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Pattern of Cervical Cytology and High Risk Human Papillomavirus Strains in Non HIV Positive Women Presenting for Cervical Cancer Screening in Port Harcourt, Nigeria

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Abstract

Background: The high risk human papilloma virus (hrHPV) is largely associated with cervical cancer with identifiable dysplastic changes on cytology. The use of cervical cancer screening strategies has largely improved the general outcome of cervical malignancies globally. **Objective:** To compare cervical cytological features against human papilloma virus genotypes in non HIV positive patients presenting for cervical cancer screening in UPTH. **Method:** A cross sectional prospective study of 82 non HIV positive women who presented for cervical cancer screening at the University of Port Harcourt Teaching hospital. A prestructured questionnaire was used to obtain socio demographic information. Cytobrush extracts of cervical samples were subjected to cytology and human papilloma virus DNA genotyping using real-time polymerase chain reaction. The information obtained was analyzed using SSPP version 20 and results presented as frequency tables, percentages and tested for significance using student t-test and chi square with p value < 0.05 at 95% confidence interval. **Results:** The mean age of the women was 36.61 ± 7.75 with an age range of 22 - 58 years. The prevalence of HrHPV was 4.88%. Twenty-two of the respondent have abnormal cytological pattern. While the 4 cases of HrHPV positivity were of normal cytological pattern and occurred in respondents that were in their reproductive age, the 22 that showed abnormal cervical cytology were mainly of low grade squamous intraepithelial lesion (LGSIL). There was no case of high grade squamous cell intraepithelial lesion (HGSIL). **Conclusion:** HrHPV prevalence rate of 4.88% occurring in low socioeconomic class patients. All the cervical abnormalies were of LGSIL, hence the risk of transformation into cervical cancer is equally low. There may be no correlation between hrHPV and cervical cytology in low risk patients.

Keywords

hrHPV, Cytology, Port Harcourt, Nigeria

1. Introduction

Globally, about 500,000 new cases of cervical cancer are diagnosed annually with 300,000 deaths per year [1] [2]; most of the deaths occurring in Sub-Saharan Africa where 75% of women are known to present at advanced stages of the disease compared to what obtained in the developed countries [3] [4]. The milestones achieved by the Nordic countries were as a result of concerted efforts by the government of these countries focusing national resources and placing legislative backing in creating organized screening programmes [5]. These measures have substantially improved the outcome of cervical cancer by reducing the morbidity and mortality by 50% [6], prior to the introduction of organized screening programmes, encouraged by having population screening coverage of more than 70% [7].

Bassey *et al.* had highlighted the lack of use of cervical cancer preventive strategies among patients with cervical cancer [8]. This observation is triggered unfortunately by pressing alternative economic demands and lack of political will on the part of most Subsaharan African country governments.

The causal link between human papilloma virus and cervical cancer have been established by various studies with about ninety nine percent of patients with cervical cancer associated with different high-risk serotypes which varies according to geographical location [9] [10]. Every sexually active female is at risk of acquiring HPV infection [11].

About eighty percent of all HPV serotypes have the tendency of spontaneous regressions of infection, without causing cyto-pathological changes in the cervical epithelium [12]. However high-grade genotypes are less likely to have spontaneous regression with eventual integration of the HPV genome into the host cells cumulating in the development of identifiable dysplastic changes which are precursors for the occurrence of cervical cancer [13]. It has been shown that every one million infected cases of HPV, about 100,000 (1 in 10) will develop precancerous changes [14]. The progression of human papilloma virus infection from precancerous condition to cervical cancer is largely unpredictable and may take up to 20 years to complete [15].

The traditional practice of cervical cancer screening is largely that of the Papanicolaou methods, which identifies specific cytological changes with grading into high grade intraepithelial lesions, low grade intraepithelial lesions among others [16]. High grade intraepithelial lesions (HGSIL) are noted to have high propensity of malignant transformations [13] which has the HrHPV for this transformation. In a resource limited environment, time is of the essence in identifying women at risk of developing cervical cancer; as earlier mentioned

this transformation can take between 10 - 20 years. It is based on this that this study seek to profile cytological changes in patients with human papillomavirus infection in a seemly normal population who had opportunistic screening for cervical cancer at the University of Port Harcourt Teaching Hospital cancer screening centre.

2. Methodology

A cross sectional prospective study on women who presented for cervical cancer screening in the University of Port Harcourt Teaching Hospital, Port Harcourt between 21st October and December 2014 was conducted. All women between 15 and 70 years were included in the study while women who had total abdominal hysterectomy, failed to give consent for study, treated for premalignant lesion of the cervix, who were adequately immunized against the HPV, women receiving anti-neoplastic therapy or immunotherapy and those who are not eligible for papanicolaou smear were excluded from the study.

The sample size was determined using the Leshe-kish formula [$N = Z^2Pq/d^2$ where N is the sample size, Z is proportion of normal distribution Corresponding to the required significance level, P is the prevalence of HPV in Port Harcourt, q is 1.00-P, and d is how close to previously reported prevalence, the current study is desired] of single proportion with prevalence of human papilloma virus in women in Ibadan used as reference. Allowing a precision of 100% the minimum study population estimated was 73. A total of 82 persons were recruited for the study.

A prestructured study proforma was administered on each of the women after counseling and consent obtained. The following information was obtained from the women: age, occupation level of education, marital status and parity.

The cervical smears were collected with the cytobrush for Papanicolaou smear and HPV genotyping. In collecting the sample, the women were placed on lithotomy position, the cervix was exposed using the bivalve speculum and then inspected. The cytobrush was introduced into the transformation zone scrapped in a clockwise manner to 360˚. The specimen for the HPV genotyping was collected in the same manner using the cytobrush. The speculum was removed after the collection of the sample. After collecting the samples, the cervical smear was smeared on an already numbered frosted glass slide and covered with a cover slip. This was inserted into a container with 95% alcohol solution and sent to the Anatomical Pathology Department of UPTH for cytology. The cyto-brush for HPV serotyping was inserted into an already numbered specimen bottle, which contained a physiological saline. This was then cut short which allowed the specimen bottle to be covered.

All the collected samples with the cyto-brush were packaged in an ice pack in a container and were sent to the Safety Molecular Pathology laboratory at Enugu, which was used for HPV DNA testing using Real time Polymerase Chain Reaction(PCR).

Information obtained at the end of this study was processed using computer software Statistical Package for Social Science version 20.0 (SPSS Inc; Chicago USA). Frequency tables were generated and the results tested for significance using student t-test and chi-square. The age-specific prevalence and the contribution of other socio-demographic factors were computed. The risk of acquiring HPV was estimated with odds ratio. Statistical test of association was carried out at the level of significance set at P value < 0.05 at 95% confidence interval.

3. Results

The mean age of the women reviewed were 36.61 ± 7.76, with age range of 22 - 58 years (P value = 0.42). The prevalence of HrHPV was 4 (4.88%). Twenty two (26.83%) of the 82 respondents had abnormal cervical cytological pattern. **Table 1** shows the Socio demographic Characteristics of respondents.

The four cases of hrHPV showed normal cervical cytology and occurred in respondents in the reproductive age group; they were mainly of low parity, poor socio economic class and were all married (**Table 2**). Out of the 78 respondents that were negative for hrHPV, 56 (68.29%) were of normal cervical cytology and of the remaining 22 that had abnormal cytological pattern, 17.03% had LGSIL and 7.32% had inflammatory cells and they were distributed among various age group, parity and socio-economic class. There was no HGSIL. There is no correlation between the 4 case of positive hrHPV and cervical cytology (**Table 3**).

4. Discussions

In this study of non HIV positive women, the presence of hrHPV was found to be low as against a three-fold increase in a comparative study done in HIV positive counterpart [17]. This is in keeping with an established observation that immune suppression increases the chance of acquisition of HPV, pre invasive phase and hence eventual transformation to cervical cancer [18]. Considering that the positive predictive value and the specificity of the traditional screening method (pap smear) is relatively low, the more precise HPV genotype screening method should improve the pick-up rate of all the exposed and infected individuals in the apparently low risk population. In this study however there is apparently no difference in terms of sensitivity to detecting cervical pathology. The pap smear have the advantage of being cheap as against the much more expensive genotype method.

All the respondents with hrHPV were of low socioeconomic class which is in agreement with global literature review [19] [20]. These four cases of hrHPV had normal cervical cytology. This is against a 15 fold chance of not only having abnormal cervical pathologies but the high grade squamous intra-epithelial neoplasium (HGSIL) type as observed in their HIV positive counterpart [17]. These HGSIL have a higher propensity for transformation into a premalignant cervical lesion. Despite the negative cytology, these women with hrHPV have higher chance of developing HGSIL later in life than those with negative HPV, hence the need to follow them up with cytology at intervals [21].

Table 1. Socio demographic characteristics of respondents.

Age (years)	Frequency	Percentage (%)
15 - 24	4	4.9
25 - 34	30	36.5
35 - 44	37	45.1
45 - 54	8	9.8
55 - 64	3	3.7
Total	**82**	**100**
Education		
Primary	3	3.7
Secondary	33	40.2
Tertiary	46	56.1
Total	**82**	**100**
Occupation		
Business	45	54.9
Civil servant	22	26.8
House wife	6	7.3
Public servant	1	1.2
Student	8	9.8
Total	**82**	**100**
Marital Status		
Single	13	15.9
Married	65	79.3
Divorced	4	4.9
Total	**82**	**100**
Parity		
Nullparity	36	43.9
Primparity	13	15.9
Multiparity	30	36.6
Grand multiparity	3	3.6
Total	**82**	**100**

The largely low grade interepithelial lesion (LGSIL) and other cervical pathologies noted on pap smear were in keeping with documented case series on non compromised groups [22] [23]. It then means that the possibility of these women having cancer of the cervix is low when HPV is negative. In this instance, yearly cytology is done for follow up.

However, for women with atypical squamous cells of undetermined significance (ASCUS) and HPV negative as is the case in this study, further screening by

Table 2. Socio demographic characteristics by presence of hrHPV.

Variables	HPV status	
	HPV+	HPV−
Age		
15 - 24	-	4
25 - 34	-	30
35 - 44	4	34
45 - 54	-	7
55 - 64	-	3
Parity		
0 - 1	2	50
2 - 3	2	20
4 - 5	-	6
>5	-	2
Social status		
Low	2	18
Middle	2	41
High	-	19
Marital Status		
Single	-	12
Married	4	63
Divorced	-	3

Table 3. Socio demographic characteristics in relation to cytological changes and hrHPV distribution.

Variables	Cytological patterns					
	N	HGSIL	LGSIL	AGUS	IC	ASCUS
Age						
15 - 24	4	-	-	-	-	2
25 - 34	12	-	11	-	2	-
35 - 44	35	-	2	-	4	-
45 - 54	7	-	1	-	-	-
55 - 64	2	-	-	-	-	-
Parity						
0 - 1	34	-	11	-	4	2
2 - 3	19	-		-	2	-
4 - 5	5	-	3	-	-	-
>5	2	-	-	-	-	-
Social status						
Low	13	-	7	-		
Middle	36	-	4	-	1	2
High	11	-	3	-	5	
Marital Status						
Single	9	-	1	-	2	-
Married	48	-	13	-	4	2
Divorced	3	-	-	-	-	-
HrHPV status						
Positive	4	-	-	-	-	-
Negative	56	-	14	-	6	2

colsposcopy and biopsy are unnecessary and periodic cytological follow up is acceptable. If HPV is positive, immediate colposcopy should be done [22].

There was no correlation noted in this study between hrHPV and pre invasive lesion as all the patients with Positive hrHPV have normal cytology. This can be explained by the fact that trigger factors are needed for cytological transformations which the uncompromised do not have.

In the social context of this study, it would be noted that all high risk oncogenic strains are associated with low socioeconomic class hence improving economic status and reducing certain high risk social behaviors of the patients may further reduce the prevalence cytologic changes. It is worthy of note that in the context of cost of screening, this study highlights the usefulness of the less expensive cytologic method of screening as against the detection of high risk oncogenic virus detection in low risk population.

5. Conclusion

This study found no correlation between high risk human papilloma virus acquisition and abnormal cervical cytological changes in non HIV positive respondents. Furthermore, in the non HIV positive women (low risk group), the traditional Pap smear and the very expensive HPV genotype methods seems to be at par in terms of detection of cytological changes. It is therefore advocated that the more expensive genotype method should be reserved for screening in the high risk population only.

References

[1] Ferlay, J., Soerjomataran, I., Dikshart, R. *et al.* (2015) Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBACAN. *International Journal of Cancer*, **136**, E359-E386. https://doi.org/10.1002/ijc.29210

[2] IARC GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. IARC. http://globocan.fr

[3] Okonofua, F. (2007) Human Papilloma Virus and Prevention of Cervical Cancer in Africa. *African Journal of Reproductive Health*, 117-122.

[4] Kamager, F., Dores, G.M. and Anderson, W.F. (2008) Pattern of Cervical Cancer Incidence Mortality and Prevalence across Five Different Continent Defining Geographical reGions of the World. *Journal of Clinical Oncology*, **24**, 2137-2150. https://doi.org/10.1200/JCO.2005.05.2308

[5] Larra, E., Dayen, E. and Hakama, M. (1987) Trend in Cervical Mortality in Nordic Countries Association with Organized Screening Programmes. *Lancet*, **30**, 1247-1249.

[6] Linday, A.T., Freddie, B., Rebbeca, I.S., Jacques, F. and Ahmedin, J. (2015) Global Cancer. *Journal of Clinical Practice*, **56**, 87-108.

[7] Anttla, A., Aasmaa, A., Fender, M., Patrick, J., Rebil, M., Nicula, F., *et al.* (2009) Cervical Cancer Screening Policies and Coverage in Europe. *European Journal of Cancer*, **45**, 2649-2658. https://doi.org/10.1016/j.ejca.2009.07.020

[8] Bassey, G., Nyengidiki, T.K. and Onwubuariri, M. (2015) Profile and Retrospective

Analysis of the Use of Preventive Strategies in Patients with Cervical Cancer in South-South Nigeria. *Nigerian Medical Journal*, **56**, 109-112. https://doi.org/10.4103/0300-1652.150693

[9] Human Papillomavirus: Genital HPV Infection. Fact Sheet. Centre for Disease Control and Prevention 2014.

[10] Boach, F.X., Lortinez, A., Munoz, N., Mejer, C.J. and Shark, K.V. (2002) The Casual Relationship between HPV and Cervical Cancer. *Journal of Clinical Pathology*, **4**, 1244-1265.

[11] Winer, R.L., Feng, Q., Hughes, J.P., Orely, S., Kivt, N.B. and Koutsky, L.A. (2008) Risk Factors of Female Human Papilloma Virus Acquisition Associated with First Male Sex Partners. *The Journal of Infectious Diseases*, **197**, 279-282. https://doi.org/10.1086/524875

[12] Magnet, S. (2010) HPV Immune Response to Infection and Vaccination. *Infectious Agent and Cancer*, 19-25.

[13] Pooja, P., Mala, Y.M., Tripathic, R., Das, B.C. and Bhambram, S. (2014) Human Papillomavirus (HPV) Infection and Abnormal Cytopathology among HIV Positive Women in India. *Journal of AIDS and HIV Research*, **6**, 1-6. https://doi.org/10.5897/JAHR10.033

[14] HPV Prevalence and Type-Distribution in Crervical Cancer and Premalignant Lesion of Cervix: A Population Based Study from Northern Ireland. *Journal of Medical Virology*, **88**, 1262-1270. https://doi.org/10.1002/jmv.24447

[15] Bud Ellien, M. (2003) Human Papillomavirus and Cervical Cancer. *Clinical Microbiology Reviews*, **16**, 1-7. https://doi.org/10.1128/CMR.16.1.1-17.2003

[16] National Cancer Institute (2015) Hpv and Cancer. http://www.cancer.gov

[17] Nyengidiki, T.K. and Athanasius, P.B. (2016) High Risk Human Papiloma Virus Genotyping and Cervical Cytology as Screening Test for Cervical Cancer in Human Immunodeficiency Virus Positive Women in Nigeria. *Journal of Cancer and Tumor International*, **3**, 1-7. https://doi.org/10.9734/JCTI/2016/25209

[18] Veldnujien, N.J., Srigder, P.J., Reiss, P., Majer, C.J. and Van de Wjgert, J.A. (2010) Factors Affecting Transmission of Mucosal Human Papilloma Virus. *The Lancet Infectious Diseases*, **10**, 862-874. https://doi.org/10.1016/S1473-3099(10)70190-0

[19] Nyengidiki, T.K., Durugbo, I.K. and Oranu, E.O. (2016) Human Papillomavirus Awareness and Uptake of HPV Vaccination among Human Immunodeficiency Virus Positive Women in Nigeria. *International Journal of Tropical Disease & Health*, **15**, 1-7. https://doi.org/10.9734/IJTDH/2016/25241

[20] Khan, M.J., Pstidge, E.E., Wang, S.S. and Shiffman, M. (2005) Socioeconomic Status and the Risk of Cervical Intraepithelial Neoplasm Grade 3 among Oncogenic Human Papillomavirus DNA Positive Women with Equivocal Abnormal Cytology. *Cancer*, **1004**, 61-70. https://doi.org/10.1002/cncr.21129

[21] Katik, H.A., Kinney, W.K., Fetterman, B., Lory, T., Poitrar, N.E., Cheung, L., *et al.* (2011) Cervical Cancer Risk for Women Undergoing Concurrent Testing for Human Papillomavirus and Cervical Cytology: A Population Based Study in Clinical Practice. *The Lancet Oncology*, **12**, 663-673. https://doi.org/10.1016/S1470-2045(11)70145-0

[22] Faruk, M.K. and Murat, M.N. (2014) Cervical Premalignant Lesion and Their Management. *Journal of the Turkish-German Gynecological Association*, **15**, 109-121. https://doi.org/10.5152/jtgga.2014.29795

[23] Stancy, B., Zaibo, L., Marshall, A. and Chegquam, Z. (2014) Low Grade Squamous

Cell Intraepithelial Lesion Cannot Exclude High Grade Squmous Cell Intraepithelial Lesion. *American Journal of Clinical Pathology*, **141**, 239-246.
https://doi.org/10.1309/AJCPM9X5RCZYEQJQ