

Prevalence of malignant disorders in 50 cases of postmenopausal bleeding

Kauser Jillani, Razia Bahadur Khoro, Safia Maqsood, Maqsood Ahmed Siddiqui
Peoples Medical College, Nawabshah, Sindh.

Abstract

Objective: To find the prevalence of malignant pathology in women with postmenopausal bleeding (PMB).

Methods: An observational cross section study was conducted in the Department of Obstetrics and Gynaecology at Peoples Medical College and Hospital Nawabshah from 1st January 2006 to 31st December 2006. All patients with a typical history of post-menopausal bleeding were evaluated under anaesthesia and diagnostic dilatation and curettage was done for histopathological assessment of endometrial lining. Cervical biopsy was taken in selected patients.

Results: Total 50 patients were included. Benign lesion was found in 24 (48%) cases, followed by malignant pathology in 15 (30%), premalignant lesion was responsible for PMB in 7 (14%) cases, while pathology remained undetermined in 4 (8%) patients.

Conclusion: Malignancy has an important role in the etiology of PMB which needs a careful evaluation. This study showed a high prevalence of malignant disorders (30%) with carcinoma of cervix and endometrium having an equal contribution. Multiparity was the most significant factor for carcinoma of endometrium (JPMA 60:540; 2010).

Introduction

Postmenopausal bleeding (PMB) is defined as any bleeding that occurs from the genital tract more than 12 months after the last menstrual period in a woman who is not receiving Hormone Replacement Therapy (HRT).^{1,2} It is a frequent and alarming sign and exclusion of genital tract malignancy, especially endometrial carcinoma is the primary aim of investigation.

Approximately one in 10 women experiences this problem.³ Usually, this occurs in early years of menopause and is less frequent after 3 or more years of menopause. Increasing time interval between menopause and onset of postmenopausal bleeding is highly indicative of malignancy. In developed countries more than 60 % cases are due to

benign lesions like atrophic vaginitis, uterine or cervical polyp, endometrial hyperplasia and atrophic endometritis.⁴⁻⁶ The situation is different in Pakistan and multiple studies conducted in different institution of the country showed a high prevalence of malignancy in patients of postmenopausal bleeding.⁷⁻⁹ Most probably it reflects the non availability of screening programmes, poverty, lack of education and ignorance regarding women's health.

The average age of menopause is 51 years.¹⁰ Any woman who is still menstruating after 55 years should be viewed with suspicion and postmenopausal blood stained discharge has an equal significance to that of PMB.¹¹ Any woman with postmenopausal bleeding must be evaluated for endometrial carcinoma.¹² The assessment includes evaluation

of risk factors like obesity, parity, family history of endometrial/breast carcinoma, personal history of breast/ovarian carcinoma, and drug history as HRT, tamoxifen and anticoagulants. A thorough physical examination followed by investigations as cervical cytology, assessment of endometrial thickness by transvaginal ultrasound (TVS) and endometrial histopathology. Hysteroscopically guided endometrial biopsy is the gold standard investigation, but due to limited facilities, Dilatation and Curretage (D & C) is the main procedure for evaluation of such cases in our setup.

This study was designed and conducted to find out the aetiological factors for PMB with histopathological aid.

Patient and Methods

This observational cross-sectional study was conducted from 1st January 2006 to 31st December 2006 at PMCH Nawabshah. A total of 50 patients with typical history of PMB attending the Gynaecology OPD of PMCH Nawabshah with postmenopausal bleeding (PMB) / Blood stained vaginal discharge, were enrolled. PMB is defined as any bleeding that occurs from the genital tract more than 12 months after the last menstrual period in a woman who is not receiving HRT.^{1,2} Patients who had received HRT were excluded from the study. The study was approved by the Ethical committee of PMCH Nawabshah.

All the patients were properly counseled and written informed consent was obtained for the study. A prompt clinical evaluation was done, which included a problem oriented history and examination. History included age, parity, age of menarche, years since menopause; details of bleeding like mode of onset, amount, number of episodes, postcoital bleeding and any abnormal discharge. Family and personal history of genital tract malignancies was asked. Documentation of associated clinical factors like hypertension, diabetes, use of drugs as HRT, tamoxifen and

anticoagulants were recorded. Complete physical examination with special attention to lymph nodes enlargement, abdominal, examination per speculum examination along with Pap smear and digital vaginal examination were carried out.

All the patients were subjected to basic haematological investigation, urine analysis and pelvic ultrasound. Examination under anaesthesia (EUA) along with D & C was carried out; cervical biopsies were taken where indicated. All the tissues obtained were analysed histopathologically to correlate with the clinical diagnosis.

Statistical analysis was performed using SPSS version 10.0 for windows. Data were expressed as mean \pm SD. Frequency and percentage were computed for continuous data like age, duration of PMB and Parity. A chi-square test was applied to compare age groups with malignancy and parity. P-value < 0.05 was considered as statistically significant.

Results

A total of 50 women with typical history of PMB were included in this study. The mean age was 59.82 ± 7.82 years (95% CI, 57.59 - 62.04). The minimum age was 47 years and maximum was 78 years. The mean parity was 4.26 ± 4.00 (95 % CI, 3.34-5.17). The majority of patients i.e. 16 (48 %) had a parity of 7 - 9, 09 (18 %) were nulliparous and 12 (24 %) patients had parity 1-3.

Malignant changes on histopathology were found in 15 (30%) patients with PMB, 07 (14%) had Ca Cervix and 08 (16%) were diagnosed as Ca Endometrium. On comparison with age groups, 05 (10%) patients were diagnosed malignant with dominance of Ca Cervix. On the other hand, 05 (10%) patients were found malignant in 61 - 70 years age group with dominance of Ca Endometrium which was not statistically significant (Table-1).

Table-1: Comparison of age group and parity with invasive carcinoma of cervix (06) and endometrium (08).

Parameter	CA Cervix n (%)	CA Endometrium n (%)	Benign n (%)	Total n (%)	P value
Age Group					
45 - 50 Years	1(2%)	Nil	4(8%)	5(10%)	0.402
51 - 60 Years	5(10%)	2(4%)	15(30%)	22(44%)	
61 - 70 Years	1(2%)	5(10%)	12(24%)	18(36%)	
> 70 Years	Nil	1(2%)	4(8%)	5(10%)	
	7(14%)	8(16%)	35(70%)	50(100%)	
Parity					
0	Nil	6(12 %)	3(6%)	9(18%)	0.002
1 - 3	1(2 %)	2(4 %)	9(18%)	12(24%)	
4 - 6	1(4 %)	Nil	10(20%)	12(32%)	
7 - 9	4(8%)	Nil	12(24%)	16(32%)	
> 9	Nil	Nil	1(2%)	1(2%)	
	7(14%)	8(16%)	35(70%)	50(100%)	

Table-2: Frequency and malignant pathology in relation to time of onset after menopause.

Onset of PMB after Menopause	Malignant Cases	Benign	Total	P=value
1 - 5 Years	2(4%)	15(30%)	17(34%)	0.005
6 - 10 Years	5(10%)	16(32%)	21(42%)	
> 10 Years	8(16%)	4(8%)	12(24%)	
	15(30%)	35(70%)	50(100%)	

It was also incidentally noted that 06 (12%) patients in nulliparity group had only Ca Endometrium and cervical cancer was more common in grand multiparous (8%). This was statistically significant ($p = 0.002$) (Table-1).

The incidence of malignancy increased with increase in period between menopause and onset of PMB. In 08 (16%) patients, malignancy was present when bleeding started ≥ 10 years after menopause ($p = 0.005$) (Table-2).

Benign pathology was encountered in 24 (48 %) cases; with benign atrophic endometrium in 07 (14 %), polyp in 06 (12%), endometrial hyperplasia in 06 (12%), senile vaginitis in 04 (8%) and one case of postcoital tear.

Premalignant lesions like adenomatous and atypical hyperplasia were seen in 07 (14%) patients, while pathology remained undetermined in 04 (8%) cases. The malignant cases included endometrial carcinomas in 8 (16%) cases and squamous cell carcinoma in 7 (14%) patients. Cervical biopsy was taken in 06 patients with clinical suspicion of malignancy, which was confirmed histopathologically. Most patients presented with multiple clinical features with common association of anaemia, hypertension, diabetes mellitus, joint pain and hot flushes.

Discussion

The famous dictum that "Postmenopausal bleeding must be considered as indicative of malignant disease until proven otherwise," still holds true in our circumstances. The general consensus regarding management of PMB is that all patients must be excluded of cancer by oriented biopsy.

In this series of 50 cases, malignancy was found in 15 (30%) cases, premalignant disorders in 7 (14%), benign pathology 24 (48%) and pathology remained undetermined in 4 (8%) cases. The earlier studies conducted in different parts of the world showed a prevalence of malignancy in PMB around 35%,^{12,13} while the more recent prevalence is quoted to be around 9.9%,^{3,4,14} -11%.¹⁵ This drop in prevalence of malignancy reflects the awareness of women and availability of screening facilities.

The situation is not satisfactory in Pakistan and malignancy of the genital tract is the existing pathology in a large number of cases. Pamela et al from India showed a prevalence of 63.6%,¹⁶ Wonderrossen Ergette from Ethiopia

60.8%,¹⁷ Liaquat et al 53.7%,⁸ Asif et al 44%⁷ and Ghazi et al 20%.¹⁸ The frequency found in our study (30%) occupies a middle position when compared with local studies.

Evaluation of PMB needs an exclusion of corpus cancer which is the fourth common cancer in women and most common gynaecological malignancy in USA.¹⁰ This situation reflects a long life span of women more than 70 years, required for development of endometrial carcinoma.

Carcinoma of cervix is the seventh most common carcinoma in USA which reflects the provision of a well organized screening programme in these countries. Worldwide it continues to be the number one cancer affecting women, with approximately 500,000 cases occurring annually.¹⁹

In the present study, endometrial carcinoma accounted for 16 % cases of PMB which is almost consistent with the reported incidence of Siyal and coworkers (14.89%).²⁰ Carcinoma of cervix was responsible for 12% cases of PMB, while it is reported to be 8.8% by Ghazi et al,¹⁷ 25.5% by Asif et al⁷ and 39.6 % by Liaquat et al.⁸

In the present study, the peak of invasive endometrial carcinoma was found at 60-70 years and that for carcinoma of cervix was 50-60 years. There is a strong correlation of carcinoma of endometrium with nulliparity and low parity. Endometrial hyperplasia, a precursor of endometrial carcinoma was found in 14% patients.

Benign lesions as a cause of PMB were found in 24 (48%) cases, consistent with the reported incidence of Ghazi et al¹⁸ and much lower than the reported incidence in the developed world.^{3,4,14} The most common lesions were atrophic endometrium (14%), polyp (12%), endometrial hyperplasia (12%) and senile vaginitis (8%). In the present study pathology remained undetermined in 8 % of cases, which is between the reported incidence quoted by Lidor A et al²² (10%), Asif et al⁷ (5.5%) and Liaquat et al⁸ (4.6%).

Conclusion

Abnormal PMB accounts for a significant proportion of gynaecological referrals. Excluding endometrial carcinoma is the primary aim of investigation. This study shows a high prevalence of malignant disorder (30%). Carcinoma of cervix and carcinoma of endometrium have almost equal contribution. Nulliparity is the significant risk factor with carcinoma of endometrium. Considering the above data, all patients with PMB need careful evaluation.

References

1. Ind Thomas. Management of Postmenopausal Bleeding. In Studd J ed. Progress in Obs & Gynae. Edinburgh, Churchill Livingstone 1998; 13: 361-77.
2. Brand AH. The woman with postmenopausal bleeding. Australian Family Physician 2007; 30: 97-192.
3. Valerie A Omicol. Postmenopausal bleeding. (Online) 2010. Available from

URL: www.mainlinehealth.org/whs.

4. Youssef A, Ben Aissia N, Gara MF. Postmenopausal uterine bleeding: Analytical study of about 65 cases. *Tunis Med* 2005; 83: 453-6.
 5. Webster SD, Cason Z, Lemos LB, Benghuzzi H. Gynaecologic correlation in patient with clinical symptoms of postmenopausal bleeding. *Biomed Sci Instrum* 2000; 36: 367-72.
 6. Mc Gregor HF. postmenopausal bleeding: A practical approach. *J Am Acad Nurse Pract* 2001; 13: 113-5.
 7. Asif KH, Hamid S. Causes of postmenopausal bleeding. *Pak J Obstet Gynaecol* 1997; 10: 22-6.
 8. Liaquat NF, Noorani K. Causes of postmenopausal bleeding: A study of 328 cases. *J Coll Physicians Surg Pale* 2000; 10: 134-7.
 9. Ahmed J, Aleem M, Khalid S, Amin D, Hussain A, Roohi M, et al. A profile of Gynaecological Cancer: A clinicopathological analysis of 580 cases during 1986 - 1994. *Professional Med J* 1996; 3: 271-82.
 10. Tindall VR. Clinical aspects of ovulation and menstruation. *Jeffcoates Principles of Gynaecology*. 5th ed. London Butterworths 1987: 80-102.
 11. Cavanagh D, Fiorica VJ, Hoffman MS, Durfee J, Nicosia VS. Adenocarcinoma of the Endometrium: An Institutional Review. *Cancer Control* 1999; 6: 354-60.
 12. Rubin SC. Postmenopausal bleeding etiology, evaluation and management. *Med Clin North Am* 1987; 71: 59-69.
 13. Cospi E, Perpimal S, Reif A. Incidence of malignancy in Jewish women with postmenopausal bleeding. *Isr J Med Sc* 1977; 13: 299-304.
 14. Kintio GA, Calvert W. Postmenopausal bleeding one hospital, one year. *J Obstet Gynaecol Surv* 1984; 39: 43-5.
 15. Gredmark T, Kvint S, Havel G, Mattsson LA. Histopathological findings in women with postmenopausal bleeding. *Br J Obstet Gynaecol* 1995; 102: 133-6.
 16. Panda S, Panda SN, Sarangi RK, Habeebullah S. Postmenopausal bleeding. *J Indian Med Assoc* 1977; 68: 185-8.
 17. Wondwossen Ergette. Abiye Tesfaye. Histopathological findings of PMB in Ethiopian women. *Ethiopian J Health Dev* 2001; 15: 39-44.
 18. Ghazi A, Jabbar S, Siddiqui N. Frequency of Endometrial carcinoma in patients with postmenopausal bleeding. *Pak J of Surgery* 2005; 21: 41-4.
 19. Mahmood I. Shafi. Premalignant and malignant disease of the cervix. In Edmonds DK ed. *Dewhurst's Textbook of Obstetrics & Gynaecology*. 7th ed. Oxford Blackwell Publishing 2007: 614-24.
 20. Siyal AR, Shaikh SM, Balouch R, Surahio AW. Gynaecological Cancer: A Histopathological Experience at Chandka Medical College and Hospital Larkana. *Med Channel* 1999; 5: 15-19.
 21. Saksouk FA, Al-Kadhi YA. Endometrium, Carcinoma. *emedicine*. Updated: Jan 12, 2010. (Online) Available from URL: <http://emedicine.medscape.com/article/403578-overview>
 22. Lidor A, Ismajovich B, Confino E, David MP. Histological findings in 226 women with postmenopausal uterine bleeding. *Acta Obstet Gynaecol Scand* 1986; 65: 41-3.
-