VOLUME - 12, ISSUE - 12, DECEMBER - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

PAP SMEAR CYTOLOGY OF CERVICAL LESIONS WITH HISTOPATHOLOGICAL CORRELATION.

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ABSTRACT **Introduction:** Cervical cancer is among the leading cause of death in Indian women owing to lack of awareness and lack of a proper screening program. Objectives: To assess incidence of various cervical lesions by Pap smear in the study area and to evaluate the accuracy of Pap smear with respect to histopathology wherever possible by estimating sensitivity, specificity, predictive values so as to find the usefulness of Pap smear in screening for cervical cancer. **Methodology:** This was a prospective and retrospective study comprising 110 specimen subjected to Pap smears followed by Histopathological examination. **Results:** The most common lesion on Pap smear was atypical cells followed by positive for malignancy, SCC and HSIL. The accuracy of cytological test considering histopathological diagnosis as gold standard yielded 80% sensitivity and 92% specificity with 97.14% PPV and 57.50% NPV. **Conclusion:** Pap smears should be routinely advised to enable early detection of premalignant and malignant cervical lesions.

KEYWORDS : cervical cancer, pap smear

INTRODUCTION

Cervical cancer is the second most frequent disease in women worldwide, and it continues to be the primary cause of cancer-related mortality for women in poorer nations. Cervical cancer is the leading cause of mortality for middle-aged Indian women and accounts for around 20% of all cancer-related fatalities in women in India. (1) It is estimated that in underdeveloped nations, where women frequently lack access to cervical cancer screening and treatment, over 85% of cases and 88% of deaths from the disease occur. (2)

Cervical cancer diagnosis carries a lifetime risk of 0.78%, while the lifetime risk of cervical cancer death is 0.26%. (3) According to a World Bank study, women who have cervical cancer typically pass away 18 years before they would have otherwise. (4) Owing to concerted and organised control measures, the incidence of cervical cancer is slowly reducing, although it still needs coordinated and planned prevention efforts. With the development of a prophylactic vaccination, control through primary prevention has become a reality, although broad use of the vaccine may take some time. Therefore, at this point, the only practical way to control cervical cancer is through secondary preventative measures.

Long term precancerous lesions turning into invasive cervical cancer can be identified through screening and properly treated with non-invasive methods, thereby averting aggressive cervical cancer. (2) Visual screening techniques, such as visual examination with acetic acid or visual inspection with Lugol's iodine (VIA/VILI), are used as screening modalities. VIA has emerged as a viable substitute for underdeveloped nations due to its low cost, speed, little training requirements, and lack of specialized equipment. The process is based on acetowhitening, in which 5% acetic acid (vinegar) causes the CIN to turn white. These qualities render it a realistic alternative for low-resource settings. Its low specificity limits its ability to identify cervical cancer and CIN, despite its great sensitivity being demonstrated in these cases. (5-7)

In contrast, VILI entails examination of the cervix with naked eye to spot mustard-yellow patches that appear after applying Lugol's iodine. Human Papilloma virus deoxyribose nucleic acid HPV-DNA) has been studied recently. But unless a low-cost, same-day HPV test and practical procedures are created (8), this option is unfeasible for poor areas (9)

The incidence of morbidity and mortality from cervical cancer has been shown to have significantly decreased in developed countries with well-organized cytology screening programs. (10-12). There are no organized screening programs for cervical cancer prevention in any part of India, despite the high disease burden and rising absolute number of cases brought on by population growth. (13). Therefore, it is evident that a practical, precise, and efficient screening technique is required to control cervical cancer.

In view of the above the present study was planned to assess incidence of various cervical lesions by Pap smear in the study area, to evaluate the accuracy of Pap smear with respect to histopathology wherever possible by estimating sensitivity, specificity, predictive values and so as to find the usefulness of Pap smear in screening for cervical cancer.

METHODOLOGY

The present study was five year retrospective and prospective study conducted in the Department of Pathology, Goa Medical College, Goa during the period of January 2012 to Dec 2016. The study was approved by the Ethical and Research Committee, Goa Medical College, GOA. Samples were collected from Department of Obstetrics and Gynaecology Goa Medical College, Goa.

8000 specimens were received for Pap smear from January 2012 to December 2016. Retrospectively i.e. from January 2012 - December 2015, a total of 6000 Pap smears were conducted out of which 70 underwent histopathological examination. Prospectively, i.e., from January 2016- December 2016, from the 2000 Pap smears conducted, 40 underwent histopathological examination. Hence a total of 110 cases were studied that is, 70 retrospectively and 40 prospectively.

Selection Criteria

Inclusion Criteria

Samples sent from department of Obstetrics and Gynaecology Goa Medical College, Goa for Pap smear and undergoing histopathological examination.

Procedure

Permission was obtained from Medical Records Department (MRD) Goa Medical College, Goa to retrieve the data about Pap smear and histopathological diagnosis to collect retrospective data. Prospectively, the details like age about specimen received was noted and the specimen was subjected to Pap smear and histopathological examination wherever indicated.

It was recommended to use the Pap test to check for premalignant and malignant cervix lesions. The natural history of HPV infection and subsequent cervical dysplasia has led to a significant revision in the recommended age of initiation of cervical cancer screening over time. Regardless of

past sexual history, cervical cancer screening starts at age 21.This recommendation was confirmed in 2012 and again in Jan 2016. Proper clinical history was taken and appropriate lab investigations (wherever required) were done on all patients.

Pap test was conducted on obtaining informed consent of the patient. During this procedure patient was made to lie on her back on the examination table in lithotomy position. Under aseptic precautions speculum was slowly inserted into the vagina; to allow for retraction of the anterior and posterior vaginal wall and provide access to the cervix. By using spatula and brush the scrapings of cells from transformation zone of the cervix were taken and smears were made on glass slides. These smears were immediately fixed using a solution containing equal amounts of ether and absolute ethanol as a fixative. The fixed smears were stained with routine haematoxylin and eosin stain and subjected for microscopic examination.

Abnormal Pap test eventually turned up as surgical biopsies, hysterectomy specimens, for which histopathological correlation was possible. The tissue specimen were grossed and multiple representative samples were taken as small 1x1cm blocks and subjected to processing by paraffin embedding. Sections were prepared and stained by haematoxylin and eosin method. The Pap test findings were compared with histopathological report wherever possible. All slides were reported in the presence of two postgraduate students and under the guidance of consultant in Department of Pathology, Goa Medical College

RESULTS

The data obtained was analysed and the final results and observations were tabulated as below.

Table 1: Distribution Of Women According To The Cyto-pathological Diagnosis

Occupation	Distribution (n=20)	
	Number	Percentage
Moderate dysplasia	23	20.91
Mild dysplasia	20	18.18
Dysplasia	16	14.55
Atypical cells	10	9.09
Positive for malignancy	10	9.09
SCC	8	7.27
Mild	3	2.73
Atypical endocervical cells	2	1.82
Dysplasia in endocervical cells	2	1.82
Dysplasia in few cells	1	0.91
Large atypical cells	1	0.91
Endocervical dysplasia	1	0.91
Few atypical	1	0.91
Few show atypical cells	1	0.91
HGSIL	1	0.91
HSIL	4	3.64
Large atypical cells	1	0.91
LSIL	1	0.91
Marked dysplasia	1	0.91
Atypical cells in endocervicals cell	1	0.91
Mild atypical changes in cells	1	0.91
Positive for SCC	1	0.91
Total	110	100.00

Table 2. Distribution Of Women According To The Type Of Lesion Based On Cytological Diagnosis

Type of lesion	Distribution (n=110)	
	Number	Percentage
Benign	70	63.64
Malignant	40	36.36
Total	110	100.00

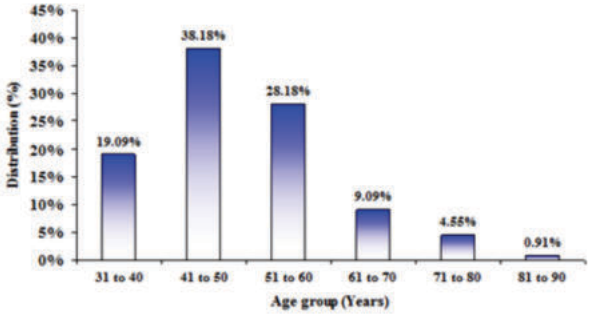
Table 3: Correlation Of Cytological Type Of Lesion And Histopathological Type Of Lesion P = <0.001

Cytological diagnosis	Histopathological diagnosis				Total	
	Benign		Malignant			
	No	%	No	%	No	%
Benign	68	97.14	2	2.86	70	100.00
Malignant	17	42.50	23	57.50	40	100.00
Total	85	77.27	25	22.73	110	100.00

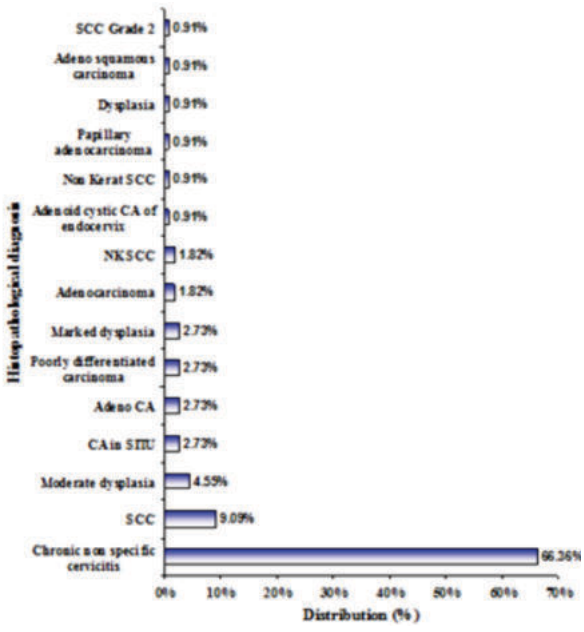
Table 4: Correlation Of Cytological Type Of Lesion And Histopathological Type Of Lesion

Cytological diagnosis	Histopathological diagnosis															Total
	Adeno Carcinoma	Adeno squamous Carcinoma	Adeno-carcinoma	Adenoid cystic Carcinoma of endocervix	Carcinoma in SITU	Chronic non specific cervicitis	Dysplasia	Marked dysplasia	Moderate dysplasia	NKSCC	Non Kerat SCC	Papillary adeno Carcinoma	Poorly differentiated Carcinoma	SCC	SCC Grade 2	
Large atypical cells	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Atypical cells	0	0	1	0	3	2	0	0	1	0	0	0	1	2	0	10
Atypical cells in endocervicals cell	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Atypical endocervical cells	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	2
Dysplasia	0	0	0	0	0	16	0	0	0	0	0	0	0	0	0	16
Dysplasia in endocervical cells	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
Dysplasia in few cells	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Endocervical dysplasia	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Few atypical	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Few show atypical cells	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1

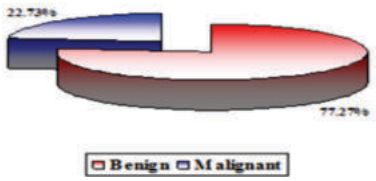
HGSIL	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
HSIL	0	0	0	0	0	1	0	0	1	0	0	0	0	2	0	4
Large atypical cells	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
LSIL	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Marked dysplasia	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Mild atypical changes in cells	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Mild dysplasia	0	0	0	0	0	23	0	0	0	0	0	0	0	0	0	23
Moderate dysplasia	0	0	0	0	0	21	0	0	2	0	0	0	0	0	0	23
Positive for SCC	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Positive for malignancy	0	0	0	0	0	4	1	0	0	1	1	0	0	3	0	10
SCC	0	1	0	0	0	0	0	2	1	1	0	0	0	2	1	8
Total	3	1	2	1	3	73	1	3	5	2	1	1	3	10	1	110



Graph 1 : Distribution Of Women According To Age



Graph 2: Distribution Of Women According To Histological Diagnosis



Graph 3: Distribution Of Women Based On Type Of Lesion On Histopathological Diagnosis

DISCUSSION

The incidence of advanced cervical cancer has decreased significantly in developed nations due to a combination of cultural barriers, lack of awareness, and economic factors. (14) That cannot be said, though, of developing nations. Only one-fourth of the cases of cervical cancer worldwide are found in India. In India, women have difficulties expressing their needs related to reproductive health as well as accessing healthcare services. Their inability to obtain timely care is a result of cultural barriers, lack of awareness, and financial constraints.(15)

The abnormal cellular or epithelial architecture in the vicinity of the uterine cervix's transformation zone, which is the junction of the squamous and columnar epithelium, is a characteristic of premalignant lesions.(16) The Papanicolaou (Pap) smear cytology test is still a crucial cervical cancer screening method. (17) Cervical cancer can be prevented because there are effective screening, diagnostic, and treatment options available. One of the gynecologist's main responsibilities is to identify genital tract neoplasms as soon as possible. By detecting cervical cancer in its preinvasive stages, cytological evaluation helps to lower the disease's morbidity and mortality. (18) The purpose of this study was to estimate the sensitivity, specificity, predictive values, and other parameters to assess the PAP smear's accuracy in relation to histopathology so as to find the usefulness of PAP smear in screening for cervical cancer.

In the present study age ranged between 35 to 82 years. Most of the women (38.18%) belonged to the age group of 41 to 50 years. The mean age was 51.14±10.75 years. (Figure 1) This indicates that most of the women in this study were middle aged. These findings were consistent with those of a prospective study conducted by Atla BL et al. (15) who reported that, the age range in their study as 20 to 70 years. Another study by Kohli B et al.(19) from Uttar Pradesh to compare pap smear and colposcopy in detection of premalignant lesions of cervix reported the mean age as 39.91±9.64 years with 30 to 39 years (33%) being the most common age group followed by 40 to 49 years (30%) which was comparable to the present study. However, the mean age noted in the present study was high compared to the study by Kohli B. et al. (19)

In the present study, 20.91% of the specimens were diagnosed to have moderate dysplasia while mild dysplasia was noted in 18.18% of the cases. Based on pap smear 63.64% of the specimen were labeled as benign lesions and the remaining were malignant lesions. (Table 1 and 2) A study by Kohli B. et al. (19) reported 49% of the specimens positive for malignancy and 51% benign lesions.

In the current study, when comparing the histopathological

examination, it was noted that majority of the specimens (66.36%) were diagnosed to have chronic non-specific cervicitis while SCC was noted in 9.09%, moderate dysplasia in 4.55%, carcinoma in SITU, adenocarcinoma, poorly differentiated carcinoma and marked dysplasia in 2.73% of the specimens each. Furthermore, based on histopathological diagnosis 77.27% of the specimens were benign lesions while malignant lesions were noted in 22.73% of the specimens. (Graph 2 and 3) In a study by Kohli B et al. (19) the rate malignancy was 30% which slightly higher but comparable to the present study.

Forty specimens in the current study were categorized as malignant lesions on pap smear out of which 23 (57.50%) were malignant lesions on histopathological examination and the accuracy of pap smear considering histopathological diagnosis as gold standard was 80% sensitive and 92% specific with 97.14% PPV and 57.50% NPV ($p<0.001$). Only 12 of the 94 studies with less biased estimates were analyzed in the systematic review, which revealed that it had a sensitivity of only 51% and a specificity of 98%, despite significant variation in methodological quality and the frequency of histological abnormalities.(20) The comparison of sensitivity and specificity observed in the present study with other studies is as depicted in Table below.

The sensitivity observed in the present study was marginally low compared to a study by Al Alwan et al. (21) who reported sensitivity of 88.9% and Adamopoulou M et al. (22) who reported sensitivity of 91.7% but higher compared to the study by Zarchi MK et al. (23) who reported sensitivity of 15%. In 2000, Nanda K. et al. (20) assessed the efficacy of novel and traditional Papanicolaou (Pap) testing techniques for the early detection of cervical cancer and its progenitors. The analysis included 94 studies that contrasted Pap testing (rescreening or computer screening, monolayer cytology, or conventional methods) with a concurrent reference standard (histologic examination, colposcopy, or cytology). Estimates of sensitivity and specificity for traditional Pap tests varied widely between individual studies. The frequency of histologic abnormalities and the quality of the methods used also differed significantly between studies. In a study by Agarwal A. et al. (12) the sensitivity of Pap smear was 84.20% and the specificity was 62.10% which was comparable to the present study.

In this study cytologically the most common diagnosis was mild and moderate dysplasia noted in 23 specimens each. Out of 23 specimen with moderate dysplasia, 21 were chronic nonspecific cervicitis on histopathology and remaining 2 were moderate dysplasia while in 23 specimen with mild dysplasia all were diagnosed as chronic nonspecific cervicitis on histopathology suggesting good correlation between pap smear and histopathological diagnosis. (Table 5)

Ultimately, the phrase "preventable but not prevented" still applies to cervical cancer because there are currently no ideal screening tests with 100% sensitivity and good specificity. Nonetheless, this study showed a strong correlation and high accuracy between histology and pap smear. Therefore, Pap smears should be performed on women who have been clinically diagnosed with an unhealthy cervix in order to detect any premalignant or malignant lesions. Additionally, Pap smear results and histopathology should be analyzed together.

The study's retrospective design, one-center investigation, and smaller sample size were its limitations. Additional large-scale prospective multicentric studies could yield precise pap smear test accuracy.

CONCLUSION

Based on the findings of this study it may be concluded that, moderate dysplasia was the most common diagnosis on Pap smear as well as on histopathological examination. The most common lesion on pap smear was atypical cells followed by positive for malignancy, SCC and HSIL. The accuracy of cytological test considering histopathological diagnosis as gold standard yielded 80% sensitivity and 92% specificity with 97.14% PPV and 57.50% NPV.

Pap smears are a good potential substitute or supplementary screening test that can be used in both resource-poor and well-equipped centers. Because pap smears are easy to perform, affordable, and suitable for an outpatient setting, they continue to be the most reliable screening and diagnostic test available in the current setup. Hence, Pap smears should be routinely advised to enable early detection of premalignant and malignant cervical lesions.

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