Visual inspection of the cervix as a primary means of cervical cancer screening: results of a pilot study

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Objective: To measure the effectiveness of unaided visual inspection (UVI) of the cervix as a primary means of cervical cancer screening.
Design: A cross sectional study.
Setting: Five primary health care clinics in Mashonaland Province, Zimbabwe.
Subjects: 1 000 women aged between 25 and 55 years.
Main Outcome Measures: Sensitivity and specificity of UVI.
Methods: 1 000 women attending primary health care clinics were screened for cervical cancer by six qualified nurses. An unlubricated bivalve speculum was inserted into the vagina under good light to visualize the cervix and a cervical cytology specimen was obtained followed by visual inspection of the cervix stained by 4% acetic acid. All women found to have abnormal cervices by visual inspection and/or by cervical cytology report were scheduled for colposcopy examination at Harare Central Hospital.
Results: 236 (23.6%) women had an abnormal cervical appearance after application with 4% acetic acid, out of which 157 (15.7%) were reported abnormal by cytology. True disease as defined by positive colposcopy and positive cytology was confirmed in 38 (3.8%) women. The sensitivity of UVI using colposcopy and cytology as a reference standard was 68.4%, specificity was 3.4%.
Conclusion: The results of this study suggest that naked eye inspection of the cervix after application of acetic acid is a practical alternative to cervical cytology in screening for cervical cancer in countries with few resources like Zimbabwe.

Introduction

Cervical cancer remains the most common cause of cancer deaths among women in developing countries.[1] A considerable reduction in cervical cancer deaths has occurred in many of the industrialized countries where screening programmes based on the cervical cytology smear (with reliable patient follow up) aimed at treating pre-cancerous lesions are in place.[2] In most developing countries however, such screening programmes are largely non existent. In a few of the developing

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countries where cervical cytology smear screening is available, it is usually opportunistic screening only in urban centres and the private sector. Logistical, technical and economic problems remain an impediment to implementing effective screening programmes in most developing countries. As a result, cervical cancer remains a significant public health problem in countries like Zimbabwe, where it contributes to 30% of cancers among females.[3]

Attention has recently been focused on alternative screening methods in countries where cytology based screening programmes are impractical. The most prominent technique is performed by washing the cervix with acetic acid solution and then visually inspecting the cervix with (aided) or without (unaided) a magnifying device. Published experiences with this approach have demonstrated that such a technique holds promise in settings with limited resources and could offer numerous advantages over traditional screening techniques such as instant feedback to the patient and most importantly, the potential to provide treatment immediately after screening.[4]

With these currently published study results in mind, a pilot project was carried out in Zimbabwe with the primary objective of measuring the effectiveness of unaided visual inspection (UVI) of the cervix performed by nurses/midwives in primary health clinics and comparing it with cytology and colposcopy as currently practiced in Zimbabwe. This report discusses the experiences and conclusions of the pilot study.

Materials and Methods

This cross sectional pilot study was conducted in five primary health care clinics in Mashonaland Central Province, Zimbabwe between April and June 1995. All women aged 25 to 60 years presenting at these clinics were offered screening regardless of their presenting complaints. Women with a history of hysterectomy or diagnosis of cervical cancer were excluded from the study. Screening was performed by six qualified nurses who had undergone a one week orientation course designed to standardise speculum examination techniques, acetic acid application to the cervix, criteria used for diagnosing intraepithelial lesions by visual inspection and collection of cervical cytology specimens. The UVI classification used in this study is shown in Table I.

Table I: UVI classification used in the study.

UVI Classification	Clinical Interpretation
Normal	Smooth, pink, uniform and featureless
Atypical	Cervicitis (inflammation/red spots)
	Discharge
	Extropion
	Polyp
Abnormal	White plaques
	Ulcer
	Aceto-white epithelium
Cervical cancer	Cauliflower-like growth/ulcer
	Obvious cancer

Each participant completed a study questionnaire before she was placed in a modified lithotomy position on an examination table. An unlubricated bivalve speculum was inserted into the vagina to visualize the cervix using a battery powered halogen flashlight. A cervical cytology specimen was immediately obtained using a wooden spatula to scrape the cervix around its entire transformation zone. Visual inspection of the exposed cervix was then performed by first thoroughly cleaning any excess mucus with a saline soaked swab. A tipped cotton applicator soaked in 4% acetic acid was applied to the cervix and after two minutes, the nurse visualised the cervix in its entirety. The findings were then recorded using standard codes (see Table I). A register of all women screened was maintained at the clinic to facilitate follow up and recall of subjects requiring colposcopy.

All women found to have abnormal cervices by visual inspection and/or by cervical cytology report, and a 10% random sample of those who tested negative (both cytology and UVI) were further scheduled for colposcopy at Harare Central Hospital. All colposcopies were performed by one of the study investigators (ZMC) and all cervical cytology smears were examined at the National Cytology Centre in Harare by cytotechnicians. All positive cervical cytology smears and a 10% random sample of negative smears were further analysed by a cytopathologist, for confirmation, and internal quality control.

All 1000 smears were read by a second pathologist at Johns Hopkins Bayview Medical Center as a means of external quality control. Women confirmed to have high grade squamous intra-epithelial lesion (HGSIL) at colposcopy who met criteria for local treatment had large loop excision of the transformation zone under local anaesthesia during the same clinic visit (see and treat).

Statistical Analysis.

Frequency distributions were used to summarize demographic data. Sensitivity and specificity results were calculated using raw pilot study data, unadjusted for differences in the rate of sequential diagnostic testing (using colposcop and cervical cytology) among women assessed as norm versus abnormal with UVI. Positive and negative predicti values and test efficiency were calculated adjusting for t prevalence of the disease. Adjustment for such work up bi was not possible in the pilot study phase due to the sma proportion of women identified as normal at screening wh ended up having a colposcopy, thus valid estimates of th specificity of UVI could not be ascertained. The sensitivit measure refers to the proportion of women diagnosed a having HGSIL or cancer by colposcopy and cytology (used a a measure of true disease status in the pilot phase) who wer classified as abnormal or cancer by UVI (i.e. true positives

Results

Between April and June 1995, 1 000 women were recruited into the pilot study. The key characteristics of these women included a median (Q1, Q3) age of 34.0 (30.0, 39.0) years and median parity of 4.0 (2.0, 6.0). The majority of women (75%) were married and in a monogamous relationship. Seventy nine percent had completed primary school education. The mean age at first intercourse was 17.8 years (SD = 2.1) and mean age at first pregnancy was 18.7 (SD = 3.1).

All the 1 000 women had the two screening procedures (Pap. smear, UVI), performed during the study. Tables II and

III list the frequency distribution for the two screening procedures according to test results. There were 236 women (23.6%) who had positive reactions after staining with acetic acid and 14 women (1.4%) suspected of having cancer on visual inspection. Ten women had missing information for their visual inspection findings and were therefore removed from the analysis. The cervical cytology (Pap. smear) was recorded as HGSIL in 57 women (5.7%) as shown in Table III.

Table II: Distribution of women screened by their UVI diagnosis.

UVI diagnosis	Frequency n= 1 000	(%)
Normal	402	(40.2)
Atypical	338	(33.8)
Abnormal	236	(23.6)
Cancer	14	(1.4)
Missing	10	(1.0)

Table III: Distribution of women screened by their cervical cytology diagnosis.

Cervical cytology diagnosis	Frequency n= 1 000	(%)
Normal	140	(14.0)
Unsatisfactory	68	(6.8)
Inflammation	5	(58.8)
Atypia	4	(4.7)
Low grade SIL	100	(10.0)
High grade SIL	57	(5.7)

A total of 213 (21.3%) women attended colposcopy as shown in Table IV, with the colposcopy findings.

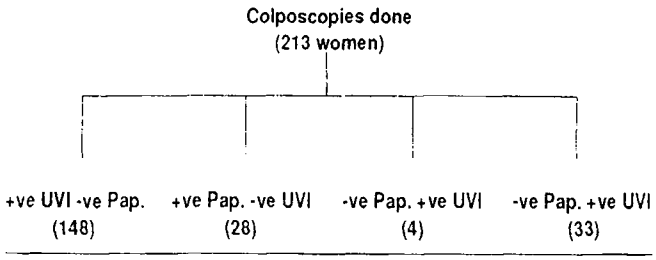
Table IV: Distribution of women screened by their colposcopy diagnosis.

Colposcopy diagnosis	Frequency n= 213	(%)
Normal	128	(60.1)
Inflammation	7	(3.1)
Low grade SIL	3	(18.3)
High grade SIL	35	(16.4)
Invasive cancer	2	(0.9)
Inadequate colposcopy	2	(0.9)

Figure I is a flow chart of women attending colposcopy clinic according to reasons of referral. The majority of these women (148) had positive UVI and negative Pap. smear.

Only four women attended colposcopy with negative Pap smear and negative UVI. All colposcopies were performed without knowledge of either UVI or Pap. smear results. Table V summarises the screening measures of UVI versus Colposcopy. The determination of sensitivity and specificity was based on the ture positives and true negatives. The true disease (positives) were defined as positive Pap. and positive colposcopy (38). True negatives were negative Pap. and negative colposcopy (89).

Figure I: Flow chart — UVI and Pap. smear results for women attending colposcopy.



Histology confirmation of pre-cancer was not used in the analysis because of inadequate numbers of cases with complete results.

Table V: Summary of sensitivity and specificity of UVI.

		Gold Standard Colposcopy True +ve	True -ve	
UVI	+ve	26	86	
	-ve	12	3	Prevalence = 6%
		38	89	

			95% CI
Sensitivity	=	68.4%	(53.6, 83.2)
Specificity	=	3.4%	(-0.4, 7.1)
Test efficiency	=	22.8%	(15.5, 30.1)
PPV	=	4.3	
NPV	=	62.6	

UVI = Unaided visual inspection
PPV = Positive predictive value
NPV = Negative predictive value

The table indicates high sensitivity of 68.4% but very low specificity of 3.4%, with a test efficiency of UVI as 22.8%.

Discussion

The prevalence of cervical cancer in the developing countries remains at epidemic levels due to inadequate screening resources. Lack of trained personnel, inadequate laboratory and technical equipment and the high cost of services are some of the reasons resulting in the current status. It is, therefore, apparent that alternatives to cytological screening need to be explored for countries with low resources like Zimbabwe. The overall study was conceived to measure the sensitivity and specificity of UVI as a screening test for cervical pre-cancer.

The use of acetic acid to investigate the presence of disease in the uterine cervix has long been in use by many clinicians. Most investigators have explored the value of visual inspection as an adjunct to cytology and relatively little field-based work has been done to evaluate the efficacy of visual inspection as

a primary means of screening cervical pre-cancerous lesions. The overall aim of our study was to evaluate the effectiveness of visual inspection of an acetic acid stained cervix compared to a standard cervical cytology smear in screening for cervical neoplasms. The pilot study design was to test the operational model of field based work before embarking on the larger study.

In this pilot project, the sensitivity of UVI was estimated at 68.4% with a specificity of 3.4%. The observed low specificity of UVI (3.4%) in this phase of the study was partly due to the difficulties the nurses had in correctly identifying cervices with acute and chronic inflammations from schistosomiasis and trichomoniasis as later confirmed at colposcopy. Only two women were confirmed to have invasive cancer out of 14 identified by UVI because the nurses had difficulties with overt warts on the cervix. Thus, UVI proved valuable in allowing early cervical cancer diagnosis even though its major thrust is to help identify women with cervical pre-cancer, because these two women were surgically treated at Parirenyatwa Hospital.

Out of the 100 women who tested negative randomly selected for diagnostic testing (both cytology and UVI), only four were followed through colposcopy and biopsy, thus creating a serious work up bias in the pilot results. Positive patients were preferentially seen at the colposcopy clinic and those with both negative cytology and UVI were under represented.

Currently cervical cytology remains the most widely used test to screen for cervical pre-cancer although false negative rates of between 10% to 35% have been reported.[5,6] In most developing countries however, the complexity and cost of cytological screening systems make it expensive and unlikely to be implemented on a national basis. Other screening methods like cervicography and human papilloma virus typing remain experimental and require expensive technological infrastructure not available to countries with low resources. Visual inspection without acetic acid wash was evaluated in India where the researchers detected 52% of lesions (early cancer) compared to 71% which were detected by cytology.[7] This approach was designed to detect early invasive cervical cancer rather than pre-invasive disease which is the ideal target in order to have a significant impact on reducing the current high morbidity and mortality from cervical cancer in developing countries. Ottaviano *et al*[4] were able to detect 96% of the atypical transformation zones by naked eye inspection of the cervix after application of acetic acid.

Among the lessons learned in this pilot study were that a field based trial of UVI is feasible but that adequate numbers of both test positive and test negative patients must be followed up with an examination by the reference standard critical to obtaining consistently reliable results. Also, histological confirmation of cervical pre-cancer would strengthen the true positivity of the disease.

In this study, UVI was able to detect 68% of lesions and this seems a reasonable pick-up rate for a setting where current cytological screening is negligible due to logistic problems. Our study results are similar to those reported by Megevand *et al*[8] in South Africa who detected 64% of women with HGSIL by visual inspection of the cervix after application of acetic acid. Screening of cervical pre-cancer by naked eye inspection of the cervix after application of acetic acid is an inexpensive, practical alternative to cervical cytology in countries with limited resources.

Acknowledgements

This study was supported by the JPHIEGO Corporation, Baltimore, USA, with funding from the United States Agency for International Development through the Commonwealth Regional Health Secretariat, Arusha, Tanzania and the Ministry of Health, Harare Zimbabwe. We wish to thank the following for their administrative, logistical and technical support: Professor S Kinoti, Dr W Mpanju-Shumbusho, Dr R Makunike, Dr R Szumel, Dr S Brechin, N Maier, Dr E Ngwale, Dr Kama Rogo, Dr F Muriu, Dr S Kaggwa, Dr P Tlebere and the following research midwives who carried out this project expeditiously: V Akino, F Chanakira, MM Kamba, P Kunaka, M Kurangwa, M Mlingo, M Mpofu and E Mutukwa.

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