ORIGINAL RESEARCH

Study of pap smears for cervical cancer screening and its correlation with cervical biopsy in Himachali women

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ABSTRACT

Introduction: Cervical cancer is change in the cells of cervix which occurs gradually leading to various conditions ranging from benign to malignant conditions. It is the major health problem faced by women of India which commonly affects the women in reproductive age. It is the third largest cause of mortality in Indian women and accounts for one fifth of the total world burden of cervical cancer. Aims and Objectives: To study prevalence of various types of lesions in cervical Pap smear cytology and correlate the changes observed in cervical Pap smear cytology with histopathology, wherever indicated in Himachali women. Materials and Methods: This was a cross sectional study done on 500 women from the OPD of Obstetrics and Gynaecology. The cytology smears were reported according to the 2014 Bethesda system and was correlated histopathologically where ever needed. Results: In our study of 500 patients, maximum number of participants were in the age group of 31-40 yrs and had no history of chronic vaginal infection. Majority of the smears were normal followed by inflammation. Cyto-histological correlation was done on 50 cases, among which 2 cases were of HSIL, 2 cases of SCC and incidental finding of cervical carcinoma on endometrial curettage. Conclusion: It was concluded that conventional Pap smear along with biopsy are best tool for cervical screening. More screening programs must be organized for maximum participation.

Key words: Pap smear, biopsy, cytohistology, HSIL, SCC

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INTRODUCTION

The conical-shaped, 2.5 cm long cervix is located at the caudal part of the uterus which extends into vagina. The internal os and the external os, which represent the upper and lower border of cervical canal, include the transition zone from squamous to the columnar epithelium. At the time of birth, the original squamo-columnar junction is located at the internal os (old squamo columnar junction). As the age advances, the cervix elongates and post-pubertal under the influence of hormones the columnar epithelium is replaced by the metaplastic epithelium. The histologic squamo-columnar junction moves towards the

external os which is now referred to asphysiologic or new squamo-columnar junction. The area between the two junctions is known as transformation zone which is a common site for malignant transformation 1,2,3,4 .

Cervical cancer is an abnormal growth of cervical cells that occurs gradually leading to various conditions ranging from benign to malignant. Cervical cancer strikes women in their prime and has devastating effects with a high human mortality, social and economic cost⁵. The main cause of death and morbidity for women worldwide is cancer of the uterine cervix⁶. With an estimated 604,000 new cases and 342,000 fatalities in 2020, it is the fourth most

prevalent cancer in women globally⁷.It is the third leading cause of death for women in reproductive age and accounts for one-fifth of the global cervical cancer burden and with high disease prevalence in India^{8, 9}.It is a serious health issue that affects Indian women⁸.Socioeconomic status, sexualorientation, reproductive status, dietary practices, viruses (mostly HPV), and long term oral contraceptive use are a few factors that have been linked to cancer development¹⁰.By 2030, it is anticipated that there will be an increase in the death rate from cervical cancer¹¹.

The lack of awareness and education leads to the late detection of cancer in the majority of cases. The early detection of precancerous lesions with effective screening programs has reduced the mortality rate in developed countries. With early identification the 5-year survival rate for cervical cancer has roughly increased by roughly $92\%^{12}$.With promotion of screening programs by several nations efforts have been made to decrease disease burden worldwide ¹³.

For early detection of disease, the screening method must be cost-effective, easy to perform, less invasive, and should be applicable on a large group of the population^{14,15}. With the availability of cheap and easy-to-use screening tools, mortality related to cervical cancer can be significantly reduced¹⁶.

The cervical cytology (Pap smear) has become an important diagnostic asset in the identification of cervical pathology since its discovery and is widely used as a mass screening method^{15, 17}. The main function of the Pap test is to detect cellular changes at an early level, so as to provide effective treatment and prevent disease progression¹⁶.

Three categories that were previously labelled "less than ideal" in "The 1991 Bethesda system" were later renamed "satisfying but constrained by". In order to better understand cervix biology and lessen clinician confusion in reporting, the system was redesigned in 2001 and again in 2014 based on clinical knowledge and technological advancements¹⁸.

With the introduction of liquid-based cytology, cervical cancer screening has become easier, but a little expensive. Our study was carried out in the areas, where Liquid based cytology is not available at present and also women are still unaware of the benefits of Pap smear. Pap smear remains to be one of the most effective methods for cervical cancer screening.

MATERIAL AND METHODS

The present study was conducted in the Department of Pathology,Maharishi Markandeshwar Medical College and Hospital Kumarhatti, Solan. The study group included all female patients coming to Department of Obstetrics and Gynaecology of the hospital for the common gynaecological complaints. It was a prospectivecross-sectional study. The study was done from 1stJanuary 2021 to 30th June 2022 and 500 cervical Pap smear samples were screened. Pap

smears taken in Gynae.Obs. OPD or OT were processed and examined in the Department ofPathology, Maharishi Markandeshwar Medical College and Hospital. Out of these, all the patients with abnormal cervical cytology undergoing cervical biopsy were studied for cytohistopathological correlation.

The women in the age group of 21-65 years attending gynaecology out-patient department with any of the complaints like abnormal vaginal discharge post coital bleeding, persistent leucorrhoea, abnormal uterine bleeding, postmenopausal bleeding and any other abnormal findings on speculum/vaginal examination were included in the study.

The women with the age < 21 years and >65 years, pregnancy, post-hysterectomy, post chemotherapy/radiotherapy were excluded from the study.

All the cervical Pap smears were reported as per the latest Bethesda System (TBS 2014) guidelines.

PROCEDURE

The consent was obtained from all the participants after detailed explanation of the procedure. Detailed history (Obstetric history and menstrual history) in addition to the signs and symptoms of the patient were record.

EXAMINATION OF THE CERVICAL PAP SMEARS

All the cervical Pap smear slides received from the gynaecology department were stained with Papanicolaou stain.

THE PAPANICOLAOU STAINING PROCEDURE

- 1. Wet fix smear in 95% ethyl alcohol for 5 minutesand hydrate them through
- 2. 80%,70%, 50% alcohol to distilled water.
- 3. Stain in Harris' hematoxylin in 4 minutes.
- 4. Wash in tap water for 1-2 minutes.
- 5. Differentiate in acid alcohol.
- 6. Bluing in tap water or 1.5% Sodium Bicarbonate.
- 7. Rinse in distilled water.
- 8. Transfer to 70%, then 95% alcohol for 1 min.
- 9. Stain in Orange Green (OG-6) for 2 minutes.
- 10. Rinse in 3 changes of 95% alcohol for 30 seconds each.
- 11. Stain in Eosin Azure (EA-36) for 2 minutes.
- 12. Rinse in 3 changes of 95% alcohol for 30 seconds each.
- 13. Dehydrate in absolute alcohol.
- 14. Clear in xylene.
- 15. Mount with DPX.

CERVICAL BIOPSY

The histopathological examination of the cervix was done in all the cervical biopsies or hysterectomies received in the histopathology laboratory of the hospital, wherever indicated. The Gynaecologist and cytopathologist were a part of the study team who worked together towards one common aim that is improving patient compliance and hence ensuring proper and early treatment there by helping the patient. For this purpose efforts were made to take adequate smears and to reduce the number of unsatisfactory smears.

STATISTICAL ANALYSIS

In all patients, statistical analysis was done to calculate the sensitivity, specificity, positive predictive value and negative predictive value of the Pap smear test in correctly diagnosing cancerous and pre-cancerous lesions.

ETHICAL CONSIDERATION

Informed and written consent (in the language they best understand) were taken from each subject before collecting data. Only those individuals, who volunteered to participate in the study, were included and the data was kept confidential. The study did not impose any burden on the subjects and the Institute; therefore, the study was ethically justified. The proposed study was undertaken after the approval by the Institutional Ethical Committee.

RESULTS

Cervical Pap smears of 500 women were included in the study and analysis was done according to the 2014 Bethesda system guidelines. A histopathological correlation was carried out in 50 available biopsies. General demographic characteristics of the study group were also studied. Out of 500 women who underwent cervical Pap smear screening majority of the women were in 4th to 5th decade i.e. 360 (72%). Out of 500 women majority received education upto senior secondary level 421 (84.2%). Multiparous women constituted the major chunk of women screened cytologically. Among the 500 conventional Pap smears screened, 422 (84.4%) cases were NILM of which 212 (42.4%) were normal, 206 (41.2%) were inflammatory and 4 (0.8%) were atrophic. The incidence of epithelial abnormalities was 18 (3.6%) which included 13 ASCUS, 1 ASC-H and 2 HSIL. There was no LSIL in our lesions. The carcinomas diagnosed were 2 (0.4%). All these were Squamous cell carcinomas. There was no Adenocarcinoma on cytologic categorization. However, 54 (10.8%) smears were considered unsatisfactory for evaluation (Fig 1).

 Table 1: Cytological Categorization on Conventional Cervical Pap Smears

Cytological impression	Frequency	Percentage	
Normal	212	42.4	
Inflammatory	206	41.2	
Atrophic	4	0.8	
ASC-US	13	2.6	
ASC-H	1	0.2	
AGC- NOS	6	1.2	
LSIL	0	0	
HSIL	2	0.4	
SCC	2	0.4	
Unsatisfactory	54	10.8	
TOTAL	500	100	

DISTRIBUTION OF INFLAMMATORY LESIONS

The causes of inflammatory lesion were divided into non-specific inflammation, infectious causes like bacterial vaginosis, trichomonas vaginalis and candida were seen in the study. Besides the above-mentioned infective causes of inflammation other causes are also there which were not seen our study.

Table 2:Distribution of Inflammatory Lesions

Lesions	No. of cases	Percentage
Non-Specific Inflammation	143	69.4
Bacterial vaginosis and Trichomonas vaginalis	61	29.6
Candida	2	1.0
Total	206	100

Out of 500 cases, histopathological correlation was studied in 50 cases. Of 50 cases majority were hysterectomies 35 (70%), cervical biopsies were 14 (28%). Besides the common an incidental finding was of a cervical carcinoma (SCC) being reported in endometrial curettage.

Table 3: Types of samples received for histopathology with significant finding

Туре	Frequency	Percentage
Cervical biopsy	14	28

Hysterectomy	35	70
Endometrial curettage	1	2
Total	50	100

Out of 50 cases majority i.e. 40 (80%) showed inflammatory changes, 5 cases were diagnosed as carcinoma. 2 (4%) cases were diagnosed as HSIL. Mild dysplastic change/CIN-I was present in 3 (6%) cases. Of the 5 cases diagnosed as carcinoma, 3 were squamous cell carcinomas and 1 was adeno-squamous carcinoma cervix. Cervical carcinoma was not found on routine screening but was an incidental finding on endometrial curettage.

Table 4: Lesions diagnosed on histopathology

Lesion	Frequency	Percentage
Inflammatory	40	80
Mild Dysplasia/CIN-1	3	6
HSIL	2	4
Carcinoma	5	10
Total	50	100

Table 5: Correlation of cytology with histopathology diagnosis (n=50)

		Histopathology				
Cytology	Cervicitis	LSIL (CIN I/Mild dysplasia)	HSIL (CIN II/CIN III/Carcinoma <i>in situ</i>)	Carcinoma	Total	
NILM	37	0	2	2	41	
ASC and AGC	3	3	0	0	6	
LSIL	0	0	0	0	0	
HSIL	0	0	0	1	1	
Carcinoma	0	0	0	2	2	
Total	40	3	2	25	50	

Concordance of the lesions between cytologic and Histopathologic diagnoses (Cytohistological correlation):

Of the total 500 cases screened for cervical cancer, a cytohistologic correlation was carried out in 50 cases for which biopsy was performed.

Of the 41 cases that were reported as NILM on Pap smear, 37 showed inflammatory changes on biopsy, 2 were upgraded to HSIL and 2 as carcinoma on histopathology.

Of the total 6 cases of atypical squamous cells and atypical glandular cells, 3 showed inflammatory changes and 3 were upgraded as CIN I.

No case was categorized as LSIL either in cytology or histopathology.

1 case of HSIL diagnosed cytologically was upgraded to squamous cell carcinoma on histopathology.

2 cases of squamous cell carcinoma on cytology were confirmed on biopsy.

Table 6: Sensitivity and specificity of Pap smear in diagnosis of Intraepitheliallesion or Malignancy (n=50)

Histopothology	Cyt		
Histopathology	Positive	Negative	Total
Positive	6	4	10
Negative	3	37	40
Total	9	41	50

Sensitivity, specificity, positive predictive value and negative predictive value of the pap smear test in the present study were 60%, 92.5%, 66.66% and 90.24% respectively. Accuracy of the test was 86%.

Sensitivity:It is the proportion of disease positives who are test positive. In the current study sensitivity was 60 % which means 60% of the women screened truly had disease and remaining 40% showed false negative result.

Sensitivity is calculated as **TP/TP+FN** = $(6/6+4) \times 100 = 60\%$

Where, TP- True positives and FN- False negatives together constitute actual diseased persons.

Specificity:It is the proportion of disease negatives who are test negative.

In the current study specificity was 92.5 % which means that 92.5% of the women screened were truly not having disease.

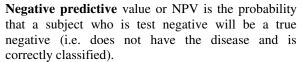
Specificity is calculated as **TN/TN+FP** i.e. (37/37+3) x 100 = 92.5%

Where TN- True negatives and FP- False positives together constitute actual non diseased persons.

Positive predictive value or PPV is the probability that a subject who is test positive will be a true positive (i.e. has the disease and is correctly classified).

PPV is calculated as **TP/TP+FP** i.e. (6/6+3) = 66.66%.

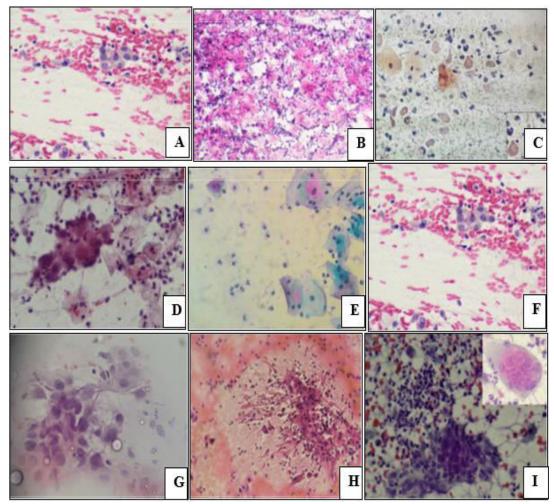
Where TP- True positives and FP- False positives are the total test positive subjects.



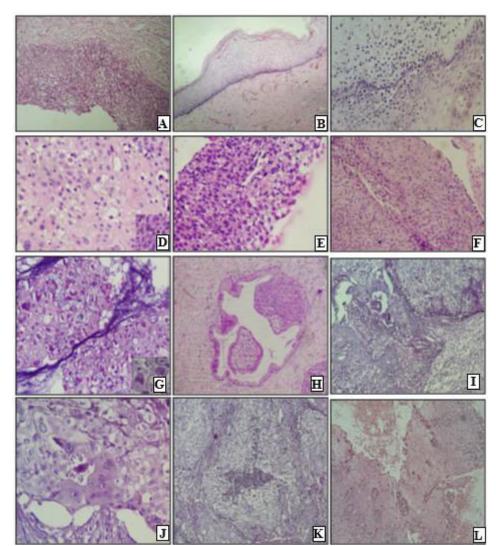
NPV is calculated as **TN/TN+FN** i.e. (37/37+4) = 90.24%.

Where, TN- True negatives and FN- False negatives are the total test negative subjects.

Accuracy of a test is its ability to differentiate the patient and healthy cases correctly. It is calculated as TP+TN/TP+TN+FP+FN i.e. (6+37/6+37+3+4) = 86%.



a) Inflammatory smear showing superficial squamous epithelial cells covered by dense inflammatory cells (Conventional Pap, 200x); b) Inflammatory smear showing pear shaped; c) Inflammatory smear showing Candida yeast form. (Conventional Pap, 400x) organism Trichomonas vaginalis (Inset). (Conventional Pap, 400x); d) & e) Smear showing atypical glandular cell cluster (Conventional Pap, 400x); f) & g) Smear showing atypical squamous cells of undetermined significance (ASCUS). (Conventional Pap, 400x); h) Smear of SCC showing cluster and singlyscattered hyperchromatic and pleomorphic tumor cells and tadpole cells. (Conventional Pap, 200x); i) Smear of HSIL showing cluster of hyperchromatic and pleomorphic cells in hemorrhagic and inflammatory background. Multinucleation also seen (Inset) Conventional Pap, 400x)



a) Cervical biopsy showing normal mature cervical squamous epithelium. (H&E, 100X); b) Cervical biopsy showing Chronic cervicitis. (H&E, 400X); c) Cervical biopsy showing tumor with moderate nuclear atypia in High grade squamous intraepithelial lesion, HSIL (CIN III-Carcinoma *in situ*). (H&E, 400X); d) Cervical biopsy showing High grade squamous intraepithelial lesion, HSIL (CIN III). (H&E, 100X); e) HSIL (CIN III- Carcinoma in situ) with extension into endocervical glands (No invasion beyond basement membrane found in all other sections); f) Section showing marked pleomorphism in Squamous cell carcinoma. (H&E, 200X); g)Section showing marked pleomorphism with prominent nucleoli and mitosis (Inset) in Squamous cell carcinoma. (H&E, 400X); h)Adenosquamous carcinoma cervix showing differentiation and conspicuous nucleoli). (H&E, 400X); j)
Adenosquamous carcinoma cervix showing glandular pattern (inset) and extracellular mucin. (H&E, 400X); k) Adenosquamous carcinoma cervix showing necrosis. (H&E, 100X); l) Squamous Cell carcinoma (well differentiated) found as an incidental finding in endometrial curettage sample). (H&E, 100X)

DISCUSSION

For more than 50 years, Pap smear has remained the primary modality for screeningwomen of all age groups but has a high false negativity rate. According to WHO and other guidelines, average age group for cervical cancer screening is 3^{rd} decade onwards². In both Nikumbh *et al.* (2012)¹⁹ and Armo *et al.* (2014)²⁰study, majority of the women who came for screening were in age group of 31-40 years which was similar to our findings. A similar age group was

screened maximum by several other studies. Also majority of the women were in the reproductive age group. Our study showed striking similarity with Bamanikar *et al.* $(2016)^{21}$, where the majority of the women were diagnosed with NILM which was 88.02%. Sohail *et al.* $(2008)^{22}$ and Verma *et al.* $(2017)^{23}$ showed that women diagnosed with NILM were 92% and 90% respectively which was also close to our findings. The studies by Sohail *et al.* $(2008)^{22}$ and Bamanikar *et al.* $(2016)^{21}$ showed almost similar

resemblance to our study in diagnosing epithelial cell abnormalities (6% and 5.99 % respectively vs 4.8% in present study). The incidence of epithelial cell abnormalities was higher i.e. 24.4% in Vaghela *et al.* $(2014)^{24}$ study.

DISTRIBUTION OF NILM (NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY)

Out of 500 patients, NILM was diagnosed in 84.4% of women. Majority of thepatients in this group were non-specific inflammation. Others included reactivechanges, candidiasis, trichomonas and bacterial vaginosis and atrophic smears.

Vaghela *et al.* $(2014)^{24}$ study showed that amongst NILM, non-specific inflammationconstituted 37.4%. 2.8% were positive for candida, 2% were positive for trichomonasand 1.6% for bacterial vaginosis. Atrophic smears constituted 2% of the cases.

In Tailor et al. (2016)²⁵study amongst NILM, nonspecific infections constituted51.6%, 3.7% were positive for candida, 0.7% were positive for trichomonas and 26.8% positive for reactive changes and atrophy in 1.33% cases. The present study like other studies showed that majority of NILM cases are non-specific inflammations and specific infections comprise a minority. The relatively higher incidence of infections like Bacterial vaginosis and Trichomonas vaginalis in our study might be due to our hospital catering to predominantly rural women.

DISTRIBUTION OF EPITHELIAL CELL ABNORMALITIES (ECA)

In our study epithelial cell abnormalities constituted 4.8%. Atypical squamous cells ofUndetermined significance being the most common among epithelial cellabnormalities constituting 2.6% followed by HSIL and Squamous cell carcinoma(0.4% each).

AGE WISE DISTRIBUTION OF EPITHELIAL CELL ABNORMALITIES

In our study since ASCUS being the most common epithelial lesion found in the agegroup of 35-40 years. HSIL, SCC were found in the age group of 40-45 years and 60-65 years respectively. Similar results were seen in the age group of 35-40 years in the study conducted by Bamanikar *et al.* $(2016)^{21}$.

DISTRIBUTION OF ASC (ATYPICAL SQUAMOUS CELLS)

In our study ASC were 2.8%. The commonest lesion found in ASC was ASCUSwhich was 2.6%. The results were closest to study conducted by Rana *et al.* $(2013)^{26}$ which was 3.2%. Nikumbh *et al.* $(2012)^{19}$ and Verma *et al.* $2017)^{23}$ carried out the studies in which incidence of the ASCUS was 0.96% and 1% respectively. The study conducted byArmo *et al.* $(2014)^{20}$ also showed almost similar results to our study and stated thatASCUS was the commonest

lesion among the ASC (3.3%). Other comparisons were similar.

DISTRIBUTION OF LSIL (LOW GRADE SQUAMOUS INTRAEPITHELIAL LESION)

There was no case of LSIL found in our study. Several studies have studied the incidence of LSIL. Nikumbh *et al.* $(2012)^{19}$ and Verma *et al.* $(2017)^{23}$ study showed it was 0.9% and 5.5%. The study conducted by Nandwani *et al.* $(2016)^{27}$ and Armo *et al.* $(2014)^{20}$ had incidence of 2.6% and 2.0% respectively. Vaghela *et al.* $(2014)^{24}$ had the highest incidence among the studies compared i.e. 12.4%.

DISTRIBUTION OF HSIL (HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION)

Our study showed the incidence of HSIL is 0.4% which was similar to study done by Tailor *et al.* $(2016)^{25}$ i.e. 0.35%. The studies by Nikumbh *et al.* $(2009)^{19}$ and Rana *et al.* $(2013)^{26}$ showed incidence of 1.9% and 1.6% respectively. In contrast to the present study, Vaghela *et al.* $(2014)^{24}$ conducted a studied which showed higher incidence of HSIL i.e. 5%.

DISTRIBUTION OF SCC (SQUAMOUS CELL CARCINOMA)

Nikumbh *et al.* $(2012)^{19}$ and Vaghela *et al.* $(2014)^{24}$ showed the incidence of SCC as 1.6% and 2.4% respectively. The present study had and incidence of 0.4% which was similar to Rana *et al.* $(2013)^{26}$ and Armo *et al.* $(2014)^{20}$ which was 0.6% and 0.5% respectively.

However, Tailor *et al.* $(2016)^{25}$ had a lower incidence of 0.1% which was lesser in comparison to the present study.

DISTRIBUTION OF AGC (ATYPICAL GLANDULAR CELLS)

The incidence of AGC in our study was 1.2% which was similar to the study carriedout by Vaghela *et al.* $(2014)^{24}$. Tailor *et al.* $(2016)^{25}$ in their study who found the incidence of AGC as 0.3%. Another study by Nikumbh *et al.* $(2012)^{19}$ found reported the incidence of AGC as 0.4%.

DISTRIBUTION OF THE CASES ON HISTOPATHOLOGY WITH CYTOHISTOPATHOLOGICALCORRELATIO N

In our study out of 500 Pap smear screened, 50 smears were correlated histologically with significant findings. Of 50 histopathologically diagnosed cases majority of the cases were inflammatory (80%). 10% cases were of carcinoma. 4% HSIL and 6% cases of Mild Dysplasia/CIN-1. A study done by Bamanikar *et al.* ²¹in 2016 also had majority of cases as inflammatory on histopathological correlation.10% cases were found to be carcinoma. 16.5% were found to be HSIL. The present study and Bamanikar *et al.* (2016)²¹showed higher incidence of inflammatory

lesions being diagnosed on biopsy. In contrast lower incidence wasfound in study carried out by Meenai et al. (2018)²⁷. Although there was no frank LSIL case found in our 50 biopsies, we had 6% CINI/Mild dyplasia cases. Bamanikar et al. (2016)²¹, Joshi et al. (2015)²⁸ and Meenai et al. (2018)²⁷ found higher incidences of the same probably due to a higher set of biopsies. HSIL, a precursor of malignancy was low in the current study which in contrast was higher (37.1%) in study by Meenai *et al.* $(2018)^{27}$. Other compared studies alsoshowed a higher incidence of HSIL. This might be explained on the basis of higher number of cases studied histopathologically by them as can be seen by the total cases studied. The incidence of carcinoma in the present study was in close proximation to different studies as can be seen from the table. It was same as that of Bamanikar et al. $(2016)^{21}$.

The present study showed sensitivity of 60% in detection of intraepithelial lesions.

The reason for low sensitivity could be low sample size, obscuration of the cellmorphology by blood or inflammation due to which important findings may havebeen missed. Another reason could be gynecologic sampling error. Two cases ofmalignancy which were missed on cytology were diagnosed as carcinomas on biopsy.

Although the Pap smear test has a high specificity, it has been discovered to have alow sensitivity and a significant likelihood of false negative results.31 Also the lessernumber of cases could also be reason for lower sensitivity in comparison to otherstudies with a larger set of study subjects. (Table 7). Turkmen *et al.* $(2013)^{29}$,Hegde *et al.* $(2011)^{30}$, Sirasagi *et al.* $(2021)^{31}$ and Bamanikar *et al.* $(2016)^{21}$ foundmuch higher sensitivity (above 80%) in their studies. On the other hand Meenai *et al.* $(2015)^{28}$ found lesser sensitivity intheir studies (61.76%, 65.2% and 65.38% respectively). The sensitivity of the presentstudy (60%) was similar

to the latter 3 studies with lower sensitivities. The contrasting comparison of sensitivites shows that this parameter is highly dependent on sampling/processing techniques as well as the number of study subjects. Limitations of cytology in diagnosing all lesions is also a factor that cannot to be ignored.

SEPECIFICITY COMPARISON

The present study showed 92.5% specficity in detection of intraepithelial lesionswhich was in line with most of studies. Only occasional study by Sirasagi *et al.* $(2021)^{31}$ had a low specificity.(Table 7) A review of literature also shows that sensitivity and specificity rates of cervicalcytology are highly variable.

Positive predictive value is the probability that a subject who is test positive will be atrue positive. This value came out to be 66.66%. The relatively low values incomparison to other studies can be explained again by the less numbers of malignancies and intraepithelial lesions being included in present analysis. Patil *et al.* (2016)³³ also found a similar lower Positive predictive value (70%). (Table 7)

Negative predictive value s the probability that a subject who is test negative will bea true negative. NPV in our study was 90.24% which means that 90.24% of thesubjects testing negative by the cytological Pap test were also negative on histopathology. Our study NPV was in closest to Hegde *et al.* $(2011)^{30}$ and Patil *et al.* $(2016)^{33}$ (97.9%) and 88.8% respectively). Accuracyof the Pap smear test in the current analysis came out to be 86% which was similar to almost all the compared studies. The above comparisons show that the cervical cytology (Pap smear) is an effective test for screening, but in case of doubt or abnormal smear findings, biopsy should be always be done further highlighting the fact that histopathology is the gold standard in diagnosing and confirming malignancies and intraepithelial lesions of the cervix.

 Table 7: Comparison of Sensitivity, Specificity, Positive predictive value, Negative predictive value and

 Accuracy of Cervical Pap smear with variousStudies

Study	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Study	(%)	(%)	(%)	(%)	(%)
Turkmen et al. (2013)	86.4	-	-	-	-
Meenai et al. (2018)	61.76	99.1	-	-	-
Jyothi et al. (2013)	65.2	96.3	89.3	-	-
Joshi et al. (2015)	65.38	95.83	94.4	71.8	80
Hegde et al. (2011)	83	98	80	97.9	-
Patil et al. (2016)	77.7	84.2	70	88.8	82.1
Chaudhary et al.	25.40	99.27	94.12	74.32	76
Sirasagi et al. (2021)	90.57	62.50	95.41	43.47	87.66
Bamanikar et al. (2016)	89.47	88.7	82.92	-	-
Present study	60	92.5	66.66	90.24	86

CONCLUSION

Pap smears are the best screening methods for detection of early cervical lesions especially

malignancies besides all other screening methods available due to the low cost and easy availability as an outpatient procedure especially in developing countries like India. Biopsy (Histopathology) still remains the gold standard in diagnosing cervical lesions especially malignancies. As early diagnosis is the key in malignancies, cervical Pap smear screening guidelines laid down must be followed for women of all age. groups and a biopsy performed wherever indicated to prevent the occurrence of adverse consequences.It is suggested that more screening programs should be conducted for maximum participation of women and for detection of disease at an early stage for reducing disease burden.

REFERENCES

- 1. Apgar BS, Zoschnick L, Wright TC Jr. The 2001 Bethesda System terminology. Am Fam Physician. 2003;68:1992-8
- Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran pathologic basis of disease. 8th. Philadelphia: Ed. Saunders Elsevier. 2010:1-2
- Sun Q, Tsutsumi K, Kelleher MB, Pater A, Pater MM. Squamous metaplasia of normal and carcinoma in situ of HPV 16-immortalized human endocervical cells. Cancer Res. 1992;52:4254-60
- 4. Kurman RJ, Ellenson LH, Ronnett BM, editors. Blaustein's pathology of the female genital tract. New York: Springer; 2011 Jan 10.
- Pankaj S, Nazneen S, Kumari S, Kumari A, Kumari A, Kumari J, *et al*.Comparison of conventional Pap smear and liquid-based cytology: A study of cervical cancer screening at a tertiary care center in Bihar. Indian J Cancer. 2018; 55(1):80-3.
- Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, *et al*. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002; 287(16):2114-9.
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*.Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021; 71(3):209-49.
- Jacob M. Information, education & communication: corner stone for preventing cancer of the cervix. Indian J Med Res. 2012; 136(2):182-4.
- Jain DK, Singh P. A study of the uterine cervix cancer in India. Sankhyā: The Indian Journal of Statistics, Series B. 1996:118-44.
- Hazra SK, Maiti S, Chaudhuri A, Banerjee D, Guha S, Das A. Cervical cancer in women with unhealthy cervix in a rural population of a developing country. J Basic ClinReprod Sci. 2013; 2(2):97-100.
- 11. Parkhurst JO, Vulimiri M. Cervical cancer and the global health agenda: Insights from multiple policy-analysis frameworks. Glob Public Health. 2013; 8(10):1093-108.
- 12. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al.American

Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin. 2012;137(4):516-42.

- 13. Shin JY, Choi KS, Suh M, Park B, Jun JK. Comparison of cervical cancer screening among women with and without hysterectomies: a nationwide population-based study in Korea. BMC Cancer. 2018; 18(1):810-6.
- 14. Andrae B, Kemetli L, Sparén P, Silfverdal L, Strander B, Ryd W, *et al*.Screening-preventable cervical cancer risks: evidence from a nationwide audit in Sweden. J Natl Cancer Inst. 2008; 100(9):622-9.
- Monsonego J, Autillo-Touati A, Bergeron C, Dachez R, Liaras J, Saurel J, *et al*.Liquid-based cytology for primary cervical cancer screening: a multi-centre study. Br J Cancer.2001; 84(3):360-6.
- 16. Bengtsson E., Malm P. Screening for cervical cancer using automated analysis of PAP-smears. *Comput Math Methods Med.* 2014; 2014: 12.
- Mainali N, Homagai N, Nepal N, Choudhary P. A correlation study of cervical cytology on Pap smear with cervical biopsy in a tertiary hospital of Eastern Nepal. J Pathol Nep. 2018; 8(2):1389-92.
- Cibas ES, Cervical and vaginal cytology. In: Cibas ES, Ducatman BS, editors. Cytology: Diagnostic principles and clinical correlates. 3rd edit.Philadelphia: Gulf Professional Publishing; 2003.p.11-8
- 19. Nikumbh DB, Nikumbh RD, Dombale VD, Jagtap SV, Desai SR. Cervicovaginal cytology: clinicopathological and social aspect of cervical cancer screening in rural (Maharashtra) India. Int J Health Sci Res. 2012;1:125-32.
- Armo M, Khunte V, Sainik S, Kanniga RG, Jatwar N. Awareness and practices of cervical cancer screening among women in Rajnandgaon district, central India: health education is the need of the hour. Int J ReprodContraceptObstet Gynecol. 2019;8:1266-70.
- 21. Bamanikar SA, Baravkar D, Chandanwale S, Dharwadkar A, Paranjape S. Study of cervical cytology and its correlation with clinical and histopathological findings. Clin Cancer Invest J. 2016;5:403-8.
- 22. Sohail R, Nazir R, Latif Y, Zaman F. Evaluation of cervical smear in women attending gynecology OPD. J Surg Pak. 2008;13:121-3.
- 23. Verma A, Verma S, Vashist S, Attri S, Singhal A. A study on cervical cancer screening in symptomatic women using Pap smear in a tertiary care hospital in rural area of Himachal Pradesh, India. Middle East FertilSoc J. 2017;22:39-42.

- 24. Vaghela B, Vaghela VK, Santwani PM. Analysis of abnormal cervical cytology in Papanicolaou smears at tertiary care center A retrospective study. Int J of Biomed &Adv Res. 2014; 5:47-9.
- 25. Tailor HJ, Patel RD, Patel PR, Bhagat VM. Study of cervical Pap smears in a tertiary care hospital of south Gujarat, India. Int J Res Med Sci. 2016;4:286-8
- 26. Rana S, Jairajpuri ZS, Jetley S. Cervical smear cytology on routine screening in a semi urban population in New Delhi: A review of 610 cases. Arch Med Health Sci. 2013;1:131-5.
- 27. Meenai FJ, Ansari SA, Gupta S, Ali MA. Cytohisto correlation of conventional Pap smear with cervical biopsy in diagnosis of precancerous and cancerous lesions of cervix.IP Arch CytolHistopathol Res. 2018;3:76-82.
- Joshi C, Kujur P, Thakur N. Correlation of Pap smear and colposcopy in relation to histopathological findings in detection of premalignant lesions of cervix in a tertiary care centre. International Journal of Scientific Study. 2015;3(8):55-60.
- Türkmen İÇ, Başsüllü N, Korkmaz P, Günenç B, Baykal CM, Güdücü N, *et al*.Patients with epithelial cell abnormality in PAP smears: correlation of results with follow-up smears and cervical biopsies. Turk PatolojiDerg. 2013;29:179-84.
- 30. Hegde D, Shetty H, Shetty PK, Rai S, Manjeera L, Vyas N, Hegde A, Mallya H, Rajesh A. Diagnostic value of VIA comparing with conventional Pap smear in the detection of colposcopic biopsy proved CIN. Nepal Journal of Obstetrics and Gynaecology. 2011;6(1):7-12.
- 31. Sirasagi AK, Arpitha K, Neha S, Pattar PM. A two year retrospective study of cytohistopathological correlation of cervical smear in a tertiary care hospital. Asian Journal of Medical Sciences. 2021;12(8):144-8.
- 32. Jyothi R, Gupta P, Rao R, Sood PL, Parasher N. Correlation between colposcopy, cytology and histopathology in high-risk patients for cervical cancer in perimenopausal women in Himachal Pradesh, India. Journal of SAFOMS. 2013;1:21.
- Patil PR, Jibhkate SN. Cytohistopathological correlation of Papanicolaou smears: a hospitalbased study. Int J Reprod Contracept Obstet Gynecol. 2016;5:1695-9.