

Factors associated with human papillomavirus infection during pregnancy: An integrative review

RESUMO | Objetivo: Identificar os fatores associados à infecção pelo papilomavírus humano em gestantes. Método: Revisão integrativa realizada nas seguintes bases de dados: BDEF, LILACS, MEDLINE e IBECs. Foram utilizados os seguintes descritores: "Papilomavirus Humano", "HPV", "Gravidez", "Infecções Sexualmente Transmissíveis" e "IST" (com respectivas traduções para o inglês). Resultados: Seis artigos compuseram a amostra final deste estudo. O design de pesquisa mais prevalente foi o estudo transversal (n: 03). Verificou-se que os fatores associados à infecção pelo HPV estavam relacionados a características sociodemográficas (menor idade, baixa escolaridade, estado civil solteira e consumo de álcool na gestação) e maternas (multiparidade). Conclusão: Verificou-se que alguns fatores podem estar associados à presença de infecção pelo HPV em gestantes, como características sociodemográficas e maternas. Faz-se necessário que os profissionais de saúde tenham um olhar mais atento a este público, afim de contribuir para disseminação da informação e consequente prevenção.

Descritores: Alphapapillomavirus; Cuidado pré-natal; Doenças sexualmente transmissíveis.

ABSTRACT | Objective: To identify factors associated with human papillomavirus infection in pregnant women. Method: Integrative review carried out in the following databases: BDEF, LILACS, MEDLINE and IBECs. The following descriptors were used: "Papilomavirus Humano", "HPV", "Gravidez", "Infecções Sexualmente Transmissíveis" and "IST" (with respective translations into English). Results: Six articles made up the final sample of this study. The most prevalent research design was the cross-sectional study (n: 03). It was found that the factors associated with HPV infection were related to sociodemographic (younger age, low education, single marital status and alcohol consumption during pregnancy) and maternal (multiparity) characteristics. Conclusion: It was found that some factors may be associated with the presence of HPV infection in pregnant women, such as sociodemographic and maternal characteristics. It is necessary that health professionals have a closer look at this public, in order to contribute to the dissemination of information and consequent prevention.

Keywords: Alphapapillomavirus; Prenatal care; Sexually transmitted diseases.

RESUMEN | Objetivo: Identificar los factores asociados a la infección por el virus del papiloma humano en mujeres embarazadas. Método: Revisión integrativa realizada en las siguientes bases de datos: BDEF, LILACS, MEDLINE e IBECs. Se utilizaron los siguientes descriptores: "Papilomavirus Humano", "HPV", "Gravidez", "Infecções Sexualmente Transmissíveis" y "IST" (con sus respectivas traducciones al inglés). Resultados: Seis artículos constituyeron la muestra final de este estudio. El diseño de investigación más prevalente fue el estudio transversal (n: 03). Se encontró que los factores asociados a la infección por VPH se relacionaron con características sociodemográficas (menor edad, baja escolaridad, estado civil soltero y consumo de alcohol durante el embarazo) y maternas (multiparidad). Conclusión: Se encontró que algunos factores pueden estar asociados a la presencia de infección por VPH en gestantes, como las características sociodemográficas y maternas. Es necesario que los profesionales de la salud tengan una mirada más cercana a este público, a fin de contribuir a la difusión de información y consecuente prevención.

Palabras claves: Alphapapillomavirus; Atención prenatal; Enfermedades de transmisión sexual.

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INTRODUCTION

A World Health Organization (WHO) estimates that over one million sexually transmitted infections (STIs) are acquired every day with over 357 million new infections per year. ⁽¹⁾ Among the STIs, the Human Papilloma Virus (HPV) stands out, which constitutes a heterogeneous group of viruses belonging to the Papovaviridae family, with recognized potential for tumor induction, with infection of the squamous epithelium. ⁽²⁾

It is a virus with more than 100 identified subtypes, of which 40 are related to lesions in the genital areas, but only 20 are considered high risk, that is, present a greater predisposition to carcinogenesis, although the main anatomical regions where HPVs are found are the cervix, vulva, vagina and penis, in addition to the oral and laryngeal mucosa. ⁽²⁾

According to the National Cancer Institute, the number of oncogenic subtypes of HPV reaches at least 13, and among these, subtypes 16 and 18 are responsible for about 70% of cervical cancer cases. ⁽³⁾ Cervical cancer is relevant for studies because it is categorized as a public health issue, mainly due to its high capacity for morbidity and mortality - affecting mostly women from more disadvantaged socioeconomic conditions. ⁽⁵⁾

Although HPV is a known cause of cervical cancer, its clinical impact on pregnancy, obstetric outcomes, and future noncommunicable diseases is less studied. The lifetime risk of HPV infections in women is approximately 80% and approximately 70% clear the infection within 1 year. ^(2,4) Because HPV targets placental trophoblast cells, infections during pregnancy can negatively affect maternal and fetal outcomes through abnormal placentation and placental function. ⁽⁵⁾

During pregnancy, the risk of HPV infection is expected to be high due to the fact that pregnancy is a kind of suppressed immunity state. ⁽⁶⁾ Pregnant wo-

men are at greater risk of HPV infection because during pregnancy major physiological and immunological changes occur that modulate the functioning of the immune system and can cause changes in HPV replication. These changes can also make clearing HPV much more difficult. HPV infection can impair trophoblast invasion of extra villi into the uterine wall, increasing the rate of trophoblast cell death and causing placental dysfunction that can result in adverse pregnancy outcomes. ⁽⁷⁾

HPV infection during pregnancy can bring several complications. Research indicates that HPV infection is significantly associated with adverse outcomes including preeclampsia, preterm delivery and low birth weight. It was found that HPV-positive pregnant women were 2.80 times more likely to develop preeclampsia compared to HPV-negative women. ⁽⁶⁾ Thus, this study aimed to identify factors associated with human papillomavirus infection in pregnant women.

METHODS

An integrative literature review study was carried out, based on the following guiding question: "What are the main factors associated with human papillomavirus infection in pregnant women?"

To conduct the study, the following steps were taken as a basis: 1) Definition of the guiding question and research objectives; 2) Establishment of inclusion and exclusion/sampling criteria for studies; 3) Search in the literature; 4) Categorization and analysis of studies; 5) Presentation and discussion of sample results and; 6) Presentation and synthesis of knowledge. ⁽⁸⁾

The investigation of the studies took place in the following databases: Nursing Database (BDENF), Latin American and Caribbean Literature in Health Sciences (LILACS) and Bibliographical Index Español en Ciencias de la Salud (IBECS) and Medical Literature Analysis

and Retrieval System Online (MEDLINE), through the Virtual Health Library (VHL).

The search took place from January to February 2022. To search the databases, a query was made to the Health Sciences Descriptors (DeCS) and the following descriptors were used: "Human Papillomavirus", "HPV", "Pregnancy", "Sexually Transmitted Infections" and "STIs". The search began by applying the descriptors individually and then crossings were performed using the Boolean operators "AND" and "OR".

The studies were selected according to the following inclusion criteria: research available electronically in the selected databases, published in Portuguese, English or Spanish from January 2016 to December 2021. Duplicate articles in the databases (duplicates), review studies (narrative, integrative and systematic), theses, dissertations and course conclusion work, book chapters, reflection articles, reports and editorials of non-scientific newspapers.

The survey in the databases took place using the Parsifal software, where the studies were submitted to the stages of data identification and analysis. The last activity of this phase was the automatic removal of article duplicates. In the second phase, the screening stage, all the titles and abstracts of the articles were examined through the software, based on the main objectives of selecting relevant studies by the reviewers.

Subsequently, the full texts of relevant studies were scrutinized by the reviewers, and if there was any discrepancy between them, a third reviewer made the final decision. For the development of this phase, a Google Sheets table shared among the researchers of the present work was used, based on the instrument proposed by the scientific literature. ⁽⁹⁾

After applying the search filters in the databases, 818 articles were initially found. Duplicate articles ⁽³⁰⁾ were registered only once, totaling 788 for reading titles and abstracts. At this sta-

ge, 677 publications that did not have a relevant approach to the theme of this study, 69 review studies and 12 opinion articles and dissertations were excluded. Thus, 30 publications were selected for reading in full, but 24 were excluded because they were studies focusing on general STIs, without specifying HPV, and because they did not report in detail the factors associated with infection of this virus during pregnancy. Thus, six articles constituted the final sample of this review, as explained in Figure 1.

The selected articles were submitted to the classification of the level of evidence, from the instrument of Hierarchical Classification of Evidence for Evaluation of Studies.⁽⁹⁾ According to this classification, levels I and II are considered strong evidence, III and IV moderate, and V to VII weak.⁽¹⁰⁾

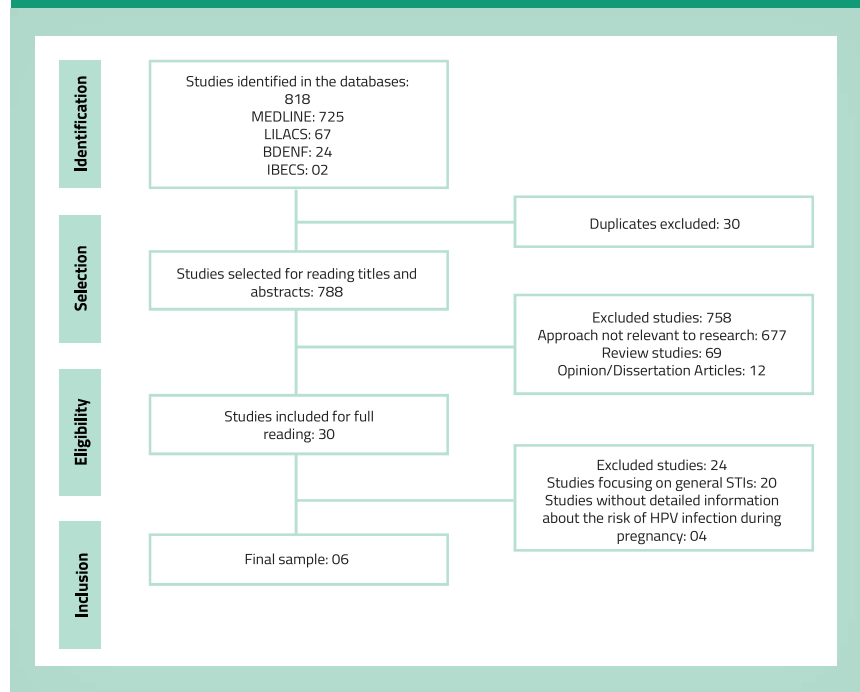
This study preserved the ethical aspects in such a way that all authors of the analyzed publications were properly referenced, according to the Copyright Law nº 9.610 of February 19, 1998.⁽¹¹⁾

RESULTS

Of the total of six articles analyzed, Table 1 shows a higher frequency of publication in 2018 (n: 02) and greater production in Brazil (n: 02). Regarding the approach of the articles found, it appears that the highest prevalence was the cross-sectional study (n: 03), with a weak level of evidence (VI), although higher levels have been identified, as in case-control and cohort studies (III), through the classification used for analysis.

Through Table 2, it is possible to analyze some important information about the studies carried out. 1,766 pregnant women participated in the analyzed studies, with an average age that ranged from 19.8 to 32.3 – young and middle-aged population. It was found that the factors associated with HPV infection during pregnancy were related to sociodemographic characteristics (younger age, low education, single

Figure 1: Flowchart of the study selection process, Recife (PE), Brazil, 2022.



Source: Data obtained in the study, 2022.

marital status and alcohol consumption during pregnancy) and maternal (multiparity).

DISCUSSION

This study analyzed the scientific production regarding the factors associated with HPV infection during pregnancy. During this period, key considerations in the management of HPV infection include concerns about disease progression, the safety of therapies (for mother and baby), and the risk of vertical transmission to the fetus and newborn.⁽¹⁸⁾

Altered immunity in pregnancy increases the risk and consequences of infections such as HPV. In addition to this factor, this viral infection is associated with a persistence of the virus in cervical epithelial cells and possible progression of subclinical/mildly symptomatic infections. During pregnancy, there is proliferation of the basal and parabasal layers of the stratified squamous epithelium of

the cervix, increasing mucus secretions in the cervical glands and activation of cervical epithelial metaplasia.⁽¹⁹⁾ It is also found that the columnar epithelium moves more towards the vaginal side of the cervix and is more exposed (ectopy) and sensitive to several factors, including infections.⁽¹⁹⁾

In light of the results, it was found that some sociodemographic characteristics may be related to a higher risk of HPV infection during pregnancy. A lower age group of pregnant women with HPV was associated with this higher risk, corroborating other published studies.^(20,21) When the incidence of HPV in pregnant women under 25 years of age is exclusively evaluated, it is significantly higher than in older pregnant women. The answer to this phenomenon may be related to the fact that HPV infection occurs more frequently in young people at the beginning of sexual and reproductive activity.⁽²²⁾

Single marital status was also as-

Table 1: Characterization of articles in the final sample, Recife (PE), Brazil, 2022.

ID	Author/ Year	Country	Journal	Study design (LE*)	Objectives
01	Ferreira et al., 2017 ⁽¹²⁾	Brazil	Revista Perspectivas Online: Biológicas & Saúde	Retrospective (VI)	To evaluate the epidemiological profile of pregnant women with human papillomavirus treated at an Outpatient Clinic for Sexually Transmitted Infections in a municipality on the border between Brazil and Paraguay.
02	Liang et al., 2018 ⁽¹³⁾	China	Reproductive Health	Case-control (III)	To investigate socioeconomic and lifestyle factors associated with HPV infection in pregnant women.
03	Sousa et al., 2018 ⁽¹⁴⁾	Brazil	Revista Pan-Amazônica de Saúde	Cross-sectional (VI)	To determine the prevalence of human papillomavirus (HPV) infection of the uterine cervix in pregnant women in the municipality of Imperatriz, state of Maranhão, Brazil.
04	Elukunbi et al., 2019 ⁽¹⁵⁾	Nigeria	Journal of Immunoassay and Immunochemistry	Cross-sectional (VI)	To identify characteristics of pregnant women infected with HPV.
05	Jordan et al., 2020 ⁽¹⁶⁾	Chile	Revista chilena de infectologia	Cross-sectional (VI)	Knowing the prevalence of genital HPV infections, identifying the clinical-epidemiological factors associated with this prevalence.
06	Værnesbranden et al., 2021 ⁽¹⁷⁾	Norway	International Journal of Infectious Diseases	Cohort (III)	To identify the prevalence of HPV in mid-pregnancy and childbirth.

*LE - Level of evidence.
Source: Data obtained in the study, 2022.

Table 2: Main factors associated with HPV infection in pregnant women, Recife (PE), Brazil, 2022.

ID	Sample; average age	Main results
01	46; 19,8	None of the pregnant women were aware of HPV infection during pregnancy. The following epidemiological characteristics indicated in the literature as facilitators of acquiring HPV infection were identified, such as: smokers (82.60%); use of oral contraceptives (69.56%) and multiparity (78.26%). We found 9.2% of pregnant women with intracervical neoplasia.
02	198; 28,15	Data analysis showed that alcohol consumption during pregnancy was the strongest significant factor (OR = 3.35, 95% CI* = 1.40-8.03, p = 0.007) when comparing the case group (HPV positive) with the control group (HPV negative).
03	167; 25,3	None of the pregnant women were aware of HPV infection during pregnancy. single/separated/widowed pregnant women were four times more likely to acquire HPV infection than married women.
04	93; 30,62	The overall HPV seroprevalence was 5.38% (5/93). The highest prevalence of infection was recorded in the age group from 26 to 35 (6.3%; 4/64) years, indicating young age as a possible risk factor for the occurrence of infection.
05	505; 28,4	The prevalence of total HPV carriers was 30.7%, and of these 71.6% corresponded to high risk (mainly HPV 16 [35.1%], 58 [10.8%] and 31 [8.1%]). HPV detection was higher in women aged 15 to 24 years and with more sexual partners.
06	757; 32,3	Several risk factors were significantly associated with mid-pregnancy HPV prevalence: being a single mother (OR€ 0.9, 95% CI* 0.9–1.0); alcohol intake during pregnancy (OR€ 1.4, 95%CI* 1.0–2.0).

Notes: *CI 95% - Confidence Interval 95%; €OR - Odds Ratio
Source: Data obtained in the study, 2022.

sociated with a higher risk of infection during pregnancy, which was identified in two studies. ^(14,17) In this context, researchers point out that, because single women are exposed to a greater number of sexual partners, they could be more exposed to the virus, since, associated with low education, contraceptive methods may not be used correctly by this population. ⁽¹²⁾

It was found that alcohol consumption during pregnancy was also associated with a higher risk factor for HPV infection. ^(13,17) For a number of reasons, alcohol consumption during pregnancy is an especially important factor in advising expectant mothers to avoid it. Alcohol can be a potent modulator of immune function that can lead to immune deficiency and increased suscepti-

bility to various chronic and infectious diseases. ⁽²³⁾

Not only chronic alcohol abuse, but also acute and moderate consumption can adversely affect the immune system. ⁽²⁴⁾ Normal defense responses to various pathogens are divided into two phases: the first phase is an inflammatory reaction, which provides protection against the immediate effects of infection, and

the second phase involves the development of immunity to the pathogen. Alcohol consumption is known to interfere with both phases of the normal immune response.⁽²⁴⁾

From these identifications, knowledge of these risk factors is essential for the adoption of preventive measures. HPV is highly prevalent in women of reproductive age and pregnancy and is of great public health interest because of its unambiguous link to cancers of the lower genital tract. It is also responsible

for genital warts, which can affect pregnancy, as well as having the potential for vertical and horizontal transmission to the neonate.⁽²⁵⁾

CONCLUSION

It was found that some factors may be associated with the presence of HPV infection in pregnant women, such as sociodemographic and maternal characteristics. Most pregnant women are still unaware of how HPV infection can oc-

cur, in addition to not having sufficient knowledge about preventive methods and forms of diagnosis, such as from the Pap smear.

In this way, it is necessary that health professionals working in Primary Care have a closer look, in order to contribute to the dissemination of information, especially in relation to STIs, as well as in the promotion of public policies, with strategies aimed at this audience. 🌱

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