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Prevalence of human papillomavirus genotypes in women treated by the Unified Health System in a population from Northeast Brazil

Prevalência de genótipos do papilomavírus humano em mulheres atendidas pelo Sistema Único de Saúde em uma população do Nordeste do Brasil

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ABSTRACT: The aim of this study was to present the circulating HPV genotypes in a population from northeast Brazil. HPV was detected by nested-Polymerase Chain Reaction (nPCR) method using primers MY09/11 and GP5+/6+. HPV sequencing was performed by the method of Sanger. The HPV 16 was the most frequent (35.7%), followed by HPV 58 (14.3%). In conclusion, we identified, in one population from Northeast Brazil, a low prevalence of HPV 18 present in the vaccine provided by Unified Health System and a high prevalence of HPV 58 which is not present in this vaccine.
KEYWORDS: HPV, Oncology and Woman Healthy.

RESUMO: O objetivo deste estudo foi apresentar os genótipos circulantes do HPV em uma população do nordeste do Brasil. O HPV foi detectado pelo método de reação em cadeia da polimerase aninhada (nPCR) usando os iniciadores MY09 / 11 e GP5 + / 6 +. O sequenciamento do HPV foi realizado pelo método de Sanger. O HPV 16 foi o mais frequente (35,7%), seguido do HPV 58 (14,3%). Concluindo, identificamos, em uma população do Nordeste do Brasil, baixa prevalência do HPV 18 presente na vacina fornecida pelo Sistema Único de Saúde e alta prevalência do HPV 58 que não está presente nesta vacina.
PALAVRAS-CHAVE: HPV, Oncologia e Mulher Saudável.

INTRODUÇÃO

Infections caused by high risk genotypes of human papillomavirus (HPV) in women are associated with the development of carcinogenesis, including cervical cancer. HPV 16 and 18 are responsible by 70% of Squamous Intraepithelial Lesion (SIL) and cervical cancers [1]. Other high risk HPV genotypes, excluding the combination HPV 16 and 18, have been shown to increase four fold more the risk of developing cervical cancer [2]. Therefore, the identification high risk HPV genotypes in a population is an important epidemiological approach to future vaccination and disease management. This study aimed to report the circulating HPV genotypes in a population from Northeast Brazil.

METHODOLOGICAL PROCEDURE

The samples were collected from women attended through the Unified Health System in Arapiraca city, Alagoas. DNA was extracted from cervical cells using Wizard® Genomic DNA Purification kit (PROMEGA). All procedures were approved by the ethical committee from Federal University of Alagoas (UFAL) in July 2014 (permit number: 739.340). Informed consent was obtained from all study participants.

HPV was detected by nested-Polymerase Chain Reaction (nPCR) method using primers MY09(5'-CGTCCMARRGGAWACTGATC-3') MY11(5'GCMCAGGGWCATAAYAATGG-3') and GP5+(5'TTTGTTACTGTGGTAGATACTAC-3')/GP6+(5'GAAAAATAAACTGTAAATCATATTC-3'). Amplification of the human β-globin gene was used as internal control of HPV detection. HPV positive samples were sequenced using the BigDye Terminator v3.1 Cycle Sequencing Kit (Applied Biosystems, USA) with electrophoresis on 3500 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) by the method of Sanger. The sequences obtained were identified using National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) search (https://blast.ncbi.nlm.nih.gov/Blast.cgi). In this analysis only the samples that showed ≥ 97% similarity with the HPVs genotypes found were included.

For consensus tree construction based on L1 partial genome, the sequences were aligned and edited using BioEdit 7.2.5 (http://www.mbio.ncsu.edu/BioEdit/bioedit.html). The evolutionary history was inferred using the Maximum Likelihood method with a bootstrap of 1000 replicates and the evolutionary distances were computed using the Tamura 3-parameter method in MEGA7 software. all samples included in the analysis showed an identity rate higher than 97% when compared to the sequences deposited in GenBank.

RESULTS

From a total of 709 samples collected in the period between September 2014 and December 2016. These samples 50,07% (n=355) were HPV positive. All HPV positive women were submitted to DNA sequencing, however, the Sanger sequencing method permits identify only simple infections.

Sixty samples (16.90%) presented sequencing data compatible to simple infections. The other samples presented multiple overlapping unreadable sequences and were inviable for sequencing alignment using BLAST algorithm. Among the 60 samples, 18 (30%) showed less than 97% of similarity to the HPV genotypes available in the NCBI database, and thus were excluded of the study. The identity of HPV genotype was possible for 42 (70%) samples with a high similarity to the NCBI database sequences.

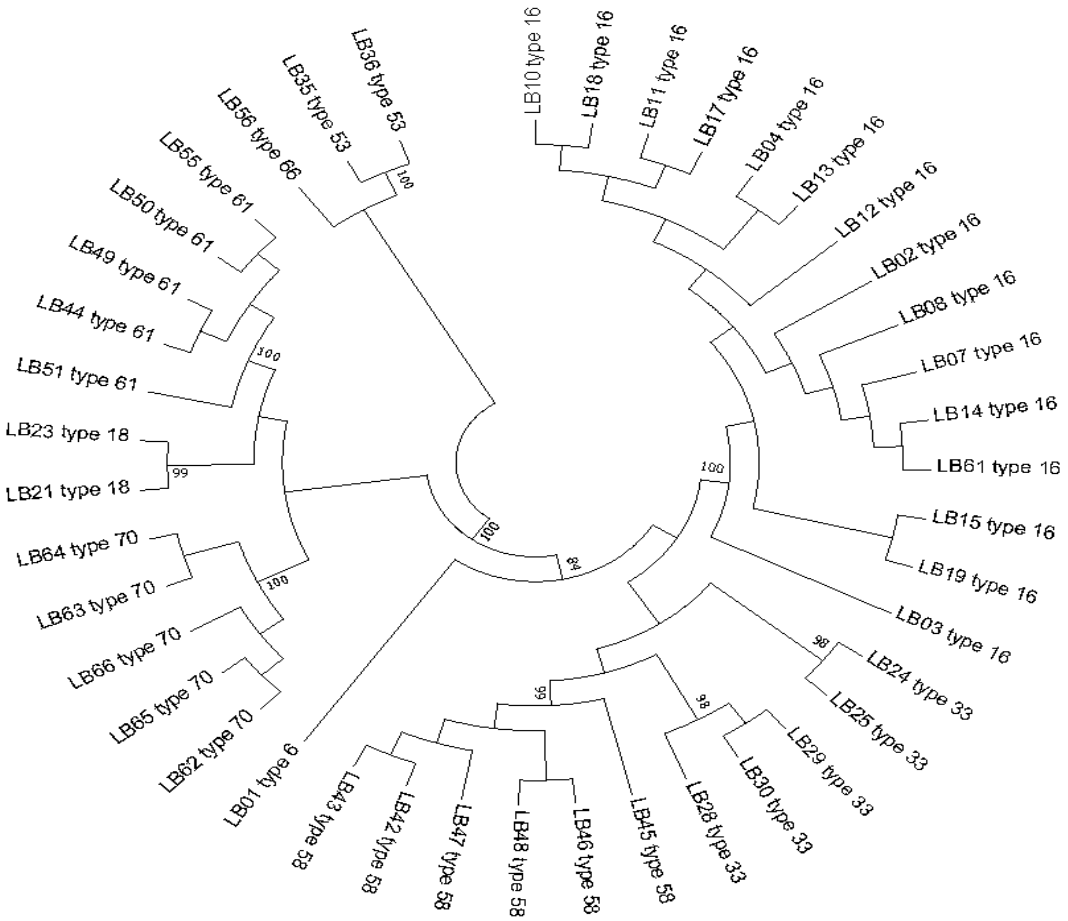
In this study, nine HPV genotypes were identified among the 42 analyzed samples, which were grouped into a consensus tree for each HPV genotypes (Figure 1). Seven high-risk (16, 18, 33, 53, 58, 66 and 70) and two low-risk (6 and 61) HPV genotypes were detected.

HPV 16 genotype was the most frequent (35.7%), followed by HPV 58 (14.3%), HPVs 33-61-70 (11.9%), HPVs 18-53 (4.8%) and HPVs 6-66 (2.4%).

This study showed a high frequency of HPV positive samples (50.07%) among women attended in Unified Health System from Alagoas state, Northeast Brazil. These women are with higher risk of developing cervical diseases, due to the permanent HPV

infection. High prevalence HPV also has been identified in other study conducted in northeast Brazil, with about 65.2% of women infected for HPV [3].

Figure 1 - Consensus tree HPV genotypes. HPV genotypes identified among the 42 analyzed samples.



Among the nine HPV genotype found in Alagoas population seven were of high-risk HPV, including 16, 18, 33, 53, 58, 66 and 70. The most prevalent HPV genotype in ours study was HPV 16, followed by HPV 58 and HPVs 33-61-70. Corroborating with our research, a study with women from Natal city, in northeast Brazilian, showed HPV 16 and 58 as the first and second most prevalent genotypes [3]. Two studies in northeast Brazil performed in Bahia and Ceará found HPVs 16-56 and HPVs 16-31 as the two most prevalent genotypes respectively [4,5]. The 4-valent HPV vaccine provided by Unified Health System in Brazil contains two low risk HPV (HPVs 6-11), and two higher risk HPV (HPVs 16-18) [6]. Interestingly, HPV 18 showed low

prevalence in studies conducted in Northeast Brazil, and other high risk HPV genotypes that are not in the vaccine were identified in these regions, indicating that some women's vaccines may not be able to protect against cervical cancer in particular populations [4,5].

Recent findings revealed that HPV 16 and HPV 18 are the most prevalent genotypes of southeast Brazil, although other high risk HPV also presented significant prevalence [7,8]. In the Amazon region (Brazil), HPV 16-58 was found to be the most prevalent [9], similarly to our findings. Vaccines containing HPVs 16-18, the inclusion of other higher risk HPV could increase the protection to approximately 90% against infections responsible for these cervix diseases [10].

In our finding was not possible to determine which genotypes were presented in almost 83% of the positive samples using the strategy described herein, this turns out to be the main limiting factor of the study.

CONCLUSION

In conclusion, we identified, in one population from Northeast Brazil, a low prevalence of HPV 18 present in the vaccine provided by Unified Health System and a high prevalence of HPV 58 which is not present in this vaccine. Accordingly, in other studies conducted in Northeast Brazil, a low prevalence of HPV 18 and significant prevalence of other high-risk HPV genotypes not included in the vaccines distributed to the local population were observed. The identification and monitoring of high-risk HPV genotypes in different populations may contribute to the improvement of current vaccines, leading to a better epidemiological control of the infections responsible for cervical cancer.

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DECLARATION OF INTERESTS

None.

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