International Journal of Reproduction, Contraception, Obstetrics and Gynecology
John JD et al. Int J Reprod Contracept Obstet Gynecol. 2017 Jun;6(6):2547-2552
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20172349

Original Research Article

Assessment of thyroid and prolactin levels among the women with abnormal uterine bleeding

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Received: 04 April 2017
Accepted: 02 May 2017

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ABSTRACT

Background: Thyroid disorders are 10 times more common in women than men.1 Menstrual disturbances usually accompany clinical alterations in thyroid function and every clinician would have encountered altered menstrual pattern among women suffering from either hypo or hyper thyroidism. A high serum prolactin level can distrurb the follicular maturation and corpus luteum function, and leads to inhibition of normal pulsatile secretion of gonadotrophin-releasing hormone in hypothalamus resulting in anovulation. The aim of the study was to assess the thyroid and the prolactin levels among the women with abnormal uterine bleeding and to evaluate the association between them by comparing with normal females.

Methods: A cross sectional study was conducted for a period of one year between Jan 2016 and December 2016 in our institution at the gynaecology OPD. Patients in the age group of 15 to 45 with the complaints of abnormal uterine bleeding and with the ultrasound findings showing normal uterus and ovary were included in the study. Hundred age and sex matched controls without any complaints of abnormal uterine bleeding in the age group of 15 – 45 years were also included in the study. Free T3, Free T4, TSH and prolactin estimation was done by chemiluminescent immunoassay for both the patients and the controls.

Results: The mean TSH levels among the cases were much higher than that of the controls and the difference in the levels found to be statistically significant. Similarly, hyperprolactinemia was found in 18 cases when compared to 2 cases in controls and the mean prolactin levels were higher in cases. The serum prolactin levels and the serum TSH levels showed a perfect positive correlation which indicates that as the TSH level increases prolactin levels also increases with the R value >0.5.

Conclusions: Early detection of hypothyroidism in such subjects saves the patient from recurrent curettage and at times hysterectomy. The financial implications of screening for prolactin/thyroid hormone abnormalities will have to be evaluated before a general recommendation can be made.

Keywords: AUB, Prolactin, Thyroid function test

INTRODUCTION

Thyroid disorders are 10 times more common in women than men.[1] Menstrual disturbances usually accompany clinical alterations in thyroid function and every clinician would have encountered altered menstrual pattern among women suffering from either hypo or hyper thyroidism. Hypothyroidism commonly causes menorrhagia. Hyperthyroidism is associated with menorrhagia followed by oligomenorrhoea and amenorrhoea proportionate to the severity of thyrotoxicosis.[2,3]

Abnormal uterine bleeding occurs due to any disruption in the normal physiology or anatomic changes in the

endometrium.[4] Initially AUB was broadly divided in to two categories→ ovulatory and anovulatory, but now after November 2010 the International Federation of Gynaecology and Obstetrics formally accepted a new classification system for causes of AUB in reproductive years. The system is based on acronym PALM-COEIN. PALM (Structural causes) → Polyps, Adenomyosis, Leiomyoma, Malignancy. COEIN (nonstructural causes) →Coagulopathy, Ovulatory disorders, Endometrial causes, Iatrogenic, not classified.[5,6]

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.[7]

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.[8] 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 oestrogen excess thereby causing menorrhagia.

There may be episodes of amenorhoea 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.[9,10]

Studies showed that 33.3% patients with hypothyroidism had menorrhagia. The mechanism explained was it seems that poor progesterone production is associated with persistent endometrial proliferation which may be responsible for massive bleeding (anovulatory bleeding). Another, mechanism for this may be failure of LH secretion. 44.4% patients with hypothyroidism had oligomenorrhoea. This was explained by the galactorrhoea-amenorrhoea syndrome in long standing hypothyroid patients.[1]

Hyperthyroidism occurring before puberty has been reported to delay the onset of menses. In women of fertile age group, oligomenorrhea and amenorrhea are the commonest abnormalities associated with hyperthyroidism.[11] These irregularities sometimes precede thyroid dysfunction. In the present times, subclinical hyper- and hypothyroidism can be diagnosed very early, whereas these would have passed unnoticed a few decades ago. Timely detection of Thyroid disorder in patients presenting with menstrual disorders and their management can prevent surgical intervention like curettage and hysterectomy. Thyroid autoimmunity has been shown to have association with various kinds of thyroid dysfunction.

A high serum prolactin level can distrurb the follicular maturation and corpus luteum function, and leads to inhibition of normal pulsatile secretion of gonadotrophin-releasing hormone in hypothalamus.[12] It also leads to deficient secretion of LH and FSH which leads to inadequate induction of proper ovarian response.[13] As of today very few studies had been done to see the association of prolactin and thyroid levels among females with abnormal uterine bleeding, so the present study was aimed to assess these levels among women with AUB.

The aim of the study was to assess the thyroid and the prolactin levels among the women with abnormal uterine bleeding and to evaluate the association between them by comparing with normal females.

METHODS

A cross sectional study was conducted for a period of one year between Jan 2016 and December 2016 in our institution at the gynaecology OPD. Patients in the age group of 15 to 45 with the complaints of abnormal uterine bleeding and with the ultrasound findings showing normal uterus and ovary were included in the study. Patients with any form of uterine and thyroid abnormalities, patients who are on hormonal drugs or steroids, IUCD users, history of bleeding disorders (hemophilia, von Willebrand's disease) and pelvic infections including endometritis, PID, PCOD were excluded from the study.

A total of hundred patients who were fitting into the above criteria were included in the study. Hundred age and sex matched controls without any complaints of abnormal uterine bleeding in the age group of 15-45 years were also included in the study.

A detailed history related to onset, duration, interval and amount of bleeding was obtained from the patients. Both the patients and the controls were subjected to routine investigations like blood counts, urine examination for sugar, albumin and microscopy, bleeding time and clotting time to rule out coagulation defect and ultrasound to rule out uterine or ovarian pathologies. Free T3, Free T4, TSH and prolactin estimation was done by chemiluminescent immunoassay for both the patients and the controls. Based on the thyroid levels patients were grouped into euthyroid, subclinical hypothyroid, hypothyroid and hyperthyroid and based on the prolactin levels they were classified as normal prolactin and hyperprolactinemia. The data were analyzed by using SPSS version 20. The socio-demographic data was analysed by simple proportions and percentages. The association and relation between different parameters were analyzed using chi-square test and pearson's correlation test.

RESULTS

Table 1: Age wise distribution of the study population.

Age group	Cases	Controls	P value
<15	2	3	0.738
15-25	20	18	
26-35	29	30	
36-45	48	46	
>45	1	3	
Total	100	100	
Mean±SD	33.8±8.3	34.2±7.4	

Table 1 shows the age wise distribution among the cases and controls. It is seen from the Table that majority of the women were in the age group of between 25 and 45 years in both the groups with the mean age of 33.8 years among cases and 34.2 years among the controls and it proves that the age was completely matched for selecting the controls. The various gynaecological symptoms with which the cases were presented to our department were shown in Table 2.

Table 2: Distribution of the cases based on their symptoms.

Symptoms	Frequency	%
Amenorrhea	2	2.0
Menorrhagia	42	42.0
Oligomenorrhoea	38	38.0
Polymenorrhagia	17	17.0
MetropathiaHaemorrhagica	1	1.0
Total	100	100.0

Menorrhagia was found to be the most common symptom among the patients with abnormal uterine bleeding (AUB) followed by oligomenorrhoea and polymenorrhagia.

Speculum examination was done for all the patients in the case group and among them 64 of them had normal cervix and 16 of them had eroded and 9 of them had hypertrophied cervix (Table 3).

Table 3: Distribution of the cases based on them per speculum findings.

Per speculum findings	Frequency	%
Cervix normal	64	64
Cervix erosion	16	16
Cervix hypertrophied	9	9
Cervix flushed with vagina	6	6
Cervix- Nabothian cyst	5	5
Total	100	100

The ultrasound abdomen which was performed on all cases showed bulky uterus for 9 patients and atrophied uterus in 3 patients and for remaining it was normal. The haemoglobin levels were assessed among both the cases and controls and it was found to be much lower in cases than the controls.

The mean Hb among cases was 9.4 gms/dl and among controls it was 11.6 gm/dl and the difference between them was found to be statistically significant (p <0.05) (Table 4).

Table 4: Comparison of haemoglobin levels among cases and controls.

Hb levels (gms/dl)	Cases	Controls	P value
<8	11	3	<0.005
8-12	85	60	
12-14	4	24	
>14	0	13	
Total	100	100	
Mean±SD (gms/dl)	9.4±1.2	11.6±2.4	<0.005

This proves that abnormal uterine bleeding has a significant impact on the haemoglobin levels. The thyroid function was assessed by measuring the free T3, free T4 and TSH levels among both the cases and controls.

Table 5: Comparison of levels of thyroid function test among cases and controls.

Thyroid function test		Cases	Controls	P value
Free T3 (pg/ml)	<2.1	37	16	<.001
	2.1-4.4	61	83	
	>4.4	2	1	
	Mean±SD	1.87±2.1	2.38±3.3	<.001
Free T4 (ng/dl)	<0.8	37	17	<.001
	0.8-2.7	60	82	
	>2.7	3	1	
	Mean±SD	1.08±0.98	1.34±1.02	<.001
TSH (µIU/ml)	<0.35	2	3	<.001
	0.35-5.5	42	75	
	>5.5	56	22	
	Mean±SD	8.34±4.8	4.32±3.7	<.001

Table 6: Comparison of prolactin levels among cases and controls.

Prolactin levels	Cases	Controls	P value
Hyperprolactenemia (Prl >1.3 nmol/l)	18	2	<.001
Normal prolactin levels (<1.3 nmol/l)	78	98	
Mean±SD (ngm/ml)	27.8±2.5	12.3±2.8	<.001

TSH levels of more than 5.5µIU/ml was considered as hypothyroidism and among the cases 56 of them and among controls 22 of them had hypothyroidism and the difference found to be statistically significant. Similarly, the mean levels of free T3, T4 and TSH showed a statistically significant difference among the cases and

controls (Table 5). Serum prolactin levels were measured among the cases and controls. Prolactin levels of more than 1.3 nmol/l was considered as hyperprolactenemia and among cases 18 and among controls 2 of them had hyperprolactenemia and the mean prolactin levels among the cases was 27.8 ngm/ml and among the controls it was 12.3 ngm/ml and the difference was found to be statistically significant ($p<0.05$) (Table 6). The serum prolactin levels and the serum TSH levels showed a perfect positive correlation which indicates that as the TSH level increases prolactin levels also increases with the R value >0.5 (Table 7).

Table 7: Pearsons correlation between TSH and serum prolactin levels.

Cases		R value	Controls		R value
Mean TSH levels (µIU/ml)	Mean prolactin levels (ngm/ml)		Mean TSH levels (µIU/ml)	Mean prolactin levels (ngm/ml)	
8.34	27.8	0.845	4.32	12.3	0.636

DISCUSSION

In the present study majority of the study subjects were in the age group between 25-45 years and it is almost in par with the studies done by Narula et al, Pahwa S et al and Kumar A et al.[14-16]

In our study majority of the women were multiparous and only 5% were nulliparous and it was almost similar to the findings quoted by Pilli etal.[17] Menorrhagia is a frequent debilitating symptom in gynaecological practice resulting in need for repeated curettage and hysterectomy with its attendant morbidity and mortality.

Objective measurements have shown that mean menstrual blood loss in each menstrual cycle is 35 ml and menstrual blood loss is considered to be excessive when it is more than 80 ml per cycle (90th percentile).[18]

In our study, we found menorrhagia to be the most common symptom (42%) among abnormal uterine bleeding and it is in par with the study done by Kumar A et al.

The present study had shown the prevalence of hypothyroidism and subclinical hypothyroidism was 56% among the patients with abnormal uterine bleeding and our results almost matches the results quoted by Doifode et al, Douglas et al, Singh L et al and Shruthi et al and in all those studies they had also shown that menorrhagia as the most common symptom in patients with hypothyroidism or subclinical hypothyroidism.[19-22]

One of the explanations is the activity of thyroid is that closely linked with the process of ovarian maturation. The thyroid gland is itself dependent on direct and indirect stimulation from the ovary to discharge its own function.

Previous studies have evaluated the prevalence of hyperprolactinemia among patients with menstruation related problems in which most of these studies included patients with oligomenorrhea or amenorrhea. For example, Lee et al studied hyperprolactinemia in adolescents and young women with menstrual problems.[23] They divided the study population in two groups based on age and found a 9.4% prevalence of hyperprolactinemia in the group aged 21-30 years compared with a 2.4% prevalence in the group aged 11-20 years. In other studies, the prevalence of hyperprolactinemia varied from approximately 0.2% in an unselected normal adult population to 15%-20% among women with reproductive disorders, whereas a study of women with a wider age range (15-45 years) found that 61% of patients with abnormal bleeding had hyperprolactinemia, whereas in our study only 18% of patients with abnormal uterine bleeding had hyperprolactenemia and 2% of women without abnormal uterine bleeding had hyperprolactenemia.[24-26]

Most of thegynaecologists today will investigate for prolactin levels only among patientswith symptoms of galactorrhea or galactorrhea associated with oligomenorrhea or amenorrhea. In the current study, galactorrhea was present in 18% of the patients with AUB overall.[27] Thus, if prolactin levels are only measured in patients with galactorrhea, hyperprolactinemia will be missed in a considerable number of patients.

The association between thyroid disturbances and hyperprolactinemia has long been postulated, although some studies have not find any correlation between prolactin and thyroid hormones.[28]

In people, TSH and prolactin secretion is controlled by an interrelated pathway. If a common regulatory mechanism is involved, the pituitary thyrotrophs and lactotrophs have shown differential sensitivity to the common stimulatory and inhibitory substances.[29]

In the current study, the association between elevated prolactin levels and abnormal TSH was evident by showing a perfect positive correlation between TSH levels and serum prolactin levels, indicating that the menstrual cycle is affected via a common pathway.

CONCLUSION

With the advent of modern hormonal assay techniques precise estimation of thyroid hormones in serum is possible in a rapid and reliable manner. Treatment of hypothyroidism is very satisfying as it usually relieves patient of all the symptoms.

Hence in investigating a patient with menorrhagia and/or menstrual irregularities, evaluation of thyroid functional status forms an essential component. Early detection of hypothyroidism in such subjects saves the patient from surgical interventions like curettage and hysterectomy.

The financial implications of screening for prolactin/thyroid hormone abnormalities will have to be evaluated before a general recommendation can be made.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: John JD, Damodaran V, Radhakrishnan S. Assessment of thyroid and prolactin levels among the women with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol 2017;6:2547-52.