

**LETTER TO EDITOR****Status of carcinoma cervix and high risk HPV 16 DNA in women with postmenopausal uterine bleeding (PMB)**Veena Kashyap<sup>1</sup>, Suresh Hedau<sup>2</sup><sup>1,2</sup>Division of Cytopathology and Molecular Oncology<sup>2</sup>, Institute of Cytology & Preventive Oncology (ICMR), I-7, Sector-39, Noida**Corresponding Author**

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Postmenopausal bleeding (PMB) is a discharge that occurs following the firm diagnosis of menopause, which is at least six months from the end of women's menstrual cycle but not to be confused with infrequent or irregular periods occurring around the time of menopause. It is a common problem representing 5% of all gynecology outpatient attendances which are to eliminate endometrial cancer as the cause of bleed and PMB should be reported urgently to the gynecologist. Uterine bleeding in postmenopausal women is highly indicative clinically of malignancy originating from cervix or endometrium and Human papilloma virus (HPV) is one of the causative agent for carcinoma cervix. Incidence of carcinoma cervix increases with the age in mature women, however, incidence of human papillomavirus (HPV) infection reduces as menopause sets in. The presence of the virus could be used as an early indication of disease potential. Because the Pap test can only detect clinical evidence of cervical disease, molecular-based diagnostic tools are being used more frequently to detect the virus before abnormal cell growth can be observed. This study was aimed to determine the status of cervical cancer and HPV 16 DNA positivity in relation to postmenopausal bleeding.

Seventy postmenopausal women aged 60 to 70 years with mean age of 65.9 years ( $\pm 2.51$ ) who had uterine bleeding for the last few months and not under hormone therapy, visited the hospital for Gynecological checkup and were examined. Pap smears were made and cervical scrapes were collected in chilled phosphate buffer saline (PBS) and

stored in -20°C for DNA extraction and further for HPV DNA testing by polymerase chain reaction (PCR) amplification. Pap smears were stained by the Pap stain and were categorized as per The Bethesda System (TBS). Amongst 70 cases of PMB, cytologically 12, were Normal (Negative for intraepithelial lesion or malignancy), 20 BCC (Benign Cellular changes, 3 LSIL-HPV (Low-grade Squamous intraepithelial lesion encompassing human papillomavirus), 4 Adenocarcinoma and 25 carcinoma cervix and 6 Atypical Glandular cells-AGUS). By HPV DNA analysis 23 cases were positive for HR-HPV 16 DNA which includes BCC (2), LSIL-HPV (1) carcinoma cervix (20). Histopathology examination was done in 28 cases of PMB and the diagnosis was chronic cervicitis (3), koilocytic changes of HPV (1), simple atypical endometrial hyperplasia (5), adenocarcinoma endometrium (3) adenocarcinoma endocervix (1), carcinoma cervix (15). The results showed that 2/20 (10%) BCC, 1/3(33.3) LSIL-HPV and 20/25 (80%) cancer cervix was positive for HR-HPV 16 DNA only. It is revealed from the results that 23/70 (32.8%) cases of PMB was positive for high risk HPV 16 DNA, 11/70 (15.7%) cases were negative for HR-HPV 16 DNA but could be positive for low risk variants and 36/70 (51.4%) cases were negative for HPV DNA which further confirms the findings that HPV declines with the increasing age of woman. The results also revealed that by Pap smear testing 29/70 (41.4%) cases of postmenopausal bleeding were detected as cancer consisting of 25 carcinoma cervix and 4 adenocarcinoma. 20/25 (80%) cancer cervix cases were positive for HR-HPV 16 DNA while all

endometrial carcinoma were negative, which is in support of our earlier observation that HR-HPV 16 is the type prevalent in cervical cancer in India.

The most likely cause of postmenopausal bleeding is an intrauterine abnormality, the physical examination gives no indication as to source of bleeding. Majority of cases had no serious problem but there are chances when the bleeding is the first symptom of serious disease including cancer. Even when the bleeding is related to cancer, if it is diagnosed early there is a very good chance that disease can be cured. The commonest innocent cause is atrophic vaginitis (inflammation of the lining of the vagina due to lower levels of the circulating hormone estrogen). Cervical and endometrial polyps

are also common but they are usually benign. About 10% cases of post-menopausal bleeding can be associated with endometrial or cervical cancer but in present study association between PMB and cancer was comparatively high, this finding can be associated with the old age of patients and longer period after cessation of menstruation when the rate of cervical cancer is comparatively high than the menstruating women. Although Pap smear is an insensitive test for detecting endometrial carcinoma, it should be done in any women presenting postmenopausal bleeding. There is growing scientific evidence to suggest that the ability to identify the presence of high-risk types of HPV is a key factor in combating this disease at the molecular level.

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