ORIGINAL RESEARCH

IMPACT OF PAP SMEAR SCREENING ON CERVICAL CANCER IN A TERTIARY CARE CENTER IN NORTH INDIA

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ABSTRACT
Background: Cervical cancer is the most prevalent malignancy in women that occurs in the cervix, considered as 2nd common cancer that affects the women after most common breast cancer. Pap smear is a simple, cost effective, non-invasive and OPD method for early diagnosis of cervical cancer and pre-cancerous cervical lesions.
Purpose: The purpose of this study was to examine the evidence for the support of patterns of different kinds of cervical lesions and prevalence of epithelial cell abnormalities in our study populations.
Materials and Methods: This retrospective study was carried out in the department of Pathology in collaboration with the department of Gynaecology at ESIC hospital, Lucknow, Uttar Pradesh, India from 01/03/2021 to 30/12/2021 with the duration of 10 months. All Pap smears were taken of women between the age group of 20-70 years in this study. A total of 150 smears were stained with Pap stain and reported by following the New Bethesda system for Reporting Cervical Cytology, 2014.
Results: Out of 150 cases, 17 (11.33%) Pap smears were reported as unsatisfactory or inadequate, 126 (84%) were NILM (negative for intraepithelial lesion or malignancy). Non-specific inflammatory smears were found to be more predominant among NILM. Epithelial cell abnormalities were reported in 07 (4.66%) pap smears examinations. Atypical squamous cells of undetermined significance (ASC-US) in 03(2%) cases, Low grade squamous intraepithelial lesion (LSIL) in 01(0.66%) case, high grade squamous intraepithelial lesion (HSIL) in 01(0.66%) case and squamous cell carcinoma (SCC) were also found in 01(0.66%) case. The most prevalent age group for epithelial cell abnormalities was 40-50 years.
Conclusion: Pap smears is an effective, non-invasive modality and useful in the detection of early diagnosis of cervical cancer and pre-cancerous cervical lesions.
Keywords: Cervical cancer, Pap smears, Malignant, Pre-cancerous cervical lesions.

INTRODUCTION

Cervical cancer is the most prevalent malignancy in women that occurs in the cervix, considered as 2nd common cancer that affects the women after breast cance.[1] Globally, estimated incidence of cervical cancer is 570,000 cases and 311,000 related deaths in 2018[2,3] that accounts for 7.5% of all women cancer deaths.[4] Incidence of cervical cancer in females is a more frequent gynecological cancer in developing countries in contrast to developed countries[5] owing to scarcity of awareness and difficulties in operating the cytology-based screening programs.[6] In India, cervical cancer in females has been a leading cause of cancer for decades with an estimated age standardized incidence rate (23.07/100,000) in the period of 1990 to 2015.[7] Several lines of evidence on cervical cancer in India showed that 126,000 new cases of cervical cancer occur in each year.[8,9] However, cervical cancer is easily detectable as well as curable malignancy in comparison to other malignancies.[10] It is treatable cancer especially in the early stage of development when tumor cells are confined on the surface of the cervix, once it is metastasized which is more troublesome to treat resulting in increased mortality and morbidity. Effective screening is the first effective way to reduce the mortality and morbidity owing to cervical cancer but for this sensitization of females and awareness among women is needed by way of community based approach. The Pap smear examination is a salvage screening modality for the diagnosis of cervical cancer and precancerous lesions, being employed in the whole world.[11,12] Sensitivity and specificity of the Pap test is about 50%-75% and 98%-99% respectively.[13] Pap smear examination detects early cervical lesions and TBS (The Bethesda System) is the most widely accepted system for describing Pap smears.[14] Despite early detection of cervical lesion, it is also helpful in the detection of other vaginal and cervical problems including infection and inflammatory conditions.[12,15] The purpose of this study is to examine the evidence for the support of patterns of different kinds of cervical lesions and prevalence of epithelial cell abnormalities in our study populations.

MATERIALS AND METHODS

The present retrospective study was carried out in our department of Pathology with collaboration with the department of Gynaecology at ESIC hospital, Lucknow, Uttar Pradesh, India from 01/03/2021 to 30/12/2021 with duration of 10 months. Pap smears were obtained from total 150 women between age ranges from 20 to 70 years who represented with different vaginal and cervical problems (menstrual irregularities, post menopausal bleeding , foul smelling discharge , abnormal vaginal discharge, dysparenuria and pelvic pain) and also post chemotherapy for cervical cancer by employing Pap diagnosing Kit (Ayres spatula, cotton swab and endo-cervical brush). The exclusion criteria were women with age more than 70 years and less than 20 years. Pap smears were fixed in 95% ethanol and immediately sent to the Department of Pathology, followed by staining with Pap stain. Pap smears were reported as described by New Bethesda system for Reporting Cervical Cytology, 2014.[16]

RESULTS

In this retrospective study, a total of 150 Pap smears were analyzed. Out of 150 cases, 17 Pap smears (11.33%) were reported as Unsatisfactory or Inadequate according to the New Bethesda System for Reporting Cervical Cytology, 2014. This study observed that 126 (84%) cases were NILM (negative for intraepithelial lesion or malignancy) (**Table-1**) in which Inflammatory cases 103 (68.7%) followed by Atrophied cases 04 (2.66%) having majority of parabasal and basal cells in microscopic examination and No Change (normal smear) in 19 (12.66%) cases. Epithelial cell abnormalities were reported in 07 (4.66%) cases. Pap smears examinations [ASC-US-04(2.7%), LSIL-01(0.66%), HSIL-01(0.66%) and SCC-01(0.66%)] (**Table-1**). In Inflammatory smears - Non-specific inflammatory cases (60%, 90 cases) were found to be more predominant and in microscopy examination showing numerous polymorphs (mild, moderate and marked) (**Figure-1**). Candida spores (4%, 06 cases), Bacterial vaginosis (4%, 06 cases) showed clue cells over the squamous epithelial cells on a dirty background (**Figure-2**) and Trichomonas (0.66%, 01 case). Atypical squamous cells of undetermined significance (ASC-US) cases (2.7%) were found to be more common among epithelial cell abnormalities showing very few suspicious atypical squamous cells .low grade squamous intraepithelial lesion (LSIL) was found in only one case (0.66%) which showed few clusters of dysplastic squamous cells and koilocytosis with perinuclear halo (**Figure 3).** High grade squamous intraepithelial lesion (HSIL) was also found in only one case (0.66%) showing tight clusters of atypical squamous cells with increased nucleocytoplasmic ratio and hyperchromatic nuclei. Squamous cell carcinoma (SCC) was also observed in only one case (0.66%) and in microscopy examination found sheets and clusters of atypical squamous cells, metaplastic cells and tadpole cells. The most prevalent age group for epithelial cell abnormalities was 40-50 years (**Table-2**). Three ASC-US cases were observed at 40-50 years of age. One case of LSIL & one case of HSIL were observed at 50-60 years of age while only one case of SCC was observed at >60 years of age. Inflammatory Pap smears reveals that the majority of cases were in the age group of 40-50 years. Non-specific inflammation was observed in all age groups with the highest one in 40-50 years of age. The cases of Bacterial vaginosis and Candida spores were observed in two age groups (30-40 and 40-50 years of age). Trichomonas case was observed in 30-40 years of age group (**Table-2**).

**Table-1: Categorisation of cytological interpretation**

Interpretation	Number of pap smear (150)examined
1. Unsatisfactory	17(11.33%)
2. NILM (Negative for intraepithelial lesion)	126 (84%)
(a) Inflammatory	103 (68.7%)
Non specific	90 (60%)
Candida spores	06 (4%)
Bacterial vaginosis	06 (4%)
Trichomonas	01 (0.66%)
(b) Atrophied	04 (2.66%)
(c) No changes (normal smear)	19 (12.66%)
3. Epithelial cell abnormality	07 (4.66%)
ASC-US	03 (2.7%)

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ASC-H	00
LSIL	01 (0.66%)
HSIL	01 (0.66%)
SCC	01 (0.66%)
[NILM- Negative for intraepithelial lesion; ASC-US- Atypical squamous cells of undetermined significance; ASC-H- Atypical squamous cells cannot exclude HSIL; LSIL- Low grade squamous intraepithelial lesion; HSIL- High grade squamous intraepithelial lesion; SCC- Squamous cell carcinoma.]	

Table-2: Cytological based detections in distinct age groups

Diagnosis	20-30 yrs	30-40yrs	40-50yrs	50-60yrs	60-70yrs
Inflammatory smear					
Non specific inflammation	10	30	38	08	04
Bacterial vaginosis	-	03	03		
Trichomonas infection		01			
Candida spores		02	04		
Epithelial cell abnormality					
ASC-US		01	03		
ASC-H			00		
LSIL				01	
HSIL				01	
SCC					01
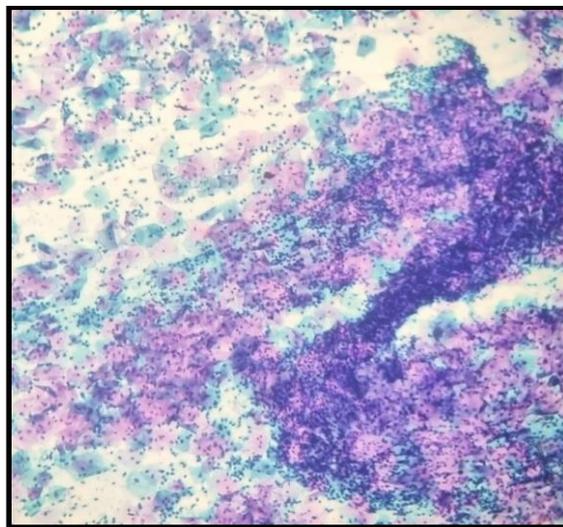
Photomicrograph-1: NILM-Marked inflammation [Papanicolaou stain, x100] showing numerous polymorphs on a background of superficial and intermediate squamous cells.
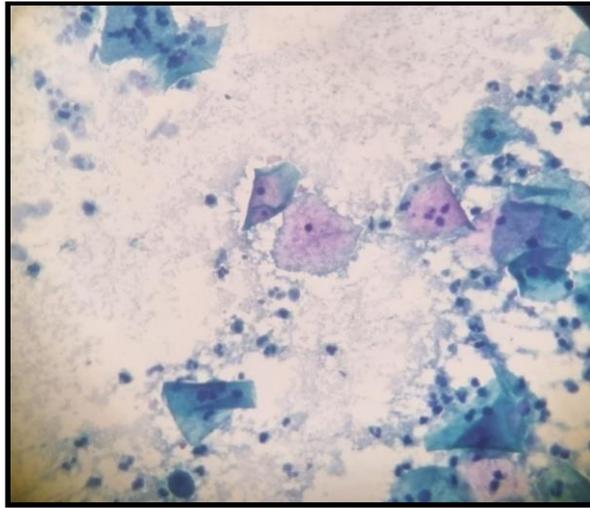
Photomicrograph-2: NILM- Bacterial vaginosis [Papanicolaou stain, x100] showing clue cells over the squamous epithelial cells and few polymorphs on a dirty background.
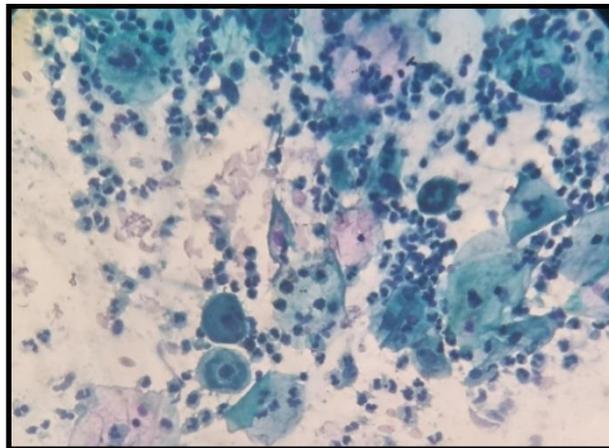
Photomicrograph-3: LSIL (low grade squamous intraepithelial lesion) [Papanicolaou stain, x100] showing koilocytosis with perinuclear clearing, polymorphs and superficial squamous epithelial cells.

DISCUSSION

The incidence of cervical cancer in women is very high owing to poorly implemented prevention programs. Cervical cancer most frequently occurs between ages of 40-50 years of age.[17] Pap smear modality is an effective method for screening of cervical cancer and a widely acceptable method worldwide. The pap smear test is a screening procedure and it should be done every 3 years according to the American Cancer Society (2012).[18] However, still morbidity and mortality associated with cervical cancer has not been completely eliminated. In 1986, approximately 1867 elder women died from cervical cancer in the United States.[19] Cervical cancer in women is the most widely screened cancer in both developed and developing countries.[12] Population based screening of cervical cancer showed that the Pap smears method decreased the mortality and incidence of cervical cancer up to 80% in developed countries in the previous five decades.[20] Declining trend of cervical cancer has been reported in developing countries especially in India.[21] According to NCRP (national cancer registry program), India; Breast and uterine cervix cancer is the leading cause of malignancies that occurs in Indian women.[14] Fruitful screening programs are

required for early detection and treatment of precancerous cervical lesions particularly in high risk age groups and reduction of morbidity and mortality associated with cervical cancer. In this retrospective study, the majority of the women had Pap Smear Test for the 1st time in their life-span because of lack of awareness and also in low socioeconomic women. Singh and Singh.[22] in their study reported 83.6% cases of NILM after cytological based screening of Pap smears. Another retrospective study reported that 97.6% of Pap smears were NILM by employing Pap technique.[23] A tertiary care centre study reported 91.3% cases of NILM after Pap staining.[24] In the present reports at our tertiary care ESIC hospital, 84% of screened Pap smears were reported to be NILM. In a study performed by Singh and Singh[22], they reported the epithelial cell abnormalities in 16% of screened Pap smears. Another study reported the epithelial cell abnormalities in 15% of screened Pap smears.[25] Sharma et al.,[24] reported the epithelial cell abnormalities in6.8% of screened Pap smears. In this study, epithelial cell abnormalities were observed only in 4.66% of screened Pap smears. One of the reports reported the ASC-US in 2.9% of screened women, HSIL in 0.48% cases and LSIL in 5.09% cases.[26] Another reports found ASC-US in 2.5% of screened women, HSIL in 6% cases and LSIL in 7.5% cases. Sharma et al.,[24] observed ASC-US in 3.3% of screened women, HSIL in 0.4% cases, SCC in 0.2% cases, and ASC-H in 0.8% cases. Lakshmi et al.,[25], in their study observed ASC-US in 2.5% of screened women, HSIL in 6% cases and LSIL in 7.5% cases. Malpani et al.,[23] found the ASC-US in 0.42% of screened women, HSIL in 0.54% cases, LSIL in 0.42 % cases and SCC in 0.48% cases. In our study, ASC-US is observed in 2.7% of screened women, HSIL in 0.66% cases, LSIL in 0.66% cases, SCC in 0.66% cases and no positive case in ASC-H. In a study carried out by Warpe et al.,[27], they found non-specific inflammation in 61.2% of screened women, bacterial vaginosis in 12.24% cases, Trichomonas infection in 7.35% and Candida spores in 0.8% cases. Numerous other reports also found similar reports.[28,29] Sharma et al.,[24] observed non-specific inflammation in 67.5% of screened Pap smears, bacterial vaginosis in 7.5%, Trichomonas infection in 0.67% cases and Candida spores in 3.5% cases. In the present study, Non-Specific Inflammation was observed in 60% of screened Pap smears, Bacterial Vaginosis in 04 % cases, Trichomonas infection in 0.66% cases and Candida spores in 4% cases. A Study conducted by Malpani et al.,[23], revealed that the majority of cases of inflammatory smears and epithelial cell abnormalities were seen in the age group of 41-50 years. Another report carried out by Naik et al.,[30] also found similar age group association with inflammatory smears and epithelial cell abnormalities. Ramprabhat et al.,[31] found that 8% of screened Pap smears were seen in the age group of >40 years of age. In the current reports, association of inflammatory smears and epithelial cell abnormalities was found with the age group of 40-50 years. In a report performed by Ramu et al.,[32], they found the atrophy in 8.91% of screened Pap smears. Another reports found the atrophy in 1.33% of screened Pap smears[33]. A prospective study performed in tertiary care centre observed atrophy in 2.4% of screened Pap smears.[34] In the current reports, atrophy was observed in 2.66% of screened Pap smears.

LIMITATION

The limitation of this study is that the Pap smear test is a screening procedure and to confirm the cases of epithelial cell abnormality, researchers must correlate this with histopathological examination which is a confirmatory procedure for epithelial cell abnormalities. Our ESIC

hospital is a tertiary care hospital and after finding out epithelial cell abnormality, we refer the case to a primary care hospital which is tied up to this hospital. So we could not correlate our impression on Pap smear to histopathology.

CONCLUSION

Cervical cancer and precancerous cervical lesions are quite high in women. Pap smears test is an effective, safe, affordable, non-invasive modality and useful in the detection of early diagnosis of cervical cancer and pre-cancerous cervical lesions. We observed that cervical cancer occurs more commonly in the age group of 40-50 years. Hence, it is recommended to have one Pap smear test prior to the age of 40 years and followed by every 3 years. Further, Periodical screening must be recommended for early diagnosis of cervical cancer and precancerous cervical lesions and to decrease the mortality and morbidity associated with cervical cancer in women.

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