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Original Research Article

Association of abnormal thyroid stimulating hormone and serum prolactin levels in women of reproductive age with abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a frequent problem in reproductive-aged women and carries substantial morbidity, anemia and reduced quality of life. The objective of this study was to evaluate the association between thyroid-stimulating hormone (TSH) levels and serum prolactin levels in women of reproductive age presenting with AUB.

Methods: This was a cross sectional, observational study carried out for 18 months in Department of Obstetrics and Gynecology, ESIC Medical College, Rajajinagar, Bengaluru. Twenty-seven women aged 19-49 years who had AUB were recruited. After clinical assessment, the serum TSH and prolactin levels were determined using chemiluminescence immunoassay (Siemens ADVIA Centaur). IBM SPSS Statistics version 25.0 was used to data analysis. Descriptive statistics, chi-square test, Pearson's correlation was applied and p value of <0.05 was regarded as statistically significant.

Results: The mean age of the study population was 34.06±9.42 years and majority of the women were multiparous (61.9%) and aged between 35-44 years (32.2%). The most common presentation was heavy menstrual bleeding (53.7%). The non-structural causes represented 63.7% of AUB, with ovulatory dysfunction being the most common cause (35.2%). In 40.0% of women, the TSH level was abnormal, with hypothyroidism (35.2%) and hyperthyroidism (4.8%). Twenty-seven.4% of participants had hyperprolactinemia. There was no correlation between TSH and prolactin levels (r=0.048, p=0.432).

Conclusions: Thyroid dysfunction and hyperprolactinemia are relatively frequent in women with AUB, but no significant relationship was found between TSH and prolactin levels. Regular hormonal testing may aid in early detection of any underlying glandular problems and help to guide treatment in women with AUB.

Keywords: AUB, Hypothyroidism, Hyperprolactinemia, Prolactin, Reproductive age, TSH

INTRODUCTION

AUB is one of the most frequently encountered gynecologic disorders in women of reproductive age and is an important cause of morbidity, health care utilization and poor quality of life. It is characterized by Abnormal bleeding from the uterine corpus, in terms of volume, frequency, regularity or duration in non-pregnant women.[1-3] It's potential complications include iron-deficiency anemia, physical exhaustion, emotional stress and social challenges, placing a heavy strain on both the patient and healthcare systems.[1-5] Menorrhagia, metrorrhagia and dysfunctional uterine bleeding have historically been used interchangeably in the discussion of menstrual variations. Since this point, there has been diagnostic confusion and inconsistencies in clinical interpretation and evidence-based practices and research.[3,5] To rectify these challenges, a standardized

terminology and classification scheme, like the PALM–COEIN system and terminology for gynecology was developed by the International Federation of Gynecology and Obstetrics (FIGO). This classification was made to encourage a systematic approach to the evaluation of a patient's AUB cause(s) as well as to ensure that multiple underlying causes may present in a single patient.[2,4] Such classification promotes a systematic approach to evaluation while emphasizing that multiple underlying causes may exist in an individual patient.[2,3]

Given the significance of hormonal/endocrine imbalance in ovulatory dysfunction, a stepwise approach needs to be organized, with focus on underlying systemic disorders that may be reversible, such as endocrine causes.[6] This suggests that there is a need to investigate thyroid and prolactin abnormalities in women who become affected.[3,5,6] Hence, the objective of this study was to evaluate the association between TSH levels and serum prolactin levels in women of reproductive age presenting with AUB.

METHODS

Study type

A cross-sectional observational study was conducted at the department of obstetrics and gynaecology ESIMC and PGIMSR Rajajinagar, Bangalore, Karnataka, India, from May 2024 to September 2025. A total of 270 women with AUB in the age group between 19-49 years were included in this study. Eligible women were recruited after obtaining written informed consent. This study was carried out in after obtaining approval from the Institutional Ethics Committee.

Inclusion criteria

Women aged between 19-49 years experiencing AUB without any clinically palpable pathologies were included in this study.

Exclusion criteria

The exclusion criteria included women with known thyroid disorders receiving treatment, women undergoing treatment for hyperprolactinemia, premenarchal or postmenopausal women, pregnant women, women receiving anticoagulant or hormonal therapy and users of intrauterine contraceptive devices (IUCDs).

Procedure

Women were informed about the study and purpose of study in detail. A detailed history regarding name, age, obstetric score, onset, duration, interval and amount of bleeding was taken. General physical examination, neck and breast examination and pelvic examination was done. All women were subjected to the routine investigations like complete blood count, coagulation profile, urine routine and microscopy. Serum TSH and serum prolactin evaluation was done by chemiluminescence immune assay method using Siemens 1600 IM analyser in ESIC biochemistry lab.

Sample size

Sample size was calculated using the prevalence estimation formula based on Prasad et al.[24]

$$n = \frac{Z^2 \times p \times q}{d^2}$$

$$n = \frac{1.96^2 \times 17.9 \times 82.1}{5^2 \times 100}$$

$$n = 225.8 \approx 226$$

The calculated minimum sample size was 226 participants. Considering a 10% attrition rate for incomplete evaluation or exclusions, the final sample size was increased to 270 participants. A study by Prasad et al was selected as the sample size as it being the most relevant and methodologically similar published study of assessment of hormonal abnormalities in women with abnormal uterine bleeding in similar population. If local institutional data cannot be found, then an appropriate sample size can be determined with reference to a previously published prevalence estimate.

Study variables

The study variables were age, parity, serum TSH level, serum prolactin level and final clinical diagnosis. These were taken and analyzed to assess whether there is a relationship between thyroid dysfunction and hyperprolactinemia and abnormal uterine bleeding.

Laboratory methods

Chemiluminescence immunoassay (CLIA) was used to measure TSH and prolactin levels quantitatively in a laboratory on Siemens ADVIA Centaur XP platform. The assay is highly sensitive, has a wide analytical range and excellent precision (intra-assay variation <3-5%, inter-assay variation <3-5%). Automated analyzer is based on acridinium ester–chemiluminescent technology with manufacturer-supplied calibration standards that are traceable to WHO international standards and routine quality control for accuracy and reproducibility. The reference range for serum thyroid-stimulating hormone (TSH) was 0.34–5.60 µIU/ml. Hypothyroidism was defined as a TSH level >5.60 µIU/ml and was further classified as subclinical (5.60–10.0 µIU/ml) or overt (≥10.0 µIU/ml). Hyperthyroidism was defined as a TSH level <0.34 µIU/ml. The reference range for serum prolactin in non-pregnant, premenopausal women was 3.34–26.72 ng/ml, according to the Siemens ADVIA

Centaur assay-specific reference intervals. Hyperprolactinemia was defined as a serum prolactin level >26.72 ng/ml. Macroprolactin testing was performed when clinically indicated.

Study tools

Structured case record proforma, serum TSH, prolactin estimation by CLIA,

Statistical analysis

Data were entered into Microsoft Excel and analysed using appropriate statistical software. Continuous variables were expressed as mean±standard deviation, while categorical variables were presented as frequencies and percentages. Associations were assessed using Chi-square or Fisher's exact test for categorical variables and independent t-test for continuous variables. A p value <0.05 was considered statistically significant.

RESULTS

Age-wise distribution

The study included a total of 270 women aged 19-49 years who had abnormal uterine bleeding. The mean age was 34.06±9.42 years, with median age of 34 years (interquartile range of 26.0–42.75 years) and the majority of the participants were in reproductive and perimenopausal age groups. The age group with the greatest percentage of participants was 35-44 years (87, 32.2%), followed by 25-34 years (79, 29.3%). Women aged 19–24 years accounted for 66 (24.4%) cases, while 38 (14.1%) were aged 45–49 years. Overall, almost two thirds (61.5%) of the study population was aged between 25 and 44 years (Table 1).

Parity distribution

Most of the women in the study were multiparas (167, 61.85%). There were 59 cases (21.85%) of women with parity P1L1 and 44 women (16.3%) were nulliparous. This suggests that there is more abnormal uterine bleeding in multiparous women in the present study (Table 2).

Abnormal uterine bleeding pattern characteristics

All women who presented with abnormal uterine bleeding (270 women) had abnormal uterine bleeding patterns, with heavy menstrual bleeding the most common symptom (145 women, 53.7%). Irregular cycles occurred in 110 cases (40.7%), followed by normal cycles. Irregular cycles followed, in 110 cases (40.7%). In 15 cases (5.6%) mixed bleeding patterns were observed (Table 3).

Distribution of PALM-COEIN etiological classification

Using the FIGO PALM–COEIN classification, the non-structural causes (COEIN) were more common than the structural causes. In total, 172 women (63.7%) were in the COEIN group and 98 women (36.3%) were in the PALM group. The most frequent etiology was leiomyoma (42 cases, 15.6%), followed by endometrial polyps (28 cases, 10.4%), adenomyosis (21 cases, 7.8%) and malignancy or endometrial hyperplasia (7 cases, 2.6%) among the structural causes.

Ovulatory disorders were the largest of the COEIN category with 95 cases (35.2%). The most common causes were endometrial (17.4%), coagulopathy (6.7%) and iatrogenic (3.0%) causes and unclassified causes (1.5%). Twenty-eight women (10.4%) were found to have multimorbidity, but classification was given according to the most prevalent etiology, following the hierarchical recommendations of FIGO (Table 4).

Primary thyroid stimulating hormone status classification

All 270 women in the study had their thyroid function tested by serum TSH estimation. Of the 162 women, 60.0% had normal TSH levels and 40.0% had abnormal thyroid function (reference range 0.34–5.60 IU/ml). The mean TSH value of the total study population was 5.50±3.76 IU/ml (Table 5).

Detailed thyroid stimulating hormone abnormality distribution

Hypothyroidism was the most common abnormality in women with abnormal TSH levels. Hypothyroidism was diagnosed in 95 women (35.2%) and their mean TSH level was 9.85±2.45 IU/ml. Of the above, 42 women (15.6%) had TSH levels ≥10 IU/ml (overt hypothyroidism) and 53 women (19.6%) had TSH levels between 5.60 and 10 IU/ml (subclinical hypothyroidism). Hyperthyroidism was diagnosed in 13 women (4.8%) and the mean TSH level was 0.21±0.09 IU/ml (Table 6).

Age-stratified thyroid stimulating hormone distribution

Age stratified analysis showed that hypothyroidism was more common in all age groups, increasing with age. Hypothyroidism was observed in 31.8% of women aged 19–24 years, 34.2% in the 25–34 years age group, 37.9% in women aged 35–44 years and 36.8% among those aged 45–49 years. The youngest age group (63.6%) had the most normal TSH levels, followed by a gradual decrease in the older age groups. Compared to this, hyperthyroidism was relatively rare and occurred in 3.4% to 7.9% of the age groups (Table 7).

Primary prolactin status classification

All 270 women in the study had their serum prolactin level estimated. Based on the reference range of 3.34-26.72 ng/ml, 196 women (72.6%) had normal serum levels of prolactin and 74 women (27.4%) had high levels of

prolactin. The overall mean serum prolactin level was 19.31±8.97 ng/ml (Table 8).

Age-stratified prolactin distribution

Emergency LSCS was the most common mode of delivery of live births (45.5%), followed by vaginal delivery (39.2%) and elective LSCS (15.4%) (Table 9). No statistical significance was found between vitamin D status and mode of delivery (p>0.05).

Association between thyroid function and serum prolactin levels

A 2×2 contingency table and chi-square test of independence were used to assess the association between thyroid status and serum prolactin levels (Table 5). Of the 162 women with normal TSH levels, 118 (73.0%) had normal prolactin levels and 44 (27.0%) had elevated prolactin levels. Likewise, of the 108 women with abnormal TSH levels, 78 (72.2%) had normal levels of prolactin while 30 (27.8%) had elevated levels of prolactin. Serum prolactin level did not show any significant correlation with thyroid status when analyzed by the statistical method. The chi-square value was 0.02 and the degree of freedom was 1, with the p value being 1.00. The strength of the association was very weak (φ=0.009). Women with abnormal TSH levels were not more likely to have hyperprolactinemia than women with euthyroid TSH (OR 1.04, 95% CI 0.62–1.74). The expected frequency for the normal TSH–elevated prolactin cell was 43.3 and 118.7 for the normal TSH–normal prolactin cell, which confirmed the appropriateness of the chi-square test.

Table 1: Age wise distribution.

Parameters	Value
Mean±SD	34.06±9.42 years
Median (IQR)	34.0 (26.0-42.75) years
Range	19-49 years
Age groups (in years)	**N (%)**
19-24	66 (24.4)
25-34	79 (29.3)
35-44	87 (32.2)
45-49	38 (14.1)

Table 2: Parity wise distribution.

Parity	Frequency (N)	%
Nulliparous	44	16.3
P1L1	59	21.85
Multiparous	167	61.85
Total	270	100.0

Table 3: AUB pattern characteristics.

AUB patterns	Frequency (N)	%
Heavy menstrual bleeding	145	53.7
Irregular cycles	110	40.7
Both	15	5.6
Total	270	100.0

Table 4: Distribution of PALM-COEIN etiological classification.

Category	Subtype	Frequency (N)	%
PALM (Structural)	**Total**	**98**	**36.3**
	Leiomyoma	42	15.6
	Polyp	28	10.4
	Adenomyosis	21	7.8
	Malignancy/Hyperplasia	7	2.6
COEIN (Non-structural)	**Total**	**172**	**63.7**
	Ovulatory disorder	95	35.2
	Endometrial cause	47	17.4
	Coagulopathy	18	6.7
	Iatrogenic	8	3.0
	Not classified	4	1.5

Table 5: Primary TSH status classification.

TSH status	Frequency (N)	%	Mean TSH (IU/ml)±SD
Normal (0.34-5.60 IU/ml)	162	60.0	2.85±1.42
Abnormal	108	40.0	9.12±2.68
Total	270	100.0	5.50±3.76

Table 6: Detailed TSH abnormality distribution.

TSH category	Reference range	Frequency (N)	%	Mean TSH (IU/ml)±SD
Hypothyroidism	>5.60 IU/ml	95	35.2	9.85±2.45
	Overt (≥10.0)	42	15.6	11.2±1.8
	Subclinical (5.60-10.0)	53	19.6	7.3±1.2
Hyperthyroidism	<0.34 IU/ml	13	4.8	0.21±0.09
Normal	0.34-5.60 IU/ml	162	60.0	2.85±1.42

Table 7: Age-stratified TSH distribution.

Age group (in years)	Normal TSH, N (%)	Hypothyroid, N (%)	Hyperthyroid, N (%)	Total
19-24	42 (63.6%)	21 (31.8%)	3 (4.5%)	66
25-34	48 (60.8%)	27 (34.2%)	4 (5.1%)	79
35-44	51 (58.6%)	33 (37.9%)	3 (3.4%)	87
45-49	21 (55.3%)	14 (36.8%)	3 (7.9%)	38
Total	162 (60.0%)	95 (35.2%)	13 (4.8%)	270

Table 8: Primary prolactin status classification.

Prolactin status	Reference range	Frequency (N)	%	Mean prolactin (ng/ml)±SD
Normal	3.34-26.72 ng/ml	196	72.6	15.8±6.2
Abnormal (elevated)	>26.72 ng/ml	74	27.4	31.4±4.8
Total	-	270	100.0	19.31±8.97

Table 9: Age-stratified prolactin distribution.

Age group (in years)	Normal, N (%)
19-24	50 (75.8)
25-34	56 (70.9)
35-44	57 (65.5)
45-49	33 (86.8)

DISCUSSION

In the present study, AUB was found to be more common among women in reproductive and perimenopausal ages with a mean of 34.06±9.42 years and almost two-third of the women aged 25-44 years. This is similar to the previous Indian studies by John et al, Wilkhu et al and Nanajudan et al which reported the highest prevalence of AUB in women during their third and fourth decade of life, which may be attributed to hormonal changes, reduced ovarian reserve and increased incidence of ovulatory dysfunction during the perimenopausal transition.[8,16,19] The high percentage of multiparous women (61.9%) versus nulliparous women (16.3%) was similar to that reported in other studies and may be related to the cumulative changes in the uterus and hormones that occur with repeated pregnancies and increasing reproductive age.[18,20] The most common clinical presentation was heavy menstrual bleeding (53.7%) followed by irregular menstrual cycles (40.7%). The high prevalence of HMB could be because of the interplay of ovulatory dysfunction, endometrial changes and underlying endocrine abnormalities, as mentioned by John et al and Wilkhu et al, making it the most common clinical presentation in various populations.[16,19] Forty percent of women with AUB had thyroid dysfunction, with hypothyroidism being the most common abnormality (35.2%) followed by hyperthyroidism (4.8%). The relatively higher prevalence of thyroid dysfunction in the present study is comparable to the previous studies conducted in India which reported that about 30-45% of women with AUB presented with thyroid dysfunction, with hypothyroidism being the more

common abnormality, though slightly less.[21,22] The prevalence of hypothyroidism was also found to be higher with age, particularly in women aged 35–44 years, as reported previously, where there is greater burden of thyroid dysfunction during the perimenopausal period.[19] Also, hyperthyroidism (15.6%) was less common but was important because thyroid hormone excess can disrupt menstrual cyclicity due to hypothalamic–pituitary–ovarian axis disturbances.[18]

Of the women with abnormal uterine bleeding (AUB), 27.4% had hyperprolactinemia and 72.6% had normal serum prolactin levels. This prevalence is similar to that reported in previous studies conducted in India where hyperprolactinemia was seen in about 25% of women with AUB with the highest being seen in the age group 35-44 years and the lowest in the 45-49 years age group, as reported earlier.[19]

This greater incidence of hyperprolactinemia may be due to alterations in hypothalamic–pituitary control, psychosocial stress or mild endocrine abnormalities, such as thyroid disease. However, the decreased prevalence in older women may be due to a relative decrease in the stimulation of the pituitary lactotroph cells by estrogen, hence the importance of biochemical screening in the diagnosis of hyperprolactinemia, which is often the only symptom in women with AUB, particularly those with ovulatory dysfunction or irregular menstrual cycles.[11,12] Hyperprolactinemia can be diagnosed and treated early and can lead to restoration of ovulatory function, improvement of menstrual regularity and prevent unnecessary invasive investigations.[14]

The present study found no significant association between thyroid dysfunction and hyperprolactinemia among women with abnormal uterine bleeding. There was no statistically significant difference between the presence of hyperprolactinemia in women with euthyroid and those with abnormal TSH levels (27.2% vs. 27.8%, χ^2=0.02, p=1.00). The small effect size (φ=0.009) and the odds ratio near one (OR=1.04, 95% CI: 0.62–1.74) further support the finding that thyroid dysfunction was not associated with an increased risk for hyperprolactinemia in this cohort. The results are similar to those of previous studies which found no significant correlation between serum TSH and prolactin levels in women with AUB. The results of the present study were corroborated by the findings of Rathore et al, who reported a weak, non-significant correlation between thyroid function and serum prolactin levels in a recent Indian study, indicating that thyroid dysfunction and hyperprolactinemia may be independent endocrine abnormalities responsible for abnormal uterine bleeding and should therefore be evaluated separately.[16,23]

The lack of significant association between thyroid dysfunction and hyperprolactinemia could be due to the polyetiology of prolactin secretion. In hypothyroidism, secretion of thyrotropin-releasing hormone (TRH) is raised and this is followed by an increase in the secretion of prolactin, but this is more apparent in overt hypothyroidism. The high prevalence of subclinical hypothyroidism in the present study, on the other hand, might not have been enough to stimulate TRH sufficiently to elicit clinically relevant hyperprolactinemia. In addition, there are other factors that affect prolactin secretion that can be independent of thyroid status, such as stress, medications and pituitary function.[11,12]

The high prevalence of isolated thyroid dysfunction (17.8%) and isolated hyperprolactinemia (16.3%) and the low prevalence of concurrent abnormalities (11.1%) further support the notion that these endocrine disorders contribute independently to abnormal uterine bleeding, rather than as a direct causal relationship. These results suggest that thyroid function is not a reliable indicator of prolactin abnormalities and that both hormones should be evaluated independently in women with AUB. Prompt diagnosis and treatment of each endocrine disorder can help to achieve better menstrual results and prevent unnecessary invasive investigations. In summary, the present results suggest that thyroid dysfunction and hyperprolactinemia are frequent, but largely distinct endocrine causes of abnormal uterine bleeding.

CONCLUSION

Abnormal uterine bleeding is a very common gynecological symptom in women of reproductive age. The present study shows that thyroid dysfunction and hyperprolactinemia are common endocrine disturbances in these women, but there was no significant relationship between the two conditions. Thus, serum TSH and serum prolactin levels should be done as part of the initial evaluation of women with AUB. Early diagnosis and timely treatment of these potentially reversible endocrine disorders can help to enhance menstrual outcomes, direct medical management and minimize unnecessary surgical and/or invasive procedures.

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