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HPV Profile of Patients Screened for Precancerous and Cancerous Lesions of the Uterine Cervix: At the Institut d'Hygiene Sociale Hospital in Dakar

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Abstract

Objectives: To evaluate the feasibility of HPV testing, to specify its indications, results and associated cervical lesions at the Institut d'Hygiène Sociale hospital in Dakar between January 1, 2022 and December 31, 2024. **Patients and Methods:** This was a retrospective, descriptive and analytical study conducted over a 36-month period from January 1, 2022, to December 31, 2024, covering all patients who underwent colposcopy and/or biopsy according to indications and HPV testing at the Institut d'Hygiène Sociale Hospital in Dakar. Analysis was performed using Excel, Epi Info and RStudio software. **Results:** We collected 150 colonoscopic examinations. The average age of patients was 51.37, ranging from 30 to 83 years. Mean gestational age was 4.73 with extremes of 0 and 10, mean parity 3.96 and extremes 0 and 9. Age at first intercourse was available for 44 patients. The mean age was 21.71, with extremes of 13 and 38. The age at first intercourse was ≤20 years for 15 patients (34.09%), between 21 and 30 years for 26 patients (59.09%), and between 31 and 40 years for 3 patients (6.82%). There were 57 married women (84.29%), with 14.29% remarried. In relation to the period of genital activity, 61.43% of patients were menopausal. We performed 51 biopsies according to colposcopy indications and recorded 18 CIN1 (38.30%), 12 CIN2 (25.53%), 6 CIN3 (12.77%), 2 carcinomas (4.26%) and 9 cervicitis (19.15%). The rate of HPV testing among the 71 patients was 47.33% for colposcopies. HPV test results were not available for 5 patients (7.04%). In the remaining 66 patients, the test was negative in 52.11% and positive in 40.85% with an HPV HR. Some patients presented high-grade lesions with a negative HPV test, even after a second sampling for control. Other patients were HPV HR positive with CIN-like lesions. The HPV HR genotypes found were: 16, 18 and 45, found 3 times,

6 times and 3 times respectively. HPV 26, 33 and 52 were found 5 times, and 58 was found 8 times. Among our patients, 7 or 24.13% were carriers of one type, 10 or 34.48% were carriers of two HPV types, 8 were carriers of three or more HPV types, 4 were unspecified and 5 tests were unavailable. The bivariate analysis was not significant, probably due to sample size. **Conclusion:** Despite the very high sensitivity of the HPV test, which makes it highly recommended for cervical lesion screening, our study showed that HPV testing and genotyping are not 100% sensitive. A cytological examination is therefore strongly recommended for all patients with no recent history of normal cytology, before proceeding with the recommended follow-up every 5 years in the event of a negative HPV test.

Keywords

Cervical Dysplasia, Cervical Cancer, Human Papilloma Virus, HPV Test Sensitivity

1. Introduction

Cervical cancer is the fourth most common cancer in women worldwide, with an estimated 660,000 new cases and 350,000 related deaths in 2022 [1]-[3]. It is caused by persistent infection with the human papillomavirus (HPV). Women living with HIV are six times more likely to develop cervical cancer than other women. Cervical cancer is a real public health problem. The highest rates of cervical cancer incidence and mortality are in low- and middle-income countries. This reflects major inequities driven by lack of access to national HPV vaccination, cervical screening and treatment services and social and economic determinants [1]-[3]. In Africa, 34 women out of 100,000 suffer from cervical cancer, and 23 women out of 100,000 die from it every year [4]. In Senegal, the incidence is estimated at 1876 new cases of cervical cancer, and there are 1367 cervical cancer-related deaths each year [5]. Since November 17, 2020, the World Health Organization Global (WHO) Strategy was officially launched on to accelerate the elimination of cervical cancer as a public health problem has been to ensure that: 90% of girls are fully vaccinated against human papillomavirus by age 15; 70% of women are screened with a high-performance test at age 35 and again at age 45; and 90% of women diagnosed with cervical disease Cervical cancer is the leading cause of death in the world; and 90% of women diagnosed with cervical disease receive treatment (90% of women with precancerous lesions are treated; 90% of women with invasive cancer are managed). Around the world, countries are striving to accelerate the elimination of cervical cancer by 2030 [1]-[3], but women who have not had this opportunity must follow the recommended screening program with cervico-vaginal smear, colposcopy and HPV testing as appropriate. HPV is the main cause of cervical cancer. It has more than 120 serotypes, including those most implicated in cervical cancer: types 16 and 18, which are targeted by vaccination. Various tech-

niques are used to determine its presence, and HPV typing is recommended by the WHO [1]-[3].

2. Methodology

Our attention was drawn to HPV testing of high-grade lesions which had come back negatively. We decided to evaluate the sensitivity of the HPV test on cervical lesions. A literature review was first carried out on the various HPV tests available and their sensitivity, including their history. We evaluated the feasibility of HPV testing, its indications, results and associated cervical lesions at the Social Institute of Hygiene Hospital in Dakar. The study period runs from January 1, 2022, to December 31, 2024, over a period of 36 months.

This was a retrospective, descriptive and analytical study conducted over a 36-month period from January 1, 2021, to December 31, 2023, and concerned all patients who underwent colposcopy and/or biopsy according to indications and HPV testing at the Social Institute Hygiene Hospital in Dakar.

All women who consulted for a colposcopy at the Social Institute Hygiene Hospital during the period and who had an HPV test before or after the colposcopy were included.

All women who consulted during the study period for a colposcopy and who did not receive the results of their HPV test were excluded.

Beforehand, the patient was informed of the purpose of the examination, the procedure and the expected results, to obtain her informed consent. Data were collected on a computerized form including the following parameters: patient's socio-demographic characteristics, reasons for consultation, results of cervico-uterine smear, colposcopy, concordance between biopsy results and HPV virus carriage. Data were entered into Excel 2021 and analyzed using Excel 2021, 2pi-Info 7 and RStudio. For the analytical part of our study, the Chi2 test was used to compare proportions, and the difference was statistically significant when the P-value was less than 0.05.

3. Results

3.1. Descriptive Results

3.1.1. Epidemiology

We recorded a frequency of HPV testing of 47.33% among the 150 patients who underwent colposcopy. The majority (62.86%) came from the suburbs of Dakar, while those from neighbouring regions and countries accounted for 5.71%. The average age of the patients was 51.37, with extremes of 30 and 83 years. Age group 3 (51 to 60 years) was the most represented with 31.03%. Mean gestational age was 4.73 with extremes of 0 and 10, and mean parity was 3.96 with extremes of 0 and 9. Age at first intercourse was available for 44 patients. The mean age was 21.71, with extremes of 13 and 38. Of these, 15 (34.09%) were aged ≤ 20 at first intercourse, 26 (59.09%) between 21 and 30, and 3 (6.82%) between 31 and 40. Married women numbered 57 (84.29%), with 14.29% remarried. In relation to the

period of genital activity, they were menopausal in 61.43%.

3.1.2. Anatomopathological Results of Biopsies

The results of cervical biopsies according to colposcopy indications showed 18 CIN1 (38.30%), 12 CIN2 (25.53%), 6 CIN3 (12.77%), 2 carcinomas (4.26%) and 9 cervicitis (19.15%).

3.1.3. HPV Test and Genotyping Results

HPV testing was positive in 40.89% of patients, negative in 52.11% and 5 patients (7%) did not receive their results. These results showed a representation of several HPV genotypes (Table 1). Among our patients, 10 or 34.48% carried two HPV types, 8 or 27.58% carried three or more HPV types, 7 or 24.13% carried one type, 4 patients had unspecified HPV HR and 5 tests were not available (Figure 1). Genotypes 16, 18 and 45 were represented 3-fold, 6-fold and 3-fold respectively. HPV 26, 33 and 52 recurred 5 times in patients, and HPV 58 8 times (Figure 2).

Table 1. Patients' results of HPV test.

HPV Result	Number	Frequency
Absence	37	52.11%
HR HPV 16 18	1	1.41%
HR HPV 18 26 52	1	1.41%
HR HPV 31 33 74	1	1.41%
HR HPV 45	1	1.41%
BR HPV 6 11	1	1.41%
HR HPV	4	5.63%
HR HPV 16	1	1.41%
HR HPV 16 18 and 45	1	1.41%
HR HPV 18 52 58	1	1.41%
HR HPV 18 and 58	1	1.41%
HR HPV 26	1	1.41%
HR HPV 26 51 56 58 68 82	1	1.41%
HR HPV 31 51	1	1.41%
HR HPV 33 58	3	4.23%
HR HPV 33 and 53	1	1.41%
HR HPV 33 and 58	1	1.41%
HR HPV 51	1	1.41%
HR HPV 51 52 58 and BR 11	1	1.41%
HR HPV 51 82 and BR 81	1	1.41%
HR HPV 52	1	1.41%
HR HPV 56	1	1.41%
HR HPV 68, 82 and LR11	1	1.41%
HR HPV 81	1	1.41%
HR HPV 82 26	1	1.41%
Unspecified	5	7.04%
TOTAL	**71**	**100%**

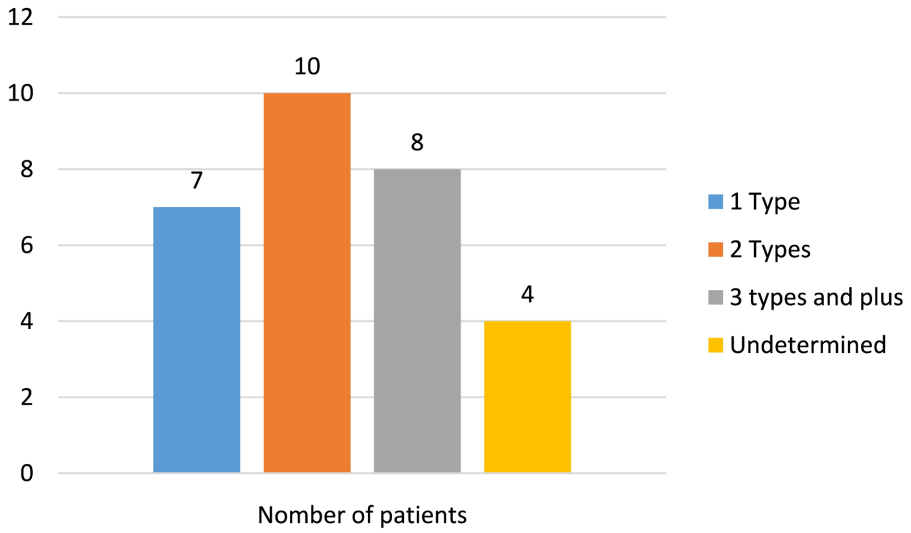

Figure 1. Carriage of one or more types of HPV.

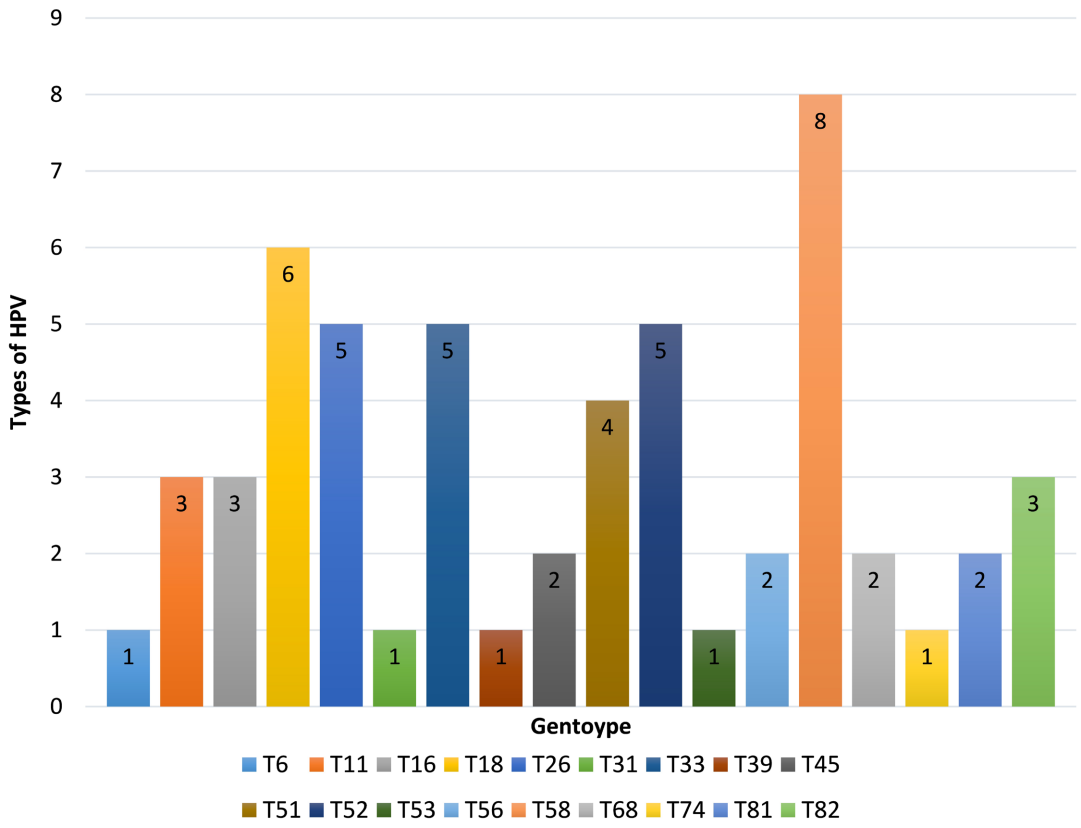

Figure 2. Representation of the frequency of different types of HPV in our patients.

3.2. Analytical Results

3.2.1. Age Class and Presence of HPV

The study of age-class and the presence or absence of HPV showed that HPV was more prevalent in patients aged between 41 and 50, and less prevalent in patients over 50.

3.2.2. Date of First Sexual Intercourse and Presence of HPV

The study of the date of first sexual intercourse in relation to HPV carriage was not statistically significant, with a p = 0.62.

3.2.3. Notion of Polygamy and Presence of HPV

The analysis shows that HPV was more present in patients who were in a polygamous marriage compared to others in their group, without there being a statistically significant relationship with a p = 0.19.

3.2.4. Relation between Presence of HPV and FCV Result

The study of the presence of HPV HR in FCV abnormalities did not find a statistically significant relationship with a p = 0.07.

3.2.5. Biopsy Results and Presence of HPV

Analysis of biopsy results and the presence of HPV HR showed that HPV HR was present in all low-grade and high-grade histological lesions. However, the presence of HPV HR could not be detected in one case of cervical carcinoma, in one case of CIN3 and in 6 cases of CIN2, without there being a statistically significant association (p = 0.51). (Table 2)

Table 2. Proportion of presence of HR HPV in dysplastic lesions of the uterine cervix.

	Absence	HR HPV	Not Available	TOTAL
Carcinoma	**1**	**1**	**0**	2
	50%	**50%**	**0%**	100%
	3.85%	**5.88%**	**0%**	4.26%
Cervicitis	**7**	**2**	**0**	9
	77.78%	**22.22%**	**0%**	100%
	26.92%	**11.76%**	**0%**	19.15%
CIN1	**9**	**7**	**2**	18
	50%	**38.89%**	**11.11%**	100%
	34.62%	**41.18%**	**50%**	38.30%
CIN2	**4**	**6**	**2**	12
	33.33%	**50%**	**16.67%**	100%
	15.38%	**35.29%**	**50%**	25.53%
CIN3	**5**	**1**	**0**	6
	83.33%	**16.67%**	**0%**	100%
	19.23%	**5.88%**	**0%**	12.77%
TOTAL	26	17	4	47
	55.32%	36.17%	8.51%	100%
	100%	100%	100%	100%

3.3. Multivariate Analysis

The logistic regression used variables included: dependent variable as a presence

of cervical abnormalities (CIN1, CIN2, CIN3, carcinoma) and independent variables as HPV test result (positive vs. negative) and Menopausal status (postmenopausal vs. premenopausal). We find that a positive HPV test is strongly associated with lesions, p-value = 0.037 (Table 3). The wide confidence intervals indicate the small sample size and an almost perfect separation in the data.

Table 3. Relation between presence of cervical abnormalities (CIN1, CIN2, CIN3, carcinoma) and HPV test result and menopausal status.

Variable	OR (IC 95%)	p-Value	Interpretation
Positive HPV test	24.5 (1.2 - 500.3)	0.037	Strongly associated with lesions
Menopause	3.2 (0.4 - 28.1)	0.27	Non-significant trend

4. Discussion

4.1. HPV Test Results

In our study, HPV testing was carried out in 71 patients, a frequency of 47.33%. It was positive in 29 of the 66 patients who had undergone HPV testing and colposcopy; 5 patients had not received their results. This rate is much higher than those reported by MBAYE [6] in Senegal and TRAORE [7] in Burkina-Faso, which were 23.2% and 25.4% respectively. The prevalence of HPV in our study was 43.93%. A study of Class-Age and the presence or absence of HPV showed that HPV was more prevalent in patients aged between 41 and 50, and less prevalent in patients over 50, which corresponds to the clearance of HPV increasing with age (p = 0.1527). This relatively high rate in our series could be explained by the fact that HPV testing was only performed on patients with lesions of cervical dysplasia, in order to refine their management. In fact, in our practice, the cervico-uterine smear remains the reference screening test, due to the limited availability of the HPV test. The worldwide prevalence of HPV infection among women with normal cytological results is estimated at 11.7% [8]. The regions with the highest prevalence are Sub-Saharan Africa (24%), Latin America and the Caribbean (16.1%), Eastern Europe (14.2%) and South-East Asia (14%). However, on a country level, the prevalence of HPV infection in cervical samples varies between 1.6% and 41.9% worldwide.

In Senegal, few data are available on the epidemiology of HPV infection. A study carried out in 4 regions of the country (Dakar, Thiès, Saint-Louis and Louga) showed an average prevalence of HPV infection of 18.1%, with extremes of 17.4% in Dakar and 23.2% in Thiès [6]. The mean prevalence of HPV-HR in our study is higher than the frequency in the study of the four regions of Senegal; this is probably related to our study population who already had an abnormality on cervico-vaginal Frottis.

4.2. HPV Genotyping

With regard to HPV genotypes, the most frequently found in our series were: HPV

58 (16.32%), HPV 18 (12.24%), HPV 26, 33 and 52 (10.20%), followed by HPV 16 and 82 (6.12%). In MBAYE's study [6], HPV 31 (4.7%) was the most prevalent genotype, followed by HPV 52 (3.5%) and HPV 53 (3%). The overall prevalence of HPV 16 and HPV 18 was 6.12% and 12.24% respectively. In another study carried out in Senegal on the molecular genotyping of human papillomaviruses in HIV-infected women compared with HIV-seronegative women, HPV 56 was the most common genotype found in both groups, with 46.62% in people living with HIV (PLHIV) versus 27.18% in HIV-seronegative people. Also NDIAYE in Senegal found that other genotypes are more frequently found than 16 and 18 [9]. A study in Mali classified HPV into P3 (31/33/35/52/58), P4 (51/59) and P5 (39/56/66/68) groups. In this study population, the P3 component represented by one of the following subtypes (31/33/35/52/58) was the most frequent, with a total of 13, or 15.3%, followed by P5 (7.1%) and HPV 16 (5.9%) [10]. In Egypt, Mouhamed found type 16 to be the most frequent (41.9%; 26/62), followed, in descending order of frequency, by HPV18 (18/62; 29.03%), HPV 31 (8/62; 12.9%), HPV 58, 59, 6 (7/62; 11.3%), HPV 45, 62, CP6108 (6/62; 9.7%), HPV 84 (5/62; 8.1%), HPV 33, 51, 66 (4/62; 6.5%), HPV35, 52, 11, 61, 68 (3/62; 4.8%), HPV 72, 81, 83 [11]. Tebeu's study found 6 HPV 18 genotypes and 2 HPV 16 genotypes. This order is different from that reported [12]. Worldwide, it is estimated that HPV-16 and 18 are responsible for almost 70% of cervical cancer cases [13]. HPV 16 and 18 are predominant worldwide, with HPV 16 being the most common genotype in all regions. HPV 18 and other high-risk genotypes such as 31, 39, 51, 52, 56, 58 and 59 show a similar prevalence and are among the most common high-risk genotypes [2]. This confirms the predominance of genotype 58 noted in our series. This analysis shows us that in our countries, other high-risk HPV genotypes are at the forefront in terms of frequency, which could justify choosing the nonavalent vaccine in primary prevention even if there would be cross-immunity with the use of bivalent and quadrivalent vaccines. usually eliminated in the immunocompetent.

4.3. Carriage of Two or Multiple HPV Types

Among our patients, 10 or 34.48% carried two HPV types, 8 or 27.58% carried three or more HPV types, 7 or 24.13% carried one type, 4 patients had unspecified HPV HR and 5 tests were unavailable (**Figure 1**). In Mohamed's study in Egypt, HPV DNA was detected as a mixed infection in 80% (28/35) of women with LSIL, in 100% (2/2) of those with HSIL, and in 64.3% (9/14) of those with invasive SCC [11].

In the Kitchener study [14], the proportion of women with a single HR-HPV type and moderate or worse cytology was 26% for HPV16, between 12% and 19% for HPV types 18, 31, 33 and 58, 7% to 9% for Types 35, 45, 51 and 52, and less than 5% for types 39, 56, 59 and 68.

Multiple HPV carriage was found in the majority of patients. Does multiple HPV carriage represent a cumulative risk for the development of low- and high-grade lesions on the cervix? A follow-up of these patients could probably shed

some light on this situation.

4.4. HPV Test Sensitivity

With regard to the sensitivity of the HPV test, the search for HPV DNA in high-grade lesions was not always successful. Of the 38 low-grade, high-grade and carcinoma lesions, HPV HR could only be detected in 15 patients, and could not be detected in 19 patients, including 9 cases of CIN2 and CIN3 and 1 case of carcinoma. Ndiaye, during his study in Senegal, the HPV test detected 85% of CIN2 and higher lesions, as we have noted, but not all high-grade lesions in women aged 43.6 with the extreme 22 and 76 years old [9]. Erik A. Gustafson's study results show that HR-HPV had a slightly higher sensitivity (94.2% vs. 92.3%) than cytology for all high-grade diseases (CIN2/3) [15].

Almost all types of cervical cancer—squamous cell carcinoma, adenosquamous cell carcinoma and adenocarcinoma—are now thought to be associated with HPV infection. When information from the 11 trials was pooled, case-control studies in nine countries identified high-risk HPV types in cervical cancers: HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-51, HPV-52, HPV-56, HPV-58, HPV-59, HPV-68, HPV-73 and HPV-82. HPV-16 and HPV-18 are associated with 70% of all invasive cervical cancers [16]. The sensitivity of HPV testing is around 90%. Although these studies showed similar performance between positive tests, in the USA, the FDA Advisory Committee recommended the Cobas system as the only HPV test for primary screening. This recommendation was based on the results of the ATHENA (Addressing THE Need for Advanced HPV diagnostics) trial, which showed that the Cobas system was more accurate than HC. For CIN, the sensitivity and specificity of the Cobas system were 93.5% and 69.3% respectively, compared with 91.3% and 70% for HC [17]. Numerous studies have shown that HPV testing, alone or combined with cervical cytology, is more sensitive than cervical cytology alone for detecting high or low-grade cervical histopathological lesions. The highest proportion of HPV-18-associated cervical cancers (23%) occurred in Africa [18]. The analysis was limited to studies using consensus PCR or hybrid capture, as other tests are much less reliable and give results that are not comparable. With modern tests, over 95% of all cancers are HPV positive [19]-[21] and 75% - 95% of high-grade CIN lesions are associated with a positive HPV test on exfoliated cells [22]-[26]. These and other comparative studies have shown that HPV testing has a higher sensitivity for CIN II/III than cytology.

The sensitivity of histological detection of HSIL+ was 64.9% for the Pap test and 100% for the Hybrid Capture 2 test, but the ratio of colposcopies per detection of each HSIL+ was more than twice as high with the Hybrid Capture 2 test as with the Pap test (5.9 vs. 2.8). Genotyping results were available for 316 samples. HPV52, HPV16 and HPV58 were the three most common genotypes in women with histological HSIL+. The performance of genotyping using HPV16/18/52/58 was superior to that of HPV16/18, with higher sensitivity (85.7% vs. 28.6%) and

negative predictive value (94.2% vs. 83.9%) [27]. Indeed, there is now ample evidence that HPV testing offers better protection against UCC than cytology screening these women [28]. This gain in efficacy would also be greater against adenocarcinoma than against squamous cell carcinoma [29]. According Kitchener, it would not be cost-effective to screen with cytology and HPV combined but HPV testing, as either triage or initial test triaged by cytology, would be cheaper than cytology without HPV testing [14]. In the Cochrane database, we found a review of the literature that included 40 studies in the analysis, involving more than 140,000 women aged between 20 and 70. Many studies had a low risk of bias. The number of studies included with adequate methodology was sufficient to make the following test comparisons: hybrid capture 2 (HC2) (threshold 1 pg/ml) versus conventional cytology (CC) (thresholds atypical squamous cells of undetermined significance (ASCUS+) and low-grade squamous intraepithelial lesions (LSIL+)) or liquid-based cytology (LBC) (thresholds ASCUS+ and LSIL+), other high-risk HPV tests versus conventional cytology (thresholds ASCUS+ and LSIL+) or LBC (thresholds ASCUS+ and LSIL+). For CIN 2+, the pooled sensitivity estimates for HC2, CC and LBC (ASCUS+) were 89.9%, 62.5% and 72.9% respectively, and the pooled specificity estimates were 89.9%, 96.6% and 90.3% respectively. Results did not vary according to the age of the women (under or over 30) or studies with verification bias. However, HC2 accuracy was higher in European countries than in other countries. Results for test sensitivity were heterogeneous, ranging from 52% to 94% for AML, and from 61% to 100% for HC2. Overall, the quality of evidence for test sensitivity was moderate, and high for specificity. The relative sensitivity of HC2 versus CC for CIN 2+ was 1.52 (95% CI: 1.24 to 1.86) and relative specificity 0.94 (95% CI: 0.92 to 0.96), and versus LBC for CIN 2+ was 1.18 (95% CI: 1.10 to 1.26) and relative specificity 0.96 (95% CI: 0.95 to 0.97). The relative sensitivity of HC2 versus CC for CIN 3+ was 1.46 (95% CI: 1.12 to 1.91) and the relative specificity was 0.95 (95% CI: 0.93 to 0.97). The relative sensitivity of HC2 versus LBC for CIN 3+ was 1.17 (95% CI: 1.07 to 1.28) and the relative specificity was 0.96 (95% CI: 0.95 to 0.97).

The authors concluded that HPV tests are less likely to miss cases of CIN 2+ and CIN 3+, and that a negative HPV test is more reassuring than a negative cytological test, as the cytological test is more likely to be falsely negative, which could lead to delays in administering appropriate treatment. However, data from prospective longitudinal studies are needed to establish the relative clinical implications of these tests [30].

These results allow us to conclude that, however high the sensitivity of the HPV test, and however superior it is to cytology, it can still be negative in the presence of a cervical abnormality. And although this percentage is low, special attention must be paid to ensure equity in the management of screening.

5. Conclusion

Our series is characterized by a higher frequency of high-risk HPV genotypes (58,

33 and 18). A larger-scale study would probably reveal the predominant HR HPV in our region. The sensitivity of the HPV test tells us that a cytological examination is just as important in a patient who does not have a history of normal cervical cytology before starting screening with the HPV test, in order to follow the recommendations of every 5 years in case of negativity, which is more beneficial in terms of screening cost. However, in view of the findings of our study, the proposal of an HPV test and cervico-vaginal smear every 5 years would be more reassuring for equity in management.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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