

Cervical Cytology in Postmenopausal Women of Lucknow Rural Areas, India

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Introduction: As carcinoma cervix mostly occurs after the age of 50 in women, it is mandatory to cytologically examine all the postmenopausal women above 45 to detect the onset of any premalignant changes in the cervix. The present study was conducted on 537 postmenopausal women living in rural areas and the collected data were analyzed in terms of predisposing factors of cervical carcinogenesis.

Methods: The 537 postmenopausal women were selected from the 183 rural camps organized during cervical cancer screening in the villages of Lucknow from May 2013 to December 2019.

Results: Though the frequency of atypical squamous cell changes of unknown significance (ASCUS) was very low (2.4%) in the postmenopausal women, but of squamous intraepithelial lesions of cervix (SIL) was very high (15.6%). A rise was observed in the SIL rate with increasing duration of menopause up to the age of 60 after which it declined. Candida albicans infection was the most common sexually transmitted disease (STD) and was mostly observed during the early menopausal years of 45-50 years. Different cervical lesions and gynecological symptoms were also observed mostly in the early menopause years. The SIL rate was higher with cervical lesions and postmenopausal bleeding (29.6%). The parity showed a reverse trend in postmenopausal women compared with perimenopausal ones, being higher in the nulliparous women and declining with increased parity.

Conclusion: The SIL rate was high in postmenopausal women living in the rural areas which increased with increasing duration of menopause up to the age of 60. The Pap smear screening is, therefore, mandatory in older women to exclude any premalignancy.

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INTRODUCTION

Though cervical cancer decreased significantly in the urban population of India, it remains a major threat in the rural areas. Since the peak age for cervical cancer in India is from 55 to 59 years, postmenopausal women should not be ignored for routine Pap smear screening [1]. A high proportion of carcinoma cervix patients are referred to hospital in late stages of the disease [2]. It is observed that only 22% of women in the age range of 15-49 years undergo cervical examination. The incidence

of cervical cancer drastically reduces with when an effective screening program and access to the treatment are available [3]. A high squamous intraepithelial lesions of cervix (SIL) rate especially high grade squamous intraepithelial lesions of cervix (HSIL) is reported by many investigators in the postmenopausal women [4-7]. Since it is observed that majority of HSIL cases progress to carcinoma cervix, it is essential to detect them by implementing organized cytological screening

programs among women in the rural population of India. This can be actualized by organizing camps through proper counseling and motivation with the help of qualified health workers [8].

Currently the authors are engaged in the rural cervical cancer screening program among women living in west Lucknow villages through counseling and motivating the people and holding the camps to perform Pap test. These women include adolescent married females from the age of 16 years to postmenopausal ones above 60 years. The elderly women did not cooperate in the counseling since they were mostly illiterate. However, among the total 2912 women registered until December 2019, 537 were postmenopausal ranging from the 45 to 70 years and the cytological findings obtained from their cervical smears were extensively analyzed in terms of predisposing factors of cervical carcinogenesis.

METHODS

Rural cervical cancer screening is in progress from May 2013 in the villages of Kakori and Malihabad of Lucknow and until December 2019, a total of 183 camps were organized during which 2912 women underwent Pap smear examination. The majority of these women were from the younger age group and the response of the elderly women was not so encouraging. Illiteracy may be the reason resulting in the ignorance of risk factors of cervical cancer and the utility of Pap smear screening for early detection of the disease. In spite the intense counseling and motivation in the current study, only 537 postmenopausal women in the age range of 45 to 70 years attended the camp and underwent Pap smear examination. There was no family history of cervical cancer in any case of the 537 women in the study group. Approximately 90% of these women were illiterate, and in most cases, the patients had a very low socioeconomic status. The women who underwent hysterectomy were excluded from the study. Informed consent was obtained from the subjects: thumb impression if they were illiterate or signature if literate. All the collected smears were stained in the Cytology Lab of the Department of Pathology of Era's Lucknow Medical College and Hospital, Lucknow and cytopathological abnormalities observed in the cervical smears were graded according to the Revised Bethesda system of classification of cervical cytodiagnosis [9].

The current study protocol was approved by the Ethics Committee of Era's Lucknow Medical College and Hospital, Lucknow before the rural screening program onset. All the collected data were subjected to stastical analysis using the Chi-square test in SPSS, version 22.

RESULTS

Cytopathological changes observed in the cervical smears of 537 postmenopausal women were found to be as follows:

- 13 (2.4%) ASCUS (Figure 1)
- 84(15.6%) SIL
- 76 (14.1%) Low grade squamous intraepithelial lesions (LSIL) (Figure 2)
- 8(1.4%) HSIL (Figure 3)

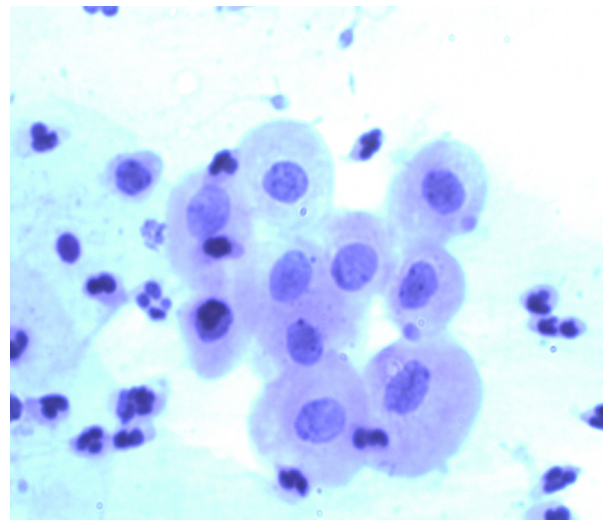


Figure 1: Atrophic ASCUS

Ectocervical smear showing atrophic squamous cells with nuclear enlargement, hyperchromasia and pleomorphism (Pap×400)

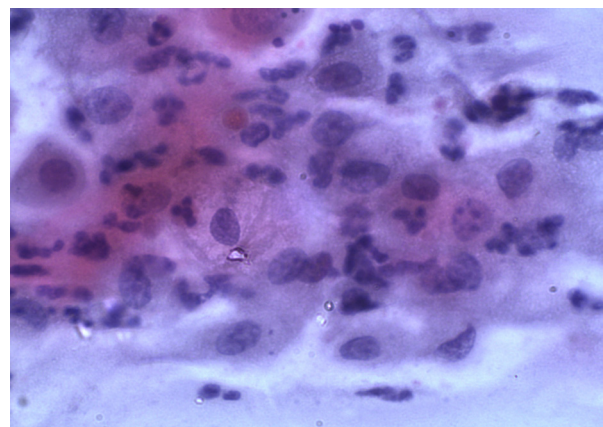


Figure 2: Atrophy With LSIL

Ectocervical cells showing atrophic changes along with nuclear enlargement and coarse chromatin (Pap×400)

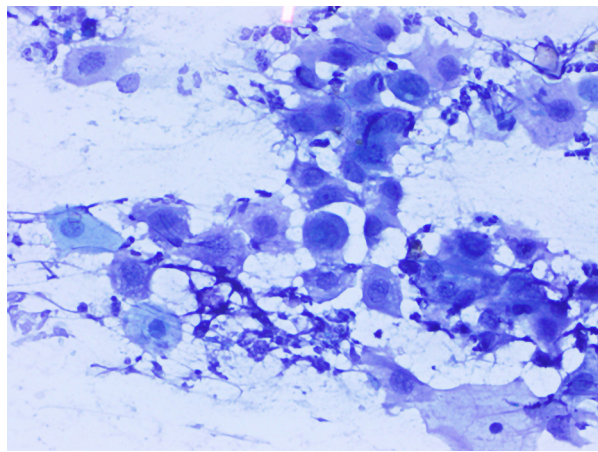


Figure 3: Atrophy With HSIL
Ectocervical basal cells showing atrophy with nuclear enlargement and coarser chromatin (Pap×400)

Cytological findings in the cervical smears of 537 postmenopausal and 2375 perimenopausal women are shown in Table 1. The atypical squamous cell changes of unknown significance (ASCUS) incidence in the postmenopausal women was 2.4% which was much lower than 7.5% observed in the perimenopausal women and the difference was statistically significant ($\chi^2=18.07$; $P<0.001$). However, there was no difference in the SIL incidence between peri- and postmenopausal women (17.2% vs. 15.6%) which was statistically insignificant ($\chi^2=0.702$; $P=0.402$). However, the HSIL incidence was higher in older women (1.4%) compared to younger ones (1.4% vs. 0.7%). Only two cases of carcinoma cervix were detected in the perimenopausal women between 35-40 years.

The incidence of different epithelial abnormalities associated with the increasing duration of menopause is shown in Table 2. All the 13 observed ASCUS cases were in the early stages of menopause aged 45-50 years (2.9%) while SIL was slightly higher in the middle age group of 45-50 years (17.7%) than in the 50-60 years age group (15.3%) but the difference was statistically insignificant ($\chi^2=0.128$; $P=0.720$). Only two SIL cases were observed in the 21 women aged above 60 years (9.5%).

Four types of STDs were studied in the cervical smears of the 537 postmenopausal women and their incidence was analyzed according to the increasing time of menopause. The most common STD was *Candida albicans* (3.4%) while *Trichomonas vaginalis*, Human papilloma virus (HPV) and Herpes simplex virus (HSV) were detected in two cases each. *Candida albicans* was associated with SIL in 18.7% of the subjects while one of the two HPV cases had SIL (50%). No SIL was observed with *Trichomonas vaginalis* or HSV infection. Most of the STDs were observed in the early menopausal group of 45-50 years while only one case of *Candida albicans* and HPV infection were observed in the 51-60 years age group. No STD was observed among the older women examined above 60 years of age. The clinical lesions of cervix were also studied in the 537 postmenopausal women (Table 3). The most common lesion was found to be erosion cervix (6.8%) followed by cystocele (6.3%). Hypertrophied cervix was observed in only two cases. The SIL was optimally observed in cases of erosion cervix (35.1%)

Table 1: Cytopathological Lesions in Postmenopausal and Perimenopausal Women^a

Cytopathological Lesions	Postmenopausal Women, No.(%) (n=537)	Perimenopausal Women, No.(%) (n=2375)
ASCUS	13(2.4%)	179(7.5%)
SIL	84(15.6%)	409(17.2%)
LSIL	76(14.1%)	391(16.5%)
HSIL	8(1.4%)	18(0.7%)
Cervical Cancer	—	2(0.08%)

^a Abbreviations: ASCUS, atypical squamous cell changes of unknown significance; HSIL, high grade squamous intraepithelial lesions; LSIL, low grade squamous intraepithelial lesions; SIL, squamous intraepithelial lesions

Table 2: Incidence of ASCUS and SIL in Relation Increasing Duration of Menopause^a

	Cases, No.(%)	ASCUS, No.(%)	SIL, No.(%)
45-50, yr	437 (81.3%)	13(2.9%)	68(15.5%)
51-60, yr	79 (14.7%)	—	14(17.7%)
Above 60, yr	21 (3.9%)	—	2 (9.5%)

^a Abbreviations: ASCUS, atypical squamous cell changes of unknown significance; SIL, squamous intraepithelial lesions

Table 3: The Relationship of Cervical Lesions of and SIL Rate With Increasing Duration of Menopause^a

	Erosion Cervix		Cervical Hypertrophy		cystocele and Other Lesions	
	Cases, No.(%)	SIL Rate, No.(%)	Cases, No.(%)	SIL Rate, No.(%)	Cases, No.(%)	SIL Rate, No.(%)
45-50, yr (n=437)	33(7.5%)	12(36.3%)	2(0.4%)	—	21(4.8%)	9(42.8%)
51-60, yr (n=79)	3(3.7%)	1(33.3%)	—	—	10(12.6%)	—
Above 60, yr (n=21)	1(4.7%)	—	—	—	3(14.2%)	—
Total, yr (n=537)	37(6.8%)	13(35.1%)	2(0.3%)	—	34(6.3%)	9(26.4%)

^a Abbreviations: SIL, squamous intraepithelial lesions

followed by cystocele and other lesions (26.4%) but the difference was statically insignificant ($\chi^2=0.228$; $P=0.633$). The SIL incidence was just double with cervical lesions (30.1% - 22/73) than 15.1% noticed in women showing a healthy cervix on clinical examination (70/464). When clinical lesions were analyzed in terms of increasing duration of menopause, erosion cervix was most common in the 45-50 years age group while cystocele and other lesions were seen in the late menopausal years after 50 years. The SIL was mostly observed in the early menopausal cases but the difference was statically insignificant ($\chi^2=0.612$; $P=0.430$).

Different gynecological symptoms observed in the 537 postmenopausal women are presented in Table 4. The SIL incidence was almost double in symptomatic subjects (23.5% - 63/267) than the 11.4% noticed in asymptomatic ones (31/270) and the difference was found to be statically significant ($\chi^2=17.94$; $P<0.001$). The vaginal discharge and pain in the lower abdomen were the most common symptoms in the postmenopausal women (21.4% and 25.1% respectively) while postmenopausal bleeding was observed in 16 cases (3.1%). The SIL rate was maximum with postmenopausal bleeding (29.4%) followed by vaginal discharge (26.9%) and pain in the lower abdomen (20.1%). When the incidence of different symptoms was analyzed in the successive years of menopause, it was observed

that all three types of gynecological symptoms and associated SIL rates were seen maximal in the early menopausal years of 45-50 years and minimal beyond 60 years but the difference was found insignificant ($\chi^2=0.115$; $P=0.734$).

The relation of parity with the SIL rate in the 537 postmenopausal women is shown in Table 5. There were nine nulliparous women of which three showed SIL (30%). The number of cases with para1 and 2 was 22 and 47 respectively and the SIL rate in these two parity groups was 18.1% and 19.1% respectively. The majority of the subjects were multiparous (85.2%) and SIL incidence was 15.1%. There was thus a declining trend in the SIL incidence from 30% in nulliparous women to 15.1% in the multiparous ones but the difference between the parity groups was found to be insignificant ($\chi^2=2.35$; $P=0.502$). The trend was reversed as the SIL incidence showed rise with increasing parity in the perimenopausal women.

The literacy status in 537 postmenopausal women was also investigated. The illiteracy rate was alarmingly higher (89.8%) in older women and only 9.2% were found literate. The SIL rate was also higher with illiteracy (16.3%) than 9.1% seen with literacy. However, the difference in the SIL rate between the two groups was statically insignificant ($\chi^2=1.899$; $P=0.168$). Lack of knowledge of personal genital hygiene in the illiterate women may be the

Table 4: Relationship of Gynecological Symptoms and SIL Rate With Increasing Duration of Menopause^{a, b}

	Vaginal Discharge		Pain in Lower Abdomen		Postmenopausal Bleeding	
	Cases, No.(%)	SIL Rate, No.(%)	Cases, No.(%)	SIL Rate, No.(%)	Cases, No.(%)	SIL Rate, No.(%)
45-50, yr (n=437)	95 (21.7%)	29(30.5%)	105(24.0%)	26(24.7%)	14(3.3%)	4 (28.5%)
51-60, yr (n=79)	15 (18.9%)	2 (13.3%)	24(30.3%)	1 (3.3%)	3(2.5%)	1 (50%)
Above 60, yr (n=21)	5(23.8%)	—	6(30%)	—	—	—
Total, yr (n=537)	115 (21.4%)	31(26.9%)	135(25.1%)	27(20.1%)	17(3.1%)	5(29.4%)

^a Abbreviations: SIL, squamous intraepithelial lesions

^b Symptomatic Women: 63/267 with SIL (23.5%), Asymptomatic Women: 31/270 with SIL (11.4%)

reason for the high SIL rate as the vaginal infections mostly remain undetected and untreated due to lack of medical amenities.

Table 5: The Relationship of SIL Rate With Parity in Postmenopausal Women ^a

	Cases, No.	SIL Rate, No.(%)
Nulliparous	10	3(30.8%)
Para1	22	4(18.1%)
Para 2	47	8(19.1%)
Para 3 and above	458	69(15.1%)

^a Abbreviations: SIL, squamous intraepithelial lesions

DISCUSSION

Cytological evaluation of cervical smears in 537 postmenopausal women revealed that ASCUS incidence (2.4%) was much lower than 7.5% observed in the perimenopausal women. The similar incidence of ASCUS was also reported by Mahadik et al., and Mulay et al., [5, 10]. However, there was no significant difference in terms of the SIL rate between the two groups (15.6% vs. 17.2%) but the HSIL incidence was double in the postmenopausal women (1.4%) compared with 0.7% observed in the perimenopausal women. Misra et al., have also found similar findings in the urban women population of Lucknow [11]. Saminathan et al., have also observed a high SIL rate in menopausal women and suggested that the squamous cell atypias can be significantly higher in postmenopausal status [4]. A high HSIL rate as observed in the present study was also reported by Mahadik et al., Ranabhat et al., and Nikumbh et al., in the postmenopausal women [5-7]. Since most of HSIL progress to malignancy, its detection and treatment are essential to prevent carcinoma cervix. In the present study, the HSIL rate was highest in 51-60 age group while no case was seen beyond 60 years. Colgan et al., reported that 80% of the HSIL cases noticed in the subjects aged above 50 years of age occurred in women with no history of Pap test or previous normal reports [12]. Since the transformation of carcinoma cervix from normal epithelium takes almost 10 years in the life of woman, a periodical cytological checkup every 3 years is mandatory to detect any pathological abnormalities in time for adequate treatment so that any advent of cervical cancer could be checked. They have also suggested that the HSIL in older women may be due to long- term lesions that do not

progress to cancer [12].

The analysis of cytopathologies with increasing duration of menopause revealed ASCUS occurring only in the early menopausal years of 45-60 years while SIL incidence was higher in late menopause of 51-60 years of age. Misra et al., have also found SIL rate rising with increasing duration of menopause in the urban women of Lucknow [11]. Mahadik et al., have also seen a high incidence of various epithelial abnormalities between 51-60 years of age [5]. Similar findings have also reported by Bukhari et al., Kaiho et al., and Thakur et al., [13-15]. A low number of STDs were seen in postmenopausal women and was found common in early menopausal years. Misra et al., have also found a low incidence of STDs in the urban women population of Lucknow [11]. However, they have reported a high HPV infection rate in postmenopausal women and have suggested that HPV infection may be latent in early years of infection and become reactivated after menopause. However, this second peak of HPV was not common in rural women. Cervical erosion cervix was the commonest cervical lesion in the postmenopausal women followed by cystocele. All these cervical lesions were mostly observed in the early menopausal years of 45-50. Similar findings were also obtained by Misra et al., in the urban counterparts [11]. Though the SIL incidence was just double in women with cervical lesions than the ones with a normal healthy cervix, a 12.9% SIL rate noticed in women with healthy cervices indicated the necessity of PAP screening even under normal conditions of the cervix.

In the present study, a high SIL rate was observed in women complaining of postmenopausal bleeding. Misra et al., also found that the SIL rate was higher in urban women with postmenopausal bleeding [11]. Thomas et al., Bukhari et al., Thakur et al., and Reddy et al., also found more likelihood of epithelial abnormalities in postmenopausal women with vaginal bleeding [13, 15-17]. Furthermore, all these symptoms were commonly observed in the early menopause years of 45-50 also reported by Barlow et al., [18]. As stated earlier, a high SIL rate was noticed in the asymptomatic women that necessitates the need for PAP screening in with no symptoms since many precursor lesions of cervix remain dormant for long. This point was also emphasized by Mahadik et al., and Velu

et al. [5, 19]. In the present study, a high SIL rate was observed in the nulliparous women which declined with increasing parity. This is a reverse trend as in the perimenopausal women the SIL rate showed rise with increasing parity. Reddy et al., have also reported a high SIL rate in nulliparous women [16], while other authors such as Gupta et al., and Mahadik et al., found a high SIL incidence in women with two parities or more [5, 20]. There is an urgent need to raise awareness among older rural women of the gynecological symptoms such as postmenopausal bleeding and vaginal discharge which are commonly associated with carcinoma cervix. These women are ignorant of the risk factors of the disease and the importance of early detection of cervical cancer through cytological examination. Raychaudhuri et al., observed that 93.7% of rural women were ignorant of signs and symptoms of carcinoma cervix [21]. Veerakumar et al., also emphasized the need of creating awareness of cervical cancer in rural women [22]. The prevalence of illiteracy and poverty in the rural population are the catalytic factors for this ignorance.

As most of the rural older women are illiterate, there is a need of raising their awareness of early detection of cervical cancer. During the present camp-based cervical cancer screening program, it was noticed that the postmenopausal women mostly refrain from undergoing Pap smear examination. They opt for a Pap test when they have some long-term severe gynecological problems. Furthermore, since HSIL cases were common in women aged above 50 years, it is necessary to include women aged up to 60 in the screening and also above 60, if they are symptomatic. Such a strategy yields large number of SIL cases in the postmenopausal women covered by the screening, the adequate treatment of which can monitor the progression of the lesions to malignancy and thus brings down the incidence of carcinoma cervix in the screened rural elderly women population. As mentioned earlier, about 90% of the postmenopausal women of the series, were illiterate and, had no knowledge of the risk factors of the disease and the importance of early detection of cervical cancer. They avoided Pap smear examination since they thought that it is an invasive process. Hence most of them avoided it in spite of the repeated motivation by authors. Only symptomatic women attended the camp to

be examined by the gynecologist and underwent Pap test based on her advice. Furthermore, there is a social taboo among rural women as they think that attending the camp proves a hindrance in their privacy.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

ETHICS APPROVAL

The current study protocol was approved by the Ethics Committee of Era's Lucknow Medical College and Hospital, Lucknow before the rural screening program onset.

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