# MOLECULAR EPIDEMIOLOGY AND SOME FACTORS ASSOCIATED WITH GENITAL HUMAN PAPILLOMAVIRUS INFECTION AMONG WOMEN IN OYO STATE, NIGERIA

**BY**

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## ABSTRACT

Genital Human Papillomavirus (HPV) infection is a well-established causative agent of cervical cancer; a major cancer in most developing countries.Persistent infection with high-risk HPV, especially types 16 and 18 have been associated with cervical cancer. Two HPV vaccines (Cervarix and Gardasil) are currently available in Nigeria, targeting two (16 and 18) and four (6, 11, 16 and 18) types, respectively. However, the distribution of HPV types varies greatly across geographical regions with little information on the circulating types among Nigerian women, thus raising concerns about the effectiveness of the available vaccines in the country. This study was therefore designed to determine the circulating HPV types among women in Oyo State, Nigeria and identify some factors associated with the infection.

A total of 295 endocervical swab samples were collected from consenting women attending routine cervical cancer screening, STI clinics and community-based outreach programme. The participants were enrolled from University College Hospital, Ibadan; Baptist Medical Centre, Saki and during an outreach in Molete community, Ibadan.Structured questionnaire was used to capture demographic, medical information and sexual history.Genomic DNA was extracted from samples using commercial extraction reagents. The presence of HPV was detected by PCR using two sets of consensus primers targeting the L1 and E6/E7 genes. Six pairs of HPV type-specific primers (16, 18, 31, 33, 35 and 6/11) were then used to genotype the HPV isolates in a nested PCR. Samples not identified by the primers used were sequenced and typed by phylogenetic analysis. Data were analysed using Chi-square at $\alpha_{0.05}$.

Fifty five (18.6%) individuals were positive for HPV infection. Primers targeting E6/E7 region detected more HPV infections (17.3%) than those targeting L1 region (9.2%). Five HPV types were detected using type-specific primers (HPV 16, 18, 31, 33 and 35), while 14 HPV types (HPV 6, 16, 18, 31, 35, 42, 43, 44, 52, 58, 66, 74, 81, 86) were identified by sequencing. In all, 15 HPV types were detected with HPV 31 being the most predominant (32.8%), followed by HPV 35 (17.2%) and HPV 16 (15.5%). About 21.0% of individuals had dual infections while high-risk HPV genotypes were found among 86.2% of HPV-

positive individuals. Highest nucleotide substitutions (n=32) were found in HPV 44 genotype while the only HPV 74 isolate had three nucleotide (CCT) insertionsat E7 gene that translated into amino acid proline. Some factors including divorce (p=0.019), illiteracy (p=0.003), polygamy(p=0.027), unemployment (p=0.023), low income earnings (p=0.018), younger age (<18years)at sexual debut (p=0.039) and passive smoking (p=0.017) were associated with HPV infection.

Multiple Human Papillomavirus types co-circulated in Oyo State, Nigeria. Most of the circulating Human Papillomavirus are high-risk type with type 31 being the most predominant. Although the implication of the rare HPV 74 with proline insertion detected for the first time in Nigeria is unknown, it may have effect on the transformation potential of the virus. Primers targeting E6/E7 region may be more appropriate for the detection of Human Papillomavirus circulating in Oyo State, Nigeria.

**Keywords:** Circulating Human Papillomavirus types, High-risk Human Papillomavirus, E6/E7 genes, Human Papillomavirus associated factors

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## CERTIFICATION

We certify that this work was carried out by Mrs. Yewande Tolulope NEJO in the Department of Virology, Faculty of Basic Medical Sciences, College of Medicine, University of Ibadan, Ibadan, Nigeria.

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## DEDICATION

This work is dedicated to my Heavenly Father, the Author and Finisher of my faith. He is my portion and the reason for my existence. To Him be glory, honour, majesty, dominion, power, wisdom, and might forever, Amen.

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## ACRONYMS

**ACOG**- American College of Obstetricians and Gynecologists

**AIDS**- Acquired Immunodeficiency Syndrome

**AIN**- Anal Intraepithelial Neoplasia

**BLAST**- Basic Local Alignment Search Tool

**BPV**- Bovine Papillomavirus

**CDC**- Center for Disease Control

**CIN**- Cervical Intraepithelial Neoplasia

**CMV**- Cytomegalovirus

**CRPV**- Cottontail Rabbit Papillomavirus

**DC**- Dendritic cells

**DNA**- Deoxyribonucleic acid

**DVI**- Direct visual inspection

**EDTA**- Ethylene di-amine tetra acetic acid

**ELISA**- Enzyme-Linked Immunosorbent Assay

**EV**- *Epidermodysplasia verruciformis*

**FDA**- Food and Drug Administration

**HHV**- Human herpesvirus

**HIV**- Human Immunodeficiency Virus

**HPV**- Human papillomavirus

**HR**-HPV- High-risk types

**HSIL**- High-grade cervical lesions

**IARC**- International Agency for Research on Cancer

**ICC**- Invasive Cervical Cancer

**ICTV**- International Committee on the Taxonomy of Viruses

**IFN**- Interferon

**LC**- Langerhans cells

**LCR**- Long control region

**LR-HPV**- Low-risk types

**LSIL**- Low-grade cervical lesions

**MCL**- Maximum Composite Likelihood

**NCBI**- National Centre for Biotechnology Information

**NC**-Negative Control

**NCR-** Non-coding region

**NHS**- National Health Service

**NK**- Natural killer cells,

**NKT**- Natural killer T

**NMPCR**- Nested Multiplex Polymerase Chain Reaction

**OC**- Oral Contraceptives

**ORFs**- Open reading frames

**PC**- Positive Control

**PCR**- Polymerase Chain Reaction

**PG**- Pico Green

**PIN**- Penile Intraepithelial Neoplasia

**PV**- Papillomaviruses

**SPSS**- Statistical Package for Social Sciences

**STI**- Sexually Transmitted Infection

**TBE**- Tris Borate EDTA

**UCH**- University College Hospital

**URR**- Upstream regulatory region

**VIA**- Visual inspection with acetic acid

**VIN**- Vulvar Intraepithelial Neoplasia

**VLPs**- Virus-like particles

**WHO**- World Health Organization