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Visual Inspection of the Cervix with (Acetic Acid or Lugol's Iodine) for Cervical Cancer Screening

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Abstract

Objective: To assess the visual inspection with acetic acid (VIA) and Lugol's iodine (VILI) as alternative screening methods for cancer cervix.

Materials and methods: Comparative cross-sectional study was conducted on 1000 women with age range from 18 to 61 years were attending the obstetrics and gynecology Department in Zagazig university hospital from January2013 to October 2015. Each one was done Papanicolaou smear (PAP), visual inspection with 5% acetic acid (VIA) and with 5% Lugol's iodine (VILI). All women underwent Colposcopy. Analyse of the sensitivity, specificity and predictive values of the results using colposcopic directed biopsy as reference was done.

Results: From 80 positive screening tests by (either PAP, VIA, VILI or colposcopy). Pap smear was positive in 14/80 (17.5%), including 4 cases of atypical squamous cell with undetermined significance (ASCU), 4 cases of low grade squamous cell intraepithelial lesion (LSIL) and 5 cases of high grade squamous cell intraepithelial lesion (HSIL) and one case with malignant cells. Biopsy was positive in 11/14 of PAP smear. VIA accounted positive in 23/80 (28.7%) and VILI results were positive in 12/80. Biopsy was positive in 21/23 for VIA and 8/12 was positive for VILI , The Pap smear had a sensitivity of 78.57%, specificity of 96.75%, and positive predictive value 75.12% and negative predictive value of 97.09%. VIA had a sensitivity of 91.30%, specificity of 85.33% and positive predictive value of 40.11% and negative predictive value of 98.05%. VILI had sensitivity of 66.54, specificity of 91.32, and positive predictive value 43.51% and negative predictive value of 98.31%.

Conclusion: Precancerous and cancerous lesions of the cervix could be well detected by VIA and VILI in low resource locality. Using both testes in matching improves the specificity of both to make them good options for screening of cancer cervix in this society.

Keywords: Visual inspection; VIA; VILI; Pap smear; Screening; Developing countries; Prevention; Cervical cancer

Introduction

A total of 84% of new cases and 86% of deaths occurred in the developing regions [1]. Cancer cervix is the fourth most common cancer in women, and the seventh overall, with an about 528 000 new cases and more than 250 000 deaths in 2012. The important reasons for this high incidence are lack of valuable Screening curriculums and poor organized resources [2]. Presence of approach for effective screening programs is very important [3]. Cevical cancer can be a preventable disease through both early detection and primary prevention. The declining of incidence and mortality related to cervical cancer in developed countries is due to efficient screening programmes through Papanicolaou (Pap) smear [4]. 80% of cervical cancers in developing countries, are untreatable at the time of discovery due to their advanced stage [5]. The Papanicolaous (PAP) smear as a cytologic methods for screening of cervical cancer have become the core stay of prevention programs as a mass screening system. It is a simple, safe, non invasive and effective but although its effectiveness, it is difficult in low socioeconomic setting because of its multifaceted process of gathering the sample, preparation, staining, reading, reporting and the delay between screening and terms of test outcomes. Subsequently, in these regions it should be looked for others. Numerous modalities of screening are currently accessible for early diagnosis of cervical cancer could be helpful in those areas [6]. Visual inspection of the cervix following application of 3–5% acetic acid (VIA) and that subsequent to the application of Lugol's iodine (VILI), have been broadly evaluated as alternative screening tests in many developing countries, because they are simple, inexpensive and feasible [7]. This study was conducted to establish the possibility of replacing Pap smear by visual inspection with acetic acid (VIA) and Lugol's iodine (VILI) even with a amalgamation of them in matching for cervical screening in low-resource settings [8].

Patients and Methods

1000 women aged 19 to 61 years, were attending the clinic of the obstetrics and gynecology Department in Zagazig university hospital from January 2013 to October 2015 were eligible to participate but only 650 women completed full work in this comparative cross section study. The protocol of our study was reviewed and approved by the local ethical and research Committee Zagazig University Hospitals. Each woman keened to join in the study gave verbal and a written informed consent. Exclusion criteria were- Pregnant women, women with active vaginal bleeding, and any one had undergone hysterectomy or management for precancer or cancer of cervix. Firstly, Appropriate

general, obstetrical and gynecological history was taken after full information about the study and reassurance that the process was painless were given to all participants. Examination of Vulva for any abnormalities then vagina and cervix was done after insertion of Cusco's bivalve speculum. Any discharge was dried by cotton swabs. Inspection of the cervix with the naked eye using a focus lamp was done then a PAP smear was taken by scrapping the squamocolumner junction gently by Ayre's spatula and cytobrush, immediately fixing the taken materials in 95% alcohol on a glass slide to stain them by papanicolau stain. Visual inspection (VIA) after freshly prepared 4% acetic acid was applied with a cotton swab and observation for 1 minute for presence of a well-defined opaque acetowhite lesion next or close to the squamocolumnar junction (SCJ). After that colposcopic examination was done to all patients by another one with no awareness to the findings of VIA. When the colposcopic examination was completed after applying acetic acid, (VILI) was done by a second physician by applying Lugol's iodine to the cervix, which was prepared by dissolving 5 gm of iodine and 10 gm of potassium iodide in 100 ml distilled water and wait for 1 minute and examined the cervix by naked eye and classify the test if, VILI negative (homogeneous staining of the cervix) or VILI positive (the presence of a well-delimited non-staining area).

Colposcopy was positive if acetowhite epithelium, punctuation, mosaic, iodine negativity or atypical vessels were seen in the transformation zone [9]. Punch Biopsy was taken if any test or colposcopy was positive so, histopathology is the reference of diagnosis if biopsies had been taken; otherwise, the gold standard reference is the colposcopy diagnosis. The PAP was evaluated by the Bethesda system [10]. A smear was considered as cytology-positive if the smear

- (ASCUS): Atypical squamous cell of undetermined significance/OR
- (LSIL): Low-grade squamous intraepithelial lesion/OR
- (HSIL): High-grade squamous intraepithelial lesion/OR
- (SCC): Squamous cell carcinoma

Any slide with dysplasia (mild, moderate, severe), carcinoma in situ (CIS) or squamous cell carcinomawere considered positive histopathologically.

The (VIA) testing's results were classified as: Negative or positive according to presence of a well-defined opaque acetowhite lesion next or close to the squamocolumnar junction (SCJ) [11]. These lesions appear in The (VILI) as non-staining areas when Lugol is applied to the cervix, and testing's results were classified into:

Negative: Homogeneous staining of the cervix.

Positive: Presence of a well-delimited non-staining [12].

Statistically analysis of Collected data was done determine specificity and sensitivity, PPV, NPV of Pap smear, visual inspection by acetic acid (VIA) or Lugol's iodine (VILI), and Pap. In comparing with colposcopy or colposcopy with histopathology results as the gold standerd reference of diagnosis with 95% confidence intervals. Using statistical package for social sciences (SPSS) version 13.

Results

1000 women registered in this study who were attending Gynaecology Outpatient clinic. 350 women were excluded due to either were not fit to inclusion criteria or failed to submit one of screening tests and 650 completed the work. The mean age of the subjects was 35.1 ± 9.8, the mean of parity was 2.43 ± 1.2 .80% were married, 16.92% were divorced and 3% were widow (Table 1). 69% has regular menstruation, 9.4% has irregular one and 21.6% were menopause.

Parameter	**Range**	**Mean**
Age	18-61	35 ± 9.8 years
Parity	0-5	2.43 ± 1.2
Parameter	**Number**	**Percentage %**
Marital state		
Married	520	80%
Divorced	110	16.92%
widow	20	3.08%
Education level		
Not	390	60%
Low	130	20%
Medium	123	18.90%
High	7	1.10%
Regularity of menstruation		
Regular	448	69%
Irregular	61	9.40%
Menopause	140	21.60%

Table 1: Sociodemographic data of screened women.

The main complaints were vaginal discharge (61%), itching at genital area (27.7%), back ache (33%), lower abdominal pain 14%, pain with sexual intercourse (2.4%), abnormal vaginal bleeding (2%), post coital bleeding (1.3%) (Table 2). The most common finding on local examination through Cusco's bivalve speculum was cervical erosion (ectropion) (36%) (Table 3). 80 cases were positive by (either PAP, VIA, VILI or colposcopy). Pap smear was positive in 14/80 cases from total 80/650 screened positive cases (17.5%), including 4 cases of atypical squamous cell with undetermined significance (ASCU), 4 cases of low grade squamous cell intraepithelial lesion (LSIL) and 4 cases of high grade squamous cell intraepithelial lesion (HSIL) and one case with malignant cells (Table 4). All participants were undergone Colposcopy and Punch Biopsy was taken when result of any screening test or colposcopy was positive to make histopathology is the reference of diagnosis. When biopsy was taken from those 14 positive; PAP smear; 11/14 were positive and 3/14 were negative. VIA accounted positive in 23/80 subjects (28.7%) and VILI results were positive in 12/80 (Table 5). After colposcopy and biopsy 21/23 was positive and 2/23 were negative for VIA. 8/12 were positive and 4/12 were negative for VILI (Tables 6 and 7) showed the sensitivity of VIA and VILI which were (91.30% 66.54%) and Specificity of them were (85.33%, 91.32%) while Sensitivity and Specificity of PAP smear were (78.57%, 96.75). Positive predictive value of both VIA and VILI were less than that of PAP (40.11%, 43.51% versus 75.12%) while the negative predictive value of the three screening tests were near to each other (98.05%, 98.31%, 97.09%) even to that of Colposcopy (99.06%).

Complaint	Number (N)=650	Percentages (%)
Vaginal discharge	400	61.50%
Pruritis vulvae	180	27.70%
Backache	210	32.30%
Lower abdominal pain	91	14%
Pain with sexual relation	15	2.30%
Abnormal vaginal bleeding	13	2%
Postcoital bleeding	8	1.23%

Table 2: Main complaints (%).

Findings by speculum examination	Number (N)=650	Percentage (%)
Looks normal	390	60%
Cervical erosion (ectropion)	234	36%
Cervicitis	123	18.90%
Hypertrophied cervix	97	14.90%
Unhealthy cervix	5	0.76%
Bleed on touch	7	1.07%
Suspicious cervix	3	0.46%

Table 3: Clinical findings of cervix by local examination (%).

Findings by speculum examination	Number (N)=650	Percentage (%)
Looks normal	390	60%
Cervical erosion (ectropion)	234	36%
Cervicitis	123	18.90%
Hypertrophied cervix	97	14.90%
Unhealthy cervix	5	0.76%
Bleed on touch	7	1.07%
Suspicious cervix	3	0.46%

Table 3: Clinical findings of cervix by local examination (%).

Pap smear	Number (N)	Percent total=17.5 % (%)
	Total = 14/80	
ASCUS	4	5%
LSIL	4	5%
HSIL	5	6.25%
Malignant cells	1	1.25%

ASCUS atypical squamous cell of undetermined significance, (LSIL and HSIL) low and high grade squamous intraepithelial lesion.

Table 4: Pap smear findings (%).

Positive results	Number (35/ 80)	Percentage
VIA	23	28.70%
VILI	12	15%

Table 5: VIA, VILI findings (%).

Screening test (positive)			Histopathology (positive)	
N=80 %				
	No	%	No	%
PAP smear	14	17.5	11	13.7
VIA	23	28.7	21	26.2
VILI	12	15	8	10
Colposcopy	31	38.75	24	30

PAP papanicolau VIA and VILI, visual inspection with acetic acid & Lugol's iodine Data are stated as N and (%).

Table 6: PAP, VIA and VILI findings in comparison to histopathology.

Screening test	VIA	VILI	PAP smear	Colposcopy
Sensitivity	91.30%	66.54%	78.57%	86.23%
Specificity	85.33%	91.32%	96.75%	95.90%
PPV (%)	40.11%	43.51%	75.12%	77,41%
NPV (%)	98.05%	98.31%	97.09%	97.54%

Table 7: Sensitivity, Specificity, Positive predictive value, Negative predictive value of VIA, VILI, Pap test and Colposcopy.

	Sensitivity (%)	Specificity (%)
Denny et al. [3]	70	79
Cronje et al. [21]	79	49
Sankaranarayanan et al. [22]	77	86
Goel et al. [23]	96	36
Ghosh et al. [19]	89	91
Present study	91	85

Table 8: Sensitivity and specificity of visual inspection with acetic acid (VIA) in different studies.

	Sensitivity (%)	Specificity (%)
Arbyn et al. [5]	91.2	84.5

Sarian et al. [24]	56.7	77.9
Denny et al. [3]	92	85
Shastri et al. [14]	75.4	84.3
Lugoma et al. [25]	68.3	76.2
Ghosh et al. [19]	100	93.3
Present study	66.54	91.32

Table 9: Sensitivity and specificity of visual inspection with acetic acid (VILI) in different studies.

Discussion

Cancer cervix is a possible avoidable cancer. Premalignant lesions take 5-15 years to progress to invasive cancer. So, if perceived and managed appropriately, it has nearly 100 per cent cure rate [13]. Programmed Pap smears as screening test for cancer cervix has long been established in the developed countries but in developing one, it seems not easy to do that due to restricted transportation, trained persons and resources [14]. So, alternative strategies for early detection of cervical cancer. Such as VIA, VILI, HPV testing, cervicography and possibly, screening colposcopy were thought to carry on [15]. The simplicity and low-cost of visual inspection of cervix with acetic acid and Lugol's iodine (VIA and VILI) make them suitable and promising approaches to become universal screening for cancer cervix in low-resource settings. They do not require a complicated laboratory communications like cervical cytology and the immediate accessibility of test's result allows diagnostic investigations similar to colposcopy and biopsy to be carried out in the same visit. This allows treatment to be planned and employed without extra recalls [16].

Most studies compared VIA, VILI with PAP, looking at sensitivity and specificity of both whilst comparing them to colposcopy with biopsy as the gold standard. Some have suggested that these tests can attain similar or better results than Pap smear in the detection of CIN. According to results of Rana et al. most cases of pre cancer and cancer of cervix can be screened with VIA. They found that VIA had better negative predictive value and lower specificity than that of the Pap smear. So, when the test's result is negative, the woman can be reassured that she is not probably have a neoplastic lesion cervical [17]. The sensitivity and specificity for cytology in the Study of Samira et al. were 52.6% and 72.1% respectively as compared to that of Cronje in 2001 with sensitivity of 19.3% and specificity of 99.3%. While it was 44.3% and 90.6% respectively in a study by Gaffikin et al. [18].

In our study, the sensitivity for cytology (PAP) smear was 78.57% which is less better than that of (VIA) which was 91% but more good than that of VILI which was 66.54%. The specificity was 96.75% which is near to that of both VIA and VILI (85%, 91.32%) respectively.

Pap smear sensitivity varied in different studies from 40% in Denny et al. [19], 50% in Goel et al., 53% in GHOSH et al. 56% in Ratnam et al. [15], 65% in Sankaranarayanan et al. So, besides low sensitivity of Pap smear, it has a variety of limitations like; the requirement for repeated visits, gathering of report, assessment of abnormal results and treatment, and necessity for laboratory infrastructure, highly trained cytopathologists and staff for large scale screening.

The sensitivity and specificity of visual inspection with acetic acid (VIA) in different study showed wide range (Table 8). Our results were comparable to that of other studies. The large variation in these results indicates that several variables may affect the characters of the test like observer training, criteria for test positivity, inter-observer variation, and light source, presence of co-existing infection, inflammation and metaplasia. VILI has lots of advantages which are easily performed, low cost, results are immediately available. The sensitivity and specificity of our study corroborated well with some studies in some studies but not with other (Table 9). VILI had a lesser sensitivity (66.54%) compared to VIA (91%). Both visual techniques (VIA,VILI) have high negative predictive value (98.05, 98.31). This means, a woman negative by VIA/VILI does not need further investigation. However, these women are advised to undergo a VIA or VILI after a minimum interval of 3 years. Only 10-15 per cent women who are test positive with visual techniques require further evaluation. Some authors adviced Combined testing to reduce the number of biopsies taken based on either test alone [20].

Conclusion

Screening of cancer cervix in low source settings could be carried on by cheap and easily obtainable methods through using visual inspection of the cevix after application of acetic acid (VIA) and Lugol's iodine (VILI) as they have good sensitivity to detect any grade of dysplasia, with a realistic specificity to facilitate the screening and obtain the highest health care to population in such society.

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