

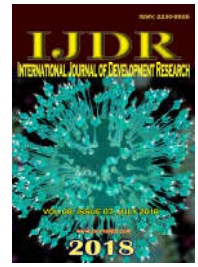


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## VARIATIONS IN THE PREVALENCE OF ISOLATED HUMAN PAPILLOMAVIRUS GENOTYPE IN CERVICAL CANCER SPECIMENS: A REVIEW

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### ABSTRACT

The uterine cervix represents a pathologically important part of the uterus because of the high prevalence of cervical cancer worldwide. The epithelium of the cervix can be infected by sexually transmitted oncogenic types of human papillomavirus (HPV). These virus cause persistent infection of the cervical epithelial cells and this leads to viral cytopathic changes associated with atypia (koilocytic atypia) in the infected cells. This is referred to as squamous intraepithelial lesions which can be low grade or high grade depending on the severity of koilocytic atypia. There are three categories of oncogenic human papillomavirus. These include the high-risk, low-risk and undetermined-risk human papillomaviruses. There are up to 19 types of high-risk human papillomaviruses that have been identified. These include types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73 and 82. More than 90% of cervical cancer is caused by high-risk human papillomaviruses. These viral subtypes are isolated more often from cervical cancer specimen than the low-risk subtypes. There are several low-risk HPVs including types 6, 11, 40, 42, 43, 44, 54, 55, 57, 61, 62, 70, 71, 72, 74, 81, 83, 84 and 89. They have been isolated from cervical cancer specimens in some cases. They have been known to be responsible for more than 90% benign cervical lesions such as condylomata accuminata. There are also undetermined-risk human papillomaviruses for cervical cancer such as types 2a, 3, 7, 10, 13, 27, 28, 29, 30, 34, 86, 87, 90 and 91. The common prevalent HPV genotypes are HPV 16, 18, 31, 33 and 45. But HPV45 have not been isolated from cervical sample specimens in some regions in the globe like southern Nigeria and Ivory Coast. HPV 16 and 18 have consistently been the most prevalent HPV subtypes isolated from the cervical specimen in most part of the world. Several studies done in Nigeria, Japan, Kenyan and Canada have shown HPV 16 and 31 as the commonest HPV genotypes isolated from cervical cancer specimen. The study by de Vuyst et al in Kenya show an equal prevalence of HPV 31 and 45. **Objective:** To do a review on the variations in the prevalence of isolated human papillomavirus genotype in cervical cancer specimens. **Methodology:** Literature search was done using google search and the following keywords were used in the search - prevalence, human papillomavirus, genotype, cervical and cancer. The literatures obtained were analyzed and used for this review. **Conclusion:** It is clear that the prevalent HPV genotypes involved in the etiology of cervical cancer in the various part of the world vary. Therefore, there is need to develop vaccines that would be able to protect women and men from HPV infections of the variable HPV genotypes. The specific HPV vaccines available do not protect against infections caused by other types of HPV that it is not specific for. With the growing knowledge of the prevalent HPV genotypes in various region of the world, a day for the perfect vaccine that would eliminate cervical cancer globally will come soon.

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## INTRODUCTION

The uterine cervix represents a pathologically important part of the uterus because of the high prevalence of cervical cancer worldwide. The epithelium of the cervix can be infected by sexually transmitted oncogenic types of human papillomavirus (HPV). These viruses cause persistent infection of the cervical epithelial cells and this leads to viral cytopathic changes associated with atypia (koilocytic atypia) in the infected cells (Leval, 2013; Forman, 2012; Blomberg, 2012 and Nordenvall, 2006). This is referred to as squamous intraepithelial lesions which can be low grade or high grade depending on the severity of koilocytic atypia. There are three categories of oncogenic human papillomavirus. These include the high-risk, low-risk and undetermined-risk human papillomaviruses. There are up to 19 types of high-risk human papillomaviruses that have been identified (Nordenvall, 2006 and Luostarinen, 1999). These include types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73 and 82. More than 90% of cervical cancer is caused by high-risk human papillomaviruses. These viral subtypes are isolated more often from cervical cancer specimen than the low-risk subtypes. There are several low-risk HPVs including types 6, 11, 40, 42, 43, 44, 54, 55, 57, 61, 62, 70, 71, 72, 74, 81, 83, 84 and 89. They have been isolated from cervical cancer specimens in some cases. They have been known to be responsible for more than 90% benign cervical lesions such as condylomata accuminata. There are also undetermined-risk human papillomaviruses for cervical cancer such as types 2a, 3, 7, 10, 13, 27, 28, 29, 30, 34, 86, 87, 90 and 91 (Luostarinen, 1999).

### Variations in the Prevalence of Human Papillomavirus in Cervical Cancer

The study by Sah et al in Nepal shows that the most common human papillomavirus genotypes isolated from cervical cancer specimens are 16, 18, 45, 33, 52, 56 and 31. Most of these were found as single infections (94.5%).<sup>6</sup> Together, HPV types 16, 18, and 45 were found in 92% of the tumor samples (Sah, 2018). Another study by Suthipintawong C in Thailand on invasive cervical cancer samples shows a 93.3% prevalence of HPV DNA in the samples and the five most common high-risk HPV genotype isolated and their prevalence are HPV types 16 (83.2%), HPV18 (59.3%), 58 (9.3%), 52 (4.1%), and 45 (3.8%). HPV types 16, 18 and 58 were the commonest with HPV 45 being the fifth commonest genotype isolated compare to the study by Sah et al with HPV 45 as the third commonest. In this study, other cervical biopsies with intraepithelial lesions were also analyzed for HPV DNA and genotype (Suthipintawong, 2011). The study by Damião et in Angola show HPV types 16 and 18 as the only HPV genotype isolated from cervical cancer specimens (Damião, 2016). Also another study by La Ruche et al in Ivory Coast show that the commonest isolated HPV types from cervical cancers and high-grade lesions are types 16, 18, 31, 33, 58 and 52 (La Ruche, 1998). However, HPV 16,18 and 31 were the three commonest HPV genotype isolated in this study (La Ruche, 1998). In this study HPV DNA was prevalent in 77.6% of the specimens. A similar study in Kenya by De Vuyst et al shows that the commonest HPV genotypes isolated from cervical cancer specimens were HPV types 16, 18, 31, 33 and 45 (De Vuyst, 2013). Human papillomavirus types 16, 18 and 31 were the three commonest HPV genotypes isolated. This is similar to the findings by La Ruche et al. In this study, HPV DNA was

detected in 96.6% of the cervical cancer specimens. Another study done by Irabor et al in Nigeria shows the detection of HPV DNA in 91.3% of the cervical cancer specimens (Irabor, 2018).

In this study, seven high-risk human papillomavirus genotypes were isolated from the cervical cancer specimens including types 16, 31, 18, 33, 35, 59 and 68. Types 16, 31 and 18 were the three commonest types of HPV isolated from cervical cancer specimen in this study. Human papillomavirus types 16 and 31 were the two most common comprising 65.2% of the HPV DNA positive samples.<sup>11</sup> In a study by De Almeida et al in Brazil the eight most frequent HPV types that were isolated from cervical cancer specimen which include 16, 18, 31, 33, 35, 45, 52, and 58. The HPV types 16, 18 and 31 were the commonest genotypes isolated in this study (De Almeida, 2017). A study done in Jamaica by Rottray show an unusually high prevalence of HPV type 45 of 13.6% among cervical cancer specimens. However, HPV 16 and 31 had the highest prevalence in cervical cancer specimens than HPV 18 and 45. This finding is similar to that by Irabor et al in Nigeria. The study by Mesher et al in the UK show that 95.8% of the cervical cancer specimens were positive for at least one high-risk (HR) human papillomavirus (HPV) type. The HPV types 31, 33, 45, 52 and 58 were isolated in 16.1% of HR HPV-positive invasive cervical cancers (Mesher, 2014). In all HPV types, 16 and 18 were isolated from 83% of the cervical cancer specimens. One study by Baay et in Belgium show an HPV DNA prevalence in cervical cancer specimens of 97% and the commonest HPV genotype isolated in this study were HPV 16, 18, 33, 45 and 58 (Carole Rattray, 1996). The commonest prevalent HPV genotypes are HPV 16, 18, 31, 33 and 45. But HPV45 have not been isolated from cervical cancer specimens in some regions in the globe like southern Nigeria and Ivory Coast. HPV 16 and 18 have consistently been the most prevalent HPV subtypes isolated from the cervical specimen in most part of the world. Several studies done in Nigeria, Kenyan and Canada have shown HPV 16 and 31 as the commonest HPV genotypes isolated from cervical cancer specimen (Baay, 2001 and Sellor, 2000). One study from de Vuyst in Kenya show an equal prevalence of HPV 31 and 45 (La Ruche, 1998). These variations in the prevalent HPV genotypes can be attributed to differences in lifestyle and geographical locations of the different places where these studies were done.

### CONCLUSION

It is clear that the prevalent HPV genotypes involved in the etiology of cervical cancer in the various part of the world vary. Therefore, there is need to develop vaccines that would be able to protect women and men from HPV infections of the variable HPV genotypes. The specific HPV vaccines available do not protect against infections caused by other types of HPV that it is not specific for. With the growing knowledge of the prevalent HPV genotypes in various region of the world, a day for the perfect vaccine that would eliminate cervical cancer globally will come soon.

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