Cervical cancer screening among women attending gynecologic OPD in Jimma Medical Center, Jimma, southwest Ethiopia, a cross sectional study

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Jimma, Ethiopia

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Abstract

Background: Cervical cancer ranks second in incidence and mortality behind breast cancer in lower Human Development Index. An appropriate screening strategy is a priority nowadays in low Human Development Index settings where incidence and mortality from cervical cancer is very high. Recently, the OncoE6™ Cervical Test (OncoE6 Test) which is a rapid, easy-to-use lateral flow method detecting HPV16/18 E6 oncoproteins that has proven to detect high-grade cervical lesions with high specificity and this technology might allow for decentralized screening of hard-to-reach populations. The aim of the study is to assess the knowledge, practice and factors associated with previous screening practices among women attending gynecologic OPD at Jimma Medical Center.

Methods: a hospital based cross sectional study was conducted on women aged 25 to 50 years visiting gynecology OPD of Jimma Medical Center from December 5th 2020 to August 31st 2021. Data were collected by trained midwives, from 437 women using an interviewer-administered questionnaire, entered to kobo tool, and exported to S**TATA** version **17** for analysis.

Results: out of the total respondents, the age range was from 25 to 50 years with a mean of 34.5 years. Previous history of screening practice was 4.6%. around 63% know risk factors of cervical cancer, and the prevalence of Onco E6 and VIA positivity was 2.1 and 0.5% respectively. There were no associated factors for previous history of cervical cancer screening.

Conclusion and recommendation: validation test for the new Onco E6 is recommended

Key words: cervical cancer screening, Onco E6

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I would like to thank Jimma University for offering me this chance of undergoing this research.

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Acronyms and abbreviations

CIN: Carcinoma in situ

DNA: Deoxyribonucleic acid

HDI: Human Development Index

HPV: Human papilloma virus

hrHPV: high risk human papilloma virus

JMC: Jimma Medical center

LMIC: Low- and middle-income countries

mAbs: monoclonal antibodies

NPV: Negative Predictive Value

RCTs: Randomized clinical trials

STD: sexually transmitted diseases

VIA: Visual inspection using acetic acid

WHO: World health organization

Chapter one: Introduction

1.1. Background

With an estimated 570,000 cases and 311,000 deaths only in 2018 worldwide, cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. It ranks second in incidence and mortality behind breast cancer in lower Human Development Index (HDI) settings(1).

In low-and middle-income countries (LMICs), it is more common, being the second most common cancer in incidence among women and the third most common in terms of mortality. The majority of new cases and deaths (approximately 85% and 90%, respectively) occur in low-resource regions or among people from socioeconomically weaker sections of society(2). Without urgent attention, deaths due to cervical cancer are projected to rise by almost 25% over the next 10 years(3).

Cervical cancer is the most commonly diagnosed cancer in 28 countries and the leading cause of cancer death in 42 countries, the vast majority of which are in Sub-Saharan Africa and South-Eastern Asia (1).

The highest regional incidence and mortality rates are seen in Africa, with rates elevated in Southern Africa (e.g., Swaziland, with the highest incidence rate), Eastern Africa (Malawi and Zimbabwe, with the highest mortality rate), and Western Africa (Guinea, Burkina Faso, and Mali(1).

1.1. Statement of the problem

It is now understood that cervical cancer is a rare long-term outcome of persistent infection of the lower genital tract by one of about 15 high-risk human papillomaviruses (HPV) types, which is termed the “necessary” cause of cervical cancer. HPV 16 and HPV 18 account for 71% of cases (4). Persistent HPV infection denotes the presence of the same type-specific HPV DNA on repeated sampling after 6–12 months. Only one-tenth of all infections become persistent, and these women could develop cervical precancerous lesions (2).

Prevention and elimination are potential possibilities, but the tragedy is that it is not yet prevented on a large scale in many LMICs due to a lack of efficient and effective intervention programs. World Health Organization (WHO) has recently given a call to action for the elimination of cervical cancer (2).

Several cervical screening strategies have been found to be useful in varied settings. The tests widely used to diagnose include conventional cytology (Pap smear), liquid-based cytology (in recent years) and HPV testing, while visual inspection with acetic acid (VIA) is also practiced in LMICs, (5).

While the Pap smear is still the major workhorse of screening, it is a challenging and resource-intensive technology that is not feasible in low-resource settings where poor organization, low coverage, and lack of quality assurance providing suboptimal outcomes (2,5).

Primary HPV screening, which has higher sensitivity and negative predictive value, allows extended screening intervals or even a single lifetime screening in low-resource settings (6,7).

VIA involves detection of acetowhite lesions on the cervix 1 minute after application of 3%–5% freshly prepared acetic acid. In view of its feasibility, VIA screening has been widely implemented in opportunistic settings in many low-income countries in Sub-Saharan Africa (8,9).

Lack of screening programs and the high prevalence of HPV infection in the population are the major factors responsible for the increased cancer risk observed in LMICs. The knowledge that persistent infection with one of the oncogenic HPV types is the necessary cause for cervical cancer has led to HPV vaccination and HPV testing as emerging strategies for prevention and early detection of cervical cancer. However, these are yet to be implemented in national programs in many LMICs, where they are most needed (10).

In the absence of effective screening, as in Eastern Europe and Central Asia (including the former republics of the Soviet Union), there have been rapid increases in premature cervical cancer mortality in recent generations (11). In such high-risk countries and regions, the challenge is to ensure that resource-dependent screening and vaccination programs are implemented to transform the situation (12).

The WHO recommends screening of women aged 30 to 49 years either through VIA and Papanicolaou tests (cervical cytology) every 3 to 5 years, or HPV testing every 5 years coupled with timely treatment of precancerous lesions(4).

In recent years, clear evidence supports the use of HPV-based tests for the detection of precursor lesions of the cervix (13); in a randomized trial in India, HPV testing offered greater protection against invasive cervical cancer than either VIA or cytology (10)

The effective integration of HPV vaccine programs with HPV-based testing via screening programs has the potential to virtually eliminate the burden of cervical cancer in every country of the world in this century (1).

Almost all types of cervical cancer: squamous cancer, adeno-squamous cancer, and adenocarcinoma—are now thought to be associated with 15 high risk HPV infection types denoted as HPV-16,18, 31,33,35,39,45,51,52,56,58,59,68,73,82 (14). The knowledge that persistent infection with one of the oncogenic HPV types is the necessary cause for cervical cancer has led to HPV vaccination and HPV testing as emerging strategies for prevention and early detection of cervical cancer. However, these are yet to be implemented in national programs in many LMICs, where they are most needed (10).

Those women with persistent HPV infection are at high risk for cervical cancer, of which HPV 16 and 18 cause 70% −75% of the cervical cancer cases across the world (15,16). The fact that high-risk HPV infections cause almost all cervical cancers, recently there have been two new approaches for cervical cancer control: i) primary prevention by vaccination of pre-adolescents and adolescents (9−18-year-old girls) and ii) early detection of cervical precancerous lesions such as CIN 3 and AIS by HPV screening in women aged 30 years and older (17).

An appropriate screening strategy is a priority nowadays in low Human Development Index (HDI) settings where incidence and mortality from cervical cancer are very high (18).

Most CIN I and up to 40% of CIN II/III lesions can regress to normal, but some lesions with viral genomic integration causing HPV E6, E7 oncoprotein overexpression may prevent regression of lesions (19).

By attacking tumor suppressor genes, p53 and pRb, respectively, these two oncoproteins lead to transcriptional activation, cell immortalization, uncontrolled cell cycling, and malignancy. Identification of cervical lesions with E6/E7 oncoprotein expression deserves special attention as they are predictive of future malignant transformation (20).

Among different methods of cervical cancer screening, cervical cytology (Pap test) has been a successful primary screening tool for more than sixty years in high-income and developed countries. Scarcity of trained cytopathologists and lack of a supporting medical infrastructure preclude universal Pap smear screening in resource-limited settings. In contrast, VIA is an approved low-cost screening alternative by the WHO (21,22). While VIA is inexpensive and gives

immediate results, false positive results range from 20 to 50% leading to colposcopy, over referral, increased screening costs, and overtreatment (23). Although HPV testing can precisely detect presence of infection; it can't differentiate between latent and transforming infections. So positive high-risk HPV test results do not represent true cancer precursors but can cause anxiety and overtreatment (18).

Among the new disease-specific molecular markers with ability to identify true cancer precursors, HPV E6/E7 mRNA is now FDA approved and while costly, is being used by some developed countries (18).

HPV DNA testing is considered the gold standard of clinical HPV-based screening due to very high sensitivity and excellent Negative Predictive Value (NPV) based on large-scale clinical studies and randomized controlled trials (RCTs) (18).

Advances in understanding human papillomavirus biology and the natural history of human papillomavirus-related precancers and cancers have led to the discovery of a range of novel biomarkers in the past decade (23).

The OncoE6 Cervical Test does not require sophisticated equipment, and operator training is simple, thus favoring its adoption in low-resource settings (22).

OncoE6 cervical test used in this study can detect two high risk HPV strains 16 and 18 which are responsible for 70 to 80% of cervical cancer globally. This lateral flow test is free from subjective operator bias and requires minimal laboratory training, minimal equipment, and providing results in two- and one-half hours (18).

In LMICs, including Ethiopia, cervical cancer is the commonest cancer affecting reproductive organs and also the leading cause of death from cancer among women. In 2010, it was estimated that 20.9 million women were at risk of developing cervical cancer in Ethiopia with an estimated 4,648 and 3,235 annual numbers of new cases and deaths, respectively (24).

Findings of maintained expression of HPV oncoproteins E6 and E7 as a prerequisite for invasive cervical cancer to develop (26), motivated the development of the OncoE6 Cervical Test (OncoE6 Test), a technology directly detecting elevated levels of the E6 oncoprotein of HPV types 16 and 18 (27). The OncoE6 Test relies on genotype-specific mouse monoclonal antibodies (mAbs) to HPV 16 E6 and HPV 18 E6 oncoproteins; these mAbs are used in the format of a lateral flow assay (strip test) of high robustness (27). HPV viral gene integration with cervical cellular genome

causes over-expression of E6 and E7 proteins which are recognized to have high oncogenic properties(5). Detection of any of these oncoproteins in CIN lesions can predict the risk of progression to cancer in the future(6).

The major limitations of VIA include: low specificity (generally less than 85%), which can lead to over-investigation and over-treatment of screen positive women and lack of standardized methods of quality control, training and competency evaluation. Furthermore, it is limited in its ability to detect endocervical disease(7).

Generally, HPV tests are characterized by high sensitivity but suffer from low specificity for true disease due to many infections resolving spontaneously or not leading to cervical cancer (HPV infection rarely result in cervical cancer)(8).

In the context of resource-constrained settings, the failure to establish and sustain cytology-based screening has necessitated research on operationally simple and less resource-intensive approaches for cancer prevention and control(10).

1.2. Significance of the study

Early detection both by screening and early clinical diagnosis represents an important component of cancer control in LMIC. In LMICs, only approximately 5% of eligible women undergo cytology-based screening in a five-year period. In virtually all LMICs, cytology-based services are confined to teaching hospitals or private laboratories in urban areas. The barriers to scale-up of cervical cytology-based screening programs in Ethiopia include the lack of trained and skilled professionals, supplies, laboratory infrastructure and equipment. Furthermore, the absence of a well-organized surveillance and recall system, let a treatment or follow-up far from decreasing the burden of death from cervical cancer. These are some of the barriers that prevent cytology-based screening programs from being effective in LMICs(11).

For low HDI countries where cost-effective, affordable and sustainable screening methods are needed, E6 oncoprotein testing can serve as an attractive and specific biomarker for cervical cancer.

Thus, the development and validation of novel, low-cost, and robust screening strategies are much needed if the unequal burden of cervical cancer worldwide is to be addressed.

Chapter two: Literature review

It is generally agreed that cytology screening for cancer of the cervix has been effective in reducing the incidence and mortality from the disease in many developed countries. There is general agreement that high quality cytology is a highly specific screening test, with estimates of the order of 98-99. Studies that have been able to assess sensitivity longitudinally have produced estimates that approximate to 75%(7).

Low-cost technologies for the detection of high-risk human papillomavirus (hrHPV) types are of particular interest for use in cervical cancer screening in developing countries. Promising technologies include those that are capable of detecting the HPV E6 oncoprotein or hrHPV DNA(9).

Despite different study settings, providers, study protocols and definitions of positive tests, the estimates of VIA sensitivity to detect high-grade precancerous lesions cluster around a mean value of 76%. In most of the studies where cytology and VIA have been provided under the same conditions, the sensitivity of VIA was found to be similar to that of cytology, whereas its specificity was consistently lower(7).

A meta-analysis by Cuzick and colleagues has shown the sensitivity of cytology to be 53·0% (95% CI 48·6–57·4) versus a sensitivity of 96·1% (94·2–97·4) for cervical HPV-DNA testing for the detection of moderate or severe cervical intraepithelial neoplasia (CIN)(12).

In a study done in Bangladesh on the role of HPV E6 oncoprotein cervical test in cervical cancer screening, it was found that E6 oncoprotein test had the highest specificity and Positive Predictive Value (PPV; 97% and 75%) compared to VIA (42% and 18%), cytology (95% and 46%) and colposcopy (94% and 59%). Sensitivity of the E6 oncoprotein test for detection of CIN3+was significantly higher than that of cytology (52% VS 25%) but lower than that of VIA (52% VS 74%)(13). It was also concluded that The HPV E6 oncoprotein test is an effective triage test to reduce colposcopy referrals for the large number of false positive test outcomes seen with VIA(13).

Clinical studies in underserved regions of India, China and Brazil have shown the feasibility and efficiency of this test to detect true cancer precursors(9,14–16).

A cross-sectional study conducted at Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from May 2018 to April 2019 has shown an association of E6 oncoprotein expression as significant for CIN III and highly significant for cervical cancer and it was concluded that the presence of E6 oncoprotein expression in CIN lesions can identify true cancer precursors with risk of cancer development in the future and can be utilized in cancer screening program(6).

Evaluation of women in rural China showed that tests for E6 and HPV DNA differ in their detection performance yet are complementary in cervical cancer assessment. HPV DNA detection showed superior screening performance, because of its high sensitivity and negative predictive value. HPV E6 detection performed better in diagnosis, because of its specificity and positive predictive value(9).

In a feasibility study of HPV Onco E6 test for the diagnosis of precancer and cervical cancer, it was demonstrated that E6 detection from cervical swab specimens is both feasible and potentially more specific for $CIN3^{+}$ than HPV DNA detection for the same HPV genotypes(17).

According to the national cancer control plan of Ethiopia (2016-2020) an objective is set to achieve 80-percent coverage of VIA to detect pre-cancerous cervical lesions among non-symptomatic women aged 30-49(25).

Chapter three: Objectives

3.1. **General objective:** at Jimma Medical Center from December 5th 2020 to August 31st 2021

3.2. Specific objectives

3.2.1. To describe sociodemographic factors
3.2.2. To determine the knowledge and practice of women
3.2.3. To assess the prevalence of ONCO E6 and VIA positivity
3.2.4. To determine factors associated with previous history of cervical cancer screening

Chapter four: Methods and materials

4.1. Study area and period:

The study was conducted in Jimma medical center. Jimma medical center is one of the public health facilities found at Jimma city, which is located 355 km away from Addis Ababa in the south

west of Ethiopia. Jimma medical center is one of the oldest governmental hospitals, which was established in 1937 and currently named as "Jimma medical center". It is inaugurated as a new Medical center on December 08, 2018 as the only teaching and referral hospital in the southwestern part of the country. It is providing services for approximately 15000 inpatient, 160000 outpatient attendants, 11000 emergency cases and 4500 deliveries in a year coming to the hospital from the catchment population of more than 15 million people. It has 1600 staff members and 800 beds.

Department of obstetrics and gynecology has got 12 consultant faculties, 41 residents from year one to year four, rotating medical interns, midwives, and clinical nurses; the department has started fellowship programs in the fields of urogynecology, gynecologic oncology and perinatology fields, and is giving services at its gynecology out patient departments, antenatal care clinics, labor, maternity and gynecology wards.

VIA, cryotherapy, colposcopy, and loop electrosurgical excisional procedure (LEEP) services are being provided in the hospital for the past five years and on average 100 clients get services for preinvasive cervical cancer screening using VIA, and those who tested positive for VIA and those with pathology results of CIN2+ are treated with either cryotherapy or LEEP according to the national guidelines.

Cytologic study for screening of cervical cancer (Pap smear) is not being practiced in our institute.

4.2. Study design:

Hospital based prospective cross-sectional study

Specimens (swabs) from all subjects were collected and subjected to the Onco***E6***™ Cervical Test and VIA was done after taking sample at the same time.

Clinical management

Women aged 25 to 50 years evaluated in Jimma Medical Center by a practicing midwife. Study participants underwent a routine pelvic exam by trained midwife, at which time cervical specimen collected for OncoE6 testing and then visual inspection after 5% acetic acid (VIA) done immediately after, results recorded during the same visit.

Control group participants (women aged 30-49) who tested positive for any of the 2 screening tests (VIA & OncoE6) was referred to colposcopy, and at the same time approximately 10% random sample of the women who tested negative for all screening tests (screen-negative women) will also undergo colposcopic evaluation by the principal investigator blindly that will include using a

biopsy protocol. Women who won't have visible lesions on colposcopic evaluation, their screening result was revealed and if there are no visible lesions, no biopsies were taken.

Laboratory tests

The OncoE6 cervical test is an immunochromatographic test using lateral flow format and performed by a trained local hospital personnel staff using a protocol suggested by Arbor Vita Corporation, Fremont, CA, USA) following the manufacturer's instructions. Three test strips constitute one test unit, with each test strip allowing for analysis of one individual clinical specimen and several units (of 3 test strips each) can be used in parallel by one operator. A control line is included on each strip, which allows for verification of detector reagent activity and proper sample solution migration up the test strip. The time from sample collection to test results is typically approximately 2.5 hours. Since there are no gold standard methods, the OncoE6 cervical test result was compared to biopsy result outcomes.

Pathology

The primary histopathologic diagnosis was provided by 2 pathologists, who are faculties of JMC after reaching an agreement and the worst of the biopsies or surgical specimen was used for the final diagnosis in these analyses.

Statistical methods

Standard contingency table methods with Pearson c2 tests were used to assess differences in risk factors and socio demographics. Sensitivity, specificity, and positive and negative predictive values for all screening tests was calculated.

4.3. Population

4.3.1. Source population:

All women who came to Jimma Medical center (JMC)

4.3.2. Study population:

Those women who came to the gynecologic OPD of JMC

4.4. Eligibility criteria:

4.4.1. Inclusion criteria**:** (i) have a cervix; (ii) not pregnant; (iii) physically able to undergo routine cervical cancer screening; and (iv) able to provide informed consent.

4.4.2. Exclusion criteria: Women who haven't fulfilled the above inclusion criteria and as the same time if they never had sexual intercourse, ages are <25 or >50 were excluded.

4.5. Sample Size Determination and Sampling Procedures

4.5.1. Sample size estimation

In this study sample size was calculated using single proportion formula. As there is no study, we used clinical assumption of 10 % positivity of Visual inspection of acetic acid in the community and 3% of margin of error.

$P=Z^2PV/d^2= 1.96*1.96*0.1*0.9/0.03*0.03=385$

By adding 10% non-response rate, the total sample size was 437

4.5.2. Sampling Technique: conventional sample collection method, in which sample was collected until the calculated sample size was reached.

4.5.3. Specimen collection and storage: sterile speculum was inserted, using cotton tip applicator cervical sample was taken and inserted into a labeled test tube, and stored in refrigerator until it is sent to laboratory for testing, on every day basis and VIA was done after that by a trained midwife.

4.6. Data collection tools and procedure: Structured questionnaire was used for basic information data collection. Residents was trained and used for data collection using ODK collect application.

4.7. Study variables

4.7.1. Dependent variables: knowledge of cervical cancer screening

4.7.2. Independent variables: age, marital status, parity, age at first sex, age at first delivery, history of hormonal contraceptive use, history of cigarette smoking, history of sexually transmitted infection

4.8. Data analysis:

Kappa was calculated as a measure of agreement for binary variables.

4.9. Data management and statistical analysis

4.10. **Quality assurance:** Standard tools, pre-tested questionnaires was used to collect information. A questionnaire was translated into Amharic/Afan Oromo by linguistic then translated back to English to check for consistency and understandability of the tool. Training was given for data collectors and supervisors on the data collection tool. Training was given for data collectors and supervisors on the data collection tool. The questionnaire was pretested prior to the actual data collection on 5% of sample size and the questionnaire was checked for its clarity, simplicity, and understandability. During data collection, the questionnaire was checked for its completeness on daily basis by data collectors, supervisors and then by the investigator.

4.11. **Plan for dissemination and ensure utilization of findings:** findings of the study result was presented for the department of obstetrics and gynecology, presented for Jimma Medical center and respective regional and national health offices for suggesting recommendations, prepared for publication, presented on reputable conferences.

4.12. **Ethical consideration:**

Ethical clearance was obtained from Ethical Review Committee, Jimma University. OncoE6 cervical test has been in practice in public health services as one modality of cervical cancer screening methods. Support letter to JMC was obtained from the department of obstetrics and gynecology. For the prevention of COVID 19 wearing of face mask, maintaining physical distance and washing of our hand in every activity during the study period was performed seriously. All eligible women were asked to complete the written, informed consent to participate in the study. Women was provided with an overview of the study and education on cervical cancer before signing consent.

Chapter five: result

Sociodemographic characteristics

In this study a total of 437 women were included, and the age range was from 25 to 50 years with a mean of 34.5 years. Nearly three- quarters were urban dwellers (74.6%), 61.8% were Muslims, less than three-quarters (74.4%) were married, 59.8% of the respondents were house wives by occupation, comparable proportion of the respondents had either no formal education or primary education (32.7%, and 31.1%) respectively, the mean monthly income of the respondents was 2956 Ethiopian birr, with a range of 500 to 15000 birr. See table 1.

Table 1. Sociodemographic characteristics of the study participants from December 5th 2020 to August 31st 2021, Jimma Medical center

Variable	Frequency	Percent
Age of the respondents (N=437)	Mean± SD	Range
	34.5± 6.6	25-50
Address		
Rural	111	25.4
Urban	326	74.6
Religion		
Muslim	270	61.8
Orthodox	98	22.4
Protestant	69	15.8
Marital Status		
Divorced	66	15.1
Married	325	74.4
Single	20	4.6
Widowed	26	5.9
Educational Status		
No formal education	143	32.7
Primary education	136	31.1
Secondary education	93	21.3
College or above	65	14.9
Occupational status		
Daily laborer	37	8.5
Government employee	72	16.5
House wife	261	59.8
Merchant	67	15.3
Total	437	100.00
Monthly Income in Birr (N=437)	Mean± SD	Range
	2956.13 ± 1616.70	500- 15,000

Reproductive and contraceptive history

Among the respondents, 69% were multiparous (para 2 to 4), while 9.2% haven't delivered any child. Thirty percent of the participants have history of an abortion at least once. Majority of the study participants (69.3%) have history of use of modern contraceptive, and 38% have used injectable contraceptive in the past five years; mean age at first sex was 19 years, with a range of 14 to 28 years, mean age at first delivery was 21 years with a range of 15 to 30 years. Fifteen percent had history of sexually transmitted diseases. More than 90% of the respondents were screened for HIV and more than a quarter of them (26.3%) tested positive. See table 2

Table 2. Reproductive and sexual history of the study participants from December 5th 2020 to August 31st 2021, Jimma Medical center

Variable	Freq.	Percent
Parity		
Nulliparous	40	9.15
1	60	13.73
2 to 4	303	69.34
≥5	34	7.78
History of abortion		
No	304	70.05
Yes	130	29.95
Ever use of any of modern contraceptive methods		
No	134	30.66
Yes	303	69.34
Age at first sex (N=437)	Mean± SD	Range
	19.2±2.7	14-28
Age at first delivery (N= 397)	21.2±2.6	15-30
Ever history of STD		
No	372	85.1
Yes	65	14.9
Ever HIV tested		
No	41	9.38
Yes	396	90.62
Total	437	100.00
If yes for HIV test, what was the result?		
Negative	292	73.74
Positive	104	26.26
Total	396	100.00

Cervical cancer screening knowledge and practice

In this study, 84.7% of the respondents have heard about cervical cancer, while 63.1% of the respondents reported that they have heard how cervical cancer screening is done it's only 4.6% of them who have ever been screened for cervical cancer with a mean of 9 months from current study. Majority of the respondents (62.7%) know risk factors for cervical cancer and mentioned at

least one risk factor, and less than three -quarters (73%) of the respondents believe that cervical cancer is preventable. See table 3

Table 3. cervical cancer screening knowledge and practice of the study participants from December 5th 2020 to August 31st 2021, Jimma Medical center

Variables	Frequency	Percentage
Previously screened for cervical cancer		
No	417	95.4
Yes	20	4.6
Time from previous screening in months (N=20)	Mean (SD)	Range
	9.1(8.5)	1 to 36
Know the risk factors for cervical cancer		
No	163	37.3
Yes	274	62.7
Cervical cancer is preventable		
No	118	27
Yes	319	73
Heard about cervical cancer		
No	65	15.3
Yes	361	84.7
Heard about cervical cancer screening methods		
No	161	36.8
Yes	276	63.2
Total	437	100.00

Outcomes of the screening tests

Among the study participants, only 2.1%, and 0.5% tested positive for Onco E6 and VIA respectively, see table 4

Table 4. VIA and Onco E6 results of the study participants of the study participants from December 5th 2020 to August 31st 2021, Jimma Medical center

Variable	**Freq.**	**Percent**
VIA result		
Negative	435	99.5
Positive	2	0.5
OncoE6 result		
Negative	428	97.9
Positive	9	2.1
Total	437	100.00

Factors associated with previous history of cervical cancer screening

Result of bivariate analysis

Age of the respondents was not significantly associated with history of previous screening practice, whereas knowledge on acquiring HIV increases risk of cervical cancer, having history of STD, having HIV infection, knowledge that early marriage is a risk for acquiring cervical cancer were associated with previous history of cervical cancer screening see table 5

Table 5. cross tab on factors associated with previous history of cervical cancer screening practices among the study participants from December 5th 2020 to August 31st 2021, Jimma Medical center

Variables	previous screening practice		
Address	No	Yes	p value
Rural	109(98.3%)	2(1.8%)	
Urban	308(94.5%)	18(5.5%)	0.1053
Marital Status			
Divorced	65(98.5%)	1(1.5%)	
Married	310 (95.4%)	15 (4.6%)	0.3418
Single	18(90%)	2(10%)	
Widowed	24(92.3%)	2(7.7%)	
Occupational status			
Daily laborer	36(97.3%)	1(2.7%)	
Government employee	66(91.7%)	6(8.3%)	0.3982
House wife	251(96.2%)	10(3.8%)	
Merchant	64(95.5%)	3(4.5%)	
Educational Status			
No formal education	140(97.9%)	3(2.1%)	
Primary education	130(95.6%)	6(4.4%)	0.2363
Secondary education	86(92.5%)	7(7.5%)	
College or above	61(93.8%)	4(6.2%)	
Parity			
0	37(92.5%)	3(7.5%)	
1	57(95%)	3(5%)	
2 to 4	290(95.7%)	13(4.3%)	0.7837
≥5	33(97.1%)	1(2.9%)	
Know Cervical cancer is preventable			
No	115(97.5%)	3(2.5%)	
Yes	302(94.7%)	17(5.3%)	0.2158

Know HIV positivity increases the chance of getting cervical cancer			
No	210(99.1%)	2(0.9%)	
Yes	207(92%)	18(8%)	0.0004#
Ever HIV tested			
No	40(97.6%)	1(2.4%)	
Yes	377(95.2%)	19(4.8%)	0.4914
Result of HIV test			
Negative	283(96.9%)	9(3.1%)	
Positive	94(90.4%)	10(9.6%)	0.0074#
History of STD			
No	359(96.5%)	13(3. %5)	
Yes	58(89.2%)	7(10.8%)	0.0096#
Know Early marriage is a risk factor for cervical cancer			
No	26(97.4%)	7(2.6%)	
Yes	149(92%)	13(8%)	0.0101#

Significant association

Result of multiple regression: variables that were associated with past history of cervical cancer with the logistic regression model and age were inserted together to look for any independent risk factor for past history of cervical cancer screening practices, and it was revealed that none of the variables were not significantly associated see table 6

Table 6. multiple regression for factors associated with previous history of cervical cancer screening among the study participants factors from December 5th 2020 to August 31st 2021, Jimma Medical center

Variable		p-value	**COR:95%, CI**	**AOR:95%, CI**
Age		0.927	1.032(0.966-1.102)	0.996(0.918-1.081)
Age at first delivery		0.132	1.188(1.004, 1.405)	1.158(0.957, 1.402)
Know that HIV positivity increases risk	1	.		
Yes		0.227	9.13(2.092, 39.847)	2.115(0.627, 7.142)
HIV test result	1	.		
Positive		0.12	3.345(1.319, 8.481)	2.402(0.797, 7.243)
History of STD	1	.		
Yes		0.516	3.333 (1.276, 8.703)	1.566(0.404, 6.074)
Know that early marriage is a risk	1	.		
Yes		0.062	3.241(1.265, 8.301)	7.627 (0.901, 64.543)

Chapter 6 Discussion:

In this study the prevalence of onco E6 cervical test and VIA positivity were 2.1 and 0.5% respectively, and only 4.6% had previous history of cervical cancer screening practices. Regarding

knowledge of risk factors for cervical cancer, 62.7% were knowledgeable, 63.2% of the respondents know methods of cervical cancer screening.

In this study, multiple regression has revealed that there are no independent factors for having screening history in the past

Limitations: the study hasn't seen results of women with high grade lesions and above, the gold standard test ie, biopsy was not done as the results of onco E were heralded after one month and the clients could not respond to their phones, and as this is a facility-based study, it may not be representative of the general population

Chapter 7 Conclusion and recommendation

Low prevalence of VIA positivity

Recommendation: further study to check validity of the new Onco E6 test is recommended

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.

2. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. Int J Gynecol Obstet. 2018;143:22–36.

3. WHO. Who Report on Cancer. 2020.

4. Test T, Follow-up T. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention.

5. Isaacson Wechsler E, Wang Q, Roberts I, Pagliarulo E, Jackson D, Untersperger C, et al. Reconstruction of Human Papillomavirus Type 16-Mediated Early-Stage Neoplasia Implicates E6/E7 Deregulation and the Loss of Contact Inhibition in Neoplastic Progression. J Virol. 2012;86(11):6358–64.

6. Ara R, Pervin S, Khatun S, Shahera U, Sultana M, Aktar MN. Low-Cost Molecular Biomarker HPV-16/18 E6 Oncoprotein Expression in Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer with Its Relation with Severity of Neoplastic State. Indian J Gynecol Oncol [Internet]. 2020;18(3):2–6. Available from: https://doi.org/10.1007/s40944-020-00416-5

7. Cervical Cancer Screening in Developing Countries. Iraqi J Med Sci. 2017;15(1).

8. Bosch FX, Broker TR, Forman D, Moscicki A-B, Gillison ML, Doorbar J, et al. Comprehensive Control of Human Papillomavirus Infections and Related Diseases. Vaccine [Internet]. 2013;31:H1–31. Available from: http://dx.doi.org/10.1016/j.vaccine.2013.10.003

9. Valdez M, Jeronimo J, Bansil P, Qiao YL, Zhao FH, Chen W, et al. Effectiveness of novel, lower cost molecular human papillomavirus-based tests for cervical cancer screening in rural China. Int J Cancer. 2016;138(6):1453–61.

10. Sankaranarayanan R, Boffetta P. Research on cancer prevention, detection and management in low- and medium-income countries. Ann Oncol [Internet]. 2010;21(10):1935–43. Available from: https://doi.org/10.1093/annonc/mdq049

11. Republic FD. Guideline for Cervical Cancer Prevention and Control in Ethiopia.

12. Cuzick J, Clavel C, Petry KU, Meijer CJLM, Hoyer H, Ratnam S, et al. Overview of the European and North American studies on HPV testing in primary cervical cancer screening. Int J Cancer. 2006;119(5):1095–101.

13. Ara R, Khatun S, Pervin S, Jahan M, Shahera U, Ferdous J, et al. Role of molecular biomarker human papilloma virus (HPV) E6 oncoprotein in cervical cancer screening. Gynecol Oncol [Internet]. 2020;158(3):590–6. Available from: https://doi.org/10.1016/j.ygyno.2020.06.496

14. Mariano VS, Lorenzi AT, Scapulatempo-Neto C, Stein MD, Resende JCP, Antoniazzi M, et al. A Low-Cost HPV immunochromatographic assay to detect high-grade cervical intraepithelial neoplasia. PLoS One. 2016;11(10):1–12.

15. Sellors JW, Schweizer JG, Lu PS, Liu B, Weigl BH, Cui JF, et al. Association of elevated E6 oncoprotein with grade of cervical neoplasia using PDZ interaction-mediated precipitation of E6. J Low Genit Tract Dis. 2011;15(2):169–76.

16. Zhao FH, Jeronimo J, Qiao YL, Schweizer J, Chen W, Valdez M, et al. An evaluation of novel, lower-cost molecular screening tests for human papillomavirus in rural China. Cancer Prev Res. 2013;6(9):938–48.

17. Schweizer J, Lu PS, Mahoney CW, Berard-Bergery M, Ho M, Ramasamy V, et al. Feasibility study of a human papillomavirus E6 oncoprotein test for diagnosis of cervical precancer and cancer. J Clin Microbiol. 2010;48(12):4646–8.

ANNEX

Annex 1: Information and Consent sheet

This is a research work by Dr. Wubshet Girma (OBGYN Specialist). Now I am conducting this research work as a part of fulfilment for his sub-specialty in gynecologic oncology.

The aim of this research work is to validate the role of Onco E6 cervical test as a screening tool for preinvasive cervical cancer. Thus, after conducting this research we want strengthen and use it at every institution to mitigate death from cervical cancer.

The interview is going to take 10 minutes

Thus, the outcome of this research work will guide us to improve the routine clinical care for similar condition for future.

The information from this interview will not be disclosed to a 3rd body and only was used for the purpose of this research work.

Participation is based your full free will.

For any questions and clarification, you can contact Dr. Wubshet Girma, and my phone number is 0911668114

Are you volunteer to participate in this study?

1. Yes 2. No

Name of study participant _____ signature _____

Name of data collector _____ signature _____

Date _____

Annex 1: Information and Consent sheet Afaan oromo

Ani Dr wubshat Girmaa jedhama ispeshalisti gadameeessa hospitaala jimmati amma qorannoo tokko gegeessuutti jirra, qorannon kuni hadholii gedemeessi jaraa gara alaa bahe ilaalleta. Qorannoon kuni rakkoo hadholii kana qunnamaa jiru sirriitti hubachuufi gara, fuulduraattis yaalii kana fooyyesuuf nu gargaara.

Infoormeeshiniin asirraa sassaabame kan qaama sadaffatiif hin saaxilamne isin hubachiisaa qorannoo kanarrati hirmaachuun bu'aa guddaa ummata kenyaaf waan qabuuf akka hirmaattanu kabajaan isin gaafanna.

Hirmaachunis hirmaachuu dhiisunis fedhii keessan.

Qoranno kanarratti hirmaachuu barbaadduu?

1) Eyyee
2) Hin barbaadu

Maqaa hirmaataa qorannichaa; _____

Maqaa Qorataa; _____

Guyaa; _____

Annex 2: Questionnaire

2.1. Sociodemographic characteristics

Registration number

2.1.1. Age (in years)
2.1.2. Address
a. Urban
b. rural
2.1.3. Marital status
  a. Single
  b. Cohabited
  c. Married
  d. Widowed
  e. Divorced
2.1.4. Educational status
  a. No formal education
  b. Primary education
  c. Secondary education
  d. College or above
2.1.5. Occupational status (mention)
  a. House wife
  b. Merchant
  c. Daily laborer
  d. Government employee
  e. Private/ NGO employee
2.1.6. Income per month (mention)
2.1.7. Religion (mention)

2.2. Reproductive health related characteristics of screened women

2.2.1. Contraception use sometime
  2.2.1.1.Yes, if yes
  2.2.1.2.No
    2.2.1.1.1. OCP, duration in months/ years (never, former, current)
    2.2.1.1.2. Injectable, duration in months/ years
    2.2.1.1.3. Implanon, duration in months/ years
    2.2.1.1.4. Jadelle, duration in months/ years
    2.2.1.1.5. IUCD, duration in months/ years
    2.2.1.1.6. Others, duration in months/ years
2.2.2. Age at first marriage
2.2.3. Age at first sex
2.2.4. Age of first delivery (mention)
2.2.5. Average birth interval (mention)
2.2.6. Menstrual history

a. Regular
b. Irregular
c. Sometimes irregular
d. Amenorrheic

2.2.7. Post coital bleeding
a. Yes
b. No

2.2.8. Parity (mention)----------

2.2.9. History of abortion
a. No
b. Yes, if yes no. of times

2.2.10. Family history of cervical cancer
a. No
b. Yes

2.3. Lifestyle and sexual behavior characteristics of screened women

2.3.1. Previously screened for cervical cancer
a. Yes
b. No

2.3.2. If yes, Time since last screening (in months)

2.3.3. Result of the last screening (for cervical precancerous lesion)

2.3.4. positive /Negative

2.3.5. Ever history of smoking

2.3.6. yes no

2.3.7. Condom use

2.3.8. Ever history of STD

2.3.9. Yes/ no

2.3.10. if yes, were you treated (yes/ no)

2.3.11. Ever history of STD on sexual partner

2.3.12. Yes/ no

2.3.13. if yes, were you treated (yes/ no)

2.3.14. Ever HIV tested (yes/ no)

2.3.15. If yes HIV status (positive/ negative)

2.3.16. Number of Life time sexual partners

2.3.17. Number sexual partners in the past six months

2.4. Test

VIA test result (Positive/ negative)

OncoE6 test result (Positive/ Negative)

If positive for either of the two, what was the colposcopy finding?

If result is positive for either of VIA or OncoE6, what was the pathology result?