ORIGINAL ARTICLE

Human Papillomavirus infection among pregnant women treated in primary health care: a cross-sectional study

Infecção por Papilomavírus Humano entre gestantes atendidas na atenção primária de saúde: um estudo transversal

Infección por Virus del Papiloma Humano en gestantes atendidas en atención primaria de salud

Nunes, Suzana Santos;[1] Azevedo, Maria Joana Nunes de;[2] Silva, Kátia Luz Torres;[3] Santos, Cristina Maria Borborema dos;[4] Rocha, Danielle Albuquerque Pires;[5]

ABSTRACT

Objective: to verify the prevalence of Human Papillomavirus in pregnant women and the concordance of detection between urine and cervical-vaginal samples. **Methods:** samples were collected from 110 women in the second trimester of pregnancy in the city of Coari, Amazonas. Detection of the virus was performed using Polymerase Chain Reaction using the PGMY09/11 primer set. **Results:** 24.6% of pregnant women were infected, with the virus present in 11.8% of urine samples and in 23.6% of cervical-vaginal samples. There was 86.4% agreement and a moderate agreement rate between biological samples (kappa = 0.543). A statistically significant association was found between Human Papillomavirus infection and the variables: age of pregnant women (p= 0.014), first pregnancy (p= 0.027) and nulliparity (p= 0.046). **Conclusions:** the cervical-vaginal sample proved to be more suitable for detecting the virus and the high prevalence found reinforces the need to closely monitor this infection during pregnancy.

Descriptors: Human papillomavirus; Pregnancy; Pregnancy Complications, infectious; Primary health care; Amazonian ecosystem.

RESUMO

***Objetivo**: verificar a prevalência de Papilomavírus Humano em gestantes e a concordância da detecção entre amostras de urina e cérvico-vaginais. **Métodos**: foram colhidas amostras de 110 mulheres no segundo trimestre de gestação no município de Coari, Amazonas. A detecção do vírus foi feita através de Reação em Cadeia da Polimerase, utilizando-se o conjunto de iniciadores PGMY09/11. **Resultados**: 24,6% das gestantes estavam infectadas, estando o vírus presente em 11,8% das amostras de urina e em 23,6% das amostras cérvico-vaginais. Houve concordância de 86,4% e índice de concordância moderado entre as amostras biológicas (kappa = 0,543). Foi encontrada associação estatisticamente significativa entre a infecção pelo Papilomavírus Humano e as variáveis: idade das gestantes (p= 0,014), primigestação (p= 0,027) e nuliparidade (p= 0,046). **Conclusões**: a amostra cérvico-vaginal mostrou-se mais adequada para detecção do vírus e a alta prevalência encontrada reforça a necessidade de acompanhar com mais atenção esta infecção na fase gestacional.*

***Descritores**: Papilomavírus humano; Gravidez; Complicações infecciosas na gravidez; Atenção primária à saúde; Ecossistema amazônico.*

1 Universidade Federal do Amazonas (UFAM). Manaus, Amazonas (AM). Brasil (BR). E-mail: suzyisb@ufam.edu.br ORCID: http://orcid.org/0009-0007-2860-8340

2 Universidade de São Paulo (USP). São Paulo, Sãp Paulo (SP). Brasil (BR). E-mail: ananunes.azevedo05@gmail.com ORCID: http://orcid.org/0000-0002-3244-2837

3 Fundação Centro de Controle em Oncologia do Estado do Amazonas (FCECON). Manaus, Amazonas (AM). Brasil (BR). E-mail: katialuztorres@hotmail.com ORCID: http://orcid.org/0000-0003-0922-5866

4 Universidade Federal do Amazonas (UFAM). Manaus, Amazonas (AM). Brasil (BR). E-mail: cris.bsantos10@gmail.com ORCID: http://orcid.org/0000-0002-1447-9759

5 Universidade Federal do Rio Grande do Norte (UFRN). Natal, Rio Grande do Norte (RN). Brasil (BR). E-mail: danielle.albuquerque@ufrn.br ORCID: https://orcid.org/0000-0002-9317-168X

How cite: Nunes SS, Azevedo MJN, Silva KLT, Santos CMB, Rocha DAP. Human papillomavirus infection among pregnant women treated in primary health care: a cross-sectional study. J. nurs. health. 2024;14(3):e1427022. DOI: https://doi.org/10.15210/jonah.v14i3.27022

RESUMÉN

Objetivo: *verificar prevalencia del Virus del Papiloma Humano en mujeres embarazadas y la concordancia de detección entre muestras de orina y cérvico-vaginales.* ***Métodos:*** *110 mujeres en el segundo trimestre del embarazo en el municipio de Coari, Amazonas tuvo la detección del virus mediante la reacción en cadena de la polimerasa utilizando el conjunto de cebadores PGMY09/11.* ***Resultados:*** *24,6% de las gestantes resultaron infectadas, estando el virus presente en el 11,8% de orina y en 23,6% de las muestras cérvico-vaginales. Hubo un 86,4% de acuerdo y una tasa de acuerdo moderada entre muestras biológicas (kappa = 0,543). Se encontró asociación entre la infección por Virus y las variables: edad de la gestante (p= 0,014), primer embarazo (p= 0,027) y nuliparidad (p= 0,046).* ***Conclusiones:*** *la muestra cérvico-vaginal demostró ser más adecuada para la detección del virus y la alta prevalencia encontrada refuerza la necesidad de monitorear esta infección durante el embarazo.*

Descriptores: *Virus del papiloma humano; Embarazo; Complicaciones infecciosas del embarazo; Atención primaria de salud; Ecosistema amazónico.*

INTRODUCTION

The Human Papillomavirus (HPV) is the most common sexually transmitted virus, which is ubiquitous. It is estimated that almost all sexually active people will have been infected by it at some point in their lives,[1-2] and about 75 to 80% of unvaccinated adults have immunological evidence of having had a primary HPV infection.[3] The peak of HPV infection occurs shortly after the start of sexual life, but most of these infections resolve spontaneously by immunological mechanisms, without causing symptoms or illnesses.[4] However, persistent infection with certain types of HPV is quite worrying, as they are related to benign and malignant epithelial neoplasms in various anatomical sites, such as the cervix, vagina, vulva, anus and oropharynx.[5-8]

In pregnant women, large genital warts and *condylomata acuminatum*, even though they are benign lesions, are sometimes dangerous as they can obstruct the birth canal. HPV infection during pregnancy has been consistently associated with some adverse outcomes, such as spontaneous abortion, premature birth, premature rupture of membranes, hypertension, placental abnormalities, low birth weight, fetal growth restriction and intrauterine death. However, the evidence of these adverse effects is quite variable, in addition to other factors also contributing to these obstetric outcomes.[1-2,4]

In addition to concerns about their own gynecological health and obstetric problems, pregnant women infected with HPV can transmit the virus to their babies, especially during natural birth. In infected children, the virus can cause recurrent respiratory and oral papillomatosis, with clinical consequences that are quite unpleasant and sometimes dangerous for the child.[2-3] International studies indicate the prevalence of HPV in pregnant women ranging from 16.9% in countries east of the Mediterranean to 46.46% in African regions.[9] In Brazil, epidemiological studies found a prevalence of HPV infection ranging from 25% to 35.3% in studies carried out in mixed groups of women,[10-12] reaching 50.5% in pregnant adolescents[13] and 84,3%[14] and 96%[15] in pregnant HIV-positive.

With proper prenatal care, the gestational period is a phase in a woman's life that presents several opportunities to strengthen her contact with health services, including for a preventive Pap smear test and/or HPV detection. If the woman has her Pap smear up to date, the possibility of less invasive sample collection methods for HPV detection can be a good strategy to increase pregnant women's adherence to the program. In this context, the urine sample becomes a less invasive and easily obtained option in this specific group of women. From this perspective, the objective of this study was to verify the prevalence of HPV infection by investigating the presence of the virus's DNA in urine and cervical-vaginal samples and to compare the concordance of positivity between these 2 types of biological samples.

METHOD

This was a cross-sectional study carried out with pregnant women undergoing prenatal care at Health Centers in the city of Coari, Amazonas, Brazil, using the STROBE (Strengthening the Reporting of Observational Studies Epidemiology) script as a guide. It was approved by the Research Ethics Committee of the Federal University of Amazonas (CAAE nº 50907415.3.0000.5020) on 11/19/2015.

The population consisted of pregnant women treated at the Health Centers in Coari City from July/2016 to March/2017. The minimum number of women estimated for this study was 58 pregnant women, based on the number of 1,729 born in 2013[16] and the expected prevalence of sexually transmitted infections (STI) of 1.4% (according to DATASUS data on STI in pregnant women in Coari in 2013), with a margin of error of 3% and a confidence interval of 95%.

Only pregnant women who were in the second trimester of pregnancy (14 and 27 weeks) participated in the study, to avoid any association between endocervical collection and any adverse effects, such as bleeding, premature rupture of membranes, etc., without age limits. Pregnant women who had already reported any associated risk factor were not included: history of vaginal bleeding, accidental fall, placenta previa, fluid loss, cervix dilation, among other factors.

A survey was carried out of the total number of pregnant women who were in the second trimester of pregnancy in the city's 12 Health Centers, totaling 249 women, all of whom were approached at home. Of these, 164 met the inclusion criteria and agreed to participate in the research, but 52 withdrew and 02 had their biological samples unviable, totaling a final sample of 110 pregnant women. The participating women signed the Free and Informed Consent Form (ICF) (minors signed an Assent Form and their guardians signed the ICF). They answered a standard questionnaire and received a sterile collection bottle. An appointment was made to go to the Health Center to perform the endocervical collection, at the same time they were instructed to collect the urine (20ml) and bring it in the collection bottle to the Health Center on the same day of collection. On the scheduled day, the cervical-vaginal sample was collected by the nurse (team member) using a sterile swab, which was immediately immersed in a tube containing 1 mL of TRIS-EDTA buffer (10 mM TRIS-HCl and 1 mM EDTA pH 8.0). The samples were taken to the laboratory and frozen at -20ºC.

Urine samples were centrifuged at 2,000g for 20 minutes. The supernatant was discarded and the pellet was washed with phosphate-buffered saline (PBS). The cervico-vaginal samples were vortexed and 1ml was transferred to a microtube. According to the manufacturers' recommendations, DNA from urine samples was extracted using the commercial QIAamp Viral RNA Mini Kit (QIAGEN, GERMANY) and DNA from cervical-vaginal samples was extracted using the QIAamp DNA Mini Kit (QIAGEN, GERMANY).

To detect HPV DNA, a Polymerase Chain Reaction (PCR) was performed using the primer set PGMY09/11[17] together with the primer pair PCO4/GH20[18] which amplify a segment of genomic DNA human. The final volume of the reaction was 25μl, containing 14.5μl of water, 2.5μl of 10x Buffer, 0.8μl of MgCl250mM, 0.5μl of 10mM dNTP, 0.5 μl PGMY09/11 5mM, 0.5μl PCO4 5mM, 0.5μl GH20 5mM, 0.2μl Platinum Taq DAN polymerase 5U and 5μl DNA. Thermocycling was: 95ºC for 5 minutes for initial denaturation, 40 cycles of 95ºC for 1 minute, 55ºC for 1 minute and 72ºC for 1 minute, followed by 10 minutes at 72ºC for final extension. The PCR products were analyzed by electrophoresis in a 1.5% agarose gel, stained with ethidium bromide and visualized using a transilluminator.

The observed agreement, the Kappa index and the respective 95% confidence intervals (95% CI) were calculated for comparing the PCR results between the urine samples and the cervico-vaginal swab. To analyze the categorical data from the questionnaire in relation to the PCR result, the chi-square test with Yates correction was applied, and if it was impossible to apply the Yates test, the

Fisher exact test was chosen. In the analysis of quantitative data, accepting the hypothesis of normality using the Shapiro-Wilk test, the mean and standard deviation (SD) were calculated. The software used for data analysis was Epi Info version 7.2 for Windows. The significance level established in statistical tests was 5%.

RESULTS

A total of 110 pregnant women aged between 13 and 41 years, with a mean age of 23.20 (SD=6.33) provided urine samples and cervical-vaginal samples collected by a health professional. HPV infection was detected in 24.6% (27/110) of pregnant women. For each sample type, HPV DNA was found in 13 (11.8%) urine samples and in 26 (23.6%) cervical-vaginal samples. Twelve (10.91%) pregnant women were positive in both samples, one (0.91%) pregnant woman was positive only in the urine sample and 14 (12.73%) pregnant women were positive only in the cervico-vaginal samples. Eighty-three (75.45%) pregnant women were negative in both samples (Table 01). There was an agreement of 86.4% (95% CI, 78.7% - 91.6%) and a moderate agreement rate between biological samples (kappa = 0.543 (95% CI, 0.372 - 0.715). A statistically significant association was found between Human Papillomavirus infection and the variables: age of pregnant women (p= 0.014), first pregnancy (p= 0.027) and nulliparity (p= 0.046).

Table 1. Distribution according to PCR results for HPV in urine and cervical-vaginal samples from pregnant women. Coari, 2023.

PCR (Urine)	PCR (cervico-vaginal swab)					
	Positive		Negative			
	f_i	%	f_i	%	Total	%
Positive	12	10,9	1	0,9	13	11,8
Negative	14	12,7	83	75,5	97	88,2
Total	26	23,6	84	76,4	110	100

fi = simple absolute frequency
Source: research data, 2015.

DISCUSSION

It is not understood exactly why 90% of people infected with HPV experience a natural "clearance" while other individuals are severely affected by the virus, although the complex immunological interactions involved are being clarified.[3,19-20] During pregnancy, hormonal and immunological changes typical of pregnancy can favor the persistence of HPV infection and transgenerational transmission, leading to an increased risk of cancer.[4] Older studies already showed that the prevalence of HPV increases during pregnancy; Smith et al (1991)[21] showed that the prevalence among pregnant women increased with gestational age: from 8.0% in the first trimester to 16.7% in the second and 23.1% in the third, suggesting that HPV infection can be activated by hormones and other effects of pregnancy (e.g., immunodeficiency) and may explain why some pregnancies are known to be associated with an increased risk of dysplasia and cancer.[2] Recent studies have found a higher prevalence of HPV in pregnant women compared to non-pregnant women. Luo et al (2021)[22] carried out a case-control study with 1,077 pregnant women (in the second trimester of pregnancy) and 1,077 non-pregnant women matched by age and found a significantly higher prevalence in the case group than in the control group (24.2 % vs.14.8%, respectively).

In our study, we found a 26% prevalence of HPV infection among pregnant women, which agrees with Brazilian studies carried out with mixed populations of women (i.e., populations of women without particularities such as adolescents, a group of HIV-positive women, etc). The study carried out by Salcedo et al (2015)[11] in the city of Porto Alegre/RS comparing HPV infection in 91

pregnant women and 92 non-pregnant women in cervical samples collected by a professional and tested for HPV by PCR found the prevalence of HPV among pregnant women (25.3%) compared to the prevalence found among non-pregnant women (13%). The study by Brandão et al (2009)[15] carried out with women in a maternity hospital in Recife between 2006 and 2007 revealed alarming levels of HIV-positive and HIV-negative HPV infection: the prevalence of HPV among HIV-positive women it was 96% and among HIV-negative women it reached 79.2%.

Study published in 2022 followed 303 pregnant teenagers in a tertiary health care service in the city of São Paulo from January 2010 to January 2016 and found an alarming rate of 50.5% of girls positive for HPV. The authors used a sample collected from the ectocervix and the outermost ¼ of the endocervical canal, and HPV detection was carried out by hybrid capture, as this procedure was already part of the protocol of that medical service.[13] The data revealed that 17.49% of pregnant adolescents had cytological changes: 9.57% had low-grade epithelial lesion (LSIL), 7.59% had squamous atypia of undetermined significance (ASC-US) and up to 1 girl (0 .33%) presented with a high-grade squamous epithelial lesion (HSIL). However, there was no association with obstetric and neonatal complications.

It needs to be highlighted that the period in which the studies described above were carried out covered a pre-vaccination period[11,15] until a period after the start of vaccination,[13] which occurred in 2014 in Brazil. Thus, it was a period of transition, in which data on vaccination coverage and acceptance were being constructed. Certainly, the start of vaccination of pre-adolescents and adolescents against HPV in Brazil in 2014 was an important milestone for Brazilian public health, which should lead to a reduction in these rates of HPV infection and cervical abnormalities. In our study we did not obtain data regarding the vaccination status of our participants, which is one of its limitations. As our collections were carried out between July/2016 and March/2017, and although the range of women's ages varied between 13 and 41 years (demonstrating the participation of adolescents), the average age was 23.20, with a deviation of standard of 6.33, it is reasonable to assume that most of the participating women had not been vaccinated at that time. Studies highlight the positive impacts that anti-HPV vaccination has on adverse effects during pregnancy, both on the mother and the fetus.[23-24]

In our service, a preventive Pap smear test is only offered to women if they are not up to date with the exam, which was the case for few participating women. The interpretation of the pregnant woman's cytological specimen is more challenging, as hormonal changes cause changes in squamous and glandular cells, including hyperplasia and reactional atypia, which can generate a higher rate of false positives, resulting in unnecessary interventions and maternal anxiety. Detection of HR-HPV through molecular tests would have good applicability during pregnancy, minimizing problems with reading slides due to changes caused by transient hormonal changes.[2]

But what type of sample would then be suitable for the molecular diagnosis of HPV for pregnant women? If she is up to date with her Pap smear, is it worth making her go through the unnecessarily stressful speculum exam to collect a sample for HPV research? If the urine sample presents good performance for the detection of HPV by molecular examination, this would facilitate women's adherence to the examination as it is a non-invasive and easy to perform method. In addition, pregnant women undergo several urine tests during their prenatal care. In our study we used 2 biological samples: urine and a cervical-vaginal sample collected by a professional. HPV DNA was found in 23.6% of cervical-vaginal samples, but in only 11.8% of urine samples, with an agreement of 86.4% (95% CI, 78.7% - 91.6%) and moderate agreement index between biological samples (kappa = 0.543 (95% CI, 0.372 - 0.715). In our study, the cervical-vaginal sample showed better performance than the urinary sample. In addition to the viral load being higher in the cervicovaginal epithelium, there are PCR inhibitors in the urine (urea, nitrites, salt crystals and hemoglobin, for example), which, if not

adequately removed in the DNA extraction process, can have an impact on the reaction when the concentration of viral DNA in urine is low, despite the fact that the samples were positive for human genomic DNA.[17]

The suitability of vaginal samples obtained through self-collection devices has also been studied. Numerous studies have already been carried out on the acceptability and efficiency in obtaining a quality biological sample for the molecular diagnosis of various sexually transmitted pathogens in the general population, showing positive results.[18-20,25] In studies with pregnant women, however, the acceptability of vaginal self-collection does not seem to be unanimous. Franciscatto et al (2014)[17] studying 133 pregnant women in Rio Grande do Sul, reported that 52.6% of the participating women refused to perform self-collection, demonstrating that urine was more accepted among them. These authors compared the detection of HPV in urine samples and samples obtained by self-collection and found a high prevalence of 54% in urine and 61.9% in self-collected samples, with substantial agreement between the samples (k=77.3%) and advocate the use of urine samples to detect HPV in pregnant women.

Among the forms of biological samples suitable for pregnant women, the collection of vaginal secretion/fluid collected with a condom brush used during ultrasound examinations in the first trimester (transvaginal route) has been tested. Pandey et al (2019)[4] used this method and detected the presence of HPV in 39.4% of pregnant women in India. In addition to showing suitability for molecular tests, this type of sample is easy to obtain and therefore well accepted by women, since in many services specular examination and collection are not part of the prenatal routine. These authors found a statistically significant association between HPV infection and pregnant women with premature membrane rupture.

Most cases of vertical transmission of HPV occur during vaginal birth, showing that cesarean section has a protective effect. The meta-analysis published by Chatzistamatiou, Sotiriadis & Agorastos[26] showed that cesarean birth had a significantly lower HPV transmission rate compared to vaginal birth (14.9 x 28.2%; CI 0.43-0.78), reducing the risk of perinatal transmission by approximately 46%. However, cesarean delivery reduces, but does not eliminate, the risk of transmission, as HPV has been isolated in amniotic fluid, placenta and fetal membranes, indicating possible intrauterine transmission to the fetus.[27-28] Monitoring the first 4 years after the introduction of the quadrivalent anti-HPV vaccine in Australia showed that rates of recurrent juvenile respiratory papillomatosis fell dramatically from 0.16/100,000 in 2012 to 0.02/100,000 in 2016.[2]

Treatment indications for HPV infections during pregnancy are similar to those for non-pregnant women HPV infections can resolve spontaneously. Genital warts do not pose a serious risk to women, but if the clinician observes their presence during a routine examination, he or she should inform the patient about their existence. If the pregnant woman presents with condyloma acuminata, the size, quantity (single or multiple), extension and whether there is any risk of obstruction of the birth canal must be assessed. Some indications are the use of trichloroacetic acid, cryotherapy, photodynamic therapy and surgical excision.[2] Administration of the anti-HPV vaccine during pregnancy has not been practiced in Brazil, but studies show that there is no greater risk of adverse effects.[29-30] In our research, no woman presented papillary/warty lesions on clinical examination.

In addition to the limitations that have already been mentioned above, we must point out some others here, the main one being the small sample. All eligible women were contacted and invited, however, there was a high refusal rate. Other limitations of this study were that women were not monitored to verify adverse outcomes and genotyping of HPV found in infected women was not done.

CONCLUSION

The high prevalence found in our study emphasizes the need to give greater importance to researching this pathogen during pregnancy. More research comparing the best type of biological sample is needed, as well as acceptance of the collection method by patients.

REFERENCES

1 Condrat CE, Filip L, Gherghe M, Cretoiu D, Suciu N. Maternal HPV infection: Effects on pregnancy outcome. Viruses. 2021;13(12):1–21. DOI: https://doi.org/10.3390/v13122455

2 Chilaka VN, Navti OB, Al Beloushi M, Ahmed B, Konje JC. Human papillomavirus (HPV) in pregnancy – An update. Eur J Obstet Gynecol Reprod Biol. 2021;264:340–8. DOI: https://doi.org/10.1016/j.ejogrb.2021.07.053

3 Benedict JJ, Derkay CS. Recurrent respiratory papillomatosis: A 2020 perspective. Laryngoscope Investig Otolaryngol. 2021;6(2):340–5. DOI: https://doi.org/10.1002%2Flio2.545

4 Pandey D, Solleti V, Jain G, Das A, Shama Prasada K, Acharya S, et al. Human Papillomavirus (HPV) infection in early pregnancy: prevalence and implications. Infect Dis Obstet Gynecol. 2019;2019. DOI: https://doi.org/10.1155/2019/4376902

5 Mix JM, Gopalani SV, Simko S, Saraiya M. Trends in HPV- and non-HPV-associated vulvar cancer incidence, United States, 2001–2017. Prev Med. 2022;164:107302. DOI: https://doi.org/10.1016/j.ypmed.2022.107302

6 Clarke MA, Deshmukh AA, Suk R, Roberts J, Gilson R, Jay N, et al. A systematic review and meta-analysis of cytology and HPV-related biomarkers for anal cancer screening among different risk groups. Int J Cancer. 2022;151(11):1889–901. DOI: https://doi.org/10.1002/ijc.34199

7 González-Guevara MB, Linares-Vieyra C, Castro-García ME, Muñiz-Lino MA, Abaroa-Chauvet C, Bello-Torrejón F. Carcinoma escamocelular bucal. Caso clínico y revisión de la literatura. Rev Med Inst Mex Seguro Soc. 2021;60(1). Disponible en: https://docs.bvsalud.org/biblioref/2022/03/1361682/4215-29326-1-pb.pdf

8 Curty G, De Carvalho PS, Soares MA. The Role of the Cervicovaginal Microbiome on the Genesis and as a Biomarker of Premalignant Cervical Intraepithelial Neoplasia and Invasive Cervical Cancer. Int J Mol Sci. 2019;21(1):222. DOI: https://doi.org/10.3390/ijms21010222

9 Ardekani A, Sepidarkish M, Mollalo A, Afradiasbagharani P, Rouholamin S, Rezaeinejad M, et al. Worldwide prevalence of human papillomavirus among pregnant women: a systematic review and meta-analysis. Rev Med Virol. 2023;33(1):1–13. DOI: https://doi.org/10.1002/rmv.2374

10 Freitas LB, Pereira CC, Checon R, Leite JPG, Nascimento JP, Spano LC. Adeno-associated virus and human papillomavirus types in cervical samples of pregnant and non-pregnant women. Eur J Obstet Gynecol Reprod Biol. 2009;145(1):41–4. DOI: https://doi.org/10.1016/j.ejogrb.2009.03.024

11 Salcedo MMBP, Damin APS, Agnes G, Pessini SA, Beitune PE, Alexandre COP, et al. Prevalence of human papillomavirus infection in pregnant versus non-pregnant women in Brazil. Arch Gynecol Obstet. 2015;292(6):1273–8. DOI: https://doi.org/10.1007/s00404-015-3752-8

12 Pereira SMM, Etlinger D, Aguiar LS, Peres SV, Filho AL. Simultaneous Chlamydia trachomatis and HPV Infection in Pregnant Women. Diagn Cytopathol. 2010;38(6):397–401. DOI: https://doi.org/10.1002/dc.21219

13 Souza HD, Waissman AL, Diório GRM, Peres SV, Francisco RPV, Galletta MAK. Prevalence of oncogenic human papillomavirus in pregnant adolescents, association with colpocytological changes, risk factors and obstetric outcomes. Clinics (Sao Paulo). 2022;77:100127. DOI: https://doi.org/10.1016/j.clinsp.2022.100127

14 Meyrelles ARI, Siqueira JD, Hofer CB, Costa TP, Azevedo AP, Guimarães BV, et al. HIV/HPV co-infection during pregnancy in southeastern Brazil: Prevalence, HPV

types, cytological abnormalities and risk factors. Gynecol Oncol. 2013;128(1):107–12. DOI: https://doi.org/10.1016/j.ygyno.2012.10.003

15 Brandao VCRAB, Lacerda HR, Lucena-Silva N, Ximenes RA de A. Frequency and types of human papillomavirus among pregnant and non-pregnant women with human immunodeficiency virus infection in Recife determined by genotyping. Mem Inst Oswaldo Cruz. 2009;104(5):755–63. DOI: https://doi.org/10.1590/s0074-02762009000500016

16 Ministério da Saúde (BR). Departamento de Informática do Sistema Único de Saúde (DATASUS). Sistema de Informação de Nascidos Vivos (SINASC). Nascimentos em Coari - Amazonas. 2013. [acesso em 2015 maio 10]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinasc/cnv/nvam.def

17 Gravitt PE, Peyton CL, Alessi TQ, Wheeler CM, Coutlée F, Hildesheim A, et al. Improved Amplification of Genital Human Papillomaviruses. J Clin Microbiol. 2000;38(1):357–61. DOI: https://doi.org/10.1128/jcm.38.1.357-361.2000

18 Bernard HU, Chan SY, Manos MM, Ong CK, Villa LL. Identification and assessment of known and novel human papillomaviruses by polymerase chain reaction amplification, restriction fragment length polymorphisms, nucleotide sequence, and phylogenetic algorithms. The Journal of Infectious Diseases.1994;170(5):1077-85. DOI: https://doi.org/10.1093/infdis/170.5.1077

19 Kudela E, Liskova A, Samec M, Koklesova L, Holubekova V, Rokos T, et al. The interplay between the vaginal microbiome and innate immunity in the focus of predictive, preventive, and personalized medical approach to combat HPV-induced cervical cancer. EPMA J. 2021;12(2):199–220. DOI: https://doi.org/10.1007/s13167-021-00244-3

20 Condrat CE, Cretoiu D, Radoi VE, Mihele DM, Tovaru M, Bordea CI, et al. Unraveling Immunological Dynamics: HPV Infection in Women—Insights from Pregnancy. Viruses. 2023;15(10):2011. DOI: https://doi.org/10.3390/v15102011

21 Smith EM, Johnson SR, Jiang D, Zaleski S, Lynch F, Brundage S, et al. The association between pregnancy and human papilloma virus prevalence. Cancer Detect Prev 1991;15(5):397–402.

22 Luo D, Peng M, Wei X, Pan D, Xue H, Xu Y, et al. Prevalence of human papillomavirus and genotype distribution in pregnant and non-pregnant women in china. Risk Manag Healthc Policy. 2021;14:3147–57. DOI: https://doi.org/10.2147/rmhp.s288838

23 Dousti R, Allahqoli L, Ayar Kocaturk A, Hakimi S. Can human papillomavirus vaccination during pregnancy result in miscarriage and stillbirth? A meta-analysis and systematic review. Eur J Midwifery. 2023;29(7):1–6. DOI: https://doi.org/10.18332/ejm/161793

24 Yuill S, Velentzis LS, Smith M, Egger S, Wrede CD, Bateson D, et al. The impact of HPV vaccination beyond cancer prevention: effect on pregnancy outcomes. Hum Vaccin Immunother. 2021;17(10):3562–76. DOI: https://doi.org/10.1080%2F21645515.2021.1936860

25 Batista SJS, Gomes AMP, Oliveira TKLD, Lobato TCL, Dantas JDS, Oliveira FGD, et al. Home Self-collection to test for Human Papillomavirus and Chlamydia trachomatis infection in riverside women in Amazonas. Research, Society and Development. 2023;12(3):e16412340171. DOI: https://doi.org/10.33448/rsd-v12i3.40171

26 Chatzistamatiou K, Sotiriadis A, Agorastos T. Effect of mode of delivery on vertical human papillomavirus transmission - A meta-analysis. J Obstet Gynaecol. 2016;36(1):10–4. DOI: https://doi.org/10.3109/01443615.2015.1030606

27 Petca A, Borislavschi A, Zvanca M, Petca RC, Sandru F, Dumitrascu M. Non-sexual HPV transmission and role of vaccination for a better future (Review). Exp Ther Med. 2020;20(6):1–1. DOI: https://doi.org/10.3892/etm.2020.9316

28 Bruno MT, Caruso S, Bica F, Arcidiacono G, Boemi S. Evidence for HPV DNA in the

placenta of women who resorted to elective abortion. BMC Pregnancy Childbirth. 2021;21(1):485. DOI: https://doi.org/10.1186/s12884-021-03937-9

29 Wang A, Liu C, Wang Y, Yin A, Wu J, Zhang C, et al. Pregnancy Outcomes After Human Papillomavirus Vaccination in Periconceptional Period or During Pregnancy: A Systematic Review and Meta-analysis. Hum Vaccin Immunother. 2020;16(3):581–9. DOI: https://doi.org/10.1080/21645515.2019.1662363

30 Arora M, Lakshmi R. Vaccines - safety in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2021;76:23–40. DOI: https://doi.org/10.1016/j.bpobgyn.2021.02.002

Recebido em: 22/05/2024
Aceito em: 16/07/2024
Publicado em: 16/08/2024