

Full Length Research Paper

Determinants of pre-cervical cancer among women visiting Hawassa University Comprehensive Specialized Hospital, Ethiopia: A case control study

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Cervical cancer is the most common and lethal form of cancer occurring among women of sub-Saharan Africa and Ethiopia. Despite its wider occurrence, cervical cancer is preventable and curable if it is diagnosed and treated in its pre-cancerous stage. Recognizing the risk factors associated with pre-cervical cancer lesion is important to design appropriate strategies for prevention of cervical cancer. However, studies on risk factors associated with pre-cervical cancer lesion in women are limited in Ethiopia as well as in the study location. A hospital based unmatched case control study was conducted at Hawassa university, Comprehensive Specialized Hospital. Bivariate logistic regression analysis was conducted to assess the strength of association between the outcome and explanatory variables. Association was declared when p-value is < 0.05. Predictive variables whose P-value is <0.25 in crude analysis were included in the final multivariate analysis. A backward stepwise approach was conducted and statistically significant association was declared based on adjusted odd ratio (AOR), 95% confidence interval (CI) and P-value <0.05. Findings from multivariate analysis showed contraceptive use [AOR: 5.16, CI (2.97-8.96)], pattern of irregular menstrual bleeding [AOR: 6.03, CI (3.40-10.69)], history of STI [AOR: 4.02, CI (2.28-7.10)] and HIV/AIDS reactive status [AOR: 7.41, CI (4.38-12.56)] were found to be independent predictors of pre-cervical cancer lesion. Being using contraceptive, having STI history, having irregular menstrual bleeding pattern and having HIV/AIDS reactive status increase the risk of developing pre-cervical cancer. These high risk groups should be encouraged to have regular screening for pre-cervical cancer.

Key words: Pre-cervical cancer, visual inspection with acetic acid (VIA), risk factors, cervical cancer.

INTRODUCTION

Globally, cervical cancer is the third most frequent cancer among women. Each year, an estimated 569,847 new

cases are diagnosed with ~311,365 deaths in 2018. Low-resource countries account for 85% of the cases, yet very

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little is spent in preventing and treating cervical cancers (ICO Information Centre on HPV and Cancer, HPV Information Center, 2019). Similarly, it is the most common and most lethal cancer among the women of sub-Saharan Africa. A considerable reduction in cervical cancer incidence and deaths has been achieved in developed countries with effective strategies for cervical cancer screening and treatment programs. However, this has not been possible in most resource-limited countries, mainly because systematic screening is rarely performed (Jemal et al., 2012).

In Ethiopia, cervical cancer ranks as the most frequent cancer among women and cause for 4,732 deaths annually. Among the general population, ~33.6% of women are estimated to harbor cervical human papilloma virus (HPV) infection at a given time. The primary screening method adopted by the Government of Ethiopia is the visual inspection with acetic acid applied to the cervix by health care providers. An accurate diagnosis depends on the ability of the provider to visualize the cervix properly and differentiate between cervical lesions (Federal Democratic Republic of Ethiopia, Ministry of Health, 2015).

Cervical cancer is usually detected in advanced stages in developing countries due to the lack of effective preventive mechanisms. An estimated 80% of all patients with cancer in developing countries are presented with advanced stages at their first consultation (Cervical Cancer Action, 2011). In low resource countries, cytology-based screening programs and DNA typing of HPV are usually beyond the capacity of many health services. Visual inspection of the cervix using acetic acid (VIA), Lugol's iodine (VILI), and Folate Receptor-Mediated Staining Solution (FRD™) to highlight precancerous lesions allows identification of pre-cancerous lesions in the clinic instead of the laboratory. With adequate training, any health care provider, including doctors, nurses, or nurse-midwives, can effectively perform the procedure (Sherris et al., 2010; Li et al., 2017).

The exact cause of cervical cancer remains unknown. Cervical cancer can occur in any women, however, there are a number of associated risk factors that have been identified. Epidemiological studies conducted during the past 30 years have consistently indicated that cervical cancer risk is strongly influenced by sexual activity, number of sexual partners and sexual behavior of women's male partners (Schiffman and Brinton, 1995). According to the UNAIDS Report (2016), several key risk factors for cervical cancer are common in sub-Saharan countries, including prolonged HPV infections and HIV/AIDS which is endemic in this region. Other risk factors include debut of sexual activity before age of 20 years old, multiple sexual partners, tobacco smoking, oral contraceptive pill use for more than 5 years, history of cervical cancer in the family, high parity (more than 3 children born), and

immune-depression due to malnutrition or other systemic diseases (WHO, 2006).

Getting the evidence in factors associated with pre-cervical cancer among screened women helps to take an action in each factor to decrease the morbidity and mortality of cervical cancer. And allocate resources at the policy level so as to control the problem and concurrent losses coming with the disease burden. Studies on the issue of factors associated with pre-cancer cervical among screened women in Ethiopia are limited. Thus, this study focused on finding out the dominant risk factor for pre-cervical lesion among women who were screened by visual inspection of the cervix using acetic acid (VIA) and their result was positive/suspicious or negative for pre-cancer lesion.

METHODOLOGY

Study design

The study was institutional unmatched case control study design. In this study, the cases were those women whose cervical cancer screening results were positive or suspicious for visual inspection with acetic acid screening for pre-cervical cancer lesion. The controls were those women whose visual inspection with acetic acid screening for pre-cervical cancer lesion result was negative. Patients' data documented for five years and 4 month were collected from the client assessment card from visual inspection with acetic acid for pre-cervical cancer (VIA) screening room in Hawassa Comprehensive Specialized Hospital, Ethiopia. The follow up period encompasses from August 13, 2012 to December 29, 2017 and the data was collected from 1st to 15th January, 2018.

Study setting and population

This study was conducted in Hawassa Comprehensive specialized Hospital (Hawassa University) which is found in Hawassa city, South Ethiopia. The city is located at 275 km South of Addis Ababa (the capital of Ethiopia). Hawassa Comprehensive Specialized Hospital has started health delivery services in 2006. It provides diversity of both outpatient and inpatient services for about 15 million populations from all over SNNPR and neighboring region. Currently, it has over 400 beds and provides high quality patient care in a broad range of services to over 90,200 outpatient, 18,116 hospitalized patients and 1,092 emergency cases annually.

The source population of this study was women who were screened for cervical pre-cancer lesion by using visual inspection with acetic acid (VIA) and their result was positive/suspicious and negative in Hawassa Comprehensive Specialized Hospital from August 13, 2012 to December 29, 2017. During this time duration there were about 1789 women screened for pre-cervical cancer and all of them are the study population for this research. Among the total population, there were 272 women with positive results and 7 had suspicious result. The study population's data were retrieved from patient registry book and client assessment card from the VIA room of the hospital.

Sample size and sampling procedure

The sample size determination for addressing objective of the study

was calculated based on two population proportions and considering three commonest risk factors for cervical cancer and by choosing one risk factor which is very frequently assessed in similar studies and had satisfactory sample size frame. The list factors were oral contraceptives, number of sexual partners, menopausal status (Mesele et al., 2015; Geeth and Santhylnt, 2013). These risk factors are taken from similar studies conducted in India and western part of Ethiopia. Then the researcher decided to consider the risk factor, number of sexual partners to calculate the sample size for the study because it allowed to have considerably sufficient study participants number in order to minimize the sample size problem.

The sample size determination for addressing objective of the study was calculated based on the following assumptions: confidence level of 95%, prevalence, power 80%, ratio of cases to control of 1:1, and proportion of cases. However, since the calculated sample size was much closer to the total number of cases that visited the hospital during the specified periods, the researcher includes all the cases which were found in the registry. Finally, the study enrolled 260 women with positive pre-cancer lesions (cases) and 260 women who tested negative (controls) with visual inspection with acetic acid result.

All women who did pre-cervical cancer screening from August 13, 2012 to December 29, 2017 at Hawassa Comprehensive Specialized Hospital were considered as a study population. It included 5 years and 4 months cervical cancer screening service collected data. This study considers all the cases found in the study population. To select the controls from the study population systemic random sampling techniques was used. Totally, there were 279 cases found in the secondary data and among them there were about 19 cases which did not have complete information. The cases which did not have complete information were excluded from the study. There were about 1510 women found in the secondary data whose VIA result was negative and among them 101 were excluded from the study due to incomplete data in the register. Then, by using systemic random sampling techniques 260 controls were selected among the total number of the controls. Every 5th client data was enrolled in the study.

Data collection instruments

Data were collected from Hawassa Comprehensive Specialized Hospital pre-cervical cancer screening room. The client assessment form and registry book which was completed during the screening service was used to collect the associated risk factors for pre-cervical cancer. In the client assessment form there were about eleven questions which helped to assess the risk factors for pre-cervical cancer in which the service providers completed after they received the response of the women during the regular and campaign screening service. As data collection tools, excel spreadsheet was used in this study. The data were collected by two trained VIA service providers. Then the researchers verified wrong or missed information from the secondary data.

Data processing and analysis

The data were cleaned, coded and entered into SPSS version 20 statistical software. Descriptive, bivariate and multivariate logistic regression analyses were conducted. COR, AOR and 95% Confidence Intervals (CI) with the P-value were computed to find statistically significant associated risk factors for the outcome variable. Statistical significance was declared if P value < 0.05 and if the 95% CI includes or crossed a value of 1.0.

RESULTS

Demographic characteristics

The total number of the study participants was 520 women. Among them 260 were cases and 260 were controls. The mean and standard deviation of the age of the study participants was 38.55 (± 6.13 SD) and the case and the controls were 37.15 (± 5.73) and 39.93 (± 6.26) old, respectively. Among the participant of the study who were under 30 years of age, 19 (70.3%) were cases and 8 (29.7%) were controls. Majority, 234 (90.0%) cases and 250 (96.15%) controls fall in the age category of 30-49 years while 7 cases and 2 participants were over 49 years old.

Among the study participant, 41 (15.77%) cases and 39 (15.00%) controls had at least college level education. Majority of the participants attended secondary education, 257 (49.42%) of which 130 (50.00%) were cases and 127 (48.85%) were controls. The study showed that about 78 (30.00%) cases and 84 (32.31%) controls attended primary education. About 22 (4.23%) participants did not attend formal education among them, 11 (4.23%) were cases and 10 (3.85%) were controls. In this study, marital status was taken as one of the independent variables. There were 204 (78.46%) cases and 227 (87.31%) controls who married whereas 29 (11.15%) cases and 21 (8.08%) controls were unmarried. Further, 18 (6.92%) cases and 3 (1.15%) controls had divorced status and 9 (3.46%) cases and 9 (3.46%) controls were widowed.

Reproductive health and sexual behavior characteristics

In this study, there were 408 (78.46%) participants who started their first sexual intercourse under the age of 20 years old. The proportion of women who experienced sexual intercourse at age below 20 years, constituted 210 (80.77%) cases and 198 (76.15%) controls. About 50 (19.23%) cases and 62 (23.85%) controls had started sexual intercourse after their 20th birth day.

There were 114 (43.85%) cases and 44 (16.92%) controls who had used contraceptives. The study showed that relatively fewer number of cases, 146 (56.15%) than controls, 216 (83.08%) were using contraceptives. In this study, there were 101 (38.85%) cases and 222 (85.38%) controls whose menstrual bleeding pattern was regular while 149 (57.31%) cases and 33 (12.69%) controls had irregular menstrual bleeding patterns. Moreover, 10 (3.85%) cases and 5 (1.96%) controls were at the menopause stage. There were about 66 (12.69%) study participants who had only one sexual partner. The finding showed that 27 (10.38%) cases and 39 (15%) controls had one sexual partner and conversely, 233 (89.62%)

cases and 221 (75%) controls had more than one sexual partner.

Life style characteristics

The number of smokers observed in the study was generally low. There were only 3 participants who had experienced smoking of cigarettes and they were all from cases. There were about 120 (23.08%) participants who were using chronic corticosteroid. Ninety two (35.38%) of cases and 28 (10.77%) of controls used corticosteroids.

Communicable diseases characteristic

In this study, there were about 179 (34.42%) participants who had sexually transmitted infection. As many as 137 (52.69%) of cases and 42 (16.15%) of controls had sexually transmitted infections. The finding shows that the number of participants infected with sexually transmitted diseases were significantly higher among cases compared to controls. In this study, there were about 186 (35.77%) participants who had HIV/AIDS reactive status. There was a significant difference between the cases and controls in the number of people infected with HIV/AIDS. About 150 (57.69%) cases and 36 (13.85%) controls had HIV/AIDS reactive status.

Bivariate analysis

The demographic factors such as age, educational and marital status of the participants were included in the bivariate model. Among the demographic factors, there was only one variable that showed significant association $p < 0.05$ in the bivariate analysis. Those with divorced marital status showed significant association [COR: 6.68, 95% CI (1.94-23.00)] with pre-cervical cancer lesion in the bivariate analysis. Among the reproductive health factors, age at first sexual intercourse, contraceptive use, patterns of menstrual bleeding and number of sexual partners were examined. Among them there were only two variables that had significant association $p < 0.05$. These included: using contraceptives [COR: 3.83, 95% CI (2.55-5.76)] and patterns of irregular menstrual bleeding [COR: 9.92, 95% CI (6.36-15.48)] in the bivariate analysis. The study examined history of smoking and using chronic corticosteroid as life style factors that might be associated with the outcome. Among them, use of chronic corticosteroid showed a significant association [COR: 4.54, 95% CI (2.84-7.24)] with pre-cervical cancer lesion in the bivariate analysis.

Sexually transmitted infection and HIV/AIDS were among communicable disease factors whose associations were examined. In this study, both

communicable disease factors showed significant association $p < 0.05$ in the bivariate analysis. Having sexually transmitted infection [COR: 5.78, 95% CI (3.84-8.71)] and HIV/AIDS reactive status [COR: 8.49, 95% CI (5.52-13.04)] have showed statistically significant association with the pre-cervical cancer lesion.

Multivariate analysis

Although six variables showed significant association in bivariate logistic regression model but in multivariate logistic regression model, only four variables showed independent significant association. Contraceptive use was among variables that showed strong significant association [AOR: 5.16, 95% CI (2.97-8.96)]. Irregular menstrual bleeding pattern was another variable that showed strong significant association [AOR: 6.03, 95% CI (3.40-10.69)]. Having sexually transmitted infection history showed strong significant association [AOR: 4.02, 95% CI (2.28-7.10)]. Having reactive HIV/AIDS status showed strong significant association [AOR: 7.41, 95% CI (4.38-12.56)]. Table 1 shows details of both bivariate and multivariate associations of different covariates with pre-cervical cancer lesion.

DISCUSSION

According to the result of bivariate logistic regression model, using contraceptive had association with the pre-cervical cancer [COR: 3.83, 95%CI (2.55-5.76)]. Moreover, multivariate logistic regression model analysis result found that women who use contraceptive had the odds of having pre-cervical cancer by 5.16 times compared to their counter parts [AOR:5.16, 95%CI (2.97-8.96)]. This study showed that use of contraceptives increased risk of cervical cancer. Consistent finding was reported by one systematic review study which revealed that women who have used oral contraceptives for 5 or more years have a higher risk of cervical cancer than women who have never used oral contraceptives. This means, the longer a woman uses oral contraceptives, the greater the increase in her risk of cervical cancer (Smith et al., 2003). Similar findings were observed by Schemik (2008), who said that long term use of oral contraceptives may lead to a more frequent persistence of HPV. This was also supported by similar study in that they opined that oral contraceptives may accelerate cervical maturation process, representing increased cell proliferation and thus a possible greater vulnerability to HPV (Hwang, 2009).

The bivariate logistic regression model analysis result revealed that menstrual bleeding pattern was significant in a way that irregular menstrual bleeding was associated with the pre-cervical cancer [COR: 9.92, 95% CI

Table 1. Bivariate and multivariate analysis of the study Hawassa Ethiopia, 2018 (n=520).

Variable category	Case (%)	Control (%)	COR (95% CI)	AOR (95% CI)
Age				
30-49	19 (7.31)	8 (3.08)	1	1
<30	234 (90.00)	250 (96.15)	0.39 (0.17, 0.92)	0.52 (0.18, 1.47)
>49	7 (2.69)	2 (0.77)	1.47 (0.25, 8.70)	2.61 (0.23, 29.89)
Age at first sexual intercourse				
<20	210 (80.77)	198 (76.15)	0.76 (0.50, 1.16)	0.86 (0.47, 1.57)
>20	50 (19.23)	62 (23.85)	1	1
Educational status				
College and above	41 (15.77)	39 (15.00)	1	1
Secondary	130 (50.00)	127 (48.85)	0.97 (0.59, 1.61)	1.03 (0.50, 2.11)
Primary	78 (30.00)	84 (32.31)	0.88 (0.52, 1.51)	0.77 (0.36, 1.64)
Illiterate	11 (4.23)	10 (3.85)	1.04 (0.40, 2.74)	0.63 (0.16, 2.50)
Marital status				
Married	204 (78.46)	227 (87.31)	1	1
Unmarried	29 (11.15)	21 (8.08)	1.54 (0.85, 2.78)	1.34 (0.58, 3.08)
Divorced	18 (6.92)	3 (1.15)	6.68 (1.94, 23.00)*	7.18 (1.73, 29.84)
Widowed	9 (3.46)	9 (3.46)	1.11 (0.43, 2.86)	1.53 (0.42, 5.50)
Contraceptive use				
Yes	114 (43.85)	44 (16.92)	3.83 (2.55, 5.76)*	5.16 (2.97, 8.96)*
No	146 (56.15)	216 (83.08)	1	1
Menstrual bleeding pattern				
Regular	101 (38.85)	222 (85.38)	1	1
Irregular	149 (57.31)	33 (12.69)	9.92 (6.36, 15.48) *	6.03 (3.40, 10.69)*
Menopause	10 (3.85)	5 (1.96)	4.40 (1.47, 13.19)	2.04 (0.51, 8.20)
STI history				
Yes	137 (52.69)	42 (16.15)	5.78 (3.84, 8.71)*	4.02 (2.28, 7.10)*
No	123 (47.31)	218 (83.85)	1	1
Number of sexual partner				
1	27 (10.38)	39 (15)	1	1
>1	221 (75)	233 (89.62)	1.52 (0.90, 2.57)	1.14 (0.54, 2.39)
History of smoking				
Yes	3 (1.15)	0 (0)	1634332547 (0.54, 0.0)	736766172.4 (0.000, 0.0)
NO	257 (98.85)	260 (100)	1	1
Chronic corticosteroid				
Yes	92 (35.38)	28 (10.77)	4.54 (2.84, 7.24)*	1.84 (0.87, 3.86)
No	168 (64.62)	232 (89.23)	1	1
HIV/AIDS status				
Reactive	150 (57.69)	36 (13.85)	8.49 (5.52, 13.04)*	7.41 (4.38, 12.56)*
Nonreactive	110 (42.31)	224 (86.15)	1	1

*Significantly associate.

(6.36-15.48)], than that of women who had regular menstrual bleeding pattern. The multivariate logistic regression model analysis revealed that having irregular menstrual bleeding increases the risk of developing pre-cervical cancer by 6.03 times than that of women counterparts who has regular menstrual bleeding pattern [AOR: 6.03, 95%CI (3.40-10.69)].

According to the bivariate logistic regression model analysis result, being having sexually transmitted infection (STI) had association with pre-cervical cancer [COR: 5.78, 95%CI (3.84-8.71)] than that of women did not had sexually transmitted infection (STI) history. Finding from multivariate logistic regression model analysis publicized that having the history of sexually transmitted infection (STI) increases the risk of developing pre-cervical cancer by 4.02 times than that of women counterparts who did not have the history of STI [AOR: 4.02, 95%CI (2.28-7.10)]. This is similar with finding of a study in Zimbabwe, where history of STIs was found as risk factors (AOR=3.10; p-value=0.02) as compared to not having any STIs (Veremichael, 2013). Likewise, study conducted in Yirgalem revealed the same finding [AOR: 8.3, 95%CI: 5.64, 12.41] (Hailemariam et al., 2017).

According to the bivariate logistic regression model analysis result using chronic corticosteroid had association with pre-cervical cancer with that of women counterparts who do not use chronic corticosteroid [COR: 4.54, 95%CI (2.84-7.24)]. However, the finding from multivariate logistic regression model analysis did not show significant association.

Based on the finding from bivariate logistic regression analysis, having HIV/AIDS reactive status had association with pre-cervical cancer than that of being nonreactive status [COR: 8.49, 95%CI (5.52-13.04)]. Finding from the multivariate logistic regression analysis shows that being HIV/AIDS reactive increases the odds of developing pre-cervical cancer than that of non-reactive for HIV/AIDS by 7.41 [AOR:7.41, 95%CI (4.38-12.56)]. Similar study conducted in Zambia revealed that HIV positive women have higher likelihood of having high grade cervical squamous intra epithelial lesion [AOR: 8.0, 95% CI: 20.54, 52.04] and cervical cancer cases are reported to occur more in the immune suppressed cases (Sun et al., 1997).

Epidemiological studies, in developed countries showed that HIV infected women are at higher risk of being infected with HPV, and are at a higher risk of persistence and associated cervical disease progression than HIV uninfected women (Blossom et al., 2007). In the present study it was observed that HIV infected women were more susceptible to pre-cervical cancer than that of their counterparts. This study assessed factors associated with pre-cervical cancer among women screened and diagnosed in consecutive 5 years (August 13, 2012-December 29, 2017) in Hawassa Comprehensive

Specialized Hospital. The following factors were identified as independent predictors of pre-cervical cancer: using contraceptives, having irregular menstrual bleeding pattern, having STI history, and having HIV/AIDS reactive status.

Conclusion

This study assessed factors associated with pre-cervical cancer among women screened and diagnosed in consecutive 5 years (August 13, 2012-December 29, 2017) in Hawassa Comprehensive Specialized Hospital. The following factors were identified as independent predictors of pre-cervical cancer: using contraceptives, having irregular menstrual bleeding pattern, having STI history, and having HIV/AIDS reactive status.

RECOMMENDATION

Health professional and health facilities should be able to encourage women who have a history of using contraceptive, sexually transmitted infection, having irregular menstrual bleeding pattern and HIV/AIDS reactive status should make consistent cervical cancer screening and follow-up. Supplementary investigation should be done in predictive variables which are not statistically significant in this study in order to compare the association with the outcome variable. Policy should provide fertile environment to integrate pre-cervical cancer screening service with HIV/AIDS, sexually transmitted infection and family planning service.

ABBREVIATIONS

AOR, Adjusted odd ratio; **COR**, crude odd ratio; **CI**, confidence interval; **SD**, standard deviation; **STI**, sexual transmitted infection; **HIV**, human immunodeficiency virus; **AIDS**, acquired immune deficiency syndrome; **VIA**, visual inspection with acetic acid; **WHO**, world Health organization; **VILI**, visual inspection with Lugol's iodine; **FRD**, folate receptor-mediated staining solution; **HPV**, human papilloma virus; **UNAIDS**, United Nations AIDS; **SNNPR**, South Nation Nationalities People Region.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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