A study of correlation between thyroid disorders and menstrual disorders in reproductive age group

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ABSTRACT
Present study to evaluate and detect thyroid dysfunction and its correlation in patients with a menstrual disorder in the reproductive age group. Research objectives are to study the prevalence of thyroid disorders in relation to menstrual disorders and study the correlation between menstrual irregularities and thyroid dysfunction. Precise assessments of thyroid hormones in serum become achievable easily and accurately with the introduction of new homographical research techniques. Hypothyroidism diagnosis is advantageous because it typically relieves the patient of all symptoms. Therefore, the assessment of thyroid activity forms an essential component for the evaluation of a female with menorrhagia or otherwise menstrual irregularities. The individuals are rescued from repeated curettage from hysterectomy by early diagnosis of hypothyroidism. Objectively measured menstrual blood losses were 35 ml per menstrual cycle (patients in the age group <20 to ≥40 years). In the present study, 211 patients out of 520 (40%) were having menorrhagia, followed by metrorrhagia (17%) and poly-menorrhoea (16%) bleeding patterns. The observations were carried out in the laboratory, and the results were validated using SPSS software. If the thyroid functioning is poorly examined, a range of diagnostic and medical therapies, including intrusive (surgical) as well as non-invasive (hormonal) treatments may result in the patients' undue exposures.

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INTRODUCTION
The natural reproductive and physiological activity of thyroid hormone depends on the existence of mostly natural levels (Topper, 1970). During the usual reproductive system, thyroid hormone plays a significant role both through direct impact on ovaries and by communicating specifically with proteins that bind sex hormone (Poppe, 2003). Menstrual abnormalities and infertility can be induced by thyroid dysfunction. Thyroid gland disorders are among the world’s second most common diabetes disorders. A specific clinical issue of excessive uterine bleeding is documented among women of reproductive age prevalence of about 17.9 per cent in India. The menstrual discharge, but for the usual length, period, regularity and incidence is irregular uterine bleeding (AUB) (Mohanty et al., 2008). The most commonly impacted are young women and perimenopause people. Thyroid hormones are 10x more prevalent in women than in men in the hormonal and reproductive process of women. Thyroid deficient women also suffer menstrual abnormalities, miscarriage and elevated pregnancy mor-
bidity (Soleymani et al., 2014). The high incidence of thyroid disorders in children, however, is not well known because of the inflammatory existence of thyroid disorders (Mazzaferri, 1997). The objective of the present study is to find the correlation between thyroid disorders and AUB in women attending gynaecology OPD.

The existence may clarify ovary thyroid sensitivity in human oocytes of thyroid-stimulating hormone receptors. Although the thyroid operation is directly connected to the ovarian maturity cycle, the thyroid gland itself depends on overt as well as indirect ovarian stimulation for the fulfilling of its function (Sharma and Sharma, 2012). Menstrual disorders may follow thyroid disease, or might even invoke it. TSH, T3 and T4 test has been tested in this analysis for the thyroid function of patients with irregular uterine bleeding. Intense menstrual bleeding (Verma et al., 2017) is typically induced by hypothyroidism. In comparison, oligomenorrhoea and reduced discharge were correlated with hyperthyroidism. In a serum-free thyroid hormone (TSH), subclinical hypothyroidism does have a serum-free thyroid-stimulating hormone (T4), with the specified upper limit of the standard set.

Various pathways are responsible for the association between menstrual abnormalities and thyroid disorders (MohanTy et al., 2008). The TSH reaction, decreased prolactin rates, modified LH responses, peripheral transfer of androgens to estrogen, enhanced globulin binding sex hormones (SHBG), and TRH impairs coagulation effects. In hypothyroidism, TRH induces hyperprolactinemia to alter pulsating GnRH secretion, which leads to defects or delays in the LH response, which again leads to defects in the luteal and anovulatory phases. For the proper production of progesterone, the synergistic effect of FSH-mediated LH receptors is essential, and they are directly affected by thyroid hormones. Hypothyroidism also changes peripheral estrogen metabolism, reduces SHBG production and causes abnormal pituitary feedback (Vinita and Ashwini, 2006). In addition to influencing ovulation, hypothyroidism also causes menorrhagia by changing the coagulation factor; namely the reduction factors VII, VIII, IX, XI. SHBG production increases in hyperthyroidism. Estrogen metabolism is altered, and the conversion of peripheral androgens to estrogen increases. Hyperthyroxinemia increases gonadotropin responses to GnRH, and initial gonadotropin concentrations also often increase. Decreased menstrual flow can also be associated with effects on hemostatic factors, including synthesis of factor VII (Mulder, 1998).

### Aim

To evaluate and detect thyroid dysfunction and its correlation in patients with a menstrual disorder in the reproductive age group.

### Objectives

1. To study the prevalence of thyroid disorders in relation to menstrual disorders.
2. Study the correlation between menstrual irregularities and thyroid dysfunction.

### REVIEW OF LITERATURE

#### Epidemiology

Thyroid disease is common throughout the world. The prevalence of thyroid disorder in India is also high. It is known that in India, an additional 42 million individuals have a thyroid disorder, as per various reports of thyroid disease (Mulder, 1998). This paper emphasizes on 5 specific thyroid disorders epidemiologies in India:

1. hyperthyroidism, 2. hypothyroidism, 3. Hashimoto’s thyroiditis, 4. thyroid cancer, 5. iodine deficiency and goitre disorders.

Thyroid disease is different from other conditions by its simple diagnosis, the availability of medical care and the relative observation that is even offered by minor thyroid swellings. However, early diagnosis and treatments remain the cornerstone of managing thyroid problems.

#### Spread

In common, hypothyroidism affects roughly 1 to 2 per cent of the women that distinguishes TSH rates beyond the standard benchmark range, including ST4 rates below the benchmark range (Unnikrishnan and Menon, 2011). Lethargy, an increase of weight, irregular lipid profiles including heart disease, can contribute to unregulated open hypothyroidism and therefore, can delay child growth and mental development (Mulder, 1998). The asymptomatic hypothyroidism is much more severe for females than males-up to 10% among females over 60 yrs of age have higher TSH. Constant hyperthyroidism impacts 1.9 per cent of TSH patients below the baseline as well as ST4 or ST3 beyond the average level. Subclinical hyperthyroidism influences around 2% of individuals and grows with ageing, where 3% of individuals over 80 years are afflicted (Usha et al., 2009).

#### Auto-immune thyroiditis

Studies show that around 16.7% of adults have antibodies to thyroid peroxidase (TPO), and about
Table 1: Age distribution

| Age(year) | Cases (N=520) | Percentage (%) |
|-----------|---------------|----------------|
| <20       | 32            | 6%             |
| 21-30     | 124           | 24%            |
| 31-40     | 364           | 70%            |

Table 2: Bleeding patterns according to age groups

| Age     | Number of cases | Poly menorrhoea | Menorrhagia | Metrorrhagia | Oligo menorrhoea | Hypo menorrhea | Poly-menorrhagia |
|---------|-----------------|-----------------|-------------|--------------|-----------------|----------------|------------------|
| <20     | 32              | 3(9%)           | 3(9%)       | 1(3%)        | 16(50%)         | 8(25%)         | 1(3%)            |
| 21-30   | 124             | 17(14%)         | 27(22%)     | 11(9%)       | 40(32%)         | 18(14%)        | 11(9%)           |
| 31-40   | 364             | 62(17%)         | 181(50%)    | 76(21%)      | 9(2%)           | 14(4%)         | 22(6%)           |

Table 3: Bleeding Pattern

| Bleeding Pattern | Number of cases | Percent (%) |
|------------------|-----------------|-------------|
| Menorrhagia      | 211             | 40%         |
| Metrorrhagia     | 88              | 17%         |
| Polymenorrhoea   | 82              | 16%         |
| Oligomenorrhoea  | 65              | 12%         |
| Hypomenorrhoea   | 40              | 8%          |
| Polymenorrhagia  | 34              | 6%          |

Table 4: Thyroid dysfunction in different age groups

| Age     | Number of cases | Hyperthyroidism | Euthyroid | Sub Hypothyroidism | Overt Hypothyroidism | Total Thyroid Dysfunction |
|---------|-----------------|-----------------|-----------|-------------------|----------------------|---------------------------|
| <20     | 32              | 0               | 25(78%)   | 4(12%)            | 3(9%)                | 7(22%)                    |
| 21-30   | 124             | 4(3%)           | 95(77%)   | 21(17%)           | 4(3%)                | 29(23%)                   |
| 31-40   | 364             | 6(2%)           | 309(85%)  | 42(11%)           | 7(2%)                | 55(15%)                   |

Table 5: Other bleeding causes

| Cause                | Patients | Percentage(%) |
|----------------------|----------|---------------|
| Leiomyoma            | 147      | 28%           |
| Adenomyosis          | 69       | 13%           |
| Polyp                | 48       | 9%            |
| Endometrial hyperplasia| 66      | 13%           |
| Pcos                 | 67       | 13%           |
| Non classified       | 42       | 8%            |
| Endometrial malignancy| 2        | 0.3%          |
| Total                | 441      | 85%           |
12.1% have antibodies to thyroglobulin (TG) (Usha et al., 2009).

**Thyroid Cancer**

The National Cancer Registration Program (NCRP) was founded by the Indian Medical Research Council (IMRC) which collected information on over 3,000,000 people with cancer from 1984 to 1993. The NCRP identified 5,614 thyroid cancer cases among these patients were 2007 men and 3617 women.

**STRUCTURE AND FUNCTION OF THYROID GLAND**

The thyroid gland is a butterfly-shaped organ, situated just below the larynx before the trachea. The medial zone, known as the isthmus, has left and horizontal wings. Every thyroid lobe is lined on its back surfaces with parathyroid glands. The thyroid tissue is primarily made up of thyroid follicles. The follicles are a single space filled with the colloid matter. The follicles are comprised of a small space filled with the colloid matter. The colloid is the centre of thyroid hormone development and therefore, is enclosed by a layer of epithelial cells that depends on the central, unique portion of the hormone: iodine (Bhavani, 2015). Thyroid development starts on day 24 as a thickening of the midline in pharyngeal soil within human embryos. The fetal thyroid gland may synthesize thyroxine within 11 weeks, but that only reacts to hypophysial secretion at weeks 22.

**Synthesis and Release of Thyroid Hormones**

Production of the hormone is initiated by iodine atom bonded mineral called upon thyroglobulin colloid, usually secreted by the follicle cells colloid. The following steps describe the hormone group:

1. TSH receptor due to its iodine binding cells active transport of thyroid follicular cells (I-) by ion cell membrane into the cytoplasm from the bloodstream. As a response, the "fall" of hair follicles are even more significant than the bloodstream concentrations.

2. The follicular cell lumen is then passed to the nucleus, that restricts the colloid. The ions oxidize (eliminate the electrons that are negatively charged). Two iodide ions (2-) are oxidized and contribute to iodine (I2). Follicular cell membrane passes via the colloid.

3. Colloidal, thyroglobulin iodine is conjugated peroxidase in amino acid tyrosine to form two intermediates: tyrosine, which binds to iodine, and tyrosine, a combination of two iodine (Sharma and Sharma, 2012). The resulting compound is triiodothyronine (T3) also termed triiodine when covalent bonds bound one of these intermediates. More often, the second mediator makes two copies of four iodine, called thyroxine (T4), a thyroid hormone with iodine (I4).

These hormones remain in the middle of the thyroid follicle colloid, and colloidal endocytosis returns to the hair follicle cells in TSH stimulation. There the lysosomal enzymes break down colloidal thyroglobulin and release T3 and T4 free from the flow and diffusion into the bloodstream. With separate flows, the T3 and T4 cycles are kept below one per cent. These free T3 and T4 can pass through the lipid bilayer membrane and are absorbed by cells. T3 and T4 cycles of the remaining 99% of the specific binding for transport proteins called thyroxine-binding globulin (TBG) with albumin or other plasma proteins (Vinita and Ashwini, 2006).

**Thyroid Hormones and it Functions**

Thyroid hormone T3 and T4, commonly known as metabolic hormones, affect the body's basal metabolic rate, the amount of energy the body uses at rest. When T3 and T4 bind to receptors located in the mitochondria of cells, this causes an increase in the interference of nutrients and oxygen to produce ATP. Besides, T3 and T4 initiate genes involved in transcription glucose oxidation. Although this upper cell mechanism produces more ATP, the process is inefficient and the amount of heat that is abnormally increased releases side products from these reactions. This is called the calorie effect (burning = "heat") of fever.

Its primary function is adequate thyroid secretion from T4 and T3 to maintain lower thyroid hormone levels in the body, which are sufficient to meet the body's metabolic needs. Thyroid hormone levels due to negative hypothalamic and anterior hypothalamic feedback. So, if the control level of T3 secretion from the TSH pituitary further decreases thyroid hormone production and secretion (Mohanty et al., 2008; Soleymani et al., 2014; Verma et al., 2017). Conversely, when T3 levels rise, TSH secretion is suppressed, reducing thyroid hormone synthesis. An adequate amount of thyroid hormone and protein synthesis is needed for fetal and child development and organizational growth (Gibbons et al., 2008). This is very important for them and the healthy development of the nervous system in children in the early womb, they continue to maintain nerve function in adults.
Thyroid hormones have a complicated relationship between reproductive hormones, and lack of respect can affect libido, fertility and reproductive function. Regulation of the thyroid hormone in vivo by increasing the sensitivity of the adrenal medulla receptors to catecholamines (adrenaline and noradrenaline). The result is rapid heart rhythm, high pulse acceleration and raised blood pressure from an excess of hormones T3 and T4. Thyroid hormones may have significant, pervasive effects as they control metabolism, heat output, protein synthesis and various other body functions. Dietary iodine is essential for the production of thyroid hormone.

**Effects of deranged thyroid on menstruation**

Hypothyroidism, as well as hyperthyroidism, are related to an abnormality in the human menstrual cycle.

**Hypothyroidism**

Thyroid hormone produces pregnenolone from cholesterol, and formation of progesterone. Hypothyroidism, may not produce enough progesterone, resulting in a lack of progesterone are the signs, including menstrual irregularities and infertility when low levels of progesterone, thyroid, brain signals are harder to produce more pregnenolones. This extra weight weakened thyroid, thereby reducing pregnenolone (less progestin), thus forming a vicious cycle.

Hypothyroidism, heavy menstruation, menstrual missing (amenorrhea) or rare menstruation (oligomenorrhea). Amenorrhea or menstrual thin hair may be due to the release of female hypothyroidism with thyroid hormone (TRH) increases.

TRH caused high levels of prolactin release by the pituitary gland. Prolactin interferes with the production of ovarian estrogen. It causes rare or missing menstruation, and other symptoms may occur, such as infertility, abnormal milk output (called galactorrhea) and menopausal symptoms such as hot flashes and vaginal dryness.

In the menstrual cycle, disorders can make pregnancy difficult. Besides, pregnant women increase the risk of miscarriage in the first trimester of hypothyroidism. These are the treatments of hypothyroidism that can improve infertility and reduce the risk of miscarriage and thyroid replacement hormone (thyroxine).

**Hyperthyroidism**

Loss or infrequent menstruation are most common in severe hyperthyroidism. And this is due to the increase in thyroid hormone indirectly cause an increase in sex hormone-binding hormone (SHBG), which can prevent ovulation. The most severe form of hyperthyroidism is plain menorrhagia. Cycles of anovulation are quite usual. There will be elevated blood. However, not many have hypothyroidism. Malcolm G et al. It was found that any pregnant patients’ menstrual disorders, especially menorrhagia, requires TSH stimulation (Marumudi et al., 2017). T4 assay sensitivity and specificity and increased TSH thyroid function testing serum-free introduction of radioimmunoassay. Analysis of serum TSH has been shown to reduce thyroid function reserve because of the sensitive indicator before increasing the level of circulating TSH hormone levels below the normal ranges.

**Menstrual abnormalities**

1. *Menorrhagia*: Cyclic leakage, extreme in volume and length, or both, at the usual intervals. The average blood loss per menstrual cell is equivalent to or more than 80 mL.
2. *Polymenorrhea*: Cyclic bleeding regular in volume but lasting fewer than 21 days at very frequently lasting periods.
3. *Polymenorrhagia*: severe and recurrent cyclic bleeding
4. *Metrorrhagia*: Profuse bleeding, i.e. acyclic, in some volume that happens during natural period irregularly or continually.
5. *Menometrorrhagia*: Uterine bleeding, i.e., usually excessive and prolonged occurring at frequent and irregular intervals
6. *Hypomenorrhea*: Menstrual bleeding which is unduly scanty or requires two or fewer days
7. *Oligomenorrhea*: Severe recurrent bleeding outbreaks typically arise more than 35 days a week.
8. *Amenorrhea*: Lack of menstruation for the span of 3 consecutive cycles, in the context of oligomenorrhoea, whether six months after normal menstruation, whether six months after normal or eighteen months following menarche menstruation.

**MATERIAL AND METHODS**

**Materials for the study**

The studies were performed at Tertiary Care Center Department of Obstetrics and Gynecology.

**Research design**

Retrospective analysis focused on the hospital.

**Period of study**

1 June 2016 to 31 June 2018.
Study population

The participants for the study comprised of women attending Obstetrics and Gynecology staff, going through menstrual disorder.

Sample size

This study consists of 520 patients by Bhavani (2015). Among 200 cases, 38 had thyroid dysfunction $n = pq \div 5 \times p$ - Prevalence $q = 1-p$ As per this formula minimum of 62 cases of abnormal uterine bleeding should be studied. The ethical committee gave a sample size of about 520.

Inclusion Criteria

All women with AUB in the reproductive age group (menarche to 40yr)

Exclusion Criteria

1. Contraceptives users: IUCD users, oc pills, inj.DMPA
2. Bleeding disorders.

Methodology

All women were visiting the department for the first time with a complaint of abnormal uterine bleeding selected for the study after taking consent according to inclusion criteria. The disorders and indications of past thyroid diseases were examined carefully, recent medical history, menstrual history, family medical history, obstetrics history, as well as relevant personal data were taken. A thorough history was made regarding age, bleeding pattern, onset, duration, the quantity of bleeding.

The full clinical evaluation was performed in respect to heartbeat, respiration, temperatures, and the blood pressure, accompanied by RS, CNS, CVS, clinical thyroid examinations, as well as gynaecological exams. The full clinical evaluation was performed in respect to heartbeat, respiration, temperatures, and the blood pressure, accompanied by RS, CNS, CVS, clinical thyroid examination, and gynaecological exam. All recruited patients underwent regular examinations such as haemoglobin, RBST, routine urine test, bleeding and clotting time, ultrasound of abdomen and pelvis.

Then all patients were subjected to TSH. If TSH deranged was observed then T3, T4 levels were checked, and patients were diagnosed according to test results, and further medical management was done. TFT was carried out by using the TOSOH AIA 360 analyzer machine.

The laboratory values were:

- T3: 52-185ng/ml,
- T4: 4.6-10.7ug/dl,
- TSH : 0.28-6.82ulU/ml.

Thyroid Test

For most instances, the original assessment of thyroid activity may be considered as a serum thyroid-stimulating hormone (STSH). For specific checks, such as FT4, serum triiodothyronine(FT3) or thyroid inhibitors requires the following abnormal results of TSH, to which may be added without requiring a second patient having a blood test original request.

Statistical Evaluations

The data collected to describe the data Microsoft Excel 2010 Compilation expressed as mean, median, standard deviation quantitative measures. Qualitative data type expressed as a percentage or proportion. Using SPSS (Statistical Social Sciences program) software version 22, openEpi version 2.3 software for data analysis. For quantitative applications significance test data is applied to qualitative data student t-test and chi-square test for; wherein "P" value of less than 0.05 was considered significant.

RESULTS AND DISCUSSION

A prospective analytical study was conducted with 520 patients to evaluate thyroid disorders and their frequency in irregular uterine bleeding. Table 1 shows the age distribution of patients. Among 520 women majority patients belong to the age group between 31 and 40 years (70%) followed by 21 to 30 years, and 6% were in the age group < 20 years.

Table 2 shows the patients by age groups and bleeding distribution; oligomenorrhea (50%) is the most common bleeding patterns in patients or equal to 20 years. Then after less (25%) and menorrhagia (9%), oligomenorrhea boxes 21-30 age group occurred in 40 (32%). The second most common bleeding pattern is menorrhagia, 31–40 years and after, menorrhagia is the most common bleeding pattern (50%)—secondly polymenore and measurement. The value "P", observed significant <0.00001.

Table 3 depicts the pattern of bleeding. The most common bleeding pattern in among 520 cases found menorrhagia 40%, followed by Metrorrhagia 17%. Among others, 16% of presented with Polymenorrhoea, 12% of them had oligomenorrhoea, 8% with Hypomenorrhoea, 6% with Polymenorrhagia.
The thyroid disorder in various age groups is reflected in Table 4. The age-wise distribution of irregular uterine bleeding patients with hypothyroidism and hyperthyroidism indicates the most frequent of 21 to 40 years (38%), while thyroid impairment has appeared in all age ranges. And in the age group less or equal to 20 it is 23%, for this table p-value was 0.08 which not significant.

Table 5 shows various other causes of bleeding; The AUB Category Symptoms include structural as well as non-structural factors, based on the most recent FIGO PALM COEIN categorization. Adenomyosis, polyps, lesion, leiomyoma, hyperplasia and non-structural causes are involved, however therefore not listed as coagulopathic. In this study 18% (91 cases out of 520) had thyroid dysfunction, 8% (42 out of 520) were non-classified causes of AUB, and 76% had abnormal uterine bleeding because of structural reasons.

Hypothyroidism thyroid disease and thyroid function in general, especially in women. Adolescent growth, menarche, physical development, the onset of the menstrual cycle, fecundity and fetal development, growth period, postnatal period, and menopause are profound effects generated by women’s thyroid function. Whether hyperthyroidism and hypothyroidism can lead to menstrual disorders. Menorrhagia is leading to need repeated curettage and hysterectomy morbidity and mortality in gynaecological practice accompanied by often debilitating symptoms. The objective measurement showed that the average per menstrual cycle and the blood loss in the menstrual cycle is 35ml if more than 80ml is produced per period (90th percentile). It is assumed abnormal. The descent is very complicated for menorrhagia. Hormonal imbalances (usually hyperthyroidism or hypothyroidism) will contribute to this., pelvic inflammatory disease, or other reproductive tracts, endometrial hyperplasia, cancer (endometrial carcinoma), endometriosis, benign tumours (fibroids, polyps) and other local lesions systemic condition thyroid dysfunction is a common cause of excessive menstrual bleeding and menstrual irregularities (Komathi et al., 2016).

In the present study, 211 patients out of 520(40%) were having menorrhagia, followed by metrorrhagia (17%) and polymenorrhoea (16%) bleeding pattern. Menorrhagia accompanied by metrorrhagia including polymenorrhoea is the most common bleeding behaviour (54%, 20%, 8% and 40%, 21%, 18%) in the similar studies conducted by Deshmukh et al. (2015) and Bhavani (2015). A study was done by Dhanapal et al. (2016) seen that menorrhagia was the most common form of bleeding (59%), followed by oligomenorrhoea (27%). A study by Parveen et al. (2017) showed that menorrhagia accompanied by metrorrhagia and oligomenorrhoea was the most common bleeding form.

CONCLUSION

The abnormal uterine bleeding is often seen by the majority of patients with impaired thyroid function and associated, even unusual menstrual dysfunction may precede clinical symptoms, and the symptoms occur such as thyroid function. Any type of thyroid function menstrual disorders ought to be considered in this case presented incomplete and may deem necessary to assess thyroid symptoms. Thyroid dysfunction is present in India to highlight the significant increase in the incidence of a recent study. Unless appropriately done, evaluate thyroid function in these patients, we tend to miss a significant cause of AUB. This can, in turn, lead to a different treatment and rehabilitation interventions that are not accurate and unsuccessful, including invasive (surgery) and non-invasive unnecessary exposure of patients (hormone) technology. Correctly diagnose the cause of AUB will help patients with abnormal menstruation while proper management of thyroid disease treatment, it would be cost-effective.

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Conflict of Interest

I hereby declare that there is no conflict of interest related to this manuscript.

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