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Original Article

Comparison of Cervical Cancer Screening by Visual Inspection with Acetic Acid versus Cervical-Cytology in Pregnancy

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Abstract

Aims: The aim of this study was to compare visual inspection with acetic acid (VIA) with cervical cytology for cervical cancer screening in pregnant women. **Settings and Design:** A prospective cohort study was conducted after institutional ethical committee approval in a tertiary care hospital in Northern India. Pregnant women of gestational age <28 weeks were randomly recruited from the antenatal clinic. **Subjects and Methods:** All eligible women had a Pap smear followed by VIA; colposcopy was performed if either test was positive. Swede score was used for grading of the acetowhite lesion; biopsy was planned if Swede score was ≥8. **Statistical Analysis Used:** The sensitivity, specificity, and predictive values for both screening methods were compared with colposcopy as the reference standard. **Results:** There were 370 low-risk pregnant women in the age group of 20–36 years in the study with a mean parity was 2.1, and the median period of gestation of 14.6 weeks. Abnormal Pap cytology was seen in 5.9% (n = 22) of patients; the abnormalities were ASCUS in 13 (59%), LSIL in 4 (18.2%), and AGC-NOS in 5 (22.7%) patients. VIA positivity was found in 8.4% (n = 31). The positive predictive value was 31.8% for cervical cytology and 48.4% for VIA (P = 0.001). No invasive lesion was detected. Positive predictive value of VIA was significantly higher than Pap cytology for detection of abnormal lesions. **Conclusions:** VIA is a cost-effective method with better predictive value than Pap smear for cervical cancer screening in pregnant women.

Keywords: *Cervical cancer screening, cervical cytology, pregnancy, visual inspection with acetic acid*

Introduction

Cervical cancer is the second most common cancer in Indian women, with age-standardized rate of 22/100,000 women per year; 96,922 new cases and 60,078 deaths per year.[1] Despite the magnitude, there is no existing national screening program for cervical screening at present in India. This, along with other factors, contributes to the high incidence of cervical cancer in our country. Pregnancy is the only time when women approach health-care professionel in India. Therefore, antenatal visits give an excellent opportunity for opportunistic screening for premalignant and malignant diseases of the cervix. However, cervical screening in pregnancy also poses a lot of problems because of hormone-induced changes in the cervix.[2,3] Abnormal findings during pregnancy are generally more difficult to evaluate due to the normal pregnancy-related metaplastic changes. There are hormonal changes in the epithelium of the ectocervix and the endocervix. Cells are hypervacoulated; nuclei are larger which may mimic abnormal cells.[2-5] All this makes cytology difficult to interpret in pregnancy; hence there is need for alternative options for screening. Visual methods such as visual inspection after application of acetic acid visual inspection with acetic acid (VIA) are very well tested and documented as a method of screening in nonpregnant women.[6] However, these methods have not been tested in pregnancy. Colposcopy in pregnancy is also not easy; extensive immature metaplasia often produces an intense acetowhitening after application of acetic acid, vascularity of the cervix is increased with fine punctuation, and mosaic patterns seen commonly.[4,5,7] Human papillomavirus screening does not seem to be a suitable option in young Indian women because of the high incidence of positivity in women <30 years of age.[8-10] Overall, cervical screening in pregnancy appears to

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be beneficial, and, at the same time, difficult to interpret. The best method of screening, therefore, remains a matter of debate. This study was conducted to see the prevalence of premalignant and malignant diseases of the cervix in pregnancy in a hospital based population and to compare the two methods for screening in pregnancy namely, cytology and VIA.

Subjects and Methods

Study design

A prospective cohort study.

Setting

This was an antenatal clinic-based study.

Sample size

Three hundred and ninety eight antenatal women in the first and second trimesters were recruited over a period of 1 year.

Inclusion criteria

Pregnant women of gestational age <28 weeks were randomly recruited from the antenatal clinic.

Exclusion criteria

- Active vaginitis
- Preterm premature rupture of membranes
- Patients unwilling for examination and follow-up
- Women in the third trimester of pregnancy.

All pregnant women in their first and second trimesters were randomly recruited from the antenatal clinic. Eligible women were then explained about the study and given printed information in their own language. Women who were willing to participate in the study and follow-up were then recruited into the study after informed consent. Detailed demographic information was recorded using a preformed questionnaire.

All women in the study had a speculum examination; cytology was taken by the conventional technique using the Ayre spatula; smear was spread on a slide and was immediately fixed with 95% alcohol spray. This was followed by visual inspection of the cervix with a good light by a trained doctor after application of 5% freshly prepared acetic acid using a swab stick (VIA). The changes on the cervix were then interpreted as VIA positive or negative. VIA test was labeled as positive if there were distinct, well-defined, acetowhite areas with regular or irregular margins, close to or abutting the squamocolumnar junction in the transformation zone. The intensity of acetowhiteness, borders of acetowhite area, and location of the acetowhite area were noted.

Bethesda system was used for reporting cervical cytology.[11] Abnormal results were categorized as atypical squamous cell of undetermined significance (ASCUS), atypical squamous cell cannot exclude high-grade squamous intraepithelial lesion (HSIL), low-grade squamous intraepithelial lesion (LSIL), HSIL, atypical glandular cell not otherwise specified (AGC-NOS), AGC favor neoplasia, adenocarcinoma *in situ*, adenocarcinoma, and squamous cell carcinoma.

Criteria for referral to colposcopy were taken as any women with VIA positivity or cervical cytology showing ASCUS or more. We used a digital video colposcope – GOLDWAY SLC 2000A for colposcopy, which was performed by an experienced colposcopist. The International Federation for Cervical Pathology and Colposcopy 2011 nomenclature was used to describe the colposcopic findings;[12] any acetowhite lesions seen on colposcopy were graded using the Swede's score. Biopsy was planned in women with Swede score was ≥8, as this was the cutoff given by our ethics committee based on earlier studies. Women with normal colposcopy findings were sent back to routine antenatal care. Women with abnormal colposcopy findings were followed in the second trimester and postpartum.

Statistical analysis

Data were categorized as the mean, median, and standard deviation. The sensitivity, specificity, and positive and negative predictive values of cervical cytology and VIA were compared in terms of their accuracy and predictive value in diagnosing preinvasive lesions of the cervix, with colposcopy as the reference standard.

Results

A total of 398 women participated in the study; 28 were lost to follow-up; therefore, a total of 370 women were included in the final analysis.

The age group of women ranged from 20 to 39 years with a mean age of 24.7 ± 3.5 years. The mean gestational age at the time of screening was 14.6 weeks. One-third of the women were recruited before completing the 10th week of gestation. Of all, 144 (39%) women were primigravida, 111 (30%) were second gravida, and 115 (31%) were third gravida and above. Majority of the women belonged to the middle and lower-middle class (86%) based on their family income.

The prevalence of abnormal Pap cytology was 5.9% (n = 22); 8.4% (n = 31) were VIA positive. Of 370, 29 smears lacked endocervical cells, and therefore, the specimen was termed inadequate [Table 1]. However, the squamous cells were reported as normal. Of the 22 women with abnormal Pap smear, 13 smears were reported as ASCUS, four as LSIL, and five as AGC. Of the 22 women with an abnormal Pap smear, colposcopy was abnormal in seven (31.8%), four with ASCUS, and three with LSIL. With an LSIL result on the Pap smear, Colposcopic findings were suggestive of a high grade lesion in the three out of four women (75%). On the other hand, ASCUS correlated poorly with abnormal colposcopy findings,

with only 3/13 (23.1%) of women with Pap smear with ASCUS had lesions consistent with cervical intraepithelial neoplasia (CIN) on colposcopy. Positive predictive value was low with ASCUS cytology, 76.9% had a normal colposcopy. There were five women with Pap smear report showing AGC-NOS. All of them had normal colposcopy; ectropion was found in three. VIA was positive in 31; on colposcopy, 38.7% (n = 12) had lesions suggestive of low-grade CIN and 9.7% (n = 3) had findings suggestive of high-grade CIN.

Overall, 43 colposcopies were performed; 16 women had the acetowhite lesions suggestive of CIN on colposcopy, 12 had lesions suggestive of low-grade CIN (Swede score <5), and 4 had lesions suggestive of high-grade CIN (Swede score >5). None of them had a score of >8 suggesting cancer. No case of invasive carcinoma was diagnosed. All the 12 women with low-grade CIN were VIA positive, whereas only three of them could be picked up on Pap cytology. Of the four women with Swede score of >5, three were VIA positive and all had abnormal cytology. Therefore, Pap cytology was more specific for high-grade lesions [Table 2]. Overall, only 10 women were screen positive on both the tests. These women were more likely to have abnormal colposcopy findings with the least number of false-positive cases.

The sensitivity, specificity, and predictive values of both the tests are given in Table 2; cytology had a sensitivity of 43.8% and specificity of 95.8%, with VIA, the sensitivity and specificity was 93.75% and 95.4%, respectively.

All the procedures were well tolerated by all women. Of 370 women, 15% had spotting or mild bleeding while taking the sample; none had heavy bleeding following the screening test. Mild pain was reported in 28.9%, moderate in 9.45%, and severe in 2.7% of women; rest were comfortable during the procedure.

Table 1: Sociodemographics of the study group

Parameters	Values
Total number of patients	370
Mother's age (years), mean	24.8
Gestational age (weeks), mean	14.6
Obstetric status	
Primigravida	144
Second gravida	111
Third gravida and more	115
Pap cytology findings	
NILM	314
Inadequate	29
ASCUS	13
LSIL	4
HSIL	0
Invasive	0
AGC	5
VIA findings (%)	
Negative	339 (91.6)
Positive	31 (8.4)

ASCUS – Atypical squamous cell of undetermined significance; LSIL – Low-grade squamous intraepithelial lesion; HSIL – High-grade squamous intraepithelial lesion; AGC – Atypical glandular cell; VIA – Visual inspection with acetic acid; NILM – Negative for intraepithelial lesion or malignancy

Table 2: Comparative analysis of the two tests

Screening test	Cervical cytology (%)	VIA (%)	Both cervical cytology and VIA positive (%)
Sensitivity	43.8	93.75	37.5
Specificity	95.8	95.4	98.8
Negative predictive value	97.4	99.7	97.2
Positive predictive value	31.8	48.4	60
P	<0.001	<0.001	<0.001

VIA – Visual inspection with acetic acid

Discussion

Recommendations from many international societies do not favor routine screening of pregnant women for abnormal cytology.[13] However, in a developing country like India where a national screening program for cervical screening does not exist, antenatal screening provides an excellent opportunity for detection of pre-invasive lesions of the cervix.

Cervical screening in pregnancy appears to be safe and well tolerated as no major side effects were noticed in the present study. Similarly, it has been reported to be safe in other studies too.[14-16] Abnormal Pap smear in pregnant women has been reported in many studies with the prevalence of abnormal Pap smear ranging between 0.3% and 7%.[17-19] In the present study, the prevalence of abnormal Pap smear in pregnant women was 5.9%, ASCUS 3.5%, LSIL 1.1%, and AGC 1.62%. Visual methods of screening have been well tested in nonpregnant women. However, there is no study as yet in the literature of visual methods for screening pregnant women.[19-21]

We found a VIA positivity rate of 8.4% in our pregnant population. The sensitivity of VIA was significantly higher with equal specificity than cytology for the detection of CIN lesions.

The positive predictive value of VIA (48.4%) was higher than Pap cytology (31.8%). This could be due to difficulties in taking a Pap smear in pregnancy due to abundant mucus and vascular cervix, resulting in inadequate sampling of the transformation zone. The sampling device was the Ayre spatula which also has a lower sensitivity and positive predictive value than liquid-based cytology sample.[22,23]

Colposcopy, in pregnancy, can be challenging because of pregnancy-associated changes in the cervix and needs a trained colposcopist to assess the images. The Swede score, has an added parameter of lesion size, and

found to have high accuracy in detecting high-grade lesions in nonpregnant women.[24] Kärrberg *et al*. in their study on colposcopy in 281 women found the Swede's score.[25] to be better for prediciting CIN in pregnancy.

The overall prevalence of CIN in pregnancy in our study was 4.32%, a majority being low grade. Insinga *et al*. reported the prevalence of CIN in pregnancy to be around 1%.[26]

The purpose of colposcopy in pregnancy is mainly to rule out invasive cancer: Preinvasive lesions can be followed up in pregnancy and postpartum as they have a high regression rate.

In the present study, no case of invasive cancer was found. High rates of spontaneous postpartum regression have been reported by many authors; up to 70% regression rates have been reported in CIN2/3 lesions.[27] The rate of progression can be as low as 5%–7%;[27,28] follow-up, therefore, can be safely carried out even in high-grade lesions.

Refraining from a biopsy in all women having the acetowhite lesions on colposcopy may be considered a limitation of our study. However, a cutoff score of ≥8 was determined by our ethics committee in view of earlier studies by Kärrberg *et al*.,[25] who found that a score of ≥5 was associated with high-grade CIN and ≥8 with cancer and suggested 8 as the cutoff score for biopsy as all women with cervical cancer in their study had a score of ≥8.[25]

The sensitivity of colposcopy in various meta-analyses has been reported as 89%–96% for diagnosing CIN and 85% for diagnosing high-grade CIN.[29-31] Unpublished data from our department show a sensitivity of 84.6% and specificity of 64.4% for detecting high-grade CIN. Since only 12% of the lesions progress during pregnancy, follow-up without biopsy in our patient group could be justified.

In the present study, VIA appears to be an efficient and better method for cervical screening than cervical cytology, especially for developing countries. The costs are low, with lesser infrastructure required.[21] Furthermore, results can be confirmed in the same sitting with no need to recall women.

Conclusions

Cervical screening appears to be a feasible and safe method in pregnancy for detection of preinvasive and invasive lesions of the cervix, especially in developing countries. VIA is an effective and accurate method for screening and also decreases the number of follow-up visits as it gives results in the same sitting in comparison to cervical cytology. Follow-up can be an effective management option for preinvasive lesions of the cervix. VIA can be performed at the booking antenatal visit to avoid discomfort to the woman late in pregnancy. Those found VIA-positive can be followed up by colposcopy if facilities exist or VIA alone can be carried out and treated at 6–12 weeks' postpartum when they come for vaccination of their babies and contraception. Since VIA needs minimal training and infrastructure, it can be easily carried out in rural health centers and providing cervical screening at the doorstep of Indian women.

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Conflicts of interest

There are no conflicts of interest.

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