PAP-Smear Study and its Utility in Cervical Cancer Screening in A Tertiary Care Hospital: An Institutional Based Study

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Abstract

Background: Cancer of uterine cervix is a leading cause of mortality and morbidity among women world-wide Papanicolaou cytological (Pap) test is, in many respects, the ideal screening test. Cervical cancer has a defined premalignant phase of many years, which allows repeated tests to significantly reduce the impact of individual false negative test results. Cervical cytology is inexpensive and readily accepted among Indian women.This is a retrospective study aimed to evaluate all previously conducted cervical smears examined at a teaching tertiary hospital during a two and half year period to find out the prevalence of abnormal pap smears. *Materials & Methods:* Detailed clinical data and Pap smear cytology reports were obtained from June 2014 to December 2016 and data noted in a structured Performa. All the smears were reported as per the revised 2014 Bethesda system. Prevalence of epithelial abnormalities was calculated in percentages. *Results:* Out of 1671 cases, 1635(97.8%) were negative for intraepithelial lesion/malignancy, 36 cases (2.15%) were positive for intraepithelial lesion. *Conclusion:* Pap smear provides supportive evidence as a tool for screening for cervical cancer. There is a need to increase the awareness among women to know the utility of this test to prevent precancerous changes in cervix can be detected before they progress to frank malignancy.

Keywords: Cervical Cancer; Screening; Bethesda System; Pap Smear; Papanicolaou.

Introduction

Cervical cancer has emerged as a major global public health problem and is the most common cancer causing death of women in developing countries [1]. Cervical cancer screening has decreased its incidence and mortality resulting from cervical cancer. Methods for screening include evaluation with the Papanicolaou (Pap) test (cytology) and testing for high-risk types of human papillomavirus (HPV).The Pap smear unquestionably is a successful screening test for cervical cancer in medical history.

Cancer of cervix is readily preventable, by early detection and appropriate timely treatment of its precursor lesions by simple Pap screening test. Though Pap smear is a routine screening test, the overall

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sensitivity in detection of high grade squamous intraepithelial lesion (HSIL) is 70 - 80%. The role of HPV in development of cervical cancer is proved beyond doubt. If Pap screening is associated with HPVDNA testing than we can increase the sensitivity.

We conducted a retrospective study and evaluated all cervical smears to find out the prevalence of abnormal pap smears in a tertiary care hospital and correlate with histopathology wherever possible.

Materials & Methods

This retrospective descriptive study conducted in Department of Pathology of All India Institute of Medical Sciences, Patna to evaluate all the pap smears reported during June 2012 to December 2016. All cytological smears were taken by gynecologists for routine screening by conventional method. After fixation in 95% isopropyl alcohol, these slides were stained with Papanicolaou's method. Specimen

Punam Prasad Bhadani et. al. / PAP-Smear Study and its Utility in Cervical Cancer Screening in
A Tertiary Care Hospital: An Institutional Based Study

13

adequacy as well as reporting was assessed according to the revised 2014 Bethesda system. Data were collected from patient's case notes & cytopathological findings from slide archive. A total of 1671 cases were studied and results were analyzed by descriptive statistical analysis. Corresponding cervical biopsy in the available cases were also correlated.

Results

The data show that mean age of the patients was 30±8 years (ranging from 18-84 years). Most of them were in age group of 25-34years (34.7 %), followed by 35-44(25.7%) and 45-54years (15.2%) respectively. A total of 1446(86.5%) samples were satisfactory for evaluation whereas 225(13.4%) samples were unsatisfactory for evaluation out of 1671 cases. The main cause for unsatisfactory were inadequate squamous component or obscuring inflammation. 1357 cases (81.2%) showed presence of transformation zone (TZ) while rest 314 cases(18.7%) didn't show transformation zone (Table 1).

Infections made up 242 cases (14.4%) while remaining were noninfectious. Bacterial vaginosis was the most common infection.

Out of 1671 cases, 1635(97.8%) were negative for intraepithelial lesion/malignancy (NILM) and 36 cases (2.15%) were positive for intraepithelial lesion, which were further classified as atypical squamous cell of undetermined significance (ASCUS, n=8, 0.47 %), atypical squamous cells cannot exclude HSIL (ASC-H, n=3, 0.17%), low grade squamous intraepithelial lesion (LSIL, n= 6, 0.35%), high grade squamous intraepithelial lesion (HSIL, n=11, 0.65%), atypical glandular cells (AGC, n=0, 0%) and Squamous cell carcinoma(SCC, n=8 , 0.47%) (Table 2 & 3); (Figure 1,2& 3).

About 121 biopsies could be retrieved and correlated with corresponding Pap smear. Cytology of 92 pap smears were correlated with corresponding histopathological biopsies,whereas 29 smears showed discrepancy with histopathological findings. (Table 4, 5).

Table 1: Age wise incidence of satisfactory & unsatisfactory smears with presence &absence of transformation zone

Age (yrs)	No. of cases	Unsatisfactory smears	Satisfactory smears	Transformation zone present	Transformation zone absent
18-24	152	21	131	132	20
25-34	581	69	512	480	101
35-44	431	37	394	377	54
45-54	255	42	213	188	67
55-64	132	31	101	94	38
65-74	76	19	57	53	23
75-84	44	6	38	33	11
Total	1671	225	1446	1357	314

Table 2: Categorization of cervical Pap smears

Category	Number of Cases
Normal Cervical Smear	237
Unsatisfactorycervical Smear	225
Inflammatory Cervical Smear	1205
-Inflammaotry (NOS)	655
-Bacterial vaginosis	124
-Trichomonas vaginalis	10
-Candidiasis	86
-Herpes simplex virus	9
-Bacterial vaginosis + Trichomonas vaginalis	5
-Bacterial vaginosis+Trichomonasvaginalis +Candidiasis	8
-Squamous metaplastic cervical smear	216
-Atrophic vaginitis	92
ASCUS	08
ASC-H	03
AGUS	00
LSIL	06
HSIL	11
Squamous cell carcinoma	8

Table 3: Categorization of Intraepithelial lesions in different age groups

Age	ASCUS	ASC-H	LSIL	HSIL	SCC	Atypical glandular cells	Total smears
18-24	01	00	00	00	00	00	01
25-34	02	01	01	03	00	00	07
35-44	02	01	02	03	01	00	09
45-54	01	01	02	02	02	00	08
55-64	01	00	01	01	02	00	05
65-74	01	00	00	01	02	00	04
75-84	00	00	00	01	01	00	02
Total (%)	08(22.2%)	03(8.3%)	06(16.6%)	11(30.5%)	08(22.2%)	00(0%)	36

Table 4: Pap smears correlating with corresponding histopathology

| Cytology (n=92)	Histopathology
Inflammatory (n=71)	Chronic cervicitis
LSIL (n=4)	CIN I
HSIL (n=9)	CIN II/III
Squamous cell carcinoma (n=8)	Squamous cell carcinoma

Table 5: Cyto- histopathological discrepancies

Cytology (n=29)	Histopathology
Inflammatory (n=15)	CIN I/II
ASCUS (n=8)	Chronic cervicitis
ASC-H(n=2)	CINII/III
LSIL (n=2)	Chronic cervicitis
HSIL(N=2)	Squamous cell carcinoma

Table 6: Various parameters of Pap smear in present study compared with other studies

Diagnoses	Present study	Kalyani et al.	Crasta et al.	Narasimha et al.	Sankaranarayana et al.
Unsatisfactory	13.46%	17.80%	1.36%	24.42%	4.10%
ASCUS	0.23%	1.46%	0.37%	4.14%	8.80%
LSIL	0.35%	0.24%	0.19%	2.70%	6.20%
HSIL	0.65%	0.41%	0.61%	2.50%	1.60%

**Table 7:** Positive pap smears in current study as compared to other studies

| Author	Sample size	Positive pap smears
Present study	n=1671	1.91%
Sankaranarayana et al.	n=4444	3.40%
Kalyani et al.	n=1501	3.08%
Tamrakar et al.	n=1506	1.70%
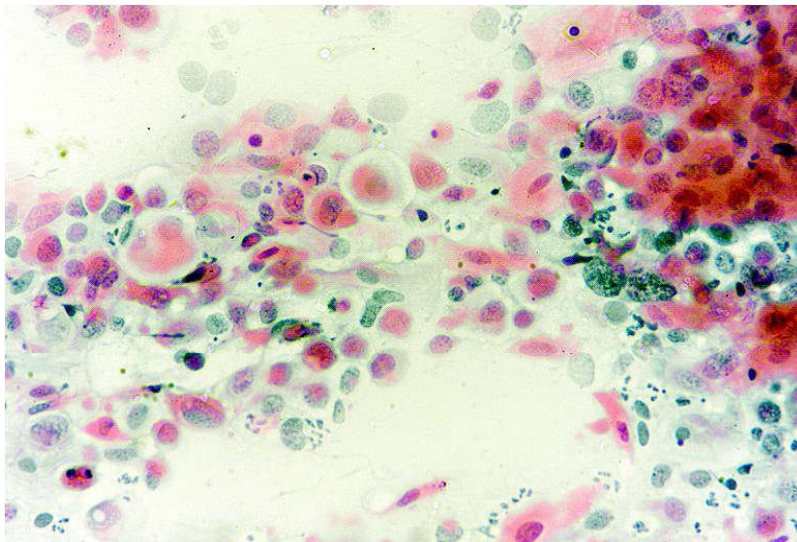
Fig. 1: Microphotograph showing cytological features of ASC-H (atypical squamous cell-cannot exclude HSIL).Atypical cells having dense cytoplasm, high nuclear to cytoplasmic ratio and irregular nuclear contours.(Papanicolaou stain; 400X)

Punam Prasad Bhadani et. al. / PAP-Smear Study and its Utility in Cervical Cancer Screening in
A Tertiary Care Hospital: An Institutional Based Study

15

Table 8: Comparison of Sensitivity, Specificity,Positive predictive value, Negative predictive value,False positive rate and False negative rate in various studies with present study

Various studies	Sensitivity	Specificity	PPV	NPV	FNR	FPR
Present study	58.33%	88.54%	63.64%	82.6%	36.4%	17.44%
Ghosh P et al.	52.6%	99.1%	76.1%	97.3%	47.3%	0.9%
Saleh HS et al.	50.1%	93.1%	89.3%	65.6%	49.9%	6.9%
Gupta V et al.	66.66%	93.54%	75%	90.60%	33.33%	6.45%
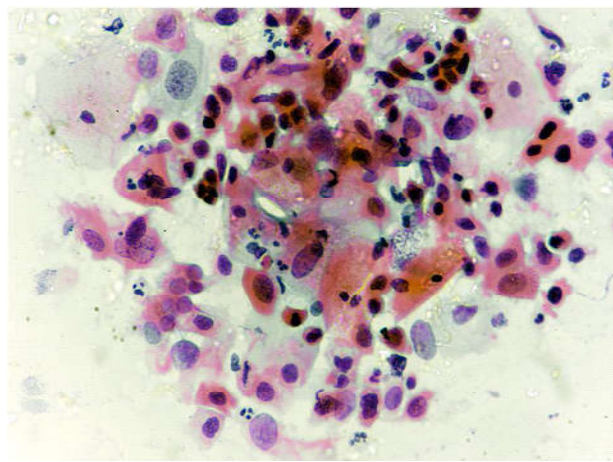
Fig. 2: Microphotograph showing cytopathological features of HSIL(High grade squamous intraepithelial lesion) .Dysplastic cells with a high nuclear to cytoplasmic ratio,hyperchromatic nuclei with irregular nuclear membrane. (Papanicolaou stain; 400X)
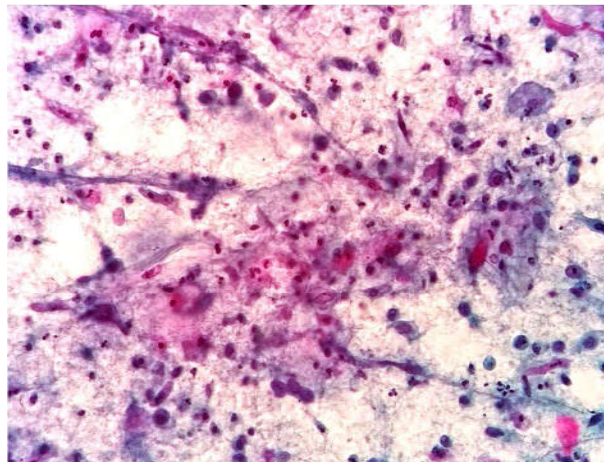
Fig. 3: Photomicrograph of Squamous cell carcinoma, keratinizing type with tadpole cells and tumor diathesis. (Papanicolaou stain; 400X)0.47, Inset "a" shows numerous tadpole cells and inset " b" shows malignant squamous cells with evidence of keratinisation and at places keratin pearl formation(Papanicoloau stain; 100X)

Discussion

Cervical cancer is the fourth most common cancer affecting women worldwide after breast, colorectal, and lung cancers. It is most commoncancer in the low resource developing countries constituting 70% of the global burden. Approximately one fifth of all new cases are reported in India. In sub- Saharan Africa, 34.8 new cases of cervical cancer are diagnosed per 100,000 women annually and 22.5 per 100,000 women die from the disease. These figures were compared with 2.5-6.6 per 100,000 women in North America. The drastic differences can be explained by lack of access to effective screening and to services that facilitate early detection and treatment [2-3].

Cervical cancer has been the most important cancer in women in India over the past two decades. The current estimates indicate approximately 132,000 new cases diagnosed and 74,000 deaths annually in India, accounting to nearly 1/3rd of the global cervical cancer deaths [4].

Conventional cervical cytology is the most widely used cervical cancer screening test in the world and cytology screening programmer in several developed countries have been associated with impressive reductions in cervical cancer burden. However the screening coverage in India is 2.6-5% and it is mainly an opportunistic screening. Even though the cancer registries show decline in cervical cancer incidence, it is mainly urban statistics. In rural areas cervical cancer still ranks number one in India [5].

The WHO recommends that in developing countries, women aged between 18-69 years should be screened for cervical cancer every 3 years. In our study, the youngest age screened was 18 years and oldest age was 84 years. Unlike many other cancers, cervical cancer occurs early and strikes at the productive period of a woman's life. The incidence rises in 30–34 years of age and peaks at 55–65 years, with a median age of 38 years (age 21–67 years) [5,6]. In our study, cervical cancer was noted between 45- 65 years.

The rate of unsatisfactory smear in the present study was 13.4%. In other studies it is 1.36%, 4.1% and 24.42%. [3,7,8] (Table 6).

The unsatisfactory rate is an important quality assurance indicator in cervical cytology as it identifies women who are being inadequately screened. High rate of unsatisfactory smears could be due to sampling errors. Hence regular training and feed back is essential to reduce the number of unsatisfactory smears.

The positive/abnormal Pap smear cytology (1.91%) in our study was lower than various studies done by Kalyani et al., (3%) and Sankaranarayanan et al., (3.4%) respectively [8-10]. But it was higher than studies done by Tamrakar et al., as our study was done on high risk semi-urban population of lower socio-economic status [11](Table 7). The relationship between the transformation zone and intraepithelial lesion is always controversial. The Bethesda System for Reporting Cervical Cytology states; "Specimens that lack EC/TZ elements are not more likely to have a squamous lesion on follow up" [11-15]. In our study 81.2% cases showed presence of transformation zone which suggests that presence transformation zone component increases the detection of intraepithelial lesions.

Considering cytohistopathology correlation, in our study of 11 HSIL cases, nine were diagnosed as CIN II/CIN III and rest 2 cases were diagnosed as Squamous cell carcinoma. The prevalence rate of biopsy – proven SIL in a patient with a previous diagnosis of ASCUS on pap smear ranges from 10-61.3%. Kurman et al stated that "follow up is not further qualified if, a reactive process is favoured." This explains our discrepancies of ASCUS as chronic cervicitis on histopathology, that it could be a reactive process or regenerative process [16].

Our study had a sensitivity of 58.33%, specificity 85.54%, positive predictive value 63.64%, negative predictive value 82.6 %, false positive rate 17.44% and false negative rate 36.4 %. The comparison in various studies is shown in Table 8.

Conclusion

Though cervical cancer is a leading cause of death in India, our Institutional based study shows a relatively low prevalence which is similar to that of developed countries. Based on the findings of this study we recommend at least a single life-time pap screening cytology of the uterine cervix of all the women aged 35 to 50 years. This study emphasized the importance of Pap smears screening for early detection of premalignant and malignant lesions of cervix.

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