Original Article

FREQUENCY OF ENDOMETRIAL HYPERPLASIA IN OBESE PATIENTS OF REPRODUCTIVE AGE PRESENTING WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background: Among women of reproductive age, one of the most common gynecological problems is abnormal uterine bleeding (AUB). The prevalence rate of this disorder is up to 30%. The causes of AUB include systemic, physician induced, hormonal related to age and endometrial pathologies like polyps, submucous myomas, hyperplasia, and endometrial carcinoma. It is always important to suspect and evaluate for endometrial pathologies. This study aimed to determine the frequency of endometrial hyperplasia in obese women of reproductive age presenting with abnormal uterine bleeding.

Material and Methods: This cross-sectional study was conducted at Obstetrics and Gynecology Department, Jinnah Hospital Lahore from December 25th 2018 to June 25th 2019. In this study, 215 obese women with abnormal uterine BMI ≥ 27 Kg/m^2 were included. Transvaginal ultrasound was performed to see the endometrial thickness and endometrial tissues were obtained by Dilatation and Curettage (D&C) method for histological findings of endometrial hyperplasia.

Results: The range of age in subjects of this study was from 18 to 35 years with a mean age of 30.33±2.66 years, mean parity 1.74±1.57, mean weight 82.99±8.09 Kg, mean height 1.61±0.10 meters, mean BMI 32.10±3.13 Kg/m^2 and mean endometrial thickness was 10.153±2.39 millimeter. Endometrial Hyperplasia was seen in 9.3% of patients.

Conclusion: The frequency of endometrial hyperplasia in obese women presenting with abnormal uterine bleeding was 9.3%. A high body mass index is the leading risk factor for endometrial hyperplasia in premenopausal women.

Key Words: Endometrial hyperplasia, Obesity, Uterine bleeding

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INTRODUCTION

The prevalence of some type of AUB in patients of the reproductive age group is up to 30%.[1] Medical expenditure in a retrospective analysis data of 1.4 million women having abnormal uterine bleeding was compared with those without abnormal uterine bleeding of more than 50 million women. It was found that women with abnormal bleeding were younger, Caucasian, obese and had poor mental and physical health.[2] The causes of AUB include systemic, induced, hormonal related to age and endometrial pathologies, including polyps, submucous myomas, endometrial hyperplasia and endometrial carcinoma. It is always compulsory to suspect and evaluate for endometrial pathologies. Infectious endometritis can cause irregular bleeding even endometrial atrophy and sometimes manifest as abnormal uterine bleeding.[3] Nowadays, diagnosis of endometrial pathologies can be made by clinical examination, through Transvaginal

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ultrasound (TVS) and saline infusion sonohysterography (SIS), hysteroscopy and sampling of the endometrium.[4] American College of Obstetricians and Gynecologists (ACOG) recommended endometrial biopsies for even young women not responding to treatment or those with increased menstrual bleeding because of unimpeded estrogen treatment. In these young women, the risk factors that have been identified include nulliparity, hypertension, obesity and family history of abnormal uterine bleeding.[5] ACOG has recently classified abnormal bleeding into various types like irregular menstrual bleeding, bleeding due to instruments and postmenopausal bleeding. ACOG has recommended that assessing irregular uterine bleeding histologically in premenopausal women should be dependent upon the symptoms and clinical features of the patient.[6] Nelson et al., in their study have concluded that obese patients of reproductive age presenting with abnormal uterine bleeding have frequency of endometrial hyperplasia of 7.3%.[7, 8] Sajitha et al. in their study, has found it to be 25% in patients with BMI greater than 30.[9]

As recommended by the United Kingdom, National Institute for Health and Care Excellence (NICE), endometrial biopsy should be taken in women with persistent intermenstrual bleeding or if their age is ≥45 years and their medical treatment has failed.[3] Royal College of Obstetricians and Gynecologists (RCOG) also recommends the same guidelines as NICE. The only exception is the age of sampling which is 40 years in case of treatment failure.[10] With the increase in endometrial cancers the gynecologists are recommended to use their clinical judgement to evaluate the risks and then prescribing biopsy accordingly.

World Health Organization (WHO), also consider anyone to be overweight if the body mass index (BMI) is equal to or greater than 25 kg/m^2 and obesity is if the Body Mass Index equals to or is greater than 30 kg/m^2. In women who are obese, the excess of estrogen and androgens may cause anovulation leading to endometrial hyperplasia.

The most common presenting complaint of endometrial hyperplasia is abnormal uterine bleeding. The abnormal uterine bleeding can present as menorrhagia, intermenstrual bleeding, postmenopausal bleeding or irregular bleeding as endometrial hyperplasia can affect premenopausal and postmenopausal women. It accounts for approximately 15% of women who present with postmenopausal bleeding. It is usually believed that most of the endometrial cancers follow a specific sequence of histologically hyperplastic lesions, which range from endometrial hyperplasia without atypia to endometrial hyperplasia with atypia to well-differentiated endometrial carcinoma.[6]

Endometrial hyperplasia can be divided into two types simple and complex, depending upon the complexity and crowding of the glandular structures. It is a challenge for the pathologist to distinguish between reversible changes dependent on hormone and neoplastic changes.

Usually, most varieties of endometrial hyperplasia do not progress to endometrial carcinoma; therefore, treatment should be individualized. Whether simple or complex, endometrial hyperplasia, in the absence of histologically distinguished atypia, is at very low risk to progress to endometrial carcinoma. Therefore, these can be treated conservatively. Most women with endometrial hyperplasia without atypia are treated with progesterone therapy. This treatment may result in complete resolution of this condition.

There is a shortage of data on this subject in our local population. Therefore, it is necessary to get further evidence by determining the frequency of endometrial hyperplasia in our setup in patients of reproductive age who are obese and have abnormal uterine bleeding and planning the course of action accordingly.

This study aimed to determine the frequency of endometrial hyperplasia in obese patients of reproductive age with abnormal uterine bleeding.

MATERIAL AND METHODS

This Descriptive cross-sectional Study was conducted from 25th December 2018 to 25th June 2019 within the Department of Obstetrics and Gynecology of Jinnah Hospital Lahore.

Following operational definitions were set;

Abnormal uterine bleeding was defined as if any one of the subsequent conditions present:

- Too frequent periods (more often than every 26 days).
- Any bleeding lasts longer than 7 days.

Women with BMI > 27 Kg/m^2 were considered obese. (the formula calculated BMI: weight (in kilogram) divided by height in meters square (Kg/m^2)).

Endometrial hyperplasia had been defined as when within 2 days after cessation of menstruation, the endometrium is quite 7 mm in thickness on ultrasound with any one of subsequent histopathology

- Endometrial polyp with irregular interspersed cystic and tubular glands in a very fibrous and focally edematous stroma (H.E., 40x).
- Non-atypical hyperplasia with closely packed endometrial glands and no cytologic atypia (H.E., 100x)
- High power view of endometrial intraepithelial neoplasia with increased glandular density and cytological atypia (H.E., 200x).
- Considerable architectural complexity and cytological atypia in endometrial intraepithelial neoplasia (H.E., 200x).

Sample size was calculated using the expected proportion of (endometrial hyperplasia) 7.3%.[7] Keeping margin of error at 5% and confidence level at 95% sample size was calculated using non-probability consecutive sampling. After rounding off, 215 participants were included in the study.

Women of age 18-35 years of any parity having BMI $\geq$ 27 kg/m^2 and presenting with abnormal uterine bleeding were part of this study. Pregnant females and those taking oral contraceptive pills were excluded from the study.

The approval from ethical committee of Allama Iqbal Medical College was taken. Data containing 215 women fulfilling the inclusion criteria were included in the study from the outpatient Department of Obstetrics and Gynecology of Jinnah Hospital Lahore. Informed consent was taken from each patient. Information of patients like age, parity, weight on weighing machine, height on height scale and BMI as per operational definition was taken. Transvaginal ultrasound was done to determine the endometrial thickness The endometrial sample was obtained by the Dilatation and Curettage method for histological diagnoses. Endometrial hyperplasia was noted as per operational definition by researcher herself on the proforma.

Data was analyzed by IBM-SPSS 23. Number and percent were determined for categorical variables like endometrial hyperplasia. Mean ± SD was taken for quantitative variables like age, parity, weight, height, BMI and endometrial thickness.

Effect of modifiers like age, parity and body mass index were minimized by stratification. Test of significance applied was Chi-Square, $p \leq 0.05$ was considered statistically significant.

RESULTS

This study concluded age range from 18 to 35 years with mean age of 30.339±2.66 years, mean parity of 1.744±1.57, mean weight 82.995±8.09 Kg, mean height 1.610±0.103 meters, mean BMI 32.108±3.13 Kg/m^2 and mean endometrial thickness was 10.153±2.39 millimeter as shown in Table-1.

Endometrial Hyperplasia was seen in 9.3% of patients as shown in Table-2.

Stratification of Endometrial Hyperplasia concerning age, parity and BMI are indicated in Table-3, 4 and 5, respectively.

Table-1: Mean ± SD of Age, parity, weight, height, BMI and endometrial thickness
n=2015

Demographics		Mean ± SD
1	Age (years)	30.33±2.66
1	Parity	1.74±1.57
1	Weight (Kg)	82.99±8.09
1	Height (m)	1.61±0.103
1	BMI (Kg/m^2)	32.10±3.13
1	Endometrial Thickness (mm)	10.15±2.39

Table-2: Frequency and percentage of patients according to Endometrial Hyperplasia
n=215

Endometrial Hyperplasia	Frequency	Age %
Present	20	9.3%
Not present	195	90.7%
Total	215	100%

Table-3: Stratification of Endometrial Hyperplasia concerning age

Age (years)	Endometrial Hyperplasia		p-value
	Yes	No	
18-27	3 (13.6%)	19 (86.4%)	0.460
28-35	17 (8.8%)	176 (91.2%)	
Total	20 (9.3%)	195 (90.7%)	

Table-4: Stratification of Endometrial Hyperplasia concerning parity

Parity	Endometrial Hyperplasia		p-value
	Yes	No	
0-3	20(10.7%)	167(89.3%)	0.069
>3	0(0%)	28(100%)	
Total	20(9.3%)	195(90.7%)	

Table-5: Stratification of Endometrial Hyperplasia concerning BMI

BMI (Kg/m^2)	Endometrial Hyperplasia		p-value
	Yes	No	
27-30	3(5.8%)	49(94.2%)	0.314
>30	17(10.4%)	146(89.6%)	
Total	20(9.3%)	195(90.7%)	

DISCUSSION

The obesity accounts for 200-400% increase in the risk of causing endometrial carcinoma with each point increase in BMI. In this study most of the patients had BMI >30 kg/m^2. No women was using estrogen in this study. Risk of malignancy and hyperplasia is significantly lower in premenopausal than in postmenopausal women.[11] It is not confirmed in this study that obesity impacts premenopausal women or postmenopausal women. Another study conducted at United states, described that a longer duration of overweight and obesity was associated with an increased risk of developing several forms of cancer. Furthermore, the degree of overweight experienced during adulthood seemed to play an important role in the risk of developing cancer, especially for endometrial cancer.[12] This study showed increased risk and higher ratio of endometrial hyperplasia (9.3%) as compared to other studies (4-17.3%).[13-15]

A study conducted by Nelson et al. showed that the frequency of endometrial hyperplasia was 7.3% in patients of reproductive age who were obese and had abnormal uterine bleeding.[7] Sajitha et al., showed in this study that the frequency of endometrial hyperplasia was 25% in the patients of reproductive age having abnormal uterine bleeding and who were also obese.[8]

A significant impact of age on endometrial pathology incidence has been shown in an extensive study based on the pathology reports. Similarly, in our study, women of higher age group also had higher risk of endometrial pathology and impacts of weight and diabetes on the probability of significant pathology.[16]

A short course of hormonal therapy will not be beneficial in women with abnormal bleeding due to obesity or thyroid disorder.[17] Though, if long-term hormonal treatment of progesterone is given, it will prevent endometrial hyperplasia and stop the excessive bleed until the existing etiology becomes cured.[18] OCPs containing progesterone and LNG-IUS efficiently treat endometrial hyperplasia through a progesterone-mediated reversal of the PTEN suppressor genes.[19,20] In this study, relatively lower rates of significant pathology were present in the comparatively younger women.[12,21]

It is essential to keep a regular follow-up to timely diagnose recurrent irregular AUB or development of endometrial hyperplasia.[18,22,23] In women having Hb ≤5 mg/dl, due to heavy vaginal bleed, more than 25% received multiple blood transfusions, yet none of these patients had been on other varieties of medicinal therapy to overcome excessive blood loss during menses.[24]

In this study, many cases were considered and an increased prevalence rate of the disease was obtained but the results are not precise. Even then, they show an estimated upper limit of remarkable pathology found in the endometrial sampling. It is an offer by us to the other investigators who are interested in this area to use our data.[25] We, however, recognize that our data will not apply to the postmenopausal patients having abnormal vaginal bleeding and using hormone therapy. This is because none of our patients were using this hormone therapy.

CONCLUSION

Body mass index (BMI) is the consistent and main risk factor for complex endometrial hyperplasia in premenopausal women. During the assessment of endometrium in symptomatic premenopausal, women's body mass index should always be considered.

AUTHOR'S CONTRIBUTION

SM: Data collection
SS: Drafting of manuscript
FN: Data analysis

REFERENCES

1. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. Clinical Practice-Gynaecology Committee: Abnormal uterine bleeding in premenopausal women. J Obstet Gynaecol Can. 2013 May;35(5):473-9. doi: 10.1016/S1701-2163(15)30939-7
2. Matteson KA, Raker CA, Clark MA, Frick KD. Abnormal uterine bleeding, health status, and usual source of medical care: analyses using the Medical Expenditures Panel Survey. J Women's Health. 2013 Nov 1;22(11):959-65. doi: 10.1089/jwh.2013.4288
3. Ghahiri A, Malekzadeh B, Tehrani HG. Comparing the Frequency of Endometritis in Unexplained Infertility and Anovulatory Infertility. Adv Biomed Res.2017 Nov 30;6:151. doi: 10.4103/2277-9175.219416
4. Kotdawala P, Kotdawala S, Nagar N. Evaluation of endometrium in peri-menopausal abnormal uterine bleeding. J Mid-life Health. 2013 Jan;4(1):16-21. doi: 10.4103/0976-7800.109628.
5. Practice bulletin no. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. Obstet Gynecol. 2013 Jul;122(1):176-85. doi:10.1097/01.AOG.0000431815.52679.bb.
6. Practice bulletin no. 149: endometrial cancer. Obstet Gynecol. 2015 Apr;125(4):1006-26. doi:10.1097/01.AOG.0000462977.61229.de.
7. Nelson AL, Vasquez L, Tabatabai R, Im SS. The yield of endometrial aspiration in women with various risk factors and bleeding abnormalities. Contraception and Reproductive Med. 2016 Dec;1(1):1-8. doi: 10.1186/s40834-016-0020-7.
8. Munro MG, Critchley HO, Fraser IS. The FIGO classification of causes of abnormal uterine bleeding: Malcolm G. Munro, Hilary OD Crithcley, Ian S. Fraser, for the FIGO working group on menstrual disorders. Int J Gynaecol Obstet. 2011 Apr;113(1):1-2. doi: 10.1016/j.ijgo.2011.01.001
9. Sajitha K, Padma SK, Shetty KJ, KishanPrasad HL, Permi HS, Hegde P. Study of histopathological patterns of endometrium in abnormal uterine bleeding. CHRISMED J Health and Res. 2014 Apr 1;1(2):76-81. doi: 10.4103/2348-3334.134265.
10. Standards for Gynaecology. RCOG; 2008. Available at: https://www.rcog.org.uk/globalassets/documents/guidelines/wprgynstandards2008.pdf.
11. Gawron I, Łoboda M, Babczyk D, Ludwin I, Basta P, Pityński K, Ludwin A. Endometrial cancer and hyperplasia rate in women before menopause with abnormal uterine bleeding undergoing endometrial sampling. Przegl Lek. 2017;74(4):139-43.. PMID: 29696944.
12. Arnold M, Jiang L, Stefanick ML, Johnson KC, Lane DS, LeBlanc ES, Prentice R, Rohan TE, Snively BM, Vitolins M, Zaslavsky O. Duration of adulthood overweight, obesity, and cancer risk in the Women's Health Initiative: a longitudinal study from the United States. PLoS medicine.

2016 Aug 16;13(8):e1002081. doi:https://doi.org/10.1371/journal.pmed.1002081

13. Beavis AL, Najjar O, Cheskin LJ, Mangal R, Rositch AF, Langham G, Fader AN. Prevalence of endometrial cancer symptoms among overweight and obese women presenting to a multidisciplinary weight management center. Gynecologic oncology reports. 2020 Nov 1;34:100643. doi:https://doi.org/10.1016/j.gore.2020.100643
14. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: A systematic review. American journal of obstetrics and gynecology. 2016 Jun 1;214(6):689-e1. doi:https://doi.org/10.1016/j.ajog.2016.01.175
15. Prakansamut N, Sirayapiwat P, Triratanachat S. The percentages of endometrial hyperplasia and endometrial cancer among polycystic ovary syndrome (PCOS) patients presenting with abnormal menstrual pattern. J Med Assoc Thai. 2014 Feb 1;97(2):159-64.
16. Iram S, Musonda P, Ewies AA. Premenopausal bleeding: When should the endometrium be investigated?—A retrospective non-comparative study of 3006 women. Europ. J Obstet Gynec. Reprod Biol. 2010 Jan 1;148(1):86-9. doi: 10.1016/j.ejogrb.2009.09.023.
17. Mackintosh ML, Crosbie EJ. Obesity-driven endometrial cancer: is weight loss the answer?. BJOG: An Int J Obstet & Gynaecol. 2013 Jun;120(7):791-4. doi:10.1111/1471-0528.12106.
18. Fader AN, Arriba LN, Frasure HE, von Gruenigen VE. Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survivorship. Gynecol Oncol. 2009 Jul 1;114(1):121-7. doi: 10.1016/j.ygyno.2009.03.039.
19. Kim MK, Seong SJ, Kim YS, Song T, Kim ML, Yoon BS, et al. Combined medroxyprogesterone acetate/levonorgestrel–intrauterine system treatment in young women with early-stage endometrial cancer. Am J Obstet & Gynecol. 2013 Oct 1;209(4):358-e1. doi: 10.1016/j.ajog.2013.06.031. (CrossRef)
20. Hubbs JL, Saig RM, Abaid LN, Bae-Jump VL, Gehrig PA. Systemic and local hormone therapy for endometrial hyperplasia and early adenocarcinoma. Obstet & Gynecol. 2013 Jun 1;121(6):1172-80. doi: 10.1097/AOG.0b013e31828d6186. (CrossRef)
21. Balbi G, Napolitano A, Seguino E, Scaravilli G, Gioia F, Di Martino L, Fusco D, Signoriello G, Grauso F. The role of hypertension, body mass index, and serum leptin levels in patients with endometrial hyperplasia during premenopausal period. Clinical and Experimental Obstetrics & Gynecology. 2021 Sep 1;39(3):321-5.
22. Lin MC, Burkholder KA, Viswanathan AN, Neuberg D, Mutter GL. Involution of latent endometrial precancers by hormonal and nonhormonal mechanisms. Cancer. 2009 May 15;115(10):2111-8. doi: 10.1002/cncr.24218
23. Kudesia R, Singer T, Caputo TA, Holcomb KM, Kligman I, Rosenwaks Z, et al. Reproductive and oncologic outcomes after progestin therapy for endometrial complex atypical hyperplasia or carcinoma. Am J Obstet & Gynecol. 2014 Mar 1;210(3):255-e1. doi: 10.1016/j.ajog.2013.11.001.
24. Nelson AL, Ritchie JJ. Severe anemia from heavy menstrual bleeding requires heightened attention. Am J Obstet Gynecol. 2015 Jul 1;213(1):97-e1. doi: 10.1016/j.ajog.2015.04.023.
25. Damle RP, Dravid NV, Suryawanshi KH, Gadre AS, Bagale PS, Ahire N. Clinicopathological spectrum of endometrial changes in peri-menopausal and postmenopausal abnormal uterine bleeding: A 2 years study. J Clin Diagn Res. 2013 Dec;7(12):2774-6. doi: 10.7860/JCDR/2013/6291.3755