Prevalence of premalignant cervical lesions among women in community-based screening program using visual inspection with acetic acid in Metro Manila

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Abstract:

BACKGROUND: Cervical cancer remains a health-care burden in our country. Majority of women afflicted with this cancer are diagnosed in advanced stage. Several groups like the Philippine Society for Cervical Pathology and Colposcopy (PSCPC) have put forth efforts to decrease and eventually eliminate cervical cancer through improvement in level of awareness on the disease and community-based cervical cancer screening programs using visual inspection using acetic acid (VIA). Data on the prevalence of premalignant lesions using this screening method are limited in our country. Thus, the initiative of the society (PSCPC) to embark on this study.

OBJECTIVE: The objective of this study was to determine the prevalence of premalignant cervical lesions among women screened in community-based screening program using VIA in Metro Manila.

METHODOLOGY: A retrospective cross-sectional study with collection of data from medical records of cervical screening programs done by the PSCPC from March 2017 to December 2019 was done. VIA was done for screening. All VIA-positive women underwent colposcopy and those with abnormal findings had colposcopically guided cervical punch biopsy.

RESULTS: A total of 1072 women were screened with a positivity rate of 14.6%. One hundred and fifty-six women were VIA positive and 79 of these women underwent colposcopically guided biopsy. Premalignant cervical lesions were seen in 21 women. The prevalence rate of premalignant cervical lesions in VIA-positive women was 13.5%. The prevalence of premalignant cervical lesions among all women screened was 2%. Risk factors associated with premalignant lesions were early coitarche and smoking.

CONCLUSION: The prevalence of premalignant cervical lesions among women who underwent community-based cervical cancer screening using VIA is lower compared to other studies at 2%.

Keywords:
Cervical punch biopsy, premalignant cervical lesion, visual inspection with acetic acid

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Introduction

Cervical cancer is the fourth most common cancer in women worldwide. About 604,127 new cases and 341,831 related deaths were noted in 2020.[1] A large majority of this global burden occurs in low- to middle-income countries. In the Philippines, cervical cancer remains a public health-care concern. It is the second most frequent cancer among women between 15 and 44 years of age, and there are about 34.30 million women aged 15 years and

older who are at risk of developing cervical cancer in the country.[2] Around 7897 women were diagnosed with cervical cancer and about 4052 died from the disease.[1]

Premalignant lesions of the cervix occur in 1%–5% of women in the general population.[3] About 69,000 new cases of low-grade lesions and 15,000 high-grade lesions were diagnosed in Europe.[3,4] The pooled prevalence of premalignant lesions of the cervix in Ethiopia, on the other hand, was 15.16 (95% confidence interval [CI]: 10.16–19.70). The lowest prevalence was 1.56% and the highest was 28.4%. In the Philippines, there is no published data regarding the prevalence of premalignant lesions of the cervix.

Persistent infection of high-risk human papillomavirus (HPV) is an established risk factor for cervical cancer. It is transmitted sexually and thru skin-skin genital contact. About 23% of young adults are already sexually active and their numbers are increasing steadily over the years.[2] However, with proper education, effective screening methods, and timely management of premalignant lesions, the development of cervical cancer may be prevented.

In the recent World Health Organization (WHO) guidelines on cervical cancer screening, HPV DNA detection is the recommended primary screening test for all individuals with a cervix and those living with HIV.[5] Use, though, is limited due to its prohibitive cost. Current approaches to cervical cancer screening such as cervical cytology and visual inspection using acetic acid (VIA) should be continued while transitioning to this screening method.

Papanicolaou smear has been the gold standard for screening cervical cancer. It has markedly decreased the incidence of cervical cancer in high-income countries where organized screening programs have been implemented. This decline, however, has not been realized in low- to middle-income countries like the Philippines. Alternative screening strategies like visual inspection of the cervix after application of 3%–5% acetic acid have been used in low-resource setting because it is simple, inexpensive, feasible, provides immediate result, and is comparable with cytology. It is for this reason that the Department of Health has issued a memorandum directing all DOH-mandated hospitals to perform cervical cancer screening using VIA to all women in the reproductive age group of 21 years and above with the aim to decrease the burden of cervical cancer in our country. Efforts have been made by various organizations both private and public to address this health concern using this alternative approach.

The Philippine Society for Cervical Pathology and Colposcopy (PSCPC) is a nongovernment organization that has started community-based screening activities using VIA, colposcopy, and cryotherapy for cervical cancer prevention. However, studies on the prevalence of premalignant cervical lesions, positivity rate of VIA, and characteristics of these women undergoing screening through these activities are limited. The results of this study may have important implication in the delivery of our cervical cancer screening program.

Objectives of the study
General objective
The general objective of this study was to determine the prevalence of premalignant cervical lesions among women screened in community-based screening program using VIA in Metro Manila.

Specific objectives
The specific objectives of this study were as follows:
1. To determine the positivity rate of VIA in a community-based screening program
2. To determine the prevalence of premalignant cervical lesions among women screened in community-based screening program using VIA
3. To determine the characteristics of women with VIA positive
4. To determine the factors associated with premalignant lesions of the cervix.

Methodology

Research design and framework
This was a retrospective cross-sectional study with collection of data from medical records of cervical screening programs done by the PSCPC from March 2017 to December 2019. The Institutional Review Board/Ethics Review Committee approved the conduct of the study.

Below is the framework of this study:
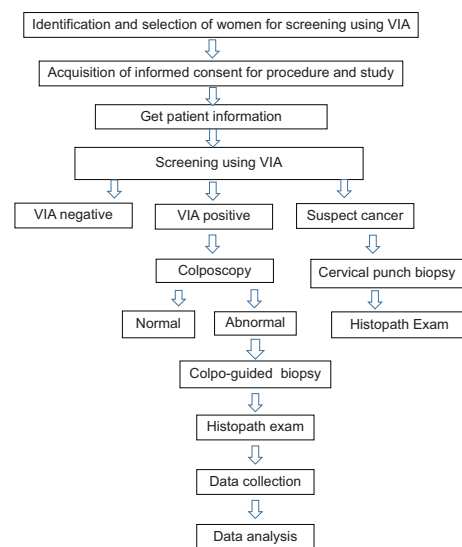
Study subjects

The study population were women who satisfied the following inclusion and exclusion criteria.

Inclusion criteria

The inclusion criteria of this study were as follows:
1. At least 21 years of age
2. Willing and able to provide consent to undergo screening and study.

Exclusion criteria

The exclusion criteria of this study were as follows:
1. Previous hysterectomy
2. Pregnancy.

Members of the vulnerable populations, including the elderly, homeless, politically powerless, or women with terminal illness, were not involved in this study.

Assessment of instrument

Screening procedure of the Philippine Society for Cervical Pathology and Colposcopy activities

Women who satisfied the criteria for cervical cancer screening using VIA were included in the program. The purpose and procedure of the activity were explained. Informed consent was obtained for the procedure and study.

All women underwent VIA. Women diagnosed as VIA positive underwent colposcopically guided cervical punch biopsy. Physicians trained for VIA and colposcopy performed the procedures.

Specimens were sent to a designated pathologist for examination. Moreover, participants of the screening activity were informed of the results once available.

Data collection

Records of screening program activities of the PSCPC from March 2017 to December 2019 were retrieved. The sociodemographic profile and characteristics of the women screened using VIA, results of VIA, colposcopy, and histologic examinations were collected and entered in Epi Info. All information gathered during the screening activity and research remained confidential.

Statistical/data analysis plan

Sample size calculation

The sample size was determined using the following formula:

$$N \geq \frac{4 \times P \times (1-P)}{d^2}$$

where N = sample size

P = expected prevalence

d = allowable error.

The prevalence rate of premalignant cervical lesions using VIA based on previous prevalence studies was 3.5%–5%. Thus, P was set at 0.05. Using the formula above, the sample size is 76.

$$N \geq \frac{4\,(0.05)\,(1-0.05)}{0.05^2}$$

$N \geq 76$.

Data analysis

Frequency, percentages, mean, standard deviation, median, and interquartile range (25th and 75th percentiles) were used to describe the variables of the study. Frequency and percentages were used to determine the prevalence of premalignant cervical lesions among women screened in community-based screening program using VIA, and the characteristics of women with VIA positive and premalignant lesions. The positivity rate of VIA in a community-based screening program was expressed in percentage. Chi-square and risk ratio were used to identify the factors associated with VIA positive and premalignant lesion results. The process produced a risk ratio and a 95% CI. STATA was used for data analysis. Null hypothesis was rejected at a 0.05-alpha level of significance.

Results

A total of 1072 women were screened in the community-based screening program using VIA from March 2017 to December 2019. One hundred and fifty-six (14.6%) of these women were VIA positive, and the demographic profile is shown in Table 1. The median age of these women was 41 years. Majority finished high school (51.9%) and college (29.3%). The median age of coitarche was 18 years. Most of the participants had 1–2 sexual partners (73.1%) followed by 3–4 partners (14.7%) and more than 4 partners (11.5%). Moreover, 9.5% were smokers and 33.3% used oral contraceptive pills.

Of the 156 (14.6%) women who were VIA positive, 79 underwent colposcopically guided cervical punch biopsy. Among those women who were VIA positive, 183 (13.5%) were diagnosed with premalignant cervical lesions. This was 2% (or 21 women) among the total women screened [Table 2]. It was also observed that there was a high false-positive rate of VIA. Fifty-eight (37.2%) women had normal histologic findings after colposcopically guided biopsy, and 76 (48.7%) women had normal findings on colposcopy.

Table 1: Demographic and clinical profile of the patients

	Total (n=156), n (%)	VIA positive with premalignant lesion on biopsy (n=21), n (%)	VIA positive with normal findings on biopsy (n=58), n (%)	VIA-positive suspect cancer (n=1), n (%)	Positive VIA but normal colposcopy and no biopsy needed (n=76), n (%)
Age, median (IQR)	41 (33.5–49)	43 (34–50)	39 (32–47)	36 (36–36)	43 (36–49.3)
Education					
Elementary	18 (11.5)	3 (14.3)	4 (6.9)	1	11 (14.5)
High school	81 (51.9)	15 (71.4)	30 (51.7)	0	35 (46.1)
Vocational	1 (0.6)	0	1 (1.7)	1	0
College	46 (29.5)	1 (4.8)	22 (37.9)	0	23 (30.3)
Postgraduate	6 (3.8)	0	0	0	6 (7.9)
N/A	4 (2.6)	2 (9.5)	1 (1.7)	0	1 (1.3)
Coitarche	18 (17–21)	18 (16–20)	19 (17–22)	16 (16–16)	18 (17.3–21)
Number of sexual partners	2 (1–3)	2 (1–3)	1 (1–2)	4 (4–4)	2 (1–3)
1–2	114 (73.1)	14 (66.7)	49 (84.5)	0	51 (67.1)
3–4	23 (14.7)	5 (23.8)	4 (6.9)	1	13 (17.1)
>4	18 (11.5)	1 (4.8)	5 (8.6)	0	12 (15.8)
N/A	1 (0.6)	1 (4.8)	0	0	0
Gravidity	3 (2–5)	3 (2–3)	3 (2–4.8)	5 (5–5)	4 (2–5)
0	8 (5.1)	0	4 (6.9)	0	4 (5.3)
1	18 (11.5)	3 (14.3)	6 (10.3)	0	9 (11.8)
≥2	129 (82.7)	18 (85.7)	48 (82.8)	1	62 (81.6)
N/A	1 (0.6)	0	0	0	1 (1.3)
Parity	3 (2–4)	2 (2–3)	2 (2–4)	4 (4–4)	3 (2–4.8)
0	10 (6.4)	1 (4.8)	4 (6.9)	0	5 (6.6)
1	25 (16)	3 (14.3)	10 (17.2)	0	12 (15.8)
≥2	119 (76.3)	16 (76.2)	44 (75.9)	1	58 (76.3)
N/A	2 (1.3)	1 (4.8)	0	0	1 (1.3)
Smoking	4 (2.6)	2 (9.5)	1 (1.7)	1	0
OCP use	53 (34)	7 (33.3)	23 (39.7)	1	22 (28.9)
History of pap smear	125 (80.1)	14 (66.7)	44 (75.9)	1	66 (86.8)

IQR: Interquartile range, N/A: Not available, VIA: Visual inspection with acetic acid, OCP: Oral contraceptive

Among all the variables associated with cervical cancer, smoking and coitarche were the only factors associated with VIA positivity and premalignant cervical lesion in the study [Table 3]. Women with early age of coitarche (median age of 18 years [16–20]) were 3.96 times more at risk with $P = 0.000$, and smokers had a fourfold increased risk of developing premalignant cervical lesion compared to nonsmokers with $P = 0.011$.

Discussion

VIA is an inexpensive cervical cancer screening tool that is suitable for low- to middle-resource setting when HPV DNA testing and cervical cytology are not available. In the Philippines, this method has been used in majority of community screening activities for its simple method, cost-effectiveness, and easily available results. Treatment following the see-and-treat approach is also feasible in this setup. HPV DNA testing and cervical cytology are preferred when these methods are logistically feasible.

The prevalence of positive VIA and premalignant cervical lesions has been studied in other countries. In 2017, Nuranna *et al.* mentioned that the prevalence of

VIA positive in the female cancer program in Jakarta was 4.7%. The risk factors of these women diagnosed with premalignant cervical lesions were the increase in number of marriages and parity, smoking, and use of hormonal contraception.[6] A similar study in 2019 conducted in Bengaluru, India, showed that VIA positivity was 11.2% and the prevalence of premalignant and malignant lesions was 3.5%.[7] The prevalence was lower compared to the 5.5% prevalence rate observed in 2018.[8] In Africa, the prevalence of VIA positive was 11%–12.9%. Studies done in Cameroon, Kenya, and Rwanda, however, found a higher prevalence of premalignant cervical lesions at 3.3%–26.7%. The difference in the rates may be related to varying ages of initiation of sexual activity, high prevalence of HIV in certain areas, higher parity, and history of sexually transmitted diseases.[3,9,10] Our study had similar findings of high VIA positivity rate at 14.6% with a prevalence of premalignant cervical lesions among those who were VIA positive at 13.5%. The prevalence of premalignant cervical lesions among all those who were screened was 2%. The prevalence of premalignant cervical lesions in this study, though lower compared to most of the studies, implies that cervical cancer remains a public

Table 2: Prevalence of premalignant cervical lesions among women screened in community-based screening program using visual inspection with acetic acid

	All patients	VIA positive	VIA positive with premalignant lesion on biopsy	VIA positive with normal findings on biopsy	VIA-positive suspect cancer	Positive VIA but normal colposcopy and no biopsy needed
Women screened in community-based screening program using VIA	1072	156	21	58	1	76
Prevalence (%)		14.6	2.0	5.4	0.1	7.1
Prevalence among VIA positive (%)			13.5	37.2	0.6	48.7

VIA: Visual inspection with acetic acid

Table 3: Factors associated with premalignant cervical lesions

	VIA positive with premalignant lesion on biopsy (*n*=21), *n* (%)	VIA positive with normal/other findings on biopsy (*n*=135), *n* (%)	Risk ratio (95% CI)	*P*
Age, median (IQR)	43 (34–50)	41 (32.3–48.8)	1.05 (0.96–1.15)	0.193
Coitarche	18 (16–20)	18.5 (17–21)	3.96 (1.87–8.39)	0.000
Number of sexual partners				
1–2	14 (66.7)	100 (74.1)	0.74 (0.32–1.70)	0.474
3–4	5 (23.8)	18 (13.3)	1.81 (0.73–4.45)	0.198
>4	1 (4.8)	17 (12.6)	0.38 (0.05–2.69)	0.335
N/A	1 (4.8)	0	-	-
Gravidity				
0	0	8 (5.9)	0.90 (0.07–12.33)	0.934
1	3 (14.3)	15 (11.1)	1.28 (0.42–3.91)	0.668
≥2	18 (85.7)	111 (82.2)	1.26 (0.40–3.97)	0.698
N/A	0	1 (0.7)	-	-
Parity				
0	1 (4.8)	9 (6.7)	0.73 (0.11–4.90)	0.746
1	3 (14.3)	22 (16.3)	0.87 (0.28–2.74)	0.817
≥2	16 (76.2)	103 (76.3)	1.00 (0.39–2.53)	0.992
N/A	1 (4.8)	1 (0.7)	-	-
Smoking	2 (9.5)	2 (1.5)	4.00 (1.38–11.62)	0.011
OCP use	7 (33.3)	46 (34.1)	0.97 (0.42–2.26)	0.947
History of pap smear	14 (66.7)	111 (82.2)	0.50 (0.22–1.12)	0.093

VIA: Visual inspection with acetic acid, N/A: Not available, CI: Confidence interval, IQR: Interquartile range, OCP: Oral contraceptive

health burden that needs direct attention. Important factors associated with cervical cancer and key strategies to prevent this disease have already been identified. Furthermore, updates in the screening strategies and creation of newer guidelines have been made by both government and nongovernment institutions. Logistics to implement such measures has to be supported for its sustainability.

The risk factors for HPV infection and cervical cancer in the Philippines as mentioned in the study of Domingo and Dy Echo. in 2009 were similar to the reported cases in other countries as well as this study.[2] Identified factors were young age at first intercourse, low socioeconomic status, high parity, smoking, use of hormonal contraception, and other risky sexual behaviors.

Our country has heeded the global call to action by the WHO on cervical cancer elimination. The Philippine Obstetrical and Gynecologic Society with its affiliate societies, such as the PSCPC, Asia-Oceania Research Organisation on Genital Infections and Neoplasia-Philippines, and Society of Gynecologic Oncologists of the Philippines, has responded to this initiative by promoting and maintaining its community-based cervical cancer prevention programs thru educational awareness, adopt-a-barangay program, screening activities, and treatment of premalignant and malignant cervical lesions and creation of screening and treatment guidelines that are applicable to our clinical practice and current health system.

Conclusion

The prevalence of premalignant cervical lesions among all women who were screened in community-based screening programs using VIA in Metro Manila is lower compared to other studies at 2%. Risk factors that play a role in the development of premalignant lesions are older age, early coitarche, and smoking. There is a need to increase the level of awareness on cervical cancer and its screening and treatment strategies as the disease remains a public health concern.

Limitations of the study

The sample may not be representative of the target population as this is a community-based cervical screening activity. A larger population sampling using regional divisions may be done for more representation. Interpretation of the screening method (VIA) is subjective, but the results were confirmed by histology.

Definition of terms

1. Visual inspection using acetic acid (VIA): Alternative screening tool for cervical cancer screening by observing for acetowhite changes on the cervix after application of 3%–5% of acetic acid
2. VIA positive: Presence of raised dense well-demarcated/defined white plaques or acetowhite epithelium near the squamocolumnar junction (SCJ) within the transformation zone
3. VIA negative: No acetowhite change or presence of fine, thin uniform acetowhite change near the SCJ or presence of acetowhite changes outside the transformation zone or before application of acetic acid
4. Suspect cancer: Presence of endophytic or exophytic lesions on the cervix
5. Squamocolumnar junction (SCJ): The area/junction between the endocervix (lined by columnar epithelium) and the ectocervix (lined by stratified squamous epithelium)
6. Colposcopically guided cervical punch biopsy: Directed biopsies of the cervix using a colposcope machine
7. Low-grade squamous intraepithelial lesion (LSIL): Presence of enlarged nuclei with vacuolated cytoplasm (koilocytosis) in the superficial and intermediate cells typical of productive viral infection limited to the lower third of the epithelium.
8. High-grade squamous intraepithelial lesion (HSIL): Presence of increased nuclear–cytoplasmic ratio as well as abnormal nuclear size and density and altered chromatin patterns of basal or parabasal cells involving the middle third to the full thickness of the epithelium.

Conflicts of interest

There are no conflicts of interest.

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