A Retrospective Study of Cervical Cancer Screening using Pap Smear and the Bethesda System 2014

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Abstract

Background: Cancer of the uterine cervix is the second most common malignancy among Indian females with very high mortality rates. Cervical cancer evolves through well understood progression model from pre-cancerous lesion to cervical intraepithelial neoplasia (CIN) with progression to invasive cancer. The identification of these pre-cancerous lesions of the cervix by cervical cytological screening will enhance cure rate by timely management and thereby reduce mortality rates. The aim of the study is to determine incidence of the various pre-cancerous and cancerous lesions of cervix using pap smear as a screening test and their incidence among different age groups.

Materials and Methods: It is a retrospective study of pap smears conducted on the 2,450 cases for two years from January 2021 to December 2022. This study was conducted by the department of Obstetrics and Gynaecology with the help of department of Pathology using The Bethesda system 2014.

Results: Pap smear was done on a total of 2450 patients on outpatient basis. Out 2450 smears, 150 (6.1%) were reported as having epithelial cell abnormalities. The most frequent epithelial cell abnormality reported in our study group was Low grade squamous intraepithelial lesions (LSIL) seen in 65 cases (2.65%), followed by high grade Squamous intraepithelial lesions seen in 40 cases (1.63%) and atypical squamous cell of undetermined Significance seen in 22 cases (0.89%). Atypical Glandular cells (AGC) were seen in 3 cases, while squamous cell carcinoma was seen in 20 cases (0.81%) on cytology. Mean age of women with abnormal pap smear was 43.4 years. LSIL was more common in age group of 41-50 years, while HSIL was more frequently noted between 31-40 years.

Conclusion: Our study highlights the importance of routine pap smear screening for detection of precancerous lesions of cervix.

Key Words: Cervical cancer screening, pap smear, cervical epithelial-cell abnormalities, cervical cancer.

Introduction

According to the GLOBCAN (IARC) 2020 statistics on cancer, cervical cancer is the fourth most common cancer among women in the world, with an estimated 6,04,000 new cases. Not only is the incidence high but the mortality reported is also high at 3,42,000 deaths in the year 2020. Approximately, 90% of the new cases of the cervical cancer were reported form the low and middle-income countries. [1] In India, cancer cervix is second most common cancer among females with 1,23,907 (18.7%) new case reported in 2020 and is associated with high mortality of 77,348 cases (62.4%). Despite the high incidence and mortality of cervical cancer, low socio-economic regions lack the screening programs for detection of cervical cancer, as according to WHO, fewer than 1 in 100 women were screened for cancer cervix in last 5 years. [2] Pap smear is not only efficient but also economical way of screening masses in low resource settings like India. Due to sensitivity of 72 % and high specificity of 92%, pap smear test is best suited for population-based screening programmes. [3] The main advantage of cervical cancer screening is due to fact that cervix is easily subjected to examination per speculum.

The aim of our study was to estimate the incidence of precancerous lesions and early cancers in our community in various age groups.

Materials And Methods

This is a retrospective study conducted by the department of Obstetrics and gynaecology in

collaboration with department of Pathology Apollo Institute of Medical Sciences and Research, Hyderabad, India from January 2021 to December 2022. Pap smears were prepared by spreading the cervical cell specimen collected using a wooden Ayers spatula from transformational zone of cervix and using cervical brush from endocervix on to glass slides. The glass slide were fixed in 95% ethyl alcohol solution and stained using Papanicolaou (PAP) staining. Results of pap smear were reported according The Bethesda System 2014. [4] Smears were checked for adequacy of specimen, inflammatory cells, infections, squamous metaplasia and abnormal epithelial cells. During the study period, 2450 pap smears were performed and analysed.

According to The Bethesda system 2014, epithelial cell abnormalities are classified into the following categories:

Squamous Cells

1. Atypical squamous cells (ASC)

- ASC of Undetermined Significance (ASCUS)

- Atypical Squamous cells, cannot rule out HSIL (ASC-H)

2. LSIL (Low grade squamous intraepithelial lesions)

3. HSIL (High grade squamous intraepithelial lesions)

4. SCC (Squamous cell carcinoma)

Glandular Cells

1. Atypical glandular cells of undetermined significance (AGUS)

2. Adenocarcinoma (ADC).

Abnormal Pap smear were correlated with cervical tissue biopsy where ever available.

Inclusion Criteria

Pap smears of all women above the age of 21 years to 65 years were included.

Exclusion Criteria

1. Known case of cervical cancers or cervical cancer growth on per speculum examination.

2. Pap smear from hysterectomised women.

Jamovi Version 2.3.22. Software was used for descriptive and statistical analysis using frequencies and percentages.

Results

Out of 2,450 pap smears performed, 150 (6.1%) pap smears were reported as abnormal with various degrees of epithelial cell abnormalities. The most frequent epithelial cell abnormality seen was Low grade Squamous Intraepithelial Lesions (LSIL) in 65 cases (2.65%). LSIL was followed by High grade Squamous intraepithelial lesions (HSIL) in 40 cases (1.63%) and Atypical Squamous Cell of Undetermined Significance (ASCUS) in 22 cases (0.89%). Squamous cell carcinoma was seen in 20 cases (0.81%), while Atypical Glandular cells were reported in only 3 cases (AGC). (Table 1)

Table 1: Incidence of various types of epithelial abnormalities

Epithelial Abnormality	Count (n)	Percentage Out of Total Smears	Percentage Out of Abnormal Smears
ASCUS	22	0.89%	14.7%
LSIL	65	2.65%	43.3%
HSIL	40	1.63%	26.7%
SCC	20	0.81%	13.3%
AGC-US	3	0.12%	2.0%
Total	150	6.1%	100%

Mean age of women with abnormal pap smears was 43.4 years with minimum age 21 years and maximum 65 years. According to age, epithelial abnormalities were more frequently noted between 41 to 50 years in 57 cases (2.33 %). Post-menopausal women accounted for approximately 1.1 % of abnormal pap smears. LSIL was also seen in the age group of 41-50 years (1.10%) but HSIL was seen more in age group of 31-40 years (0.7%). ASCUS was more common in age group of 41-50 years, while SCC was frequent in cases with age more than 50 years. (Table 2 and 3)

Table 2: Number of abnormal pap smears according to different age groups

Age Groups	Number	Percentage
21-30	18	0.73%
31-40	48	1.95%
41-50	57	2.33%
>50 y	27	1.10%

Table 3: Frequency of various epithelial abnormalities according to age groups

Epithelial Abnormality	Age Groups (years)	Count (n)	% of Total	% of Abnormal Pap Smears
ASCUS	21-30	2	0.08	1.3
	31-40	6	0.24	4.0
	41-50	8	0.33	5.3
	>50	6	0.24	4.0
LSIL	21-31	12	0.48	8
	31-40	18	0.73	12
	41-50	27	1.10	18
	>50	8	0.33	5.3
HSIL	21-30	4	0.16	2.7
	31-40	17	0.7	11.3
	41-50	14	0.57	9.3
	>50	5	0.20	3.3
SCC	21-30	0	0.00	0
	31-40	6	0.24	4
	41-50	6	0.24	4%
	>50	8	0.33	5.3%
AGC-US	21-30	0	0.00	0.0%
	31-40	1	0.04	0.7%
	41-50	2	0.08	1.3%
	>50	0	0.00	0.0%

Among the high grade lesions, HSIL and SCC on pap smear accounted for 60 cases (2.44%) and needed confirmation by biopsy with subsequent histopathology. However histopathology reports for cervical biopsy was available for 32 cases only for correlation. On histopathology of cervical biopsies, benign (chronic cervicitis) was reported in 10 cases (31.25%), cervical intra epithelial neoplasia (CIN 1) in eight cases (25%) , CIN 2 in one case (3.12%) , CIN 3 in five cases (15.62%) and invasive cancer in eight cases (25%).(Table 4)

Table 4: Result of Cervical biopsies from high grade lesions (HSIL and SCC) on pap smears

Category	Number	Percentage
Benign	10	31.25%
CIN 1	8	25%
CIN 2	1	3.12%
CIN 3	5	15.62%
SCC	8	25%
Total	32	100%

Genital tract infection was present in 16.6% of abnormal pap smears. Most common type of infection seen with epithelial abnormalities was Bacterial Vaginosis (9.3 %). Bacterial Vaginosis was mostly associated with LSIL (6.7%). Vaginal candidiasis was present in 8 cases (5.3%) and Trichomonas Vaginalis was present in 3 cases (2 %) of abnormal pap smears. (Table 5 and table 6)

Table 5: Frequency of various genital infections with epithelial cell abnormalities on Pap smears

	Infection	Count(n)	Percentage
Epithelial Abnormality (150)	No infection	125	83
	Bacterial vaginosis	14	9.3
	Candida	8	5.3
	Trichomonas vaginalis	3	2

Table 6: Frequency of infections in various types of epithelial cell abnormalities

Epithelial Abnormality	Infection	Count (n)	Percentage
ASCUS	No infection	17	11.3 %
	Bacterial vaginosis	2	1.3 %
	Candida	2	1.3 %
	Trichomonas Vaginalis	1	0.7 %
LSIL	No infection	51	34.0 %
	Bacterial vaginosis	10	6.7 %
	Candida	3	2.0 %
	Trichomonas Vaginalis	1	0.7 %
HSIL	No infection	37	24.7 %
	Bacterial vaginosis	1	0.7 %
	Candida	1	0.7 %
	Trichomonas Vaginalis	1	0.7 %
SCC	No infection	18	12.0 %
	Bacterial vaginosis	0	0.0 %
	Candida	2	1.3 %
	Trichomonas Vaginalis	0	0.0 %
AGC-US	No infection	2	1.3 %
	Bacterial vaginosis	1	0.7 %
	Candida	0	0.0 %
	Trichomonas vaginalis	0	0.0 %

Discussion

The Cytological cervical cancer screening, a great public health success in prevention of cervical cancer was introduced by George Papanicolaou in the late 1940s. [5] Population based cervical cancer screening programmes by Pap smear tests every 3–4 years have reduced the incidence as well as the mortality of cancer cervix by 80% in developed countries in last 5 decades. [6] A Global estimate of Incidence and mortality of cervical cancer in 2020 shows incidence is three times higher in countries with low Human Development Index (HDI) than countries with very high HDI, whereas mortality rates are six times higher in low HDI countries compared to very high HDI countries. This reduction of cervical cancer burden in high HDI countries signifies the favourable effect of mass screening and vaccination. [7] Despite increased morbidity and mortality due to cervical cancer HPV vaccination has not been put in place by more than 75% of low income countries whereas more than 85% of developed countries have already adopted HPV vaccination. [8] Lack of effective and regular screening, poor to moderate living conditions and increased prevalence of HPV (Human papilloma virus) contributes to increased burden of cervical cancer in India.

Our study aimed to provide an insight on the magnitude of abnormal pap smears in women attending Medical College Hospital in Telangana, South India. In our study, 6.1% pap smears were abnormal as reported on cytology. Various studies across India have reported cervical intraepithelial abnormalities varying from 8% to 16%. [9-12] As compared to our and other Indian studies, Sengul et al [13] and Nayir et al[6] from Turkey have reported very low

incidence of abnormal pap smears of 1.73% and 2.5 % respectively. In United States annually 3.1 million pap smears are done out of which 5% are reported as abnormal. [14] Sirovich BE et al, from USA reported that 20% of women have at least one abnormal smear. [14] This wide variation between different nations can be justified by various reasons like type of study population, geographical locations, religious and cultural beliefs, age groups and socioeconomic status.

In our study, LSIL (2.6%) was the most common epithelial abnormality noticed followed by HSIL (1.6 %). Verma et al and Padmini et al have also reported higher incidence of LSIL (5.5 % and 5%) followed by HSIL (2.5 % and 3%) in their studies.[9,10] Similarly, Nayani et al reported LSIL in 8.65% cases and HSIL in 3.8% cases.[12] However much low incidence of LSIL was reported by Nayir et al[6] and Sengul et al[13] reported as 0.5% and 0.39%. They also reported low incidence of HSIL in 0.1% and 0.16% cases only. While, studies from USA reported atypical squamous cells of undetermined significance as most common abnormality in 60% of abnormal smears and low-grade squamous intraepithelial lesions in 33% of abnormal pap smears. [15]

In our study the mean age group of women with abnormal smear was 43.4 years. The most common age group affected by cervical epithelial cell abnormality was between 41-50 years (2.33%).This is similar to a study conducted by Joshi et al in 2015. [16] We found that HSIL was more common among cases aged 31-40 years (0.7%), similar to the studies from Verma et al and Padma et al.[9,11] This may be because in our country women in this age group tend to visit hospital more often due to other coexisting

gynaecological conditions. Cervical cancer was seen more after the age of 50 years. Bobdey et al in review of literature on cervical cancer also reported that maximum number of cervical cancer cases occur between 50-59 years of age, amounting to 27.37%. [17] However, a study by Shanmugham D et al in 2014 reported that the common age to develop cervical cancer is between 40 and 50 years and its precursor lesions usually occurs 5–10 years earlier.[18] Our study also suggests that pap smear done between age 31-40 years detects more precancerous lesions like HSIL. We also recommend at least one pap smear test before the age of 45 years as recommended by Shanmugham D et al. [18]

Infection of genital tract were present in approximately 16% of abnormal pap smears in our study. The most common being Bacterial vaginosis which was found to be associated more with LSIL (6.7 %). This is in accordance to a meta-analysis by Gillet E et al in 2012 who reported a positive association between bacterial vaginosis and cervical pre-cancerous lesions with an overall estimated odds ratio of 1.51 (95% CI, 1.24-1.83). [19] This emphasizes the potential role of a disturbed vaginal microflora in gynaecologic cancers.

Our study is not without limitations. First one being the retrospective study based on a tertiary care centre. It may not represent the actual scenario in general population.

Conclusion

The findings of our research implicates that there is need for implementation of nation-wide cervical screening programmes in our country in order to reduce the burden of cervical cancer and detect the precancerous lesions early to reduce morbidity and mortality. The way to go ahead is to do Pap smear, which is an inexpensive and non-invasive method of detecting precancerous and cancerous lesions of cervix. Also emphasis should be laid on spreading the awareness among masses about early identification of epithelial cell abnormalities using pap smear. We need more robust National cervical cancer screening programmes for masses and universal HPV vaccination programme.

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