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CLINICAL ARTICLE

Prevalence of hyperprolactinemia and thyroid disorders among patients with abnormal uterine bleeding

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ABSTRACT

Objective: To evaluate the prevalence of hyperprolactinemia and thyroid disorders among patients with abnormal uterine bleeding (AUB) compared with matched controls. *Methods:* In 2013–2014, an observational study of women with AUB (group A) and women with regular menstruation (group B) was undertaken at one center in Egypt and one in the United Arab Emirates. Eligible women were aged 20–35 years and were not obese. Participants underwent clinical examinations, vaginal ultrasonography, office hysteroscopy (in selected cases), and measurement of hormone levels. *Results:* Hyperprolactinemia was present in 17 (16.2%) of 105 patients in group A and 4 (3.2%) of 125 patients in group B ($P = 0.009$). In group A, a high thyroid-stimulating hormone (TSH) level was observed in 8 (7.6%) patients and low levels of free triiodothyronine/thyroxine were found in 5 (4.8%) patients, compared with 2 (1.6%) patients and 1 (0.8%) patient in group B ($P = 0.012$ and $P = 0.008$, respectively). Polymenorrhea was the most frequent presentation of AUB (n = 60 [57.1%]). Five (29.4%) patients with hyperprolactinemia had galactorrhea. In group A, 8 (47.1%) patients with a high TSH had hyperprolactinemia, whereas 1 (1.1%) patient with a high TSH had a normal prolactin value ($P = 0.008$). *Conclusion:* Screening by evaluating prolactin and thyroid hormone levels is recommended for all patients with AUB, even in the absence of galactorrhea.

1. Introduction

Abnormal uterine bleeding (AUB) occurs in 9%–14% of women between menarche and menopause; the condition has a considerable quality-of-life and financial implications [1]. AUB is the complaint in approximately one-third of all gynecology consultations [2].

Hyperprolactinemia is a condition of elevated serum levels of prolactin, a 198-amino-acid protein (23 kD) produced in the lactotroph cells of the anterior pituitary gland [3]. In many cases of AUB, after ruling out various causes such as cervical or uterine pathology, or pregnancy, patients are usually managed by hormonal treatment or blind surgical therapy [4]. The prevalence of hyperprolactinemia varies from 0.4% in the normal adult population to as high as 9%–17% among women with menstrual conditions such as amenorrhea or polycystic ovarian syndrome [5,6]. A high serum prolactin level can disturb follicular maturation and corpus luteum function [7], and leads to inhibition of the normal pulsatile secretion of gonadotropin-releasing hormone in the hypothalamus. It also provokes deficient secretion of luteinizing hormone and follicle-stimulating hormone, in amounts not adequate to induce a proper ovarian response [8].

Thyroid disorders are common in the female population, with approximately 0.8 per 1000 women per year developing hyperthyroidism and 3.5 per 1000 per year developing spontaneous hypothyroidism [9]. Thyroid hormones are thought to affect the menstrual pattern directly through an effect on ovarian-specific thyroid hormone receptors [10] and indirectly via their effects on sex hormone binding globulin, prolactin, and gonadotropin-releasing hormone secretion, and on coagulation factors [11]. Although National Institute for Health and Care Excellence guidelines [12] do not recommend the routine performance of thyroid function tests in women with menorrhagia, several studies [2,13] have shown that 15%–26% of menstrual cycle disorders result from thyroid dysfunction. Moragianni et al. [14] also highlighted the importance of thyroid function tests in patients with menorrhagia and concluded that medical treatment given in an appropriate timeframe can resolve the symptoms and preserve fertility potential.

Although hyperprolactinemia and thyroid disorders are well-known causes of oligomenorrhea and amenorrhea, there is no consensus on whether screening for these disorders is recommended in patients with menstrual irregularities. Therefore, the present study was conducted to

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measure the prolactin and thyroid hormone levels among patients presenting with an abnormal menstrual pattern (defined as any change in the duration, amount, or frequency of menstrual flow, excluding oligo- and amenorrhea), and to compare these levels with those in patients with regular menstruation to evaluate the usefulness of screening.

2. Materials and methods

The present cross-sectional, observational study was conducted from September 1, 2013, to September 30, 2014. Patients attending the outpatient gynecology and infertility clinics at Ain Shams University (Cairo, Egypt) or the Hendawy Medical Center (Abu Dhabi, United Arab Emirates) were recruited. Eligible women were aged 20–35 years and had a body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) of less than 30. Group A included consecutive patients attending the clinics who had AUB in the form of menorrhagia (bleeding for 7 days or more with the same heaviness throughout, as stated by the patient), polymenorrhea (frequent cycles of fewer than 21 days), intermenstrual bleeding, or mixed patterns. Group B comprised age- and BMI-matched healthy women with regular menstruation, recruited from couples presenting with male factor infertility.

The exclusion criteria for group A were: other forms of AUB (oligomenorrhea, primary or secondary amenorrhea); endocrine disorders leading to AUB, such as adrenal disorder and polycystic ovarian disease; organic causes of AUB, such as fibroids, polyps, or ovarian cysts; and hormonal treatment or treatment with medications that might have an impact on the menstrual flow or prolactin level, such as anticolitic treatment. Patients with suspected malignancy were also excluded, as were pregnant women, patients with a coagulation disorder, and those taking anticoagulation therapy. The exclusion criteria for group B were similar to those for group A; in addition, other causes of female factor infertility were excluded.

The local medical ethics committees in both clinics granted approval for the study design and all participants provided informed consent.

All participants underwent the following investigations to detect the presence of any organic pathology: medical history, history of drug intake, general examination, neck examination, examination for hyperandrogenic manifestations, determination of weight and BMI, breast examination for galactorrhea (performed after the determination of serum prolactin), and vaginal speculum examination.

Subsequently, all patients were assessed by vaginal ultrasonography (Accuvix V10; Samsung Medison, Seoul, South Korea), which was performed by one sonographer in each department. In addition, the following hormone levels were assessed on days 1–3 of menstruation: luteinizing hormone and follicle-stimulating hormone (measured by radioimmunoassay; DIAsource ImmunoAssays, Nivelles, Belgium); prolactin (measured by radioimmunoassay; Siemens Healthcare Diagnostics Products, Marburg, Germany); thyroid-stimulating hormone (TSH) (measured by enzyme immunoassay; BioCheck, Foster City, CA, USA); and free triiodothyronine (T3) and free thyroxine (T4) (measured by enzyme-linked immunosorbent assay; BioCheck, Foster City, CA, USA). If a uterine lesion was suspected, hysterosonography or diagnostic hysteroscopy was performed. Sampling was done with the precautions described by Orija et al. [15].

Hyperprolactinemia was defined as a prolactin level of more than 1.13 nmol/L. An abnormal TSH level was defined as a value outside the range of 0.5–5.5 IU/L. Abnormal T3 and T4 levels were defined as values outside the ranges of 3.5–6.5 pmol/L and 10–23 pmol/L, respectively.

A power calculation was performed to determine the required sample size, with a power of 80% and a confidence level of 95%. At least 100 patients needed to be recruited in each group. The data were analyzed using SPSS version 13 (SPSS Inc, Chicago, IL, USA). The χ^2 test was used to compare categorical data. $P < 0.05$ was considered statistically significant.

Table 1
Demographic and obstetric characteristics of the study participants.[a]

Parameter	AUB (n = 105)	Regular menstruation (n = 125)	*P* value
Age, y	27.8 ± 0.1	28.9 ± 0.0	0.742
BMI[b]	24.5 ± 0.0	26.8 ± 0.0	0.190
Parity	0–2	0–3	0.256
Ethnic origin			
White	85 (81.0)	94 (75.2)	0.134
Asian	15 (14.3)	25 (20.0)	0.095
African	5 (4.8)	6 (4.8)	0.879

Abbreviations: AUB, abnormal uterine bleeding; BMI, body mass index.
[a] Values are given as mean ± SD, range, or number (percentage).
[b] Calculated as weight in kilograms divided by the square of height in meters.

3. Results

The present study included 105 patients presenting with AUB and 125 controls who were recruited from the infertility clinic. There were no significant differences between the groups in terms of age, BMI, parity, and ethnic origin (Table 1).

The frequency of elevated prolactin levels was significantly higher in group A than in group B (16.2% vs 3.2%), and the mean prolactin level also differed considerably between the groups (Table 2). Moreover, elevated TSH levels were significantly more common in group A than in group B (7.6% vs 1.6%), and low levels of free T3 and T4 were also present in more patients in group A than in group B (4.8% vs 0.8%). By contrast, the frequencies of a low TSH level and elevated free T3/T4 levels did not differ significantly between the groups.

Polymenorrhea was the most frequent type of AUB, affecting 60 (57.1%) patients (Table 3). Hyperprolactinemia was recorded in 10 (16.7%) of these patients, and an elevated TSH level was present in 5 (8.3%). A subanalysis including only group A revealed that galactorrhea was significantly more common among women with hyperprolactinemia than among those without hyperprolactinemia ($P = 0.76$) (Table 4).

In another subanalysis involving only group A, an elevated level of TSH was significantly more common among patients with AUB who had hyperprolactinemia than among those who had a normal prolactin level (Table 5).

4. Discussion

The present study evaluated the prevalence of hyperprolactinemia and thyroid disorders among patients with AUB (excluding women with oligo-/amenorrhea), as compared with asymptomatic controls. A higher prevalence of hyperprolactinemia was identified among patients

Table 2
Prolactin and thyroid hormone levels among women with and without AUB.[a]

Endocrine disorder	AUB (n = 105)	Regular menstruation (n = 125)	*P* value
Hyperprolactinemia			
High prolactin (>1.13 nmol/l)	17 (16.2)	4 (3.2)	0.009
Prolactin, ng/mL	29.5 ± 16.7 (7.4–67.4)	11.7 ± 6.9 (1.9–31.2)	0.010
Hypothyroidism			
High TSH (>5.5 IU/L)	8 (7.6)	2 (1.6)	0.012
TSH, IU/L	3.4 ± 3.0 (0.3–16.3)	2.4 ± 0.9 (1.3–6.3)	0.025
Low free T3 and T4	5 (4.8)	1 (0.8)	0.008
Hyperthyroidism			
Low TSH (<0.5 IU/L)	1 (0.9)	1 (0.8)	0.950
TSH, IU/L	2.6 ± 1.3 (1.5–5.4)	2.1 ± 1.0 (0.4–4.1)	0.086
High free T3 and T4	1 (1.0)	1 (0.8)	0.950

Abbreviations: AUB, abnormal uterine bleeding; T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone.
[a] Values are given as number (percentage) or mean ± SD (range).

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