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REVIEW

Association between genital mycoplasmas infection and human papillomavirus infection, abnormal cervical cytopathology, and cervical cancer: a systematic review and meta-analysis

Hui Ye[1,2] · Tiange Song[2] · Xi Zeng[1] · Lin Li[1] · Minmin Hou[1] · Mingrong Xi[1,3]

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Abstract

Background Some studies demonstrated that female genital mycoplasmas play important roles in human papillomavirus (HPV) infection, abnormal cervical cytopathology, and cervical cancer. However, those results remained inconclusive. We aimed to perform a systematic review and meta-analysis to investigate the association between female genital mycoplasmas and those disorders.

Methods Computerized databases were comprehensively searched before 26 January 2017. Pooled odd radios (ORs) and correlative 95% confidence intervals (CIs) were adopted to evaluate the strength of association.

Results Our meta-analysis included 22 studies with 16,181 participants. *Ureaplasma urealyticum* and *Ureaplasma parvum* were associated with a significantly increased risk of overall HPV infection (OR 1.57, 95% CI 1.05–2.34; OR 3.02, 95% CI 2.10–4.33, respectively), and *U. urealyticum* and *Mycoplasma genitalium* were associated with a significantly increased risk of high-risk HPV infection (OR 1.37, 95% CI 1.05–1.80; OR 1.50, 95% CI 1.11–2.02, respectively). In addition, *U. urealyticum*, *U. parvum*, and *Mycoplasma hominis* were associated with a significantly increased risk of abnormal cervical cytopathology (OR 1.51, 95% CI 1.23–1.85; OR 1.41, 95% CI 1.10–1.80; OR 1.48, 95% CI 1.10–1.99, respectively).

Conclusion We found that *U. urealyticum* and *M. genitalium* may increase the risk of high-risk HPV infection, while *U. urealyticum*, *U. parvum*, and *M. hominis* may increase the risk of abnormal cervical cytopathology.

Keywords Mycoplasma · Ureaplasma · Human papillomavirus · Abnormal cervical cytopathology · Cervical cancer

Introduction

Epidemiological and laboratory evidence have shown that human papillomavirus (HPV) infections play an important role in the progression of uterine cervical dysplasia and squamous cell cervical carcinoma (SCC) [1, 2]. However, among all HPV infections, only a small fraction of them would progress to uterine cervical dysplasia (10% of HPV infections) and SCC (< 1% of HPV infections) [1–4], which suggests that other factors may participate in this variable natural history. Among various risk factors associated with HPV infections and progression to abnormal cervical cytopathology, sexually transmitted infections (STIs) other than HPV, commonly presented as genital mycoplasmas, are gradually becoming more important. Evidence accumulated that genital mycoplasmas infections could cause serious long-term adverse sequelae in women [5–7].

Genital mycoplasmas are groups of small free-living pathogenic bacterium belonging to class Mollicutes that

Hui Ye, Tiange Song, and Xi Zeng contributed equally to this work.

✉ Mingrong Xi
xmrjzz@126.com

[1] Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Number 20-9, Third Section of People's South Road, Chengdu 610000, China

[2] West China School of Medicine, Sichuan University, Chengdu 610000, China

[3] Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China

lives on the ciliated epithelial cells of the urinary and genital tracts in humans [8], generally transmitted through direct interaction between hosts—venereally through genitogenital or orogenital contact and vertically from mother to child (either in utero or at birth) [9]. Genital mycoplasmas often refer to six species that colonize in the genital tract, involving *Ureaplasma urealyticum*, *Ureaplasma parvum, Mycoplasma hominis*, *Mycoplasma genitalium*, *Mycoplasma primatum*, and *Mycoplasma spermatophilum*, the latter two of which are considered non-pathogenic for humans [10]. There is growing evidence suggesting that genital mycoplasmas have now become a group of common etiological pathogen in women and exerted adverse effects on female reproductive health [11]. Specifically, in a Britain national survey, *M. genitalium* was found in 1.3% (0.9–1.9%) women aged 16–44 years and 2.4% (1.2–4.8%) women aged 16–19 years [12]. In addition, a recent meta-analysis also demonstrated that *M. genitalium* infection was significantly associated with significantly increased risk of cervicitis, pelvic inflammatory disease, preterm birth, and spontaneous abortion [7]. Current studies indicated that mycoplasma infections may arouse those changes through inducing chromosomal alterations that may lead to transformation of mammalian cells, especially in a chronic pattern [13, 14].

In recent decades, a substantial number of epidemiological studies investigated the association between genital mycoplasmas infection and HPV infections, abnormal cervical cytopathology, and cervical cancer [15–17]. However, their results remained inconclusive. Therefore, we aimed to perform the first systemic review and meta-analysis to assess the association between genital mycoplasmas infection and HPV infections, abnormal cervical cytopathology, and cervical cancer.

Methods

Literature search

We searched all published studies regarding the association between the genital mycoplasmas infection and HPV infections, abnormal cervical cytopathology, and cervical cancer using computerized databases (Embase and PubMed) and by manually searching references of included studies. The databases were searched before 26 January 2017. The following strategy was employed: (Uterine Cervical Neoplasms OR cervical cancer OR uterine cervical dysplasia OR cervical precancerous lesions OR abnormal cervical cytology OR abnormal cervical cytopathology OR cervical intraepithelial neoplasia OR squamous intraepithelial lesion OR atypical squamous cells OR human papillomavirus) AND (ureaplasma OR mycoplasma).

Study selection

Two reviewers (HY and TS) independently selected the included studies based on previously established standards. The included studies must meet the following criteria: (1) original peer-reviewed English articles concerning the association between genital mycoplasmas and HPV infections and related disorders; (2) cross section, case–control, or cohort studies; and (3) studies contain adequate methods to assay genital mycoplasmas. Studies meeting the following criteria were excluded: (1) animal studies, genomic studies, and in-vitro experiments; (2) conference, review, guideline, letter, and editorials; and (3) non-sufficient data to assess the associations between genital mycoplasmas and above-mentioned disorders.

Data extraction and quality assessment

Two reviewers (HY and XZ) independently extracted the following items: first author, year of publication, study region, study design, sample size, recruitment period, source of study population, age range, pregnancy or not, genital mycoplasmas assay, numbers of patients presented with genital mycoplasma, or/and HPV infections. Discrepancies were solved by discussing among reviewers to reach consensus. We also performed quality assessment of the included studies, adopting the Newcastle–Ottawa Scale (NOS) for case–control or cohort studies and the Agency for Healthcare Research and Quality (AHRQ) for cross-sectional studies [18]. The NOS consists of nine items with three components: selection (4 scores); comparability (2 scores); and exposure belong to case–control or outcome belong to cohort (3 scores). A study is considered as high quality if it has a score ≥ 7 [19]. The AHRQ is composed of 11 items with yes/no/unclear options: the "yes" response is scored 1 and, otherwise, is scored 0, and 8–11 scores are regarded as high quality [20].

Data synthesis and statistical analysis

We calculated overall odds ratio (OR) and correlative 95% confidence interval (CI) to assess the strength of the association between the genital mycoplasma infection and HPV infections and related disorders. We utilized Q test and I^2 statistic to evaluate the heterogeneity between each study, and heterogeneity was considered significant if $p < 0.1$ or $I^2 > 50\%$ [21]. We used random effects model to generate the pooled OR if significant heterogeneity was found; otherwise, the fixed-effects model was used. In addition, we performed subgroup analysis based on different types of cervical cytopathology (LSIL group included low-grade

squamous intraepithelial lesion, cervical intraepithelial neoplasia I; HSIL group included high-grade squamous intraepithelial lesion, cervical intraepithelial neoplasia II or III.). We also performed Egger's asymmetry tests and visually examined funnel plots to evaluate potential publication bias [22, 23]. Besides, we performed sensitivity analysis by excluding individual studies separately from analysis. All data analyses were performed by Revman software (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.).

Results

Literature search

After removing the duplicate records from Embase and PubMed databases, a total of 225 records were recognized. After screening for title and abstract, we excluded 199 records due to irrelevant content. The remained 26 records were screened by reviewing the full text. We excluded two studies [24, 25] with duplicate recruited population and two studies [26, 27] without detailed data on mycoplasmas. Eventually, 22 studies with a total of 16,181 participants were included in this meta-analysis. The screening process is shown in Fig. 1. Most of these studies were case–control or cross-sectional studies, except McNicol's study, which was cohort design [28]. Among these studies, 12 studies [5, 6, 17, 29–37] reported *U. urealyticum*, 5 studies [5, 15, 32, 38, 39] reported *U. parvum*, 9 studies [5, 17, 28, 30, 35–39] reported *M. hominis*, and 8 studies [5, 16, 39–44] reported *M. genitalium*. Recruited control group included community-based women ($n=6$), hospital-based patients ($n=15$), and female sex workers ($n=2$). Among those 22 studies, 9 studies investigated non-pregnant women, 2 studies involved pregnant women, and the rest of studies ($n=11$) did not describe the status of pregnancy. The characteristics of eligible studies are presented in Table 1. The pooled results are shown in Table 2.

Association between genital mycoplasmas infection and HPV infections (Fig. 2)

U. urealyticum and HPV

Eight studies with a total of 7006 participants were included, and the pooled analysis showed that women infected with *U. urealyticum* had a significantly increased risk of HPV infections compared with *U. urealyticum*-negative women.

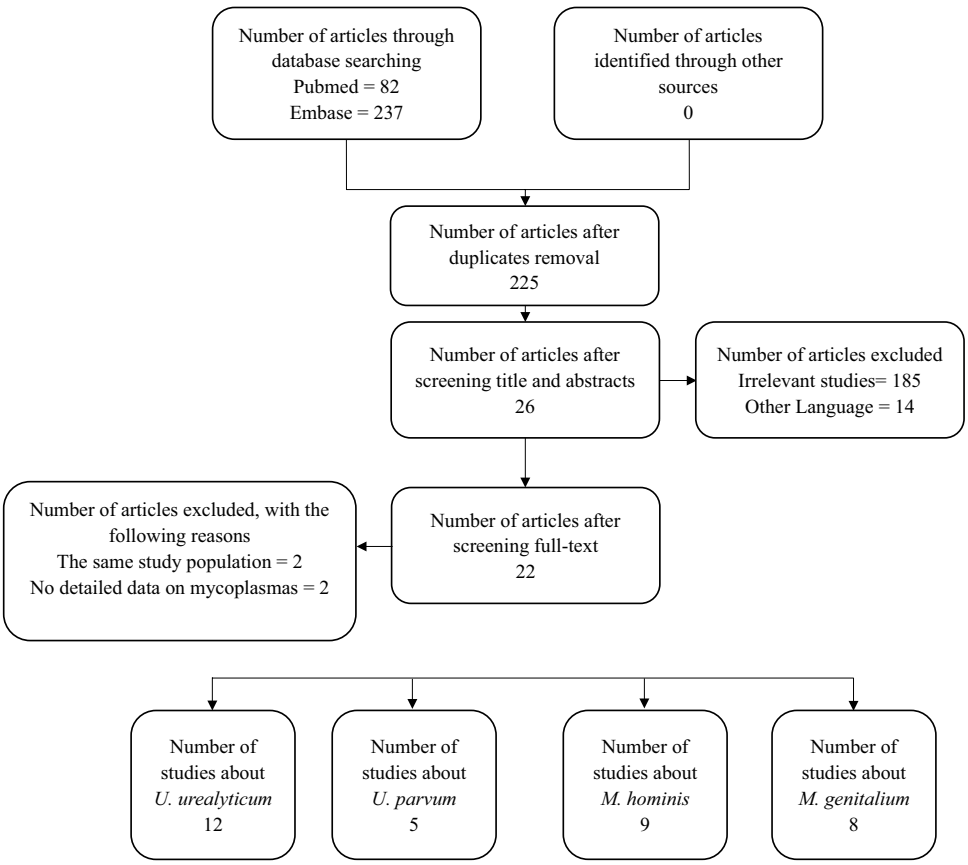

Fig. 1 Flow chart of study selection process

Table 1 Summary of eligible studies in the meta-analysis

References	Year	Country	Recruitment period	Study Design	Age range[a] (year)	Samples	Study population	Pregnancy	Mycoplasma assay	Sample size	Quality assessment
Liu et al. [6]	2016	China	From July 2013 to June 2014	Cross section	18–66	Cervical secretion	HB	NA	PCR	4290	8
Kim et al. [5]	2016	Korea	From January 2012 to May 2013.	Case–control	NA	Cervical secretion	HB	NA	PCR	1000	6
de Abreu et al. [39]	2016	Brazil	From August 2012 to March 2013	Cross section	18–68	Vaginal, cervical, endocervical secretion	CB	No	PCR	838	7
Casillas-Vega et al. [40]	2016	Mexico	From September 2013 to August 2014	Cross section	14–78	Endocervical secretion	HB	Yes	PCR	662	7
Camporiondo et al. [37]	2016	Italy	In March 2013	Cross section	34–60	Cervical secretion	CB	NA	PCR	309	8
Magaña-Contreras et al. [15]	2015	Mexico	From January 2013 to November 2014	Cross section	16–47	Ecto- and endo-cervix secretion	CB	No	PCR	201	8
Xiaolei et al. [28]	2014	China	From December 2011 to June 2012	Case–control	20–67	Cervical secretion	HB	NA	PCR	233	7
Dehon and McGowin [16]	2014	USA	From November 2012 to January 2013	Case–control	20–70	Cervical secretion	HB	NA	PCR	347	8
Choi et al. [29]	2014	Korea	From April 2008 and December 2012	Case–control	20–45	Cervicovaginal secretion	HB	No	PCR	124	7
Gomih-Alakija et al. [42]	2014	Kenya	From August 2009 to March 2011	Cross section	18–48	Cervicovaginal secretion	FSW	NA	TMA	350	8
Yin et al. [43]	2013	China	From July 2009 to September 2009	Cross section	16–NA	Cervical secretion	FSW	NA	PCR	802	8
Mendoza et al. [17]	2013	Paraguay	NA	Cross section	23–41	Endocervical secretion	CB	No	PCR	181	7
Biernat-Sudolska et al. [39]	2011	Poland	NA	Case–control	NA	Cervical secretion	CB	No	PCR	387	6
Verteramo et al. [31]	2009	Italy	From 2001 to 2006	Cross section	17–57	Ecto- and endo-cervix secretion	CB	No	Culture	857	8
Ekiel et al. [32]	2009	Poland	NA	Case–control	NA	Posterior vaginal fornix secretion	HB	No	Culture + PCR	182	8
Denks et al. [33]	2007	Estonia	From May 2004 to May 2005	Cross section	14–76	Cervical secretion	HB	No	PCR	798	9

Table 1 (continued)

References	Year	Country	Recruitment period	Study Design	Age range[a] (year)	Samples	Study population	Pregnancy	Mycoplasma assay	Sample size	Quality assessment
Lukic et al. [34]	2006	Italy	From June 2003 to December 2004	Case–control	18–50	Cervicovaginal secretion	HB	No	Culture	357	7
Pisani et al. [44]	1999	Italy	NA	Case–control	19–54	Cervical secretion	HB	NA	PCR	148	6
McNicol [28]	1994	Canada	From November 1988 to December 1989	Cohort	19–35	Vaginal secretion	HB	NA	Culture	19	8
Guijon et al. [35]	1992	Canada	NA	Case–control	17–33	Endocervical canal secretion	HB	Yes	Culture	185	7
Guijon et al. [36]	1985	Canada	NA	Case–control	NA	Endocervical canal secretion	HB	NA	Culture	87	6
Hare et al. [37]	1982	UK	NA	Case–control	NA	Endocervical mucus and cells	HB	NA	Culture	322	7

NA not available, *HB* hospital-based, *CB* community-based, *FSW* female sex worker, *PCR* polymerase chain reaction, *TMA* transcription-mediated amplification

[a]This indicates age range from minimum to maximum

Pooled OR was 1.57 (95% CI 1.05–2.34, $p = 0.03$), with $I^2 = 80\%$ for heterogeneity.

U. parvum and HPV

A total of three studies with 692 participants were included, and the pooled analysis demonstrated that *U. parvum* was associated with a significantly increased risk of HPV infections (OR 3.02, 95% CI 2.10–4.33, $p < 0.01$), and $I^2 = 55\%$ for heterogeneity.

M. hominis and HPV

A total of three studies with 549 participants were included, and we failed to find a significant statistical association of *M. hominis* infection with HPV infections. Pooled OR was 1.64 (95% CI 0.93–2.91, $p = 0.09$), with $I^2 = 0\%$ for heterogeneity.

Association between genital mycoplasmas and high-risk HPV infections (Fig. 3)

U. urealyticum and high-risk HPV

Pooled analysis of four studies with 6197 participants showed that *U. urealyticum* infection was associated with a significantly increased risk of high-risk HPV infections. Pooled OR was 1.37 (95% CI 1.05–1.80, $p = 0.02$), with $I^2 = 54\%$ for heterogeneity.

M. genitalium and high-risk HPV

A total of five studies with 3336 participants were included, and analysis showed that women infected with *M. genitalium* had a significantly increased risk of high-risk HPV infections. Pooled OR was 1.50 (95% CI 1.11–2.02, $p < 0.01$), with $I^2 = 6\%$ for heterogeneity.

Association between genital mycoplasmas and abnormal cervical cytopathology (Fig. 4)

U. urealyticum and abnormal cervical cytopathology

A total of 9 studies with 2751 participants were included in the pooled analysis, and the results demonstrated that *U. urealyticum* infection was associated with a significantly increased risk of abnormal cervical cytopathology. Pooled OR was 1.51 (95% CI 1.23–1.85, $p < 0.01$), with $I^2 = 36\%$ for heterogeneity. Based on different abnormal cervical cytopathologies, we performed a subgroup analysis by LSIL group and HSIL group. The pooled results from six studies showed that *U. urealyticum* infection was associated with both increased risk of LSIL (OR 2.02, 95% CI 1.49–2.74, $p < 0.01$, $I^2 = 47\%$) and HISL (OR 1.91, 95% CI

Table 2 Summary of pooled results

Study variable	Studies, No.	OR (95% CI)	*p*	Heterogeneity test	
				I^2, %	$P_{Q\ test}$
Abnormal cervical cytopathology					
U. urealyticum					
Overall	9	1.51 (1.23–1.85)	0.0001	36	0.13
LISL group	6	2.02 (1.49–2.74)	< 0.00001	47	0.09
HSIL group	6	1.91 (1.38–2.66)	0.09	48	0.09
U. parvum					
Overall	4	1.41 (1.10–1.80)	0.006	2	0.38
LISL group	4	1.27 (0.95–1.70)	0.11	0	0.86
HSIL group	3	1.71 (1.21–2.43)	0.002	70	0.04
M. hominis					
Overall	6	1.48 (1.10–1.99)	0.009	0	0.76
LISL group	3	1.30 (0.77–2.21)	0.33	0	0.79
HSIL group	3	1.28 (0.73–2.25)	0.39	0	0.97
M. genitalium					
Overall	5	0.78 (0.48–1.26)	0.31	22	0.28
LISL group	4	0.60 (0.34–1.05)	0.08	86	< 0.0001
HSIL group	3	1.72 (0.88–3.38)	0.12	56	0.1
High-risk HPV infections					
U. urealyticum	4	1.37 (1.05–1.80)	0.02	54	0.09
M. genitalium	5	1.50 (1.11–2.02)	0.008	6	0.37
HPV infections					
U. urealyticum	8	1.57 (1.05–2.34)	0.03	80	< 0.0001
U. parvum	3	3.02 (2.10–4.33)	< 0.00001	55	0.11
M. hominis	3	1.64 (0.93–2.91)	0.09	0	0.85

HPV human papillomavirus, *LSIL* group included low-grade squamous intraepithelial lesion, cervical intraepithelial neoplasia I, *HSIL* group included high-grade squamous intraepithelial lesion, cervical intraepithelial neoplasia II or III, *OR* odd ratio, *CI* confidence interval

1.38–2.66, $p = 0.09$, $I^2 = 48\%$) with moderate heterogeneity. Besides, as shown in Fig. 5, the symmetric shape of funnel plots suggested that there was no significant publication bias among the studies. The results of sensitivity analysis also remained stable when omitting each individual study.

U. parvum and abnormal cervical cytopathology

A total of four studies with 1750 participants were included, and pooled analysis showed that *U. parvum* infection was associated with a significantly increased risk of abnormal cervical cytopathology. Pooled OR was 1.41 (95% CI 1.10–1.80, $p = 0.006$), with $I^2 = 2\%$ for heterogeneity. The subgroup analysis showed that *U. parvum* infection increased risk of HSIL (OR 1.71, 95% CI 1.21–2.43, $p = 0.002$). Compared with HSIL group, we failed to find any significant result in LSIL group analysis (OR 1.27, 95% CI 0.95–1.70, $p = 0.11$).

M. hominis and abnormal cervical cytopathology

A total of 6 studies with 2037 participants were included. The results showed that *M. hominis* was associated with a significantly increased risk of abnormal cervical cytopathology. Pooled OR was 1.48 (95% CI 1.10–1.99, $p = 0.009$), with $I^2 = 0\%$ for heterogeneity. In the subgroup analysis, no significant association was found between *M. hominis* infection and LSIL (OR 1.30, 95% CI 0.77–2.21, $p = 0.33$) or HSIL (OR 1.28, 95% CI 0.73–2.25, $p = 0.39$) group.

M. genitalium and abnormal cervical cytopathology

A total of five studies with 2415 participants were included, no significant statistical association was found between *M. genitalium* infection and abnormal cervical cytopathology. Pooled OR was 0.78 (95% CI 0.48–1.26, $p = 0.31$), with $I^2 = 22\%$ for heterogeneity. In the subgroup analysis, we also did not observe that any significant result was found.

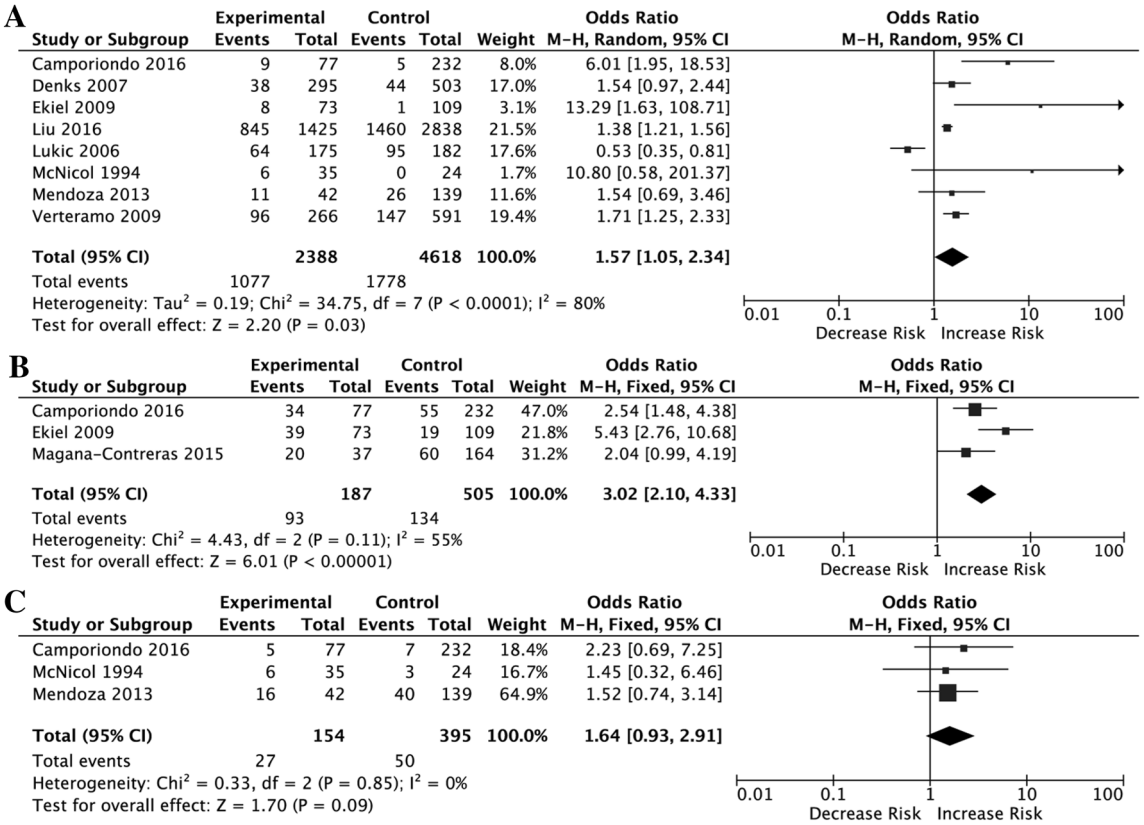

Fig. 2 Forest plot of association between genital mycoplasmas infections and HPV infection. **a** *U. urealyticum* and HPV infection. **b** *U. parvum* and HPV infection. **c** *M. hominis* and HPV infection

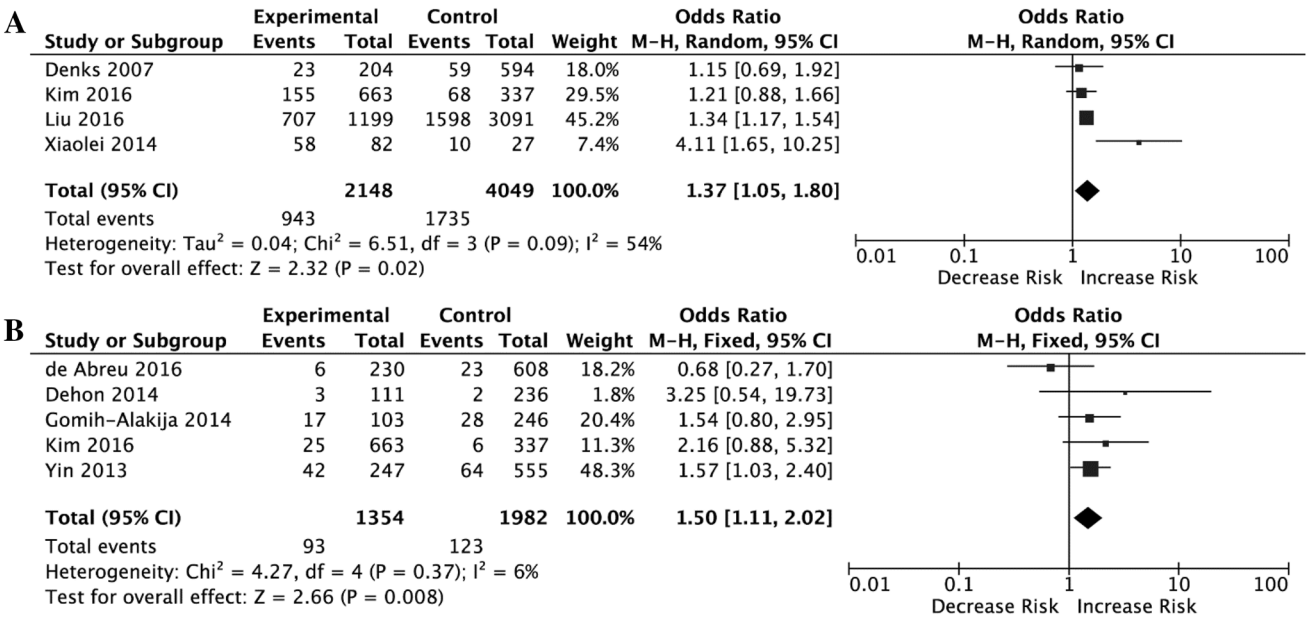

Fig. 3 Forest plot of association between genital mycoplasmas infections and high-risk HPV infection. **a** *U. urealyticum* and high-risk HPV infection. **b** *M. genitalium* and high-risk HPV infection

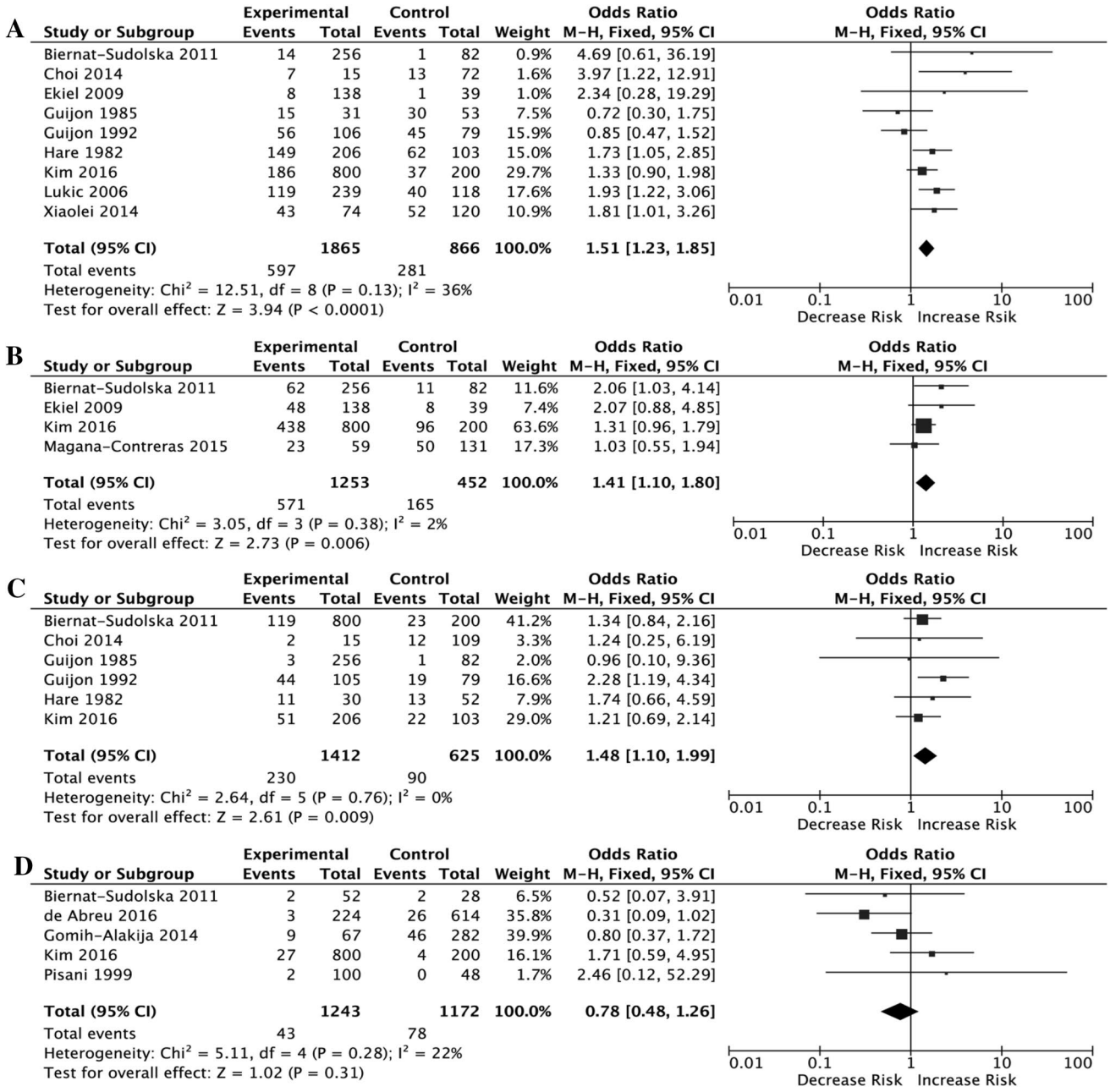

Fig. 4 Forest plot of association between between genital mycoplasmas infections and abnormal cervical cytopathology. **a** *U. urealyticum* and abnormal cervical cytopathology. **b** *U. parvum* and abnormal cervical cytopathology. **c** *M. hominis* and abnormal cervical cytopathology. **d** *M. genitalium* and abnormal cervical cytopathology

Association between genital mycoplasmas and cervical cancer

As the number of studies concerning the association between genital mycoplasma infection and cervical cancer was limited, we did not perform quantitative analysis of the results. Biernat-Sudolska and his colleagues found that the proportion of women infected with *U. urealyticum* was significantly higher in women with cervical cancer than women with normal cytopathology. However, they did not analyze *M. hominis* or *M. genitalium* infections in women with cervical cancer [39]. While in the study conducted by Hare and his colleagues, *U. urealyticum* and *M. hominis* were isolated with similar frequency from both cervical cancer group and normal cytopathology group [37].

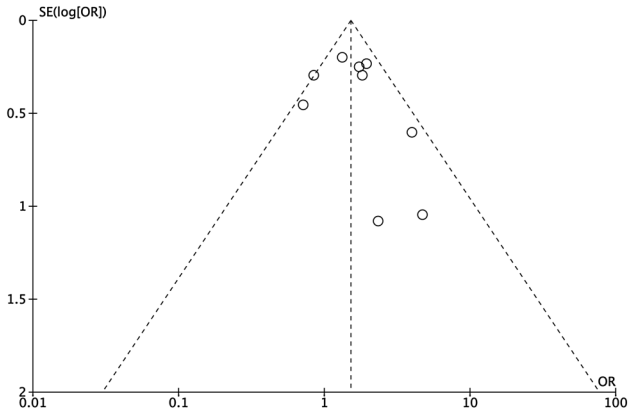

Fig. 5 Funnel plot of association between *U. urealyticum* and abnormal cervical cytopathology. The circles represent the nine included studies about association between *U. urealyticum* and abnormal cervical cytopathology. The horizontal axis represents the size of association, while the vertical axis represents the standard error. The fixed-effects summary estimate is indicated by the vertical line, and the expected 95% CI of the standard error is indicated by the vertical line

Discussion

To our knowledge, this study is the first systemic review and meta-analysis investigating the association between genital mycoplasmas infection and HPV infections, abnormal cervical cytopathology, and cervical cancer. Our findings suggested that both *U. urealyticum* and *U. parvum* infection may increase the risk of high-risk HPV infections and abnormal cervical cytopathology. While *M. genitalium* infection may increase the risk of high-risk HPV infections and *M. hominis* infection may increase the risk of abnormal cervical cytopathology.

Concurrent co-infection of multiple pathogens was considered to be one of the most important risk factors for progression of HPV infections or cervical dysplasia [30, 38]. Previous studies suggested that genital mycoplasmas, as a common type of vaginal pathogen, may influence the natural history of HPV infections by initiating cellular anomalies [13]. Our meta-analysis further explored their relationships through pooling epidemiological data and found that *U. urealyticum and M. genitalum* may increase the risk of high-risk HPV infections. Despite the large number of patients included, our results still need to be interpreted with caution, as moderate heterogeneity existed among the included studies. Besides, the included studies were mostly cross-sectional studies, lacking in a longitudinal view of the HPV infections process in patients; thus, it was hard to investigate the relationship between genital mycoplasma infection and persistent HPV infections. Future prospective cohort studies are needed to explore the relationships of multiple co-infected pathogens with persistent HPV infections in a longitudinal perspective.

Abnormal cervical cytopathology, as an advanced pathological change largely caused by high-risk HPV infections, represented moderate or severe cervical intraepithelial neoplasia or cervical carcinoma in situ. Our results showed that *U. urealyticum, U. parvum,* and *M. hominis* can increase the risk of abnormal cervical cytopathology transformation. No heterogeneity was observed among studies concerning *U. urealyticum, U. parvum,* and *M. hominis* infections. In clinical practice, the management of LSIL and HSIL is quite different, LSIL tends to be observed during follow-up, while HSIL tends to receive further progressive treatment. Therefore, we then performed a subgroups analysis by analyzing LSIL and HSIL separately, and we found that *U. urealyticum* infection can increase both the risk of LSIL and HSIL, which suggested that *U. urealyticum* might have a distinct effect on progression of LSIL and HSIL. The possible mechanism of the association between *U. urealyticum* infection and abnormal cervical cytopathology might be related to the combination of several complex infection-associated inflammatory responses [15], involving production of reactive oxidative metabolites, increased expression of cytokines, chemokines, and growth and angiogenic factors, decreased cell-mediated immunity, and the generation of free radicals [45].

A potential association between cancers and infection with mycoplasma has been suspected since the 1960s [46]. However, early evidence was restricted by difficult culture conditions of these microbes until the widespread of techniques like PCR, immunohistochemistry, and serum antibody status. Recent study by Barykova et al. was the latest one that indicated a strong link between mycoplasma species and prostate cancer [47]. Besides, Baczynska et al. found that *M. hominis* and *M. genitalium* infections might play an important role in ovarian cancer [48]. In addition to those findings in other cancers, several a few studies investigated the association between genital mycoplasma and cervical cancer, which found significant increased positive rate of *U. urealyticum* in women with cervical cancer, compared to women with normal cytology findings [39]. Furthermore, laboratory studies confirmed the ability of mycoplasma to cause or promote oncogenic transformation [49]. Several different species have been proven to transform rodent and human lines of diverse lineages in vitro [50]. However, as limited numbers of studies available, the role of genital mycoplasmas in cervical cancer is still in ambiguity, and further epidemiological studies and prospective prognosis studies are needed in the future.

Some limitations must be addressed when interpreting our results. First of all, our results were based on pooled analysis of crude epidemiological data. Most included studies did not provide adjusted OR for the association between genital mycoplasmas infection and related disorders, and matching of baseline and other risk factors was also not available. Second, there were some innate heterogeneities in

our study due to inclusion of different designs of studies, i.e., cross-sectional and case–control studies. Third, description of the details about concurrent co-infection of other pathogens, such as *C. trachomatis* and *T. vaginalis*, was not available in some included studies, which might result in possible selected bias of the patients. Fourth, most included studies concerning HPV infections were cross-sectional studies, which limited us to explore the association between genital mycoplasmas infection and persistent HPV infections. Fifth, the association between ureaplasma and mycoplasma infection and HPV infection related disorders may also be resulted from a more promiscuous sexual life which leads to a higher incidence and prevalence of sexually transmitted diseases. This confounding factor should be taken into account when interpreting our results.

Conclusions

Our systemic review and meta-analysis found that *U. urealyticum* and *U. parvum* may increase the risk of HPV, *U. urealyticum* and *M. genitalium* may increase the risk of high-risk HPV infections, and *U. urealyticum, U. parvum,* and *M. hominis* may increase the risk of abnormal cervical cytopathology. More well-designed longitudinal studies investigating the changes of the natural history of concurrent co-infection of genital mycoplasmas and persistent HPV infection are warranted in the future.

Author contributions HY: project development, data collection, data analysis, and manuscript writing. TS: data collection and manuscript writing. XZ: data analysis and manuscript writing. LL and MH: data analysis and manuscript editing. MX: project development, data analysis, and manuscript editing.

Compliance with ethical standards

Ethical approval and informed consent No patient consent or ethical approval was required, because analyses were based on the previous published studies.

Conflict of interest All authors declare that they have no conflict of interest.

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