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High-Risk HPV Detection and Cytological Correlation in Cervical Cancer Screening: A Cross-Sectional Study in Dakar, Senegal

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Abstract

Background: Cervical cancer is a significant global public health issue, with an effective screening strategy being a key challenge in its prevention. The primary objective of this study was to determine the prevalence of HPV and assess the contribution of molecular screening to primary cervical cancer detection in Dakar. **Patients and Method**: This cross-sectional study was conducted from January 2016 to December 2020. We compared cervico-vaginal smear results, classified according to the Bethesda 2014 system, with molecular screening results from the Cobas® 4800 HPV test (Roche). Additionally, we conducted a survey of health facilities in the Dakar medical region to evaluate the availability and accessibility (cost) of molecular testing. **Results**: A total of 106 patient files were analyzed. The mean age of the patients was 43.6 years (range: 22 - 76 years). Smears were normal in 41.5% of cases. Detected lesions included ASCUS (49.1%), LSIL (5.7%), and HSIL (3.8%). The overall prevalence of HPV infection was 30.2%, with non-genotype 16/18 high-risk HPV (HR HPV) infections being the most common (73%). Genotypes 16 and 18 were found in 16% and 11% of cases, respectively. Among normal smears, HPV was present in 11.3% of cases. HPV typing was positive in 40.3% of ASCUS smears and 83.3% of LSILs. HPV testing identified 85% of lesions classified as CIN2 or higher, compared to only 70% detected through cytology. The survey revealed that molecular HPV screening was unavailable in referral hospitals, and the high cost of testing in the private sector posed a significant barrier to access. **Conclusion**: Cervical cancer remains a serious public health issue in Senegal. The proven effectiveness of preventive measures, such as

vaccination against the most oncogenic HPV types and molecular screening for HPV detection, could significantly reduce the incidence of this disease.

Keywords

Cervical Cancer, HPV, Cytology, Screening, Senegal

1. Introduction

Cervical cancer remains a significant global public health issue, primarily caused by the DNA virus, human papillomavirus (HPV). This disease is particularly prevalent in many low- and middle-income countries. It ranks as the fourth leading cause of both cancer incidence and cancer-related mortality among women worldwide [1]. In 2020, there were approximately 604,127 new cervical cancer cases reported globally, resulting in around 341,831 deaths [2]. HPV infections are responsible for nearly 5% of all cancers worldwide and are the leading cause of sexually transmitted viral infections [3].

In Africa, cervical cancer is the second most common type of cancer and accounts for the highest number of cancer deaths [4]. Preventive measures, such as vaccination against high-risk oncogenic HPV genotypes (HR HPV) and screening methods that detect the HPV genome, have proven highly effective. These strategies render cervical cancer a largely preventable disease. However, countries with a high human development index have witnessed the most progress in reducing cervical cancer incidence and mortality, thanks to well-established, high-quality screening services, timely treatment, and comprehensive follow-up care [5].

Persistent infection with high-risk HPV is the primary risk factor for developing cervical cancer. However, only a small proportion of women infected with oncogenic HPV develop precancerous cervical lesions, which may progress to carcinoma *in situ* and, eventually, to invasive cancer [6].

In Senegal, cervical cancer surpasses breast cancer as the leading cancer in women, with 1937 new cases and 1312 deaths reported in 2020 [2]. Several programs and grassroots initiatives have been established to combat cancers in general, and cervical cancer in particular. Implementing an effective primary screening strategy could play a crucial role in preventing cervical cancer. In this context, our study aimed to explore the contribution of molecular diagnosis of Papillomaviruses to primary cervical cancer screening in Senegal. Specifically, we sought to determine the prevalence and genotypic distribution of Papillomaviruses, evaluate the concordance between molecular screening and cervico-vaginal smear cytology, and assess the accessibility of molecular screening within the Dakar medical region.

2. Materials and Methods

- **Study Design**: We conducted a retrospective, cross-sectional, descriptive study to assess the contribution of molecular diagnostics in cervical cancer screening

in Dakar, Senegal.

- **Study Setting and Population**: Data were collected from patients who visited the Institut Pasteur de Dakar between January 2016 and December 2020. Patient files were sourced from various hospitals and clinics across Senegal, following these inclusion criteria: women aged 18 - 65, sexually active, and with no prior history of cervical cancer treatment. Patients were excluded if they were pregnant, had an active cervical cancer diagnosis, or had incomplete medical records. To reduce selection bias, patient files were randomly selected from a range of urban and rural health centers, with stratified sampling ensuring demographic representation. Potential confounding variables were controlled through multivariate analysis.
- **Variables**: The variables collected included age, indication for screening, cervico-vaginal smear (CVS) result, HPV molecular screening result, and HPV genotypes.
- **Data Sources and Measurements**:
  - **Sampling**: Cervical cell samples were collected using a brush, which was rotated in the ectocervix and endocervix. The brush was then agitated in the transport medium (PreservCyt ThinPrep®, Hologic), and the same sample was used for both CVS and molecular typing.
  - **Cervico-vaginal Smear (CVS)**: After filtration, smears were spread using Hologic's ThinPrep processor, producing thin-layer smears. These were stained with Papanicolaou and interpreted using the Bethesda 2014 terminology.
  - **HPV Molecular Screening**: HPV screening was performed using the Cobas® HPV test on the Cobas® 4800 system (Roche®), an automated qualitative test detecting human papillomavirus (HPV) DNA. The assay targets 14 high-risk (HR) HPV types using polymerase chain reaction (PCR) amplification and nucleic acid hybridization. It specifically identifies HPV16 and HPV18 while simultaneously detecting the other high-risk types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). The test had an analytical sensitivity of 500 copies/ml and used the β-globin gene as an internal control to ensure sample integrity [7].
  - **Survey of HPV Molecular Testing in Dakar**: A survey was conducted among health facilities in the Dakar medical region to assess the availability and cost accessibility of HPV molecular tests.
- **Statistical Methods**: Data entry was performed using Microsoft Excel® 2010, and statistical analysis was carried out using R version 4.1.3. Bivariate analyses were conducted using the Chi-square method, and statistical significance was defined as a p-value ≤ 0.05.
- **Ethical Considerations**: Ethical approval for the study was obtained and is securely maintained by the authors in accordance with international or institutional standards. All patient information was anonymized and coded to protect confidentiality. Test results were communicated to patients.

3. Results

We included 106 patients with a mean age of 43.6 years, ranging from 22 to 76

years. The [40 - 50] and [30 - 40] age groups were more represented, with 42 (39.6%) and 28 (26.4%) patients respectively (Table 1).

The prevalence of HPV infection was 30.2%, predominantly in the 40 - 50y age group. However, no statistically significant difference was found between HPV infection and the different age groups (p = 0.139).

Table 1. Distribution of HPV infection by age groups of study participants (N = 106), received at Institut Pasteur Dakar (Senegal).

Age groups	Negative, N (%)	Positive, N (%)	Total	p-value
[20 - 30]	4 (5.4)	5 (15.6)	9 (8.5)	
[30 - 40]	23 (31.1)	5 (15.6)	28 (26.4)	
[40 - 50]	26 (35.1)	16 (50.0)	42 (39.6)	0.139
[50 - 60]	16 (21.6)	5 (15.6)	21 (19.8)	
≥60	5 (6.8)	1 (3.1)	6 (5.7)	

CVS was normal in 44 cases (41.5%), and among patients with abnormal CVS, we noted low-grade lesions (6 cases, 5.6%), ASCUS lesions (52 cases, 49.1%) and high-grade HSIL lesions (4 cases, 3.8%).

HPV typing was positive in 21 cases (40.4%) of ASCUS smears and in 5 cases (83.3%) of those with low-grade lesions.

However, HPV was found in 11.4% of patients with a normal CVS (5 cases out of 44 normal smears). A statistically significant difference was found between molecular typing and CVS result (p < 0.001) (Figure 1).

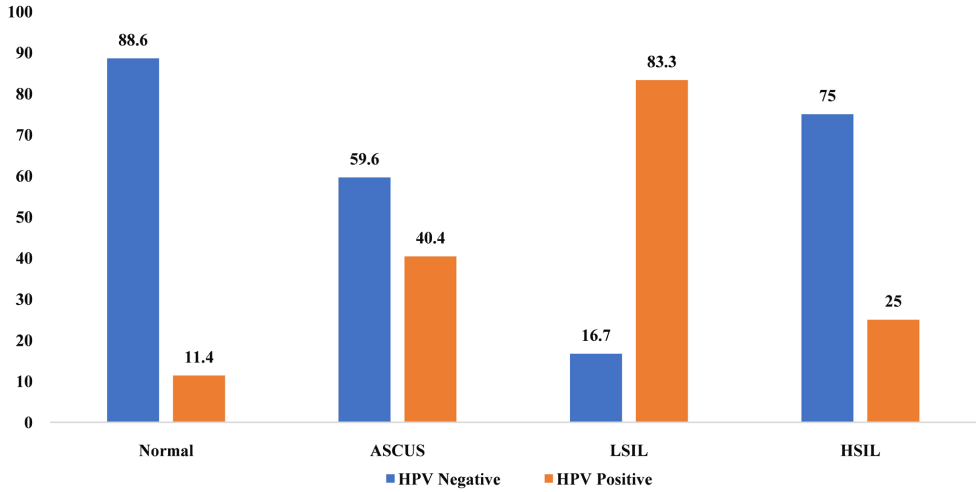

Figure 1. HPV detection according to smear results of women recruited during the study period.

HPV-HR other than genotypes 16 and 18 accounted for the majority (73%) of Papillomaviruses detected. Genotypes 16 and 18 were found in 6 cases (16.2%) and 4 cases (10.8%) respectively (Figure 2).

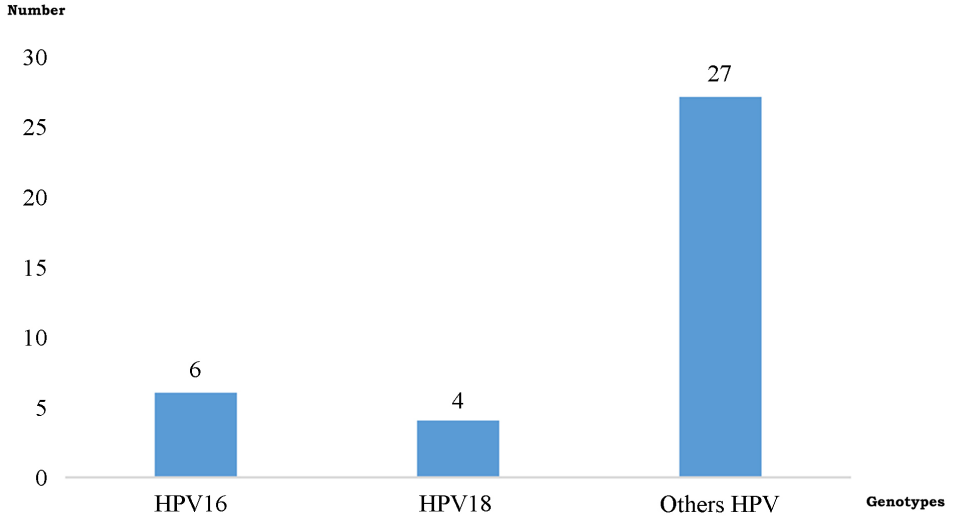

Figure 2. Distribution of HPV genotype by molecular screening using the Cobas® HPV test on the Cobas® 4800 system (Roche®).

The distribution of HPV genotypes according to CVS result showed a predominance of high-risk oncogenic HPVs other than 16 and 18, whatever the smear result (**Figure 3**).

In this study, the sensitivity and specificity of HPV testing were higher compared to cytology in detecting high-grade cervical lesions. HPV testing identified 85% of lesions classified as CIN2 or higher, while cytology detected only 70%.

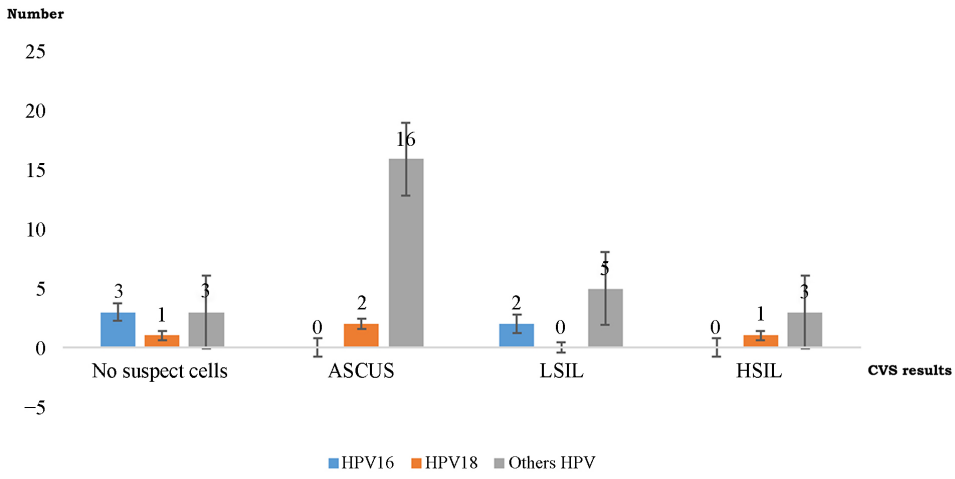

Figure 3. Distribution of HPV genotypes according to cervico-vaginal smear results.

Analysis of Papillomavirus availability and cost in the Dakar medical region: The survey of public and private health facilities in the Dakar medical region showed that molecular screening for the Papillomavirus was not available in referral hospitals. In some health centers, such as Gaspard Kamara, Wakhinane Nimzatt and HLM, an ongoing project run by the Non-Communicable Diseases Department has made molecular testing free of charge as part of a pilot project. A

single private laboratory carried out screening on site, charging CFAF 30,000. Another private laboratory outsourced the analysis for CFAF 47,500.

4. Discussion

In this study, we focused on cervical cancer screening as a preventive measure, specifically evaluating the value of molecular screening in cervical cancer diagnosis in Senegal. The study included patients with an average age of 43.6 years, ranging from 22 to 76 years. Comparable studies conducted in Senegal by Diouf and Sy-Diallo M reported mean ages of 41 and 41.1 years, respectively [8] [9]. Similarly, Samira *et al.* in Gabon included patients aged between 19 and 67, with a mean age of 43.78 years [10]. Current guidelines recommend cervical cancer screening for women aged between 25 and 65 years, with particular focus on older women due to the increased risk of persistent HPV infection leading to cervical cancer [11]. HPV-HR (high-risk) infection plays a critical role in the natural history of cervical cancer, being closely associated with the development of precancerous and cancerous lesions [12].

Our study found an HPV prevalence of 30.2%, which is slightly higher than the 22.7% prevalence reported in 2016 during primary cervical cancer screening in Senegal [13]. Globally, a meta-analysis by Krishnakumar Vinodhini reported an overall HPV prevalence of 32.1%, though it varies geographically, with an average of 42.2% in less-developed countries like those in Africa [14]. Human papillomavirus is widely recognized as the leading cause of cervical cancer. Persistent infection with high-risk oncogenic HPV types induces the progression of normal cervical cells to precancerous lesions, eventually leading to cancer [15]. Given the clear causal relationship between HPV-HR infection and cervical cancer risk, molecular screening for HPV has become an essential part of primary screening strategies, offering higher sensitivity compared to cytology [16].

In our study, HPV infection was most prevalent in the 40 - 50 age group, accounting for 50.0% of all HPV cases. This is consistent with findings from a meta-analysis by Silvia de Sanjos *et al.*, who observed a second peak in HPV prevalence among women aged 45 and older [17]. According to the French National Authority for Health, HPV testing is unnecessary in women under 30, as transient infections are common early in sexual life, with the virus typically being cleared naturally without treatment within two to five years [18].

We observed a predominance of other high-risk HPV types (73%) besides genotypes 16 and 18. This finding aligns with previous studies in Senegal, including that of Sy *et al.*, where HPV52 was the most frequently identified genotype, followed by types 53, 31, 16, and 45. In another Senegalese study, HPV16 was present in 9.5% of infections, and HPV18 in only 1.6% [13]. Similar results had also been reported in 2014 in Senegal [19].

Similar results were also reported by Diop-Ndiaye Halimatou among female sex workers in Senegal [20].

It is important to note that 15 high-risk HPV genotypes are recognized as key

risk factors for cervical intraepithelial dysplasia and cervical cancer, with genotypes 16 and 18 persisting longer and carrying a higher risk of developing high-grade lesions or cervical cancer [12] [19].

Globally, an estimated 291 million women carry HPV DNA, with 32% infected with HPV16, HPV18, or both. The most frequently detected types are also those most commonly associated with precancerous and cancerous lesions, although HPV16 and 18 have a lower relative contribution in women with normal cytology [17]. Among our patients with normal cytology, 5 (11.3%) tested positive for HPV, a result consistent with De Sanjosé's 2007 meta-analysis, which reported a 10.2% prevalence of HPV in women with normal cytology worldwide [17]. However, prevalence can be significantly higher in certain high-risk populations. For instance, among sex workers in Senegal, a 79.8% HPV prevalence was reported [19]. In Gabon, HPV DNA was detected in 57.5% of women with normal cervixes and 76.9% of women with abnormal cytology, underscoring the potential value of introducing HPV testing as part of routine primary cervical cancer screening [10].

We also found HPV in patients with ASCUS (atypical squamous cells of undetermined significance) or low-grade squamous intraepithelial lesions (LSIL) in 40.3% (21/52 cases) and 83.3% (5/6 cases), respectively. Burcu Kasap *et al.* reported abnormal cervical cytology in 30% of HPV DNA-positive cases and 5.4% of HPV DNA-negative cases [21]. In Senegal, Halimatou Diop-Ndiaye *et al.* reported an 84.2% HPV prevalence in patients with cervical neoplasia [22].

The cervico-vaginal smear (CVS) remains highly specific (96.3%, CI 96.1 - 96.5) but lacks sensitivity (53%, CI 48.6 - 57.4) for detecting high-grade intraepithelial lesions (HGIL). In contrast, HPV testing offers higher sensitivity (95%) for HGIL detection [23]. While cytology has a higher positive predictive value (PPV) than HPV testing, reducing the cost of unnecessary colposcopies, its lower sensitivity in screened populations leads to a higher incidence of cervical cancer in "well-screened" women. The superior sensitivity of HPV testing results in a higher negative predictive value, allowing for longer screening intervals and minimizing unnecessary colposcopy referrals [23].

Our survey revealed that molecular testing for HPV is nearly unavailable in health facilities in the Dakar medical region, except within certain projects. In the private sector, costs ranged from 30,000 FCFA ($55) to 47,500 FCFA ($85), presenting a significant barrier to access. This highlights the need for policies that improve access to HPV molecular screening as a primary test for cervical cancer, as recommended by international guidelines.

While the size of our study population and the specific identification of other high-risk HPV genotypes are limitations, the findings underscore the importance of molecular diagnostics in cervical cancer prevention. These results call into question the effectiveness of vaccines containing only HPV genotypes 16 and 18 in Senegal.

5. Conclusions

Cervical cancer remains a critical public health issue in Africa, where HPV

prevalence is high. Our study demonstrates the value of molecular diagnostics in primary screening for cervical cancer. In particular, we found that 11.3% of patients with normal cytology tested positive for HPV. Proven preventive measures, including vaccination against the most oncogenic HPV types and primary HPV screening, make cervical cancer largely preventable. To improve access to HPV testing in Senegal, public-private partnerships with organizations like GAVI or the Global Fund could provide funding for HPV vaccination and screening programs. Technology transfer agreements with diagnostic companies could introduce cost-effective HPV testing equipment to local health centers. Additionally, community-based programs offering HPV self-sampling kits could increase screening coverage, particularly in remote areas. Implementing these strategies, along with robust national screening guidelines, could significantly reduce the burden of HPV-related cervical cancer in Senegal.

What is known about this topic

- HPV represents a significant health issue in Senegal, with a 30.2% prevalence of infection.
- HPV was detected in 11.4% of patients with a normal cervico-vaginal smear (CVS).
- The majority (73%) of high-risk HPV infections involve genotypes other than 16 and 18.
- There is a question regarding the relevance of vaccines targeting only HPV genotypes 16 and 18, given the diversity of types detected.

What this study adds

- The study shows that relying exclusively on smear testing for cervical cancer screening is limited and may result in missed HPV cases.
- It underscores the need to make molecular diagnostic testing for cervical cancer both accessible and affordable. Additionally, it calls for an evaluation of appropriate vaccination strategies, considering the diverse HPV genotypes present in the region.

Authors' Contributions

All the authors have read and agreed to the final manuscript. The authors would like to thank the study participants. Adama Sene collected the data and Mareme Seye Thiam analyzed them. Babacar Ndiaye, Mama SY, Fatoumata Diombo DIAO and Abdoulaye SECK wrote the first draft of the manuscript and jointly developed the structure of the article. Abdou DIOP, Rena Derwiche, Samba DIAO, Thierno Abdoulaye DIALLO, Chantal MAHOU made critical reviews and approved the final version. All authors agree with the results and conclusions of the manuscript and have reviewed and approved the final manuscript.

Conflicts of Interest

The author(s) declare no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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