EU
85	110954	33	1	10	90	MPH(Acyclical)	0.89	7.9	1.86	EU
86	116096	36	3	9	30	Menorrhagia	1.43	8.8	16.96	SUB
87	116320	22	UM	7	20	Polymenorrhagia	1.07	9.7	1.49	EU

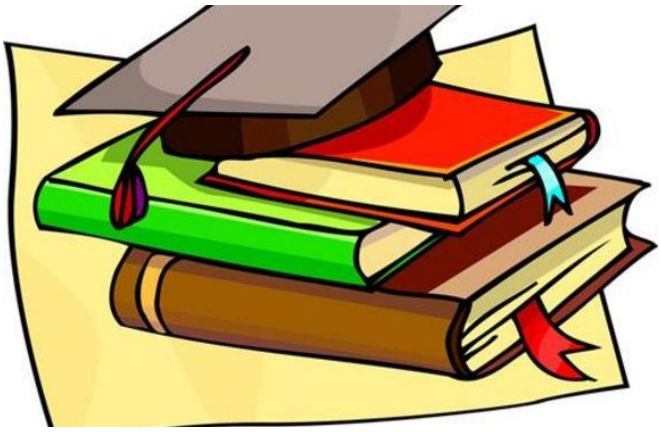
88	120400	33	2	8	30	Menorrhagia	0.84	10.2	8.49	SUB
89	119595	16	UM	7	30	Menorrhagia	1.71	11.7	3.21	EU
90	123069	27	0	2	45	Oligomenorrhoea	1.69	5.9	0.83	EU
91	123006	31	3	6	20	Polymenorrhoea	1.56	6.8	1.24	EU
92	154363	29	1	7	30	Menorrhagia	1.48	7.6	2.35	EU
93	173055	42	2	1	30	Hypomenorrhoea	1.74	8.7	1.16	EU
94	169359	18	UM	2	45	Oligomenorrhoea	0.46	2.2	72.7	HYPO
95	171309	34	4	10	90	MPH(Acyclical)	0.87	9.5	1.91	EU
96	169148	30	2	7	30	Menorrhagia	0.98	10.8	2.06	EU
97	102107	38	3	2	Irregular	Metrorrhagia	1.29	11.9	3.22	EU
98	142497	46	5	10	60	MPH(Acyclical)	1.49	5.1	12.42	SUB
99	147682	40	2	1	45	Oligomenorrhoea	0.86	6.2	1.76	EU
100	152391	20	UM	7	30	Menorrhagia	1.56	7.3	1.62	EU
101	161923	22	UM	10	45	MPH(Acyclical)	1.64	8.4	1.64	EU
102	169246	31	3	6	20	Polymenorrhagia	1.36	9.5	2.03	EU
103	170162	24	2	1	45	Oligomenorrhoea	2.94	15.57	0.03	HYPER
104	170986	19	UM	7	30	Menorrhagia	0.97	10.6	0.91	EU
105	171223	33	3	7	20	Polymenorrhagia	1.46	11.1	1.88	EU
106	184267	27	2	2	30	Hypomenorrhoea	1.97	6.1	1.57	EU
107	190996	45	2	6	20	Polymenorrhagia	1.87	7.3	1.22	EU
108	191901	17	UM	10	90	MPH(Acyclical)	1.68	8.5	2.32	EU
109	192467	37	4	8	30	Menorrhagia	1.59	9.7	1.33	EU
110	194686	27	1	7	20	Polymenorrhagia	1.76	4.9	3.73	EU
111	196789	29	2	1	45	Oligomenorrhoea	1.84	5.4	14.64	SUB
112	197971	38	4	8	30	Menorrhagia	1.02	6.9	2.8	EU
113	198672	36	3	10	90	MPH(Acyclical)	0.79	7.4	2.54	EU
114	199720	41	2	7	20	Polymenorrhagia	1.62	8.8	3.08	EU
115	202116	37	5	1	45	Oligomenorrhoea	1.58	11.2	3.68	EU
116	207227	16	UM	6	20	Polymenorrhoea	0.97	10.6	1.14	EU
117	204642	39	2	7	20	Polymenorrhagia	1.96	9.7	1.2	EU

118	206283	17	UM	2	45	Oligomenorrhoea	0.36	1.4	86.7	HYPO
119	211497	22	0	10	60	MPH(Acyclical)	0.89	8.7	19.28	SUB
120	214962	47	3	7	20	Polymenorrhoea	1.39	7.9	2.3	EU
121	229877	36	4	2	45	Oligomenorrhoea	2.46	17.46	0.16	HYPER
122	231912	23	1	6	30	Menorrhagia	1.46	6.8	1.36	EU
123	232114	15	UM	10	90	MPH(Acyclical)	1.56	8.9	3.73	EU
124	233233	37	5	7	30	Menorrhagia	1.64	9.7	2.64	EU
125	234102	24	2	7	20	Polymenorrhagia	1.72	5.4	2.47	EU
126	234991	27	3	8	30	Menorrhagia	1.86	8.6	2.63	EU
127	239632	31	3	7	20	Polymenorrhagia	1.91	9.7	1.57	EU
128	240024	29	2	1	30	Hypomenorrhoea	0.82	10.8	2.8	EU
129	241412	20	UM	2	45	Oligomenorrhoea	1.74	11.9	2.4	EU
130	249678	33	2	10	90	MPH(Acyclical)	1.86	5.7	2.47	P
131	250123	29	3	9	30	Menorrhagia	1.29	6.6	27.86	SUB
132	251521	35	4	1	45	Oligomenorrhoea	1.37	7.8	8.92	SUB
133	256778	30	2	8	30	Menorrhagia	0.93	6.9	1.22	EU
134	257862	27	2	2	45	Oligomenorrhoea	0.86	9.6	4.01	EU
135	259965	47	5	7	20	Polymenorrhagia	0.93	8.7	3.63	EU
136	260123	38	3	8	20	Polymenorrhagia	1.28	7.8	0.86	EU
137	261486	14	UM	6	30	Menorrhagia	1.19	5.3	1.43	EU
138	262962	35	3	10	60	MPH(Acyclical)	0.29	3.5	78.61	HYPO
139	264687	28	2	8	30	Menorrhagia	1.44	6.8	1.65	EU
140	267899	29	2	7	30	Menorrhagia	1.66	8.6	1.76	EU
141	268962	37	3	2	Irregular	Metrorrhagia	1.86	10.4	3.22	EU
142	269127	28	2	8	30	Menorrhagia	1.37	5.1	1.91	EU
143	271247	18	UM	10	60	MPH(Acyclical)	1.49	10.1	32.6	SUB
144	274686	31	2	9	30	Menorrhagia	1.52	11.2	10.4	SUB
145	275723	27	1	7	20	Polymenorrhagia	1.67	5.8	1.88	EU
146	277868	33	4	6	30	Menorrhagia	1.82	6.9	1.72	EU
147	279103	45	3	7	20	Polymenorrhagia	1.74	7.4	1.96	EU

148	288197	20	UM	8	30	Menorrhagia	1.7	8.5	2.1	EU
149	291923	38	2	7	30	Menorrhagia	1.09	9.3	14.61	SUB
150	295917	21	0	6	20	Polymenorrhoea	0.87	10.2	1.14	EU
151	296793	29	2	7	30	Menorrhagia	1.66	5.9	0.96	EU

INTRODUCTION


objective



Review of literature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