A two year retrospective study of cytohistopathological correlation of cervical smear in a tertiary care hospital

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ABSTRACT

Background: Cervical cancer in women is the second most common cancer and the commonest cause of mortality in developing countries. The introduction of Pap smear test changed the scenario of cervical cancer with an intense drop in the incidence and mortality due to invasive cervical cancer. **Aims and Objective:** To evaluate the patterns of cervical smear cytology and to correlate the cervical smear diagnosis with histopathological diagnosis and to assess the efficacy of Pap smears in diagnosing cervical lesions. **Materials and Methods:** This two-year retrospective study (January 2018 to December 2019) was done in the department of Pathology in a tertiary care hospital. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated considering histopathological diagnosis of cervical biopsy as the gold standard. **Results:** A total of 316 Pap smears were studied, out of which we selected 154 cases who also undergone biopsy or hysterectomy. Epithelial cell abnormalities (ECA) were found in 28 cases (18.2%). Among this the most common ECA was Atypical squamous cells of undetermined significance (ASCUS) seen in 10 cases (6.5%) followed by Low grade squamous intraepithelial lesion (LSIL) (5.2%), High grade squamous intraepithelial lesion (HSIL) (3.2%) and SCC of cervix (3.2%). The overall correlation between cervical cytology and histopathology was found in 125 out of 154 cases (81.16%). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of pap smear was 90.57%, 62.50%, 95.41%, 43.47% and 87.66% respectively. **Conclusion:** Pap smear is a simple, safe, non-invasive and effective method for detection of lesions of the cervix and ECA. Hence, better awareness and periodical cytological screening programs can help in the early detection of malignant cervical lesions and thereby reducing the morbidity and mortality related to this malignancy.

Key words: Atypical squamous cells of undetermined significance (ASCUS); Carcinoma cervix; High grade squamous intraepithelial lesion (HSIL); Low grade squamous intraepithelial lesion (LSIL); Pap smears

INTRODUCTION

Cervical cancer in women aged between 15-44 years is the second most common cancer and the commonest cause of mortality among women in developing countries.[1]

India, a developing country shows the trend of cervical cancer in higher magnitude. As per the World Cancer statistics, developing countries and those with limited resources attributes to more than 80% of all cervical cancer which in turn are attributable to lack of awareness and striving in running cytology based screening programs.[2] An estimate of 122,844 women are diagnosed with cervical cancer every year in India and 67,477 women die from the disease.[3]

Preventable nature of cervical cancer is due to its long pre invasive stage. However, robust approach like screening method in the form of Pap smear test if implemented can detect invasive cervical cancer in early stage, precancerous cervical intraepithelial neoplasia and hence suitable treatment can be instituted promptly.[4]

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The introduction of Pap smear test changed the scenario of cervical cancer in worldwide with an intense drop in the newer cases and mortality due to cervical cancer which are invasive in nature.[5] Though cervical biopsy an invasive technique remains a gold standard for detection of cervical lesions, Pap smear is a simple, safer, effective and non-invasive method.[6,7]

Aim of the study was to evaluate the patterns of cervical smear cytology and to correlate the cervical smear diagnosis with histopathological diagnosis and to know the accuracy of Pap smears, so as to assess the efficacy of Pap smears in diagnosing cervical lesions.

MATERIALS AND METHODS

This was a two year retrospective study conducted in the Department of Pathology, ESIC Medical College & Hospital, Kalaburagi, from January 2018 to December 2019. After taking Institutional Ethics Committee permission (Approval No: ESICMC/GLB/IEC/16/2021), medical records data pertaining to demographic details, detailed clinical history including parity and complaints like discharge through vagina, post coital bleeding, post-menopausal bleeding, pain in lower abdomen, inter-menstrual bleeding etc. were taken from hospital records who underwent Pap smear and cervical biopsy. Pregnant women, Unmarried women and women without sexual exposure were excluded from the study.

The Pap smears were taken with the Ayer's spatula on a clean glass slide and fixed instantly in ninety five percent ethanol and ether equal parts. Staining of the slides was performed by conventional Pap staining. Pap smears were reported as per the Bethesda System 2001 classification. Ten percent neutral buffered formalin solution was used to fix cervical biopsies or hysterectomy specimens and processed with final embedding in blocks prepared with paraffin and stained with haematoxylin and eosin (H & E).

The histopathological findings were correlated with Pap smear findings and specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were also calculated considering histopathological diagnosis of cervical biopsy as the gold standard. Data was collected in Microsoft Excel sheet and inferred by applying descriptive analysis using IBM SPSS Statistics for Windows, Version 22.0.

RESULTS

A total of 316 Pap smears were studied, out of which we selected 154 cases who were also undergone biopsy or hysterectomy during the period from January 2018 to December 2019 retrospectively. Majority of the patients (35%) were in age group of 41-50 years and belong to para 2 (42%) followed by para 3 (25.6%). Most common complaint presented by patients was of whitish discharge per vaginum (42%) and pain lower abdomen (35.7%) followed by the other complaints like intermenstrual bleeding, menorrhagia, postcoital bleeding and postmenopausal bleeding in 15.2%, 3.5%, 3.2% and 0.4% cases respectively.

In the pap smear findings of 154 cases, the majority of cases 116 (75.3%) were categorised as Negative for Intraepithelial lesion or malignancy (NILM). Epithelial cell abnormalities (ECA) were found in 28 cases (18.2%). Among the ECA; Atypical squamous cells of undetermined significance (ASCUS) was most common and was seen in 10 cases (6.5%) followed by low grade squamous intraepithelial lesion (LSIL) in 8 cases (5.2%) (Figure 1), high grade squamous intraepithelial lesion (HSIL) in 5 cases (3.2%) (Figure 2) and 5 cases (3.2%) of squamous cell carcinoma were reported (Table 1).
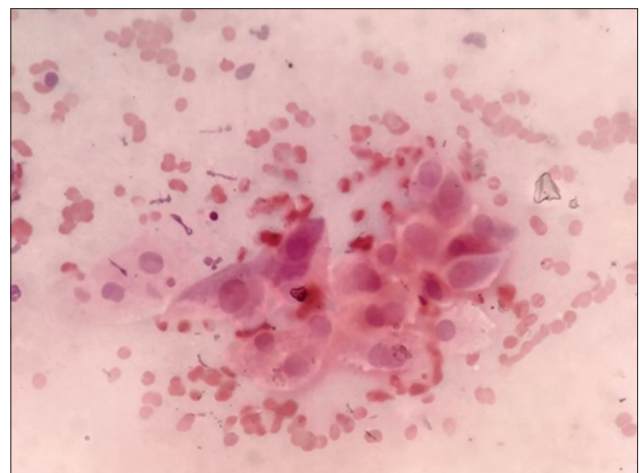
Figure 1: LSIL showing enlarged hyperchromatic nuclei with regular nuclear borders (Pap 40X)
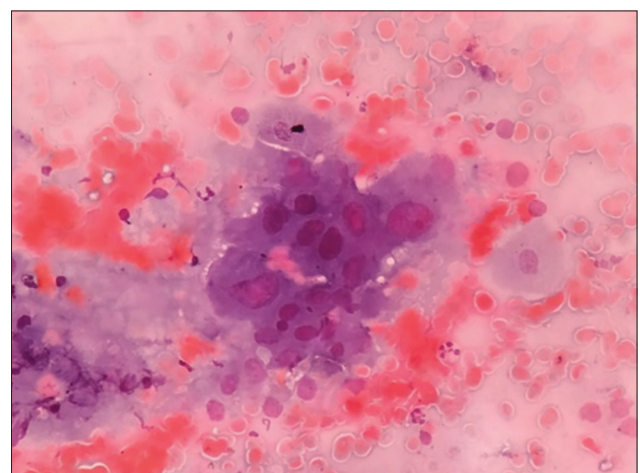
Figure 2: HSIL showing enlarged nuclei with irregular coarsely clumped chromatin and irregular nuclear borders (Pap 40X)

Table 1: Cyto-histopathological correlation of Pap smears and cervical biopsies/ hysterectomies

HP Pap	Cervicitis	CIN I	CIN II	CIN III	Carcinoma in situ	SCC	Total
NILM	115	01	-	-	-	-	116 (75.4%)
ASCUS	07	01	01	01	-	-	10 (6.5%)
LSIL	03	-	01	01	-	03	08 (5.2%)
HSIL	01	01	-	-	01	02	05 (3.2%)
SCC	-	02	-	-	-	03	05 (3.2%)
Inadequate	08	-	-	-	-	02	10 (6.5%)
Total	134 (87.0%)	05 (3.2%)	02 (1.3%)	02 (1.3%)	01 (0.7%)	10 (6.5%)	154

(HP- Histopathology, CIN- Cervical Intraepithelial Neoplasia, SCC- Squamous cell carcinoma, NILM- Negative for intraepithelial lesion/malignancy, ASCUS- Atypical squamous cells of undetermined significance, LSIL- Low grade squamous intraepithelial lesion, HSIL- High grade squamous intraepithelial lesion)

Table 2: Sensitivity and Specificity of Pap smear

Sensitivity	90.57%
Specificity	62.50%
Positive predictive value	95.41%
Negative predictive value	43.47%
Accuracy	87.66%

With regard to histopathological diagnosis of cervical biopsies or hysterectomies, out of 154 cases 45.4% cases were diagnosed as chronic cervicitis, followed by chronic cervicitis with squamous metaplasia (41.5%), Cervical intraepithelial neoplasia (CIN I) (3.2%) (Figure 3a), CIN II (1.3%) (Figure 3b) and CIN III (1.3%). Squamous cell carcinoma was diagnosed in 10 cases (6.5%) (Table 1).

In our study the sensitivity, specificity, PPV, NPV and accuracy of pap smear was 90.57%, 62.50%, 95.41%, 43.47% and 87.66% respectively (Table 2). The overall correlation between cervical cytology and histopathology was found in 125 out of 154 cases (81.16%), thereby the pap smears have an important role in screening different types of cervical lesions.

DISCUSSION

Gynaecological malignancy in the form of cervical cancer is an ideal malignancy for screening. Since it has extended premalignant latent phase, Pap smear test as a screening method will be an effective way to detect early and prevent the progress of cervical cancer. However, awareness of Pap smear test within the community settings is very low.[8]

The present study included 154 pap smear cases who also undergone biopsy or hysterectomy with most patients (35%) in the age group of 41-50 yrs and belong to para 2 (42%) followed by para 3 (25.6%). It has accordance with Sachan et al.,[8] and Parija et al.[9]

The maximum number of patients presented with complaints of whitish discharge per vaginum (42%) and pain lower abdomen (35%) correlates with the study conducted by Bamanikar et al.,[10] Atla et al.,[11] and Bindroo et al.[12]
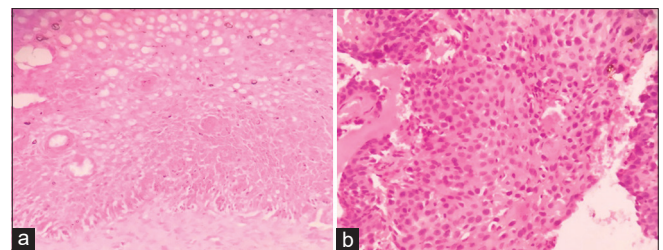
Figure 3: (a) CIN I: Increased nuclear density and variable nuclear hyperchromasia in upper epithelial layer (H&E 40X). (b) CIN II: Cytological atypia in lower two thirds of epithelium with high N/C ratio and irregular nuclear membrane contour (H&E 40X)

In our study out of 116 cases of NILM, 99% of cases correlated on histopathology which corroborated with the studies done by Atla et al.,[11] and Bindroo et al.[12] The incidence of Epithelial cell abnormality (ECA) was seen in 18.1% which correlated with Patil et al.[13] But this incidence was higher than the study conducted by Malpani et al.,[14] this may be because we had small sample size.

Regardless in the level of expertise or years of training, variability with regards to interobserver and intraobserver reporting is high and is well documented in the literature. At times diagnostic challenges due to variations corroborating to hormone replacement therapy and perimenopausal changes and may lead to over diagnosis of ASCUS especially in elderly women. Reluctance to diagnose LSIL in women during peri-menopausal and postmenopausal period may also lead to more interpretations of ASCUS.[11]

In our study out of 10 cases of ASCUS on cytology, 30% cases correlated on histopathology while 70% cases were diagnosed as cervicitis with or without metaplasia. This discrepancy of pap smear on histopathology can be attributed to the fact that those cases had perimenopausal changes like cervical erosions or ulcers, which shows inflammatory atypia and these cells on cytology may be considered as atypical squamous cells.

Out of 8 cases of LSIL, 2 cases showed CIN, 3 cases showed cervicitis and 3 cases showed invasive cancer. Out

Table 3: Comparison of pap smear values with other studies

Study	Sensitivity	Specificity	PPV	NPV	Accuracy
Bamanikar et al[10]	89.47	88.70	82.92	-	-
Atla et al[11]	94.11	64.28	82.75	85	78.2
Bindroo et al[12]	75.24	97.98	96.20	85.38	88.80
Patil et al[13]	77.7	84.2	70.0	88.8	82.1
Malpani et al[14]	86.61	73.33	96.49	39.29	85.21
Present study	90.57	62.50	95.41	43.47	87.66

(PPV- Positive predictive value, NPV- Negative predictive value)

of 5 cases, 4 cases of HSIL correlated on histopathology, but 1 case showed chronic cervicitis with metaplasia. These false negative results in cytohistologic comparison may be because of sampling error and artifacts during preparation like inadequate fixations, drying artifacts, background materials and thick smears. Though false negative rates are usually misjudged when using follow up controls, our value observation against immediate histologic 'gold-standard' reflects an effective screening program for cervical cancer.[13]

In our study, the overall sensitivity, specificity, PPV, NPV and accuracy of pap smear was 90.57%, 62.50%, 95.41%, 43.47% and 87.66% respectively. These values were comparable to Bamanikar et al.,[10] Atla et al.,[11] and Malpani et al[14] (Table-3). This study shows a good correlation between cervical cytology and histopathology.

CONCLUSION

Pap smear is a simple, safer, non-invasive, and effective method for detection of lesions of the cervix and ECA. But the accomplishment of screening is based on adequate sample collection and correct interpretation. Therefore better awareness, periodical cytological screening programs along with the use of thin-prep pap liquid based cytology technique, HPV and DNA testing can reduce inadequate sampling errors and help in early detection of cervical cancer.

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