

Impaired Thyroid Functions in Patients with Menstrual Disturbances (An Experience of a Private Clinic)

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Abstract: To determine the frequency of impaired thyroid function in patients with menstrual disturbances. This non-interventional study of four months was carried in private clinical setup at Hyderabad Sindh, Pakistan from December 2008 to March 2009. All patients, above 12 years of age, presented with history of menstrual disturbances were evaluated and enrolled in the study. All such patients were assessed for their thyroid function. The data was collected and analyzed in SPSS version 10.00 and p-value =0.05 was considered as statistically significant. Forty patients of impaired thyroid function with different menstrual disturbances were identified; 82% of hypothyroidism and 18% of hyperthyroidism, 88% patients married while 12% were single. The most common menstrual disturbance detected was menorrhagia (40%). The thyroid dysfunction is frequently associated with disturbance in menstrual cycle; therefore thyroid assessment should be done in concerned to detail history and thyroid examination. The relevant and specific investigation in relation to thyroid function should be performed in patients with menstrual disturbances.

Key words: Thyroid dysfunction • Menstrual disturbance • Hypothyroidism • Hyperthyroidism

INTRODUCTION

The Thyroid tissue is present in all vertebrates and located immediately below the larynx on each side of and anterior to the trachea, is one of the largest endocrine glands, normally weighing 15 to 20 grams in adults. The thyroid secretes two major hormones, thyroxine (T_4) and triiodothyronine (T_3), commonly called T4 and T3, respectively. Both of these hormones profoundly increase the metabolic rate of the body. Complete lack of thyroid secretion usually causes the basal metabolic rate to fall 40 to 50 per cent below normal and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 per cent above normal [1]. The thyroid gland also secretes calcitonin, an important hormone for calcium metabolism. Secretion of T_3 and T_4 is stimulated by thyroid stimulating hormone (TSH), which is released from the pituitary in response to thyrotropin-releasing hormone

(TRH) secreted by the hypothalamus. T_3 and T_4 inhibit secretion of TSH in a typical negative arrangement, T_3 and T_4 decrease the sensitivity of pituitary thyrotropes to TRH by down-regulating TRH receptors. [2] Low T_3 syndrome is a condition with impaired peripheral conversion of T_4 to T_3 [3]. To form normal quantities of thyroxine, about 50 milligrams of ingested iodine in the form of iodides are required each year or about 1 mg/week. About 93 percent of the thyroid hormone released from the thyroid gland is normally thyroxine and only 7 percent is triiodothyronine. However during the ensuing few days about one half of the thyroxine is slowly deiodinated to form additional triiodothyronine. Therefore, the hormone finally delivered to and used by the tissues is mainly triiodothyronine, a total of about 35 micrograms of triiodothyronine per day [4]. T_3 is more active as compared to T_4 because it has a very high affinity to enter the cellular thyroid hormone receptors [5].

Hyperthyroidism is characterized by nervousness, weight loss, hyperphagia, heat intolerance, increased pulse pressure, a fine tremor of the outstretched fingers, a warm and soft skin, sweating and a BMR from +10 to as high as +100. It has various causes, however the most common cause is Graves' disease (Graves' hyperthyroidism), which accounts for 60–80% of the cases, this produces marked T_4 and T_3 secretion and enlargement of the thyroid gland (goiter). However, due to the feedback effects of T_4 and T_3 plasma TSH is low, not high [4].

The syndrome of adult hypothyroidism is generally called myxedema, although this term is also used to refer specifically to the skin changes in the syndrome. However the children who are hypothyroid from birth or before are called cretins. They are dwarfed and mentally retarded and have potbellies and enlarged, protruding tongues [4].

In Pakistan, the prevalence of hyperthyroidism and sub-clinical hyperthyroidism was 5.1 and 5.8%, respectively and the prevalence of hypothyroidism and sub-clinical hypothyroidism was 4.1 and 5.4% respectively [6]. Prevalence of hyperthyroidism and sub-clinical hyperthyroidism was higher in females than males and the prevalence of hypothyroidism and sub-clinical hypothyroidism was higher in females than males [6].

Thyroid dysfunction is frequently the reason behind problems with woman's menstrual cycle. There are some established linkages between menstruation and thyroid disease that are well-established [8] i.e. (a) Early Menstruation / Precocious Puberty (Hypothyroidism in girls may trigger very early menstruation i.e. before the age of 10 years and this early puberty is known as precocious puberty. Occasionally, if hyperthyroidism occurs very early during puberty, menstrual periods may also begin earlier than usual). (b) Late Menstruation / Delayed Puberty (Hyperthyroidism in a teenage girl can delay the onset of puberty and onset of menstruation into the mid-teens, in some cases after the age of 15 years). (c) Lighter Periods (Lighter than normal periods are frequently associated with hyperthyroidism). (d) Infrequent or Sporadic Periods (Infrequent or sporadic periods are frequently associated with hyperthyroidism). (e) Absent Periods / Amenorrhea (Hyperthyroidism can cause menstruation to stop for longer periods, a condition known as amenorrhea). (f) Heavy Periods / Menorrhagia (Menorrhagia is defined as excessively heavy or prolonged menstrual bleeding, for example, soaking through pad every hour for several hours. Hypothyroidism is associated with menorrhagia). (g) More Frequent, Longer Periods (Hypothyroidism is

known to cause periods to come more frequently for example some women will find their 28 day cycle shortens to a 25 day cycle and their normally 5-day long menses lasts 6 or 7 days). (h) Painful Menstruation / Dysmenorrhea (Hypothyroidism is associated with painful menstrual periods known as dysmenorrhea, an achy or stabbing low backache, nausea, leg aches, feeling of fullness, headaches and bowel disturbances). The rationale of this study is to determine the frequency of thyroid dysfunction in patients with disturbance in their menstrual cycle. Early detection and management of thyroid abnormality can prevent the patients from severe life threatening complications of thyroid dysfunction.

MATERIALS AND METHODS

This non-interventional study of four months was carried in the private clinical setup located in the central commercial area of Hyderabad Sindh, Pakistan from December 2008 to March 2009. All patients who were above 12 years of age presented with history of disturbance in their menstrual cycle / disturbance in monthly periods at a private clinic were evaluated and enrolled in the study. The detail history and relevant clinical examination was performed and the data was collected through a pre-formed proforma / questionnaire. An informed consent was taken from every patient after full explanation of procedure regarding the study. The detail history was taken; relevant clinical examination and routine investigations were performed. The 5 ml venous blood sample of all enrolled patients was taken and sent to laboratory for assessment of thyroid function (T_3 , T_4 and TSH). The data of all such patients was collected, saved and analyzed in SPSS version 10.00. By using analytical statistics the frequency, mean and standard deviation of variables were obtained and $p = 0.05$ was considered as statistically significant. The non-cooperative patients or patients who refused to give consent or did not have interest to participate in the study were considered to be in exclusion criteria. Regarding the ethical justification all the expenses of this study will be paid by researcher themselves.

RESULTS

During our study period forty (40) patients of impaired thyroid function with menstrual disturbances were detected. The mean age and standard deviation (SD) of patient of hypothyroidism with menstrual disturbance was 28.55 ± 5.546 while the mean age and standard deviation (SD) of patients of hyperthyroidism with

Table 1: Clinical Presentation of Patients with Impaired Thyroid Function in Menstrual Disturbances

Thyroid abnormality	n = 40	Known cases (n = 4)	Newly diagnosed (n = 36)	P-value
Hypothyroidism	33 (82.5%)	03 (75%)	30 (83.3%)	p = 0.027*
Hyperthyroidism	07 (17.5)	01 (25%)	06 (16.6%)	

*P-value is statistically significant

Table 2: Marital Status of Patients with Impaired Thyroid Function in Menstrual Disturbances

Marital status	Hypothyroidism (n = 33)	Hyperthyroidism (n = 7)	Total n = 40	P-value
Unmarried	03 (9%)	02 (29%)	05 (12%)	
Married	30 (91%)	05 (71%)	35 (88%)	0.204*

*P-value not significant

Table 3: Patients of Impaired Thyroid Function with Menstrual Disturbances in Relation to Parity

Parity	Hypothyroidism (n = 33)	Hyperthyroidism (n = 7)	Total (n = 40)	P-value
0	15 (45.5%)	-	15 (37.5%)	
1-2	06(18.2%)	-	06 (15%)	
3-4	04(12.1%)	-	04 (10%)	
≥ 5	08 (24.2%)	07 (100%)	15 (37.5%)	0.001*

*P-value is statistically significant

menstrual disturbance was 35.00 ± 2.160 . Out of forty patients twenty seven (68%) were from periphery of Sindh province (rural) while thirteen (32%) were from Hyderabad City (urban). All patients were belonged to poor socio economical community. Four patients (10%) complained of weight loss, two patients (5%) had complain of change in their voice, the tremor was found in nine patients (23%), hyperreflexia in seven patients (18%) while delayed tendon reflex in two patients (5%). Nine patients (23%) complained of palpitation where as seven (18%) were gave history of diarrhea. The sweating was predominant in seventeen patients (43%) and pruritus in six patients (15%). The palmer erythema was found in seven patients (18%) where as five patients (13%) were complained of dry skin, dry hair, periocular pigmentation and alopecia therefore they were referred to dermatologist for expert opinion. Five patients (13%) was found to have enlarged thyroid gland (goiter), ten (25%) patients gave history of excess lacrimation, three (8%) cases were found to have loss of lateral eyebrows, two (5%) patients were found to have periorbital edema where as eleven patients (28%) complained of heat intolerance. The menstrual disturbances identified were menorrhagia 16 (40%), metrorrhagia 04 (10%), menometrorrhagia 08 (20%), hypomenorrhea 06 (15%), secondary amenorrhea 05 (12.5%) and primary amenorrhea 01(2.5%) The clinical presentation, marital status and parity of all such patients with their frequency, mean, standard deviation and probability value (p-value) is mentioned in Table 1-3.

DISCUSSION

Thyroid disorders causes early or late onset of puberty and disturbance in menstrual cycle. In addition abnormally high or low levels of thyroid hormone can cause very light or very heavy menstrual periods, very irregular menstrual periods, or absent menstrual periods. The relation between thyroid function and menstruation, puberty and menopause has long been recognized, [8] and our study detected forty patients had disturbances in their menstrual cycle with impaired thyroid function.

The menorrhagia is one of the common abnormality of menstrual cycle disorders and in our study 16 patients were found to have such abnormality where as menorrhagia due to thyroid dysfunction was also found in the study by Wilansky *et al.*, in which beside detection of menorrhagia, the follow up was also made after giving the thyroxine therapy and it results in the decline of thyroid stimulating hormone (TSH) [9].

Some workers have reported the occurrence of infertility, premenstrual syndrome and menorrhagia in women with sub clinical hypothyroidism [10]. It has been stated that menorrhagia is more common in hypothyroidism or myxoedema, while oligomenorrhea is common in hyperthyroidism [11]. Therefore, in the study of Tachman *et al.*, menorrhagia is reported to occur in 32-56% of cases of myxoedema [12]. Hypothyroidism or hyperthyroidism is not only responsible for the menstrual irregularities but can produce abortions, stillbirths and

failure of lactation [13]. There are different mechanisms through which menstrual disturbance occurs e.g. altered TRH response, altered luteinizing hormone (LH) response, peripheral conversion of androgens to estrogens, change in androstendione metabolism, catecholoeestrogens and altered sex hormone binding globulin levels [14].

Ross *et al.*, [15] reported severe uterine bleeding in 02 cases of unrecognized myxoedema, both women had typical features of hypothyroidism like dry skin, bradycardia, puffiness of skin and delayed tendon reflexes. The pattern of thyroid dysfunction detected in our study was alteration in the level of TSH, T₃ and T₄. Theoretically in some cases TSH levels can also be normal but the TRH response may be altered. Brayshaw *et al.*, [10] reported that out of 54 cases of menstrual disturbance 35 had sub-clinical hypothyroidism as evidenced by abnormal TSH test. They further observed clinical relief of symptoms in 34 out of 54 women who had been treated with levothyroxine. Wilansky *et al.*, [9] detected abnormal TRH level in cases of thyroid abnormality with menorrhagia.

In our study the thyroid gland enlargement (goiter) was seen in five (13%) patients where as in another study 38 cases (out of 87) with goiter had abnormal menstrual pattern and another striking feature was that in more than 45% of cases with hypo/hyperthyroidism the menstrual abnormality preceded the appearance of goiter or clinical symptoms and signs sometimes by a period of several years through follow up [16]. In some cases T₃, T₄ and TSH levels may be within normal limits and only the TRH response may be altered. Such a situation may be observed prior to the development of goiter.

Moragianni and Somkuti reported the case of a 31-year-old patient with acute menorrhagia leads to life threatening anemia that resulted from profound hypothyroidism and despite timely institution of thyroid replacement she required emergent embolization of a uterine arteriovenous malformation after dilatation and curettage failed to control her bleeding [17].

All the available evidence supports a causative association between hypothyroidism and excessive menstrual loss. Prentice *et al.*, [18] asserts that routine thyroid function tests are of no value in the investigation of women with menorrhagia however; all women with unexplained menorrhagia should be tested for thyrotropin releasing hormone (TRH).

In hyperthyroidism, amenorrhea is common and was described as early as 1840 by von Basedow while in

hypothyroidism polymenorrhea (increased menstrual bleeding) is more common. In juvenile hypothyroidism precocious puberty has been described [19]. This is probably due to a "spillover" effect of the glucoprotein hormones: TSH which is markedly increased in hypothyroidism has a small follicle stimulating hormone (FSH) and luteinizing hormone (LH) like effects. The galactorrhea may also be present in hypothyroidism [19]. On the other hand, the data of two studies [20-21] demonstrated that hypothyroidism or hyperthyroidism in women was less frequently associated with menstrual disturbances and this statement is totally against to our study.

Since the BMR (body mass index) in patients with hyperthyroidism is elevated many patients with an overactive thyroid do, indeed, experience some weight loss, where as the BMR in the patient with hypothyroidism is decreased; an under-active thyroid is generally associated with some weight gain. In our study we identified patients with history of weight loss; however changes in thyroid function can cause fatigue and alteration in weight [22]. The most specific and discriminating features of hypothyroidism are change in voice, cold intolerance, delayed tendon reflexes and periorbital oedema [23]. However in our study such features were also predominant. The common dermatological features in thyroid dysfunction are hyperpigmentation / periocular pigmentation, dry and thickening of skin, urticaria, sweating and alopecia [24] and in our study five (13%) patients of thyroid dysfunction with menstrual disturbance were presented with skin manifestation.

Hypothyroidism can cause alterations in the pubertal process; this is usually a delayed type, but occasionally it can result in pseudo-precocious puberty and in mature women hypothyroidism not only associated with abnormal menstruation i.e. anovulatory cycles but also increases the incidence of fetal wastage [25]. Most of the literature reported that menorrhagia is more common in hypothyroidism and amenorrhoea or oligomenorrhoea in hyperthyroidism but any type of menstrual irregularity can occur with either hypo or hyper function of the thyroid gland and women presenting with menstrual irregularities are usually investigated for thyroid function. Therefore it is to be summarized that any type of menstrual disorder should be considered as a possible presenting symptom of thyroid dysfunction and it may indicate clinical or sub clinical abnormality.

CONCLUSION

The thyroid dysfunction is frequently associated with disturbance in menstrual cycle; therefore thyroid assessment should be done in concerned to detail history and thyroid examination. The relevant and specific investigation in relation to thyroid function should be performed in patients with menstrual disturbances.

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