DOI: https://doi.org/10.53350/pjmhs20221611808

ORIGINAL ARTICLE

Assessment Clinical Association of Thyroid Function in Women of Reproductive Age Group with Abnormal Uterine Bleeding

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ABSTRACT

Background: Abnormal Uterine Bleeding occurs when the frequency and quantity of menstrual bleeding in females is significantly altered. It is the most prevalent clinical presentation in gynecology, affecting more than 20% of the female population, and is characterized by variations from normal menstruation in terms of irregularity in periods, frequency, duration of blood flow, amount of blood loss, and cyclicity. Thyroid hormones had significant effects on the female reproductive system, such as delayed puberty, infertility, premature menopause, recurrent abortions, and AUB. The AUB is significantly associated with thyroid secretions, and any patient who complains of AUB or irregular menstruation must have thyrotoxicosis ruled out.

Objectives: This study was conducted at the Department of Obstetrics and Gynecology, Nishtar Hospital, Multan, Pakistan, (2021-22) in order to evaluate the clinical association between thyroid function and AUB in women of different reproductive age groups.

Methods: This cross-sectional study was conducted in the outpatient department of Obstetrics & Gynecology, Nishtar Hospital, Multan, from 1st December 2021 to 31st May 2022. 320 patients participated in the study and were examined clinic-pathologically and were allocated into three groups based on their thyroid profile (euthyroid, hyperthyroid and hypothyroid, respectively) and further predisposition risk factors were recorded and analyzed.

Results: It was discovered that extreme age groups of adolescence and pre-menopause phase significantly ($p<0.05$) increased the incidence of AUB. The incidence of AUB was also elevated ($p<0.05$) among patients with an abnormal BMI, women with multiple pregnancies, and married women. The menstrual bleeding pattern was also studied in females, with polymenorrhea (131/320) being the most prevalent ($p<0.05$), followed by menorrhagia (79/320), metrorrhagia (59/320), oligomenorrhea (42/320), and amenorrhea (9/320) having a significantly lower incidence ($p<0.05$). The incidence rate of thyroid disorders was 28.12% (90/320), with hypothyroidism affecting 77(24.06%) and hyperthyroidism affecting 13(4.06%) patients ($p<0.05$).

Practical implication: AUB is significantly associated ($p<0.05$) with thyroid hormones, therefore for early diagnosis of the underlying etiology and treatment of the patients by preventing hysterectomy and other serious surgical interventions, all patients presenting to OPD clinics with the complaint of AUB or irregular menstruation must be ruled out for a thyroid profile in the first instance.

Conclusion: It was concluded that thyroid disorders directly affected the BMI, fertility and menstrual cycle of gynecology patients and increased the incidence of AUB along with the medical and gynecological complications.

Keywords: Amenorrhea; Hyperthyroidism; Hypothyroidism; Polymenorrhea; Thyrotoxicosis.

INTRODUCTION

In normal menstruation, the uterine bleeding occurs in 21 to 35 days, and the menstrual bleeding lasts for 2 to 7 days, with 5-80 milliliter of blood loss per cycle. But when the frequency or quantity of the menstrual bleeding is significantly increased, this is termed as Abnormal Uterine Bleeding (AUB) [1]. It is the most common clinical presentation in the gynecology, affecting more than 20% female population and is the bleeding from uterus clinically characterized by variations from the normal menstruation pertaining to the irregularity in periods, frequency, duration of blood flow, extent of blood loss and cyclicity [2]. It can be seen in all age group females commencing from menarche to menopause and this disorder significantly affect the physical, sexual and emotional health and quality of life of the patients [3, 4].

International Federation of Obstetrics and Gynecology (FIGO) classified the etiological factors of AUB in two categories: structural and non structural [5]. The structural causes involve polyps formation, fibroids, hyperplasia, malignancies, cancers, adenomyosis, while, non structural causes are side effects of birth control pills, endometrial and blood clotting disorders [6]. Any disorder, in the endometrium or hormonal imbalance of pituitary gland, thyroid gland, ovaries or hypothalamus result in the disrupted menstruation and lead the AUB [2]. Thyroid hormones play a vital role in the reproductive physiology of females, therefore, any kind of thyroid abnormalities including both hyperthyroidism or hypothyroidism significantly affect the normal menstruation and consequently AUB in all age group females [7]. The females most commonly affected with AUB due to hormonal imbalances are of age groups of extreme reproductive stages like adolescence, pre-menopause phase, post-partum or post-abortion [8].

The menstrual cycle is based on the complex interaction of reproductive organs and endocrine system of the females and any disruption between these two systems, is the etiology of abnormal menstruation or AUB. The characteristic features of the AUB are: polymenorrhea (bleeding at less than 21 days interval), oligomenorrhea (bleeding at more than 35 days interval), menorrhagia (heavy blood flow of more than 80ml per cycle), metorrhagia (inter-menstrual irregular bleeding) and amenorrhea (stopped bleeding in non-menopause female patients) [9]. In early thyrotoxicosis, the reproductive associations are polymenorrhea and menorrhagia, while, in later and chronic stages amenorrhea develop in thyroid associated problems. In case of hyperthyroidism, the amenorrhea and hypomenorrhea are more frequently evidenced, while 5% of the patients complain for menorrhagia. In contrary to this, in case of hypothyroidism, most often maladies are amenorrhea or anovulation [10]. In brief, thyroid hormones had profound effects on female reproductive system including delayed puberty, infertility, premature menopause, recurrent abortions and AUB. The AUB is significantly associated with the thyroid secretions and any patient complaining the AUB or irregular menstruation must be ruled out for thyrotoxicosis [11]. Therefore, this study was specifically executed to assess the clinical association of thyroid function in ladies of different reproductive age groups with AUB, presented at the Department of Obstetrics & Gynecology, Nishtar Hospital, Multan.

MATERIALS & METHODS

Study Design: This was hospital based retrospective cross-sectional observational study, which was conducted on the 320 female patients, visiting the outpatient department (OPD) at the Department of Obstetrics & Gynecology, Nishtar Hospital, Multan, from 1st December 2021 to 31st May 2022.

Inclusion and Exclusion Criteria: The data was collected from all the female patients with age ranging from 15-50 years, complaining the abnormal uterine bleeding, on an approved study questionnaire. While, the females complaining AUB with known thyroid problems, blood clotting or coagulopathy, were excluded from the study. All those women who were already diagnosed with the uterine polyps, fibroid, cancers, ovarian cysts, cervical tumors, malignancy, or enometriosis were also excluded from the study recruitment [3].

Examination of the Patients: The detailed gynecological history pertaining to the menarche, menstrual cycle variations, extent and volume of the menstrual flow, menorrhagia etc was taken from each patient along with her age and marital status description along with the medical examination including gynecological examination was conducted to rule out the pathological or structural problems associated with the ovaries and uterus. The genetic history of the patients for thyroid diseases was obtained and the weight as well as body mass index of the patients was also evaluated. The ultrasound of all the patients was done for ruling out any structural abnormality in the uterus or pelvic organs of the participants [9]. Moreover, the patients were urged to conduct diagnostic tests including complete blood count, blood biochemistry, blood sugar, and thyroid profile in particular for T3, T4 and TSH levels.

On the basis of their thyroid profiles, the patients were classified under three categories **(Table 1),** on the basis of their thyroid profile [12].

Table 1: Categorization of the subjects according to their serum thyroid profile

Category	Thyroid Status	Serum T3 level	Serum T4 level	Serum TSH level
Euthyroid	Normal	0.77- 1.98 ng/dl	6-12 µg/dl	0.34-5.12 µIU/L
Hyperthyroid	Over secretion	Above 1.98 ng/dl	Above 12 µg/dl	Below 0.34µIU/L
Hypothyroid	Under secretion	Below 0.77 ng/dl	Below 6 µg/dl	Above 5.12µIU/L

Ethical Clearance: The ethical clearance was acquired from the Ethical Review Committee of Nishtar Hospital, Multan and the study did not violate the ethical norms and privacy of the participants.

Statistical Analysis: All the data was recorded on pre-designed questionnaires and compiled on MS Excel sheets (2010). The prevalence of AUB associated with thyroid dysfunctions was determined using percentage, frequencies and the data between the treatment groups was analyzed Chi-square test. While, the quantitative variables were shown in mean and standard deviation of error with proportions of categorical variable. One-way ANOVA including Tuckey HSD test, was used for the analysis of significance between the variables at the p<0.05 difference, using IBM Statistical Package for Social Sciences version 24.

RESULTS & DISCUSSION

Patients' Profile and Comorbidities: This was a hospital based retrospective observational study AUB and comorbidities, conducted at the Department of Obstetrics & Gynecology, Nishtar Hospital, Multan, from 1st December 2021 to 31st May 2022 (FY 2021-22). The study included 320 participants, with the complaint of AUB, of 03 age groups (Table 2), as per inclusion criteria. There were 76 (23.75%) patients enrolled in Group A having age 13-25 years, 230 (71.87%) patients in Group B of age 26-38 years and 14 patients of age 39-50 years. There was statistically significant difference among these age groups (p<0.05) whereby the number of patients in Group B were highest, followed by Group A and C, respectively. The incidence of AUB due to imbalance of thyroid hormones is associated with the extreme reproductive stages like adolescence, pre-menopause phase, post-partum or post-abortion [8]. Similar flux of population was reported in a study in which the majority of females presented with AUB were euthyroid (77%) and 23% were affected with thyroidism, while, our findings revealed that 71.87% AUB patients were euthyroid and 28.13% were affected with thyroid disorders [3, 14, 15]. Similar findings were reported that most patients presented with AUB were from category of euthyroid and the menorrhagia was the common matter of complain [16]. Another study revealed that the AUB patients at the OPD clinics were mostly euthyroid (19%), while, 16.5% were hypothyroid and 2.5% were hyperthyroid, the results of which are in close agreement with our findings [19]. Our results were also in collaboration with the study completed in a tertiary care hospital, in which the AUB cases for euthyroid, hypothyroid and hyperthyroid category showed the ratio of 77.6, 17.6 and 4.7%, respectively [20]. Similarly, statistically elevated percentage of hypothyroid patients (16/116) was reported than hyperthyroid patients (3/116), which are also in agreement of our results [2]. The findings of a study are in accordance with our findings that AUB presented gyne patients were 65% euthyroid, 32% hypothyroid and 3% were hyperthyroid [9].

Table 2: Age-wise group allocation of the subject participants

S. No	Age Group	Age Range	No. of patients (n)	Percentage	p-value
1	Group A	13-25 years	76	23.75%	0.00001*
2	Group B	26-38 years	230	71.87%	
3	Group C	39-50 years	14	4.38%	
Total			320	100%	

SS= 4947.71
MS= 2473.86
df=14
F= 92.30846
P= 0.00001* (P is significant at p<0.05)

The body mass index (BMI) of the patients was also calculated using their height and weight values and women were categorized into 04 groups on the basis of BMI standards, to investigate the correlation of body fats and AUB. These were; underweight, normal, overweight and obese patients complaining the AUB were with BMI lower than 18.5, BMI between 18.5 and 24.9, with 25-30 and BMI above 30, respectively (Figure 1). It was evident from the results that the patients with the normal BMI and body fats were suffered the least (p<0.05), affecting only 13% population while, the obese patients (51%) were found predominantly suffered (p<0.05) from AUB. The incidence in weak and overweight patients was non-significantly (p≥0.05) different, with the percentage of 21 and 15%, respectively. Therefore, as per perspectives of this study, the obesity was found the predominant key factor significantly (p<0.05) causing AUB. Our findings were correlated with the study in which the endometrial hyperplasia was reported in gyne patients with increased BMI, resulting in uterine dysfunction and AUB [23]. Another research also depicted that the incidence of AUB was closely associated with BMI, whereby 81% presented patients with abnormal BMI had complaint of AUB [24]. Similar results were retrieved in a study, reporting that due to elevated BMI of the females, the endometrial thickness was increased and caused atyptical endometriosis, resulting in polymenorrhea and AUB [25]. Our results were corroborated with a study, in which it was reported that heavy menstrual bleeding (polymenorrhea) was the most common bleeding pattern of AUB patients and affected 58.45% patients [27].

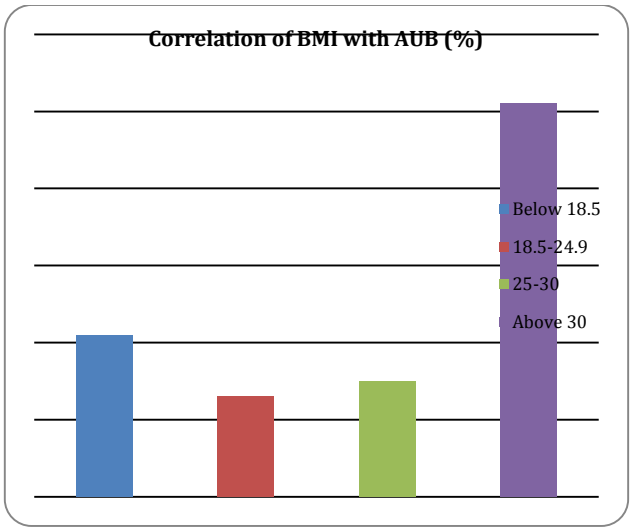

Figure 1: Correlation of patients' BMI with AUB

The history of the patients with AUB was taken on an approved questionnaire performa for analysis of the study parameters. The incidence of AUB was comparatively studied with the marital status and parity of the women. As far as the marital status of the AUB patients was concerned, it was revealed that AUB was mostly prevalent ($p<0.05$) in married population of the females and 212/320 (66.25%) AUB patients were married. Further parity of the females was also correlated with AUB and significantly highest incidence ($p<0.05$) of AUB was seen in the women with multiple pregnancies, followed by unmarried females, and lower incidence was recorded in primipara (females who delivered their first young one) and multipara (females who gave more than one birth) women **(Figure 2)**. The results of our study are in close agreement with the study, in which it was found that the prevalence of AUB was significantly higher ($p<0.05$) in multiparous patients (94%), followed by nulliparous (4%) and primaparous (2%) [21]. The incidence of AUB was significantly higher ($p<0.05$) in multiparous patients and reported 78% cases of AUB associated with multiple parity [28]. Similar findings were reported in a study that AUB was significantly higher in patients with Para-2 having 40.71 and 32.80% incidence of AUB [29].

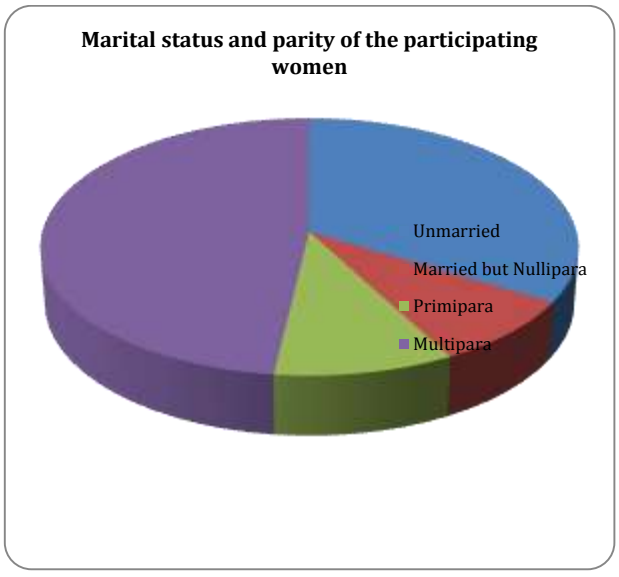

Figure 2: Classification of AUB patients according to their marriage status and parity

Bleeding Patterns of Patients Suffering from AUB: The bleeding pattern of the menstruation in AUB females was also asked and recorded in the questionnaire and was also analyzed statistically. The highest female population ($p<0.05$) with AUB was with the complaint of polymenorrhea (131/320), followed by menorrhagia (79/320), metrorrhagia (59/320), oligomenorrhea (42/320) and significantly lowest incidence ($p<0.05$) was found with the complaint of amenorrhea (9/320) **(Figure 3).** It was reported in a study that the female patients arriving with AUB were mostly complaining for menorrhagia (43%), followed by the bleeding pattern of ploymenorrhea (29%), oligomenorrhea (16.50%) and metorrhagia (2%) [16]. A study reported that the common type of bleeding pattern in the AUB patients is menorrhagia followed by polymenorrhea with the percentage of 44 and 16%, respectively [9]. Other studies also reported the same results that the AUB gyne patients were mostly complaining of menorrhagia and polymenorrhea with the percentage of 37.5, 46.15% and 22, 57.13%, respectively [22]. A study was conducted in the gynecology department, Moi Hospital Kenya and it was reported that 79.6% patients of AUB were suffering with prolonged bleeding during their menstruation [26]. Menorrhagia and polymenorrhea were the common and most prevalent clinical outcomes of the AUB in gyne patients [28].

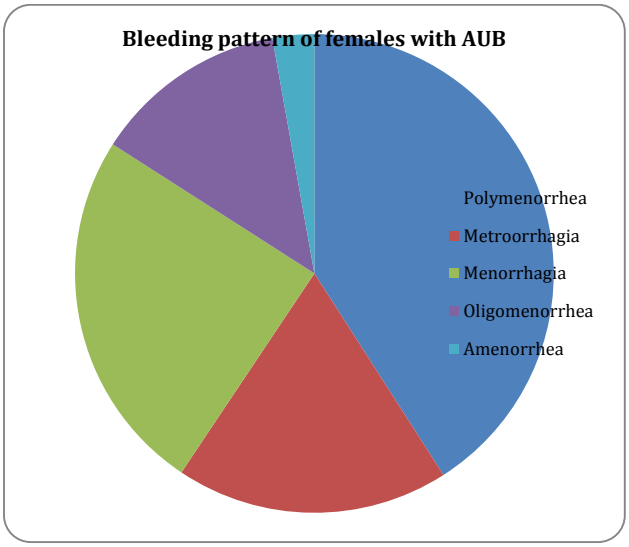

Figure 3: Bleeding pattern in patients suffering from AUB

Association of Thyroid Dysfunction with AUB: Thyroid hormones play a vital role in the reproductive physiology of females; therefore, thyroid abnormalities including both hyperthyroidism and hypothyroidism were keenly correlated in this study and it was revealed that thyroid disorders significantly affected ($p<0.05$) the normal menstruation and consequently AUB was resulted in all age group females. All the presented 320 AUB patients were investigated through their serum thyroid profile and out of these AUB cases, 90 were directly associated with the thyroid disorders **(Figure 4)**, in which 77(24.06%) patients ($p<0.05$) were affected with hypothyroidism and 13(4.06%) with hyperthyroidism **(Table 3)**. Our findings were strongly supported by a study in which the significantly higher incidence ($p<0.05$) of AUB was found in hypothyroidism than hyperthyroidism at the rate of 13.9 and 1.50%, respectively [16]. Our study is supported by the findings of a study in which 12.14% (17/140) cases were associated with thyroid disorders [29].

The association of thyroidism was also compared with AUB incidence in different age groups of the females and it was evident from the results that significantly highest ($p<0.05$) incidence of AUB due to thyroid abnormities was seen in the age Group C (39-50 years) (78.57%) and Group A (13-25 years) (38.15%), while,

significantly lowest AUB incidence due to thyrotoxicosis (p<0.05) was seen in Group B (26-38 years) with the prevalence of 21.73% **(Table 4).** The findings of our study were in accordance with the studies in which the prevalence of AUB due to thyroid disorders was highest in old age females [3, 13]. Another study stated that 67.2% of the female patients of age 35-45 years were affected with AUB due to thyroid disorders [17, 18]. The findings of a study revealed that 55.26% aged females were affected with AUB due to throtoxicosis [19]. Our findings are corroborated with a study conducted in Patil Medical College, Karnataka, India comprising 140 patients of AUB, in which 17 patients were suffering from thyroid abnormalities. The incidence of AUB was significantly higher (p<0.05) in hypothyroid patients than hyperthyroid patients with the percentage of 7.14 and 1.4%, respectively [29]. Similar findings were reported that AUB due to thyroidism had 30% more prevalence than the control group [30]. A study was conducted in a Medical College Mangalore comprising 85 subjects. It was revealed during the study that 29/85 patients of AUB had etiology of thyroidism, whereby, 24 patients were diagnosed with hypothyroidism and 5 patients with hyperthyroidism [31].

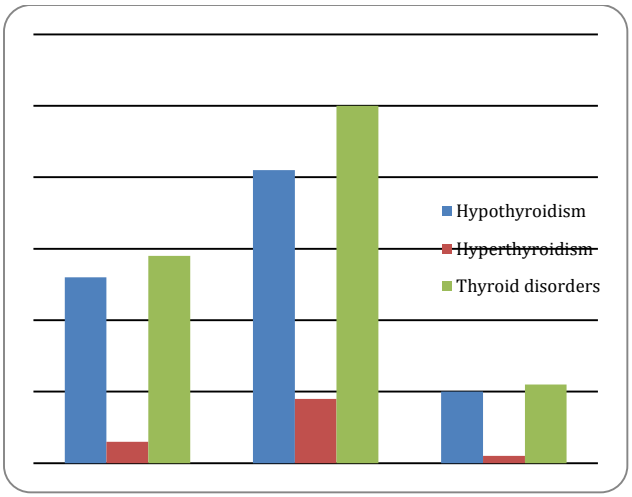

Figure 4: Association of thyroid dysfunction with the age groups of patients

Table 3: The participant's ratio with thyroid hormones

S. No	Total No. of Patients (n)	Euthyroid n (%)	Hyperthyroid n (%)	Hypothyroid n (%)	X^2	p-value
1	320	230 (71.87)	13 (4.06)	77 (24.06)	168.6605	0.00001*

Chi-square value= 168.6605
P-value= 0.00001* (P is significant at p<0.05)

Table 4: Association of different age groups of AUB with thyroid disorders

S. No	Age range (Y)	No. of AUB patients (n)	Hypo-thyroidism n(%)	Hyper-thyroidism n(%)	Total thyroid disorder n	Percentage of Thyroid disorders associated with AUB (%)	p-value
1	13-25 years	76	26(34.21)	3(3.94)	29	38.15	
2	26-38 years	230	41(17.82)	9(3.91)	50	21.73	
3	39-50 years	14	10 (71.42)	1(7.14)	11	78.57	
Total		320	77(45.26)	13(14.99)	90	-	0.00001*

Chi-square value= 168.6605
P-value= 0.00001* (P is significant at p<0.05)

CONCLUSION

It has been revealed from this retrospective observational study that thyroid disorders directly affect the BMI and menstrual cycle of the gyne patients and increase the incidence of AUB. Therefore, all the patients presented at the OPD clinics with the complaint of AUB or irregular menstruation must be ruled out for her thyroid profile at the first instance for early diagnosis of the underlying etiology and treatment of the patients by preventing them from hysterectomy and other serious surgical interventions.

Authors' Contribution: All the authors contributed equally in this research study.

Acknowledgments: The study was funded by a regular budget grant, from the Government of Punjab, Pakistan.

Conflict of Interest: The authors declared no conflict of interest.

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