Journal of Advances in Medicine and Medical Research

33(15): 138-147, 2021; Article no.JAMMR.70037
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Cervical Cancer Screening via Self-Sampling for High-Risk Human Papilloma Virus: A Community-Based Pilot Study in Lagos, Nigeria

Yusuf A. Oshodi[1*], Kayode A. Adefemi[2], Ayokunle M. Olumodeji[2], Oluwarotimi I. Akinola[1], Ephraim Ohazurike[3], Taiwo O. Kuye[1], Adedoyin A. Ogunyemi[2] and Adekunbiola A. Banjo[4]

[1]Department of Obstetrics and Gynaecology, Lagos State University College of Medicine/Lagos State University Teaching Hospital, Lagos, Nigeria.
[2]Department of Community Health and Primary Healthcare, Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria.
[3]Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, Lagos, Nigeria.
[4]Department of Pathology and Forensic Medicine , Lagos University Teaching Hospital, Lagos, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author OIA conceived the study and contributed to the study design. Authors YAO and MOA contributed to and implemented the study design, and drafting of the manuscript. Author AAO did the data analysis, produced the figures and tables (in consultation with the coauthors). Authors AAB and KAA performed laboratory testing of all samples (together with the corresponding author) and authors EO, TOK, EO contributed to the drafting of the manuscript. Author OIA provided the funds and provided critical revision to the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i1530994
Editor(s):
(1) Dr. Elvira Bormusov (Rtd.), The Lloyd Rigler Sleep Apnea Research Laboratory, Israel.
Reviewers:
(1) Amani Saber, Minia University, Egypt.
(2) Azza Mohamed Adel Abdelaziz, Ain Shams University, Egypt.
Complete Peer review History: https://www.sdiarticle4.com/review-history/70037

Original Research Article

Received 27 April 2021
Accepted 02 July 2021
Published 12 July 2021

ABSTRACT

Background: Cervical cancer is the second most common cancer in women globally after breast cancer. It is a preventable cancer with a well-defined premalignant phase where treatment could be offered before invasive cancer develops.

**Corresponding author: E-mail: yusufoshodi@gmail.com, yusufoshodi@yahoo.com;*

Objective: To determine the prevalence, socio-demographic characteristics and serotypes of high-risk HPV amongst positive women using self-sampling HPV-based cervical cancer screening.
Methods: A cross-sectional pilot study in an urban setting in Lagos, Nigeria where one hundred women, following community-based counselling on cervical cancer and its prevention, underwent cervical cancer screening via self-sampling for hr-HPV. Structured questionnaires were administered for data collection. Appropriate instruction for self-sample collection using Flobam cervical sampling kit was given to each subject. The samples were processed using DNA analysis via PCR (polymerase chain reaction) amplification and flow through hybridization to identify the hr-HPV serotypes. Women who tested positive for hr-HPV had colposcopic-guided biopsy. The data obtained were analysed using SPSS version 20.0.
Findings: Almost all (97%) the women were successful at self-sampling. The prevalence of hr-HPV positivity was 19% with peak (31.6%) of hr-HPV positivity observed in subjects aged 31-40 years. HPV 53 was the commonest (36%) serotype, HPV 33 and 39 were the least (7%) identified and 47% of hr-HPV positive subjects had infection with two or more HPV serotypes. Two-third (66.7%) of hr-HPV positive subjects attended follow-up for colposcopy guided biopsy and 10.5% of the hr-HPV positive subjects had premalignant/malignant cervical lesion.
Conclusion: Infection with more than one hr-HPV serotype is common in our study. Self-sampling modality of HPV cervical cancer screening is feasible in this environment.

Keywords: Cervical cancer screening; high risk - human papilloma virus; hr-HPV screening; hr-HPV self-sampling; hr-HPV serotypes.

1. INTRODUCTION

Cervical cancer ranks as the fourth most commonly diagnosed and cause of cancer death among women globally [1]. Nigeria lacks a well-implemented national cervical cancer policy, and late presentation of cervical cancer in majority of patients is common [2,3]. With the absence of organized screening policy, the screening offered to women occurs at the request of patients, suggestion of health personnel, or through awareness programs organized by individuals or non-governmental organizations [4]. Some of the screening programs are episodic, often concentrated around the period of cervical cancer prevention week or occasional infrequent free health services organized by politicians, philanthropists, and citizens in diaspora rather than being available all-round the year [4].

It is a preventable cancer with well-defined premalignant phase where treatment is possible before invasive cancer develops. Human papillomavirus (HPV) is a necessary cause of cervical cancer carcinogenesis, as at least one of the 15 identified genital high-risk HPV types were detected in 99.7% of cases [5]. HPV is the commonest viral infection of the reproductive tract and is one of the most common causes of sexually transmitted infection worldwide [6]. While most HPV infections are asymptomatic and self-limiting, persistent high risk HPV infection occurs in 10–15% of women and is associated with various forms of cancer [7]. HPV subtypes 16 and 18 were found to be the most pathogenic of the high-risk HPV types, together accounting for 70–80% of cervical cancers, 40–50% of vulvar and oropharyngeal cancers and 70–80% of anal cancers [8].

Early detection of precursor lesions of cervical cancer through cytology screening has drastically reduced the incidence of the disease, especially in Western countries [9]. Conversely, in resource-constrained countries such as Nigeria, cervical cancer incidence and mortality have remained high [4]. However, cytology-based screening is labour and time intensive and lacks sensitivity and reproducibility in detecting precancerous cervical lesions or cervical cancer and sampling is clinician collected [10,11]. Lack of mass participation in this screening is a major challenge in developing countries [12]. There is now overwhelming evidence from randomized clinical trials that carcinogenic HPV DNA screening is more sensitive than cytological screening for detecting histological cervical intra-epithelial neoplasia (CIN3) [13,14].

HPV DNA test is widely recognized as the primary screening modality for cervical cancer worldwide [15]. The use of similarly effective and relatively more convenient, self-collected specimens, as against clinician-collected specimens, for high-risk human papillomavirus (HPV) DNA testing may increase cervical cancer

screening uptake among women in developing countries [15]. While geographical variation in HPV serotypes distribution exist, knowledge about the distribution of HPV serotypes in different regions of Nigeria would be useful in guiding optimal vaccination strategy [16].

Since most of the available data on cervical cancer screening in Nigeria are majorly hospital based [17], this pilot study was designed to screen women for cervical cancer via self-sampling for hr-HPV test in the community and determine the prevalence, socio-demography and serotypes of high-risk HPV amongst positive women.

2. MATERIALS AND METHODS

2.1 Setting and Participants

Following ethical approval for the Lagos State University Teaching Hospital, one hundred consenting and eligible women, in a community-based prospective cross-sectional study which was conducted between 1st of November 2019 and 29th February, 2020. The study period comprises two-week hr-HPV sample collection period and 15weeks for sample processing, recall for colposcopy and processing cervical biopsy for histology. A randomly selected religious community in Ikeja, Lagos was engaged by meeting with its key religious and opinion leaders. Eight group meetings involving 15-20 women each were conducted in which the study protocol and how the vaginal samples will be collected using the hr-HPV kit were explained. Eligibility Criteria:

Healthy sexually active women aged between 21 to 65 years were included in the study. Women who were less than 21 and above 65 years of age, those who were yet to have sexual debut, pregnant, currently menstruating or had undergone hysterectomy were excluded.

2.2 Study Procedure

All the participants had structured questionnaire administered to them by the researchers. Information was obtained on socio-demographics, sexual health and behaviour, obstetrics and gynaecology history and cervical cancer screening history. They were all educated on how to perform the self-sampling collection of the vaginal specimen in groups of ten. Women who screened positive had follow-up colposcopy guided biopsy at the Colposcopy clinic of the Lagos State University Teaching Hospital.

2.3 Sample Size Calculation

The sample size was determined using the Leshe-kish formula single proportion [18], which is

$$n=z2\ p\ (1-p)\ /d2$$

p = 6.2 %, using the prevalence of hr-HPV physician collected samples in Ile-Ife, Nigeria [19].
d = 0.05 at confidence interval of 95%,
z = 1.96
n = 90.

Allowing for ten percent attrition, a total of 100 women were recruited for the self-test.

2.4 Sample Collection

Each participant had a Flobam cervical sampling kit. Each contained a pair of disposable gloves, a dry flocked swab, an information leaflet and a 5ml-specimen bottle containing fixative. Convenient and private rooms were provided for self-sample collection. The women were taught to part their labia and gently introduce the flocked swab sampler gently into their vagina until a resistance was felt and then perform a 360 degree rotatory movement with the swab in place. The swab was then removed and its tip broken along a marked line. The broken tip was then placed in the properly labelled specimen bottle containing the fixative and submitted at a designated collection centre from where they were transported within 2 hours to the laboratory for storage in the refrigerator and batch analysis.

2.5 Laboratory Analysis

Samples in HPV DNA collection kits were frozen at -20°C in the laboratory until analysis. DNA analysis was performed using the Hybribio 21 HPV Geno array test kit (Hybribio Limited, Hong Kong) which uses PCR amplification and flow through hybridization to characterize the HPV serotypes. The results were interpreted by direct visualization of the membrane for colour change of specific serotype.

2.6 Data Analysis

The data was entered and cleaned with Microsoft Excel and thereafter analyzed using Statistical

Package for social Sciences, version 20.0 (SPSS v20.0) Chicago, Illinois. Frequencies were calculated for demographic variables, knowledge of cervical cancer and hr-HPV serotypes. HPV distribution and co-infection with hr-HPV serotypes were represented with charts. Student's t-test was used to determine the relationship between hr-HPV result and variables. P-value of less that 0.05 was considered statistically significant.

3. RESULTS

Considering the socio-demographic characteristics of the subjects, majority were the age range of 41-50 years (29%) and 31-40 years (28%) respectively. Similarly, main parity ranges were Para 3-4 accounting for 44% while Para 1-2 was 35%. About three-quarter of the subjects (76%) had tertiary level of education compared to 20% who completed secondary education. About 69% of the subjects were premenopausal with only 18 (26%) of the currently using modern contraceptive methods. Intra-uterine contraceptive device excluding Mirena accounted for 55.6% of the contraceptive method used by the subjects while hormonal and barrier methods accounted for 22.2% each. The socio-demographic characteristics of subjects did not reveal any statistically significant difference (Table 1).

Table 1. Socio-demography and contraceptive use

Variables	Description	hr-HPV –ve	hr-HPV +ve	Total (Freq(%)	P value
Age range	21 -30	9	3	12	=0.929
	31 – 40	22	6	28	
	41 – 50	24	5	29	
	51 – 60	18	3	21	
	61 - 65	8	2	10	
		81	19	100	
Parity	0	10	2	12	0.974
	1-2	27	8	35	
	3-4	37	7	44	
	> 4	7	2	9	
		81	19	100	
Education Level	Primary	3	1	4	0.975
	Secondary	16	4	20	
	Tertiary	62	14	76	
		81	19	100	
Menopausal Status	Pre-menopausal	56	13	69	0.305
	Menopausal	25	6	31	
		79	19	100	
Contraceptive Use	Yes	16	2	18	0.305
	No	65	17	82	
		81	19	100	
Type of Contraceptive	1UCD	9	1	10	
	Barrier	2	-	2	
	Tubal ligation	2	-	2	
	Injectable	1	-	1	
	Mirena	1	-	1	
	OCP	1	-	1	
	Implanon	-	1	1	
	Total	16	2	18	

Table 2. Awareness, screening and vaccination against cervical cancer

Variables	Description	HR-HPV -VE	HR-HPV +VE	P value
Aware of Ca Cervix	Yes	65	15	0.985
	No	16	4	
		81	19	
Knowledge of Screening method	Yes	43	9	0.413
	No	34	10	
	Don't Know	4	-	
		81	19	
Screened Before?	Yes	28	4	0.118
	No	53	15	
		81	19	
Methods	Pap Smear	23	3	
	VIA*	4	1	
	Pap/VIA	1	-	
		28	4	
Previous Vaccination?	Yes	1	-	0.600
	No	80	19	
		81	19	

** VIA - visual inspection of the cervix using acetic acid.*

Table 3. Occupational distribution of respondents

Occupation	Frequency (%)
Trading	23 (23%)
Nursing	14 (14%)
Civil Servants	11 (11%)
Medical Practitioners	9 (9%)
Pensioners	7 (7%)
Seamstress	6 (6%)
Teaching	7 (7%)
Catering	4 (4%)
Applicant	3 (3%)
House Wife	3 (3%)
Cleaning	2(2%)
*Others	11

**Others include Accountant (1), Architect (1), Banker (1), Broker (1), Corper (1), Nanny (1), Security Personnel (1), Laboratory scientist (1), Aviation ticketing (1), Student (1), and Apprentice (1)*

Table 4. Colposcopic findings and histology IN HR-HPV +VE women (n=19)

	Colposcopy	Histology
1	Normal (10)	Normal findings
2	Suspicious for cancer (2)	(LSIEL)* 1 Cervical carcinoma 1
3	Loss to follow-up (7)	[Not done] (7)

LSIEL – Low grade squamous intra-epithelial lesion

Eighty percent (80) were aware cervical cancer but only 54(65%) of them have knowledge of the screening methods. Only thirty-two percent (32) of all subjects have had cervical cancer screening before with 26 via Pap smear. Of the 19 subjects that were positive for hr-HPV, 15 of them have not had any previous screening. Contraceptive usage, prior HPV vaccination, awareness and knowledge of cervical cancer screening methods were similar in both hr-HPV positive and hr-HPV negative subjects (Table 2). Only one (1%) subject had had HPV vaccination before. Using logistic regression analysis, there was no statistical significance noted in any of the

variables and hr-HPV test result. In the occupational distribution, most of the subjects were traders (23%), nurses (14%) and civil servants (11%) – Table 3.

Out of the participants, 97% were successful at self-sampling while 3% (3 subjects) had the swab detached and dislodged into their vagina. They had it removed by sterile digital vaginal examination without difficulty. Eighty-one subjects were hr-HPV negative (81%) giving a prevalence of hr-HPV positivity of 19%. About two-third (63.2%) of HPV positive subjects scheduled for follow-up attended. The proportion of hr-HPV positive subjects with premalignant /malignant lesion was 10.5%.

HPV 53 was the commonest (36%) serotype identified in the screened population, HPV 16, 51 and 58 were the 2nd commonest serotypes, all occurring in 29% of the subjects. HPV 33 and 39 were the least identified (7%) serotypes (Fig. 1). Almost half (47%) of the hr-HPV positive subjects had infection with more than one HPV serotype (Fig. 2). Of the hr-HPV positive subjects who required follow-up colposcopy, 36.8% defaulted, 52.6% of the hr-HPV positive women had normal colposcopy findings (Table 3). The two subjects with LSIEL and Carcinoma of the cervix following biopsy were referred to the oncology unit of the department where they were managed according to our protocol.

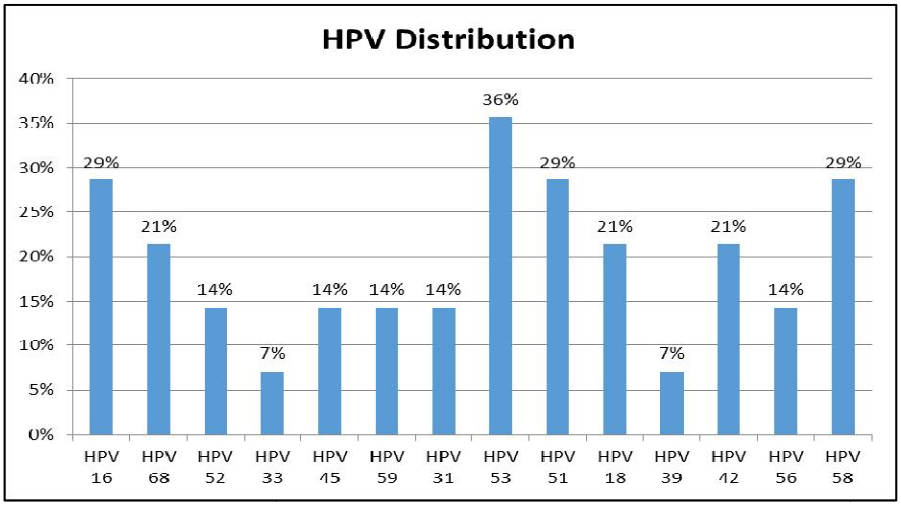

Fig. 1. Distribution of HPV serotypes in the screened population

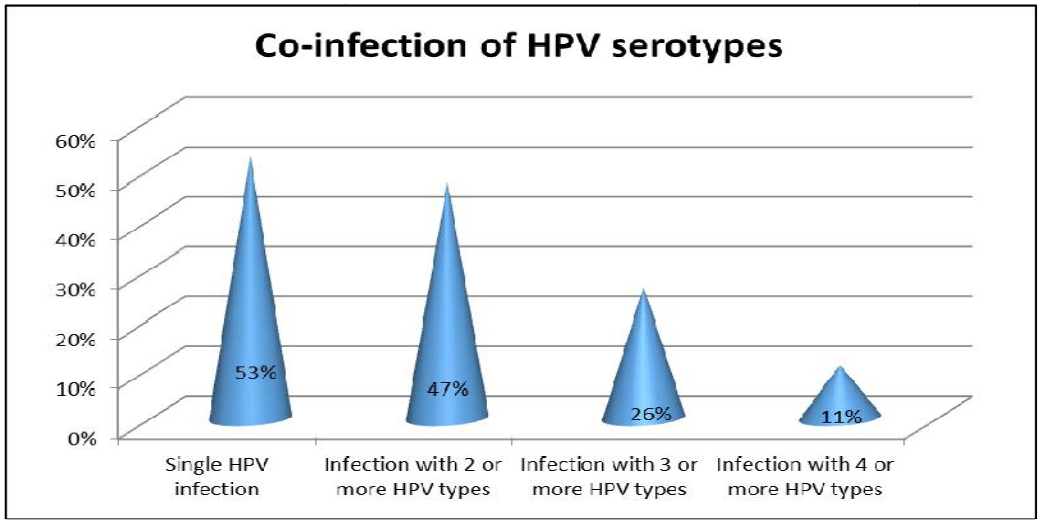

Fig. 2. Proportion of co-infection in the study population

4. DISCUSSION

In this study, 97% of the screened subjects were successful at self-sampling. This suggests that self-sampling is a feasible method of obtaining sample for cervical cancer screening in developing countries. The quality of cervico-vaginal samples collected by self-sampling in all the screened women was adequate for HPV DNA detection and typing. This is similar to the report of Modibbo et al in Abuja [12] and Bansil et al. in Uganda [20] on the feasibility of self-sampling as a modality of HPV cervical cancer screening in low- and middle- income countries.

The parity distribution in this study indicated that most positive cases were recorded among Para 1-4. While they constituted the majority of the respondents at over 90%, analysis of the difference between those who were positive and negative for hr-HPV was not significant. However, Jensen et al. [21] reported that childbirth increased the subsequent risk for immediate precursor lesions to cervical cancer, particularly among women with persistent high-risk HPV infection. They also posited that local tissue damage during vaginal delivery or cellular oxidative stress with increased likelihood of DNA damage and HPV integration may be possible mechanisms responsible [22].

In this study, 96% of the respondents had secondary and tertiary education with 95% of positive hr-HPV cases coming from them. This was contrary to the findings of other workers where lack of education had been associated with the high risk sexual practices and poor health seeking attitude; cumulating in the increased presence of sexually transmitted infections like HPV [23,24].

The prevalence of contraceptive use among respondent was only 18% with IUCD being the predominant method constituting 55.6%. Role of contraception in acquiring high risk HPV has been inconclusive especially with regard to the method. Jensen et al. [21] found no association between IUD use and a subsequent diagnosis of cervical intra-epithelial neoplasia (CIN3+). It was suggested that women who use IUD often are well screened, and precursor lesions are therefore more likely to be eliminated than in non-IUD users. Furthermore, IUD-induced chronic, low grade, sterile inflammation of the local mucosa might modify HPV carcinogenesis [25]. While Mark et al. [26] in Thailand observed that long-term use of hormonal contraception, laboratory confirmed Chlamydia infection, and bacterial vaginosis was associated with an elevated prevalence of any HPV and any hr-HPV, Jensen and co-workers observed no increased risk with pregnancy, contraceptive use, or sexual behaviour.

In this study, there was increased awareness of cancer of the cervix among participants accounting for 80% contrary to the findings of Oluwole et al. [27] in a Lagos rural community a few years ago where 85% of their respondents have never heard of cervical cancer before. Possible explanation for this was increased post-secondary educational attainment in 96% of the subject as noted earlier. Other studies in Nigeria have subjects only moderate levels of awareness of cervical cancer even among female healthcare and professional workers [28,29]. About half of the subjects (52%) knew of any conventional screening method to detect changes that predates cancer of the cervix. However, only 32% all subjects have been screened before with different methods including Pap smear and VIA but Pap smear accounted for 81% of those methods. McCarey et al. [30] observed in their series that Pap smear was the most widely and consistently known screening method for cervical cancer. Similar reports of low uptake of screening services among those with awareness of cervical cancers have been reported in different parts on Nigeria [27,31,32].

The prevalence of hr-HPV positivity of 19% found in this study is similar to 19.6% reported in Okene [33] but lower than 21.6% in Ile-Ife [16] and higher than 16.6% in Ibadan [34] and 8.9% in Northern Nigeria [12] among similar subjects. This variation may be due to differences in the study population and geographical location as the study by Modibbo et al [12] was in a semi-urban district in Northern Nigeria while ours was in an urban population in South-western Nigeria. The peak of hr-HPV positivity in our study was in women aged 31-40 years (31.6%). Modibbo et al reported a peak of 20.9% in age group 30–49 years compared to 39.0% among subjects aged 35–44years by Fadahunsi et al [16].

HPV 53 was the commonest serotype identified among our subjects followed by HPV 16, 51 and 58 which were the 2nd commonest serotypes with all occurring in 29% of them. HPV - serotypes 33 and 39 were the least identified serotypes (Figure 1). Serotype 16 was the commonest identified in Ibadan [34] and Ile-Ile [16]. Serotype 53 was the 2nd commonest in Ile-

Ile, Nigeria [16]. In Abuja, North-Central Nigeria, HPV serotypes 35, 52 and 18 were the most prevalent among their series [12]. Serotypes 33, 35, 45, and 68 were the least identified by Fadahunsi et al [16]. It thus appears that HPV serotypes 16 and 53 are relatively more common in South-western Nigeria.

Although HPV 16 [50-70%] / 18 [7-20%] infections account for majority of the disease worldwide, the contributions of HPV 16 to invasive cervical cancer from Sub-Saharan Africa and in particular West Africa is among the lowest globally [35,36]. We found a multiple infection rate of 47% which was higher than 41.7% reported Ile-ife [16], 33.9% in Ibadan [34] and 10.3% in Abuja [12]. Liao et al [37] observed multiple infection rates of 25.8% in China while Chaturvedi and co-workers reported 43.2% in Costa Rica [38].

Sixty six per cent of HPV positive women in our study attended follow-up for colposcopy. This was lower than 85% in Chile [39] and 94.1% in a Norway [40]. The lower follow-up rate in our study is probably attributable to the relatively poorer health seeking behaviour despite adequate counselling before the screening in low- and middle- income countries. One (10.05%) of the participants who tested hr-HPV positive was diagnosed of cervical cancer following colposcopy-guided biopsy while the remaining 52.6% of the hr-HPV positive women had normal colposcopy findings (Table 3). This attrition may be related to the multiple patient visits required by this method along with its personnel requirement; the asymptomatic patient is thus easily lost to follow‑up [17].

5. LIMITATIONS

This study was a pilot one with small sample size, the findings of which cannot be applicable to the general population. Although hr-HPV testing has a high sensitivity, a positive test cannot distinguish between HPV transient infection and persistent infection [41]. One-third of our hr-HPV positive subjects failed to turn-up for colposcopy and biopsy, which was a major drawback.

6. CONCLUSION

HPV 53 and 16 were the prevalent serotypes in this study correlates with findings of other workers in South-western Nigeria. Infection with more than one hr-HPV serotype is common and the self-sampling modality of HPV cervical cancer screening is feasible in our environment. Barriers to uptake of cervical cancer screening in low and middle-income countries such as cost, lack of infrastructure and concerns about health care workers' attitudes can be overcome by using self-collection of vaginal samples for hr-HPV DNA test. It offers effective screening by detecting more true-positive precursor lesions than cervical cytology and it is possible for women to perform self-HPV sampling and testing. Regional and Nationwide community-based screening is recommended to validate our findings.

CONSENT AND ETHICAL APPROVAL

Following ethical approval for the Lagos State University Teaching Hospital, one hundred consenting and eligible women, in a community-based prospective cross-sectional study which was conducted between 1st of November 2019 and 29th February, 2020.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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: a cancer journal for clinicians. 2018;68(6):394–424.
2. Oguntayo O, Zayyan M, Kolawole A, Adewuyi S, Ismail H, Koledade K, et al. Cancer of the cervix in Zaria, Northern Nigeria. Ecancermedicalscience. 2011;5:219.
3. Eze JN, Emeka‑Irem EN, Edegbe FO. A six‑year study of the clinical presentation of cervical cancer and the management challenges encountered at a state teaching hospital in Southeast Nigeria. Clin Med Insights Oncol. 2013;7:151‑8.
4. Ndikom CM, Ofi BA. Awareness, perception and factors affecting utilization of cervical cancer screening services among women in Ibadan, Nigeria: A qualitative study. Reprod Health 2012;9:11.
5. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Muñoz N. Human papillomavirus is a necessary cause of

invasive cervical cancer worldwide. J Pathol. 1999;189(1):12–9.
6. Burd EM. Human papillomavirus and cervical cancer. Clin Microbiol Rev. 2003;16(1):1-17.
7. Kitchener HC, Almonte M, Wheeler P, Desai M, Gilham C, Bailey A, et al. HPV testing in routine cervical screening: Cross sectional data from the ARTISTIC trial. Br J Cancer. 2006;95:56–61.
8. Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. WHO International Agency for Research on Cancer Monograph Working Group. A review of human carcinogens–Part B: biological agents. Lancet Oncol. 2009;10:321–2
9. Jordan J, Arbyn M, Martin-Hirsch P, Schenck U, Baldauf JJ, Da Silva D, et al. European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, part 1. Cytopathology. 2008;19(6):342–54.
10. Cuzick, J. Screening for cervical cancer. In: Rohan T.E, Shah K.V, editors. Cervical cancer: From etiology to prevention. Norwell: Kluwer Academic Publishers. 2004;261-93.
11. McCrory DC, Matchar DB, Bastian L, Datta S, Hasselblad V, Hickey J, et al. Evaluation of cervical cytology: Evidence report/technology assessment no. 5. Rockville, MD: Agency for Health Care Policy and Research; AHCPR Publication No. 99-E010; 1999.
12. Modibbo F, Iregbu KC, Okuma J, et al. Randomized trial evaluating self-sampling for HPV DNA based tests for cervical cancer screening in Nigeria. Infect Agent Cancer. 2017;12:11
13. Ronco G, Giorgi-Rossi P, Carozzi F, et al. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: A randomised controlled trial. Lancet Oncol. 2010;11(3):249–257.
14. Shiffman M, Wentzensen N, Wacholder S, Kinney W, Gage JC, Castle PE. Human papillomavirus testing in the prevention of cervical cancer. J Natl Cancer Inst. 2011;103:368–383.
15. Gupta S, Palmer C, Bik EM, Cardenas JP, Nuñez H, Kraal L, et al. Self-sampling for human papillomavirus testing: Increased cervical cancer screening participation and incorporation in international screening programs. Frontiers in Public Health. 2018;6:77
16. Fadahunsi OO, Omoniyi-Esan GO, Banjo AAF, Esimai OA, Osiagwu D, et al. Prevalence of high risk oncogenic human papillomavirus types in cervical smears of women attending well woman clinic in ile ife, Nigeria. Gynecol Obstet. 2013;3:185.
17. Sowemimo OO, Ojo OO, Fasubaa OB. Cervical cancer screening and practice in low resource countries: Nigeria as a case study. Trop J Obstet Gynaecol. 2017;34:170-6.
18. Jekel JF, Katz DL, Elmore JF. Sample size, randomization and probability theory. Epidemiology, biostatistics and preventive medicine. 2nd edition Philadelphia. WB Saunders. 2001;196-204.
19. Ajenifuja OK, Ikeri NZ, Adeteye VO, Banjo AA. Comparison between self-sampling and provider collected samples for Human Papillomavirus (HPV) Deoxyribonucleic acid (DNA) testing in a Nigerian facility. Pan Afr Med J. 2018;30:110
20. Bansil P, Wittet S, Lim J, Winkler J, Paul P, Jeronimo J. Acceptability of self-collection sampling for hpv-dna testing in low-resource settings: A mixed methods approach. BMC Public Health. 2014;14:596.
21. Jensen KE, Schmiedel S, Norrild B, Frederiksen K, Iftner T, Kjaer SK. Parity as a cofactor for high-grade cervical disease among women with persistent human papillomavirus infection: A 13-year follow-up. Brit J Cancer. 2013;108:234–239.
22. Williams VM, Filippova M, Soto U, Duerksen-Hughes PJ. HPV-DNA integration and carcinogenesis: Putative roles for inflammation and oxidative stress. Fut Virol. 2011;6:45–57.
23. Esere MO. Effect of sex education programme on at-risk sexual behaviour of school-going adolescents in ilorin, Nigeria. Afr Health Sci. 2008;8:120-125.
24. Temin MJ, Okonofua FE, Omorodion FO, Renne EP, Coplan P, et al. Perception of sexual behavior and knowledge about sexual transmitted infections among adolescents in Benin City, Nigeria. Int Fam Plan Pers. 1999;25:186-190.
25. Castellsague X, Diaz M, Vaccarella S, de Sanjose S, Munoz N, Herrero R, et al. Intrauterine device use, cervical infection with human papillomavirus, and risk of cervical cancer: A pooled analysis of 26

epidemiological studies. Lancet Oncol. 2011;12:1023–1031.
26. Marks MA, Gupta S, Liaw K, Tadesse A, Kim E, Chailert Phongnarisorn C, et al. Prevalence and correlates of HPV among women attending family-planning clinics in Thailand. BMC Infectious Diseases. 2015;15:159
27. Oluwole EO, Mohammed AS, Akinyinka MR, Salako O. Cervical cancer awareness and screening uptake among rural women in lagos, Nigeria. Journal of Community Medicine and Primary Health Care. 2017;29(1)81-88.
28. Ayinde OA, Omigbodun AO. Knowledge, attitude and practices related to prevention of cancer of the cervix among female health workers in Ibadan. J Obstet Gynaecol. 2003;23:59–62.
29. Hyacinth HI, Adekeye OA, Ibeh JN, Osoba T. Cervical cancer and pap smear awareness and utilization of pap smear test among Federal civil servants in North Central Nigeria. PLoS ONE 2012;7:e46583.
30. McCarey, Pirek D, Tebeu PM, Boulvain M, Doh AS, Petignat P. Awareness of HPV and cervical cancer prevention among Cameroonian healthcare workers. BMC Women Health. 2011;11:45
31. Utoo BT, Ngwan SD, Ansaku AS. Utilization of screening services for cancer of the cervix in Makurdi, Nigeria. J Reprod Biol Health. 2013;1(1):1.
32. Oladepo O, Ricketts OL, John-Akinola Y. Knowledge and utilization of cervical cancer screening services among Nigerian students. Int Q Community Health Educ. 2008;29:293-304.
33. Schnatz PF, Markelova NV, Holmes D, Mandavilli SR, O'Sullivan DM. The prevalence of cervical HPV and cytological abnormalities in association with reproductive factors of rural Nigerian women. J Womens Health. 2008;17(2):279-85.
34. Thomas JO, Herrero R, Omigbodun AA, Ojemakinde K, Ajayi IO, Fawole A, et al. Prevalence of papillomavirus infection in women in Ibadan, Nigeria: a population-based study. Br J Cancer. 2004;90(3):638-45.
35. Gm C, Gallus S, Herrero R, Munoz N, Pj S, Vaccarella S, et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the international agency for research on cancer hpv prevalence surveys: A pooled analysis. Lancet. 2005;366(9490):991–8.
36. Bruni L, Diaz M, Castellsague X, Ferrer E, Bosch F, De Sanjose S. Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. The Journal of Infectious Diseases. 2010;202(12):1789–99.
37. Liao G, Jiang X, She B, Tang H, Wang Z, Zhou Het al. Multi-infection patterns and co-infection preference of 27 human papillomavirus types among 137,943 gynecological outpatients across China. Front. Oncol. 2020;10:449.
38. Chaturvedi AK, Katki HA, Hildesheim A, Rodríguez AC, Quint W, Schiffman M, et al. Human papillomavirus infection with multiple types: Pattern of coinfection and risk of cervical disease. J Infect Dis. 2011;203(7):910-920.
39. Léniz J, Barriga MI, Lagos M, Ibáñez C, Puschel K, Ferreccio C. HPV vaginal self-sampling among women non-adherent to Papanicolaou screening in Chile. Salud Publica Mex. 2013;55(2):162-9.
40. Enerly E, Bonde J, Schee K, Pedersen H, Lönnberg S, Nygård M. Self-sampling for human papillomavirus testing among non-attenders increases attendance to the norwegian cervical cancer screening programme. PLoS ONE. 2016 ;11:e0151978.
41. Zhang R, Ge X, You K, Guo Y, Guo H, Wang Y, et al. p16/Ki67 dual staining improves the detection specificity of high-grade cervical lesions. J Obstet Gynaecol Res. 2018;44(11):2077-2084.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/70037