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DIAGNOSTIC ACCURACY OF PAPANICOLAOU'S SMEAR IN DETECTION OF CYTOLOGICAL ABNORMALITIES OF CERVIX

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Abstract

Objective: To study the accuracy of Pap test in detecting cytological abnormalities of the cervix and comparing with histopathological findings that is considered to be the gold standard. Methods: The present study is a prospective clinical study carried out in the department of Obstetrics and Gynaecology, SNMC & HSK Hospital and research centre, Bagalkot from 1st December 2015 to 30th November 2016 in 324 symptomatic women. All were subjected to Pap test, Colposcopy and Colposcopic directed biopsy. Patients were given appropriate treatment as per their Histopathological findings. Result: In present study the sensitivity of Pap smear was found to be 32.43%, specificity 90%, Positive predictive value 48.98%, Negative predictive value of 81.82%, and an overall Accuracy of 76.85%. Conclusion: Pap smear is simple, acceptable, cost effective and a non-invasive test for early detection and management of cervical cancer. Regular screening should be advised to the patients. However the sensitivity of Pap smear test is enhanced by Colposcopy and or HPV testing strategy. Regular screening should be advised to the patients. Government should take appropriate steps to encourage this screening method through National Programmes.

Keywords: Pap smear, Sensitivity, Specificity, Colposcopy, Colposcopic directed biopsy

INTRODUCTION

Globally, every year 5, 27, 624 women are diagnosed with cervical cancer and 2, 65, 672 die from disease (Ref: WHO ICO 2017). Cervical cancer is the fourth most frequent cancer among women in the world and is the second most common cause of death from cancer in women. Fortunately, the incidence of cervical cancer has decreased by more than 50% in the past 30years and more, largely due to the increasing use of cervical cancer screening with cervical cytology. In India, a woman dies every two seconds due to cervical cancer and is the second leading cause of death in women. There are 1, 22, 800 new cases and 67,500 women succumb to the disease annually (2016). Indian women face a 2.5% cumulative life time risk of suffering from cervical cancer and 1.4% cumulative death risk from cervical cancer [1]. Every fourth woman in world suffering from cervical cancer is an India. The cases are on a rise, especially

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

in the rural population. As per the information from Cancer Registry in Barshi, in urban areas cancer cervix accounts for 40% of cancers while in rural areas it accounts for 65% of cancers. Accesses to health center and awareness of screening programme have seen a reduction of cervical cancer incidence in urban population. In fact, the incidence of cervical cancer in the United States has decreased from 14.8 cases per 1, 00, 000 women in 1975 to 6.5 cases per 100,000 women in 2012. This corresponds to approximately 10,000 new diagnoses and 4,000 deaths attributable to the disease annually in this country. Although worldwide cervical cancer rates have decreased dramatically with the increase in screening efforts, incidence and prevalence in developing countries remains high due to lack of screening programmes, with approximately 80% of all cervical cancer deaths occurring in the developing world. India, China, Brazil, Bangladesh, Nigeria accounts to more than half the burden of global deaths due to cervical cancer. Australia is last on the list [2-4]. The incidence of cervical cancer is much higher in developing countries where resources are limited for health care and screening programme are not implemented on a strict basis. It is estimated that this incidence is going to rise. By 2020, there will be approximately 6.39 lakh cases from the developing world and only 92,000 cases from the developed world.1 Health care providers in developing countries regularly see women with advanced, incurable cervical cancers. At this late stage, there is a little they can do to save women‘s lives. Even the drugs designed to ease the pain related to the cancer are also not freely available in the developing countries [5]. Yet, cervical cancer can be readily prevented, even in the women at high risk for the disease, through screening and treatment using relatively simple techniques.

When precancerous changes in cervical tissues are found and the abnormal tissues successfully treated, a woman will not develop cancer. The mainstay of cervical cancer screening for the last 60years and more has been the Papanicolaou‘s test [6]. The Papanicolaou‘s test, also known as the Pap test or the Pap smear, was developed in the 1940s by Georgios Papanikolaou. It involves exfoliating cells from the transformation zone of the cervix to enable examination of these cells microscopically for detection of cancerous or precancerous lesions.

AIMS & OBJECTIVES OF THE STUDY

- Accuracy of Pap test in detecting premalignant lesions of cervix in symptomatic women
- To obtain Colposcopic directed biopsy from suspicious areas
- To provide guidelines for appropriate treatment and follow up

METHODOLOGY MATERIAL AND METHODS:

This prospective study was conducted in the Department of Obstetrics and Gynaecology SNMC & HSK Hospital and Research Centre Bagalkot from 1 st December 2015 to 30th November 2016 after taking approval from the review board of Institutional Ethical Clearance committee.

SAMPLE SIZE CALCULATION: done by using Open Epi software Version 2.3.1 At 95% confidence level, 80% power of the study. Specificity for detecting abnormalities by Pap smear: 34.6%. Specificity for detecting abnormalities by Colposcopy: 50%. Sample size was found to be 324. The material for the present study was collected from 324 women attending OPD who

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

met the inclusion criteria and gave informed and written consent after a brief explanation of the need for Pap smear, Colposcopy & Colposcopic biopsy.

Inclusion criteria:

1. Women > 18 years, symptomatic with abnormal cervix

2. Married women

Exclusion criteria:

1. Pregnant and puerperal women

2. Clinical visible growth on the cervix

3. Prior total hysterectomy

4. Women who are not sexually active

5. Past history of cervical neoplasia

6. During menstrual cycle

Procedure: A detailed history including age, socioeconomic status, education, parity, age of marriage were obtained. Details regarding her complaints were obtained. Menstrual and Obstetric history and history of any previous surgery was noted. General examination and systemic examination were done and information was noted on a pretested proforma.

Examination: Patient was placed in dorsal position, labia separated and the Cusco's self-retaining speculum gently inserted without the use of lubricant or jelly. The cervix was exposed and visualized for any gross pathological features under adequate light and findings were recorded.

Pap smear: After preliminary inspection of the cervix, a Pap smear was taken using Ayre's spatula. The squamocolumnar junction was scraped with Ayre's spatula by rotating full 360 degree. The scrapings were evenly spread on a glass slide and immediately fixed by dipping in the jar containing equal parts of 95% ethyl alcohol and ether and transported to cytopathological laboratory. Smears were analyzed by a senior pathologist. Revised Bethesda system was used for describing Pap smear results. After Pap smear, all women were subjected to Colposcopic assessment. Colposcopy was performed using digital ColpoITPro using manual and automatic focus with 1- 55x magnification with depth view of Ø200mm-5mm. Procedure done using normal saline, green filter, 5% dilute acetic acid and Lugol's iodine. Findings were recorded and colposcopy diagnosis was made based on Modified Reid Colposcopic Index (RCI). Reid et al (1983) defined 3 objective categories based on Colposcopic index using four colposcopic signs i.e. color, margin (including surface contour), vascular pattern and iodine response. Each category is offered scores of 0-2. Then summation of scores is done [8].

0-2: Predictive of minor lesion (CIN I or HPV)-grade 1

3-5: Middle grade lesion (CIN I-II)-grade 2

6-8: Significant lesion (CIN II-III) – grade 3

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

Feature	0 Point	1 Point	2 Points
Color of Acetowhite (AW) Area	☐ Low Intensity Acetowhitening ☐ Snow White ☐ Shiny AW ☑ Indistinct AW ☑ Transparent AW ☐ AW Beyond Transformation Zone	☐ Intermediate shade - grey/white color AW and shiny surface (most lesions should be scored in this	☐ Dull ☐ Opaque ☐ Oyster White ☐ Grey
AW Lesion Margin & Surface Configuration	☐ Feathered Margins ☐ Angular Lesions ☑ Jagged Lesions ☐ Flat Lesions with Indistinct Margins ☐ Microcondylomatous Surface ☐ Micropapillary Surface ☐ Satellite Lesions Beyond the Margin o Transformation Zone	☐ Regular-shaped, symmetrical lesions with smooth, straight outlines	☐ Rolled ☐ Peeling ☑ Internal demarcations (a central area of high-grade change and peripheral area of low-grade change)
Vessels	☐ Fine/Uniform-Calibre Vessels ☐ Poorly Formed Patterns of Fine Punctation and/or Fine Mosaic ☐ Vessels Beyond the Margin of the Transformation Zone ☐ Fine Vessels within Micro-condylomatous or Micropapillary	☑ Absent vessels	☐ Well defined coarse punctation or mosaic ☐ Sharply demarcated - and randomly and widely placed
Iodine Staining	☐ Positive iodine uptake giving mahogany-brown color ☑ Negative uptake of insignificant lesion, i.e., yellow staining by a lesion scoring 3 points or less on the first 3criteria ☐ Areas beyond the margin of the transformation zone, conspicuous on colposcopy, evident as iodine-negative	☐ Partial iodine uptake by a lesion scoring 4 or more points on above 3 categories - variegated ☐ Speckled Appearance	☐ Negative iodine uptake of significant lesion, i.e., yellow staining by a lesion already scoring four points or more on the first three criteria

Table 1: Modified Reid's Colposcopic score.

Colposcopic guided biopsy: Biopsy was taken from abnormal area under colposcopic guidance using cervical punch biopsy forceps. Four quadrant biopsy was taken from ectocervix at the sqamocolumnar junction if no abnormality was detected on colposcopy. The specimen was sent for Histopathological examination in formalin solution. Slides were analyzed by senior pathologist. Biopsy results were categorised as 1. Cervicitis 2. ASCUS, ASC-L, ASC-H 2. LSIL correlating with Mild dysplasia (CIN-I) 3. HSIL correlating with moderate to severe dysplasia (CIN-II and CIN III) 4. Squamous cell carcinoma 5. Adenocarcinoma Statistical Analysis Data were entered in MS Excel and analyzed in SPSS Version 22. Descriptive statistics for the qualitative data i.e. Percentages were done. The Accuracy, Sensitivity, Specificity, positive predictive value, Negative predictive value, False positive rate, False negative rate with 95% confidence interval were calculated for Pap smear comparing with histopathological results which is considered the gold standard.

RESULTS The Objectives of the study was to correlate the findings in women with unhealthy cervix by Pap smear cytology and colposcopy, colposcopic directed biopsies in detecting the premalignant and malignant lesions of the cervix. Outcome variable: ASCUS, LSIL, HSIL, Carcinoma. Explanatory variable: Parity, Socioeconomic status, age. The 324 women who were recruited in the study belonged to age group of 21 - 65 years.

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

Age	No of cases	Percent
21-30	106	32.7
31-40	99	30.6
41-50	81	25.0
51-60	33	10.2
>60	5	1.5
Total	324	100.0

Table 2: Age distribution

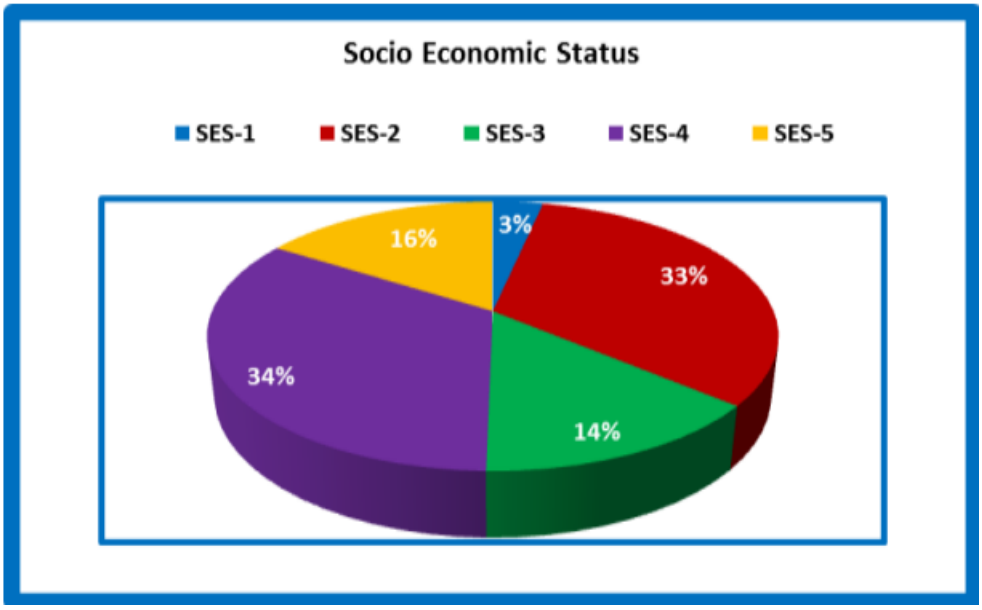


Figure 1: Socio Economic Status

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

Symptoms	No of cases	Percent
WDPV	202	62.3
Pain abdomen	69	21.3
Menorrhagia	20	6.2
Low backache	12	3.7
Polymenorrhoea	9	2.8
Postmenopausal	5	1.5
Postcoital bleeding	5	1.5
Oligomenorrhagia	2	0.6
Total	324	100.0

Table 3: Symptom distribution

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

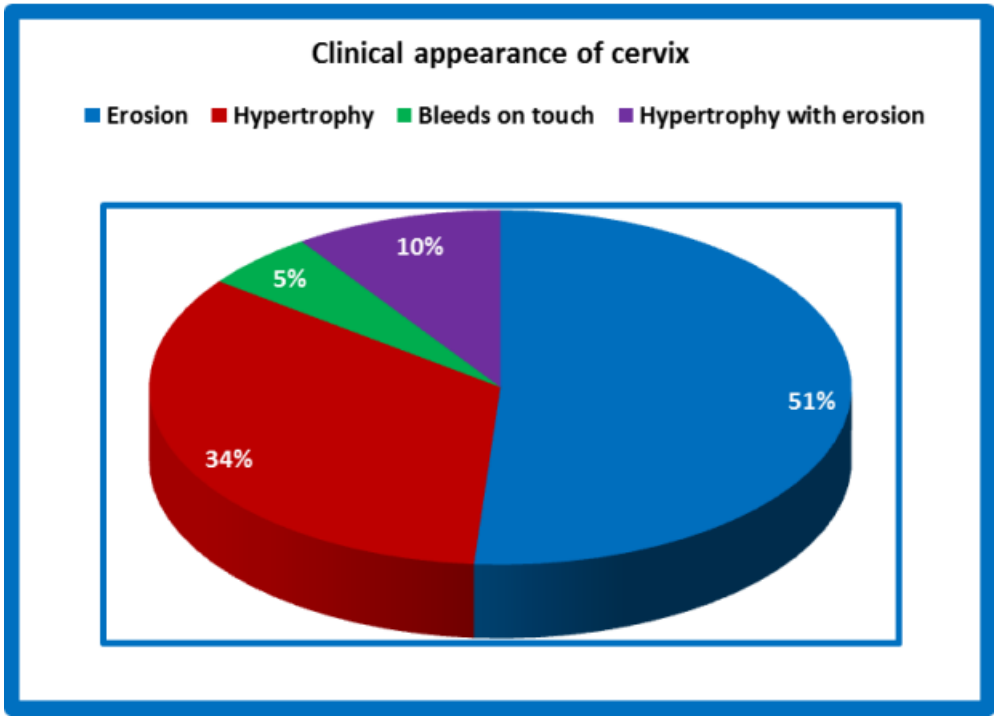
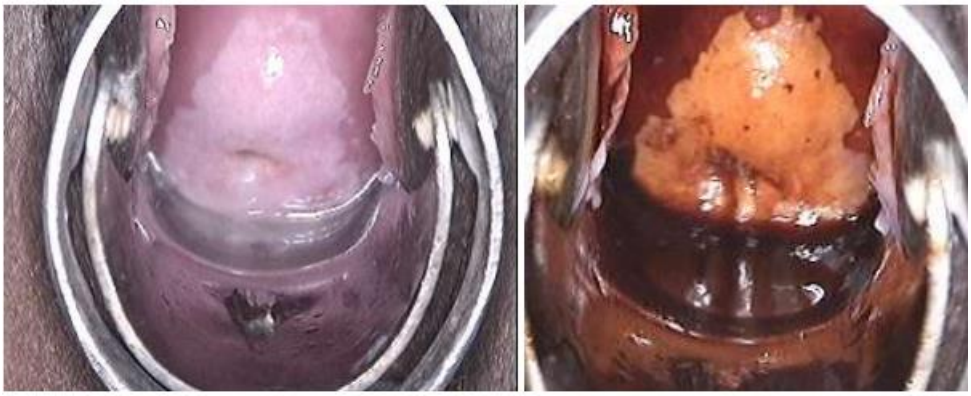


Figure 2: Clinical appearance

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

PAP smear findings	No of cases	Percent
NILM	253	78.1
ASCUS	13	4.0
ASC-H	7	2.2
LSIL	33	10.2
HSIL	13	4.0
SSC	1	0.3
AGC	2	0.6
Unsatisfactory	2	0.6
Total	324	100.0

Table 4: PAP smear clinical findings



(a) (b)

Vol. 20, No. 1. (2024)
E ISSN: 1672-2531

Figure 3: Colposcopic picture showing (a) acetowhite areas with 5% acetic acid (b) unstained areas with lugol's iodine in (CIN III).

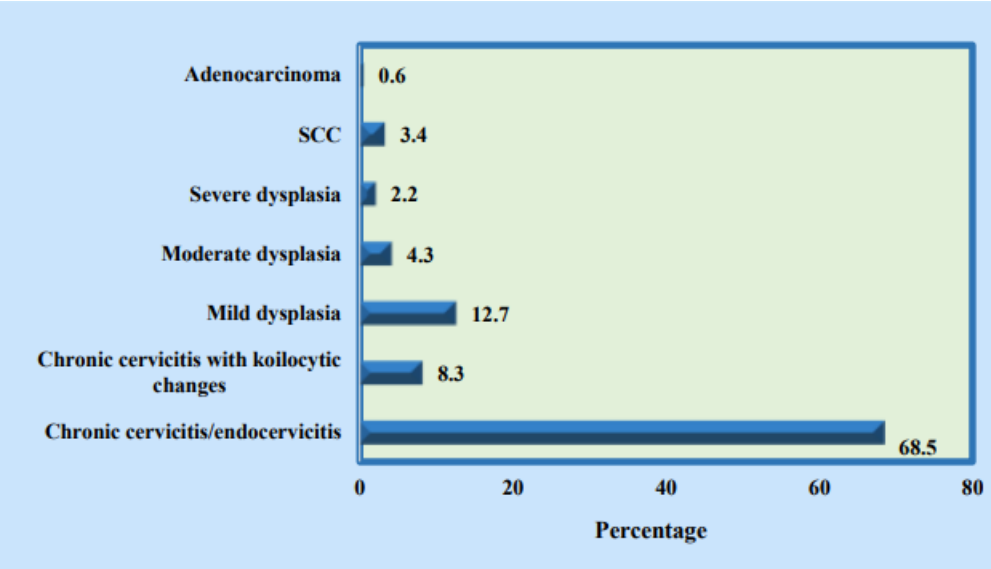


Figure 4: Histopathological findings

Pap smear	Chronic cervicitis / endocervicitis	Chronic cervicitis with koilocyte	Mild dysplasia	Moderate dysplasia	Severe dysplasia	SCC	Adenocarcinoma	Total
Unsatisfactory	-	-	1	-	-	-	1	2
NILM	201	9	31	8	2	2	-	253
ASCUS	4	6	3	-	-	-	-	13
ASC-H	3	1	2	-	1	-	-	7
LSIL	10	8	4	5	3	3	-	33
HSIL	4	2	-	1	1	5	-	13
SSC	-	-	-	-	-	1	-	1
AGC	-	1	-	-	-	-	1	2
Total	222	27	41	14	7	11	2	324

Table 5: Correlation of Pap with Histopathological report

Discussion:

Pap test has dramatically declined the incidence of cervical cancer, a major health burden especially in the underdeveloped nations such as Latin America and Southern Asia. Age between 35-55years age group is the most vulnerable. Screening should be increased based on resources as cervical cancer is a preventable disease [9]. In developing countries several attempts were made and targeted a smaller group by camp approach, hospital based screening, high risk screening but was not successful. The reason is difficulties in launching population based programs. The present study was carried out in the Department of Obstetrics and Gynaecology, SNMC and HSK Hospital Bagalkot from 1st December 2015 to 30th November 2016 [10]. About 324 women were recruited. Maximum number of cases was found to be less than 40 years. Mean age was 37.71 years. Shalini et al showed the mean age of patients with cancer cervix were 41 versus 32 in patients with benign pathology of cervix. In a study conducted by Vidhya Rani et al mean age for CIN was 41.2 years.2 Many authors have discussed strong influence of multiparity on the risk of cervical cancer as in present study. Kustagi and Fernandez showed the prevalence of CIN was significantly higher in parity of more than 2.54 In the present study majority were para-three and above (54.3%) [11]. In a study conducted by Manjula A, white discharge per vagina was the most common symptom and was seen in 74% cases.55 In present study also the commonest symptom with which the patient presented was white discharge per vaginum(62.3%). This was comparable to study done by Chaudhary RD et.al. In a study conducted by Manjula A, clinical status of cervix in majority of patients was cervical erosion in 54% cases. Similarly in the present study 166(51.2%) of cervical erosion were seen. The most common colposcopic finding was acetowhite areas seen in 40% of cases reported by Manjula A. In the present study 240 cases (74.1%) had acetowhite areas.55 In a study conducted by Manjula A, on Pap smear examination, NILM was found in 60% cases, LSIL IN 14% cases, HSIL in 12% cases and SCC in 4% cases. In the present study, 8.1% cases reported as NILM and frank malignancy reported in 0.9% cases. Low grade SIL and HSIL was reported in 10.2% and 4.0% respectively [12]. In the present study, maximum number of cases on histopathological examination were those of infection, among them majority had chronic cervicitis (68.5%). Cervical intraepithelial lesions were seen in 19.3% cases. CINI is seen in 12.7% cases and CIN II and CIN III were reported in 6.5% cases. Squamous cell carcinoma and adenocarcinoma were reported in 4% cases. Dhakal R, Makaju reported frank malignancy in 5.3% cases.17 Our study shows adenocarcinoma in 0.6% cases only and Bodel and Brar reported adenocarcinoma was seen in 2% of cases [13-15].

CONCLUSION

The concept of pre-invasive disease of the cervix which denotes changes that are confined to the cervical epithelial cells was first introduced in 1947. Early detection of pre-invasive disease has the potential in decreasing the disease burden and helps in reducing cancer related morbidity and mortality.

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Vol. 20, No. 1. (2024)
E ISSN: 1672-2531