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Original Article

Sensitivity and Specificity of Visual Inspection with Acetic Acid (VIA) and with Lugol Iodine (VILI) in the Diagnosis of Cervical Cancer in the Northern Region of Cameroon

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Cervical cancer is one of the major causes of women death worldwide. The aim of this study was to test the sensitivity and specificity of visual inspection with acetic acid (VIA) and visual inspection with lugol iodine (VILI) as a diagnostic test for cervical cancer in comparison with Pap smear in the North Cameroon region. 309 women aged between 20 to 62 years were recruited in this study. 307 were included in the statistical analyzes. Each woman was screened for cervical cancer by a conventional smear and visual inspection with acetic acid 5% and the lugol solution. The prevalence of precancerous lesions of cervix was 12.70%. The risk factors of cervical cancer identified were age, matrimonial status, age of first sexual intercourse, and parity. The association of VIA and VILI showed sensitivity, specificity, positive and negative predictive values of 93.58%, 97.01%, 82.01%, and 99.04%, respectively. VIA-VILI were revealed as good screening tests for cervical cancer in the present context. Early detection and treatment of cervical lesions and also faith against the risk factors should help to reduce the mortality and morbidity of this pathology.

Keywords: Sensitivity, specificity, diagnosis, visual inspection, cervical cancer

Cervical cancer is the second most common cancer affecting women (1). In 2002, nearly 493.000 new cases and 274.000 deaths were recorded (2). With more than 527 600 new cases and about 265700 deaths in 2012, 80% of these deaths occurred in developing countries, where this cancer is the leading cause of cancer deaths in the female population (3-4).

In Cameroon, the prevalence of cervical cancer is 7.9% in women between 30 and 60 years old (5). In the developed countries, the incidence and mortality due to cervical cancer is decreasing. For example in United States, between 1955 and 1992, mortality due to cervical cancer decreased at 70% and the rate continues to decline about 3% each year. Similarly, in the United Kingdom the rate has decreased to 70% in 2008 compared to 30 years earlier (6). However, in Cameroon, these rates are progressively increasing. This growth may be due to insufficiency of strategy and program of fight against cervical cancer that limits access to screening; the high cost and rarity of human papilloma virus (HPV) vaccine in the country; and the unavailability of early detection services.

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Consequently, cancer is diagnosed at a very advanced stage in Cameroon. 80% of cancer cases are diagnosed at a late stage and most patients die within 12 months of diagnosis (7). Cervical cancer is an avoidable and curable disease, provided that it is detected early and treated. The slow progression of precancerous lesions to invasive cervical cancer stage leaves a period about 10 years, which may involve the detection and treatment of these lesions before they reach the invasive cancer stage (8). In developed countries, regular screening of the target population would reduce the incidence of cervical cancer more than 90% (9). However, in developing countries, screening is non-existent or covers only a small part of the target population (10). In Cameroon, there is a cancer control committee that carries out sporadic screening activities across the country, but there is no national program to fight against cervical cancer. These screenings are limited because they do not reach the large proportion of the target population. Furthermore, the demands of vaginal cervical smears by physicians are tiny and confined in large cities like Douala and Yaoundé which have anatomy pathology laboratories. All these difficulties make epidemiological surveillance of cervical cancer difficult in Cameroon and even more in the Northern region where there is not yet an anatomy laboratory pathology. The effectiveness of cervical smear in the detection of cervical lesions has been demonstrated and this technique has significantly reduced the relative incidence of cervical cancer in developed countries since 1950. But the limits of this technique for developing countries are important, including cost, logistics and trained human resources to mobilize (11). The possibility of detecting HPV by molecular biology methods offers another additional approach in screening, but its cost is still high and this technique requires sophisticated equipment that is expensive in our context.

Several cases of cervical cancer die in Cameroon without diagnosis or are diagnosed at an advanced stage of the disease where management of the disease is unlikely to conclude favorably. Confronted to these challenges, the use of visual inspection tests such as visual inspection with acetic acid (VIA) and visual inspection with lugol iodine (VILI), which require minimum equipment and a lower cost than other techniques appears to be a viable alternative for low-income countries (12). The aim of this study was to test the sensitivity and specificity of VIA-VILI as a diagnostic test for cervical cancer in relation to cervical smear and to evaluate the feasibility and efficiency of epidemiological surveillance of cervical cancer based on early diagnosis in health facilities in the Northern region of Cameroon.

Materials and methods

Patients

This cross-sectional study was conducted in the Northern region Cameroon from May to August 2016 in Regional Hospital of Garoua, District Hospital of Guider, and Esperance Hospital of Djamboutou (Garoua). Among 309 recruited women, 307 were included in the statistical analyzes. Inclusion criteria were all women between the ages of 20 and 65 years attending hospitals and consenting to participate. Exclusion criteria were women with hysterectomy or cervical conisation, pregnancy, active vaginal bleeding and those with a history of precancerous and cancerous lesions. After obtaining written consent, a questionnaire on the socio-demographic characteristics and the gynecological and obstetric history was administered to each woman. Then they were screened for cervical cancer by a conventional smear, visual inspection after applying 5% acetic acid and lugol iodine.

Conventional smear

The patient was reassured and installed in the gynecological position. Then, a sterile speculum was introduced into her vagina until perfect observation of the cervix. A spatula and cytobrush were used to remove the cells by simple scraping. The sample was spread on a slide and immediately

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fixed with alcohol and dried. All the slides were sent to the anatomo-cytopathology laboratory of the University Hospital Center of Yaoundé, colored and interpreted by an anatomo-pathologist. The results were given according to the classification of Bethesda system 2001.

Visual inspection with 3-5% acetic acid (VIA)

Freshly prepared 5% acetic acid was applied on cervix using cotton swap and the test was interpreted after 1 min under bright light. Acetic acid colors the abnormal cells. The test was considered positive if a white area, well delimited and near the squamous junction appeared on cervix, and negative in the absence of this whitening (13).

Visual inspection with lugol (VILI)

Lugol's iodine solution was applied on cervix using cotton swap and the test was interpreted after 1 min. The normal cells of the cervix contain glycogen and the precancerous or cancerous cells contain very little or not. Through the glycogenic effect on lugol, normal cells absorb lugol and take black or brown coloration. In case of a positive test, iodo-negative areas appear and take a mustard or saffron yellow color. The iodo-negative areas are clearly delineated and clearly visible (14).

Statistical analyzes

The software R commander version 13.2.0 was used for the analysis of the data. The bilateral Chi2 test was used. A variable was considered as statistically significant at $P < 0.05$. The evaluation of the performance of the tests was carried out by calculating the sensitivity, specificity and the positive and negative predictive values.

Results

Conventional smear performance

Pap smears revealed 39 positive cases. A prevalence of 12.70% of precancerous lesions were reported in the northern region of Cameroon. Table 1 shows the distribution of lesions according to grade.

Performance of visual inspection after application of acetic acid (VIA)

According to VIA, 45 cases (14.65%) were positive. Corresponding results are represented in Table 2 were 2 cases of false negative and 8 cases of false positive were identified.

Performance of visual inspection after application of lugol's iodine (VILI)

The visual inspection after application of lugol's iodine revealed 44 (14.33%) positive cases. According to Table 3, 3 cases of false negative and 8 cases of false positive were identified.

The sensitivity, specificity, positive and negative predictive values VIA and VILI tests are presented in Table 4.

Relationship between socio-demographic characteristics and results of smear

Table 5 represents the relationship between socio-demographic characteristics and the onset of cervical dysplasia.

Table 1. Distribution of dysplastic lesions according to grade

Diagnosis	Effectif	Percentage (%)
ASC-H	1	0.32
ASC-US	6	1.95
HSIL	9	2.93
LSIL	23	7.49
NIL/M	268	87.29
Total	307	100

ASC-H: atypical squamous cell cannot exclude high grade; ASC-US: atypical squamous cell of undefined signification; HSIL: high squamous intra-epithelial lesion; LSIL: low squamous intra-epithelial lesion, NIL/M: no intra-epithelial lesion or malignancy.

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Table 2. Contingency of smear results with VIA results

	Results of VIA	
Results of smear	**Negative**	**Positive**
ASC-H	0	1
ASC-US	0	6
HSIL	0	9
LSIL	2	21
NIL/M	260	8

ASC-H: atypical squamous cell cannot exclude high grade; ASC-US: atypical squamous cell of undefined signification; HSIL: high squamous intra-epithelial lesion; LSIL: low squamous intra-epithelial lesion, NIL/M: no intra-epithelial lesion or malignancy.

Table 3. Contingency of smear results with VILI results

	Results of VILI	
Results of smear	**Negative**	**Positive**
ASC-H	0	1
ASC-US	0	6
HSIL	0	9
LSIL	3	20
NIL/M	260	8

Table 4. Diagnostic values of VIA and VILI

	Se (%)	**Sp (%)**	**PPV (%)**	**NPV (%)**
VIA	94.87	97.01	82.22	99.23
VILI	92.30	97.01	81.81	98.85
VIA/VILI association	93.58	97.01	82.01	99.04

Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value.

Table 5. Relationship between the socio-demographic characteristics and the results of the smear

Socio-demographic variables	**Effectives**	**Dysplasia (%)**	**P value**
Age (years)			
(20-29)	97	6.10	0.040
(30-39)	123	13.83	
(40-62)	87	18.39	
Marital statut			
Married	236	11.44	0.027
Not married	71	16.90	
Age of first sexual intercouse (years)			
(13-18)	212	16.03	0.008
(19-30)	95	5.26	

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Table 5 Cont. Relationship between the socio-demographic characteristics and the results of the smear

Socio-demographic variables	Effectives	Dysplasia (%)	P value
Number of sexual partners			
1	147	10.88	0.35
2-10	160	14.37	
Number of births			
0	36	2.77	0.015
1-4	156	10.25	
5-14	115	19.13	
Number of pregnancies			
0	27	3.70	0.35
1-3	109	10.09	
4-15	171	15.78	

Discussion

The prevalence of precancerous lesions of cervix was 12.70% in the studied population. Significantly lower rates were reported in Cameroon's rural and urban zones with 7.9% and 4.9% prevalence, respectively (5, 15). In the present study, low-grade lesions accounted for 74.43% versus 25.64% for high-grade lesions. Doh and Kouam found in 1999 a prevalence of 78.4% and 21.6% for low grade and high grade lesions, respectively (16). These results show the real necessity for screening of cervical cancer in the Northern region and elsewhere in Cameroon. Screening being the only mean of achieving complete cure of the disease, after treatment.

We found that VIA was a good screening test for precancerous lesions with a sensitivity of 94.87% and a specificity of 97.01%. The VIA identified 100% of precancerous lesions of high grade and mistook only 2 precancerous lesions of low grade among the 29 cases confirmed by the Pap smear. Therefore, an error of 6.89% on the lesions of low grade occured. The sensitivity of VIA was higher than that obtained in a study in Gabon (17).

The sensitivity and specificity of VILI were almost similar to those of VIA. We found that VILI had a sensitivity and specificity of 92.30% and 97.01%, respectively.

The association of the VIA with the VILI was beneficial. It reduced the false negatives left by one or the other. This association gave a sensitivity, specificity, positive and negative predictive values of 93.58%, 97.01%, 82.01%, and 99.04%, respectively.

A higher proportion of dysplastic lesions occurred in women over 30 years old. The average age of beginning of precancerous lesions is relatively low at 36.89 years. The study reports a significant difference between age and appearance of dysplasia ($P< 0.04$). This is consistent with data reported by Mpiga et al. in Gabon in 2015 and Nkegoum et al. in 2001 in Cameroon who found a peak appearance of dysplasia between 36 and 40 years (15, 17).

Marital status was associated with the presence of cervical dysplasia lesions. Unmarried women had significantly ($P< 0.02$) more dysplasia than those who were married. These results are in accordance with the epidemiology of cervical cancer because unmarried women are a priori more likely to have multiple sexual partners and therefore a higher risk of developing the disease. The present study

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benefited from information on the number of sexual partners for each participant. Although women with multiple sexual partners had a higher proportion of dysplastic lesions, we did not find a significant difference (P< 0.35) between the number of sexual partners and precancerous lesions.

The average age of first sexual intercourse was 17.52 years, and 75% of women had had sexual intercourse before the age of 19 years. We noticed a statistically significant association (P< 0.008) between age at first intercourse and dysplasia lesions. Those who had sexual intercourse between 13 and 18 years had significantly more dysplasia. This result is in agreement with data reported by Duport in 2008 and the WHO report in 2007 which evoke early first sexual intercourse as a determining risk factor. As HPV is sexually transmitted, the early sexual intercourse has an association with the risk of infection (18).

Parity is also a cervical cancer risk factor. A parity greater than or equal to 5 is considered as a risk factor for cervical cancer (19). The present study has considered at the same time the number of pregnancies and parity. We noted an increasing proportion of dysplasia in relation to the number of pregnancies in the studied population. However, we did not find a statistically significant association (P< 0.35) between the number of pregnancies and the presence of precancerous lesions. On the other hand, we found a significant association (P< 0.01) between parity and dysplasia. Women with a number of births greater than or equal to 5 had more dysplasia than those with a lower number of births.

Taken together, reducing mortality and morbidity caused by cervical cancer requires early screening and the fight against the risk factors that must be included in a national control program.

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Conflict of interest

The authors declared no conflict of interest.

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