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VIA /VILI Guided Cervical Punch Biopsy for Detection of CIN and Early Invasive Cervical Cancer in Low Resource Setting

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Abstract

Aim of Study *- Evaluation of VIA/VILI guided cervical biopsy for diagnosis of cervical pre invasive and early invasive lesions of cervix for resource poor settings.*

Introduction and background *- India has one fifth of burden of cervical cancer. In absence of an organized screening program most women present in advanced stages of cancer which is beyond surgical treatment. Due to lack of resources and trained personel for Pap based screening and colposcopy many patients remain undiagnosesd and untreated.*

VIA based screening have been extensively studied and have been found to be highly sensitive, cost effective and simple procedure for screening of patients in low resource settings. However after screening the need for colposcopy and LEEP leaves this patients untreated due to lack of facilities and trained personel in remote areas for colposcopy and LEEP .hence we studied VIA /VILI guided biopsy without using colposcopy as a method of diagnosis of cervical preinvasive lesions.

Material and Methods *- This study was conducted in CCM medical college hospital, kachandur, a tertiary medical college hospital in Durg district of Chhatisgarh. This hospital caters to the rural population of remote areas of Chhattisgarh community camps are organised three times a week in remote areas. All female patients coming to gynae OPD with any complaint are screened with VIA+VILI.*

All patients with Positive VIA/VILI were subjected fro VIA/VILI guided biopsy under local an aesthesia histopathological reports reviewed and correlated, and compared with the final histopathology report for those who underwent hysterectomy for various reasons, to calculate sensitivity, specificity, positive and negative predictive value or VIA /VILI guided biopsy for detection of CIN and early invasive cervical lesions.

Conclusion *- VIA /VILI guided cervical biopsy is a good alternative for very low resourse setting where both infrastructure and trained personnel for colposcopy and LEEP are lacking. As lack of these resourses and personel in periphery forces the women to travel long distances for a diagnostic test. Or they are left undiagnosed if they cannot travel to centres equipped with these facilities.*

Keywords *- **VIA; VILI; cervical biopsy; CIN; cervical cancer; colposcopy.***

AIM of study

VIA /VILI guided cervical punch biopsy for diagnosis of cervical pre-invasive lesions and early invasive lesions in a low resource setting.

Introduction and background

India has one fifth of burden of cervical cancer. In absence of an organized screening program most women present in advanced stages of cancer which is beyond surgical treatment. Due to lack of resources and trained personnel for Pap based screening and colposcopy many patients remain undiagnosed and untreated.

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Visual screening methods like VIA/VILI have been extensively studied and have been found to be highly sensitive, cost effective and simple procedure for screening of patients in low resource settings. However after screening the need for colposcopy and LEEP leaves this patients untreated due to lack of facilities and trained personnel in remote areas where facility for colposcopy and LEEP is not available. Hence we studied VIA /VILI guided biopsy without using colposcopy as a method of diagnosis of cervical pervasive lesions and early invasive lesions.

Material and Methods

This is a Retrospective observational study conducted in CCM medical college hospital, kachandur Durg a tertiary medical college hospital in Durg district of Chhatisgarh. This hospital caters to the rural population of remote areas of Chhattisgarh. Community camps are organised three times a week in remote areas, patients are brought to hospital in hospital vehicle. All female sexually active patients of age group 20-70 yrs coming to gynae OPD with any complaint are screened with VIA+VILI and PAP. All patients were subjected to a speculum examination by a medical officer who screens all new patients coming to gynae OPD with any complaint. Screening is done by single person to avoid observer bias. After speculum examination 5% acretic acid was applied with help of a cotton swab gently and after 1 min the findings recorded. Following that Pap smear taken and then Logol's iodine applied to look for iodine negative areas.

Unaided visual inspection of cervix after application of 5 % acetic acid and lugol's iodine was done and findings recorded. All positive screen patients on either VIA or VILI or both were subjected to cervical biopsy with punch forceps under local an aesthesia. VIA guided biopsy was done in 715 patients over a period of one year from May 16 to May 17. histopathology results were then studied.

We studied results of VIA /VILI guided biopsy and compared it with the final histology in patients who underwent hysterectomy for one or other causes like AUB, Fibroids, ovarian tumours, prolapse in order to study the sensitivity specificity, positive and negative predictive value of VIA guided biopsy for detection of cervical pre invasive and easly invasive lesions which are amenable to treatment. VIA screening and biopsy was done as a routine pre-op workup for all these patients. Histopathological results of VIA guided biopsy and final histopathology was correlated. statistical analysis done with X2.

Observations and Results

This is a retrospective observational study conducted at CCM medical college, kachandur, Durg, Chhattisgarh over a period of 1 year from May 16 to May 17.

All patients coming to gynae OPD with various symptoms were screened with VIA /VILI and PAP smear, irrespective of their primary complaint.

Our observations and results are tabulated here

Table 1 VIA Screen Results

Total women screened	3000	% out of total screened patients	% out of total biopsy done
VIA positive	765	25.5%	
Biopsy done	715	23.8%	
Biopsy positive	263	8.7%	36.7%
CIN	195	6.5%	27.2%
Ca cx	68	2.26%	9.5%
Biopsy negative	452		63.2%

VIA screening was done in 3000 patients over a period of 1 year from May 2016 to May 2017.

765 patients (25.5%) were VIA positive in our study.

Out of that 715 patients were subjected to VIA guided biopsy.

263 patients (36.7%) were biopsy positive (CIN 1 and above) while 452 (63.2%) were negative on biopsy. they had either chronic cervicitis or normal report. Out of 263 biopsy positive patients, 195 had CIN while 68 patients of early invasive cervical cancer were diagnosed.

Table 2- Results of VIA guided biopsy

Total VIA guided biopsy done	715	
Biopsy negative (chronic cervicitis /normal)	452	63.2%
Biopsy positive (CIN 1 and above)	263	36.6%
CIN total	195	74.1%
CIN 1	137	70.2%
CIN 2	50	25.6%
CIN 3	8	4.1%
Ca cx	68	25.8%

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Out of the 3000 screened patients VIA was positive in 765 patients. Out of that 715 patients were subjected to VIA guided cervical punch biopsy. 263 patients were positive on biopsy. CIN 1 and above report was considered biopsy positive in our study. While chronic cervicitis or inflammation and normal cervical cells were considered biopsy negative.

Out of 263 patients 195 (27.2%) patients had CIN on biopsy and 68 (9.5%) had invasive cervical cancer on VIA guided biopsy. Out of 195 patients with CIN; 137 had CIN 1, 50 patients had CIN 2 and 8 had CIN 3.

Thus out of 3000 screened patients 68 patients of invasive cervical cancer and 58 patients of high grade CIN were detected with VIA guided biopsy.

Table 3-Association of VIA guided biopsy and final biopsy report

		Final histopathology report (LEEP/hysterectomy)			
		final biopsy positive (True positive)	final biopsy negative (False positive)	final biopsy negative (True negative)	Final biopsy positive (False negative)
Total VIA guided biopsy done	715				
Hysterectomy or LEEP done	650				
VIA guided Biopsy positive	263	218	45		
VIA guided Biopsy negative	387			366	21

Out of 715 patients who had VIA guided biopsy, 650 patients had undergone either hysterectomy or LEEP for various causes like AUB, Fibroids, prolapsed, adenomyosis, etc we compared the histopathology report of VIA guided biopsy with that of the final histobiopsy report of Hysterectomy specimen or LEEP, to calculate the Sensitivity and specificity, PPV and NPV of VIA guided biopsy for diagnosis of cervical pre invasive and invasive lesions of cervix.

Table 4: Statistical analysis result for VIA guided biopsy

SENSITIVITY	91.21339
SPECIFICITY	89.05109
POSITIVE PREDICTIVE VALUE	82.88973
NEGATIVE PREDICTIVE VALUE	94.57364

Sensitivity of VIA guided biopsy was 91.2% and specificity was 89.05%. VIA guided biopsy correlates well with final biopsy negative cases hence the negative predictive value of VIA guided biopsy is 94.5%. And positive predictive value was 82%. thus VIA guided biopsy over diagnosed CIN 1 in 41 cases, CIN 2 in 3 cases and CIN 3 in 1 case. CIN 3 was found in cervical polyp which was removed hence final biopsy report did not show the lesion.

Table 5: statistical analysis of association of VIA guided biopay with final biopsy report

	Final Biopsy Positive	Final Biopsy Negative	X^2 Calculated	P-VALUE
Test (VIA guided biopsy) Positive	218(True Positive)	45(False Positive)	404.14	<0.00001
Test ((VIA guided biopsy) Negative	21(False Negative)	366(True Negative)		

Table 6- Correlation of VIA guided biopsy with the final histopathogy report (LEEP /hysterectomy)

		Hysterectomy or LEEP done	Final biopsy not done	Biopsy positive	True +ve	False +ve
Total VIA guided biopsy done	715	650	65	263	218	45
CIN 1	137	135	2 (<25 yrs.)	94	94	41
CIN 2	50	50	0	47	47	3
CIN 3	8	8	0	7	7	1
Ca cx	68	68	0	68	68	0
Biopsy negative	452	391	63	21		

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Majority of false positive in VIA guided biopsy were for CIN 1 which on final histological report were reported as Chronic cervicitis. Only 3 cases of CIN 2 reported on VIA guided biopsy was reported as false positive.

21 patients who were false negative on VIA guided biopsy had CIN 1 on final hitological report. no case of high grade CIN or invasive cervical cancer was missed on VIA guided biopsy. In 2 cases VIA guided biopsy showed CIN 2 while final biopsy was reported as micro invasive ca cx. Which can happen with punch biopsy specimen. There is a possibility of missing microinvasion in cervical punch biopsies however the number is small as compared to the no of positive cases picked up.

Discussion

Cervical cancer continues to be a major public health problem in India with an incidence of 134,420 cases and mortality of 72,825 cases in the year 2008.[1] Only a few organized cervical screening programs exist in India, even though the disease burden is high.

Many studies now provide evidence of the feasibility and cost-effectiveness of screening and treatment approaches for cervical cancer prevention. These can be easily adopted for various settings.[2,3,4,5,6,7,8]

Most recent data have shown limitations of pap smear including low sensitivity, high false negative rates and inter observer variability. These limitations have forced may observers to revisit its utility as a primary screening method esp. compared with HPV testing and Visual screening methods.

HPV testing has shown a lot of promise as a primary screening method as well as secondary triaging.

But the cost of the test is a major hurdle in adopting this test as a primary test for screening population esp. in low resource countries where 80% of burden of cervical cancer exists.

In low resource setting use of Visual screening methods has been widely studied and advocated for detection of precancerous lesions of cervix.

A significant reduction in cervical cancer mortality was shown following a single round of screening with HPV testing or VIA screening in a randomized trial in India.[9,10]

Visual inspection with acetic acid (VIA) is a simple, inexpensive test with moderate sensitivity and specificity for screening that can be combined with simple treatment procedures for early cervical lesions.[11] Studies have also shown the safety, feasibility, and efficacy of conservative treatments for pre-cancers.[12,13]

Health workers or nurses can be trained as test providers; the results are available immediately. VIA is feasible in many low-resource areas where it is difficult to sustain high-quality cytology programs.

An expert group also recommended to the Government of India the use of VIA as the primary screening test to be performed by trained nurses or health workers in primary healthcare.[14] Scaling up and inclusion of VIA-based programs into national programs is already taking place in many low- and middle-income countries.[15,16]

VIA has been found to be highly sensitive in various studies but less specific than cytology.

The downside quoted in many studies is that due to its high sensitivity it leads to more patients referred for colposcopy and guided biopsy.

According to ACCP 2004; although VIA reveals pre-tumors with more accuracy than a typical Pap smear, it also has more false positives. Because VIA-positive lesions are not unique to precancer, a considerable proportion of women will be unnecessarily treated for precancer or referred for further management, which can overload the service site where treatment is being offered [17]

Colposcopy with guided biopsy is the gold standard for diagnosis of CIN and its role can't be denied however; many developing countries do not have facilities for colposcopy and LEEP in remote areas and even if facilities are there trained personel are lacking. Hence if all screen positive women with VIA /VILI (15-30%) are referred to centres with these facilities then it will increase the burden on these centres as VIA /VILI is very sensitive test with a high percentage of false positives as has been found in various studies .as many of these screen positive women who are found to have only cervicitis or CIN can easily be managed at peripheral centres with cryotherapy or observation.

In the screening model where women are screened in peripheral clinics/community camps and referred for colposcopy and biopsy to secondary or tertiary level centre this leads to either dropout of women who are screen positive without having confirmation of diagnosis or leads to increased inconvenience and cost to travel to the centre for a diagnostic test without any confirmation that they have a lesion. It adds to the cost of screening if the agency doing screening has to arrange for travel of these screen positive women.

Many screen positive women with genuine lesions but lack of resources to travel to higher centre may be missed out inspite of being screened and found positive. Which is usually the case with rural population. Women who do not have a confirmed diagnosis if asked to go to higher center

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for diagnostic test may not comply. But if they have a confirmed diagnosis and are then asked to go for treatment they would do.

However, when screening tests with the inherent potential for overtreatment, such as visual methods, are combined with an outpatient diagnostic tests and treatment method that is safe, relatively inexpensive, and acceptable, the overall benefit can outweigh the limitations.

Thus if diagnostic testing can be done at the screening clinic itself many women will participate and also acceptance will increase.

There is lack of resources as well as trained colposcopists and pathologists in remote areas. Hence to implement colposcopic guided biopsy for all screen positive women in peripheral screening clinic may not be feasible in the current scenario. Hence we studied - feasibility and efficacy of VIA /VILI guided cervical punch biopsy for diagnosis of CIN and Cx cancer.

Cervical Biopsies Guided by Visual Inspection With Acetic Acid(18) have been studied by Ahmad Sameer Sanad, MD, Emad Mousa Ibrahim, MD, MRCOG, and Wafaey Gomaa, MD; Departments of Gynaecology and Obstetrics and Pathology, Faculty of Medicine, Minia University, El-Minia, Egypt; Article published in Journal of Lower Genital Tract Disease June 2013 They studied the accuracy of visual inspection with acetic acid (VIA) in determining the site, the size, and the number of cervical biopsies in patients with positive cervical cytology.

And concluded that Visual inspection with acetic acid and VIA guided biopsy is a good test for aiding the diagnosis of CIN and may be helpful in determining the site, the size, and the number of biopsies in patients with positive cytological results. Instead of colposcopy, VIA can be used in developing countries where colposcopy services are not available.

VIA guided biopsy can easily be done at the peripheral clinic with limited resources by trained nurses or paramedics or medical officer level staff after proper training. They can do VIA /VILI screening and do a biopsy at the same sitting or second sitting after treatment of infection if present. it has the advantage that it avoids inconvenience of travelling for the patient for a diagnostic test. And the patients can be better convinced by the health worker who is present locally and has a good rapport with the community and who acts as their community health worker. Biopsy samples can then be transported to the labs in secondary level hospital or centres and patient advised antibiotics for 1 or 2 weeks if cervicitis present and asked to come back after 1 or 2 weeks. Till that time biopsy report will be available and the positive ones with cervicitis and CIN 1 can be treated locally with cryotherapy which is feasible in peripheral clinic setting. Those with CIN 2/3 (3-4%) can bereferred to secondary level centre for LEEP. and those with CA in situ /invasive cancer (<%) can be referred to tertiary level hospital for radical surgery or radiotherapy or RT+CT.

This will lead to reduction in burden at all levels of care whether it is primary or secondary or tertiary levels, and complete spectrum of care from screening to diagnosis to treatment can be implemented with existing facilities and infrastructure with no additional cost burden.

Conclusion

VIA as screening test has been widely studied and has been recommended for low resource setting by WHO as well as Govt of India for community and mass screening. However the need for colposcopy guided biopsy and LEEP for VIA positive patients and lack of these facilities in resource poor settings and remote areas, either leaves these patients undiagnosed or compels them to travel long distance for just a diagnostic test. Many of these VIA positive patients do not have disease and can be easily managed at the primary care level by simple procedures like cryotherapy or antibiotic treatment for cervicitis. VIA guided biopsy can easily be done at the peripheral clinic with limited resources by trained nurses or paramedics or medical officer level staff after proper training. Thus VIA guided cervical punch biopsy can be used for diagnosis of CIN or early cervical cancer in primary cares level where the infrastructure, facilities and trained personnel for colposcopy and LEEP are not available.

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