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Prevalence of Cancerous and Pre-malignant Lesions of Cervical Cancer and their Association with Risk Factors as seen among women in the Regions of Uganda

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Abstract

Introduction: Cervical cancer is the second cause of death among women in Uganda. Little is known about the prevalence and risk factors associated with cancerous and pre-malignant lesions of cervical cancer in the regions of Uganda.

Methods: A cross sectional survey was carried out in the regions of Uganda. Women who reported to Gynecology Clinics were consecutively screened for cancerous and pre-malignant lesions using the Papanicolaou method. A structured questionnaire was used to collect data on risk factors. The power of associations between the risk factors and cancerous and pre-malignant lesions of cervical cancer were determined using the odds ratio and 95% confidence interval. The p value <0.05 was considered as statistically significant.

Results: Prevalence of 1.2% of cancerous and 11.2% of pre-malignant lesions was detected in all the regions. The risk factors for both cancerous and premalignant lesions were: Early coitus (OR 3.03, CI:1.01.10-10.05; p<0.024) and (OR 1.41 CI:0.98-2.20; p<0.032) respectively, sexually transmitted infections (STDs) (OR 6.07, CI: 1.77-27.22; p<0.001) and (OR 6.52, CI:4.33-9.10; p<0.001) respectively, polygamy (OR 3.13, CI: 0.98-11.77; p<0.027) and (OR 2.74, CI:1.71-4.43; p<0.001) correspondingly, alcohol (OR 3.72, CI: 1.19-13.77; p<0.011) and (OR 1.71, CI:1.20-2.47; p<0.001) respectively, increased sexual partners (OR 8.03, CI:2.20-53.1; p<0.001) and (OR 3.69, CI:2.51-5.48; p<0.001) respectively. Smoking and high parity were risk factor for only cancerous lesions. Although there was no statistical difference between women who had married more than once and those who had single marriage , the likelihood that women who had married more than once would get cancerous and premalignant lesions was high (OR 1.18, p<0.389) and (OR 1.36, p<0.122) respectively.

Conclusion and Recommendations: Age at 1st coitus, STDs, polygamy, smoking, increased sexual partners and alcohol were the risk factors for cancerous and premalignant lesions. Sensitization of the communities and regularly screening for cervical cancer should be encouraged for its control and management.

Keywords: Cervical cancer; Cancerous; Premalignant; Risk factors

Introduction

Globally, cervical is the second cancer to breast cancer and is the fourth among all the detectable cancers [1,2]. According to the report on incidence of cancer in Africa, it is estimated that by the year 2000, cancer of the cervix will constitute 22.2% of all cancers among women in Sub-Saharan Africa [3]. While cancer of the cervix is one of the cancers that can be treated if diagnosed early, it has been noted that in most of the developing countries, cervical cancer presents at its late stages thus making its management difficult [4]. As a result, cervical cancer, therefore remains one of the female cancers associated with high mortality and morbidity in women in developing countries [5]. In Uganda, cervical cancer is the number one cancer killer disease among women, followed by breast cancer [1,6-8]. According to the studies that have been carried out, it has been noted that determination of the risk factors for cervical cancer is vital for understanding the disease occurrence and its management. Occurrence of cervical cancer has been linked to risk factors such as age at first coitus, sexually transmitted infections, parity, number of sexual partners, use of contraceptives and smoking [9]. In another related study, cervical cancer occurrence has been associated with high parity, early marriage and human papilloma virus (HPV) [10]. Although several studies on cervical cancer have been done in Uganda, no studies have been done to determine the prevalence and risk factors for cancerous and premalignant lesions of cervical cancer in the regions of Uganda. The understanding of the risk factors for cancerous and pre-malignant lesions of cervical cancer and establishment of an organized screening program would therefore be essential for the control and management of cervical cancer among women in Uganda.

Materials and Methods

Study design

This was cross sectional survey study.

Study sites

Eastern, Central, Western, Southwestern, Northern and Northwestern regions of Uganda [11]. They are as shown in Figure 1. The total of 14 health facilities was involved in cervical cancer screening. Three from Eastern region, 2 Central, 2 Southwestern, 2 Northern, 2 Northwestern and 3 Central.

A study population

Comprised of women between the age of 18-70 years with mean age of 44 years.

Sampling procedure

Pre-visit was made to one of the regions and a few questionnaires which had been developed were administered by research assistants who had been trained to randomly selected participants. The data generated was then analyzed to determine the completeness of the tool. Adjustments were made in the questionnaire which was finally used for the study. In the subsequent visit, with the assistance of the nursing officers, women who attended antenatal and gynecology clinics were consecutively recruited into the study. They were first briefed on the purpose of the study after which informed consent was obtained using consent form. The participants who were not fluent in English language were interpreted using the language they comprehended by an interpreter. The pretested structured questionnaire was used to generate the data on risk factors from each of the participants after which a cervical smear was take from each participant with the aid of Ayre speculum. The glass smear was then fixed while still wet in 95% ethanol for 5 minutes and dried at room temperature.

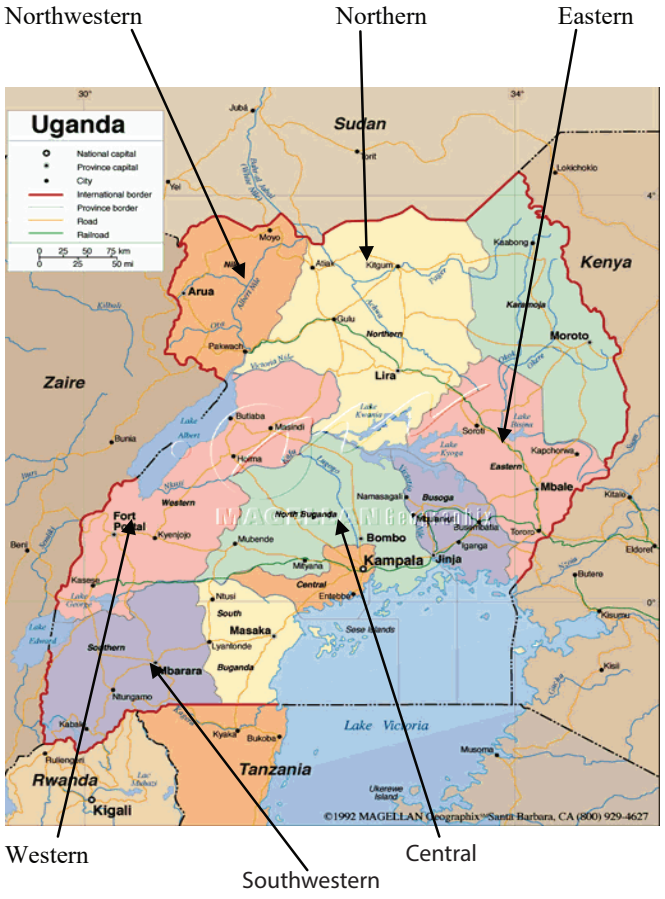

Figure 1: Map of Uganda showing the selected study regions, Adopted after

Laboratory procedure

The smears were stained using Papanicolaou protocol [12]. First the smears were stained in Haematoxylin and rinsed in water for 10 minutes. They were then rinsed in 95% alcohol and stained in Orange G for 2-3 minutes. This was followed by rinsing in 95% alcohol. They were stained in Eosin Azure (EA) for 2-3 minutes and rinsed in two changes of 95% alcohol. They were cleared in two changes of xylene and finally mounted under the cover slip using Destrene Polystyrene Xylene (DPX).

Interpretation of the slides

The slides were examined under the microscope using 10x and 100x magnification. Cancerous lesions were interpreted as cells with a high nuclear cytoplasmic ratio with loss of polarity, cells that exhibited hyperchromatic staining and loss of maturation, had pleomorphic features and intra-cytoplasmic keratinization. While precancerous cells were interpreted as cells with moderate increased nuclear cytoplasmic ratio with no loss of polarity and were hyperchromatic. Normal cells were interpreted as cells that were monotonous, oriented and had normal shape, normal nuclear cytoplasmic ration and exhibited normochromatic staining picture.

Bethesda 2014 was used for the classification and interpretation of cervical smears stained by Papanicolaou method. Histology is ongoing as follow up study for all those smears that were found to be high grade. Three senior histopathologists examined the Pap smears and the findings were included into the analysis when at least two histopathologists were in complete agreement.

Variables

Dependent variables were considered as cancerous and premalignant lesions while independent variables were socio-demographic characteristics such as - age, education, marital status and religion. Other independent variables included parity, sexual partners, smoking, alcohol drinking, use of contraceptives and sexually transmitted infections (STDs).

Data analysis

The data were entered and analysed using software package for social sciences 10.0 (SPSS 10.0) [13]. The power of associations between the risk factors and occurrence of cancerous and premaligant lesions was determined using Open Source Epidemiologic Statistic Program for Public Health version 2.2.1 (OPENEPI) using 2 × 2 contingency tables [14]. Odds ratio and 95% confidence interval were used and $p<0.05$ was considered as statistically significant.

Results

Socio-demographic characteristics

Overall total number of 1210 women were screened for cancerous and premalignant lesions of cervical cancer from the selected regions of Uganda. Their ages ranged between 18 and 70 years with mean age of 44 years. The highest number of respondents were married and the lowest were widowed. Most of the participants had primary education followed by secondary. The details are as shown in Table 1.

Variable	Region						
	Eastern (n=351)	Central (n=170)	Western (n=125)	Southwestern (n=151)	Northern (n=193)	Northwestern (n=220)	Overall Total (n=1210)
Age in years							
18-30	164 (46.7)	39 (23.0)	59 (47.2)	117 (77.5)	93 (48.2)	128 (58.2)	600 (49.6)
31-40	120 (34.2)	56 (32.9)	24 (19.2)	17 (11.2)	57 (29.5)	55 (25.0)	329 (27.2)
41-50	52 (14.8)	19 (11.2)	12 (9.6)	14 (9.3)	36 (18.7)	32 (14.5)	165 (13.6)
51 above	15 (4.3)	56 (32.9)	30 (24.0)	3 (2.0)	7 (3.6)	5 (2.3)	116 (9.6)
Education							
Informal	10 (2.9)	07 (4.1)	07 (5.6)	09 (6.0)	10 (5.2)	11 (5.0)	54 (4.5)
Primary	209 (59.5)	51 (30.0)	75 (60.0)	109 (72.2)	112 (58.0)	136 (61.8)	692 (57.2
Secondary	95 (27.1)	66 (38.8)	27 (21.6)	18 (11.9)	60 (31.1)	61 (27.7)	327 (27.0)
Tertiary	33 (9.4)	24 (14.2)	13 (10.4)	12 (7.9)	09 (4.7)	09 (4.1)	100 (8.3)
University	04 (1.1)	22 (12.9)	03 (2.4)	03 (2.0)	02 (1.0)	03 (1.4)	37 (3.0)
Marital status							
Married	294 (83.8)	115(67.6)	85 (68.0)	104 (68.9)	170 (88.1)	182 (82.7)	950 (78.5)
Single	42 (11.9)	41 (24.1)	35 (28.0)	36 (23.8)	10 (5.2)	25 (11.4)	189 (15.6)
Divorced	08 (2.3)	09 (5.3)	02 (1.6)	08 (5.3)	04 (2.1)	06 (2.7)	37 (3.1)
Widowed	07 (2.0)	05 (2.9)	03 (2.4)	03 (2.0)	09 (4.6)	07 (3.2)	34 (2.8)
Only for married							
Polygamous	41 (14.0)	16 (5.4)	12 (4.1)	15 (5.1)	24 (8.2)	26 (8.8)	134 (45.6)
Monoganous	49 (16.7)	19 (6.5)	14 (4.8)	18 (6.1)	29 (9.9)	31 (10.4)	160 (54.4)
Religion							
Catholics	104 (29.6)	50 (29.4)	37 (29.6)	45 (29.8)	58 (30.1)	66 (30.0)	360 (29.7)
Protestants	115 (32.8)	56 (32.9)	41 (32.8)	50 (33.1)	63 (32.6)	72 (32.7)	397 (32.7)
Muslim	66 (18.8)	32 (18.8)	23 (13.5)	28 (18.5)	36 (18.7)	41 (18.6)	226 (18.7)
Orthodox	11 (3.1)	5 (2.9)	4 (3.2)	5 (3.3)	6 (3.1)	7 (3.2)	38 (3.1)
Redeemed	55 (15.7)	27 (16.0)	22 (17.6)	23 (15.2)	30 (15.5	34 (15.5)	194 (15.8)

Table 1: Socio-demographic characteristics

Region	Premalignant lesions	Cancerous cases	Negative
Eastern N=351	47 (13.4)	3 (0.9)	301 (85.7)
Northern N=193	27 (14.0)	4 (2.1)	163 (84.4)
Northwestern N=220	28 (12.7)	3 (1.4)	188 (85.5)
South Western N=151	9 (5.9)	1 (0.7)	141 (93.4)
Western N=125	8 (6.4)	1 (0.8)	116 (92.8)
Central N=170	17 (10.0)	2 (1.2)	151 (88.8)
Overall Total	**136 (11.2)**	**14 (1.2)**	**1,060 (87.6)**

Table 2: Cancerous and pre-malignant lesions detected per region

Cancerous and pre-malignant lesions detected per region

Northern region had the highest prevalence of premalignant lesions (14.0%) followed by Eastern (13.4%) and Northwestern 12.7%. Central, Western and Southwestern regions had the lowest prevalence of premalignant lesions. Northern and Northwestern regions had the highest prevalence of cancerous lesions (2.1) and (1.4%) respectively. The details are as shown in Table 2.

Cancerous and pre-malignant lesions according to age

The participants between 31-40 years and 41-50 years recorded the highest cases of premalignant lesions (65.0%) and (63.5%) respectively, while those above 50 years had the highest recorded cases of cancerous lesions (26.7%) respectively. The details are as shown in Table 3.

Association between risk factors and cancerous lesions among the participants

Smoking was found to be the highest risk factor for cancerous lesions of cervical cancer (OR13.8, CI: 2.92-50.37; p<0.001) , followed by increased sexual partners (OR8.03, CI: 2.02-53.1; p<0.001), sexually transmitted infections (OR 6.07, CI: 1.79-27.22; p<0.001), alcohol (OR3. 72, CI: 1.19-13.77; p<0.011). parity (OR3.67, CI: 1.17-13.58; p<0.012), polygamy (OR3.13, CI: 0.98-11.77; p<0.027) and age at 1st coitus (OR3.03, CI: 1.01-10.05; p<0.024) and increased marriages (OR1.18, CI: 0.18-4.76; p<0.389). However, there was no statistical difference between women who had more than one marriage and those with single marriage (p>0.389), although the likelihood that women with more than one marriage would get cancerous lesions was high (OR1.18). The details are as shown in Table 4.

Association between risk factors and pre-malignant lesions among the participants

STDs was found to be the highest risk factor for premalignant lesions (OR 6.52, CI: 4.33-9.10; p<0.001), followed by polygamy (OR 2.74, CI: 1.17-4.43; p<0.0001), alcohol (OR1.71, CI: 1.19-2.47; p<0.001) and age at first coitus (OR1.41, CI: 0.98-2.02; p<0.032) and marriages (OR 1.36, CI: 0.80-2.25; p<0.122), Similarly, there was no statistical difference between women who had more than one marriage compared to those with single marriage. The details are as shown in Table 5.

Discussion

This study sought to determine the prevalence and risk factors associated with cervical cancer and pre-malignant lesions in the regions of Uganda. In overall we screened 1210 women using Papanicolou method and the prevalence of cancerous lesions was found to be 14 (1.2%) and precancerous lesions 136 (11.2 %). There was variability in the prevalence of cancerous and precancerous lesions in the study regions. Surprisingly, Eastern region with 351 women screened had 3 (0.9%) and 47 (13.4%) cancerous and pre-cancerous lesions, respectively, which was lower than 4 (2.1%) and 27 (14%) cancerous and precancerous lesions detected in the Northern region respectively out of 220 women screened. While this could be attributed to differences in the number of women screened in these regions, it is also possible that the war conflicts which have largely affected Northern region could have probably influenced these findings

Variable	Region						
	Eastern	Central	Western	South western	Northern	North western	Total
Pre-malignant lesions n= 136)							
18-30 (n=164)	4 (2.4)	0 (0.0)	0 (0)	3 (2.2)	7 (4.3)	4 (2.4)	18 (11.0)
31-40 (n=120)	29 (24.2)	12 (10.0)	5 (4.2)	4 (2.9)	12 (10.0)	16 (13.3)	78 (65.0)
41-50 (n=52)	12 (23.1)	4 (7.7)	2 (3.8)	2 (1.5)	6 (11.5)	7 (13.5	33 (63.5)
>50 (n= 15)	2 (13.3)	1 (6.7)	1 (6.7)	0 (0)	2 (13.3)	1 (6.7)	7 (46.7)
Cancerous cases (n= 14)							
18-30 (n=164	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.6)
31-40 (120)	0 (0)	1 (0.83)	0 (0)	0 (0)	1 (0.83)	1 (0.83)	3 (2.5)
41-50 (n=52)	1 (3.8)	1 (1.9)	1 (1.9)	0 (0)	2 (1.9)	1 (1.9)	6 (11.5)
>50 (n= 15)	1 (6.7)	0 (0)	0 (0)	1 (6.7)	1 (6.7)	1 (6.7)	4 (26.7)

Table 3: Cancerous and pre-malignant lesions according to age.

Risk factor	Malignant lesions	Odds Ratio	95% CI	P-value Mid-P exact
Parity				
1-4 (n= 716)	4 (0.6%	3.67	1.17-13.58	0.012
>5 (n= 494)	10 (2.0%)			
Age at 1st Coitus				
13-17 (n= 417)	9 (2.2)	3.03	1.01-10.05	0.024
>18 (n= 693)	5 (0.7)			
Marriages				
1 (n= 815)	12 (1.5)	1.18	0.18-4.76	0.389
>1 (n= 115)	2 (1.7)			
Only for married (n=294)				
Polygamous (n=134)	10 (7.4)	3.13	0.98-11.77	0.027
Monogamous (n=160)	4 (2.5)			
Sexual partners				
1 (n= 687)	2 (0.4)	8.03	2.02-53.1	0.001
>1 (n=523)	12 (2.1)			
Smoking				
Yes (n=26)	3 (8.3)	13.8	2.92-50.37	0.001
No (n=1184)	11 (0.9)			
Alcohol intake				
Yes (n=550)	10 (1.8)	3.72	1.19-13.77	0.011
No (n=660)	4 (0.6)			
Contraceptives				
Yes (n=353)	2 (2.6)	0.40	0.06-1.60	0.115
No (n=857)	12 (1.4)			
History of STDs				
Yes (n=461)	11 (2.4)	6.07	1.77-27.22	0.001
No (n=749)	3 (0.4)			

Table 4: Association between risk factors and cancerous lesions among the participants

Risk factor	Pre-malignant lesions	Odds Ratio	95% CI	P-value Mid-P exact
Parity				
1-4 (n=716)	93 (13.0)	0.64	0.43-0.93	0.010
>5 (n=494)	43 (8.7)			
Age at 1st Coitus				
13-17 (n=417)	61 (14.6)	1.41	0.98-2.02	0.032
>18 (n=693)	75 (10.8)			
Marriages				
1 (n=815)	115 (14.1)	1.36	0.80-2.25	0.122
>1 (n=115)	21 (18.6)			
Only for married (n=294)				
Polygamous (n=134)	80 (59.7)	2.74	1.71-4.43	0.001
Monogamous (n=160)	56 (35.0)			
Sexual partners				
1 (n=687)	40 (5.8)	3.69	2.51-5.48	0.001
>1 (= 523)	96 (18.4)			
Smoking				
Yes (n=26	1 (3.8)	0.31	0.01-1.68	0.117
No (n= 1184	135 (11.4)			
Alcohol intake				
Yes (550)	78 (14.2)	1.71	1.20-2.47	0.001
No (660)	58 (8.8)			
Contraceptives				
Yes (n= 353)	27 (7.6)	0.82	0.52-1.27	0.194
No (n= 857)	109 (12.7)			
History of STDs				
Yes (n= 461)	104 (22.6)	6.52	4.33-9.10	0.001
No (n= 749)	32 (4.3)			

Table 5: Association of risk factors and pre-malignant lesions among the participants

given the fact that women from this region became more vulnerable to sexual abuse and were thus at high risk of sexually transmitted infections. While our study did not look at the HPV in association with the prevalence of cancerous and premaligant lesions in the regions of Uganda, it is possible HPV had a major role to play in the mergence of these lesions. This therefore, calls for another multicentred study to determine the association between HPV and cervical lesions in the regions of Uganda.

The prevalence of 14 (1.2%) of the cancerous lesions detected in our study, was lower than 17 (1.7%) recorded in Rwanda, (9) and 24% in Cameroon [15]. However, it was found to be higher than 1.0% recorded in Ethiopia [16]. The prevalence of 136 (11.2%) of the precancerous lesions found by our study was higher than 60 (5.9%) reported in Rwanda [9], 31 (7.9)% in Ethiopia [16] and 9 (4.5%) and 14 (7%) reported in Nigeria [17,18]. However, was lower than 798 (13.3%) reported in Thailand [19]. The variations in the prevalence of cervical cancer and precancerous lesions between our study and other studies was probably due the differences in reliability of the screening methods used in these studies [20]. While our study used Papanicloau as a screening method, other studies used visual inspection with acetic acid (VIA).

Notably, the prevalence of cervical cancer and premalignant lesions was equally found to vary according to age by this study. The prevalence of 1 (0.6%) cancerous lesions seen among the women below 30 years, was lower than 3 (2.5%) seen among women between 31-40 years, 6 (11.5%) between 41-50 and 4 (26.7%) above 50 years. On contrary, the study in

Cameroon [21] found the prevalence of 164 (20.5%) of cancerous lesions among women below 30 years which was higher than the findings of this study. Similarly the study in Korea [22], found 2.5%-8.3% prevalence, and that in Rwanda [9], found 4 (0.8%) prevalence among women below 35 years which was also higher than1(0.6%) found in our study. The lower prevalence of cervical cancer seen among women below 30 years in our study, could probably have been influenced by luck of properly established and effective screening programs for early detection of cervical cancer among young reproductive women in our country, as it is practiced by countries such as Rwanda [9] and Nigeria [23].

Women aged between 41-50 years and above 50 years exhibited highest prevalence of cancerous lesions 6 (11.5%); 4 (26.7%) respectively, as compared to those below 30 years. This was in agreement with the study done in India [24] which found women above 55 years to be having the highest incidence of cervical cancer. It is possible that the high prevalence of cervical cancer found among women above 40 years by our study, was probably because since cancer evolvement is progressively slow process, and coupled with the absence of comprehensive and organized programs for early detection of cervical cancer in Uganda, it is most likely that it is detected late in life.

This study found strong association between cancerous and premalignant lesions of cervical cancer with risk factors such as polygamy, age at 1st coitus, alcohol, STDs and increased sexual partners apart from parity and smoking which were risk factors associated only with cancerous lesions. This is in concurrence with the study, which found among others early coitus, alcohol and smoking tobacco as risk factors for cancerous lesions [17]. Similar observations were made by another study which found high parity, early coitus, STDs and tobacco among others as associated risk factors for cancerous lesions [18]. Our findings are also in conformity with the study done in Rwanda which noted that high parity and early coitus were risk factors for cancerous lesions [9]. The study done in 8 countries namely; Morocco, Algeria, Philippines, Thailand, Madras, Colombia, Paraguay and Peru equally found early coitus as one of the risk factors for cervical cancer [25], while a study done in Nigeria found increased number of pregnancies to be linked to cervical cancer [18]. All these findings were in agreement with the findings of our study.

It worth noting that, most of these risk factors we found in our study were highly linked to one another. The fact that high prevalence of cancerous and premalignant lesions were detected among women who had had more than one sexual partner and who were in polygamous marriage, probably explains why many of the women who had cancerous and premalignant lesions had history of STDs since increased sexual partners and polygamy are predisposing factors for STDs such HPV. This observation is in agreement with the study which found that having many sexual partners and being in polygamous relationship predisposes partners to STDs and thus to cervical cancer [18]. This was also noted by other studies which found many sexual partners to be associated with STDs which was a high risk for cervical cancer [26, 27].

Interestingly, in overall, most of the risk factors appeared to be linked to alcohol . Since alcohol is associated with increased urge for sex, it may therefore be hypothesized that increase in urge due to sex, may expose one to early sex with the possibility of getting STDs and unwanted pregnancies which may also lead to high parity since one may get married early. There is also likelihood of marrying a person who is already married thus ending up in a polygamous relationship with the possibility of increasing the risk of contracting STDs. This observation is in agreement with the report by (WHO/UNAIDS) which noted alcohol intake among the youth, is believed to promote early coitus, acquisition of STDs and unwanted pregnancies [28]. This is also in agreement with the studies done in Belarus, Nairobi and Cape town [29,30,31] which found that drinking alcohol by the adolescents exposes them to early sexual encounter, unwanted pregnancies and STDs. Alcohol abuse has also been linked to increase in multiple partners and thus promiscuity which in end can culminate into polygamy [29,32].

Although our study did not find contraceptives and many marriages as risk factors for cervical cancer and premalignant lesions, a study done Indonesia found women who use contraceptives to be at higher risk of getting cervical cancer [33]. Similarly, women who had married many times were found to be at high risk of cervical cancer [34]. While widowed and divorced women were not considered among the risk factors by our study, some of the studies found divorced women to be at higher risk of getting cervical cancer [35].

Conclusion

Early coitus, STDs, polygamy, increased sexual partners, alcohol and smoking were the risk factors for both cancerous and premalignant lesions of cervical cancer. Sensitization of the communities about the risk factors and regularly screening women of reproductive age for cervical cancer should be encouraged for its control and management. Using multipronged approach to integrate screening as essential component of reproductive health should be developed as a policy.

Ethical Consideration

Permission to carry out this study was sought from the then Faculty of Medicine Research and Ethical Committee and from the Ministry of Health Ethics and Research Committee.

Conflict of Interest

There is no conflict of interest among authors.

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