POSTMENOPAUSAL BLEEDING: CAUSES AND RISK OF GENITAL TRACT MALIGNANCY

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Background: Postmenopausal bleeding (PMB) is bleeding occurring after 6–12 months of amenorrhea in a woman of age where the menopause can be expected. Objectives of this study were to ascertain various causes and prevalence of genital organ malignancy in patients presenting with postmenopausal bleeding. **Methods**: A prospective observational study carried out in the Department of Obstetrics and Gynaecology, Fauji Foundation Hospital, Rawalpindi comprising of 167 consecutive cases presenting with postmenopausal bleeding one year after menopause. Women having undergone hysterectomy and bilateral salpingo-oophorectomy, receiving radiotherapy or chemotherapy, suffered trauma to the genital tract, having coagulation disorder or on anticoagulant or hormone replacement therapy were excluded. Detailed history was obtained and a thorough clinical examination was conducted. Data were entered into hospital computer database (Medix™) system. Mean±SD were calculated for age, percentage was calculated for types of histopathological findings. **Results**: The commonest cause of PMB was atrophic endometritis and vaginitis 33 (21.2%). Overall incidence of various genital tract malignancies was 25 (16.0%). **Conclusion**: The overall incidence of genital tract malignancies in patients presenting with PMB is high (16.0%), therefore, it needs to be taken seriously and requires prompt and thorough investigations.

Keywords: Bleeding, postmenopausal, female genital tract, malignancies, prevalence, aetiology

INTRODUCTION

Menopause is derived from Greek *men* (month) and *pauos* (to stop). WHO has defined menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity,[1] thus it is an important phase for dramatic hormone and other changes in lifespan of a woman. Postmenopausal bleeding (PMB) is bleeding occurring after 12 months[2] (or six months according to some)[3] of amenorrhea in a woman of age where the menopause can be expected (on the average 50 years)[4]. It can also apply to younger women following premature menopause. It is a common gynecologic problem seen in about 5%-10% of all gynecologic patients[5] and is likely to increase further. About 25 million women pass through menopause each year. By 2030, the world population of menopausal and postmenopausal women is projected to increase to 1.2 billion, with 47 million new entrants each year.[6] The PMB can be quite upsetting for the patient and challenging for treating physician. The differential diagnosis is usually limited to lesion in uterus, cervix, vagina, vulva, fallopian tubes or be related to ovaries. The bleeding can be from non-gynaecological sites, such as the urethra, bladder and lower gastrointestinal tract. The literature is full of a large number of causative factors frequently of benign nature, most common being atrophic vaginitis or endometritis.[4,7] It is an important presenting symptom of malignant tumours of genital organs.[8] The reported incidence of endometrial carcinoma has a very wide range from as low as 1.5%[9] to as high as 54%[10] in different population groups. Being a symptom of varied aetiologies and its strong association with malignancy, it should not be taken lightly. It warrants a thorough diagnostic evaluation,[11] in order to identify the cause and to institute appropriate management at an early stage. This includes a complete history with assessment of various risk factors, history of use of hormones and anticoagulants. Clinical examination constitutes examination of abdomen for any mass. Speculum examination is performed to identify tumours of vulva, vagina, cervix, atrophic vaginitis and cervical polypi. Pap smear from suspicious cervix is taken. Bimanual examination is performed for uterine size, mobility, position and adnexal masses. Rectovaginal examination may reveal nodularity in cul-de-sac. Biopsy is the gold standard, which can be obtained by office endometrial sampling[12] or diagnostic D&C. Hysteroscopy guided biopsies[13] may be carried out in patients where office endometrial sampling fails, in cervical stenosis, persistent bleeding after negative biopsy or inadequate specimen.[14,15] Transvaginal ultrasound is noninvasive procedure to detect endometrial polypi, hyperplasia and endometrial cancer. Endometrial thickness measurement by transvaginal ultrasound having a cut-off of >4.0 mm may yield 98% sensitivity for the detection of cancer.[16] Hysterosalpingogram combined with transvaginal ultrasound may further increase diagnostic accuracy.[17] The primary aim of investigating a woman with PMB is to exclude endometrial malignancy and any significant additional abnormality. The present study was carried out to ascertain various causes of PMB and to determine prevalence of endometrial carcinoma and other genital tract malignancies in our population.

MATERIAL AND METHODS

A total of 167 consecutive patients presenting with spontaneously occurring PMB after one year of menopause were included in the study. The study was carried out in the Department of Obstetrics and Gynaecology, Fauji Foundation Hospital/Foundation University Medical College, Rawalpindi. An informed consent was obtained and complete medical history was taken. Physical examination was conducted and relevant laboratory investigations were carried out, ultrasound scan was performed, and appropriate biopsy specimen was obtained. Confounding variables were controlled by excluding women having undergone hysterectomy and bilateral salpingo-oophorectomy, receiving radiotherapy or chemotherapy, suffered trauma to the genital tract, having coagulation disorder or on anticoagulant or hormone replacement therapy. Data were entered into hospital computer database (Medix™). Mean±SD were calculated for age, percentage was calculated for types of histopathological findings.

RESULTS

Out of 167 cases 11 were lost to follow up. Age range of our patients was 40–81±8.59 years. Age distribution is shown in Figure-1. Maximum number of patients (81/156, 51.9%) were in sixth decade. Only 11 (7.1%) patients were below 50 years of age. The mean age of menarche was 13±2 years. The mean age of menopause was 49±2 years. Parity varied from nulliparous to para 11. The duration of bleeding had a vast range (1–3 years) with a mean of 5.04±6.64 weeks. At the time of examination 34 patients were having episode of vaginal bleeding. Non-malignant causes were seen in 131/156 (84.0%) cases. Table-1 shows distribution of uterine, cervical and ovarian pathologies, whereas organ-wise breakdown of cases is shown in Table-2. Atrophic vaginitis/endometritis was the most common histopathological finding (33/156, 21.2%) followed by proliferative endometrium in 30 (19.2%), and cystic hyperplasia in 14 (9.0%) cases. Incidence of malignancy of genital tract was 25 (16.0%) as detailed in Table-1 and Table-3. Time since menopause in malignancy group was 1–25 years with a mean of 10.36±8.18 years. The endometrial thickness ranged from 1.5–20.0 mm with a mean 8.69±4.65 mm.

Table-1: Distribution of causes of postmenopausal bleeding (*n*=156)

Cause/age (years)	≤50	50–54	55–59	60–64	65–69	≥70	*n*	%
Atrophy	3	8	8	3	5	6	33	21.2
Proliferative endometrium	2	16	6	1	4	1	30	19.2
Cystic hyperplasia	1	7	2	2	1	1	14	9.0
Secretary endometrium	2	4	1				7	4.5
Endometrial polypi				4	1	3	8	5.1
Necrosed decidua	1	2					3	1.9
Ch nonspecific endometritis		2					2	1.3
Pyometra		1		1			4	2.6
Fibroid uterus		1	1	1			3	1.9
Tuberculosis		1					1	0.6
Disordered proliferation		3					3	1.9
Adenocarcinoma	1	5		3	2	2	13	8.3
Leiomyosarcoma		1					1	0.6
Chronic cervicitis		1	1	3	2	3	10	6.4
Cervical polyp			1	2	1		4	2.6
Cervical ectopy	1	1		1			3	1.9
Decubitus ulcer		1	1	2			4	2.6
Carcinoma in situ cervix			2				2	1.3
Carcinoma cervix			1	2		2	5	3.2
Carcinoma ovary		1	2	1	1		5	3.2
Carcinoma vagina						1	1	0.6

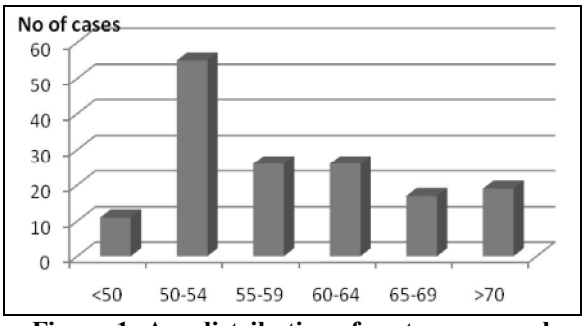

Figure-1: Age distribution of postmenopausal bleeding (n=156)

Table-2: Distribution of pathology of postmenopausal bleeding according to genital organ (*n*=156)

Organ	Number	%
Uterus	122	78.2
Cervix	28	17.9
Ovary	5	3.2
Vagina	1	0.6

Table-3: Frequency of genital organ carcinomas (n=25)

Organ	Number	%
Endometrium	14	56
Cervix	5	20
Ovary	5	20
Vagina	1	4

DISCUSSION

Patients presenting with PMB comprised of 5.0% of all gynaecological outpatients in our study which is in accordance with the reported incidence of 4.1%[7] and 5%.[13,18] The mean age at presentation was 63.6±9.3 years which is similar to other reports.[19,20] In our study time lapse between onset of bleeding and hospitalisation was 5.0±0.7 weeks which is significantly lower than the reported time lapse of 19.2 weeks.[7] It may be due to the fact that all our patients are fully entitled for free medical treatment, therefore they are promptly referred by primary care doctors to our unit for investigations and management by the consultant gynaecologist. The shorter time lapse is a significant finding as it would have been of benefit to more patients presenting with PMB in stage I & II of endometrial carcinoma.[21] There is no recommendation for screening general population for endometrial carcinoma. PMB is most common presenting symptom[14] and a warning sign for endometrial carcinoma, therefore it helps women to seek an early medical advice.[4]

A wide variety of benign causes were observed related to uterus, cervix and vagina consistent with other studies.[22] Amongst benign causes atrophic endometrium was the most common followed by proliferative endometrium as in many other studies.[4,23,24] However, chronic cervicitis has also been seen as the predominant cause in few studies.[22] The differences could be real based on different patterns of diseases according to geographic or ethnic differences or simply because of different selection criteria among various study populations. In order to clarify these differences larger, multicentre studies would be required. Atrophic endometritis needs no treatment; on the other hand atrophic vaginitis needs to be treated with local oestrogen creams, pessaries, tablets and oestradiol vaginal rings.[25] Fibroids of various sizes were seen in four patients. They usually shrink after menopause but if they enlarge or are associated with bleeding should be removed due to potential malignant change. Endometrial polypi should be removed to prevent malignant change. Simple hyperplasia can be treated with medicines but atypical hyperplasia requires surgical management. Cervical causes included decubitus ulcer due to uterine prolapse, cervical polypi, carcinoma in situ and carcinoma cervix. Cervical polypi are usually tiny in size which can be avulsed.

The reported incidence of malignancy in postmenopausal women has major differences in different population groups. It has been as low as 1%[26] – 1.5%[9] in Jewish women probably due to low incidence of carcinoma cervix to as high as 54%[10] in African women. In our study incidence of malignancy was 16% inclusive of carcinoma cervix, endometrium, ovary and vagina. The risk factors for endometrial carcinoma include obesity, hormones, Tamoxifen, diabetes and hypertension,[27,28] The risk of endometrial carcinoma increases with age with approximately 1% at age of 50 years to 25% at age 80.[29] The peak age incidence of endometrial carcinoma was significantly lower in our women between 50–54 years as compared to other studies which showed peak incidence between 60–64[23] and 65–69[29] years. Other genital tract malignancies were seen in relatively older age group (50–80 years). The ratio of carcinoma endometrium to carcinoma cervix in this study was 2:1, similar to one already determined in our[30] as well as Jewish population,[26] while the ratio by other study was in reverse order.[22] In our study only 5/156 (3.8%) cases of ovarian malignancy were seen which is similar to reported by others.[31]

Rare causes of PMB have been reported in literature such as pinworm infestation,[32] primary vaginal malignant melanoma[33] or its urethral metastasis,[34] hydatidiform mole,[35] leiomyosarcoma,[37] non-caseating sarcoid granuloma[37] and genital tract tuberculosis[38] responsible for approximately 1% cases. Although genital tuberculosis is fairly common among our population but its rarity as a cause of PMB is most probably attributed to decreased vascularity of endometrium.[39] It is recommended that a one-stop clinic be established as it is effective for early diagnosis of genital tract malignancy in majority of patients with PMB and which can significantly help in reducing the hospital waiting list.[40] It is thus concluded that all patients presenting with PMB how much slight may be or with thickened endometrium or bulky uterus should be investigated considering it malignant until proved otherwise. Strategy for population screening and investigations of patient with PMB still needs to be clearly defined.

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