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Original Research Article

Screening of premalignant and malignant lesions of cervix by visual inspection with (acetic acid or Lugol's iodine) and PAP smear

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ABSTRACT

Background: Cervical cancer is the primary cause of morbidity and fatality globally among women. It is essential to unfold a screening test with high sensitivity and specificity. This study compared the effectiveness of visual inspection of the cervix with acetic acid (VIA) and lugol's iodine (VILI) versus the Pap smear in detecting cervix cancer.
Methods: In this prospective diagnostic validation study, 1000 patients were included and screened for cervix cancer using VIA, VILI and pap smear. The outcomes were obtained, contrasted, and statistically analysed.
Results: Among enrolled patients, 17.8% had a positive PAP smear, 43.2% had a positive VIA/VILI, and 14.0% had a positive COLPO. The patients' biopsies revealed that 7.6% had chronic cervicitis, and 5.9% had cervical intraepithelial neoplasia (CIN1). The sensitivity was 87.64% for VIA/VILI and PAP smear, whereas the specificity was only 66.4%. PAP smear and biopsy had a sensitivity of 37.58% but a specificity of 85.43%. The sensitivity of VIA/VILI and biopsy was 89.93%, whereas the specificity was 64.98%.
Conclusions: The current investigation showed that VIA/VILI is more sensitive than PAP.

Keywords: Cancer of cervix, Visual inspection, Acetic acid, Pap smear, Lugol's iodine, Cervical intraepithelial neoplasia

INTRODUCTION

With approximately 604,000 new cases in 2020, cervical cancer is the 4th most prevalent cancer worldwide. It is also the fourth highest cause of cancer-related deaths among women, with an estimated 342,000 deaths in 2020. There is a 10-fold difference between the greatest and lowest incidence rates of cervical cancer and a greater than 15-fold difference among the highest and lowest fatality rates. India accounts for one-fifth of all cervical cancer cases worldwide. GLOBOCAN 2018 estimated over 96,922 new cases of cervical cancer and a fatality rate of 60,078 per year in India.[1] In civilised nations, cytology screening has considerably reduced the incidence of cervical cancer-related morbidity and fatality.[2-4] In India, approximately 122,844 women are diagnosed with cervical cancer yearly, and 67,477 succumb to the disease.[5]

The WHO guidelines for cervical cancer prevention are essential to achieving the Sustainable Development Goals for health and gender equality. Attaining the following targets by 2030 will place all nations on the path to eliminating cervical cancer as a public health problem by 2100, defined as a threshold of four cases per 100 000 women per year.[6,7] Screening can detect precursors and premalignant early-stage disease in cervical cancer and effectively prevent squamous cell carcinoma and adenocarcinoma. Early treatment of pre-existing conditions and premalignant disease can prevent the development of invasive cervical cancer and decrease disease-related mortality. In other terms, cervix cancer screening is one of the most prevalent and effective. In India, the Pap smear test is primarily limited to urban locations. Visual inspection with acetic acid and Lugol's iodine has been proven to be viable alternatives to cytology

in settings with limited resources.[8] Our goal was to compare the diagnostic efficacy of visual inspection of the cervix with acetic acid and Lugol's iodine versus Pap smear cytology in screening asymptomatic women for cervix cancer.

METHODS

This investigation was carried out at the Al-Ameen medical college and Hospital in Vijayapura, Karnataka, from 1 January 2021 to 1 January 2023. We included nulliparous and multiparous non-pregnant women attending the gynaecology department and hospitalised in gynaecology wards who were willing to undergo the test. However, pregnant and menstruating women were excluded. After receiving ethical certification and informed consent, one thousand patients underwent a general physical, clinical, per abdomen, and per speculum exam. Then, screening for cervix cancer was performed using Pap smear cytology, visual examination with acetic acid and Lugol's iodine.

Statistical analysis

All characteristics are described in detail. For continuous variables, N, mean, and standard deviation (SD) were used as summary statistics. In the data summaries for categorical data, the number and percentage were used. Using bivariate correlation analysis with Pearson's correlation coefficient (r), the amplitude and direction of relationships between interval levels of variables were determined. A sensitivity-specificity analysis utilising PPV, NPV, and precision was performed to evaluate relative efficacy. Results were considered significant if the value of p-value was less than 0.05. Regression analysis assessed the adjusted effect of the study variable's determinants. The data were analysed using Statistical Package for the Social Sciences (SPSS) version 20.0.

RESULTS

Of the 1000 enrolled patients, most were aged between 31 and 40 (34.8%), were married before the age of 18 (42.3%), had three children (42.0%), and belonged to the lower socioeconomic class (84.5%). The majority of cases (70.6%) had a regular menstrual history. WDPV was the most prevalent presenting complaint (35.7%), followed by abdominal discomfort (30%) (Figure 1). On further examination, only 1.9% of women had post-coital bleeding, 4.4% had postmenopausal bleeding, and 3.5% had IMB. Lumbar pain was reported by 3.4% of individuals. 88.5% of 1000 patients had had a tubectomy, and 7 had a history of STD (Figure 2). A speculum examination revealed that most patients were healthy. 17.8% of Pap smears were positive, 43.2% of VIA/VILI tests were positive, and 14.0% of COLPO tests were positive; 56 patients had CIN1, 45 had CIN2, and 39 had CIN3. Biopsies revealed that the majority of patients were negative. Among the enrolled patients, 72.8% of the patients receiving treatment received reassurance, while 12.2% were treated with a yellow kit, 5.9% with cryotherapy, 4.3% with a hysterectomy, and 2.2% were under follow-up (Table 1, Figure 3).

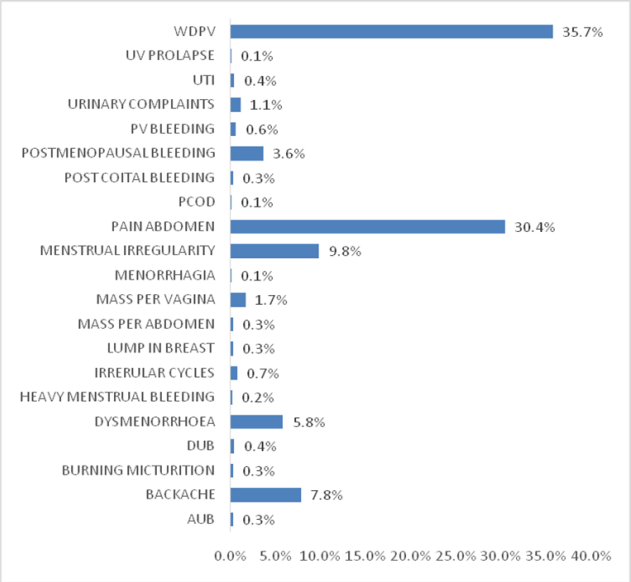

Figure 1: Distribution of the presenting complaints.

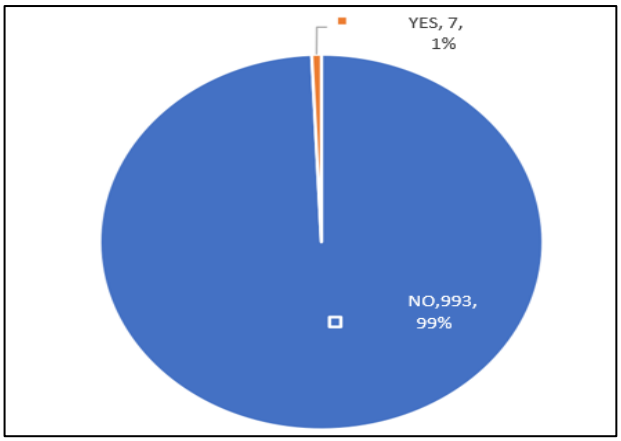

Figure 2: Distribution of history of STD.

Comparing the VIA/VILI and PAP smear results of 1000 cases, 156 were true positives, and 22 were false positives. The specificity of VIA/VILI was 66.42%, while its sensitivity was 87.64%. The positive predictive value of VIA/VILI is consequently low at 36.11%. However, the negative predictive value is quite high at 96.13%, and the accuracy was 70.20%. Pap smear and biopsy comparisons of 1000 cases revealed 56 true positives and 122 false positives, 93 true negatives and 729 false negatives. PAP had a sensitivity of 37.58% but a specificity of 85.43 %. Consequently, the positive predictive value of PAP is extremely low at 31.11%. However, the negative predictive value is quite high at 86.66%, and the accuracy was 78.30 %. Comparing the VIA/VILI and biopsy results for 1000 cases, 134 were true positives, and 298 were false positives. Furthermore, we recorded the specificity of VIA/VILI as 64.98 %, while its sensitivity was 89.93%.

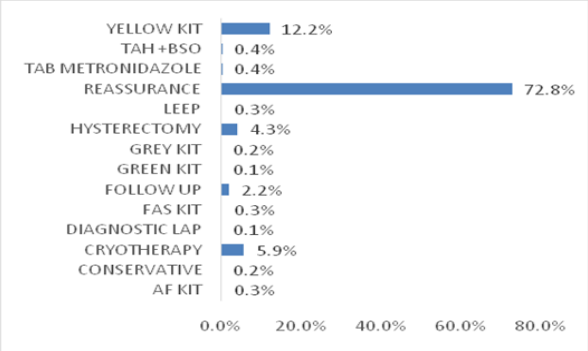

Figure 3: Distribution of treatment.

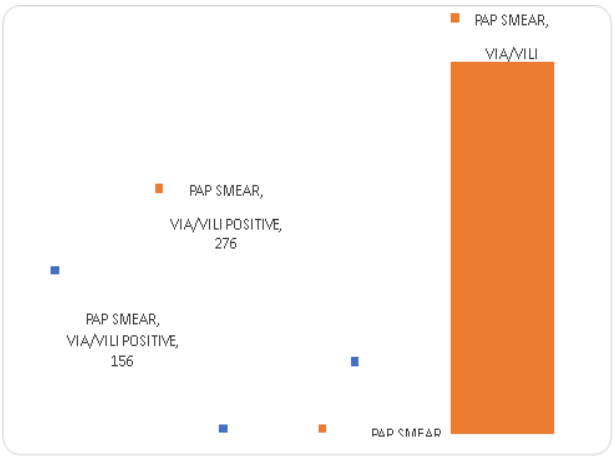

Figure 4: Distribution of VIA/VILI and a PAP smear.

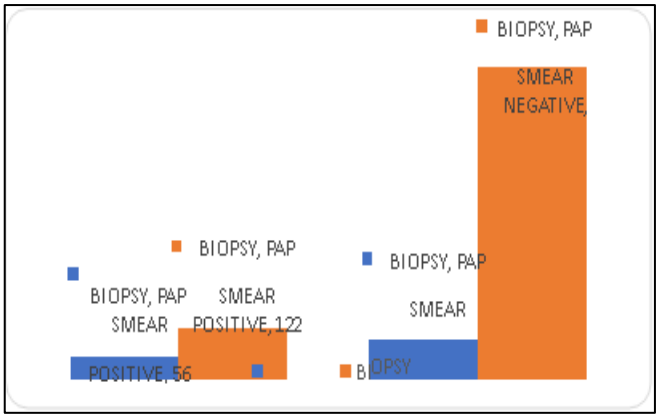

Figure 5: Distribution of pap smear and biopsy.

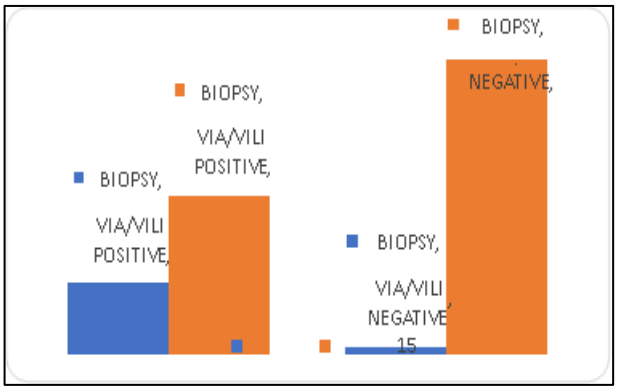

Figure 6: Distribution of VIA/VILI and biopsy.

Table 1: Clinico-demographic parameters of enrolled patients (n=1000).

		Frequency	Percentage
Age group (in years)	<20	14	1.4%
	21-30	324	32.4%
	31-40	348	34.8%
	41-50	203	20.3%
	51-60	82	8.2%
	>61	29	2.9%
Age of marriage (in years)	<18	423	42.3%
	19-20	352	35.2%
	21-25	221	22.1%
	>26	4	0.4%
Parity	Nulligravida	4	0.4%
	P1	83	8.3%
	P2	327	32.7%
	P3	420	42.0%
	P4	124	12.4%
	P5	35	3.5%
	P6	6	0.6%
	P8	1	0.1%
Menstrual history	Irregular	143	14.3%
	Menopause	151	15.1%
	Regular	706	70.6%

Continued.

		Frequency	Percentage
SES	Lower	845	84.5%
	Middle	153	15.3%
	Upper	2	0.2%
WDPV	No	543	54.3%
	Yes	457	45.7%
PCB	No	981	98.1%
	Yes	19	1.9%
PMB	No	956	95.6%
	Yes	44	4.4%
IMB	No	965	96.5%
	Yes	35	3.5%
Lumbar pain	No	966	96.6%
	Yes	34	3.4%
Patient using any fpm	Copper t	50	5.0%
	Inj. DMPA	39	3.9%
	Tubectomised	885	88.5%
	No	26	2.6%
PS	Ectropion	114	11.4%
	Healthy	688	68.8%
	Hypertrophy	16	1.6%
	Normal	6	0.6%
	Prolapse	1	0.1%
	Unhealthy	173	17.3%
Pre PAP	Not done	986	98.6%
	Acute inf	1	0.1%
	Na	1	0.1%
	Normal	12	1.2%
PAP	Normal	822	82.2%
	Ascus	62	6.2%
	ASC-H	16	1.6%
	LSIL	45	4.5%
	HSIL	39	3.9%
	SCC	16	1.6%
PAP Smear	Negative	822	82.2%
	Positive	178	17.8%
VIA/VILI	Negative	568	56.8%
	Positive	432	43.2%
COLPO	Negative	860	86.0%
	Positive	140	14.0%
COLPO	CIN1	56	5.6%
	CIN2	45	4.5%
	CIN3	39	3.9%
	Negative	860	86.0%
Biopsy	CA cervix	1	0.1%
	Chronic cervicitis	76	7.6%
	CIN1	59	5.9%
	CIN2	8	0.8%
	CIN3	5	0.5%
	Normal	851	85.1%
	Total	1000	100.0%

Table 2: Comparing the sensitivity and specificity of VIA/VILI, PAP smear and biopsy of enrolled patients (n=1000).

VIA/VILI and a PAP smear	Sensitivity	87.64%
	Specificity	66.42%
	PPV	36.11%
	NPV	96.13%
	Accuracy	70.20%
PAP smears and biopsies	Sensitivity	37.58%
	Specificity	85.43%
	PPV	31.11%
	NPV	88.66%
	Accuracy	78.30%
VIA/VILI and biopsy	Sensitivity	89.93%
	Specificity	64.98%
	PPV	31.02%
	NPV	97.36%
	Accuracy	68.70%

Consequently, the positive predictive value of VIA/VILI is meager at 31.02%. However, the negative predictive value is excellent, at approximately 97.36%, and the accuracy was 68.70% (Table 2; Figure 4-6).

DISCUSSION

Our study calculated the sensitivity and specificity of VIA/VILI and biopsy. The sensitivity of VIA/VILI was 89.93%, but the specificity was 64.98%. The positive predictive value (PPV) of VIA/VILI thus is very low at 31.02%. But the negative predictive value (NPV) is commending, about 97.36% and the accuracy was 68.70%. The sensitivity and specificity of PAP smears and biopsies were calculated. The sensitivity and specificity of the Pap smear were 37.58%, and 85.43%, respectively. The PPV of PAP thus is very low at 31.11%. But the NPV is quite good, about 86.66%, and the diagnostic accuracy was 78.30%. Similarly, Doh et al conducted a study on African women, where cancer of the cervix is the second leading cause of mortality in women after breast cancer. They observed that the VIA test showed better results as a screening tool for cervix cancer.[9] The sensitivity of the VIA test was higher (70.4%) than the Pap smear (47.7%). Contrastingly, the specificity of Pap was higher (94.2%) than that of VIA (77.6%). The PAP smear was more specific but less sensitive than the VIA test, and thus the VIA test can be used to screen a large mass population in low resource settings, such as impoverished developing countries.[9] Goel et al conducted a study with 400 women attending a gynaecological outpatient clinic in India. They noticed that the sensitivity of the VIA test was higher than the Pap smear (96.7% and 50%, respectively), and specificity was greater in Pap (97%) than in VIA (36.4%). Visual inspection with acetic acid has a very high sensitivity and a relatively inexpensive, making it an appropriate test for detecting cervical precancerous lesions in developing nations with limited resources.[10] In addition, Basu et al. found in their study that the VIA is more sensitive than a specific screening tool, corroborating our findings.[11] Megevand et al stated that in areas with limited access to cytopathologists, a visual examination of the cervix with dilute acetic acid could be a suitable alternative.[12] Furthermore, Ghosh et al. also concluded that Pap smear screening for cervical cancer could be substituted by visual inspection methods such as VILI, as it has shown the maximum sensitivity (100%) and specificity (93.3%) for detecting any grade of dysplasia.[13] Accordingly, Consul et al found that the sensitivity of VIA and VILI was analogous to that of the Pap smear, making them an appropriate potential alternative/additional detecting test not only in situations with limited resources but also in well-resourced centres.[14] Another study revealed that the sensitivity and specificity of the VIA in comparison to the histopathological report (HPR) were 80% and 67%, respectively. The corresponding values for VILI were 80% and 87%, respectively.[15] According to Kaur et al Pap smear screening has not lessened the incidence of cervical cancer in areas with limited resources. Simultaneously the VIA and VILI are less expensive, more broadly accessible, and can be utilised by medical and paramedical professionals in numerous instances.[16]

CONCLUSION

We tried to evaluate the Pap smear, VIA, and VILI as screening tests for cervix cancer. Regarding sensitivity, the VIA/VILI were similar to that of the Pap smear test. Therefore, these two tests can be considered a substitute for screening the cancer of the cervix. The VIA and VILI are both appealing tests in meagre resource environments. We noted that the sensitivity of the PAP test was extremely low, whereas the specificity was good. As reports are only available after 4-5 days and many patients do not return for follow-up, many positive cases may be overlooked. The

VIA/VILI test are more sensitive, while the PAP smear test is more specific. Additional large-scale trials are necessary to clarify further the efficacy of VIA/VILI in other clinical settings.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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