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Precancerous lesions of the cervix: prevalence and associated risk factors in the city of Ebolowa

Lésions précancéreuses du col de l'utérus: prévalence et facteurs associes dans la ville d'Ebolowa

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Article original

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ABSTRACT

Introduction: The prevalence of precancerous lesions of the cervix is increasing worldwide. The aim of our study was to determine associated risk factors of precancerous lesions of cervix in the city of Ebolowa.
Methodology: This was a cross sectional analytical study conducted over a 3 years' period from March 2021 to April 2024 at the Ebolowa Regional Health Center (ERHC). We included all records of women who had undergone cervical cancer screening at ERHC from March 2021 to April 2024. Date was collected using a previously tested and validated questionnaire. Descriptive analysis was done and multivariate logistic regression used to identify predictors of precancerous lesions of the cervix. Statistical significance was taken to be P<0.05.
Results: A total of 226 patients were included in the study. Our study revealed that the prevalence of precancerous lesions was 11.5% (26/226). The mean age of the participants was 38.3 ±11 years. The main associated factors to precancerous cervical lesions were: Bamiléké ethnicity (p=0.015), secondary education (P=0.011), use of a contraceptive method (p=0.009), menopause (p=0.049), history of contact bleeding (P = 0.004) and history of syphilis infection (p= 0.012). After multivariate analysis, the independent risk factors were a history of contact bleeding (p=0.004) and a history of syphilis infection (P = 0.012).
Conclusion: the prevalence of precancerous cervical lesions was higher in our study than in other similar studies conducted in Cameroon, underlining the importance of intensifying cervical cancer prevention efforts in resource-limited countries.

RESUME

Introduction : La prévalence des lésions précancéreuses du col de l'utérus est en nette augmentation. L'objectif était de déterminer les facteurs associés aux lésions précancéreuses du col de l'utérus dans la ville d'Ebolowa.
Méthodologie : il s'agissait d'une étude transversale analytique menée sur une période de 3ans de mars 2021 à avril 2024 au Centre Hospitalier et Régional d'Ebolowa (CHRE). Etaient inclus tous les dossiers des femmes ayant bénéficié d'un dépistage du cancer du col de l'utérus au CHRE durant cette période. Les données étaient recueillies à l'aide d'un questionnaire préalablement testé et validé. Une analyse descriptive et une régression logistique multivariée ont été réalisées pour identifier les facteurs associés. La signification statistique a été fixée à P<0,05.
Résultats : au total, 226 patientes ont été incluses. La prévalence des lésions précancéreuses était de 11,5 % (26/226). Les principaux facteurs associés des lésions précancéreuses du col de l'utérus étaient l'ethnie bamiléké (p=0.015), le niveau d'instruction secondaire (p=0.011), l'utilisation d'une méthode de contraception (p=0.009), la ménopause (p=0,049), l'antécédent de saignement de contact (p=0.004) et un antécédent d'infection à syphilis (p=0,012). Après analyse multivariée, les facteurs de risque indépendants étaient la notion de saignement de contact (p=0,022) et l'antécédent d'infection à syphilis (p=0,015).
Conclusion : la prévalence des lésions cervicales précancéreuses était élevée. Ceci souligne l'importance d'intensifier les efforts de prévention du cancer du col de l'utérus dans les pays aux ressources limitées.

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Introduction

Cervical cancer is a tissue neoplasm caused by excessive, abnormal, anarchic and autonomous cell proliferation in the cervix [1].

Cervical cancer is currently the second most common gynecological cancer in women worldwide after breast cancer, with an estimated 604,000 new cases in 2020 [2]. Unfortunately, the incidence of this cancer is steadily increasing in sub-Saharan Africa, with more than 75,000 new cases per year, favoured by HPV infection [3]. The highest incidence and mortality rates are in sub-Saharan Africa, particularly in southern, eastern and western Africa [1,2,3,4]. In 2020, 34,000 people died from cervical cancer, 90% of them in low- and middle-income countries [2]. A study conducted in Cameroon from 1 January 2010 to 31 December 2019 (10 years) at the Douala General Hospital by Ekono et al showed that cervical cancer is the second most common gynaecological cancer after breast cancer, with a prevalence of 38.17%[5].

A precancerous lesion of the cervix is an abnormality of the cervico-pavimentous junction near the external os of the uterus, consisting of the replacement of existing tissue by other tissue [1]. Persistent infection with high-risk human papillomavirus (HR-HPV) leads to the development of precancerous cervical lesions that can progress to cervical cancer [1]. It is now clear that human papillomavirus (HPV) is the major cause of cervical cancer. Other sexual and non-sexual factors contribute to the progression of HPV infection to cervical cancer [5]. Nearly 85% of cervical cancer cases occur in low- and middle-income countries, where cases are detected at late stages due to inadequate screening, lack of awareness campaigns and HPV vaccination programmes [4].

To reduce the number of new cases of cervical cancer and associated mortality, the current secondary prevention and screening programme is based on VIA (Visual inspection under acetic acid) combined with colposcopy and biopsy. These early detection interventions are very important in reducing the incidence of certain types of cervical cancer [6,7,8, 9].

This method is recommended by the WHO in low-income countries such as ours, as it is less expensive than the cervical smear [6]. Several studies have been carried out on the prevalence of precancerous cervical lesions in Cameroon [6, 8, 9,10 ,11,12] , but none in the southern region of Cameroon, hence the interest in conducting this pioneering study in this region.

Methodology

This was a descriptive cross-sectional study with an analytical component conducted over a three-year period, from March 2021 to April 2024, at the Ebolowa Regional Health Centre (CHRE), a second-tier hospital in the Cameroon health pyramid, with an active cervical cancer screening unit. Women from the south region of Cameroon and neighbouring countries (Gabon and Equatorial Guinea) are screened on daily basis and during cervical cancer free screening campaigns by a team of trained healthcare professionals, comprising two gynaecologists and three nurses. The study included all sexually active women aged 25 years or older who were screened for cervical cancer at the CHRE during the study period and who gave their consent to participate. .Women with at least one of the following criteria were excluded from the study: current menstruation, pregnancy, total hysterectomy, cervicitis, and suspected invasive cervical cancer.

Data were collected on socio-demographic characteristics (age, parity, marital status), clinical data (age at first sexual intercourse, number of sexual partners, history of sexually transmitted infections, HIV (human immunodeficiency virus) infection status, smoking, previous screening for cervical cancer, use of oral contraception and menopause). A previously tested and validated questionnaire was used to collect information on patients. Screening was done using cervical visual inspection under acetic acid (VIA) and visual inspection under Lugol Iodine.

The screening was carried out as follows; each participant was admitted to the examination room and placed in the gynaecological position. After thorough counselling on risk factors of cervical cancer and the screening procedure, the cervix was exposed with a speculum and illuminated with a spotlight. The cervix was treated with a cotton swab soaked in 5% acetic acid solution for one minute. The cervix was then examined one minute after the swab was removed. Two different readers examined the cervix. If there was a match, the results were recorded and noted on the examination form. However, if there was disagreement, a third reading was done by a more experienced reader. Lugol iodine solution was also used and VILI positive patients underwent a colposcopy guided

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biopsy. (Figure 2).The biopsy specimen was conditioned using formalin and sent for pathological examination.

Microscopic examination of the slides was performed blindly by two experienced cytologists and confirmed by a pathologist. The results were classified as normal, atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL) according to the Bethesda 2014 guidelines. Patients with a positive result for invasive cervical cancer were excluded. Data were analysed using SPSS version 23 software. To identify factors associated with precancerous lesions, we compared two populations: patients with precancerous lesions and patients without precancerous lesions. Multivariate analysis was performed using binary logistic regression to identify independent risk factors for cervical precancer, with ORs having a 95% confidence interval and a significance threshold of $p<0.05$.

Results

Of the 236 participants, 10 women were excluded for the following reasons: history of total hysterectomy (1 case), ongoing menstruation (6 cases), ongoing pregnancy (1 case), cervicitis (1 case) and suspected cervical cancer (1 case). The suspected case of cervical cancer was confirmed by biopsy and referred to a tertiary hospital for management.

The general characteristics of the 226 women screened are shown in **table 1**.

The mean age of the women was 38.3 ± 11.1 years. Almost half of the 110/226 participants (48.1%) were married. The mean age at first sexual intercourse was 18 ± 2.7 years, and the mean cumulative number of sexual partners was 3.5 ± 1.9. Eighty-eight (38.9%) had ever had a sexually transmitted infection. Only 24% (56/226) had ever been screened for cervical cancer and only 3% had ever been vaccinated against HPV. Of the 226 participants, 7.1% (16/226) reported contact bleeding during screening.

Nearly ¼ of the study population had a positive visual inspection test after application of acetic acid (28.3%: 64/226) .Of the 64 patients with a positive VIA test, all 64 underwent biopsy with anatomopathological examination. After anatomopathological analysis of the 64 samples, 26 were found to be precancerous, for a prevalence of precancerous cervical lesions of 11.5% (26/226). (**Figure 1**)

Table 1: *socio-demographic data of women who underwent cervical cancer screening at the CHRE*

Variable	Modalities	Patients (N=226)	Percentage(%)
Nationality	Camerounian	206	91.2
	Guinean	10	3.8
	Gabonese	4	1.8
	Unknown	6	2.9
Tribe	Bulu	115	50.8
	Ewondo	23	10.2
	Fang	1	0.5
	Bamiléké	33	14.6
	Others	52	23.1
Residence	Urban	186	82.3
	Rural	40	17.7
Matrital status	Maried	110	48.7
	Single	110	48.7
	Widow	6	2.7
Education level	Not scholarized	10	4.4
	Primary	26	11.5
	Secondary	101	44.6
	University	89	39.4
Age (years)	≤25	22	9.7
	[25 ; 35[	80	35.4
	[35 ; 45[	66	29.2
	≥45	58	25.7

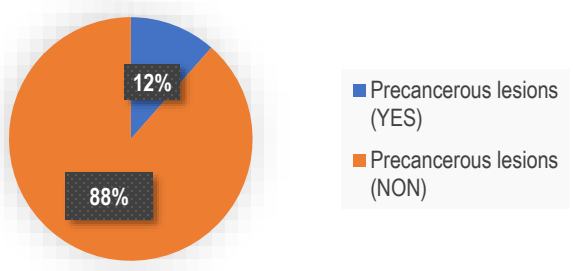

Figure 1. *prevalence of precancerous lesions of the cervix at the Ebolowa Regional Health Center*

In a univariate analysis looking for factors associated with cervical precancerous lesions, patients of Bamileke ethnicity were 3.9 times more likely to have cervical precancer [OR=3.909; 95% CI;1.303-11.727; P=0.015]. Secondary education [OR=3.532; 95% CI; 1.341- 9.306; P=0.011], a history of contact bleeding [OR=5.643; 95% CI; 0.979- 32.513; P=0.004], and menopause

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[OR=2.77; 95% CI; 1.006- 7.513; P=0.049] were risk factors for the development of cervical precancerous lesions as seen on Table 2. Other factors, such as a history of contraceptive use, increased the risk by 3.2 times [OR= 3.21; 95% CI; 1.34-7.7.13; P=0.009]. A history of syphilis infection [OR= 5.390; 95% CI; 1.456- 19.95; P=0.012] and multiparity [OR= 8.774; 95% CI; 1.069- 72.01; P=0.043] also increased the risk of developing cervical precancerous lesions. (**Table 2**)

Table 2: *risk factors associated with precancerous cervical lesions*

Variable	Precancerous lesion (NO) N= 200 ; n (%)	Precancerous lesions (YES) N= 26 ; n (%)	OR (95% CI)	P value
Tribe				
Bulu	106(53.1)	9(34.4)	1	
Ewondo	19(9.9)	4(15.6)	2.443[0.667 ; 8,955]	0.178
Fang	0(0.0)	1(3.8)	NC	1.000
Bamiléké	25(12.3)	8(31.3)	3.909[1.303 ; 11,727]	**0.015**
Others	49(24.7)	4(15.6)	0.977[0.299 ; 3,189]	0.970
Education level				
Non scholarized	10(4.9)	0(0.0)	NC	
Primary				0.522
Secondary	25(12.3)	1(3.8)	0.486[0.053 ; 4,431]	**0.011**
University	81(40.7)	20(75.0)	3.532[1.341 ; 9,306]	
	84(42.0)	5(21.9)	1	
Contact bleeding				
Yes	2(1.2)	6(21.9)	5.643[0.979 ; 32.513]	**0.004**
No	198(98.8)	20(78.1)	1	
Menopause				
Yes	25(12,3)	7(28.1)	2.778[1.006 ; 7.673]	**0.049**
No	175(87,7)	19(71,9)	1	
Contraception				
Yes	79(39.5)	18(67.7)	3.216[1.341 ; 7.713]	
No	121(60.5)	8(32.3)	1	**0.009**
Past history of Syphilis				
Yes	10(4.9)	6(21.9)	5.390[1.456 ; 19.950]	**0.012**
No	190(95.1)	20(78.1)	1	
Parity				
0	40(19.8)	1(3.1)		
]0 ; 2]	67(33.3)	9(34.4)	6.519[0.768 ; 55.319]	0.086
]2 ; 5]	77(38.3)	14(53.1)	8.774[1.069 ; 72.018]	**0.043**
>5	16(8.6)	2(9.4)	6.857[0.603 ; 77.984]	0.121

Table 3: *Independent risk factors associated with precancerous cervical lesions*

Variable	OR	95% confidence interval	Ajusted P value
Tribe			
Bulu	1		
Ewondo	1.333	0.244 -7.288	0.740
Fang	NC	NC	NC
Bamiléké	2.738	0.645-11.627	0.172
Others	0.850	0.201-3.592	0.825
Education level			
Non scholarized	NC		
Primary	0.270	0.012- 5.911	0.405
Secondary	3.139	0.870-11.334	0.081
University	1		
Contact bleeding	20.121	1.543-262.381	**0.022**
Contraception	2.491	0.766- 8.105	0.129
Past history of Syphilis	7.971	1.498- 42.404	**0.015**
Parity			
0	1		
]0 ; 2]	2.900	0.267- 31.483	0.382
]2 ; 5]	2.350	0.204-27.027	0.493
>5	4.312	0.224- 83.150	0.333

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Multivariate analysis looking for independent risk factors for cervical precancer identified contact bleeding [OR= 20.12; 95% CI; 1.54- 262.38; adjusted P=0.022] and history of syphilis infection [OR= 7.971; 95% CI; 1.498- 42.40; adjusted P=0.015] as the 2 independent risk factors for developing cervical precancer. (**Table 3**)

Discussion

The mean age of participants was 38 ± 11,1 years, extremes ranging from 22 to 88 years, in line with a study by Kemfang *et al*. in Yaoundé and Essome *et al.* at the Laquintinie Hospital in Douala, who found a mean age of 40 years among women presenting for cancer screening women from the age of 25, suggesting a late uptake of screening by women in the southern region of Cameroon [9].

Only 24% of patients reported having undergone previous screening for cervical cancer; these results are lower than those reported by Kemfang et al. where 31% and Assoumou *et al*. in Gabon (65,1%) of participants reported having undergone previous screening [8,13]. This low screening rate suggests the need to investigate the obstacle to mass screening of women in Ebolowa in particular. This may be due to the absence of regular mass screening campaigns and education of women about the importance of screening. This remains a thorny problem in Cameroonian cities outside Yaoundé and Douala.

Only 3% of the population had been vaccinated against HPV, in line with results published by Essome *et al.* and consistent with the literature highlighting low vaccination coverage in African countries [10,13], probably due to lack of awareness and refusal of vaccination. This also could be linked to the high cost of vaccination against cervical cancer (35,000 CFA francs per dose for a total of 105,000 CFA francs for full vaccination at the Yaoundé International Vaccination Centre). To reduce the prevalence of precancerous lesions, more young girls aged 9-13 years should be vaccinated against cervical cancer, according to WHO recommendations [9].

HIV prevalence in our study was 5.3%, higher than that of Kemfang et al. (3.1%) and similar to that of Essome et al (5.7%) [8,10]. This high prevalence reflects statistics from the 2018 Demographic and Health Survey (DHS), which placed the South Cameroon region at the top of the list of those most affected by HIV with a prevalence of 5.8%, followed by the East Cameroon region with a prevalence of 5.6%. In our study, 54.9% of participants had sexual intercourse before the age of 18, which is higher tham that reported by Essome *et al*. (40.2%)[10]. This early age of first sexual intercourse indicates a high risk of developing cervical cancer, and the need to lower the age of cervical cancer screening in our context.The prevalence of precancerous cervical lesions in our study was 11.5% (**Figure 1**). Geographical variations in the prevalence of precancerous cervical lesions do exist. Our results are lower than those obtained by Tagne Simo et al. in 2023 in a study carried out in two hospitals in the city of Douala on precancerous lesions of the uterine cervix, where they reported a prevalence of 17% [11] and Kalgong *et al.* in the north of Cameroon where the prevalence of precancerous cervical lesions was 12.7% [12]. On the other hand, Kemfang *et al* [8] found a prevalence of 6.4%. Binalfew Tsehay and Mekbeb Afewok in a meta-analysis on precancerous lesions of the cervix and its determinants among Ethiopian women in 2020 found a pool prevalence of precancerous cervical lesions of 9.43% [14]. Differences in the socio-behavioural characteristics of the population, the availability of screening centres, and the accuracy of the screening test used may explain differences in the regional distribution of cervical cancer prevalence. In a study carried out by Kalgong et al. in 2017, VIA-VILI were revealed as good screening tests for cervical cancer in low resource settings like ours, and results were better if VIA-VILI was associated to a colposcopy guided biopsy [12]. This high frequency in our population could also be explained by the fact that our sample size was smaller than most of the above mentioned studies and the use of colposcopy guided biopsies in our case increased the accuracy of our results.

Patients of Bamiléké ethnicity and those with secondary education had respectively 3.9 times and 3.5 times more risk of developing a precancerous lesion of the cervix with a statistically significant P value. No study carried out to date in Cameroon has revealed this particularity, which we can explain by the fact that the Bamiléké ethnic group in Cameroon is known to have very fertile women who give birth several times. The role of multiparity as a risk factor for cervical cancer is clearly described in the literature, as delivery causes cervical trauma and increased HPV linked modifications of the transformation zone hence leading to precancerous cervical lesions.

As outlined in relevant literature, postmenopausal women exhibited an increased likelihood of

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developing a precancerous cervical lesion, with a reported risk of 2.7. This increased risk is attributed to factors such as advanced age, decreased oestrogen levels, and alterations in vaginal flora, which have been linked to the development of cervical cancer [1].

In an analysis to determine the risk factors for precancerous lesions, multiparity, a notion of contact bleeding, a past history of syphilis infection and contraceptive use were other risk factors for developing a precancerous lesion of the uterine cervix (**Table 2**.), in accordance with the literature on this subject, where it has been shown that changes in the junction zone caused by multiparity and hormonal contraception favour the development of a precancerous lesion of the uterine cervix: Our study also confirms the work of Kemfang *et al.* and Essome *et al*., in which contraception was also found to be a risk factor. Paramita et al. in 2010 identified an elevated risk of precancerous lesions among oral contraceptive users in Ethiopia [15]. Although the role of oral contraceptives in the initiation of precancerous cervical lesions has been subject to controversy, several authors who ascertained the association such as Paramita et al. suggested the association is contingent upon the duration of hormonal contraception use. [16].

On the other hand, HIV infection appeared to be a protective factor in our study without a statistically significant p-value, in disagreement with several studies and the literature. It is controversial whether HIV-positive women are more likely to develop cervical cancer than HIV-negative women [16,17,18]. A study done in Brazil showed that the detection of HPV in HIV-infected women reflects either reactivation or persistence of pre-existing HPV infection rather than recent HPV acquisition [17,18]. Self- reported HIV status could explain the lack of association between HIV and cervical precancerous lesions in this study.

Finally, in our multiple logistic regression analysis to determine the independent risk factors for developing a precancerous lesion of the cervix, only contact bleeding and syphilis infection were independent risk factors for developing precancerous lesions (**Table 3**). To the best of our knowledge, no study other than that published by Sorba *et al.* in 1939 has highlighted syphilis infection as an independent risk factor for precancerous lesions of the uterine cervix [19]. However, any co-infection (syphilis, chlamydia, HIV, herpes simplex virus) may be a factor aggravating oncogenic HPV infection and thus favour the development of precancerous lesions of the cervix. as confirmed by our study. Contact bleeding, being a sign of cervical pathology, is logically a clinical element which increases the probability of finding a precancerous lesion of the uterine cervix.

Conclusion

The prevalence of precancerous cervical lesions remains high in the southern region of Cameroon. The results of this study underline the importance of intensifying cervical cancer prevention efforts in resource-limited countries such as Cameroon to reduce associated mortality. Masse screening should be encouraged and Population based health talks done on cervical cancer prevention and treatment of precancerous lesions.

Conflict of interest: The authors declare no conflict of interest

Authors' contribution:
Data design and acquisition: Messakop M.Y, Moaffo N.Y, Data analysis and interpretation: Messakop M.Y, Moaffo N.Y, Mboua N.V, Bisay S.U, Bilo'o L, Atangana E.H, Editing of the article: Messakop M.Y, Critical review of intellectual content: Ekono G.M, Foumane P

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