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High-risk Human Papillomavirus infection in women with normal and altered cytology in Amazonas, Brazil

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Abstract

Objective: To analyze high-risk Human Papillomavirus (hrHPVs) infection in women with normal and abnormal cytology in Amazonas, Brazil. **Methods:** 455 women participated in the study. The samples were collected by Liquid Based Cytology (LBC) and the detection of hrHPVs was performed by the HPV BD Onclarity® kit, through the BD ViperTM LT system, which identifies six types individually (16/18/31/45/51/52) and eight types by genotype groups (P1: HPV33/58; P2: HPV56/59/66 and P3: HPV35/39/68). **Results:** 99.3% (452) of the slides were classified as satisfactory and 7.3% (33) of them showed altered results. Among the abnormal samples, 31 samples were suitable for molecular tests, with hrHPVs being found in 70.9% of them (22/31): 80.9% (17/22) of the women classified as low-grade squamous intraepithelial lesion (LSIL), 60% (3/5) of high-grade squamous intraepithelial lesion (HSIL) and 50% (2/4) of atypical squamous cells of undeterminated significance (ASC-US) were positive and the most common genotypes were HPV 52 and those of the HPV group P3. 42 women with normal cytological results were selected, of which 11.9% (5) had hrHPVs infection, the most common genotypes being HPV 52 and the HPVP3 group. **Conclusions:** Our results reinforce the good performance of LBC, the suitability of the sample obtained by LBC for molecular testing and the presence of hrHPVs in a large number of women with altered cytology. Strategies, therefore, can be created to implement these innovative tracking tools in this region.

Keywords: Cervical Cancer, Screening, Liquid Based Cytology

Infecção por Papilomavírus Humano em mulheres com citologia normal e alterada no Amazonas, Brasil. Objetivo: Analisar a infecção por Papiloma Vírus Humano de alto rico (hrHPVs) em mulheres com citologia normal e anormal no Amazonas, Brasil. **Métodos:** participaram do estudo 455 mulheres. As amostras foram coletadas por Citologia Líquida (CL) e a detecção de hrHPVs foi realizada pelo kit HPV BD Onclarity®, por meio do sistema BD ViperTM LT, que identifica seis tipos individualmente (16/18/31/45/51/52) e oito tipos por grupos de genótipos (P1: HPV33/58; P2: HPV56/59/66 e P3: HPV35/39/68). **Resultados:** 99,3% (452) das lâminas foram classificadas como satisfatórias e 7,3% (33) delas apresentaram resultados alterados. Entre as amostras anormais, 31 amostras eram adequadas para testes moleculares, sendo hrHPVs encontrado em 70,9% delas (22/31):

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80,9% (17/22) das mulheres classificadas como Lesão epitelial de baixo grau (LSIL), 60% (3/5) das mulheres com lesão epitelial de alto risco (HSIL) e 50% (2/4) de mulheres com atipias de células esquamosas de significado indeterminado (ASC-US) foram positivos e os genótipos mais comuns foram o HPV 52 e os do grupo P3 do HPV. Foram selecionadas 42 mulheres com resultados citológicos normais, das quais 11,9% (n) apresentavam infecção por hrHPVs, sendo os genótipos mais comuns o HPV 52 e o grupo HPVP3. **Conclusões:** Nossos resultados reforçam o bom desempenho da CL, a adequação da amostra obtida pela CL para testes moleculares e a presença de hrHPVs em um grande número de mulheres com citologia alterada. Estratégias, portanto, podem ser criadas para implementar essas ferramentas inovadoras de rastreamento nessa região.

Palavras-chave: Câncer Cervical, Rastreamento, Citologia Líquida.

1. Introdution

Human Papillomavirus (HPV) is the most common sexually transmitted pathogen worldwide and it is believed that most sexually active people will come into contact with the virus at some point in their lives. However, most HPV infections are transient and do not progress to the development of lesions, as it is considered that many may indeed persist in the population in a commensal way (DOOBAR et al. 2011; BRÄUTIGAM et al. 2022; WILLIAMS et al. 2022). Currently, more than 300 Papillomaviruses (PV) have been identified and completely sequenced, including more than 200 PV that infect humans. Of these, about 40 genotypes infect the female anogenital tract and have different potential for neoplastic transformation, being classified into low-risk (lrHPVs) or high-risk (hrHPVs) HPVs. lrHPVs are involved in the development of benign neoplasms in the skin and mucous membranes, while hrHPVs are present in premalignant and malignant lesions of the cervix, vagina, vulva, anus and oropharynx (BRÄUTIGAM et al. 2022; WILLIAMS et al. 2022).

Among malignant neoplasms related to persistent infection by hrHPVs, Cervical Cancer (CC) is certainly the one with the greatest epidemiological impact, as it is the fourth most common type of cancer in women worldwide. In 2020, an estimated 604,000 women were diagnosed with CC worldwide and around 342,000 of them died from the disease (INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC) 2022). In Brazil, estimates by the National Cancer Institute (INCA) (INCA 2019) for the three-year period 2020-2022 were that approximately 16,590 new cases of CC would occur each year, making it the third most common type of malignant neoplasm in the female population (with the exception of non-melanoma skin cancer). Still in this triennium, in the North Region of Brazil, the expected incidence rate of CC was 21.20/100,000 women, equaling the estimated rate for breast cancer in this region (21.34/100,000). Specifically for the State of Amazonas, the numbers are even more worrying, as the projected incidence was 27.60/100,000 women, far surpassing the estimated incidence rate for breast cancer for each year of the triennium (21.40/ 100,000) (INCA 2019).

This high incidence of CC in the Amazonas is alarming and requires strategies that increase the effectiveness of screening for precursor lesions and invasive cancer to be sought. Currently, conventional Pap smear cytology has been used as the main screening tool, and the guidelines of the Brazilian Ministry of Health recommend cytopathological examination in asymptomatic women aged between 25 and 64 years, every 3 years, after two consecutive normal examinations. In case of a low-grade lesion, the indication is to repeat the exam in six months (Ministério da Saúde. Brasil 2016). Despite the recognized effectiveness of this technique in reducing the rates of CC in the places where it has been successfully implemented (LONGATTO-FILHO et al. 2015), in Brazil screening remains

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opportunistic, with many communities suffering from low coverage and incomplete follow-up, while in other places many women are screened at smaller intervals than those recommended by the government, resulting in disparities in CC numbers (RIBEIRO et al. 2021). Also, in certain settings Pap testing has substantial shortcomings: limited sensitivity for cervical precancer forces repetition at short intervals, inadequate reproducibility introduces unwanted variability, and the requirement of a cytology infrastructure with continuous training of skilled providers limits applicability in many regions (RODRÍGUEZ AND SALMERÓN, 2017). In Amazonas there are certainly gaps in tracking coverage due to its enormous territorial extension and the difficulty of accessing almost all cities and riverside communities in the interior, as it is a "region between rivers" (ROCHA et al. 2013; BATISTA et al. 2023). More consistent public policies that guarantee the inclusion of these women in screening programs and innovative technologies that allow improving the quality of the sample - reducing the rates of unsatisfactory cytopathological slides, false-negative results and expanding the range of possibilities for using diagnostic methods - are interesting in this context.

Liquid-Based Cytology (LBC) has some advantages over conventional cytology, as it reduces factors that usually limit sample quality: the transfer of cells to the slide is standardized, the cells are homogeneously distributed over the surface of the slide, there is elimination of red blood cells, inflammatory exudate and mucus; also allows the use of residual material for the preparation of additional slides and/or special stains from the same material, in addition to the preservation of protein molecules and nucleic acids that may be used for the detection of infections by sexually transmitted pathogens, including the detection and HPV genotyping (LONGATTO-FILHO et al. 2015; SIMION et al. 2014). The aim of this study was to investigate hrHPVs infection in women whose samples were collected and processed by LBC, analyzing this strategy in the Brazilian Amazonian context.

2. Methods

Study Population - This is a cross-sectional, convenience study with 455 women who spontaneously sought a routine gynecological examination at the 12 Basic Health Units (UBS) that make up the Primary Health Care Network in Coari City, between September and December 2014. Coari is a city located in the Middle Solimões Region (Solimões River), 363 km from Manaus, capital of the State of Amazonas. At the time of the study, the estimated population was around 76,000 inhabitants, with around 62,000 living in the urban center of the municipality and the remaining 14,000 living in 206 riverside communities, which are small villages organized on the banks of the rivers and lakes of the region. The territorial extension of the city is enormous (57,921 km2), as well as the demographic dispersion (demographic density of 1.3 people per km^2) (IBGE - Instituto Brasileiro de Geografia e Estatística 2010). In these isolated communities, there are almost no permanent medical posts, and practically all health care is provided in the urban center of the city, whose distance from the communities varies between 30 minutes and 30 hours of travel, depending on the vessel used (GAMA et al. 2018).

All the women who participated in our study were residents of the urban area of the city. Inclusion criteria were: women over 18 and sexually active. Pregnant, menstruating, hysterectomized, using endovaginal medication in the last 7 days, or self-declared virgins were excluded. The women were invited and explained about the research objectives. Those who met the inclusion criteria and agreed to participate in the study signed the Informed Consent Form and answered the epidemiological,

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sociodemographic and risk factor questionnaire for HPV infection. Subsequently, they were submitted to cervical sample collection by LBC.

Collection and processing of samples - To collect cervical samples, a Rovers® Cervix Brush Combi (Rovers® Medical Devices) was used. After collection, the brush head, which is completely removable, was dispensed into the proper collection bottle containing fixative solution (BD SurePathTM Preservative Fluid Collection). Cytological slides were prepared using semi-automated BD PrepMateTM and BD PrepStainTM equipment at the Sebastião Ferreira Marinho Laboratory, in Manaus. They were analyzed and classified according to the Bethesda classification.

DNA extraction and hrHPVs detection - All women with a diagnosis of cytological alteration were tested for hrHPVs (n=33). Among the women without cytological alteration, a sample of 42 women was drawn, which were stratified according to age, matching the group of women with altered cytology. The test used for the extraction, detection and genotyping of HPV was the BD OnclarityTM HPV Assay, used in the BD ViperTM LT equipment. It is a real-time PCR DNA extraction and amplification assay for the qualitative detection of 14 types of hrHPVs (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68), and the detection of genotypes 16, 18, 31, 45, 51 and 52 is done in isolation and the other genotypes are identified in groups: P1 = 33/58, P2 = 56/59/66 and P3 = 35/39/68. These analyzes were performed at Fundação Oncocentro de São Paulo (FOSP).

Statistical analysis - The analyzed data are described and presented in tables in the form of absolute and relative frequency and/or mean or median. To verify statistical differences between the groups, the t-Student test was used. The analysis of the significance of difference in proportions and subsequent assessment of the existence or not of association between variables was performed using Pearson's Chi-Square Test and/or Fisher's Exact Test for cases in which the expected frequency was less than five ($p<0.05$). The significance level used in the tests was 5%, with a 95% confidence interval. All analyzes were performed using SPSS software version 20.

Ethical Aspects - This research was approved by the Human Research Ethics Committee of the Amazonas State Oncology Control Center Foundation – FCECON (CAAE1281221340000004).

3. Results

Socioeconomic, clinical, and behavioral characteristics - 455 eligible women agreed to participate in this study, most of them from Coari (75.9%), married or living in a stable relationship with a partner (74.5%). The age of the participants ranged from 18 to 77 years old with a mean age of 36.7 years old (SD=11.5). Low education predominated among the participants, as the majority (59.1%) claimed to have studied for up to 8 years. Regarding occupation, those who declared themselves self-employed (25.1%) predominated, followed by housewives (24.3%). Most women (80%) reported having a family income of up to 1 minimum wage (Table 1).

Regarding the sexual behavior of the participants, the age of the first sexual intercourse ranged from 11 to 32 years, with a mean of 16.1 years (SD=2.6). Most (84.8%) said they had only 1 sexual partner in the last 12 months and 76.5% of them declared having only 1 to 4 sexual partners throughout their lives. Low adherence to condom use

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was found, as 79.7% of participants said they "never" use or use "sometimes". As for parity, 93.8% of the participants reported having children, with a significant number of women (45.9%) who claimed to have had 4 or more children, with normal delivery being more common among women (79, 6%). When asked about taking the preventive Pap smear, 9.2% of the participants reported that they had "never taken the test", but most reported taking the test once a year (69.5%) (Table 2).

Cytological results - Of the 455 women participating in this study, the slides made by LBC were considered satisfactory for 452 of them (99.3%), with only 3 slides (0.7%) considered unsatisfactory due to lack of cell representativeness. Of the 452 cytologies classified as satisfactory, 419 (92.7%) presented results within the normal range and 33 (7.3%) presented altered results, which were: 4 (0.9%) Squamous Atypia with Undetermined Significance (ASC-US), 24 (5.3%) Low Squamous Intraepithelial Lesion (LSIL) and 5 (1.1%) High Squamous Intraepithelial Lesion (HSIL). Some sociodemographic, clinical and behavioral variables were compared between the group of women with normal and abnormal cytology and the variables that showed a statistically significant relationship with cytological changes were young age at first delivery (p=0.017), marital status "single/divorced /widow" (p<0.0001) and low education (up to 8 years of study) (p=0.040).

Molecular results – Of the 33 women with altered cytology, hrHPVs DNA screening was performed on all of them, but 2 samples (both LSIL) were inconclusive, even after repeat testing. For comparison between groups, 42 samples from participants with normal cytology were randomly selected, according to age, and matched with samples with altered cytology. hrHPVs positivity was detected in 11.9% (5/42) of samples with normal cytology and in 70.9% (22/31) of abnormal cytology. Of the women diagnosed with LSIL, 80.9% (17/22) were positive for hrHPVs, in the samples diagnosed with ASC-US, hrHPVs was detected in 50.0% (2/4) and in 60.0% (3/5) the presence of hrHPVs was confirmed in the samples with HSIL.

The most frequently detected type of hrHPVs individually was HPV 52, followed by HPV-16, and among the hrHPVs detected by genotype group was P3, which corresponds to HPVs 35/39/68 (Figure 1). Socioeconomic, clinical and behavioral data of women with abnormal and normal cytology, submitted to molecular testing, were compared, but none of the variables showed a statistically significant relationship.

All women infected with hrHPVs and all those with cytological changes were referred for colposcopy and follow-up with a gynecologist.

4. Discussion

While in developed countries, types of cancer related to urbanization and development predominate (lung, prostate, female breast, colon and rectum), in developing countries there is still a high occurrence of types of cancer associated with infections (cervix, stomach, esophagus and liver). There is great variation in the magnitude and types of cancers between different regions in Brazil that accompany this relationship between development; in the South and Southeast Regions, as well as in the Midwest, the incidence pattern shows that breast tumors are the most prevalent among women, but in the Northeast and maily in the North Regions, CC has the greatest impact on the female population. The incidence and prevalence data show that the North Region is the only one in the country where the rates of female breast and cervical cancer are equivalent (INCA, 2019). Considering this alarming epidemiological situation, there is a need to study

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better strategies for "who to screen", "when to screen", and especially "how to screen" CC and its precursor lesions in women in the Amazonas.

Table 1: Distribution according to sociodemographic data of women sampled in Cori City, Amazonas, Brazil, 2023.

Variables	n = 455	
	n	%
Age		
Media ± SD	36.7 ± 11.5	
Amplitude	18 - 77	
18 |--- 24	64	14.1
25 |--- 34	159	35.0
35 |--- 44	125	27.5
45 |--- 54	69	15.1
55 |--- 64	32	7.0
≥ 65	6	1.3
Place of birth		
Coari	345	75.9
Other cities in Amazonas	98	21.5
Other Cities in Brazil	12	2.6
Marital status		
Single/Divorced/Widowed	116	25.5
Married/Stable Union	339	74.5
Schorality		
≤ 8 years	269	59.1
> 8 years	186	40.9
Ocupation		
Retired or Pensioner	11	2.4
Salaried	79	17.4
Self-employed	114	25.1
Housewife	111	24.3
Civil Servant	86	18.9
Studant	22	4.8
Unemployed	23	5.1
Others	9	2.0
Family income		
Up to 1 Minimum wage	364	80.0
From 2 to 3 Minimum wage	75	16.5
Above 3 Minimu wage	16	3.5

n = Number of Samples; SD = Standard deviation Fonte: Reis RS, et al (2023)

In terms of "how to screen", studies show that the advantages of LBC over conventional cytology cannot be disputed. Qualitatively superior material can be obtained due to the method of preparation, resulting in easier examination and interpretation, increased specificity and sensitivity, significantly decreasing the proportion of unsatisfactory slides, and even increasing the efficiency of laboratory processing and emission of the cytopathological report, since it is a semi-automated reading system (LONGATTO-FILHO et al. 2015; SIMION et al. 2014; KHAKWANI et al 2022). We consider, however, that the main impediment to the application of this method in tracking centers nationwide is linked to the initial costs of investing in equipment and setting up infrastructure (SIMION et al. 2014).

Studies have shown that LBC offers increased positivity rates and a consistent and marked reduction in unsatisfactory slides (KHAKWANI et al, 2022; SINGH et al. 2016). Longatto-Filho et al (2015) in a large study carried out with 218,594 women in the State of São Paulo (206,999 samples collected by conventional cytology and 11,595 collected by LBC), found an index of unsatisfactory slides of 3% among women samples from

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conventional cytology and 0.3% of unsatisfactory slides from samples from LBC. The authors make a projection considering that, if the Brazilian Government performs more than 10 million cytological exams per year, this means that if the laboratories in Brazil followed these same rates of unsatisfactory slides, approximately 300,000 women would have to be recalled for a new collection every year. However, for these authors, the rates of cases of unsatisfactory slides in Brazil generate much less optimism than that found in the FOSP laboratory (Fundação Oncocentro de São Paulo, which is a reference laboratory in terms of quality in Brazil). Regarding the positivity rate, a significant increase in positivity from 3% (conventional cytology) to 5.7% (LBC) was found. For these authors, this represents a significant impact on public health strategies for CC control.

Table 2: Distribution according to the clinical and behavioral data of the women sampled in Coari City, Amazonas, Brazil, 2023.

Variables	n = 455	
	n	%
Age of first sexual intercourse		
Media ± SD	16.1 ± 2.6	
Amplitude	11 – 32	
Age at first delivery (n=429)		
Media ± SD	18.6 ± 3.5	
Amplitude	12 – 38	
Number of sexual partners in the last 12 months		
None	36	7.9
1	386	84.8
≥2	33	7.3
Number of lifetime sexual partners		
1 to 4	348	76.5
5 to 8	82	18.0
≥ 9	25	5.5
Condom use		
Never	199	43.7
Sometimes	164	36.0
Always	92	20.3
Have children		
Yes	427	93.8
No	28	6.2
Number of children		
1 to 3	231	54.1
4 or more	196	45.9
Type of Delivery (n=427)		
Normal	340	79.6
Cesarean	87	20.4
Pap test (455)		
Never took the exam	42	9.2
Once a year	316	69.5
More than 2 years	97	21.3

n = Number of Samples; SD = Standard deviation
Fonte: Reis RS, et al (2023)

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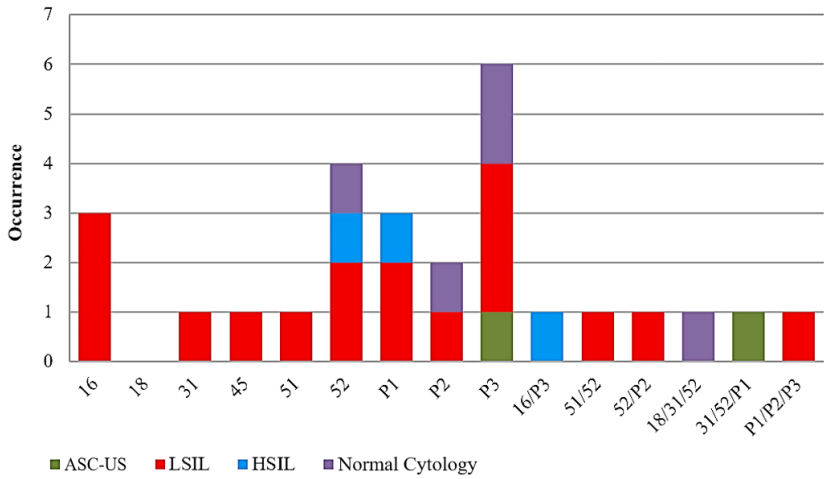

Figure 1: Distribution of hrHPVs genotypes in women with normal and altered cytology. Coari, Amazonas, Brazil, 2023. ASC-US (Atypical squamous cells undeterminated significance); LSIL (Low grade squamous intraepithelial lesions); HSIL (High grade squamous intraepithelial lesions); P1 (HPV 33/58), P2 (HPV 56/59/66) and P3 (HPV 35/39/68).

The results of our study show that 99.3% of the slides were considered satisfactory for cytopathological analysis, which we consider an excellent result. In the study carried out by Rocha et al (2013) also in the city of Coari, in Amazonas, the authors found 11% of unsatisfactory slides, made by conventional cytology. Coari is a small urban center, and although it does offer many health services of medium and high complexity, access to Basic Health Units by the population is extremely easy. In this case, for those who live in the urban area of the city, despite the expense by the government to repeat the collection and the time spent and the inconvenience generated for women, the setbacks for carrying out a new collection are not so great. But when we refer to women who live in isolated and difficult-to-reach communities, as is the case in most of the territory of Amazonas, this situation becomes very complicated. Since most cities do not have consolidated programs that systematically use river mobile units to go to communities to carry out collections, women again need to face all the difficult conditions for carrying out the new collection (difficulty in communication to make an appointment, which is aggravated by the fact that there is a need to schedule an appointment according to their menstrual cycles, long distances traveled by boat to the urban center, financial difficulties for the trip, etc). Therefore, unsatisfactory slides are a means of discouraging and losing follow-up of these women.

In this study, the percentage of abnormal cytopathological exams corresponded to 7.3% of the sample, with a greater number of women presenting LSIL (5.3%). 70.9% of the women with cytological alterations had hrHPVs infection, with a predominance of infection by HPVs 52, 16 and those in the P3 group. The percentage of women with normal cytology infected by hrHPVs was much lower: 11.9%. Rocha et al (2013), studying 361 women in routine gynecological examination also in the city of Coari, found prevalence of HPV in women with similar altered cytology: 71.4%; however, among women with normal cytology, detection was much higher than our study: 29.2%. However, these authors investigated all types of HPV, not just hrHPVs, which may partly explain this high detection. In the study carried out by Torres et al (2018), the authors obtained self-collection samples from 412 women living in the rural area (riverside) of the municipality of Coari and detected the presence of HPV DNA in 18.6% of the participants, but also without making a distinction between high- and low-risk HPV. Batista et al (2023) also

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studied the prevalence of HPV in riverside women in Coari with samples obtained by self-collection and found 15.7% of infected women, but also without distinction between the types of HPV.

As can be seen in figure 01, we consider that our results exhibit genotypic variety, with a slight predominance of HPV in the P3 group (35/39/68), followed by HPV 52. Other studies carried out in the Amazonas region also show a high prevalence and wide variety of types of HPV: in the study by Rocha et al (2013) the authors found 15 types of HPV, with a predominance of HPV 16 and 58. Teixeira et al (2018) studied HIV-positive women in the city of Manaus, capital of the state, and found a prevalence of 31.1% of infected by hrHPVs, with about 9 types found. The study by Fonseca et al (2015), carried out among indigenous people in different isolation conditions, found a high prevalence of 39.7% of HPV infection (all types, not just hrHPVs), with prevalence of types 31, 16, 18 and 68. Our study and the study by Rocha et al (2013) did not find HPV-18, while the studies by Teixeira et al (2018) and Fonseca et al (2015) found a very low prevalence of this type virus. These data, taken together, show how important it is to determine the presence of circulating genotypes in the Brazilian Amazonian region, since the administration of the 9-valent vaccine (which includes protection against HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58) rather than the quadrivalent (which only covers types 6, 11, 16 and 18) proves to be of great regional value.

Our data on the socioeconomic, clinical and behavioral characteristics of the women studied corroborate with other regional studies that point to a profile of vulnerability, not only to HPV infection, but also to other sexually transmitted infections: low education, low income, low adherence to the condom use, multiparity, among others; however, it was not observed in our findings that the data related to early sexual initiation and multiple partners had the same magnitude as in other local studies (ROCHA et al. 2019a; ROCHA et al. 2019b; AZEVEDO et al. 2019; PINTO et al, 2011). However, these data related to sexual behavior should always be considered with a certain reservation, since several cultural conditions can prevent the narration of true facts, such as shame, fear of moral judgments and even fear of breaching secrecy and confidentiality. Anyway, no statistically significant associations were found between these mentioned variables and positivity for HPV; however, regarding cytopathological results, the analyzes showed a statistically significant relationship with cytological changes and young age at first delivery ($p=0.017$), marital status "single/divorced/widowed" ($p<0.0001$) and low education (up to 8 years of study) ($p=0.040$).

Our study has some limitations. Although there was collection in all Basic Health Units in the city, the research design is not a true population-based study, but a survey with a convenience sample, so that its results cannot be extrapolated and considered representative of the local female population. Another limitation concerns the fact that the Onclarity HPV Assay kit for HPV detection does not allow the detection of all types of hrHPVs individually, and this grouping of HPV types makes the interpretation and comparison of results more difficult.

Anyway, we consider that the high rate of satisfactory slides, and the high prevalence of hrHPVs found in women with altered cytology compared to women with normal cytology provide us with a good indication that this can be a good screening strategy in women who live in regions with a high rate of CC, and more research is needed to analyze its implementation feasibility for tracking. In remote areas, with difficult access and low financial and human resources, such as in the interior of the Amazonas, studies have already been carried out suggesting that molecular tests for HPV (with genotyping for hrHPVs) in samples from self-collection and referral of positive women

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immediately to ablation treatment may be the best screening/screening strategy (RIBEIRO et al. 2021; TORRES et al. 2018). For screening, other tests are suggested and need to be researched in this context, such as double immunocytochemical labeling (p16/Ki67) of cells from liquid cytology, methylation of HPV DNA and even the use of artificial intelligence through Automated Visual Examination (AVE), whose algorithms are programmed to recognize cervical pre-cancer images even with the use of a smartphone camera (RIBEIRO et al. 2021; DESAI et al. 202; PEETERS et al. 2019).

5. Conclusion

The conventional Pap smear test is one of the most impactful cancer prevention tools in the world, as it has led to a reduction in the incidence and mortality of CC in the places where it has been successfully implemented. However, its limitations – such as low sensitivity and poor reproducibility – have led to the search for more strategies that increase the effectiveness of CC screening and screening. This study demonstrated the applicability of using LBC for CC screening in the studied population, achieving a high rate of satisfactory slides - very important in the sociogeographical context of the Amazonas - a high rate of positivity and suitability of the biological sample for molecular testing for the detection of hrHPVs. More studies related to the feasibility of implementing this screening strategy in these populations need to be carried out, since this is an area with a high rate of this disease.

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