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Cervical HPV infection in Brazil: systematic review

ABSTRACT

OBJECTIVE: To assess the prevalence of human papillomavirus (HPV) infection in women in Brazil.

METHODS: A systematic literature review was conducted with an active search in PubMed and Virtual Health Library databases using the terms "human papillomavirus," "HPV," "prevalence," and "Brazil". Of 155 articles retrieved, 82 were selected after reading their title and abstract. After a thorough examination, 14 articles were included in the study.

RESULTS: The 14 articles selected were published between 1989 and 2008 and comprised studies from four Brazilian macroregions (Southeast – 43%; South – 21.4%; Northeast – 21.4%; and North – 7.1%). Nine were cross-sectional studies. Eight articles used polymerase chain reaction and seven used hybrid capture for HPV detection. The study samples ranged from 49 to 2,329 women. The overall prevalence of HPV cervical infection was between 13.7% and 54.3%; and women with cytologically normal results had 10% to 24.5% prevalence of HPV cervical infection. Four articles described the most common HPV types.

CONCLUSIONS: The cytology techniques available use different classifications leading to different HPV prevalence estimates. However, considering the studies individually according to the detection technique used, the HPV prevalence has increased. HPV16 was the most prevalent type among women, regardless of the cytology result. The concentration of studies in the Southeast region, especially in metropolitan regions, evidences that further investigations are needed to improve information coverage of Brazilian women.

DESCRIPTORS: Papillomavirus Infections, epidemiology. Uterine Cervical. Neoplasms, prevention & control. Scientific and Technical Publications. Review.

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INTRODUCTION

Cervical cancer is the sixth most common cancer in the general population and the second most common among women.[39] In Brazil it is estimated 20,000 new cases of cervical cancer per year, an estimated rate of 20 per 100,000.[a] Mortality rates from cervical cancer show a steady trend with significant reductions in capital cities.[60,b] There is epidemiological evidence showing that human papillomavirus (HPV) infection is necessary but not sufficient for the development of cervical cancer.[5,35] Low screening coverage and changes in exposure to risk

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[a] Ministério da Saúde. Secretaria de Atenção à Saúde. Instituto Nacional de Câncer. Coordenação de Prevenção e Vigilância. Estimativa 2008: Incidência de câncer no Brasil. Rio de Janeiro; 2007.
[b] Gamarra CJ. Magnitude da mortalidade por câncer do colo do útero no Brasil, 1996-2005 [doctoral thesis]. Rio de Janeiro: Instituto de Medicina Social da Universidade do Estado do Rio de Janeiro; 2009.

factors for HPV infection have been described in the analysis of the epidemiology of cervical cancer.[6,34]

Studies on the prevalence of HPV infection published in Brazil mostly analyzed data from women who sought health services for screening or treatment. Many of them showed exclusively data of women with abnormal cervical cytology results. HPV detection methods and terminology used for reporting results have improved, which may influence the assessment of exposure to HPV and cytological diagnosis. Moreover, the findings have not been analyzed together, making it difficult to understand the distribution of this infection based on the literature.

The lack of consistent results on the magnitude of cervical cancer creates limitations to the planning of surveillance and control actions. A critical review of studies of Brazilian women on the estimated prevalence of HPV infection may provide epidemiological knowledge necessary for strengthening and redirecting policies for cervical cancer control. The objective of the present study was to assess the prevalence of HPV infection among Brazilian women, especially in women with normal cytology results, as this estimate would be close to the prevalence of exposure to HPV in the general population.

METHODS

A systematic review of studies on HPV infection in Brazilian women was conducted. There were reviewed publications indexed in the Medical Literature Analysis and Retrieval System (Medline), accessed through PubMed database, the Latin American and Caribbean Health Sciences (LILACS), Cochrane Library, and Scientific Electronic Library Online (SciELO). No period of publication was pre-defined. Two independent reviewers used a free search strategy using the terms "human papillomavirus," "prevalence," and "Brazil" and the Boolean operators "NOT HIV" and "NOT pregnant." This search was conducted in April 2009. All articles were retrieved in both PubMed and Virtual Health Library.

There were retrieved 155 references that were assessed based on their titles and abstracts and sorted by date of publication (Figure). Most (133) were from PubMed/MEDLINE. There were selected 82 articles that met the inclusion criteria: they must be conducted with Brazilian women and include cervical cytology results, HPV detection methods, the overall prevalence of HPV in women with cervical cytology results and the prevalence by HPV type in these women.

There were excluded from the review studies on women only with abnormal cervical cytology, immunocompromised or women who underwent hysterectomy or other surgical procedures with excision of the entire uterus or part of it including the cervix; and studies only reporting laboratory test results with no reference to the population of women studied.

A thorough examination of the articles retrieved was performed and an additional 22 articles were found in the references of these articles. The examination of the entire content of the texts led to the identification of other exclusion criteria, previously not identified, and the exclusion of more articles. The articles were then submitted to a process of data extraction and quality assessment by two independent reviewers.

In the case of publications with data from the same study, we chose to include the article that was most recent, with the largest sample and study period, and more complete data. A total of 14 articles were selected for the study.

All articles retrieved were stored using the open source application Jabref Reference Manager, v. 2.5.[c]

Data on methodology and study results from the articles were stored in a separate instrument. The authors of three of the articles selected were contacted for complete information.

For quality assessment it was used an instrument consisting of 24 items, adapted from 22 criteria proposed by the STROBE Statement based on epidemiological investigation principles.[64] This assessment aimed to identify the relevance of articles for the preparation of a panel where information could be easily identified and captured to guide recommendations for future studies.

Eighteen criteria items were used for assessing the quality of the studies and six for assessing availability of data for extraction. Each question was given either a score of 0 or 1 (no or yes). The highest score of articles reporting hybrid capture (HC) for HPV detection was 23, and for those reporting polymerase chain reaction (PCR) was 24 as item 12 was only applicable to the latter. Agreement of results was measured by the intraclass correlation coefficient (ICC) proposed by Shrout[58] (1998) and estimated using SPSS, version 17.0.

RESULTS

Table 1 shows the distribution of the articles included in the review. Three of them were published between 1989 and 1995;[63,18,19] and the remaining were published from the year 2000.[4,7,8,22,25,28,31,32,41,44,61] Three articles were originally published in Portuguese and 11 in English language journals.

Most studies were conducted in the Southeast region, followed by the South and Northeast (three articles each), and the North (one article). One article is about a study conducted in two regions, Northeast and Southeast.

As for study design, nine were cross-sectional, two were cohort, two were case-control and one was an experimental study. Four articles reported the prevalence of HPV in women with any cervical cytology test results, and ten reported the prevalence in women by cytology results, including women with normal cytology.

The samples studied ranged from 49 to 2,329 women.[7,63] Eight articles included up to 1,000 women and six

Table 1. Description and quality assessment of the studies selected.

Study	Site	Study design	n	n of cervical cytology subgroup	Age (years)	Quality score[a]
Villa & Franco,[63] 1989	Recife/PE and São Paulo/SP	Cross-sectional	2,329	normal – 2,301; class III or higher (LSIL or higher) – 28	≤ 25 to ≥ 42	21.5
Eluf-Neto et al,[18] 1994	São Paulo/SP	Case-control	376	normal (controls) – 190;cancer (cases) – 186	cases: 52.1 (mean) controls: 52.4 (mean)	20.0
Franco et al,[19] 1995	João Pessoa/PB	Cross-sectional	525	normal – 502; LSIL – 15; HSIL – 8	41.2 years old (mean)	16.5
Becker et al,[4] 2000	Porto Alegre/RS	Cross-sectional	956	normal – 867; ASCUS– 62; LSIL– 21; HSIL–6	16–70 (mean: 39.1; SD=11.48 years)	21.5
Lorenzato et al,[32] 2000	Recife/PE	Nested case-control	448	normal – 295; ASCUS/AGUS –38; LSIL – 42; HSIL – 42; cancer – 21	cases – 13–84 (mean: 36.5; SD =13)	20.0
Lopes et al,[31] 2001	São Paulo/SP	Cross-sectional	209	–	32.4 (mean)	13.5
Brito et al,[7] 2005	Brazilian Indian villages,[b] Novo Repartimento and Itupiranga/PA	Cross-sectional	49	normal – 31; ASCUS – 4; AGUS – 3; LSIL – 6; HSIL – 4	women older than 10	17.5
Trottier et al,[61] 2006	São Paulo/SP	Cohort	2,050	–	15–59	19.5
Holanda Jr. et al,[25] 2006	Crato, Sobral, Pedra Branca, Redenção, Ibiapina/CE	Intervention	878	–	15–69	17.0
Girianelli et al,[22] 2006	Duque de Caxias and Nova Iguaçu/RJ	Cross-sectional	1,777	conventional cervical cytology: normal – 1604; ASCUS/AGUS – 94; LSIL – 38; HSIL – 39; liquid-based cervical cytology: normal – 1447; ASCUS/AGUS – 171; LSIL – 28; HSIL – 80	25–59	21.5
Carestiato et al,[8] 2006	State of Rio de Janeiro	Cross-sectional	1,854	normal – 672; ASCUS – 152; HPV cytopathic; effect – 429; LSIL – 476; HSIL – 125	11–70 (mean 27.2 years)	19.0
Rama et al,[41] 2008	São Paulo and Campinas/SP	Cross-sectional	2,300	normal – 2080; ASCUS – 122; AGUS – 7; LSIL – 46; HSIL – 27; cancer – 2	15–64 (mean 35.7 years)	23.0
Krambeck et al,[28] 2008	Blumenau/SC	Cross-sectional	84	normal – 57; NIC I – 9; NIC 2 – 13; NIC 3 – 3	15–60 (mean 32.6 years)	19.0
Rosa et al,[44] 2008	Porto Alegre/RS	Cohort	1,204	normal – 1099; ASCUS/HPV cytopathic effect – 85; LSIL ("NIC I = LIEBG") – 16; HSIL ("NIC II-NIC III=LIEAG") – 4	43 (mean, SD =13)	19.0

[a] The quality assessment scoring was based on a 1-23 scale for hybrid capture studies and 1–24 for polymerase chain reaction (PCR) studies.
[b] Parakanã, Paranatinga, Maroxewara, Paranowaona, Itaigoa and Inaxinganga
SP: São Paulo; PB: Paraíba; RS: Rio Grande do Sul; PE: Pernambuco; PA: Pará; CE: Ceará; RJ: Rio de Janeiro; SC: Santa Catarina

Table 2. Characteristics of studies with the use of polymerase chain reaction (PCR) for HPV DNA detection and prevalence of HPV infection among Brazilian women.

Study	Site	Primer used for typing	Study population		HPV prevalence	
			General population	Women with normal cervical cytology	General population	Women with normal cervical cytology
Eluf-Neto et al[18] 1994	São Paulo, SP	GP5/GP6	-	194	-	17.0%
Franco et al[19] 1995	João Pessoa, PB	MY09/MY11	525	-	18.3%	-
Becker et al[4] 2000	Porto Alegre, RS	generic probe	956	867	23.0%	20.5%
Lorenzato et al[32] 2000[a]	Recife, PE	MY09/MY11	-	295	-	14.3%
Trottier et al[61] 2006	São Paulo, SP	MY09/MY11	2,050	-	16.8%	-
Krambeck et al[28] 2008	Blumenau, SC	MY09/MY11	84	57	28.6%	18.0%
Rosa et al[44] 2008	Porto Alegre, RS	MY09/MY11	1,204	1,099	24.6%	24.5%

[a] Only tested high-risk HPV
SP: São Paulo; PB: Paraíba; RS: Rio Grande do Sul; PE: Pernambuco; SC: Santa Catarina.

included more than 1,000 women. Eleven articles described that women were stratified according to their cervical cytology results while no references in this regard were made in the remaining articles.

The minimum age was "older than ten years" and the maximum age was 84 years.[7,32] Four articles reported only the mean age of the women studied. In 12 articles women were recruited from health services and two articles were population-based studies.

The mean score in the quality assessment was 19.18. All articles met at least 15 out of the 18 epidemiological research criteria and at least four criteria for data extraction.

There was a significant agreement between scores assigned by reviewers, ICC = 0.81 (95% CI: 0.408, 0.939, p = 0.003).

With respect to the techniques for cervical cytology most articles reported the use of conventional cervical cytology. Three articles reported using liquid-based and conventional cytology in the same study and sample of women. One article reported the use of "cytology" but the technique applied could not be identified. As for terminology used for reporting test results, the Bethesda System for Reporting Cervical Cytology was mentioned in ten articles, the Bethesda System including the Richart Classification in two articles, Papanicolaou Classification in one article and one article did not mention any classification.

As for HPV detection method, eight articles reported the use of PCR and seven HC. Two articles described both techniques and one article reported in situ hybridization, not currently employed.

Tables 2–4 present the HPV prevalence estimates obtained from the articles studied. Table 2 shows the studies that reported PCR for HPV detection. Six of them reported the use of MY09/11 primer set, one used the GP5/GP6 prime and another one used a generic probe.

Table 3. Characteristics of studies with the use of hybrid capture for HPV DNA detection and prevalence of HPV infection among Brazilian women.

Study	Site	Study population		HPV prevalence	
		General population	Women with normal cervical cytology	General population	Women with normal cervical cytology
Becker et al[4] 2000	Porto Alegre, RS	956	867	14.0%	11.6%
Lopes et al[31] 2001	São Paulo, SP	209	-	21.1%	-
Girianelli et al[22] 2006	Nova Iguaçu e Duque de Caxias, RJ	1,777	1,604	13.7%	10.4% (AR 7.2%; BR 3.2%)
Holanda Jr. et al[25] 2006	Crato, Sobral, Pedra Branca, Redenção e Ibiapina, CE	878	-	33.9%	-
Carestiato et al[8] 2006	Niterói, RJ	1,854	672	54.3%	12.6% (AR 7.4%; BR 1.8%; ambos 3.4%)
Rama et al[41] 2008	São Paulo and Campinas, SP	2,300	2,080	17.8%	14.3%

HR: High-risk HPV for cervical cancer; LR: Low-risk HPV for cervical cancer; SP: São Paulo; RS: Rio Grande do Sul; CE: Ceará; RJ: Rio de Janeiro.

The overall prevalence of HPV infection among women, not stratified by cervical cytology results, ranged from 16.8% (Trottier et al[61], 2006) to 28.6% (Krambeck et al[28], 2008). Eluf-Neto et al[18] (1994) and Lorenzato et al[32] (2000) articles were not included in the overall HPV prevalence as they were case-control studies. However, data from controls are presented in Table 2 that shows the studies on women without any lesions. In the articles that included women with normal cytology tested with PCR, the number of women ranged from 57[28] to 1,099.[19]

Two articles showed the overall prevalence of HPV types detected by PCR (Table 4). Franco et al[19] (1995) showed that the overall prevalence of low-risk HPV infection was between 0.2% (HPV54 and HPV68) and 2.3% (HPV11). The same study showed an overall prevalence of high-risk HPV infection between 0.2% (HPV68) and 5.3% (HPV16); 4.0% were not detected.

In Rosa et al study[44] (2008), the overall high-risk HPV prevalence was 3.3% (HPV18) to 18.6% (HPV16).

Two studies estimated the prevalence of HPV types by cytology results, including women with normal cytology (Table 4). Eluf-Neto et al[18] (1994) reported a 50.0% prevalence of high-risk HPV types (HPV18) in women with low-grade squamous intraepithelial lesion (LSIL), of low malignant potential and high potential for cure. Women with normal cytology had 0.5% prevalence of low-risk HPV infection (HPV6); 6.3% prevalence of multiple HPV types; 10.0% prevalence of non-detected HPV types; and 0.5% (HPV18) to 5.3% (HPV16) prevalence of high-risk HPV. Krambeck et al[28] (2008) reported among women with normal cytology 2.0% (HPV6 and HPV54) and 4.0% (HPV72) prevalence of low-risk HPV. The prevalence of HPV CP4773 was 2.0% regardless of risk classification. In women with LSIL the prevalence of low-risk HPV was 4.5%

Table 4. Overall prevalence of HPV types detected by polymerase chain reaction (PCR) and by cytology results.

HPV type detected		Overall prevalence[a]		Prevalence by cervical cytology			
		Franco et al[19]	Rosa et al[14]	Eluf-Neto et al[18,b]	Krambeck et al[28,c]		
Cervical cytology result		All	All	Normal	Normal	LSIL	HSIL
Low-risk							
	HPV 6	2.1%	-	0.5%	2.0%	-	-
	HPV 11	2.3%	-	-	-	4.5%	-
	HPV 54	0.2%	-	-	2.0%	-	-
	HPV 62	-	-	-	-	4.5%	-
	HPV 72	-	-	-	4.0%	-	-
	HPV 81	-	-	-	-	4.5%	-
High-risk							
	HPV 16	5.3%	18.6%	5.3%	2.0%	9.0%	67.0%
	HPV 18	2.1%	3.3%	0.5%	-	-	-
	HPV 31	0.6%	15.8%	-	-	-	-
	HPV 33	2.5%	-	-	2.0%	-	-
	HPV 35	0.8%	-	-	-	-	-
	HPV 45	0.6%	-	-	-	4.5%	-
	HPV 52	0.8%	-	-	-	4.5%	-
	HPV 53	1.0%	-	-	4.0%	-	-
	HPV 56	0.4%	-	-	-	-	-
	HPV 58	1.3%	-	-	-	-	-
	HPV 66	1.3%	-	-	-	4.5%	-
	HPV 68	0.2%	-	-	-	-	-
HPV CP4773[d]		-	-	-	2.0%	-	-
Not detected		4.0%	-	10.0%	-	9.0%	-
Multiple types		-	-	6.3%	-	-	-

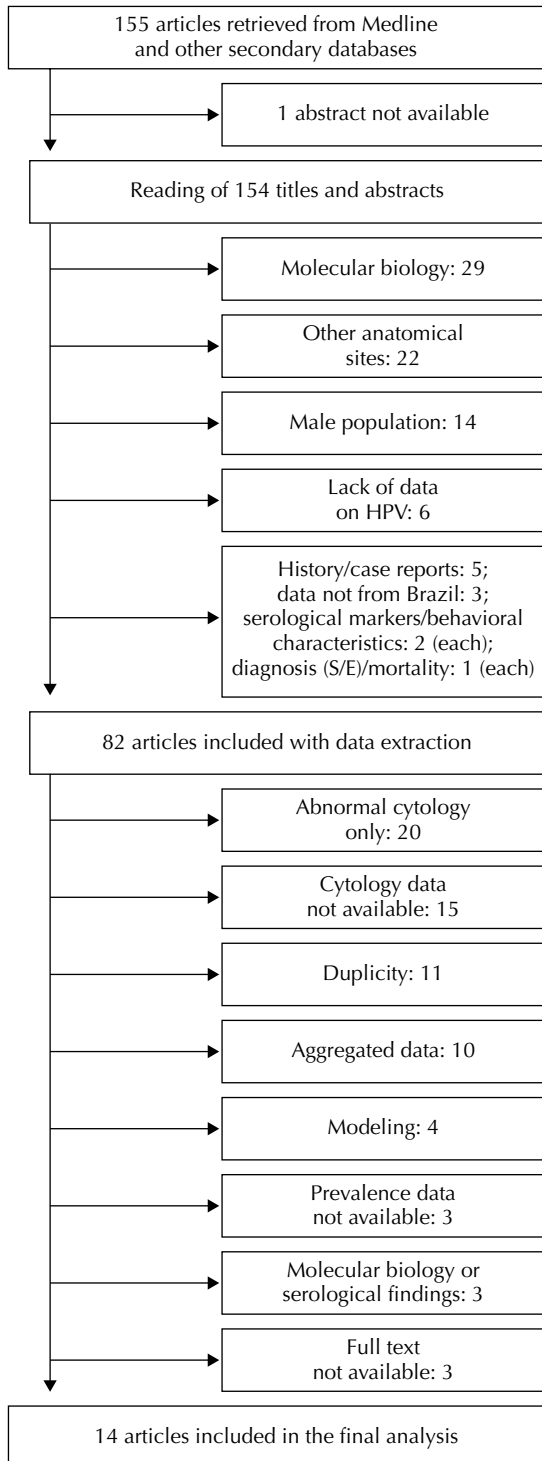[a] women with all cervical cytology results were aggregated
[b] GP5/GP6 primer set
[c] MY09/MY11 primer set
[d] not classified according to cervical cancer risk
SP: São Paulo; PB: Paraíba; RS: Rio Grande do Sul; SC: Santa Catarina.

(HPV 11, HPV 62 and HPV 81), and the same was seen for high-risk HPV types (HPV45, HPV52 and HPV66); 9.0% of HPV types were not detected. In women with high-grade squamous intraepithelial lesion (HSIL) including moderate to severe dysplastic, precancerous lesions, and carcinoma in situ, the prevalence of HPV was 67.0% (HPV16).

The studies that reported the use of HC for HPV detection are shown in Table 3. The prevalence of HPV infection in all women was between 13.7%[22] and 54.3%.[8] The number of women with normal cytology ranged from 672[8] to 2.080.[41] One study[31] reporting the use of HC described only the overall prevalence and no information was given on the prevalence in women with normal cytology. In those women tested with HC, the prevalence of HPV infection ranged from 10.4%[22] to 14.3%.[41] Two articles reported HPV groups detected in women with normal cytology, stratifying them into high- and low-risk. Girianelli et al[22] (2006) and Holanda et al[25] (2006) reported the prevalences of HPV in physician and self-collected samples. Two studies reported the prevalence of HPV by groups: women with normal cytology had prevalence between 1.8% and 3.2% for low-risk HPV and 7.2% and 7.4% for high-risk HPV.[8,22]

Only one study[7] described HPV detection by both techniques (PCR and HC); however, the prevalences were not reported by technique used. The overall prevalence was 42.8% and the prevalence in women with normal cytology (n=30) was 29.0%. This study is highly relevant since it shows the prevalence in a very specific population of Brazilian Indian women.[7]

DISCUSSION

The overall prevalence of cervical HPV infection ranged from 13.7% to 54.3%. The prevalence of HPV infection among women with normal cytology ranged between 10.4% and 24.5%. Meta-analyses conducted in other settings or that included data from South America countries including Brazil showed prevalence rates in women with normal cytology between 10.0% and 15.9%.[2,16]

The articles selected showed differences regarding: technique used in cervical cytology; terminology used for reporting results; and methods used for HPV detection or typing.

The articles reported HPV DNA detection and typing of high and low-risk types in women with normal cytology. Studies including women with normal cytology results have gained importance because of improved accuracy of estimates from population-based studies. Studies that include only women with abnormal cytology who were referred to health services because of previous abnormal findings or clinical symptoms tend to overestimate the prevalence of HPV infection in the general population. Studies that include women recruited in family planning or women's health care units tend to report low or intermediate prevalences.

Figure 1. Flowchart of the selection process of studies on the prevalence of human papilloma virus infection among Brazilian women.

Thus, prevalence estimates obtained in women recruited at health care services can be over- or underestimated,[65] and understanding the dynamics of HPV infection in women with normal cytology is expected to minimize selection bias.[16] Knowing the distribution of HPV infection is essential for the development of new HPV tests and for the assessment of the impact of vaccines in different scenarios.[62]

The analysis of the distribution of studies over time showed an increasing number of articles published since 2000. It is parallel to the growth of epidemiological research on HPV infection following the establishment of a causal relationship between HPV and cervical cancer. In addition, advances in technologies and methods for HPV detection and typing have improved the estimates.

The cytology techniques available use different classifications leading to different HPV prevalence estimates, which prevents a direct comparison between results. The prevalent HPV type varies depending on cervical cytology results, either normal or not. HPV prevalence also varies according to cytological abnormalities found (type-specific; by cytology results; or both).[2,14] Also, prevalences vary with the use of certain primers for HPV detection that may be more sensitive to some viral types than others.[13] Therefore, the sampling issue should be considered from a statistical and inferential perspective. Noncompliance of these aspects may introduce bias in the estimates.[40]

The increased use of liquid-based cytology and HC in recent years led to lower prevalence estimates compared to those reported in studies using conventional cytology and PCR. These inconsistencies, which sometimes are seen within a group of women, support the findings of other studies reporting different sensitivity and positive predictive value of cytology techniques, methods of sample collection (physician or self-collected samples), and HPV detection methods by comparing them and often with colposcopy plus biopsy, using the histopathological result as reference.[1,26,68]

The present review found that the prevalences estimated using PCR are generally higher than those using HC, although no differences in variability between estimates obtained with PCR and HC are seen (ANOVA, p>0.2861). Articles reporting the use of HC are more common in recent years and show lower estimates.[4,8,22,25,31,41] They are studies with larger samples (956 to 2,300 women) than those using PCR (84 to 2,050 women). Only Trottier et al[61] (2006) and Rosa et al[44] (2008) studied samples with more than 1,000 women, which may have affected the precision of their estimates. Thus, the use of PCR seems to produce increased HPV prevalences. For example, Becker et al[4] (2000) reported 23.0% prevalence with PCR and 14.0% with HC in the same sample of

956 women. HC seems to produce more consistent estimates with less variability over time. However, considering the studies individually according to the detection technique used, higher HPV prevalences were described in more recent studies. Among the articles that reported the use of PCR, the first one (a 1994 study[18]) showed a prevalence of 17% and the last one (a 2008 study[44]), of 24.5%. Among those reporting the use of HC, the prevalences were 11.6% and 14.3% in 2000[4] and 2008,[42] respectively.

In the present review estimates of HPV prevalence by type and cytology results are in part coherent with the findings in the literature. A meta-analysis[67] carried out with women across all continents found that HPV16 was the most prevalent type among women, regardless of the cytology result. However, estimates of HPV prevalence among women with normal cytology described in these studies are not consistent concerning the level of importance of HPV18. Studies using HC reported a prevalence of high-risk HPV about two times higher than that of low-risk HPV. As for low-risk types, we found low prevalence of HPV6 in women with normal cytology in contrast to data reported by other study[67] that detected it only in women with LSIL. Although eight studies used PCR and were able to detect HPV types in all women studied, only two of them reported HPV types found in women with normal cytology. This fact stresses the need for further investigating the prevalence of HPV types by Brazilian states and macroregions and exploring differences in estimates that may due to regional population characteristics.

The analysis of the prevalence and types of HPV by age was prevented by the fact that different age groups were studied and data was not available for each group.

There was a concentration of studies in women in the Southeast region, followed by South, then Northeast and North, and no reports were found for the Central-west region. We identified two large groups of longitudinal studies comprising several substudies using the same sample: the Latin American Screening Study (LAMS)[17,23,24,29,30,38,42,50,51,59] and the Ludwig-McGill Study.[20,21,27,33,45-48,53-57] Both were prospective cohort studies for expanding the knowledge about incidence, persistence, and regression of HPV infection.

Although there were retrieved research studies on the subject matter of interest conducted in the state of Rio de Janeiro,[9-11] Minas Gerais,[3,36,37] and the Federal District,[12,15] these articles did not provide prevalence estimates including women with normal cytology and thus were not included in the present review.

The concentration of studies in the Southeast region, especially in metropolitan regions, evidences that further investigations are needed to improve information

coverage of Brazilian women. Brazil has Because of Brazil's continental dimension and socioeconomic and cultural diversity, it is reasonable to assume that Brazilian women have different risks for factors associated with HPV infection. These differences should be considered in the development of cervical cancer actions and decisions must be taken based on regional contexts and the resolving capacity of health services. Increased screening coverage with assurance of appropriate follow-up treatment will certainly promote a more favorable scenario.[52,66]

The articles included in this review do not allow to performing a meta-analysis since the period in which they were published coincided with great improvements in molecular biology techniques. It per se may lead to the calculation of a summary measure based on studies developed in the wake of technology advances in terms of diagnosis. Thus, a meta-analysis would provide results that are difficult to interpret and inaccurate. A systematic review including 22 studies was conducted in the United States in 2005 and pointed out similar arguments for not performing a meta-analysis.[43]

With respect to the limitations of this review, it is possible that other articles of interest were not identified with the search strategy. However, we believe this is unlikely to have occurred considering that the main databases were searched and less important articles were also retrieved.[49]

As for the completeness of the articles selected, one should bear in mind that they do not always describe all data from studies. Three out of seven authors contacted provided complementary information. Some study designs did not allow prevalence estimates as they were based on the number of cervical cytology slides examined instead of total women included in the sample. In conclusion, studies to estimate the prevalence and distribution of HPV types among women with normal cytology should be encouraged in Brazil, especially in deprived areas with difficult access to health services. It is crucial to assess factors associated with regression, progression and persistence of HPV cervical infection and to identify those groups at high risk and susceptibility to infection for the development of prevention and control strategies.

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