ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

The cytological pattern of cervical papanicolaou smear in a tertiary hospital of India

Ajay Gupta[1], Pushpendra Singh[2], Krishna Dubey[3], Sushil Mewara[4], Mayank Sharma[5], Yogesh Gupta[6]

[1,4]Assistant Professor, [2,3,5]Senior Demonstrator, Department of Pathology, Government Medical College, [6]Consultant Pathologist, Sudha Hospital and Research Centre, Kota, Rajasthan, India

Submission: 22-02-2023 Revision: 28-06-2023 Publication: 01-08-2023

ABSTRACT

Background: Cervical cancer continues to be listed among the top gynecologic cancers worldwide. According to current data, it is ranked fourteenth among all cancers and fourth-ranked cancer among women worldwide. In India alone 1,30,000 new cases occur with the death toll of 70,000 per year. A "PAP' test should be performed during the second half of the menstrual cycle (Day 14). The patient is placed in lithotomy position and the cervix is visualized by means of a speculum. The smaller end of the Ayre's spatula is introduced through the external os and the squamocolumnar junction is scraped by rotating the spatula to 360°. **Aims and Objectives:** The objective of the study is to evaluate the use of the Pap smear screening method for detection of precancerous lesions. Cervical cancer accounts for 15% of all cancers in females.If treated or detected earlier, cervical cancer can be prevented. **Materials and Methods:** This study was done on 1000 patients during reproductive and later age groups (postmenopausal), attending Obstetric and Gynaecological Outpatient Department of Panna Dhai Hospital associated with RNTMC, Udaipur during the period of November 2012–April 2014 with history of white discharge per vagina, bleeding per vagina, pain in lower abdomen and post coital bleeding. **Results:** Most of the smears (90.1%) were NILM and 9.9% of smears showed cytological abnormality. Majority 834 (83.4%) of smears were inflammatory, Bacterial vaginosis was seen in 119 cases (11.9%), Candidiasis in 78 cases (7.8%), Trichomoniasis in 35 cases (3.5%), Atrophic vaginitis in 4 cases (0.4%) and Radiation changes in 4 cases (0.4%). There were 99 samples reported as having epithelial cell abnormality. Out of which 75 were LSIL, 14 were high grade squamous intraepithelial, 5 were atypical squamous cells (ASC)-US, 1 was ASC-H and 4 were squamous cell carcinoma. **Conclusion:** Due to high sensitivity, specificity and accuracy found in this study Pap test is proved to be highly useful to detect precancerous and cancerous lesions of cervix. From the above facts, it can be concluded that early diagnosis and prompt specific treatment of pre-invasive or early stages of the disease (mainly in high risk women), reduces the prevalence of invasive carcinoma of uterine cervix.

Key words: Cervix cancer; Papanicolaou smear; Non-neoplastic lesion of cervix; Epithelial cell abnormality in cervix

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i8.52702

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Cervical cancer continues to be listed among the top gynecologic cancers worldwide. According to current data, it is ranked fourteenth among all cancers and fourth-ranked cancer among women worldwide.[1] 5 lakh new cases of cancer cervix are reported annually worldwide. In India alone 1,30,000 new cases occur with the death toll of 70,000 per year. Cervical cancer accounts for 15% of all cancers in females. Cervical screening increased the cancer awareness among the patients but also the frequency of early detection and significantly decreased the deaths due to cervical cancer.[2]

Address for Correspondence:
Dr. Krishna Dubey, Senior Demonstrator, Department of Pathology, Government Medical College, Kota, Rajasthan, India.
Mobile: +91-7014331773. **E-mail:** drkrishnadubeydnb@gmail.com

A "PAP" test should be performed during the second half of the menstrual cycle (Day 14). The patient is placed in lithotomy position and the cervix is visualized by means of a speculum. The smaller end of the Ayre's spatula is introduced through the external OS and the squamocolumnar junction is scraped by rotating the spatula to 360°.

From the above facts, it can be concluded that early diagnosis and prompt specific treatment of pre-invasive or early stages of the disease (mainly in high risk women), reduces the prevalence of invasive carcinoma of uterine cervix. The widespread use of "PAP" smear permits the identification of patients with cervical dysplasia or CLS, who are at high risk of developing invasive carcinoma of uterine cervix. These patients can then be treated with simple and often non-invasive measures. Due to this diagnostic test, 58% decrease in the incidence of carcinoma of cervix occurred since the mid-1940.[3] It has been found to reduce the incidence of cervical cancer by about 80% in developed countries.[4]

In the present study, cervical "PAP" smear will be used for early diagnosis of cervical malignancy.

Aims and objectives

1. To detect the prevalence of abnormal epithelial changes and its types in Udaipur region
2. To study various types of neoplastic and non-neoplastic lesions of cervix by cervical "PAP" smear study and its interpretation by Bethesda system 2001
3. Early detection of pre-cancerous conditions and treating them before they progress to invasive cancer.

MATERIALS AND METHODS

Material and Methods are described separately
Out of 1000 smears examined in the present study 901 (90.1%) smears were Negative for intraepithelial lesion or malignancy.

The Pap test is not a diagnostic test; it is only a screening test for cervical cancer or cervical changes that are precancerous.

Source of data

Institute of study

This Study was done in prestigious Panna Dhai Hospital associated with Ravindra Nath Tagore Medical College, Udaipur, Rajasthan, India.

Patients during reproductive and later age groups (postmenopausal), attending Obstetric and Gynaecological Out Patient Department of Panna Dhai Hospital associated with RNTMC Udaipur with history of white discharge per vagina, bleeding per vagina, pain in lower abdomen, post coital bleeding are taken for study during November 2012-April 2014.

Sample size

Prospective study was done and patients appeared for cervical smear examination were taken for this study during November 2012-April 2014. The sample size for the study was calculated using the formula: n=z2pq/d2. Where: n=desired sample size when population >10,000, z=level of significance at 95% CI (=1.96), P=proportion of the study population who are aware of cervical cancer and screening from similar previous study=0.24, q=1–p=0.76 and d=degree of accuracy desired, usually set at 0.05.

Sample size (n)=z2pq/d2=(1.96) 2×(0.24)×(0.76)/(0.05) 2=1.96×1.96×0.24×0.76/0.0025=0.700707/0.0025=280. The minimum sample size required for this study was 280.

Inclusion criteria

1. Patients with abnormal symptoms like profuse white discharge, post coital bleeding, intermenstrual bleeding or post-menopausal bleeding
2. Patients with clinically unhealthy cervix diagnosed by speculum examination like cervical erosion, cervicovaginitis, cervical polyp, condylomas etc.
3. Patients with previously diagnosed "PAP" smears showing dysplasia.

Exclusion criteria

1. Patients with bleeding at the time of examination
2. Women with frank invasive cancer
3. Women who underwent total hysterectomy
4. Pregnant women.

This prospective study was conducted on 1000 patients during reproductive and later age groups (postmenopausal), attending Obstetric and Gynaecological Out Patient Department of Panna Dhai Hospital associated with RNTMC, Udaipur during November 2012-April 2014.

Written informed consent was obtained from all women. Patients were placed in the lithotomy position, and a sterile bivalve speculum was inserted into the vagina. The posterior vaginal wall was retracted posteriorly and the anterior vaginal wall anteriorly to allow proper visualization of the cervix and vaginal wall.

A a wooden Ayre spatula 360° was used for sample from the ectocervix by rotating. The sample was smeared onto a labeled glass slide and fixed with 95% ethyl alcohol in a jar. The glass slides were sent with proper fixation to the Department of Pathology for cytopathological examination. All results were reported according to the new Bethesda System for Reporting Cervical Cytology 2014.

RESULTS

Distribution of cases among "PAP" smears examined

Evaluation of 1000 smears revealed normal cytology Graph 1 (NILM) in 901 cases (90.1%) and cytological abnormality in 99 cases (9.9%) as shown in Table 1.

Cytological diagnosis of "PAP" smears Negative for intraepithelial lesion or malignancy

Out of 1000 smears examined in the present study 901 (90.1%) smears were Negative for intraepithelial lesion or malignancy. NILM includes Normal smear (Figure 1), Inflammation, Trichomonas vaginalis (Figure 2), Candidiasis (Figure 3), Bacterial vaginosis (Figure 4), Atrophy and Radiation changes.

Percentage of smears showing epithelial cell abnormality

There were 99 samples reported as having epithelial cell abnormality. Out of these samples, 05 (0.5%) smears were ASCUS (Atypical Squamous Cells of Undetermined Significance), ASC-H(Atypical Squamous Cells HSIL cannot be excluded) in 01 (0.1%), Low Grade Squamous Intraepithelial Lesion (Figure 5) in 75 (7.5%), HSIL High Grade Squamous Intraepithelial Lesion (Figure 6) in 14 (1.4%) and squamous cell carcinoma Figure 7 (SCC) in 04 (0.4%) samples as shown in Table 2.

Distribution of neoplastic lesions

The percentage of malignant lesion was 4.3% and of premalignant lesion was 95.7%. Ratio of premalignant to malignant lesions was 22.3:1.

In the premalignant lesions, HSIL constituted 15.05% and LSIL 80.65% as shown in Graph 2.

DISCUSSION

The cytologic diagnosis of cervical smears has become a very important screening test for the detection of preinvasive and invasive cervical epithelial abnormalities. Screening of female population for cervical neoplasia is a simple, inexpensive and reliable method which greatly reduces the mortality and morbidity associated with carcinoma cervix, if detected in its preinvasive stage.[5]

Cervical cytodiagnosis has been the subject of several investigations evaluating the efficacy of this method as a diagnostic test.[6]

Comparison of distribution of cases among "PAP" smears examined

In study done by Ranabhat et al.,[7] it is seen that 98.29% smears were diagnosed as NILM and only 1.71% of smears were

Table 1: Distribution of cases among "PAP" smears examined

S. No.	Category	No. of cases	% of cases
1	NILM	901	90.1
2	Epithelial cell abnormality	99	9.9

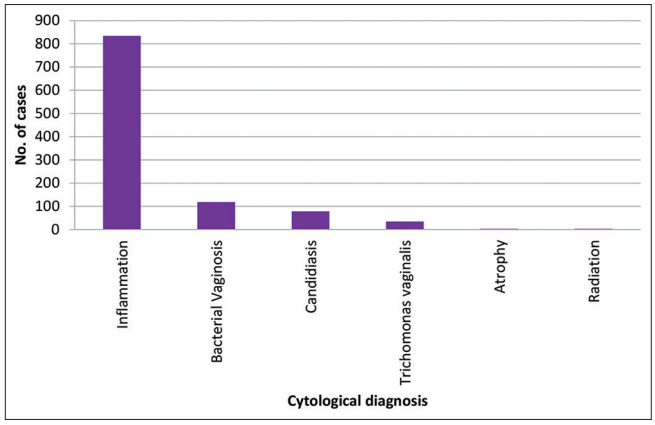
Table 2: Percentage of smears showing epithelial cell abnormality

Epithelial cell abnormality	n	TAPS% n=99	TSE% n=1000
ASC-US	05	5.05	0.5
ASC-H	01	1.01	0.1
LSIL	75	75.75	7.5
HSIL	14	14.14	1.4
CA	04	04.04	0.4
Total	99	100	9.9

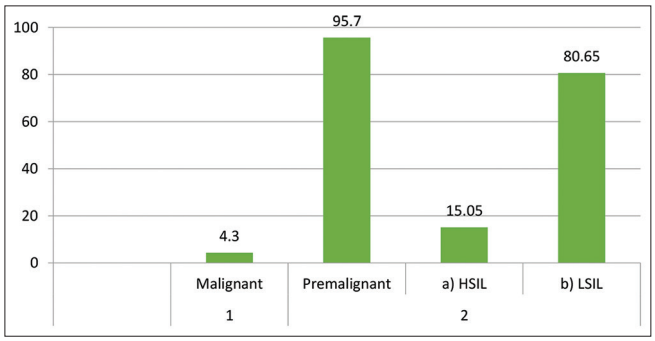
HSIL: High grade squamous intraepithelial, ASC: Atypical squamous cells

Table 3: Percentage of smears showing epithelial cell abnormality in different studies

S. No.	Category	Ranabhat et al., (2011)		Present study (2015)	
		(No. of cases)	% of cases	(No. of cases)	% of cases
1	NILM	865	98.29	901	90.1
2	Epithelial cell abnormality	15	1.71	99	9.9
	Total	880	100	1000	100



Graph 1: Cytological diagnosis



Graph 2: Distribution of neoplastic lesions

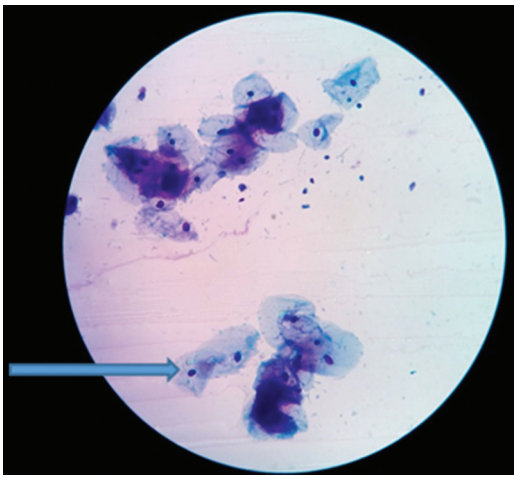


Figure 1: Normal "PAP" smear. Note normal looking superficial and intermediate squamous epithelial cells (MGG ×400)

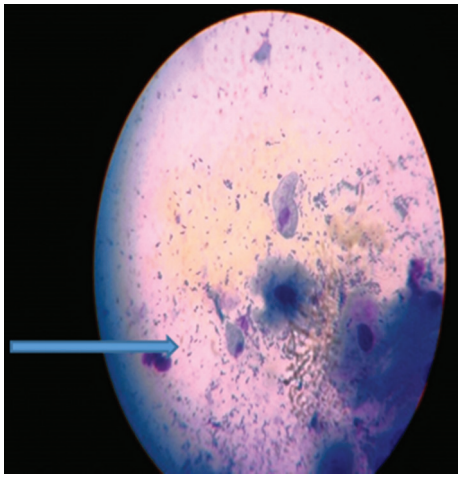


Figure 2: *Trichomonas*- pear-shaped organism morphologically consistent with *Candida* species. Note pseudohyphae. (MGG ×1000 oil immertion)

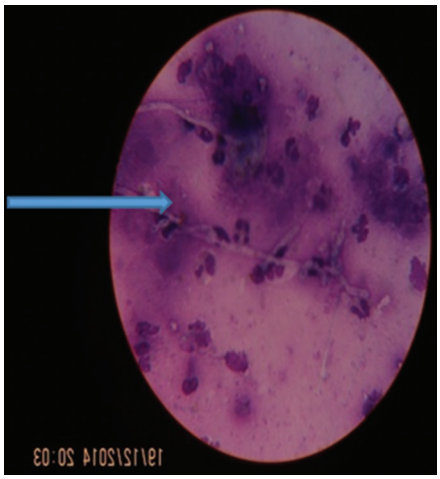


Figure 3: *Candida*- fungal organisms

showing epithelial cell abnormality in comparison to this present study shows 90.1% of smears are NILM and 9.9% of smears are showing epithelial cell abnormality as shown in Table 3.

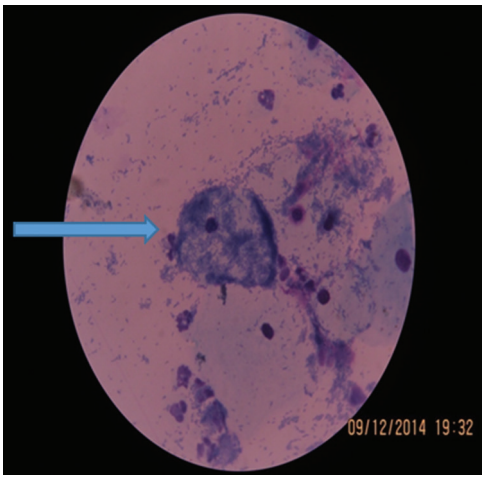


Figure 4: Bacterial vaginosis-shift in flora

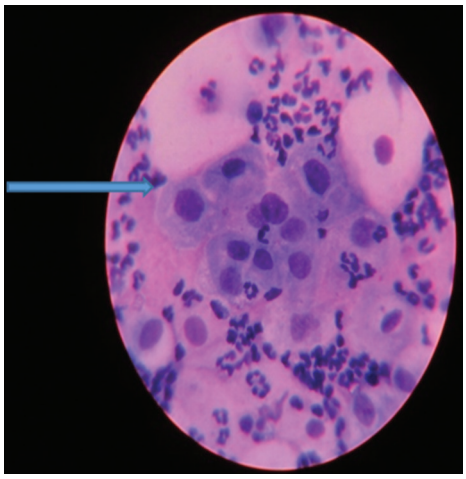


Figure 5: Low-grade squamous intraepithelial lesion

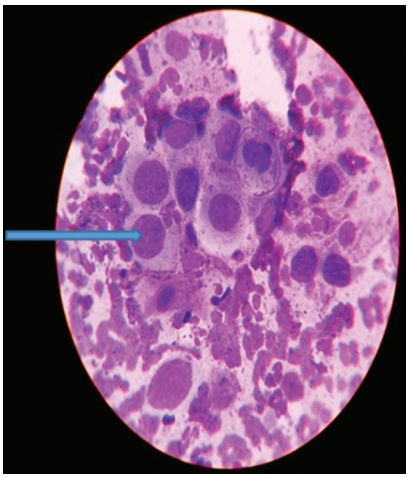


Figure 6: High-grade squamous intraepithelial lesion

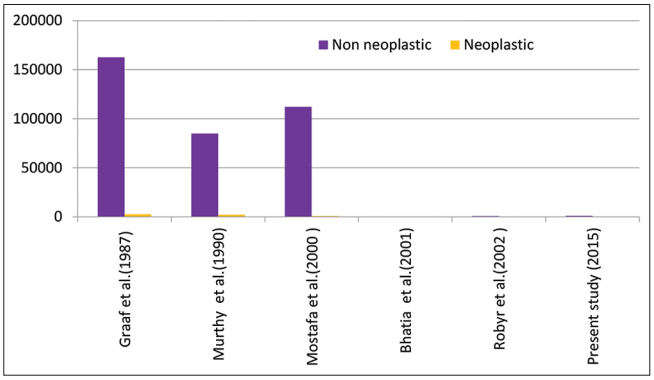
Comparison of ratio of non-neoplastic to neoplastic lesions

The Graph 3 below shows wide variation in the ratio of non-neoplastic to neoplastic lesions in different studies,

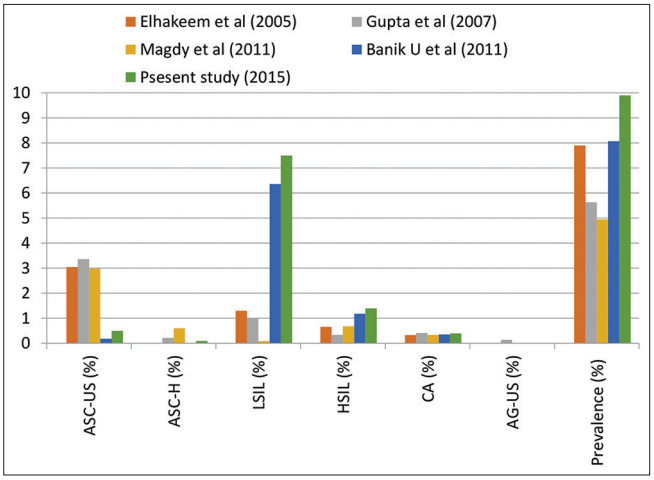
Table 4: Prevalence of abnormal epithelial abnormalities in different studies

Study	No. of cases	Mean age (years)	ASC-US (%)	ASC-H (%)	LSIL (%)	HSIL (%)	CA (%)	AG-US (%)	Prevalence (%)
Elhakeem et al., (2005)	2100	46.9	3.05	0	1.3	0.66	0.33	0	7.9
Gupta et al., (2007)	27367	41.7	3.36	0.22	1	0.34	0.41	0.14	5.64
Magdy et al., (2011)	1171	42.8	2.99	0.6	0.09	0.68	0.34	0	4.95
Banik et al.,(2011)	0	0	0.18	0	6.36	1.18	0.35	0	8.07
Present study (2015)	1000	38.63	0.5	0.1	7.5	1.4	0.4	0	9.9

ASC: Atypical squamous cells



Graph 3: Ratio of non-neoplastic and neoplastic lesions



Graph 4: Prevalence of abnormal epithelial abnormalities in different studies

indicating the geographical influence on occurrence of cervical carcinoma. The results in the present study are comparable to that reported by Graaf.[8] However, others found increase in the ratio indicating the higher rate of neoplastic lesions in developing countries as compared to developed countries.

Comparison of different cytologic categories

In the present study, the ratio of premalignant to malignant lesions is 22.3:1 as shown in Graph 2, which is comparable to study of Klinkhaemer et al.,[9] where the ratio was 29:1. However, the rate of premalignant lesions was much higher as reported by Lozowski et al.,[10] with ratio of 62.5:1. Mostafa et al.,[11] had found a lower rate of premalignant

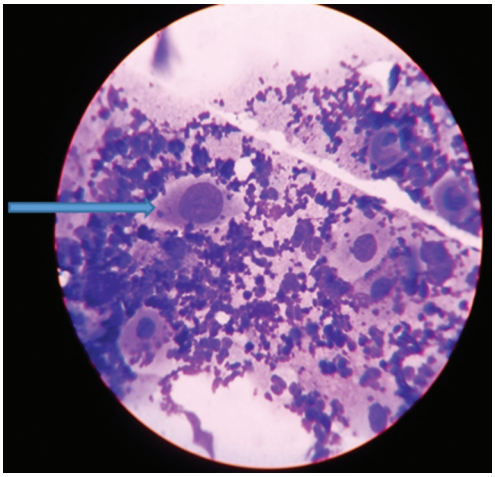


Figure 7: Squamous cell carcinoma

lesions, the ratio being 3.2:1. Premalignant lesions were higher in the studies conducted by Lozowski et al.,[10] and Klinkhaemer et al.,[9] indicating that malignant lesions were less common in developed countries. Early detection of premalignant lesions in developed countries prevent the progress of premalignant lesions to malignant lesions.

Prevalence of abnormal epithelial abnormalities in different studies

Elhakeem et al.,[12] (2005) studied 2100 cases with mean age of 46.9 years reported an overall incidence of epithelial abnormalities as 7.9%. Abnormal cervical cytology lesions such as ASCUS, HSIL, LSIL and carcinoma represented 3.05%, 0.66%, 1.3% and 0.33%, respectively. This study showed a similar overall prevalence of the epithelial abnormalities (9.9%) and CA (0.4%) as that of present study. However, we recorded more cases of HSIL and LSIL.

Gupta et al.,[13] studied 27367 cases with mean age of 41.7 years reported an overall incidence of epithelial abnormalities as 5.64%. Abnormal cervical cytology lesions such as ASCUS, ASC-H, LSIL, HSIL, carcinoma and AG-US represented 3.36%, 0.22%, 1%, 0.34%, 0.41% and 0.14%, respectively. The mean age and CA cases were concordant with the present study. The low figures in the present study may be due to the larger samples and widely used screening programs.

Magdy et al.,[14] (2011) studied 1171 cases with mean age of 42.8 years reported an overall incidence of epithelial abnormalities as 4.95%. Abnormal cervical cytology lesions such as ASCUS, ASC-H, LSIL, HSIL and carcinoma represented 2.99%, 0.6%, 0.09%, 0.68% and 0.34, respectively.

This may be explained by the different conditions prevalent in each study, with less prevalence in the urban studies as they may represent situations of good screening programmes and also the hygienic conditions could not be guaranteed in the settings of low resources.

As this study was conducted in a tertiary care hospital, there was relatively high prevalence of epithelial abnormalities.

The results of current study is quite high in comparison to some of the available literature. The reason may be that the study is carried out in symptomatic as well as clinically suspicious patients, thus more chances of positive results.

In a hospital based study done by Banik et al., (2011) showed 0.18% of cases were ASCUS, 6.36% cases were LSIL, HSIL included 1.18% and 0.35% cases were diagnosed as invasive cervical cancer. These results were almost similar to the present study (Table 4 and Graph 4).

Limitations of the study

As with all screening tests, cervical cytology is also limited by both false negative and false positives. To bring down false negative and false positive rates pathologists should have sufficient time to screen every slide completely and thoroughly with knowledge, concentration, skilled judgment and a relaxed mind.

CONCLUSION

The regular screening of population by "PAP" smear is a cost-effective method for early detection of premalignant and malignant cervical lesions and down staging of carcinoma cervix. The procedure is simple, inexpensive and can be performed in the outpatient department. Hence, it should be recommended routinely as a method of improving reproductive health. Considering the high rate of cervical neoplasia in developing countries, there is a great need for an organised, well-targeted screening program. It should include periodic gynaecological examinations along with education of women about danger signals. It will certainly bring down the high mortality due to carcinoma cervix and above all will alleviate the suffering caused by this disease.

ACKNOWLEDGMENT

The completion of this study provides a welcome opportunity to sincerely acknowledge the guidance and personal support extended too many kind souls during the course of my study like my professors, mentor, colleagues, family, friends and patients.

Dr. Ajay Gupta., Dr. Shashi Sajnani, Dr. Dharmendra Garg.

REFERENCES

1. Brisson M and Drolet M. Global elimination of cervical cancer as a public health problem. Lancet Oncol. 2019;20(3):319-321. https://doi.org/10.1016/S1470-2045(19)30072-5
2. Jayant K, Nene BM, Badwe RA, Panse NS, Thorat RV and Khan FY. Rural cancer registry at Barshi, Maharashtra and its impact on cancer control. Natl Med J India. 2010;23(5):274-277.
3. Ahuja P and Reddy D. Carcinoma of cervix-a statistical study on review of 3081 cases. Indian J Obstet Gynaecol. 1963;13:511-520.
4. Miller AB, Nazeer S, Fonn S, Brandup-Lukanow A, Rehman R, Cronje H, et al. Report on consensus conference on cervical cancer screening and management. Int J Cancer. 2000;86(3):440-447. https://doi.org/10.1002/(sici)1097-0215(20000501)86:3<440:aid-ijc22>3.0.co;2-a
5. Bhatia R, Goel S, Pal S and Sareen AR. Down staging of carcinoma cervix by Pap smear in high risk women. Obstet Gynaecol. 2001;4(1) 36-29.
6. Wilkinson EJ. Pap smears and screening for cervical neoplasia. Clinl Obstet Gynecol. 1990;33(4):817-825. https://doi.org/10.1097/00003081-199012000-00017
7. Ranabhat SK, Shrestha R and Tiwari M. Analysis of abnormal epithelial lesions in cervical Pap smears in Mid-Western Nepal. J Pathol Nepal. 2011;1(1):30-33. https://doi.org/10.3126/jpn.v1i1.4447
8. Van der Graaf VD and Voolis GP False negative rate in cervical cytology. J Clin Pathol. 1987;40(4):438-442. https://doi.org/10.1136/jcp.40.4.438
9. Klinkhaemer PJ, Vooijs GP and de Haan AF. Intraobserver and interobserver variability in the diagnosis of epithelial abnormalities in cervical smears. Acta Cytol. 1988;32(6):794-800.
10. Lozowski MS, Mishriki Y, Talebian I and Solitare G. The combined use of cytology and colposcopy in enhancing diagnostic accuracy in preclinical lesions of the uterine cervix. Acta Cytol. 1982;26(3):285-291.
11. Mostafa MG, Srivannaboon S and Rachanawutanon M. Accuracy of cytological findings in Abnormal cervical smears by cytohistologic comparison. Indian J Pathol Microbiol. 2000;43(1):23-29.
12. Elhakeem HA, Al-Ghamdi AS and Al-Maghrabi JA. Cytopathological pattern of cervical Pap smear according to the Bethesda system in Southwestern Saudi Arabia. Saudi Med J. 2005;26(4):588-592.
13. Gupta S, Sodhani P, Halder K, Chachra KL, Sardana S, Singh V, et al. Spectrum of epithelial cell abnormalities of uterine cervix in a cervical cancer screening programme: Implications for resource limited settings. Eur J Obstet Gynecol Reprod Biol. 2007;134(2):238-242. https://doi.org/10.1016/j.ejogrb.2006.07.022
14. Balaha MH, Al Moghannum MS, Al Ghowinem N and Al Omran S. Cytological pattern of cervical papanicolaou smear in eastern region of Saudi Arabia. J Cytol. 2011;28:(4):173-177. https://doi.org/10.4103/0970-9371.86343

Authors' Contributions:
AG- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **PS**- Design of study, statistical analysis and interpretation; **KD**- Prepared draft of manuscript , review of Literature, implementation of study protocol, data analysis, manuscript preparation and submission of original article; **SM**- Review manuscript; **MS** -Literature survey and preparation of figures; **YG**- Coordination and manuscript revision.

Work attributed to:
Department of Pathology, Government Medical College, Kota, Rajasthan, India.

Orcid ID:
Ajay Gupta - https://orcid.org/0000-0002-9275-4111
Pushpendra Singh - https://orcid.org/0009-0009-1624-5049
Krishna Dubey - https://orcid.org/0000-0002-4949-9098
Sushil Mewara - https://orcid.org/0009-0006-1997-1239
Mayank Sharma - https://orcid.org/0009-0008-2532-5369
Yogesh Gupta - https://orcid.org/0009-0005-4516-8880

Source of Support: Nil, **Conflicts of Interest:** None declared.