Spectrum of Cervical Pap Smears in a Tertiary Teaching Hospital in Manipur, India

[1]Phirthangmoi Fimate, [2]Rothangpui Pui and [1]Pinky Soraisham

[1]Department of Pathology, Jawaharlal Nehru Institute of Medical Sciences, Manipur, India
[2]Department of Medicine, Jawaharlal Nehru Institute of Medical Sciences, Manipur, India

ABSTRACT

Background and Objective: Cervical cancer is a worldwide leading cause of morbidity and mortality among women. This is a retrospective study to evaluate the pattern of cervical smear abnormalities and to assess the role of Pap smear screening in detecting early cervical cancer among women attending a tertiary teaching hospital in Manipur, India, for 1 year. **Materials and Methods:** Pap smear reports and slides of all women over the age of 21 years who visited the gynaecology outpatient department during this one year were retrieved and reviewed. The smears were obtained using Ayre's spatula and endocervical brush spread on two clean glass slides for each patient, which were immediately wet-fixed in 95% ethyl alcohol, stained by Pap stain and subsequently examined by trained cytopathologists of the cytopathology division of the pathology department. Frequencies of all the findings including epithelial abnormalities were calculated. **Results:** There were a total of 1,562 cases in the age range of 21-84 years. Vaginal discharge was the most common symptom. The majority of 1,499 (95.97%) of the cases were negative for intraepithelial lesion or malignancy. Epithelial cell abnormalities 63 (4.04%) including atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesions and high-grade squamous intraepithelial lesions were seen in 3.27, 0.26 and 0.51%, respectively. **Conclusion:** Pap smear test is a simple, safe and cost-effective screening tool to detect pre-invasive cervical lesions. There is a need for well-organized screening programmes to motivate every sexually active woman above the age of 21 years to undergo active cervical screening, to reduce the burden of cervical cancer.

KEYWORDS

Cervical cancer, Pap smear, screening, intra-epithelial lesion, epithelial cell abnormalities, inflammatory smear

INTRODUCTION

Cervical cancer is a major public health problem, being the fourth most common cancer as well as the fourth leading cause of cancer deaths worldwide among women in 2018[1]. In many developing countries like India, it is the second most common cancer with over 75% of incidence and mortality[1-4].

The incidence of cervical lesions, whether inflammatory or neoplastic, appears to be much more common in developing countries like India as compared to the Western countries, possibly due to the absence of effective cervical screening programmes, low socioeconomic status and lack of awareness of cervical cancer prevention[3].

Unlike most other malignancies, cervical cancer is easily detected and highly treatable in the early stages of development or carcinoma in situ, due to the long pre-invasive stage and well-defined pre-malignant lesions, if robust screening programmes are implemented[3-6].

Many studies have shown that there has been a reduction in the burden of cervical cancer worldwide because of early detection through organized screening programmes[5,7-9].

The main objective of cervical cancer screening, therefore, is the early detection and timely treatment of these early cervical intra-epithelial lesions before they develop into invasive cervical cancer since these early lesions are treatable as the cancer cells are still localized and confined to the surface of the cervix and have not yet spread into the adjacent tissues. Once the cancer cells invade and metastasize to other parts of the body, the disease becomes more difficult to treat and thus increases morbidity and mortality[3,10].

These early lesions can be identified by a Papanicolaou (Pap) smear test, which is a simple, easy, convenient, cost-effective, versatile and reliable test. The Pap smear test was first introduced in 1941 and has now become the primary standard screening test and is being used globally for the detection of pre-cancerous Cervical Intraepithelial Neoplasia (CIN) and the early stage of invasive cervical cancer. Not only does a Pap smear play a crucial role in detecting cancer but it also helps in the diagnosis of inflammatory lesions, identification of causative organisms and cervical epithelial changes due to therapeutic agents[4,10]. A Pap smear test is performed using a brush or spatula (Ayre's spatula) to gently scrape the cellular material from the squamocolumnar junction of the cervical canal and this material is smeared onto a clean glass slide. The cells are then wet-fixed, stained and visually examined under a microscope[10,11].

The new 2014 Bethesda system terminology is the most widely used system for describing and reporting pap smears and also reflects important advances in the biological understanding of cervical neoplasia and cervical screening technology[5].

Pap smear screening has a sensitivity of 50-75% and specificity of 98-99%[3].

There are several screening guidelines for the successful implementation of cytological screening, like those of the US Preventive Services Task Force (USPTF)[9,12].

The current study aimed to analyze the cytological profile of pap smears by characterizing the age and pattern of Pap smear abnormalities among patients during the study period in a tertiary teaching hospital in Manipur, India and also to assess the role of Pap test screening in detecting any early cervical intraepithelial lesions in women.

MATERIALS AND METHODS

Study area: This study was an observational study of available Pap smear results of all women who had attended the gynaecology Out-Patient Department (OPD) and subsequently underwent Pap smear tests during the period from April, 2019 to March, 2020, at Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Manipur, India.

Inclusion criteria: All sexually active women coming to gynaecology OPD between the ages of 21-84 years and consenting to Pap smear test were included in the study.

Exclusion criteria: Women unwilling to give consent for Pap smear test, known or treated cases of cancer cervix, pregnant women and women with local douche or antiseptic cream were excluded from the study.

Ethical approval was obtained from the institutional ethical committee: Each patient was placed in a dorsal lithotomy position and a Cusco's bivalve speculum was introduced through the vagina and the cervix was visualized. The longer projection of Ayre's spatula was placed in the cervix near the squamocolumnar junction of the cervical canal and rotated through 360 degrees, followed by an endocervical brush. The cellular material thus obtained was quickly but gently smeared onto two clean glass slides for each patient, which were then immediately put into a Coplin jar containing 95% ethyl alcohol (fixative) and then stained by trained cytotechnologists using the Pap method (RAPID-PAP kit). The stained Pap smear slides were then analyzed in the Cytopathology Division of Pathology Department, Jawaharlal Nehru Institute of Medical Sciences, Manipur, India by cytopathologists according to the New Bethesda System for Reporting Cervical Cytology 2014. Based on the Bethesda system, cervical lesions were broadly classified into Negative for Intraepithelial Lesion or Malignancy (NILM) and Epithelial Cell Abnormalities (ECA) including squamous and glandular cells as follows:

- Adequacy of sample
- Satisfactory
- Unsatisfactory
- Squamous cell abnormalities
- Atypical Squamous Cells (ASCs)
- ASC of Undetermined Significance (ASC-US)
- ASC that cannot rule out high-grade lesion (ASC-H)
- Low-grade Squamous Intraepithelial Lesion (LSIL)
- High-grade Squamous Intraepithelial Lesion (HSIL)
- Squamous Cell Carcinoma (SCC)
- Glandular cell abnormalities
- Atypical glandular cells, specify the site of origin, if possible
- Atypical glandular cells, favour neoplasia
- Adenocarcinoma *in situ*
- Adenocarcinoma

Other cancers (such as lymphoma, metastasis and sarcoma).

All women with abnormal Pap smear reports were advised for follow-up and treatment as per the standard guidelines by the WHO.

Those with LSIL and HSIL were counselled and advised to undergo colposcopic examination and biopsy for further histopathological examination.

Data analysis: The data collected were analyzed with Statistical Package for Social Sciences (SPSS) version 20 for Windows (IBM Corp., Armonk, NY, USA).

RESULTS AND DISCUSSION

A total of 1,562 cases of cervical pap smears were received in our cytopathology laboratory during this 1 year study period. The age of all the patients ranged from 21-84 years. The majority 641 (41%) of the women in the study group were from the reproductive age group (20-40 years).

Of the total 1,562 cases, 1,499 (95.97%) cases were reported as Negative for Intraepithelial Lesion or Malignancy (NILM), including 26 (1.66%) normal smears in Table 1.

Of the remaining 1,473 (94.3%) cases, 1,149 (73.56%) cases showed moderate to severe non-specific inflammation with no definite aetiology and 297 (19%) cases showed features of atrophic vaginitis, all of whom were postmenopausal and belonged to the age group of 40-84 years in Table 2. Specific infectious aetiology was seen in 27 cases of which, Candida infection (16 cases, 1.02%) characterized by the presence of pseudohyphae with budding yeast forms closely related to groups or clumps of squamous cells in a background of acute inflammation was the most common, followed by Bacterial vaginosis (11 cases, 0.7%) characterized by altered vaginal flora. Infection by other organisms such as Actinomyces, Trichomonas and Aspergillus was not seen in this study.

Epithelial cell abnormalities were seen in 63 (4.04%) cases in Table 3.

These cases with epithelial cell abnormalities belonged to the age range of 21-80 years with a mean age of 45.57 years, the majority of the patients 22 (34.92%) presented in the fifth decade of life in Table 4.

Table 1: Cytological diagnosis of Pap smears with percentage distribution

Cytodiagnosis	Number of cases	Percentage
NILM		
Normal	26	1.66
Inflammatory		
Non-specific	1,149	73.56
Candida	16	1.02
Bacterial vaginosis	11	0.70
Atrophic vaginitis	297	19.02
Intra-epithelial lesions/ECA		
Squamous		
ASCUS	51	3.27
LSIL	4	0.26
HSIL	8	0.51
Total	1,562	100.00

Table 2: Age-wise distribution of cases with inflammatory lesions

Age (years)	Non-specific	Bacterial vaginosis	Candida	Atrophic	Total
21-30	153	0	4	0	157
31-40	438	4	4	4	450
41-50	489	5	5	88	587
51-60	69	2	3	130	204
61-70	0	0	0	68	68
71-80	0	0	0	6	6
81-90	0	0	0	1	1
Total	1,149	11	16	297	1,473

Table 3: Comparison of the current study with previous clinical studies of epithelial cell abnormality (ECA)

Authors	Sample size	Results (abnormal Pap smear (%))
Sachan et al.[2]	n = 1,650	8.48
Rana et al.[3]	n = 610	6.8
Ekta et al.[4]	n = 500	6.6
Pudasaini et al.[7]	n = 4,160	0.5
Rose[8]	n = 630	3.8
Tamrakar et al.[11]	n = 1,506	1.7
Vedavathi[14]	n = 800	4.8
Present study	n = 1,562	4.04

Table 4: Age-wise distribution of cases with epithelial cell abnormalities

Age (years)	ASCUS	LSIL	HSIL	Total	Percentage
21-30	3	1	0	4	6.35
31-40	14	2	3	19	30.16
41-50	19	1	2	22	34.92
51-60	12	0	2	14	22.22
61-70	2	0	1	3	4.76
71-80	1	0	0	1	1.59
81-90	0	0	0	0	0
Total	51	4	8	63	100.00

Table 5: Comparison of epithelial cell abnormalities with other studies and the present study

| Study groups | Sample size | ECA (%) | | | |
		ASCUS	LSIL	HSIL	SCC
Sachan *et al.*[2]	1,650	2.9	5.09	0.48	-
Rana *et al.*[3]	610	3.27	1.31	1.63	0.65
Ekta *et al.*[4]	231	0.86	0.0	0.0	0.43
Akinfolarin *et al.*[5]	2,048	6.5	11.6	6.2	-
Pudasaini *et al.*[7]	4,160	0.1	0.2	0.2	-
Rose[8]	630	0.9	0.5	0.6	0.8
Shaki *et al.*[10]	1,100	4	6.8	6	2.3
Vedavathi *et al.*[14]	200	4	3.5	1	0.5
Present study	1,562	3.27	0.26	0.51	-

The 51 cases (3.27%) of the ECA were Atypical Squamous Cells of Undetermined Significance (ASCUS), 8 cases (0.51%) were High-grade Squamous Intraepithelial Lesion (HSIL) and 4 cases (0.26%) were Low-grade Squamous Intraepithelial Lesion (LSIL) in Table 5.

The majority 641 (41%) of the women in the study group were from the reproductive age group (20-40 years), similar to studies by others[4,7,13]. It was observed that vaginal discharge was the most common (38%) presenting complaint in our study, which is comparable to other studies[2,4,14]. There were 1,499 (95.97%) cases of NILM, with the most common lesion 1,149 (72%) being of non-specific inflammation, similar to studies by others[2,4]. The ECA was detected in 4.04% of the cases, comparable to the ECA detection rates of 0.5% and 8.48% in various studies[2-4,7,8,11,14] (Table 3). In the present study, most (22, 34.92%) of the abnormal cytology was detected in patients in the age group between 41 and 50 years (Table 4), with a mean age of 45.5 years, similar to other studies[2]. This study revealed ASCUS 51(3.27%) to be the most common ECA, which was similar to those obtained in other studies[3,4,8,14] (Table 5).

Our study implies that cervical lesions are still prevalent among women, even though our hospital caters to a small demographic region in a developing country like India. This high prevalence might be due to lifestyle, personal hygiene, age of the individuals, the existence of other coexisting sexually transmitted diseases, awareness about screening and the presence or absence of cervical screening programmes.

The Pap smear test can be applied as a screening tool to effectively detect early cervical cancer to prevent the subsequent development of invasive cervical cancer as its precursor lesions usually occur 5-10 years earlier. This test can also be used to detect any infectious or inflammatory lesions, followed by adequate prompt treatment as persistent inflammation may predispose to pre-malignant changes. Thus, the Pap smear test is a fundamental tool for the screening, prevention and early diagnosis of cervical cancers.

There is an urgent need to promote cervical cancer screening awareness programmes through any available media, educate women regarding the symptoms of cancer and motivate them to visit the hospital for cancer screening and regular follow-ups. Therefore, must also strengthen our healthcare system to include screening at primary health care centres as well as organize active regular health checkup camps across rural and urban areas. This will benefit women who hesitate to come to the hospital and also educate them regarding Pap smear tests and their effectiveness in cervical cancer detection.

The results of the current study may not be very accurate due to the limited number of cases in a tertiary care hospital as well as our study being confined to a small geographic location, hence generalization to the whole country may not be possible.

CONCLUSION
Cervical cancer remains an easily preventable and treatable (if intervention is done at the right time) huge burden which drains a person economically, emotionally and physically. Thus, there is a need to create awareness about cervical cancer among women and motivate them to attend screenings from time to time as routine health check-ups. The community as a whole should be educated and made aware of the availability of the Pap smear test, including its goal and the required frequency of tests, by widespread educational and media programmes, especially in developing countries like India. A Pap smear test is a simple, cheap, safe and practical diagnostic tool for early detection of cervical cancer and should be established as a routine screening procedure for every woman above the age of 21 or after the onset of sexual activity to reduce the treatment burden, morbidity and mortality which arises due to cervical cancer.

SIGNIFICANCE STATEMENT
This present study emphasizes the need to ramp up and re-organize the existing screening programmes for the early detection of cervical cancer among women. Despite its ease of detection by Pap smear test and treatability especially in the early stages, this disease is still a major public health problem worldwide. This will further reduce the load on individual and public funds while at the same time increasing the standards of living for women.

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