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Original Research Article

"A Comparative Study of Visual Inspection with Acetic Acid and Papsmear in Screening Cervical Intraepithelial Neoplasia"

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Abstract

Background: Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. Almost 70% of the global burden of cervical cancer falls in areas with lower levels development, and more than one-fifth of all new cases are diagnosed in India. Cancer cervix has been considered preventable because it has a long pre-invasive state and availability of screening programs and treatment of pre- invasive lesion is effective. No form of cancer documents the remarkable effects of screening, early diagnosis and curative therapy on mortality rate in a better way than does cancer cervix. ***Aim:*** To compare the diagnostic value of Visual Inspection of Cervix with Acetic Acid with Papsmear for screening of Cervical intraepithelial lesions keeping Histopathology as gold standard. ***Material and Method:*** It is a cross sectional and comparative study of 522 women who fulfilled inclusion criteria attending outpatient Department of Obstetrics and Gynaecology at St Philomena's Hospital for a period of 2 years (December 2016 to November 2018). Both pap smear and VIA are done in these cases. In positive cases, colposcopy guided cervical biopsy done and sent for histopathological studies. All results compiled and analyzed. Sensitivity, specificity, positive predictive value and negative predictive value are calculated and compared for pap smear, visual inspection with acetic acid by taking colposcopy guided cervical biopsy (histopathology) results as gold standard. ***Result and observations:*** In the present study , diagnostic values of VIA are comparable with papsmear with sensitivity of 86.6% and 80.6% respectively, specificity of 97.8% and 98.9% respectively, PPV of 85.3% and 91.5 % respectively and NPV of 98% and 97.2% respectively with histopathology as the gold standard. ***Conclusion:*** VIA has comparable results to Pap smear regarding its sensitivity, specificity, positive predictive value and negative predictive value and can be used as good alternative to pap smear in mass screening of large population. VIA can be combined with Pap smear to improve the efficacy of screening procedures in detection of pre-cancerous and cancerous lesions of cervix.

Keywords: Cervical cancer, Pap smear, VIA, Histopathology, sensitivity, specificity, positive predictive value and negative predictive value.

INTRODUCTION

Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women with an estimated 570,000 cases and 311,000 deaths in 2018 worldwide. Cervical cancer ranks second in incidence and mortality in lower Human Development Index settings [1]. Almost 70% of the global burden of cervical cancer falls in areas with lower levels development, and more than one-fifth of all new cases are diagnosed in India. For women in India, cervical cancer is the second most common cancer. Cervical cancer is also the second most common cause of cancer deaths when both genders are combined [2]. Cancer cervix has been considered preventable because it has a long pre-invasive state and availability of screening programs and treatment of pre- invasive lesion is effective[3]. No form of cancer documents the remarkable effects of screening, early diagnosis and curative therapy on mortality rate in a better way than does cancer cervix [4].

The introduction of cervico-vaginal cytology as a means to detect precancerous lesions of cervix has played central role as a tool in prevention of cervical cancer [5]. The decline in mortality and increase in detection frequency of early cancer and precancerous lesions is due to effectiveness of Pap test in detecting cervical cancer and accessibility of cervix to

colposcopy and biopsy [4].Papanicolaou (PAP) smear is a simple, safe, non-invasive and effective method for detection of pre-cancerous, cancerous and non-cancerous changes in the cervix and vagina [6]. It has been known that squamocolumnar junction of cervix is the site of predilection for carcinoma. In an effort to study early malignant changes in squamous cells thrown off from this focus, spatula cytology technique was developed and this is a means of collecting cells before their exfoliation [7].

Colposcopy is a worldwide accepted method for detection of early cervical neoplasia [8]. Colposcopy is close examination of vagina and cervix. It is diagnostic procedure to examine an illuminated magnified view of the cervix and tissue of the vagina and vulva. It is low power, binocular microscope for study of surface epithelium and underlying connective tissue stroma along with vascular pattern [9]. It provides an enlarged view of the areas, allowing colposcopist to visually distinguish normal from abnormal appearing tissue and take directed biopsies for further examination. Common problems encountered in colposcopy are lack of expertise, interpretation difficulties and failure to follow standard protocol [10]. The use of acetic acid during visual examination of the cervix, termed visual inspection with acetic acid, has been advocated as an alternative screening method to Pap smears in developing countries. The attractive features of VIA include low cost, simple administration, real time screening, of results and accuracy comparable to good quality Papsmears [11,12].

The present study is being undertaken to assess and compare the sensitivity, specificity, predictive accuracy of visual inspection of cervix with acetic acid and Pap smear in screening of cervical intraepithelial lesions keeping histopathology as the gold standard.

AIMS AND OBJECTIVES

To compare the diagnostic value of Visual Inspection of Cervix with Acetic Acid with Papsmear for screening of cervical intraepithelial lesions keeping Histopathology as gold standard.

MATERIALS AND METHODS

The present study is a Cross sectional, Hospital based, Comparative study carried out for 2 years (from December 2016 to November 2018) in 522 women who fulfilled selection criteria attending outpatient Department of Obstetrics and Gynaecology at St Philomena's Hospital, Bangalore.

Sample size Calculation

By taking 6% absolute precision, with 95% Confidence limits, sample size was calculated using the formula

$$\text{Sample Size} = \frac{Z^2 * p * q}{L^2}$$

Z score = 1.96,
Z is the Standard NormalVariate for 95% of Confidence Interval.
p = 89%, q = 100-p = 11%

L = Absolute Precision or Maximum Allowable Error = 3%

Accordingly, Sample size calculated was 418. With Design Effect of 1.25, Final Sample Size calculated to be 522. Hence 522 study subjects were recruited for the study. Sampling technique: Systematic Randomised Sampling

SELECTION CRITERIA

Inclusion Criteria

1. Women in age group of 18 years to 60 years attending outpatient Department with or without symptoms.
2. Women with symptoms like profuse white discharge, post coital bleeding, menstrual irregularities, post-menopausal bleeding.

Exclusion criteria

1. Unmarried and sexually inactive women.
2. Women below 18 years and above 60 years.
3. Women with active infection at the time of examination.
4. Women with frank invasive cervical cancer
5. Women with active vaginal bleeding at time of examination.

METHODOLOGY

1. After taking a detailed clinical history, informed written consent is taken for the screening
2. Patient was put in dorsal position.
3. Unlubricated sim's speculum was inserted into the vagina and cervix is examined
4. Two smears were taken with Ayre's spatula by gentle scraping at squamocolumnar junction, exfoliated material was transferred to two glass slides and fixed with 95% alcohol and stained by Papanicolaou stain. If subsequent pap smear results were abnormal then patient was subjected to colposcopy guided biopsy in separate setting.
5. Subsequently, 5% acetic acid was applied to cervix using a cotton swab. After 1 minute, visual inspection of cervix was done.
6. The results were interpreted as positive with detection of any distinct, opaque, dense or well-defined aceto-white area. If no aceto-white area was recorded or if a whitish appearance was doubtful, the test result was considered negative. The sites and characteristics of the lesions were mapped.

7. In women with positive VIA findings, colposcopy directed biopsy was done in the same setting. Biopsy was done using a punch biopsy forceps from abnormal areas detected under colposcopic guidance. The excised tissue thus obtained was fixed in 10% formalin and was sent for histopathological examination.
8. All results were then compiled and analyzed. Sensitivity, specificity and predictive accuracy was then calculated for pap smear and VIA by taking colposcopy guided cervical biopsy (histopathology) results as gold standard.

DATA ANALYSIS AND INTERPRETATION

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Sensitivity, Specificity and Predictive Accuracy was calculated for VIA & Pap smear by taking Histopathology (cervical biopsy report) as Gold Standard. Level of significance was set at 0.05.

RESULTS & OBSERVATIONS

The present study was carried out with an aim to compare the efficacy of Visual inspection of cervix with acetic acid and Papsmear for screening of cervical intraepithelial lesions keeping histopathology as gold standard. The observations of the study were discussed below.

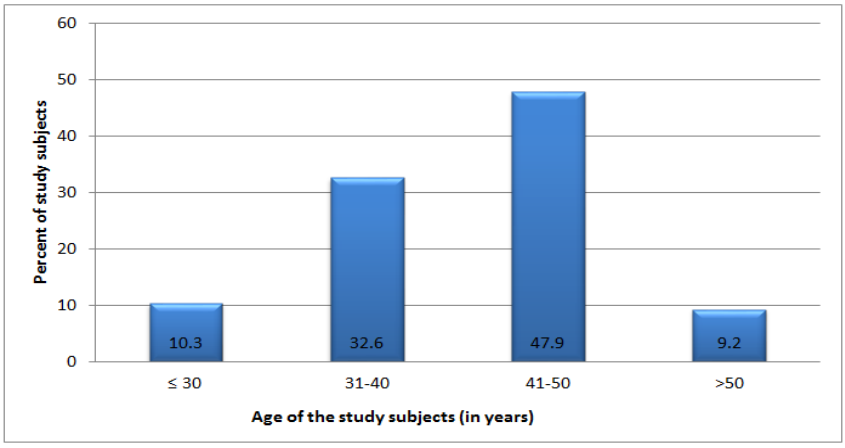

Fig-1: Distribution of Study Subjects according to their Age Group

The women studied were mostly in the age group 41-50 years accounting for 47.9% of total women studied. 32.6% were in age group of 31-40 years, 10.3% were in age group of ≤ 30 years , 9.2% were in age group of >50 years.

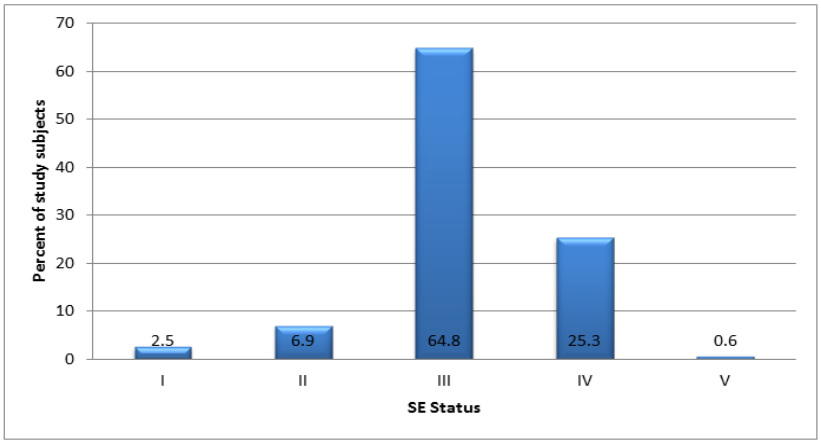

Fig-2: Distribution of Study Subjects according to the Socio-Economic Status

Most of the women studied belong to lower middle class, accounting for 64.8% of total women studied. 25.3 % belonged to upper lower class. 6.9% belonged to upper middle class, 2.5 % belonged to upper class and 0.6% belonged to lower class.

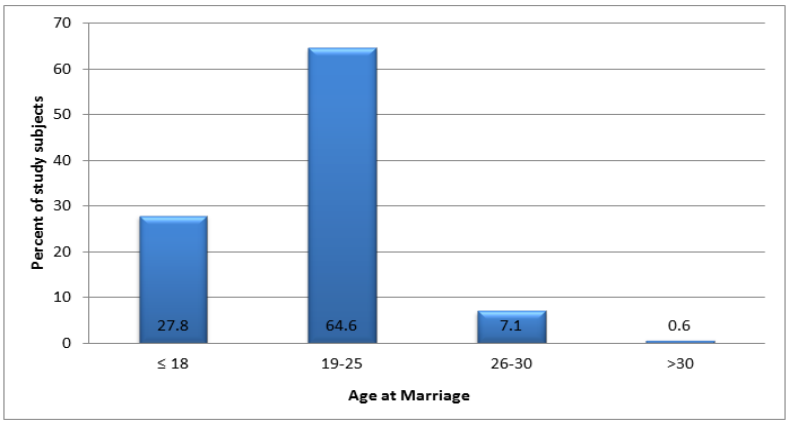

Fig-3: Distribution of Study Subjects according to the Age at Marriage

Most of the women studied were married between 19-25 years of age accounting for 64.6 % of total women studied. Women married at or before 18 years of age were 27.8%, those who married between 26-30 years were 7.1% and those who married after 30 years were 0.6% of total women.

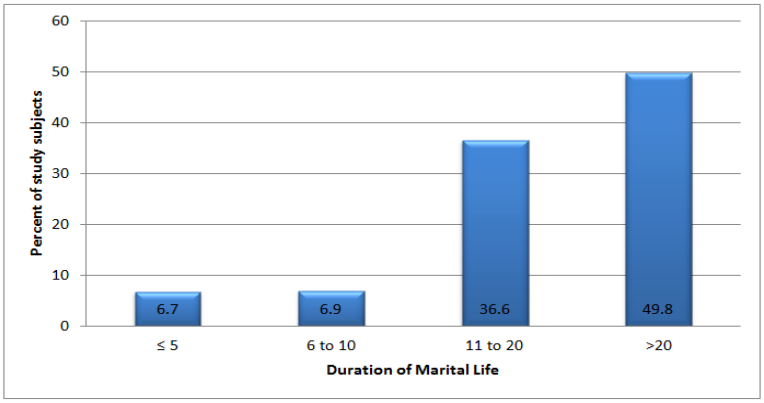

Fig-4: Distribution of Study Subjects according to the Duration of Marital Life

Duration of marital life of most of women studied was >20 years accounting for 49.8%, 36.6% for duration of 11-20years, 6.9% for duration of 6-10 years, 6.7% for duration of ≤ 5 years.

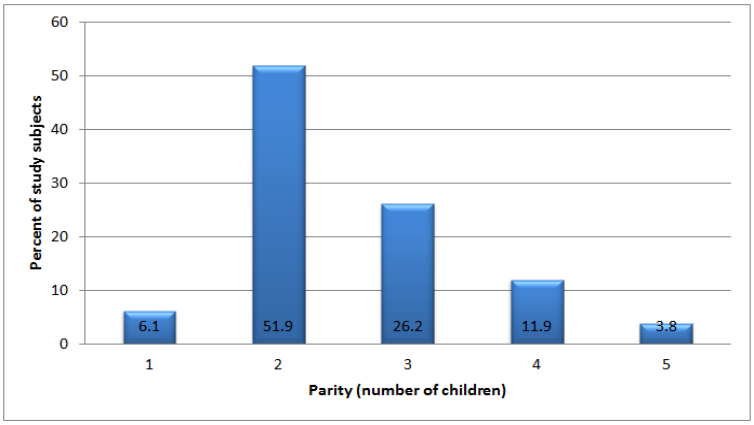

Fig-5: Distribution of Study Subjects according to the Parity

Most of women studied had 2 children accounting for 51.9% of women studied. Women with 3 children were 26.2%, women with 4 children were 11.9%, women with 1 child were 6.1% and women with 5 children were 3.8% of total women studied.

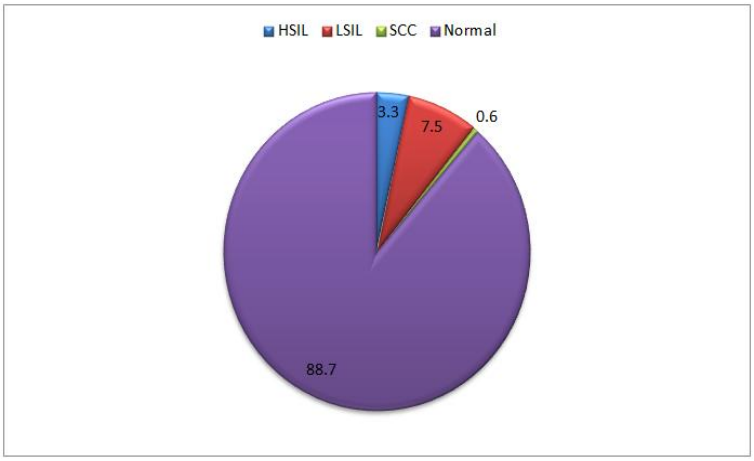

Fig-6: Distribution of Study Subjects according to Pap smear

In most of the women studied, Pap smear report was normal accounting for 88.7%, 7.5% it was LSIL, 3.3% it was HSIL and 0.6% it was SCC.

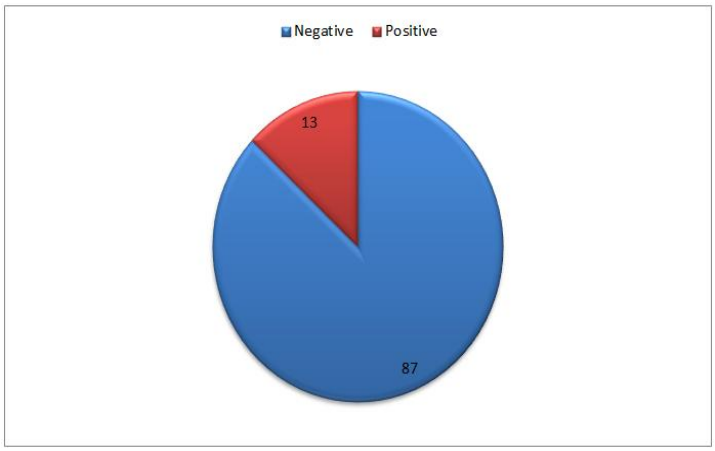

Fig-7: Distribution of Study Subjects according to the VIA

In most of the women studied, VIA was negative accounting for 87% and among 13% it was positive.

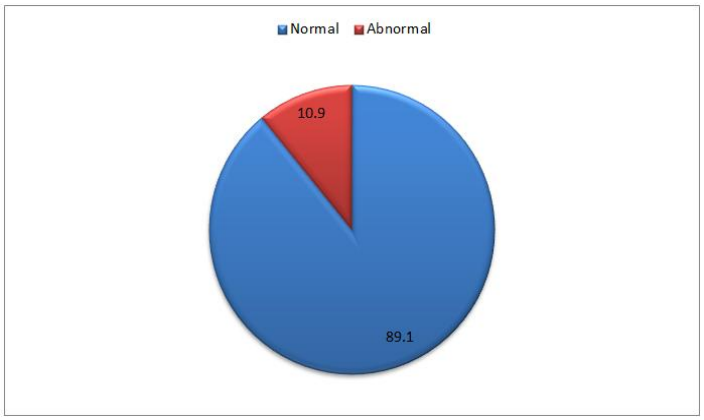

Fig-8: Distribution of Study Subjects according to the Colposcopy

In most of the women studied, colposcopy findings were normal accounting for 89.1% and 10.9% findings were abnormal.

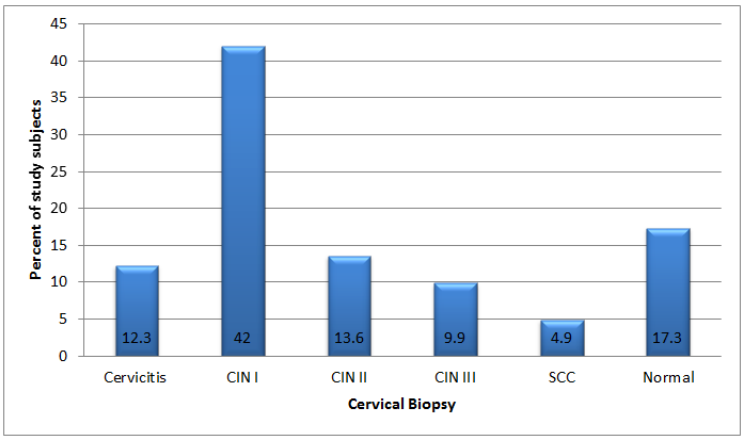

Fig-9: Distribution of Study Subjects according to the Cervical Biopsy

Most of women who have undergone cervical biopsy, report was CIN I accounting for 42%, 17.3% report was normal, 13.6% report was CIN II ,12.3% report was cervicitis , 9.9% report was CIN III and 4.9% report was SCC.

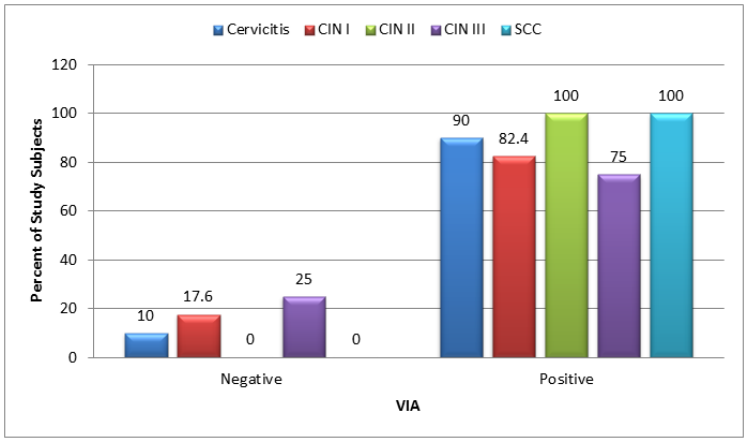

Fig-10: Distribution of Cervical Biopsy Results according to VIA

Among women with cervicitis as cervical biopsy result, 10% VIA was negative and 90% VIA was positive. Among women with CIN I as cervical biopsy result, 17.6% VIA was negative and 82.4% VIA was positive. Among women with CIN II as cervical biopsy result, in none of them VIA was negative and 100% VIA was positive. Among women with CIN III as cervical biopsy result, 25% VIA was negative and 75% VIA was positive. Among women with SCC as cervical biopsy result, in none of them VIA was negative and in 100% VIA was positive.

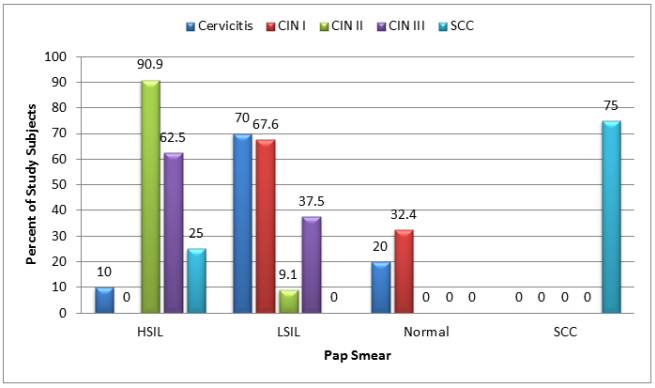

Fig-11: Distribution of Cervical Biopsy Results according to Pap smear

Among women with cervicitis as cervical biopsy result, Papsmear result was HSIL in 10%, LSIL in 70%, normal in 20%. Among women with CIN I as cervical biopsy result, Papsmear result was LSIL in

67.6%, normal in 32.4%. Women with CIN II as cervical biopsy result, Papsmear result was HSIL in 90.9%, LSIL in 9.1%. Women with CIN III as cervical biopsy result, Papsmear result was HSIL in 62.5%, LSIL in 37.5%. Women with SCC as cervical biopsy result, Papsmear result was HSIL in 25%, SCC in 75%.

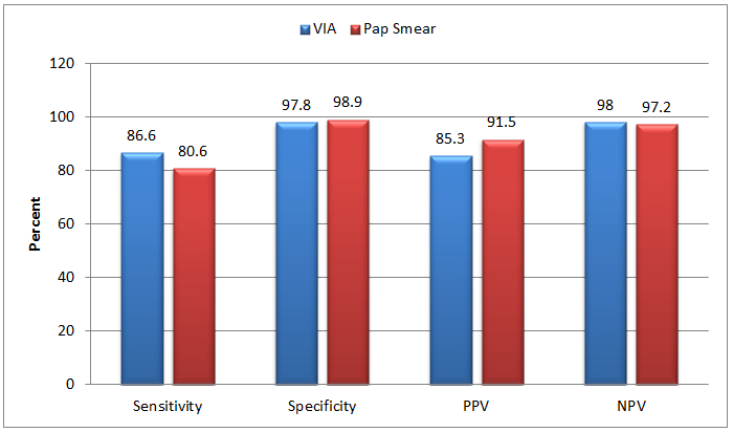

Fig-12: Comparison of sensitivity, specificity and predictive accuracy of Papsmear and VIA

Diagnostic values of VIA are comparable with papsmear with sensitivity of 86.6% and 80.6% respectively, specificity of 97.8% and 98.9% respectively, PPV of 85.3% and 91.5% respectively and NPV of 98% and 97.2% respectively.

DISCUSSION

About 80% cervical cancers occur in developing countries. This disproportionate burden of cervical cancer in such countries is mainly due to the lack of well organised screening programs. Organised and frequently repeated cytological screening has resulted in a substantial reduction of cervical cancer burden in developed countries. Several cervical cancer screening strategies have been proposed which are more cost effective than cytological screening [13].

The ultimate goal of screening for carcinoma cervix is to diagnose preinvasive and preclinical carcinoma cervix. But in low resource countries where organised cytological based cervical cancer screening programs cannot be implemented due to financial , technical and logistic barriers ,low cost technologies like pap smear based approaches have been successfully tested and proposed to address the need to effectively improve and extend screening services in the country [14].

The use of acetoacetic acid during visual inspection of cervix, termed visual inspection with Acetic acid (VIA), has been advocated as an alternative screening method to Pap smears in developing countries because of its low cost, simple administration, immediate availability of results and accuracy comparable to good quality Pap smears [11,12]. Hence the present study was carried out to compare efficacy of visual inspection of cervix with acetic acid and Pap smear in picking up pre-malignant lesions of cervix keeping histopathology as Goldstandard.

Women in the age group of 18 to 60 years were involved in our study similarly Hegdeet al. [15] included women of 20-50 years of age. Mean age of women enrolled in study was 40.83 years and is in consonance with Ghaemmaghamiet al. [16] where it was 42.1 years. Our study period extended over a period of 2 years. Hegdeet al. [15] also conducted their study within the same time frame. The mean parity in our study was 2.55 and is in consonance with Saleh et al. [17] where it is 2.61 .The mean age at marriage in our study was 20.57 years and is in consonance with Pourshadet al. [18] where it was 20 years.. The most common presenting complaint in present study was menstrual irregularity and similar complaint was most common in Hegdeet al. [15] study.

Most of women in present study belong to Lower middle socioeconomic status and is in consonance with Hegdeet al. [15]study most of women belong to Lower middle socioeconomic status. Most of women in present study duration of marital life is greater than 20 years. Mean years of duration of marital life in this study is 20.12 years and is in concurrence with Jeronimo J et al. [19]where it was 20 years.VIA positive rate in our study was 13% and is in concurrence with Consul et al. [20]where it was 13.87%. Pap smear positive rate in our study was 11.3% considering LSIL and above as abnormal and is in consonance with Hegdeet al. [15] study where it was 11.7%. The incidence of biopsy confirmed dysplasia in our study was 10.91% and is in consonance with Sankarnarayananet al. [21] where it was 10.2%.

In the present study VIA was more sensitive (86.6%) than Pap smear (80.6%), however specificity of VIA (97.8%) was lower than Pap smear (98.9%). The PPV of VIA was 85.3% versus 91.5% for Pap smear. The NPV of VIA was 98% versus 97.2% for Pap smear. In similar studies, in Sankarnarayananet al. [21]study sensitivity of VIA (90.1%) was more than

Pap smear (86.2%), specificity of VIA (92.2%) was higher than Pap smear (91.3%). The PPV of VIA was 17% versus 17.2% for Pap smear. The NPV of VIA (99%) was similar to Pap smear (99%). In Ghaemmaghami Fet al.[16] study sensitivity of VIA (74.3%) was more than Pap smear (72%), however specificity of VIA (94%) was lower than Pap smear (90.2%). The PPV of VIA was 68.1% versus 55.1% for Pap smear. The NPV of VIA was 95.5% versus 94.9% for Pap smear.

In Hegdeet al. [15] study VIA was less sensitive (70.8%) than Pap smear (83%), specificity of VIA was also lower (95%) than Pap smear (98%). The PPV of VIA was 96.5% versus 97.9% for Pap smear. The NPV of VIA was 62.9% versus 80% for Pap smear.

In Consul S et al. [20] study VIA and papsmear has equal sensitivity (84.2%), however specificity of VIA (55.2%) was lower than Pap smear (62.1%). The PPV of VIA was 55.2% versus 59.3% for Pap smear. The NPV of VIA was 84.2% versus 85.7% for Pap smear. In Pourasad Set al. [18] study VIA was more sensitive (71.4%) than Pap smear (14.3%), however specificity of VIA and Pap smear was equal (50%). The PPV of VIA was 35.7% versus 10% for Pap smear. The NPV of VIA was 81.8% versus 60% for Pap smear. In Saleh et al. [17] study VIA was more sensitive (90%) than Pap smear (50.1%), however specificity of VIA was lower (37%) than Pap smear (93.1%). The PPV of VIA was 52% versus 89.3 % for Pap smear. The NPV of VIA was 81% versus 65.6% for Pap smear.

Table-1: Comparison of Diagnostic Values of VIA and Pap smear with other studies

Studies	Screening test	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
Sankarnarayananet al. [21]	**VIA**	90.10	92.2	17.0	99.0
	Papsmear	86.2	91.3	17.2	99.0
Ghaemmaghami Fet al.[16]	**VIA**	74.3	94.0	68.1	95.5
	Papsmear	72.0	90.2	55.1	94.9
Hegdeet al. [15]	**VIA**	70.8	95.0	96.5	62.9
	Papsmear	83.0	98.0	97.9	80.0
Consul Set al.[20]	**VIA**	84.2	55.2	55.2	84.2
	Papsmear	84.2	62.1	59.3	85.7
Pourasad S et al.[18]	**VIA**	71.4	50.0	35.7	81.8
	Papsmear	14.3	50.0	10.0	60.0
Saleh et al. [17]	**VIA**	90.0	37.0	52.0	81.0
	Papsmear	50.1	93.1	89.3	65.6
Present Study	**VIA**	86.6	97.8	85.3	98.0
	Papsmear	80.6	98.9	91.5	97.2

CONCLUSION

Cancer screening is the main weapon for early detection of cervical cancer at a pre-malignant stage. The lack of effective and implementable screening programme lead to reporting of advanced cases of Cancer cervix. If detected at CIN or early stage of cervical cancer, effective treatment can be provided with encouraging results. Because of the limitations of the Pap smear like inadequate coverage of large population, lack of infrastructure and resource required for cytological screening, alternative strategies such as VIA have been studied.

Many aspects of VIA make it an appealing approach for use in low-resource settings. In most cases, costs associated with launching and sustaining VIA screening are lower than those associated with other methods. VIA is a relatively simple, easy-to-learn approach that is only somewhat reliant upon infrastructure for its adequate performance, assuming that sufficiently trained providers are available. The results of the procedure are available immediately, making it possible to provide further management, including an offer of immediate treatment of some suspected precancerous lesions during the same visit.

Since diagnostic values of VIA are comparable to Pap smear, VIA can be used as a good alternative to papsmear in mass screening of large population. VIA can be combined with Pap smear to improve the efficacy of screening procedures in detection of pre-cancerous and cancerous lesions of cervix.

Limitation of our study

1. This is a hospital‑based study. The study sample is small and population is not representative of general population. Hence when these tests are used for screening in general population the estimated sensitivity and specificity may not be achievable.
2. Biopsy is taken only from those with lesions observed in VIA positive and Papsmear positive. Those with normal VIA and Pap have not undergone biopsy to confirm the negative test. These patients are assumed to be negative even in biopsy for statistical analysis. Hence, calculation of sensitivity taking biopsy as reference standard has been biased. Actual sensitivity of each test based on biopsy may be lower than the detected.

Ethical approval

The study was approved by the institutional Ethics Committee.

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