A study on association of abnormal uterine bleeding with metabolic syndrome in women of reproductive age group attending a teritiary care hospital

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Abstract
Aim
To determine the association between abnormal uterine bleeding and metabolic syndrome among women in their reproductive age group [30-49yrs].
Objectives
1. To determine the association of individual parameters of metabolic syndrome with AUB
2. To assess the association of metabolic syndrome with Aub Material and Methods
Study Area: The study was conducted among patients attending Inpatient and Outpatient of obstetrics and gynaecology department of Malla Reddy Medical College for Women and hospital, Hyderabad
Study Design: Hospital based Prospective observational study
Study Period: September 2022 to February 2024
Study Population: Women of reproductive age group presenting with signs & symptoms or already diagnosed abnormal uterine bleeding (cases) to the department of obstetrics and gynaecology of Mallareddy Medical College for Women and hospital, Hyderabad.
Results
This prospective study was conducted in the department of Obstetrics and Gynaecology ofMallaReddy Medical College for Women and hospital, Hyderabad with an aim to determine the association between abnormal uterine bleeding and metabolic syndrome among women in their reproductive age group [30-49yrs]. The study was done between September 2022 to February 2024.
A total of 86 subjects were included in the study and divided equally into two groups of 43 each namely cases and controls. After obtaining consent from all the subjects and their attendants detailed history and clinical examination was noted using a pre-tested questionnaire.
The results of the study showed the overall mean age was 39.7± 8.4 years with majority of them belonging to middle class. Most of the women were P2L2 followed by P3L3.
The most common symptom observed in the cases was heavy menstrual bleeding and all of them had HTN and DM whereas none of the controls had any symptoms nor comorbidities.
The mean BMI and waist circumference in the cases was 34.03± 3.6 kgs/m2and 92.3± 12.2 respectively.
The mean blood pressure was higher than the controls. Investigations showed more than half of the cases had higher FBS, triglycerides and lowered HDL levels.
Conclusion
The metabolic syndrome factors were compared between cases and controls there was a significant 59difference and association between them suggesting AUB is associated with metabolic syndrome. Counselling the patients regarding Lifestyle modifications would reduce the incidence of Metabolic syndrome and AUB.

Keywords: Abnormal uterine bleeding (aub), metabolic syndrome, reproductive age women, hypertension and diabetes (htn and dm), lifestyle modifications

Introduction

The physiology of menstruation is the periodic shedding of endometrium during a woman's reproductive years due to hormonal changes. The proliferative or follicular phase and the secretory or luteal phase are the two phases of the menstrual cycle. The duration of the menstrual cycle, which typically spans 28± 7 days6 [7]. The menstrual cycle is governed by an interaction between reproductive hormones (LH, FSH, oestradiol, progesterone) that results in growth of a follicle, ovulation and formation of corpus luteum.

AUB, or abnormal uterine bleeding, is a common but dangerous symptom that can vary in normal menstrual cycle regularity, frequency, length, and blood loss throughout the menses. Globally, AUB is a primary factor in gynaecological consultations [8, 9]. The International Federation of Gynaecology and Obstetrics (FIGO) Menstrual Disorders Working Group has classified Abnormal uterine bleeding into four categories based on four main features: regularity, frequency, heaviness of flow, and duration. Menstrual bleeding can be categorised as heavy, heavy and protracted, light, extended and shortened, irregular, nonexistent, infrequent, frequent, and heavy [1]. Globally, the prevalence of AUB varies throughout populations. In women, the overall prevalence ranges from 10% to 30% [12, 13]. The causes of menstrual irregularity include: [5]

▪ Pregnancy and Lactation.

▪ Endocrine causes such as poorly controlled DM, polycystic ovary syndrome (PCOS), Cushing disease,

thyroid dysfunction, premature ovarian failure, and late-onset congenital adrenal hyperplasia.

- Acquired conditions such as stress-related hypothalamic dysfunction, medications, exercise-induced amenorrhea, and eating disorders (both anorexia and bulimia) and Ovarian tumors, adrenal tumors and prolactinomas.

- Menstrual disorders are a known marker for underlying insulin resistance (IR). IR is well known to be related to type 2 diabetes mellitus (DM), hypertension (HTN), and dyslipidemia. Therefore, menstrual disorders are likely also associated with metabolic syndrome (MetS) [2, 3, 4].

Depending on age and gender, metabolic syndrome can affect 10–50% of people in India. There has been evidence of greater morbidity among female Metabolic Syndrome patients in middleaged populations compared to male patients [19, 20, 21].

The significance of diagnosing and treating people with Metabolic Syndrome was emphasised by the Expert Panel of the National Cholesterol Education Programme Adult Treatment Panel III. Metabolic Syndrome could be identified using two criteria. As to the 2005 revised criteria by the NHLBI and AHA, an individual is classified as having metabolic syndrome if they have at least three of the five disorders listed below [11].

- Fasting plasma glucose level ≥100 mg/dl or receiving drug therapy for hyperglycaemia.

- Blood pressure ≥130/85 mm Hg or receiving drug therapy for hypertension.

- Triglycerides ≥150 mg/dl or receiving drug therapy for hypertriglyceridemia.

- HDL cholesterol (HDL-C) < 40 mg/dl in men or < 50 mg/dl in women or receiving drug therapy for reduced HDL-C.

- Waist circumference ≥102 cm (40 inch) in men or ≥88cm (35inch) in women for south Asian, ≥90 cm (35 inch) in men or≥80 cm (32 inch) in women.

Rationale
MetS has been found to be more common in women with PCOS, according to earlier research. On the other hand, not much research has been done on the general population's regularity of cycles and MetS relationship. Due to the high prevalence of metabolic syndrome in Indians, there is currently a lack of information in the literature about the relationship between menstrual and obstetric patterns, cardiometabolic risk factors, and metabolic syndrome and AUB in women of reproductive age group. In order to ascertain the relationship between abnormal uterine bleeding and metabolic syndrome in women of reproductive age group [30-49 years old], a prospective study was conducted.

AIM
To determine the association between abnormal uterine bleeding and metabolic syndrome among women in their reproductive age group [30-49yrs].

Objectives
1. To determine the association of individual parameters of metabolic syndrome with AUB

2. To assess the association of metabolic syndrome with AUB

Material and Methods
Study Area
The study was conducted among patients attending Inpatient and Outpatient of obstetrics and gynaecology department of Malla Reddy Medical College for Women and hospital, Hyderabad

Study Design
Hospital based Prospective observational study

Study Period
September 2022 to February 2024

Study Population
Women of reproductive age group presenting with signs & symptoms or already diagnosed abnormal uterine bleeding (cases) to the department of obstetrics and gynaecology of Mallareddy Medical College for Women and hospital, Hyderabad.

Inclusion criteria
1. Age between 30 to 49 years
2. All suspected and diagnosed women with abnormal uterine bleeding
3. Consented subjects

Exclusion Criteria
1. Subjects < 30 and >49 years
2. Pregnant and lactating
3. Fibroid uterus, adenomyosis, polyps, endometrial TB and foreign body
4. Currently on OCP 's or any other hormonal treatment
5. Patients on tamoxifen therapy
6. Ovarian malignancy 7. Cervical and vaginal malignancies
7. Coagulopathies
8. Thyroid disorders
9. Iatrogenic causes
10. Puberty menorrhagia
11. Other systemic diseases
12. Puerperal period up to 3 months
13. Post abortal up to 3 months

Sample Size
The sample size was calculated according to the study by Yerram *et al* (2017), who reported the proportion of patients with Metabolic Syndrome in each of the groups as follows: Group AUB:

27%Group controls: 1%P1 (Proportion in First Group) = 0.27P2 (Proportion in Second Group) =

$$ n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2\,\overline{P}\,(1-\overline{P})} + Z_{1-\beta} \sqrt{P_1\,(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2} $$

Where,

$$ \overline{P} = \frac{P_1 + P_2}{2} $$

0.01Type I error (α) = 5%, Zα (Value of Standard Normal Distribution for α = 5%) = 1.96 Type II error (β) = 5%, Power (1 – β) = 95%, Z1-β = 1.65 Using the formula

The minimum sample size required was 43 patients with the above formula for each group i.e 43 cases and 43 controls were included.

Study Methods

- All patients attending Inpatient and Outpatient of obstetrics and gynaecology department of Malla Reddy Medical College for Women and hospital, Hyderabad during the study period were screened to determine eligibility for inclusion in the study.

- The subjects meeting study criteria were explained about the nature and purpose of this study and were included in the study after their informed consent is taken.

- A Study proforma was used to collect the patients details and findings. The patients were divided equally of 43 each i.e test group (with AUB) and control group (with gynaecological complaints other than AUB) keeping confounding factor to the minimum.

- A detailed clinical history regarding age, parity, socioeconomic status, duration, character of AUB, obstetric parameters, prior treatment history, drug history and medical comorbidities (hypertension, diabetes etc) were taken.

- Physical examination including general examination-vitals, presence of pallor, icterus, clubbing, cyanosis, lymphadenopathy, pedaledema, abdominal examination and pelvic examination (per speculum and bimanual examination) was done to rule out local conditions like fibroids, polyps, adnexal Pathologies, local infections.

- Height, weight, waist circumference and blood pressure were noted using standardised methods for anthropometry measurements.

- Pap smear was taken as a part of routine screening.

- Endometrial biopsy was done in cases with AUB in premenstrual phase. Metabolic syndrome was diagnosed according to NCEP- ATP III criteria.

Study tools

- **Measurement of waist circumference**: Waist circumference was measured at a point midway between lowest rib and iliac crest with the subject in standing position at the end of normal expiration using measuring tape.

- **Measurement of BMI:** Using wt. (kgs)/ Ht. (m2)

Measurement of blood pressure

Blood pressure was recorded in sitting position using a sphygmomanometer. The measurement was performed twice with an interval of five minutes and if there was a difference of >10 mm hg between the two measurements either systolic or diastolic then the third measurement will be recorded after 10 minutes resting period. The mean of the two readings taken 5 minutes apart was recorded

Measurement of FBS, triglycerides and HDL: Blood was collected after a minimum of eight hours fasting from antecubital vein following standardised protocol. The blood sample for fasting blood sugar (FBS) measurement was collected in a vacutainer with sodium fluoride and potassium oxalate as an anticoagulant and glycolysis inhibitor. FBS was determined by hexokinase method. Serum total cholesterol was measured by CHOD-POD method, serum triglycerides by GPO-POD method and serum HDL by AHDL (automated HDL assay).

Ultrasound abdomen & pelvis: To rule out structural gynaecological conditions

PAP smear: Done in both cases and controls as a part of routine screening

Procedure: After taking informed consent, patient placed in dorsal lithotomy position, under aseptic precautions A metal cuscos speculum placed to visualise the cervix .sample obtained by Ayres spatula and cytobrush from ectocervix and endocervical respectively and sent for cytology 57

Endometrial biopsy: Done in cases presenting with AUB by Pipelle endometrial suction curette after taking informed and written consent.

Statistical analysis Plan

- The data collected was entered into Microsoft excel work sheet and exported to SPSS.
- Data was analysed using statistical package for social sciences (SPSS) version 26.
- Qualitative data is presented as percentage in categories and then presented as tables and diagrams.
- Quantitative data is presented as means and standard deviations.

- ▪ Paired t test and chi- square test were used for test of significance (comparison between both the groups). A p- value of 0.05 was considered statistically significant for all statistical tests performed.

Results
Distribution according to age

Table 1: Distribution according to age

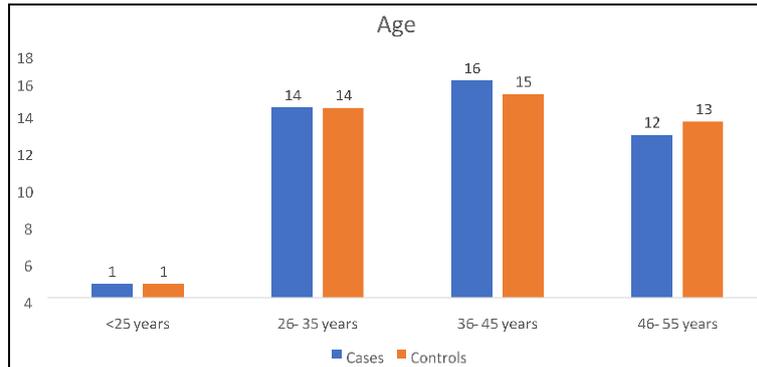| Age	Cases	Controls	Total
<25 years	1	1	2 (2.4%)
26- 35 years	14	14	28 (32.6%)
36- 45 years	16	15	31 (36%)
46- 49 years	12	13	25 (29%)
Total	43	43	86 (100%)
Mean age	39.6± 8.3	39.8± 8.6	39.7± 8.4

Fig 1: Column chart showing age

Distribution according to menstrual symptoms

Table 2: Distribution according to menstrual symptoms

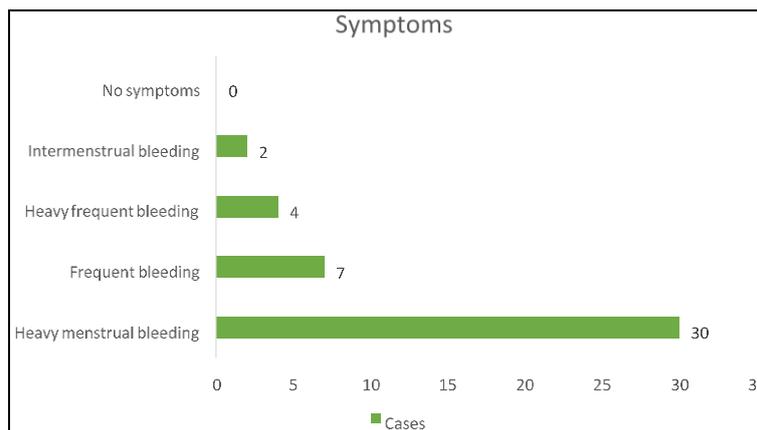| Symptoms	Cases	Controls
Heavy menstrual bleeding	30	-
Frequent bleeding	7	-
Heavy frequent bleeding	4	-
Intermenstrual bleeding	2	-
No symptoms	-	43
Total	43	43

Fig 2: Bar chart showing menstrual irregularities

Comorbidities in study

Table 3: Comorbidities in the study

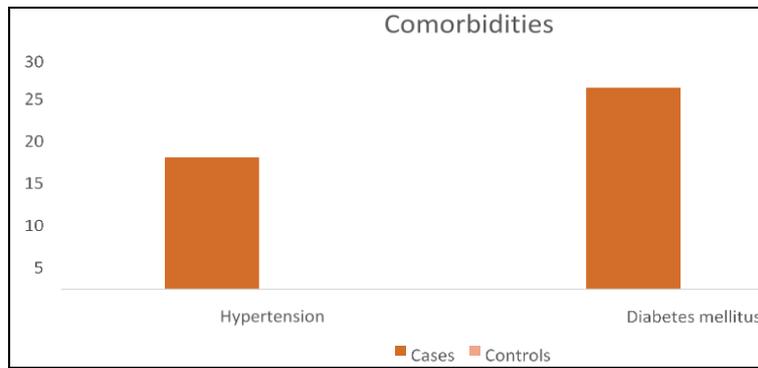| Comorbidities	Cases	Controls	Total
Hypertension	17	0	17 (19.8%)
Diabetes mellitus	26	0	26 (30.2%)

Fig 3: Column chart showing comorbidities

Distribution According to Bmi And Wc

Table 4: BMI distribution and waist circumference

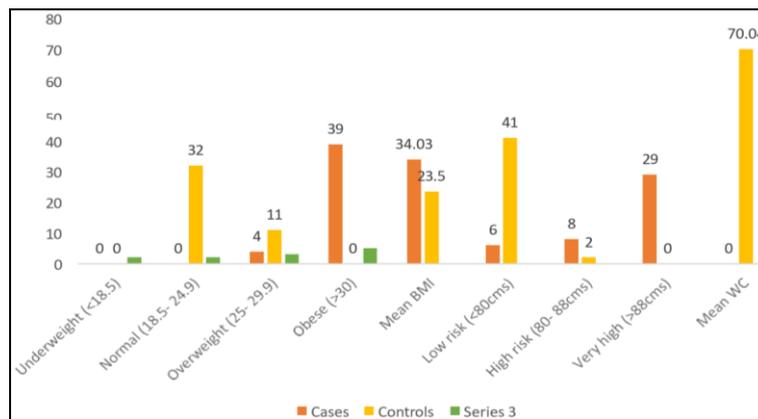| BMI/ WC	Cases	Controls	Percent
Underweight (<18.5)	-	-	
Normal (18.5- 24.9)	-	32	32 (%)
Overweight (25- 29.9)	4	11	15 (%)
Obese (>30)	39	-	39 (%)
Mean BMI	34.03± 3.6	23.5± 1.6	28.7± 2.6
	Waist circumfer ence		
Low risk (<80cms)	6	41	47 (%)
High risk (80- 88cms)	8	2	10 (%)
Very high (>88cms)	29	-	29 (%)
Mean WC	92.3± 12.2	70.04± 6.8	81.1± 9.5

Fig 4: Column chart showing BMI distribution and waist circumference

Table 5: Blood pressure distribution

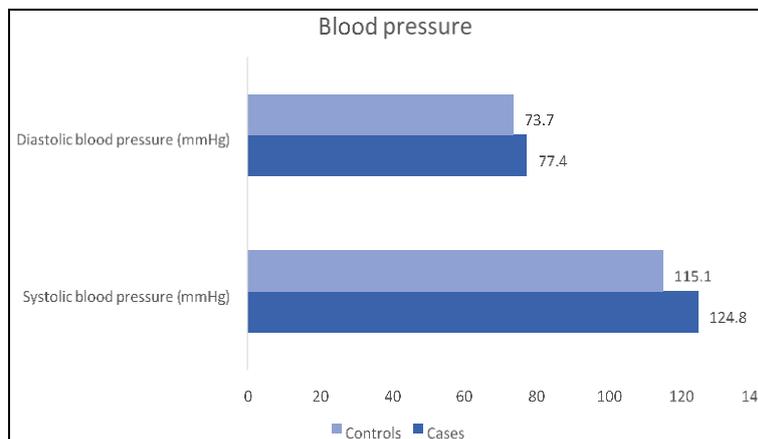| Blood pressure	Cases	Controls
Systolic blood pressure (mmHg)	124.8± 14.2	115.1± 10.08
Diastolic blood pressure (mmHg)	77.4± 9.02	73.7± 5.7

Fig 5: Bar chart showing blood pressure

Distribution According to Fbs, Tg, Hdl

Table 6: Investigation findings

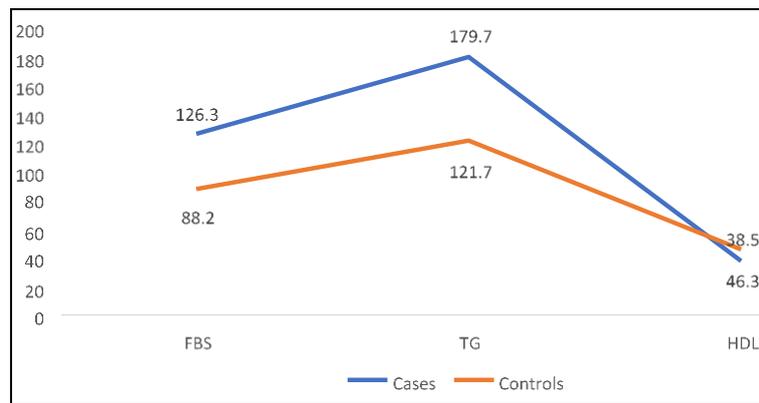| Investigations	Cases	Controls
Fasting blood sugar		
<126 mg/dl	23	-
>126 mg/dl	20	43
Mean FBS:	126.3± 34.2	88.2± 9.9
Triglycerides		
<150 mg/dl	12	43
>150 mg/dl	31	-
Mean triglyceride:	179.7± 51.1	121.7± 9.5
HDL		
<40 mg/dl	32	11
40- 60 mg/dl	11	32
>60 mg/dl	-	-
Mean HDL	38.5± 7.2	46.3± 6.1

Fig 6: Column chart showing investigations

Distribution of Metabolic Syndrome Factors Between Cases & Controls

Table 7: Comparison of metabolic syndrome factors between cases and controls

MS	Cases Mean	Controls Mean	95% CI Lower	95% CI Upper	p-value
WC	92.3± 12.2	70.04± 6.8	18.2	26.5	<0.001*
BMI	34.003± 3.6	23.5± 1.6	9.09	11.8	<0.001*
SBP	124.8± 14.2	115.1± 10.08	4.9	14.5	<0.001*
DBP	77.4± 9.02	73.7± 5.7	0.4	6.9	<0.002*
FBS	186.3± 34.2	88.2± 9.9	27.3	48.9	<0.001*
TG	179.7± 51.7	121.7± 9.5	41.9	73.9	<0.001*
HDL	38.5± 7.2	46.3± 6.1	10.5	5.06	<0.001*
	*L	evel of significance: $p<0.05$			

The metabolic syndrome factors were compared between cases and controls were a highly statistically significant difference and association was noted between them suggesting strong association ($p<0.05$) between abnormal uterine bleeding and metabolic syndrome

Pap Smear Findings
The PAP smear among the cases showed NILM (n= 17), inflammatory smear (n= 9), AGUS
(n= 7), LSIL (n= 6) and ASCUS (n= 4). Among the controls NILM (n= 22), inflammatory smear (n= 13) and ASCUS (n= 8)

Endometrial biopsy findings
The endometrial biopsy in the cases showed proliferative phase (n= 17), secretory phase (n= 15), hyperplasia with atypia (n= 7) and hyperplasia without atypia (n= 4).

Summary and Conclusion
This prospective study was conducted in the department of Obstetrics and
Gynaecology ofMallaReddy Medical College for Women and hospital, Hyderabad with an aim to determine the association between abnormal uterine bleeding and metabolic syndrome among women in their reproductive age group [30-49yrs]. The study was done between September 2022 to February 2024. A total of 86 subjects were included in the study and divided equally into two groups of 43 each namely cases and controls. After obtaining consent from all the subjects and their attendants detailed history and clinical examination was noted using a pre-tested questionnaire. The results of the study showed the overall mean age was 39.7± 8.4 years with majority of them belonging to middle class. Most of the women were P2L2 followed by P3L3.The most common symptom observed in the cases was heavy menstrual bleeding and all of them had HTN and DM whereas none of the controls had any symptoms nor comorbidities. The mean BMI and waist circumference in the cases was 34.03± 3.6 kgs/m2and 92.3± 12.2 respectively. The mean blood pressure was higher than the controls. Investigations showed more than half of the cases had higher FBS, triglycerides and lowered HDL levels. The ultrasound findings showed among the 43 cases 10 had bulky uterus. Among the cases PAP smear showed NILM (n= 17), inflammatory smear (n= 9), AGUS (n= 7), LSIL (n= 6) and ASCUS (n= 4) Among the controls NILM (n= 22), inflammatory smear (n= 13) and ASCUS (n= 8). Endometrial biopsy in the cases showed proliferative phase (n= 17), secretory phase (n= 15), hyperplasia with atypia (n= 7) and hyperplasia without atypia (n= 4). The metabolic syndrome factors were compared between cases and controls there was a significant 59difference and association between them suggesting AUB is associated with metabolic syndrome. Counselling the patients regarding Lifestyle modifications would reduce the incidence of Metabolic syndrome and AUB.

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