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Analysis of the Association between Abnormal Uterine Bleeding and Insulin Resistance

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Annotation: According to the International Federation of Gynecology and Obstetrics, abnormal uterine bleeding ranged from 3% to 30% internationally, where the endocrine cause is the most common cause of abnormal uterine bleeding, accounting for up to 50% of cases, and 20% of this is related to amenorrhea, the most observed endocrine pattern being insulin resistance, which occurs in most patients diagnosed with abnormal uterine bleeding. This study aimed to 1) evaluate the outcomes of women who were diagnosed with abnormal uterine bleeding in comparison with the control group and to 2) investigate the association between abnormal uterine bleeding and insulin resistance of the patients who participated in this study.

Based on the study's goal, a cross-sectional study was performed on 200 women who were referral to Thi Qar-Iraq hospitals during a 12-month period, ranging from April 2024 to April 2025. Women's data were classified into two groups, including 100 samples with abnormal uterine bleeding and 100 samples who presented as the control group (regular menstrual cycles). As well as we also evaluated insulin resistance in participants through the HOMA-IR index in correlation with fasting glucose, insulin, and lipid profile, as well as hormonal assays.

To compare with the control group, our study showed a rise in insulin resistance with a 4.0 ± 1.8 HOMA-IR Index, total cholesterol of 198 ± 32 mg/dL, triglycerides of 145 ± 58 mg/dL, LH of 8.5 ± 4.1 IU/L, FSH of 6.8 ± 2.3 IU/L, LH/FSH ratio of 1.3 ± 0.6, and total testosterone of 48.5 ± 18.2 ng/dL and a drop in HDL-C of 48 ± 9 mg/dL in a group of women with abnormal uterine bleeding.

In conclusion, our outcomes indicate that women with abnormal uterine bleeding have a positive association with high insulin resistance, LH/FSH ratio, and total testosterone in comparison with women in the control group.

Keywords: Abnormal Uterine Bleeding [Aub], Insulin Resistance, Homa-Ir Index, And Total Testosterone.

Introduction

Abnormal uterine bleeding (AUB) is described as the abnormality in duration, quantity, frequency, and regularity in the bleeding of the uterine body. It decreased the quality of life in terms of the following aspects: emotional, physical, and social; school attendance; work; and limit of participation in sports and social life {1, 2, 3}. The menstrual cycle has been described as having a duration between 21 and 34 days, within which seven days or less of uterine bleeding occurs, with an average blood loss of 30-40 ml, which could be quantified as 3-6 sanitary towels or tampons per day. {4, 5}

Abnormal uterine bleeding is a very frequent entity of consultation, both in adolescent women from menarche and in postmenopausal women, with an immense range of possible pathologies that vary

according to age group, which have been classified by the International Federation of Gynecology and Obstetrics (FIGO). {6, 7, 8}

IR is the common metabolic defect of the alterations that are grouped in the metabolic syndrome, such as obesity, glucose intolerance, arterial hypertension, dyslipidemia, and type 2 diabetes mellitus {9}. Insulin resistance, defined as a decrease in the glucose response to a certain amount of insulin, is a condition that represents a risk factor for developing diabetes mellitus, coronary heart disease, and arterial hypertension in the long term. Therefore, it is important to achieve a suitable intervention that reduces the risk of suffering from these diseases {10}. Insulin is a hormone that facilitates the homeostasis of glucose in the human body through the active stimulus it exerts on the target tissues (adipocytes and cardiac and skeletal muscle) and by suppressing the production of glucose by hepatocytes. Glucose intolerance is one of the main clinical problems in women with polycystic ovary syndrome and can vary between 23% and 35%. {11, 12}

Teenagers make up 18% of the global population, and their growth will continue until around the year 2030 {13}. A Canadian study identified that there is a strong correlation between a high BMI in adolescents with gynecological problems in an adolescent clinic over a period of more than 6 years, with 24% obesity and 17% overweight, representing a total of 41% of patients {14}. The main gynecological problems related to obesity in childhood were the early onset of puberty, menstrual irregularities during adolescence, and polycystic ovary syndrome. {15}

In women with polycystic ovary syndrome, hyperinsulinemia has usually altered the production of different proteins by the liver cells. Hyperinsulinemia decreased the production of Sex Hormone-Binding Globulin (SHBG), which is a plasma glycopeptide produced by the liver function that regulates the metabolism of beta-estradiol and testosterone. This current study largely contributed to enrolling clinical outcomes and describing a correlation between abnormal uterine bleeding and insulin resistance (IR). {16, 17}

Patients & Methods

According to the database of medical records at Thi Qar, Iraq, hospitals, we designed a cross-sectional study during a 12-month follow-up from April 2024 to April 2025. Two hundred patients were selected who had complete data, including the quantification of HOMA, and who were used for the present study. All cases were participated within the age range between 28 and 42 years and with a body mass index in the range of 25–34 {kg/m²}. This current study evaluated the extent of correlation between abnormal uterine bleeding (AUB) and insulin resistance for 200 women who were diagnosed using the PALM-COEIN classification.

In terms of data collection, all data were collected through a database in medical records at Thi Qar, Iraq, hospitals. Collected data of 200 women were categorized into two groups based on status. The patient group represented 100 women who suffer from abnormal uterine bleeding (AUB), while the second group is a control group, which is presented as 100 women with normal menstrual cycles. Our study defined demographic characteristics of women who were diagnosed with AUB including age (ranging from 28 to 42 years), BMI in (kg/m2), smoking status, blood pressure measurements, and waist circumference alongside with all data from women's blood samples were obtained after 8 hours of fasting and included fasting glucose (mg/dL), fasting insulin (μIU/mL), HOMA-IR Index, HbA1c, total cholesterol (mg/dL), triglycerides (mg/dL), and HDL-C (mg/dL).

Furthermore, we defined the most marked causes of women with abnormal uterine bleeding (AUB) through the PALM-COEIN classification, which was a more effective system for managing abnormal uterine bleeding. The HOMA-IR index, serum SHBG levels, and BMI registration were also calculated, where the HOMA was calculated by means of the following method:

HOMA= (Insulin μu/mL) (Glucose mmol/L) / 22.5

We measured the ratio of insulin resistance in comparison between both two groups, based on the underlying causes of AUB existing in patients. Furthermore, it also measured the hormonal profile

parameters of women in both groups, including LH (IU/L), FSH (IU/L), etc. We analyzed a significant Pearson's correlation of hormonal factors and HOMA-IR with metabolic syndrome. It also defined insulin resistance in only 100 AUB women. In addition, a multivariate logistic regression of factors related to AUB women was conducted. The data are described as averages and standard deviations (SD), or frequencies or percentages, according to SPSS, version 24.0.

Results

A total of 200 samples were enrolled the outcomes in this cross-sectional study. All patient groups were closed in age and smoking status, which age of 35.2 ± 6.1 years, with smoking 24.3% in the AUB group, while 34.8 ± 5.7 years with 12.5% in the control group. In addition to anthropometric measurements, we had measured each of systolic blood pressure and diastolic blood pressure. It noticed 124 ± 11 mmHg of systolic BP and 82 ± 8 mmHg of diastolic BP in the AUB group, but systolic blood pressure was 118 ± 9 mmHg and diastolic BP was 77 ± 6 mmHg in the control group.

TABLE – 1: Baseline and demographic parameters of women who participated in this cross–sectional study.

Characteristic	AUB Group (n=100)	Control Group (n=100)	p-value
Age (years)	35.2 ± 6.1	34.8 ± 5.7	0.812
BMI (kg/m²)	29.5 ± 4.8	24.1 ± 3.5	<0.002
Waist Circumference (cm)	92.3 ± 9.1	78.6 ± 7.4	<0.002
Systolic BP (mmHg)	124 ± 11	118 ± 9	0.02
Diastolic BP (mmHg)	82 ± 8	77 ± 6	0.003
Smokers	24.3%	12.5%	0.642

In terms of insulin resistant in both groups, this study has a high level of IR in the AUB group, with 73.50% with 4.0 ± 1.8 of HOMA-IR Index in comparison with the control group with 23.50% of 1.6 ± 0.6, which belongs to these IR to 200 women who participated in our study.

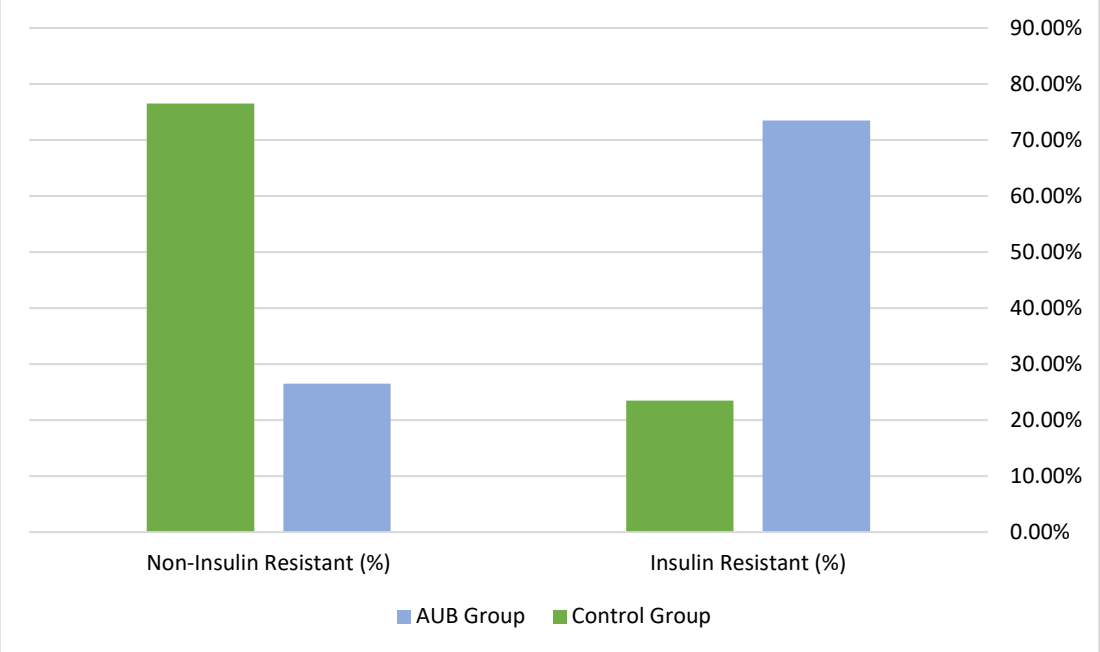

FIGURE - 1:- Distribution of insulin resistance on women who HOMA-IR lower than 2.5.

TABLE – 2: Identifying the correlation among women with abnormal uterine bleeding and insulin resistance.

Exposure	Odds Ratio (OR)	95% CI	p-value
Insulin Resistance (HOMA-IR ≥ 2.5)	8.33	2.92 – 24.81	<0.002

Also, our outcomes showed notably metabolic factors in AUB group including fasting glucose was 102.4 ± 11.3 (mg/dL), fasting insulin was 15.8 ± 6.2 (µIU/mL), HbA1c (%) was 5.8 ± 0.5, total cholesterol was 198 ± 32 (mg/dL), triglycerides was 145 ± 58 (mg/dL) and drop in HDL-C was 48 ± 9 (mg/dL) in comparison with control group fasting glucose was 89.2 ± 6.5 (mg/dL), fasting insulin was 7.1 ± 2.8 (µIU/mL), HbA1c (%) was 5.2 ± 0.3, total cholesterol was 185 ± 28 (mg/dL), triglycerides was 92 ± 35 (mg/dL) and rise in HDL-C was 55 ± 8.

TABLE – 3: Enroll diagnostic outcomes of metabolic factors.

Parameters	AUB Group (n=100)	Control Group (n=100)	p-value
Fasting Glucose (mg/dL)	102.4 ± 11.3	89.2 ± 6.5	<0.001
Fasting Insulin (µIU/mL)	15.8 ± 6.2	7.1 ± 2.8	<0.001
HOMA-IR Index	4.0 ± 1.8	1.6 ± 0.6	<0.001
HbA1c (%)	5.8 ± 0.5	5.2 ± 0.3	<0.001
Total Cholesterol (mg/dL)	198 ± 32	185 ± 28	0.072
Triglycerides (mg/dL)	145 ± 58	92 ± 35	<0.001
HDL-C (mg/dL)	48 ± 9	55 ± 8	0.001

According to PALM-COEIN classification, it analyzed all underlying causes of abnormal uterine bleeding (AUB) in women, where leiomyoma (AUB-L) was the most common factor with 32.35%, followed by ovulatory dysfunction (AUB-O), which was 20.59%, and Polyp (AUB-P) was 20.59% in all AUB women patients.

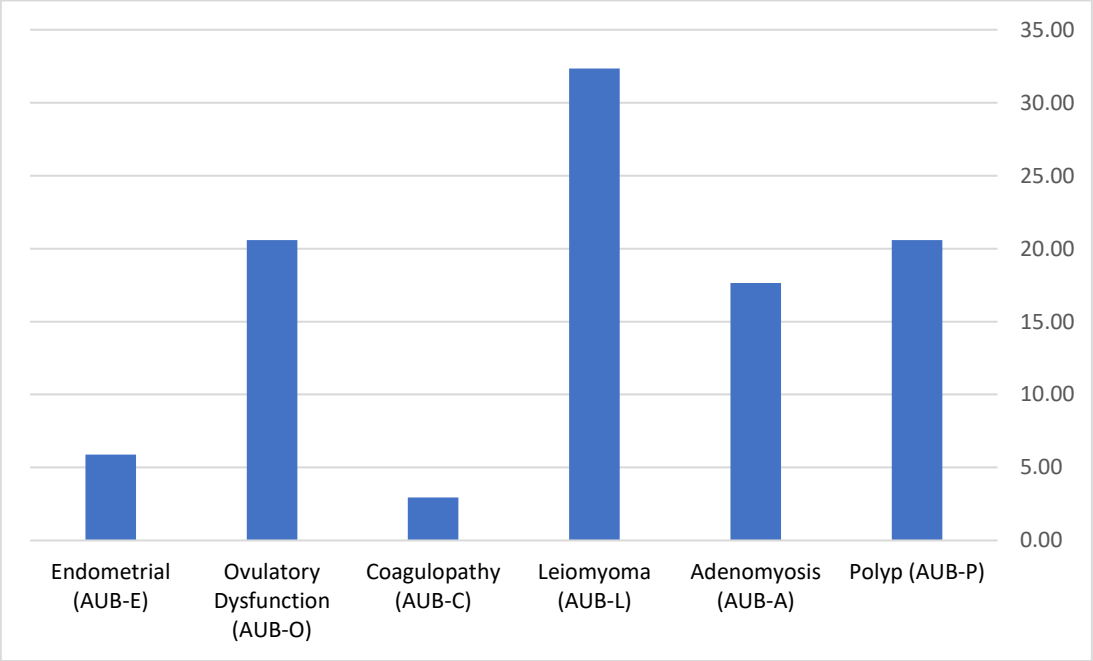

FIGURE 2:- Categorization of underlying causes related to abnormal uterine bleeding (AUB) by PALM-COEIN classification.

TABLE 4:- Determining insulin resistance at 100 women group with abnormal uterine bleeding (AUB).

AUB Causes	Frequency and percentage of AUB women		Insulin resistance of each AUB woman	
Variables	**Frequency**	**%**	**Frequency**	**%**
Polyp (AUB-P)	20	20%	17	85%
Adenomyosis (AUB-A)	16	16%	4	66.67%
Leiomyoma (AUB-L)	33	33%	28	84.85%
Coagulopathy (AUB-C)	4	4%	4	100.00%
Ovulatory Dysfunction (AUB-O)	21	21%	18	85.71%
Endometrial (AUB-E)	6	6%	6	100.00%

In term of hormonal profile, we found that almost parameters of hormonal profile in the AUB groups had significantly higher than control groups of LH (8.5 ± 4.1) IU/L, FSH (6.8 ± 2.3) IU/L, total testosterone (48.5 ± 18.2) ng/dL, free androgen index (5.2 ± 2.1), except lower SHBG (38.2 ± 12.5) (nmol/L), which it noticed evidence of hyperandrogenic alongside with dysregulated state.

TABLE – 5:- Enroll hormonal profile data of women in both groups.

Hormone factors	AUB Group (n= 100)	Control Group (n= 100)	p-value
LH (IU/L)	8.5 ± 4.1	6.2 ± 2.5	0.007
FSH (IU/L)	6.8 ± 2.3	7.1 ± 2.1	0.562
LH/FSH Ratio	1.3 ± 0.6	0.9 ± 0.3	0.001
Total Testosterone (ng/dL)	48.5 ± 18.2	35.1 ± 12.4	<0.001
SHBG (nmol/L)	38.2 ± 12.5	55.8 ± 14.1	<0.001
Free Androgen Index (FAI)	5.2 ± 2.1	2.1 ± 1.0	<0.001

TABLE – 6: Pearson's correlation of hormonal factors and HOMA-IR with metabolic.

Factors	AUB Group (n= 100)	Control Group (n= 100)
BMI	0.61	0.45
Waist Circumference	0.65	0.51
Triglycerides	0.58	0.49
HDL-C	-0.52	-0.41
Total Testosterone	0.48	0.22
SHBG	-0.57	-0.38

TABLE – 7: Multivariate logistic regression of factors related to AUB women.

Predictor Variables	Adjusted Odds Ratio (aOR)	95% CI	p-value
Insulin Resistance (HOMA-IR ≥ 2.5)	6.12	1.85 - 20.28	0.003
BMI ≥ 30 kg/m²	3.45	1.12 - 10.64	0.031
Age	1.01	0.92 - 1.11	0.821
High Triglycerides (≥150 mg/dL)	2.88	0.95 - 8.75	0.062

Furthermore, it indicated that 40% of women suffer with PCOS had more insulin resistant with androgen at the women's group with AUB compared to compare at AUB without insulin resistant.

TABLE 8:- Classify women with abnormal uterine bleeding (AUB) and based on insulin resistance.

Characteristic	AUB with IR (n=25)	AUB without IR (n=9)	p-value
BMI (kg/m²)	30.3 ± 5.1	24.1 ± 4.0	<0.001
HOMA-IR Index	4.3 ± 1.4	1.0 ± 0.2	<0.001
Free Androgen Index	5.5 ± 1.3	3.4 ± 1.2	0.002
Prevalence of PCOS	40%	10%	0.046

Discussion

Menstruation is the process in which the peeling of the surface layer of the endometrium occurs in response to decreased progesterone levels, the clinical manifestation of which is bleeding {18}. It has been seen as a consequence of the evolution of the species, since not all animal species, nor do all mammals, have menstruation. Menstruation in women is necessary to achieve adequate hemochorial placentation in case a pregnancy occurs {19, 20]

We discovered that women with (AUB) abnormal uterine bleeding had far greater levels of androgen and IR than those without the condition. A further study showed that women have a significant relationship between the severity of insulin resistance (IR) and menstrual irregularity during the length of time between vaginal bleeding. {21}

Some studies indicated a connection between insulin resistance (IR) and abnormal uterine bleeding, with obese people who suffer from abnormal uterine bleeding having a greater chance of developing insulin resistance. Women who are of normal weight and experience abnormal uterine bleeding have been reported to experience an IR of approximately 32% in the circumstances, whereas in obese PCOS, it has been reported to be higher, beyond 90%.{22}

Participants suffering from abnormal uterine bleeding had a substantially greater BMI than controls in our study, where normal follicular growth and ovulation were hampered by hyperandrogenism, IR-induced hyperinsulinemia, as well as variations in intrafollicular paracrine signaling. Studies have shown a possible connection between IR and poor egg and embryo quality development, which further connects IR to lower-than-average rates of fertilization and implantation in PCOS-affected women. Better pregnancy outcomes in these women may arise with the development of clinical indications that may accurately identify IR obtained early in PCOS instances. Consistent with other research, our study revealed a correlation between the severity of IR and irregularities in the menstrual cycle {23, 24}. This suggested that measuring the degree of menstrual irregularity as a simple clinical parameter may be a useful predictor of the severity for metabolic syndrome along with endocrine disorders. The length of the vaginal bleeding interval was positively correlated with HOMA-IR; in the longest intervals, getting the highest HOMA-IR {25}.

AUB patients had higher testosterone levels, which rose as vaginal bleeding intervals grew longer. A report found a positive correlation between serum androgen levels in women with irregular uterine bleeding. By impairing normal follicular development, hyperandrogenism during times of abnormal uterine bleeding may interrupt menstruation. {26}

Hyperandrogenic people in vaginal bleeding interval categories ranging from 45–90 days, as well as 90 days or more, exhibited more severe IR, according to an examination of abnormal uterine bleeding subgroups {27}. It showed that hyperandrogenism may exacerbate the severity of IR in PCOS patients {28}. According to the results of earlier research, hyperandrogenism was independently linked to the risk of type 2 diabetes as well as obesity. A potential reason for the result is that hyperinsulinemia promotes the continuous overproduction of androgen. {29}

Conclusion

The current outcomes indicate that women with abnormal uterine bleeding are predominantly characterized by a higher insulin resistance index and body mass index compared to the control group, where there is evident hormonal and metabolic syndrome imbalance, indicating worsening insulin resistance and dyslipidemia, which is supported by the positive correlation between insulin resistance and the interval between vaginal bleeding. Moreover, the increased insulin resistance and hyperandrogenism in these women are associated with a longer menstrual cycle, resulting in menstrual irregularities.

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