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Prevalence of cervical HPV infection in women with systemic lupus erythematosus: A systematic review and meta-analysis

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ABSTRACT

Objective: The objectives of this systematic review and meta-regression were: 1) to compare the prevalence of cervical HPV infection between SLE patients and healthy controls and 2) to evaluate the relationship between cervical HPV infection and traditional and SLE-related risk factors for cervical HPV infection in these patients.
Methods: We conducted a systematic literature review (PubMed, Cochrane Library, Embase, Virtual Health Library and SciELO databases) following PRISMA guidelines and using meta-regression to investigate the pooled prevalence of cervical HPV infection in adult women with SLE. The articles included were independently evaluated by two investigators who extracted information on study characteristics, defined outcomes, risk of bias and summarized strength of evidence [Quality of evidence using the Oxford Centre for evidence-based medicine (EBM) Levels of Evidence]. Using meta-regression, we further analyzed whether factors such as multiple sexual partners and immunosuppressive therapy were associated with HPV prevalence. We evaluated the quality of evidence included using the Oxford Centre for EBM levels of evidence. Pooled odds ratios (ORs) and 95% confidence intervals (CI) were calculated for studies providing data on HPV prevalence in women with SLE and in healthy controls.
Results: A total of 687 articles were identified; 9 full-text articles examining the prevalence of cervical HPV infection in SLE women were included, comprising 751 SLE women. Eight studies employed PCR using general primers. The HPV prevalence varied from 3.1% to 80.7%. In the random effects meta-analysis, the pooled prevalence of cervical HPV infection in SLE vs. controls was 34.15% (95% CI: 19.6%–52.5%) vs. 15.3% (95% CI 0.79–27.8%), OR = 2.87 (95% CI: 2.20–3.76) $p < .0001$, with large between-study heterogeneity ($I^2 = 95.4\%$). When only SLE women were evaluated, meta-regression showed no significant differences between patients with and without a background of multiple sexual partners and any immunosuppressive therapy. In addition, the prevalence of cervical HPV infection did not significantly differ between SLE patients on azathioprine or cyclophosphamide.
Conclusions: This meta-analysis suggests that the prevalence of cervical HPV infection is higher in SLE women than in healthy controls. However, multiple sexual partners and any immunosuppressive therapy or specific immunosuppressive treatment (azathioprine and cyclophosphamide) were not associated with the prevalence of cervical HPV infection.

Abbreviations: CI.UB, confidence interval upper bound; EBM, evidence-based medicine; GCT, glucocorticoid; HGSIL, high-grade squamous intraepithelial lesions; HPV, human papillomavirus; HR, high-risk; IC, interval confidence; INTRCPT, intercept; MSP, multiple sexual partners; PCR, polymerase chain reaction; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLE, systemic lupus erythematosus

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1. Introduction

Systemic lupus erythematosus (SLE) is a chronic condition that may affect young women [1] and is associated with activation of the activation autoreactive T and B cells and the release of proinflammatory cytokines that may increase the risk of some cancers [2]. In addition, the immunosuppressive therapy frequently administrated in autoimmune disorders such as SLE may be responsible, in part, for a decrease in the host immune response against malignancy [3–5]. The risk of infection is also increased in these patients.

The human papillomavirus (HPV) is the main risk factor for cervical cancer, which is the leading cause of cancer mortality in women in the majority of developing countries [6,7]. Most HPV infections are transient and spontaneously clear in less than one year, but the persistence of high-risk HPV infections in the cervix, especially HPV types 16 and 18, are related to the progression of cervical dysplastic lesions [8]. In immunocompromised hosts, the risk of HPV infection has been described as much higher than in the general population, due to high-loads and persistent infection with high-risk HPV genotypes [9]. In addition, the immunocompromised host is less likely to clear spontaneously and produces more severe cytopathology [10].

An increased risk of cervical pre-malignant and malignant lesions has been reported in SLE women. In Swedish registers [11], SLE was a risk factor for cervical neoplasia, in particular for pre-malignant cervical lesions. In a recent meta-analysis, the risk of high-grade squamous intraepithelial lesions (HGSIL) was significantly greater in SLE women compared with healthy female controls [12]. Several SLE cohort studies have found a high risk of HPV-associated cancer [11,13,14]. Early detection of pre-malignant lesions may have decrease morbidity and mortality in the general population because population-based screening programs have significantly contributed to early recognition and treatment [15]. Although there is an increased risk, no specific HPV guidelines have been developed for patients with systemic autoimmune diseases.

The prevalence of cervical HPV infection in women with SLE has been summarized in several observational studies [16–20], although no statistical pooling of the results has been made. In addition, the results on the influence of immunosuppressive drugs on HPV infection in these patients are unclear. This led us to carry out a systematic review and meta-regression of the available evidence to determine (i) the prevalence of cervical HPV infection in patients with SLE and (ii) whether immunosuppressive therapy is a risk factor for cervical HPV infection in these patients.

2. Methods

2.1. Search strategy

A systematic literature review was conducted using the following electronic databases: PubMed (1946-Week 2, January 2018), Cochrane Library (1985-Week 2, Week 2, January 2018), EMBASE (1974-Week 2, January 2018), Virtual Health Library (VHL) (1998-Week 2, January 2018), and SciELO (1997-Week 2, January 2018) for published studies. We followed the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analysis, see Supplementary file 1) for the meta-analysis of observational studies [21] in the data extraction, analysis, and reporting. References of all included full-text articles were hand-searched in order to search for references that seemed to be relevant for the review. We combined Medical Subject Heading (MeSH) terms and Key words (or exploded terms where possible) using Boolean operators with the following search strategy (see Supplementary file 2): (HPV OR human papillomavirus OR papillomaviridae) AND (systemic lupus erythematosus OR SLE OR lupus OR lupus nephritis). In addition, each MeSH term/ Key word was translated into DeCS (Health Sciences Descriptors), which permits navigation between records and sources of information through controlled concepts and is organized in Spanish and English, in order to search the Virtual Health Library and SciELO databases. The articles were downloaded into Mendeley Desktop and duplicates were deleted. No limits regarding publication type were set. All titles were screened by one reviewer. Abstracts and full text articles were reviewed in the search for eligible studies. Articles published in Spanish and English were considered.

2.2. Eligibility criteria

Inclusion criteria were: observational (retrospective or prospective cohort, case-control and cross sectional) studies in which (1) the HPV prevalence in SLE women and controls or only SLE cases is analyzed; (2) specimens for HPV detection were obtained from the cervix; (3) information about HPV detection methods was clearly stated. Articles were not eligible if they included the same data published in another eligible study.

2.3. Data extraction

We extracted from every article: first author, year of publication, country where the study was carried out, study design, race, the number of SLE patients and/or controls, the mean age, glucocorticoid use and dose in SLE participants, HPV detection method, the general primers used for HPV detection by PCR and HPV genotyping methods. Data extraction was conducted by two reviewers independently (CMP and MGC); two databases were constructed and the results were compared and disagreements resolved by consensus between the two researchers.

2.4. Risk of bias (quality) assessment

The Oxford Centre for Evidence-Based Medicine (EBM): 2011 Levels of Evidence criteria were used to assess the strength of the evidence for all studies included [22]. Clinical evidence was categorized into 5 levels ranging from I to V as follows: Level 1 Systematic review of cross-sectional studies with consistently applied reference standard and blinding; Level 2 Individual cross-sectional studies with consistently applied reference standard and blinding; Level 3 Non-consecutive studies, or studies without consistently applied reference standards; Level 4 Case-control studies, or “poor or non-independent reference standard; Level 5 Mechanism-based reasoning. Any disagreement was resolved through discussion and investigator consensus. Studies were not excluded from the systematic review based on this quality assessment.

2.5. Statistical analysis

Since not all studies had information of cases and controls simultaneously (see for example Amaral 2017) we fitted a multilevel linear (mixed-effects) model for the logit-transformed proportion (i.e. log odds). The multilevel structure has two levels: the first corresponds to a single effect measure, several of which can be nested in a single study (or author). This model is similar to that where odds ratios are analyzed, with the additional possibility of including studies where data on only one group is available [23].

We analyzed two data sets: 1) studies involving information on cases and controls and 2) studies involving only cases. For case-control studies we fit a model with fixed effects associated with the case and control status and random effects associated with the study (or author) level. For a subset of studies that had information on multiple sexual partners (9 studies) we fit several models exploring fixed effect interactions between case-control status and multiple sexual partners. The most parsimonious mean structure was chosen on the basis of the likelihood ratio test and AIC criteria. Similarly, for the cases data set we fit a model with fixed effects associated with HPV status (positive or negative) and for the subset of studies with information on multiple sexual partners we fit several models exploring fixed effect interactions

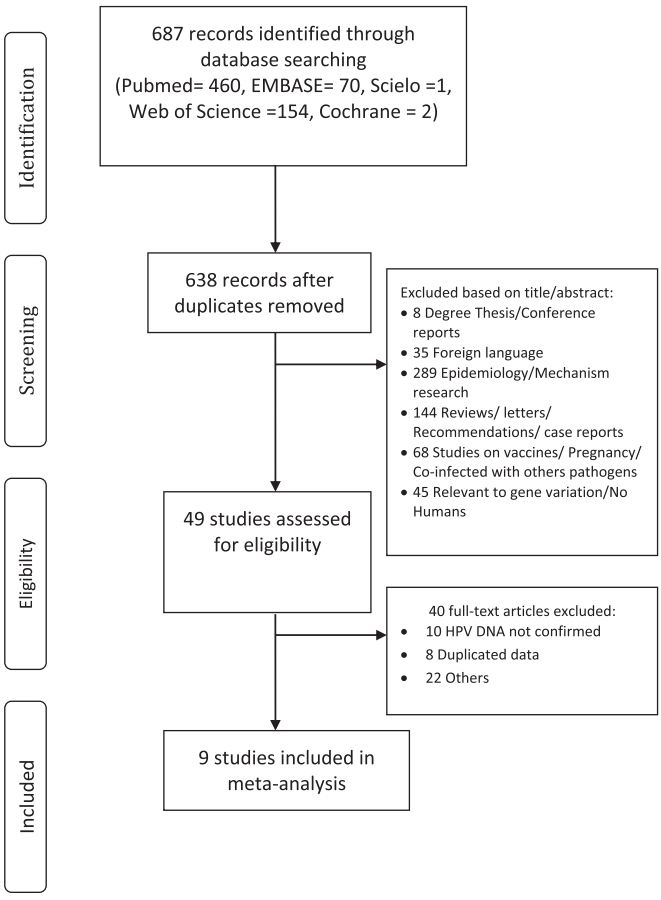

Fig. 1. PRISMA flow diagram for identification of studies for meta-analysis.

between HPV status and multiple sexual partners. As before, the random effect at the level of author was included and the most parsimonious mean structure was chosen.

Heterogeneity was calculated using Higgins's (I^2) test statistic. The I^2 test showed the proportion of observed dispersion that was real rather than spurious and was expressed as a ratio ranging from 0% to 100%. I^2 values of 25%, 50%, and 75% were qualitatively classified as low, moderate, and high, respectively.

The rank correlation test for funnel plot asymmetry was assessed to check for publication bias. The analysis was performed with the R 3.3.2 metafor package.

3. Results

3.1. Characteristics of the studies

The systematic search with the defined parameters retrieved 687 records. After duplicates were removed there were 638 potentially relevant articles. Based on title or abstract, 49 were chosen for full text review and assessed for eligibility and the remaining 589 were excluded (see detailed information in Fig. 1). Finally, 9 studies that examined the prevalence of cervical HPV in SLE women were included (Fig. 1), [17,18,20,24–29]. The studies were published between 2007 and 2017 and included 751 SLE cases. A description of the articles included is shown in Table 1. The studies were conducted in Latin America ($n = 5$) [20,26–29], Asia ($n = 3$) [17,18,25] and Europe [24] ($n = 1$). The size of the studies was relatively small: in 4 studies [18,24–26] the sample size was < 50 cases of SLE.

For the detection of cervical HPV infection, PCR-based methods were used in 8 studies [17,20,24–29] and non-PCR-based methods (immunostaining detection) in 1 study [18] (Table 2).

3.2. Prevalence of cervical HPV infection in SLE patients and controls

Fig. 2 contains a forest plot of the 9 selected studies and shows the prevalence of cervical HPV in healthy women and SLE women for each study and the pooled prevalence of HPV for each group. The prevalence of cervical HPV varied markedly from 3.1% [18] to 80.7% [28]. In the random effects meta-analysis, the pooled prevalence of cervical HPV infection in SLE vs. controls was 34.15% (95% CI: 19.6%–52.5%) vs. 15.3% (95% CI 0.79–27.8%), OR = 2.87 (95% CI 2.20–3.76) $p < .0001$, with wide between-study heterogeneity ($I^2 = 95.4\%$).

Publication bias was not evident from the funnel plot ($p = .2912$) (Table 3 and Supplementary file 3). The traditional risk factor of multiple sexual partners was analyzed in SLE patients with and without cervical HPV infection. Multiple sexual partners was measured using different definitions in each study. Three or more sexual partners were considered in two studies [17,27], four or more sexual partners in two studies [20,26] and five or more in one study [24]. We found no effect of multiple sexual partners on cervical HPV infection in SLE women.

3.3. Prevalence of cervical HPV infection in SLE patients with and without immunosuppressive therapy

The prevalence of cervical HPV infection in SLE women taking any immunosuppressive therapy at the time of the study did not significantly differ from that of SLE patients without this therapy (78.3%, 95% CI 58.2–90.3% vs. 77.5%, 95% CI 58.0–89.6%; $p = .85$) (Fig. 3).

Table 1
Characteristics of studies included comparing SLE cases and controls.

Author, year	Setting	Ethnicity	SLE patients		Controls		GCT use in SLE (%)	GCT dose[a]	Level of evidence
			Total	Age[a]	Total	Age[a]			
Nath 2007	UK	Caucasian 90%	26	39	67	29	85%	Median 0.13 mg/kg/day, range 0.02–0.3 mg/kg/day	Level 2
Lee 2010	Korean	Asian	134	40	4595	NR	75.9%	Prednisolone ≤20 mg/day	Level 2
Klumb 2010	Brazil	Caucasian 34.1% Afro-Brazilian 35.8%	173	40	217	37	NR	NR	Level 3
Yu 2012	Hong Kong	Asian	46	NR	29	NR	93% in HPV-positive 77% in HPV-negative	NR	Level 3
Rojo-Contreras 2012	Mexico	Hispanic	34	38	146	37	90.9%	Mean of 7.65 ± 9.17 mg/day	Level 3
Mendoza-Pinto 2013	Mexico	Hispanic	148	43	0	–	NR	Mean of 10.5 ± 6.8 mg/day	Level 3
Lyrio 2013	Brazil	NR	88	41	70	29	NR	NR	Level 3
Al-Sherbeni 2017	Egypt	32	32	31	20	30	100%	Mean of 25.2 ± 10.6 mg/day	Level 3
Amaral 2017	Brazil	NR	70	NR	0	–	NR	NR	Level 4

GCT: glucocorticoid; NR: Not reported.
[a] GCT dose described in each study included.

Table 2
Description of studies reporting the prevalence of HPV DNA in SLE patients.

Author, year	HPV detection method	General Primers used for HPV detection in PCR	HPV genotyping method	HPV types detected	HPV prevalence	
					General population	SLE women
Nath 2007	PCR	MY09/MY11 HPV-	PCR using type specific primers	16	6.6%	57.7%
Lee 2010	PCR (HPV chip, Mygene)	MY09/MY11 GP5+/GP6+	HPV chip, Mygene	16 types of high-risk HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 54, 56, 58, 59, 66, 68) and 8 types of low-risk HPV (6, 11, 34, 40, 42, 43, 44, 70)	7.9%	24.6%
Klum 2010	PCR	MY09/MY11 GP5+/GP6	PCR using type specific primers	6, 11, 16 and 18	7.3%	20.1%
Yu 2012	PCR	PGMY09/PGMY11	Linear Array	37 types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 56, 57, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, and CP6108)	24.1%	32.6%
Rojo-Contreras 2012	PCR	CPI/CPII	RSA1 digestion pattern of PCR products	14 types (5, 6, 8, 11, 16, 18, 31, 33, 35, 39, 45, 51, 56, 58)	30.8%	14.7%
Mendoza-Pinto 2013	PCR	PGMY09/ PGMY11	Linear array	37 types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 56, 57, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, and CP6108)	–	29%
Lyrio 2013	Nested-PCR	MY09/MY11 (first round) GP5+/GP6 (second round)	No genotyping	NR	35.7%	80.7%
Al-Sherbeni 2017	Immunostaining detection	–	Inmmuno detection	Monoclonal antibody anti HPV16	0%	3.1%
Amaral 2017	PCR	MY09/MY11	qPCR with specific probes	9 types (6, 11, 16, 18, 31, 33, 35, 52, 58)	–	22.8%

HR: High-risk; HPV: human papillomavirus; NR: Not reported; PCR: polymerase chain reaction; qPCR: quantitative PCR.

Four studies analyzed the role of azathioprine and cyclophosphamide, either oral or intravenous [17,25,27,29]. The prevalence of cervical HPV infection did not significantly differ in patients with or without either immunosuppressant therapy (azathioprine or cyclophosphamide) (Fig. 4).

4. Discussion

Evidence, including national registers and systematic reviews, has demonstrated that women with SLE are at increased risk of HSIL [11,12,14]. An increased rate of HPV infection could be, in part, responsible for the increased frequency of cervical dysplasia in those patients. Several observational studies have reported the prevalence of cervical HPV in SLE women compared with healthy controls [17,20,24,28]. However, the findings have not been analyzed together, making it difficult to interpret the distribution of infection based on individual studies. To the best of our knowledge, our report is the first meta-analysis of the prevalence of cervical HPV in women with SLE.

In this systematic review, overall, the prevalence of cervical HPV infection in SLE women was higher than in healthy controls, and the pooled prevalence of cervical HPV infection was 34.15% (95% CI: 19.6%–52.5%). The pooled OR was 2.87 (95% CI: 2.20–3.76), indicating that the odds of cervical HPV infection were greater in SLE women than in healthy women. A large meta-analysis estimated the prevalence of cervical HPV DNA in women with normal cytology worldwide and the estimated prevalence was 11.7% (95% CI 11.6%–11.7%) [30]. The increased HPV prevalence in SLE patients may be related to acquiring more new infections, delayed clearance of infections, or greater reactivation of latent HPV infections. The increased rate of HPV infection could also be responsible for the increased risk of cervical dysplasia. In fact, we previously showed that Latin-American SLE patients have a higher prevalence of high risk-HPV than low risk-HPV, with a prevalence of 20.9% and 8.1%, respectively [31]. In addition, we showed that 13,5% of SLE patients present HPV co-infection (defined as ≥ 2 HPV genotypes) in a first measurement and that in patients with persistence (defined as HPV in cervical samples over six months or in 2 samples) co-infection was a significant associated factor when compared to patients with clearance. The different HPV prevalences in the studies analyzed in the present meta-analysis could be the result of the method used, and the low prevalence of HPV reported by Al-Sherbeni et al. [18] could be the result of the low sensitivity of the diagnostic method (immunohistochemistry). The other reports used PCR, but the general primers differed in some studies and the HPV genotypes detected by each study also differed and could have modified the sensitivity of the method. The prevalence of HPV may have varied in the study populations, as reported in a meta-analysis [32]. However, independently of the diagnostic method and the study population, we found differences in the prevalence of HPV prevalence between SLE patients and the control groups.

Further insights into the increased risk of HPV infection in SLE patients have been described recently. Several factors, such as the immune production of chemokines and cytokines and their interplay may influence the high prevalence of HPV infections in SLE patients. Interleukin-17 (IL-17) has been identified as a critical immunosuppressive [33] determinant in HPV-associated epithelial hyperplasia (premalignant lesions), and these results are corroborated by reports on elevated IL-17 concentrations in cervical secretions of women with persistent high risk HPV infection compared with specimens from HPV-negative controls. These results could be interesting in light of the recent implications of IL-17 and Th17 cells and their important roles in the pathogenesis of SLE [34]. Furthermore, HPV has evolved mechanisms capable of inhibiting key host antivirus natural and adaptive responses, including the modulation of the cascade of inflammatory or immunoregulatory cytokines and chemokines and interferon (IFN) production, as well as the activity of cytotoxic T cells and natural killer cells, and the humoral antibody response [35]. These HPV

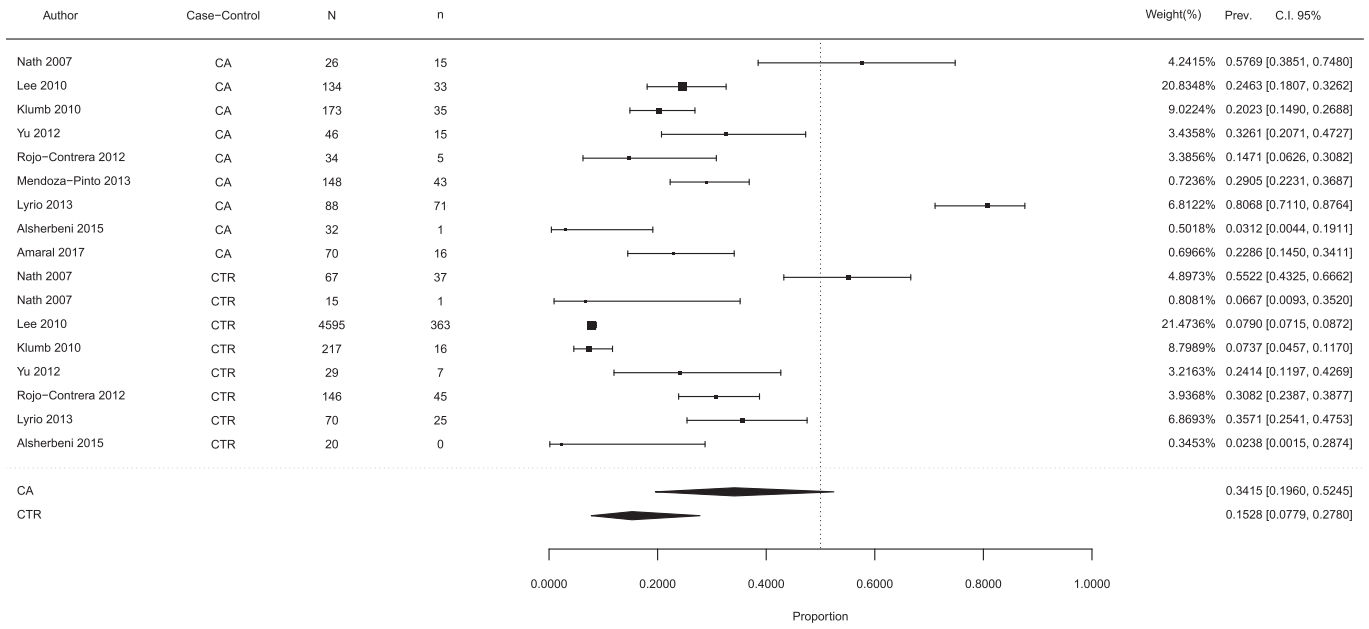

Fig. 2. Forest plot of studies meta-analyzed: Cervical HPV infection prevalence between SLE patients and controls.
CA: case; C.I.: Confidence Interval; CTR: Control; Prev: Prevalence.

Table 3
Results of the most parsimonious models for the groups of studies.

Group	Mean structure	Estimate	ci.lb	ci.ub	pval
Case-controls	intrcpt	−1.7127	−2.4708	−0.9546	< 0.0001
	Cases	1.056	0.7872	1.3247	< 0.0001
	$Sigma^2$	1.2107	0.4373	4.3989	< 0.0001
	I^2				95.42743
Multiple sexual partners	intrcpt	−1.7222	−2.6954	−0.749	0.0005
	Individual	0.986	0.524	1.4481	< 0.0001
	MSP	0.0117	−0.023	0.0463	0.5091
	$Sigma^2$	−0.0042	−0.0305	0.022	0.7513
	I^2	0.8324	0.268	4.1482	< 0.0001
Immunosuppresive therapy	intrcpt	1.2869	0.3323	2.2414	0.0082
	Individual	−0.0453	−0.5163	0.4257	0.8504
	$Sigma^2$	0.9365	0.1798	6.7102	< 0.0001
	I^2				87.4806

Heterogeneity by means of Higgins's test.
Abbreviation: ci.lb.: confidence interval lower bound; ci.ub: confidence interval upper bound; MSP: multiple sexual partners.

infection mechanisms are important, given that SLE patients have altered innate immune responses to IFN-I, with IFN-α being the dominant mediator, and could be central to the pathogenesis of SLE [36].

Evidence of a possible role of HPV in SLE patients suggests a mechanism behind this association, with immune cross-reactivity between human proteins and HPV proteins possibly being the cause of SLE onset [37–39]. Therefore, it would be necessary to promote HPV vaccines that convey no homology to the human proteome to avoid the possibility of cross-reaction especially in individuals prone to developing SLE [40].

The role of immunosuppressive therapy on the prevalence of cervical HPV infection in women with SLE is unclear. A study which demonstrated a threefold increase in the prevalence of HPV infection in SLE patients compared with controls also found that this high prevalence was associated with the use of immunosuppressive drugs [20]. Likewise, taking into account the fact that cervical neoplasia is caused by HPV infection which persists and causes the malignant transformation of infected cervical cells, in a case-control analysis with SLE women with cervical neoplasia defined as cases and SLE women without cervical neoplasia (controls), performed in 113 women, there were no significant differences between cases vs. controls for factors related to SLE such as the use of immunosuppressive drugs or disease severity [41]. By contrast, the use of immunosuppressive drugs was not associated with a higher prevalence of genital HPV infection [28]. In our systematic review, immunosuppressive therapy was evaluated using meta-regression analysis in SLE patients. Firstly, overall immunosuppressive drugs were analyzed; we found no association with cervical HPV infection. Secondly, when possible, individual immunosuppressive drugs (azathioprine and cyclophosphamide) were measured. Neither azathioprine nor cyclophosphamide was associated with the prevalence of cervical HPV infection according to the pooled analysis of four cross-sectional studies. A possible explanation for these findings could be the lack of duration and cumulative exposure measurements of almost all studies evaluating the relationship between immunosuppressive drugs and cervical HPV infection. Therefore, the influence of immunosuppression due to therapy for lupus control on the prevalence and incidence of HPV infection should be evaluated in further prospective studies analyzing the intensity of the exposure.

The study had some limitations. First, only studies published in Spanish and English were included, which might limit the results. Secondly, since the individual studies included did not determine the prevalence of HPV infection in patients with and without normal cervical cytology, we were not able to evaluate the differentiated frequency of HPV infection according to cytology findings. Thirdly, because most studies detected HPV using PCR, it was not possible to determine differences in HPV prevalence in terms of HPV detection methods. Moreover, the prevalence of specific high-risk HPV genotypes was not pooled in our systematic review due mainly to few studies reporting these data. Fourthly, studies have described having multiple HPV infections as a risk factor for HPV persistence. Multiple infections may increase the overall viral load, which may overcome immune control. It may be speculated that this risk is even stronger in immunocompromised patients. Unfortunately, we were not able to obtain data on multiple infections from original studies because most studies do not describe multiple HPV genotypes infection according to immunosuppression therapies. Fifthly, there was clear heterogeneity

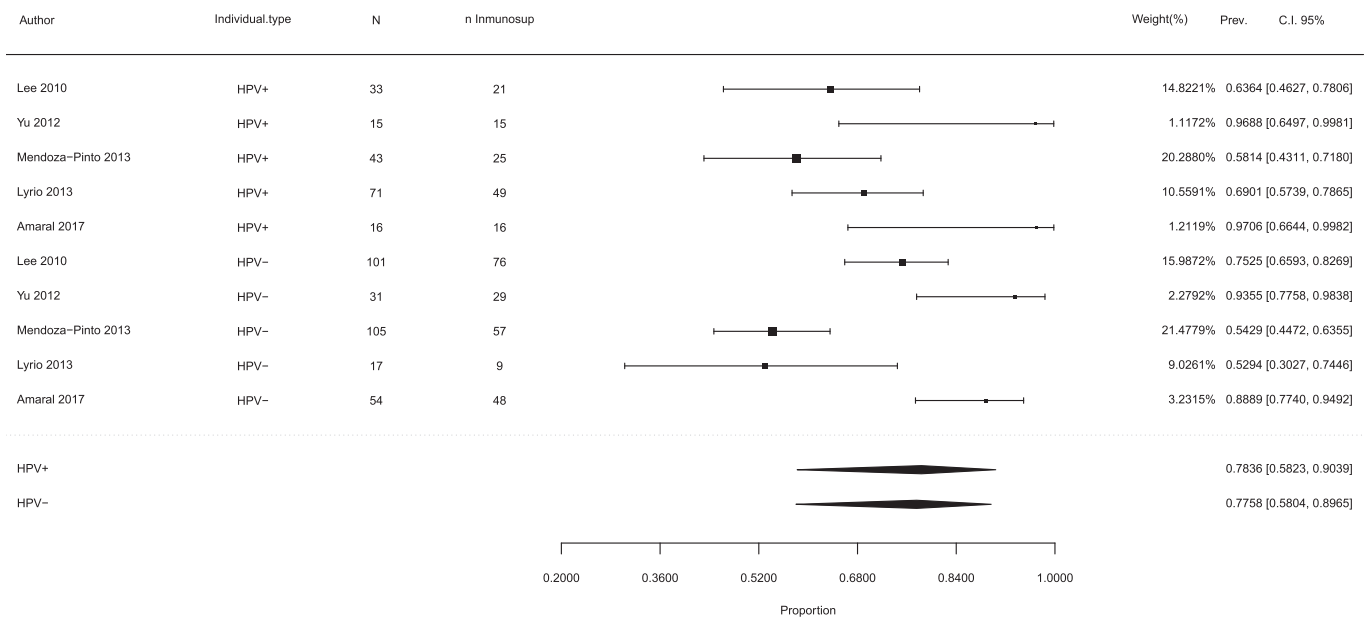

Fig. 3. Forest plot of studies meta-analyzed: Cervical HPV infection prevalence between SLE patients with and without any immunosuppressive therapy. C.I.: Confidence Interval; HPV: Human papillomavirus; Prev: Prevalence.

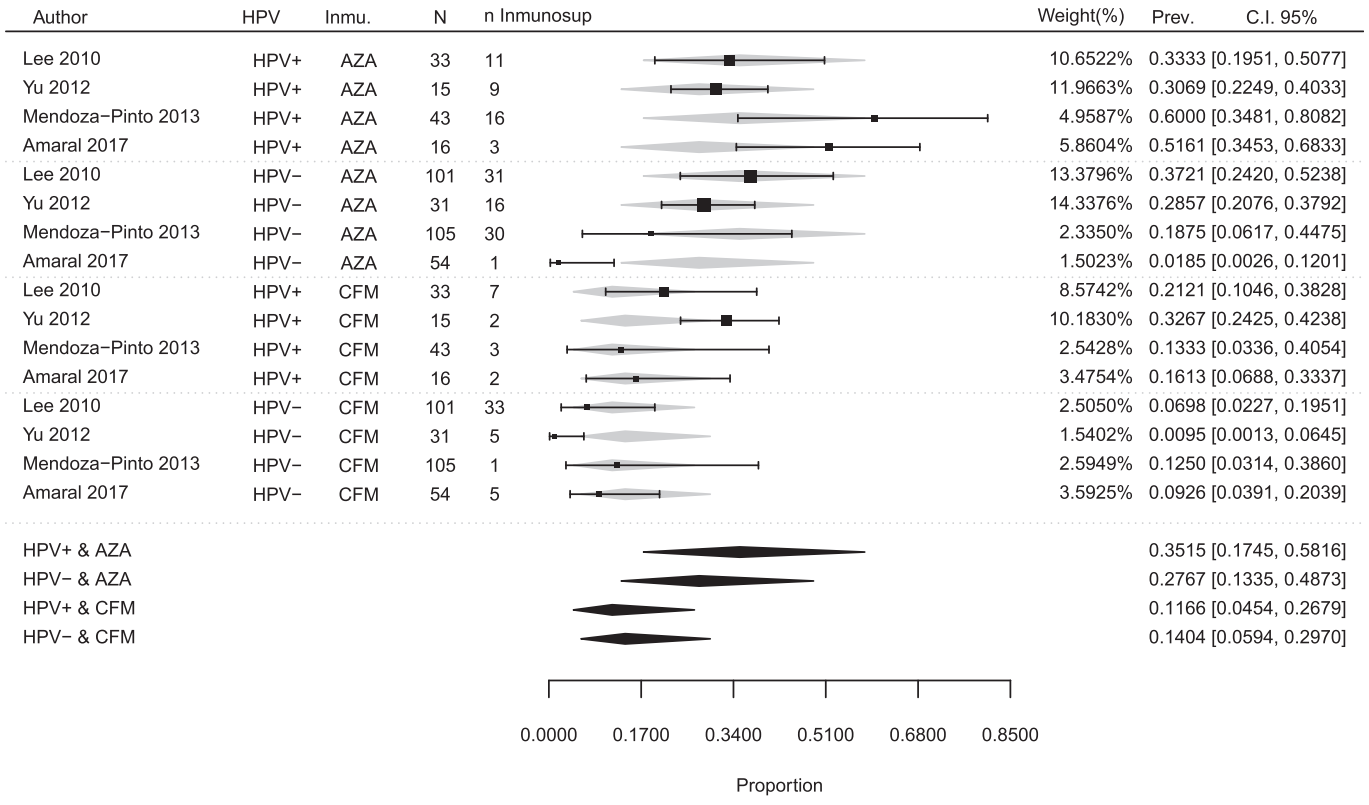

Fig. 4. Forest plot of studies meta-analyzed: Cervical HPV infection prevalence between SLE patients with azathioprine or cyclophosphamide. AZA: azathioprine; C.I.: Confidence Interval; CFM: cyclophosphamide; HPV: Human papillomavirus; Prev: Prevalence.

among the studies included, which may be attributed to the different settings from which the study population was derived. Finally, potential biases and confounders could not be prevented completely, since all studies included had cross-sectional designs and, therefore, reversal causality cannot be excluded.

In summary, our systematic review and meta-regressions suggests a significantly increased risk of cervical HPV infection in SLE women compared with healthy controls. This increased susceptibility and/or

reluctant clearing may be due to immune dysfunction secondary to SLE or impaired immune surveillance due to immunosuppressive drugs. However, not any immunosuppressive therapy, whether azathioprine or cyclophosphamide, was associated with the increased rate of cervical HPV infection. Since potential biases or confounders could not be ruled out completely, our results should be verified by further studies.

Based on the present results, we encourage rheumatologists and physicians evaluating SLE patients to follow cervical cancer screening guidelines closely, as indicated by research groups like the United States Preventive Services Task Force [42], which recommends that women aged 21 to 65 years should have Pap smear screening every 3 years or, for women aged 30 to 65 years, the Pap smear may be combined with HPV testing, which extends the screening interval to every 5 years. Following these guidelines will allow a preventive health care approach for SLE patients with respect to cervical cancer.

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Conflict of interest

All authors declare no financial conflict of interest.

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