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REVIEW ARTICLE
The prevalence and risk of human papillomavirus infection in pregnant women

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SUMMARY

A series of observational studies were evaluated concerning the risk of human papillomavirus (HPV) infection in pregnancy; however, the results were controversial. We systematically reviewed and collected data on studies regarding HPV prevalence published up to 30 April 2013, in which HPV was detected in pregnant women or both in pregnant and non-pregnant women. In total, 28 eligible studies were included that provided data on HPV infection concerning 13 640 pregnant women. The overall HPV prevalence in pregnant and age-matched non-pregnant women was 16·82% [95% confidence interval (CI) 16·21–17·47] and 12·25% (95% CI 11·50–13·01), respectively. The prevalence in the in three trimesters was 18·20%, 14·38%, and 19·32%, respectively. HPV-16 was the most frequently observed type, with a prevalence of 3·86% (95% CI 3·40–4·32). The overall HPV prevalence varied by study region, age, and HPV type. The meta-analysis showed a significantly increased risk of HPV infection in pregnant women, with a summary odds ratio (OR) of 1·42 (95% CI 1·25–1·61), especially for those aged <25 years (OR 1·79, 95% CI 1·22–2·63). The results suggest that pregnant women, especially those aged <25 years, are more susceptible to HPV infection.

Key words: Human papillomavirus, meta-analysis, pregnancy, prevalence.

INTRODUCTION

There are more than 100 types of human papillomavirus (HPV) divided into three broad categories (high-risk types, probable high-risk types, low-risk types) depending on their oncogenic potential [1]. Persistent infection with high-risk HPV and the integration of viral genomes into the host genome have been implicated in the aetiology of malignant and pre-malignant diseases of the female lower genital tract [2]. A series of investigations found that specific types of HPV were closely associated with many kinds of cancers, such as laryngeal cancer, anal cancer, vulva cancer and bladder cancer [3, 4].

Many factors could increase the risk of HPV infection, for example, sexual behaviour, the number of both recent and lifetime male sexual partners, co-infection with other sexually transmitted diseases and vaginal infection, and early onset of sexual activity. Diet, smoking, genetics and immune suppression are also related to HPV infection [5–8].

It has been shown that pregnancy is a state of mild immunosuppression due to the decrease in natural

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killer cells or reduction in the helper T-cell type 1 cell-mediated response [9]. Sillman & Sedlis found that immunosuppressed women had a higher incidence of cervical neoplasia [10]. Furthermore, Gloss *et al*. reported that the transcriptional promoter of HPV-16 contained a steroid hormone receptor-binding element that promoted HPV transcription, suggesting a hormonal activation effect on HPV replication [11]. These observations indicated that the possible temporary altered state of immunity and the increased levels of steroid hormones during pregnancy might have an effect on HPV replication and its subsequent progression to disease development.

In addition, Merckx *et al.* [12] reported that there was a significantly higher risk of children born to HPV-positive mothers becoming HPV positive, resulting in infantile anal and genital condyloma acuminatum, and juvenile laryngeal papillomatosis, although some HPV infections were almost cleared by age 6 months. Hence, the question regarding whether pregnant women are more susceptible to HPV infection than non-pregnant women is crucial. We hypothesize that pregnant women, with a state of mild immunosuppression [9], have a higher susceptibility to HPV infection, increasing the HPV prevalence in this population.

Until now, many observational studies have reported the risk of HPV infection in pregnant women, but the results are controversial. A few studies reported that pregnant women had a higher HPV prevalence [6, 13–18]. However, several reports suggested a lower prevalence in pregnant women or no statistical difference compared to those of age-matched non-pregnant controls [19–26]. In addition, we did not find any articles estimating the age, trimester and type-specific prevalence of cervical HPV DNA in pregnant women. Therefore, we set out to estimate the prevalence of cervical HPV in pregnant women and clarify the risk of HPV infection in pregnant women by conducting a meta-analysis after a systematic literature review.

METHODS

Literature search

Articles published in English and Chinese were all considered. Articles in English were identified through PubMed, Medline, Elsevier Science, and Web of Science (ISI) databases from their earliest available date to 30 April 2013. The key words ('human papillomavirus' or 'HPV') and ('pregnant' or 'pregnancy' or 'conceive' or 'conception' or 'gravidity' or 'be with child' or 'fetation' or 'to bear children') were used in combination in order to retrieve the relevant literature in these databases. Articles in Chinese were identified through the China National Knowledge Infrastructure (CNKI), Database of Chinese Scientific and Technical Periodicals (VIP), Wan Fang database, and the China Biology Medical Literature database (CBM), four commonly used databases, which were searched from 1979, 1989, 1990, 1970 to 30 April 2013, respectively. Moreover, we reviewed the reference lists from retrieved articles to search for further relevant studies.

Inclusion criteria

Inclusion criteria were as follows: (1) the HPV prevalence in asymptomatic pregnant and non-pregnant women could be directly extracted or calculated from the original article. Pregnant women were those who attended a routine antenatal visit and non-pregnant woman were from a cervical cancer screening centre located at the same hospital; (2) if studies contained non-pregnant women, they were age-matched with pregnant women; (3) specimens for HPV detection were exfoliated cells that had been scraped or lavaged from the cervix and vagina; (4) information about HPV DNA types and detection methods had to have been clearly stated. If there were duplicate reports of the study, the article published earlier or providing the more detailed information was included.

Data extraction

The following information was extracted from each study: first author, journal and year of publication, country where the study was performed, study design, study period, the number of pregnant and/or non-pregnant women, their mean age, specimen source, HPV DNA types, HPV DNA detection methods and prevalence. Data extraction was conducted independently by two authors (P.L., Y.S.), and consensus was reached on all items. The study quality was assessed using the criteria for non-randomized observational studies (see Appendix) [27, 28].

Statistical analysis

We used the prevalence rate and odds ratio (OR) with their 95% confidence intervals (CIs) of the HPV

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prevalence in pregnant women compared to that in non-pregnant women. A summary OR with 95% CI was estimated by using both fixed-effects and random-effects models. In the presence of substantial heterogeneity ($I^2 > 50\%$), the random-effects model was adopted as the pooling method, otherwise, the fixed-effects model was used to estimate the summary OR. Meta-regression was performed to assess the potentially important covariates exerting substantial impact on between-study heterogeneity. Stratified analyses were subsequently performed with respect to the characteristics of HPV DNA detection techniques [fluorescence *in situ* hybridization (FISH), Southern hybridization (SH), polymerase chain reaction (PCR), ViraPap (VP)], regions (Asia, Europe, North America), and the number of detected HPV types. Publication bias was examined by visual inspection of funnel plots and then evaluated formally with Begg's adjusted rank correlation test and Egger's regression asymmetry test. 'Leave one out' sensitivity analysis was performed to strengthen the result of the meta-analysis. The influence of each study was evaluated by estimating the summary ORs in their absence.

Data were analysed by Review Manager 5.1.2 software (USA) and Stata v. 11.1 (StataCorp., USA). All P values were two-sided and $P < 0{\cdot}05$ was considered significant.

RESULTS

Literature search

For HPV infection in pregnant and non-pregnant women, the primary search generated potentially 314 relevant articles in PubMed, 190 articles in Medline, 243 articles in ISI and 192 articles in the four common Chinese databases. Three hundred and eighty articles were duplicated in the databases and excluded. Four hundred and seventy-eight articles were excluded based on screening of titles and/or abstracts using eligibility criteria. Fifty-seven articles were excluded after full-text review (one duplicated report on the same study populations, 51 failing to meet criteria and five with incomplete data), four articles were identified from reference lists. Finally, 28 articles were included in the present study, which contained 13 640 pregnant women in total. Study populations were from Asia [18, 24, 29–37], Europe [14–16, 19, 21, 23, 25, 26, 38, 39], North America [6, 17, 20, 22, 40, 41], Australia [42]. The 28 studies included are shown in Fig. 1.

The prevalence of HPV infection in pregnant and age-matched non-pregnant women

Twenty-eight eligible studies provided data on 13 640 pregnant women for HPV prevalence, in which 14 studies provided data for HPV detection only in pregnant women and the other 14 studies provided data for HPV detection both in pregnant and age-matched non-pregnant women.

The HPV prevalence in pregnant women varied from 9·58% to 46·67%, with a summary estimate of 16·82% (95% CI 16·21–17·47), and it varied from 8·9% to 23·5% in age-matched non-pregnant women, with a summary estimate of 12·25% (95% CI 11·50–13·01). The difference between the summary estimates was significant ($P < 0{\cdot}001$, Table 1). In pregnant women, the prevalence rates of HPV infection in Australia, North America, Asia, and Europe were 36·60%, 30·37%, 15·72%, and 13·19%, respectively, showing a significant difference worldwide. The difference between the groups of pregnant and non-pregnant women in North America, Asia and Europe was seen with $P < 0{\cdot}05$ (<0·001, 0·026, and 0·038, respectively).

The prevalence rates of HPV infection were 23·94%, 13·34%, and 14·79% in pregnant women aged <25 years, 25–29 years, and ⩾30 years, respectively, and prevalence rates in non-pregnant women were 18·00%, 12·08%, and 11·43% in three age groups, respectively, the differences were significant with $P = 0{\cdot}025$, 0·039, and 0·023, respectively.

In pregnant women, the remaining most frequently identified HPV types (prevalence rate) were HPV-16 (3·86%), HPV-6 (2·45%), HPV-18 (1·80%), and HPV-11 (1·76%). The prevalence rates of different HPV types had no statistical difference in this group compared to that in the non-pregnant women group.

The HPV prevalence rates in the three trimesters were 18·20%, 14·38%, and 19·32%, and the ORs of HPV infection were 1·59 (95% CI 1·39–1·82), 1·20 (95% CI 1·08–1·34), and 1·71 (95% CI 1·55–1·90), respectively, compared to non-pregnant women (Table 2).

The risk of HPV infection in pregnant women

To estimate the risk of HPV infection in pregnant women, 14 studies containing both pregnant and age-matched non-pregnant women were included in the meta-analysis. Pregnant ($n = 3455$) and age-matched non-pregnant ($n = 7190$) women were enrolled, and their details are given in Table 3. The ORs for each

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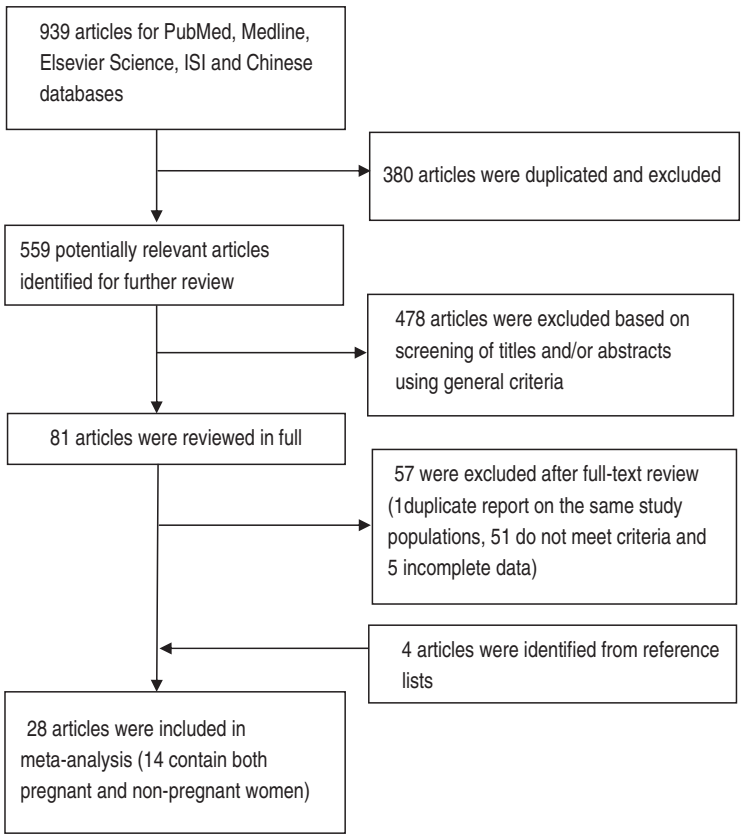

Fig. 1. Selection of studies for inclusion in the meta-analysis.

study and overall studies can be seen in the Forest map (Fig. 2). According to the heterogeneity, the random-effects model was chosen to evaluate the summary OR. The result showed that pregnant women had a higher risk (OR 1·42, 95% CI 1·25–1·61) of HPV infection.

As shown in Table 4, when pregnant women were aged <25 years, the OR was 1·79 (95% CI 1·22–2·63) for HPV infection, compared to non-pregnant women. When the ORs were pooled by region, a significantly increased HPV infection risk was shown in North America (OR 1·70, 95% CI 1·16–1·93), but this was not the case for Europe (OR 1·16, 95% CI 0·99–1·36) or Asia (OR 0·87, 95% CI 0·52–1·46). When the number of detection types was >10, there was a significantly increased HPV infection risk (OR 2·05, 95% CI 1·68–2·50) in pregnant women. There was a significantly increased risk of HPV infection in pregnant women when HPV DNA was detected using Hybrid Capture System II (HC2) (OR 3·57, 95% CI 2·65–4·82), FISH (OR 1·76, 95% CI, 1·09–2·85) and VP (OR 1·79, 95% CI, 1·16–1·93). However, there was only one study that used HC2, where the OR 3·57 (95% CI, 2·65–4·82) was not accurate. Notably, a significantly increased risk was observed in publication date periods of 1987–1999 (OR 1·19, 95% CI 1·02–1·38) and 2000–2012 (OR 2·01, 95% CI 1·62–2·50).

Sensitivity analysis

To explore the heterogeneity between studies, we performed a sensitivity analysis. After omitting one study at a time and calculating the summary ORs for the remainder of the studies, the results demonstrated that there was no evidence of any individual study having an excessive influence on the summary effect (Fig. 3).

Publication bias

The publication bias in the studies was evaluated with Egger's and Begg's tests with the results $P = 0{\cdot}458$ and $P = 0{\cdot}350$. The conclusion was that there was no significant publication bias and the shapes of the funnel plots (Fig. 4) did not reveal any obvious asymmetry.

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Table 1. *Prevalence rate of HPV infection in women across region, age and individual types*

Variable	Pregnant			Non-pregnant			
	n	No. of HPV+	Prevalence, % (95% CI)	*n*	No. of HPV+	Prevalence, % (95% CI)	*P*
Total	13640	2294	16·82 (16·21–17·47)	7190	881	12·25 (11·50–13·01)	**<0·001**
Region							
Asia	9198	1446	15·72 (14·98–16·46)	308	35	11·36 (7·82–14·91)	**0·038**
Europe	2972	392	13·19 (11·97–14·41)	5330	613	11·50 (10·64–12·36)	**0·026**
North America	1317	400	30·37 (28·15–32·93)	1552	233	15·01 (13·24–16·79)	**<0·001**
Australia	153	56	36·60 (28·97–44·23)	—	—	—	—
Age (yr)							
<25	1537	368	23·94 (21·81–26·07)	300	54	18·00 (13·65–22·35)	**0·025**
25–29	5651	754	13·34 (12·45–14·2)	6234	753	12·08 (11·27–12·89)	**0·039**
⩾30	3867	572	14·79 (13·67–15·91)	656	75	11·43 (9·00–13·86)	**0·023**
HPV type							
HPV-16	6684	258	3·86 (3·40–4·32)	882	35	4·00 (2·71–5·29)	0·876
HPV-6	1512	37	2·45 (1·67–3·23)	416	11	2·60 (1·07–4·13)	0·819
HPV-18	6376	115	1·80 (1·48–2·13)	882	19	2·20 (1·23–3·17)	0·469
HPV-11	795	14	1·76 (0·85–2·68)	416	10	2·40 (0·93–3·87)	0·446
HPV-58	6014	105	1·75 (1·41–2·08)	461	9	2·05 (0·72–3·28)	0·745
HPV-31	2731	38	1·39 (0·95–1·83)	461	2	0·40 (0·00–0·98)	0·087
HPV-33	2429	13	0·54 (0·25–0·83)	461	5	1·10 (0·15–2·05)	0·169

HPV, human papillomavirus; CI, confidence interval.

Table 2. *Prevalence rate and the risk for HPV infection in three trimesters*

Trimester	No. of studies	No. of pregnant women	No. of HPV+	Prevalence, % (95% CI)	OR* (95% CI)
1st	15	2000	364	18·20 (16·51–19·89)	**1·59 (1·39–1·82)**
2nd	11	4556	655	14·38 (13·36–15·40)	**1·20 (1·08–1·34)**
3rd	17	4193	810	19·32 (18·12–20·52)	**1·71 (1·55–1·90)**

HPV, Human papillomavirus; OR, odds ratio; CI, confidence interval.
* The OR was evaluated by comparing with the HPV prevalence in non-pregnant women.

DISCUSSION

In this meta-analysis on the prevalence and risk of HPV infection in pregnant women, 28 studies were included and summarized. The overall HPV prevalence in pregnant women was estimated to be 16·82% (95% CI 16·21–17·47). HPV-16 was the most frequently observed type, with a prevalence of 3·86% (95% CI 3·40–4·32). The risk of HPV infection in pregnant women increased to 1·42 (95% CI 1·25–1·61).

In 2007, de Sanjosé *et al*. set out to estimate the prevalence of cervical HPV DNA in women with normal cytology worldwide by meta-analysis and their prevalence estimate was 10·4% (95% CI 10·2–10·7) [43]. The women in that meta-analysis represented a large age range (25–54 years) and there were no data for pregnant women. In our meta-analysis, a higher risk of HPV infection in pregnant women (OR 1·42, 95% CI 1·25–1·61) was found and the overall HPV prevalence in age-matched non-pregnant women was 12·25% (95% CI 11·50–13·01), which was comparatively higher than that in de Sanjosé *et al*.'s meta-analysis (10·4%, 95% CI 10·2–10·7). One of the reasons that non-pregnant women in our paper were in the optimal child-bearing period, was that there was higher sexual frequency than for non-pregnant women in de Sanjosé *et al*.'s meta-analysis.

Many studies have simply discussed the prevalence of HPV in different age groups in non-pregnant

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Table 3. *Main characteristics of the published studies included in the meta-analysis*

Study [reference]	Publication year	Country	Main methods for HPV detection	HPV types detected in original articles	Pregnant			Non-pregnant			OR	Quality of study
					n	Mean age, yr	Prevalence (%)	*n*	Mean age, yr	Prevalence (%)		
Schneider [14]	1987	Germany	SH	11, 16, 18	92	27·6	28·0	96	27	12·5	2·76	7
Czegledy [15]	1989	Hungary	FISH	6, 11, 16, 18	101	28·2	34·6	108	—	20·4	2·07	8
Soares [19]	1990	Finland	VP	6, 11, 16, 18, 31, 33, 35	748	33	9·6	503	32	8·9	1·08	8
Smith [20]	1991	North America	VP	16, 18, 31, 33, 35	69	24·7	15·9	54	25·8	14·8	1·09	8
De Roda Husman [21]	1995	Netherlands	PCR	6, 11, 16, 18, 31, 33	709	30	9·6	3948	30	10·9	0·87	8
Morrison [22]	1996	North America	SH	11, 16, 18	107	25·6	34·6	74	25·6	18·9	0·91	8
Chang-Claude [16]	1996	Germany	VP	6, 11, 16, 18, 31, 35	108	29·7	13·9	192	32·8	15·1	2·27	10
Fife [17]	1996	North America	VP	16, 18, 31, 33, 35, 45, 51, 52, 56, 6, 11, 42, 43, 44	245	22·8	31	246	29·2	18·6	1·96	8
Tenti [23]	1997	Italy	PCR	16, 18*	313	30	9·6	313	29	11·8	0·79	9
Chan [24]	2002	Hong Kong	PCR	16, 18, 26, 31, 33, 58, 6, 11, 53, 54, 57, 61, CP8061, CP8304	308	28·9	10·1	308	29·1	11·4	0·87	8
Zlatkov [25]	2003	Bulgaria	FISH	6, 11, 16, 18, 31, 33	166	26·5	17·7	84	26·5	13·1	1·40	8
Hernandez-Giron [6]	2005	Mexico	HC2	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68	274	25·7	37·1	1062	26·2	14·2	3·57	8
Aydin [18]	2010	Turkey	PCR	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	164	30·6	29·2	153	33·3	19·6	1·70	8
Schmeink [26]	2012	Netherlands	PCR	6, 11, 34, 40, 42, 43, 44, 53, 54, 66, 70, 74, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68·73	51	27·4	21·6	51	27·6	23·5	0·89	9

HPV, Human papillomavirus; OR, odds ratio; SH, Southern hybridization; FISH, fluorescence *in situ* hybridization; VP, ViraPap; PCR, polymerase chain reaction; HC2, Hybrid Capture System II.

* Other types that were not specified in the original article.

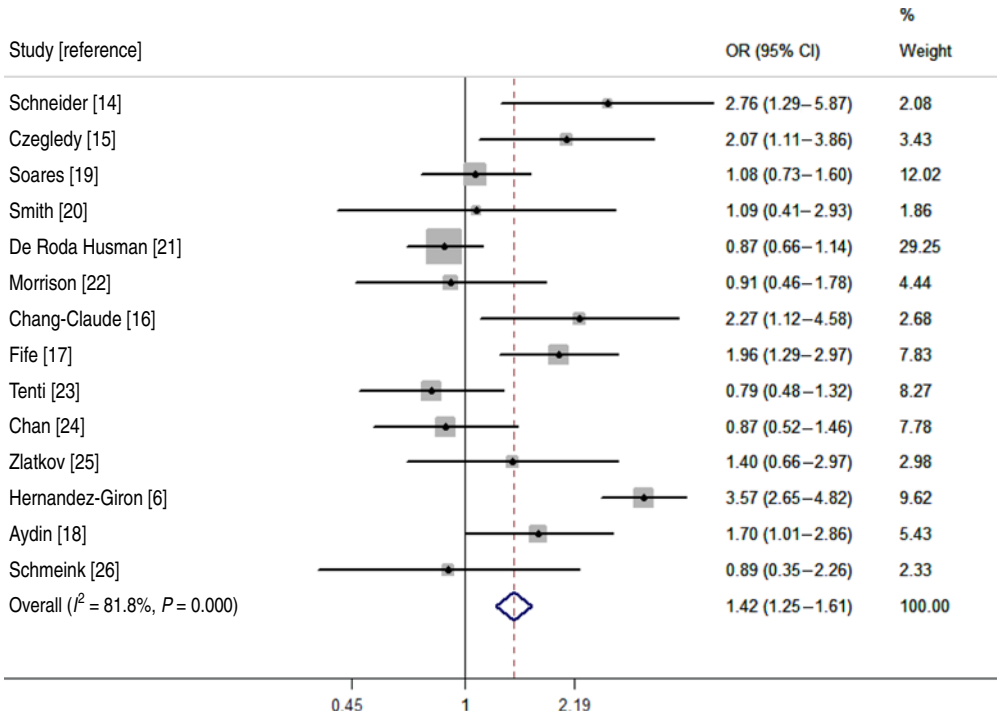

Fig. 2. Meta-analysis of odds ratio (OR) with 95% confidence interval (CI) for HPV infection in pregnant women.

[44–46] or pregnant [21, 47, 48] women. The relationship between the age of the women when pregnant and the risk of HPV infection was not considered. Fourteen studies, which provided the prevalence of HPV infection both in pregnant women and age-matched non-pregnant women, were included in our meta-analysis. In each study, the pregnant women and age-matched non-pregnant women were from the same source population and they were comparable in terms of sociodemographic variables such as age, background history of sexual activity (including number of sexual partners) and particularly, gestational age. In addition, the method for HPV detection was the same in each study. Hence, pregnant women compared to non-pregnant women in terms of HPV prevalence had little heterogeneity, and the comparisons with non-pregnant women were made feasible. This meta-analysis indicated that pregnant women who were aged <25 years had a greater risk for HPV infection.

The prevalence of HPV infection in three trimesters displayed a V-shaped trend in our study. The low HPV prevalence during the second pregnancy was partly due to HPV clearance [49]. Whereas Yamasaki *et al.* [50] reported that the HPV prevalence in the third trimester was not high, this was probably related to the changes in sexual behaviour (greater stability of partnerships, less frequent intercourse), than biologically induced impacts of pregnancy upon HPV infection susceptibility and persistence. Nevertheless, data from other authors [51] showed that there were 42·9% of pregnant women newly infected by HPV between the first/second and third trimesters. Due to the clearance of virus in the first/second and third trimesters (50·4% and 71·8%, respectively), HPV prevalence remained unchanged in different periods. Hence, more research is needed to investigate the variation trend in the three trimesters of pregnancy.

Our study showed that in North America, Asia and Europe, HPV prevalence rates in pregnant women were significantly higher than those in non-pregnant women. Pregnant women in North America were more susceptible to HPV infection compared to those in Europe and Asia. In earlier investigations in Hungary and Hong Kong, HPV-16 was the most common type in asymptomatic pregnant women. The other common types were HPV-6, -18, -11, -58, -31 and -33. The sequence was a little different from that in non-pregnant women (HPV-16, -6, -11, -18, -58, -33 and -31) and other women worldwide with normal cytology (HPV-16, -18, -31, -58, -52) [43].

There was no risk of HPV infection in pregnant women when using PCR-based methods. Possible reasons are listed as follows. First, the PCR-based methods contains GP5/6 or GP5+/6+, MY09/11 or

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Table 4. *Meta-analysis for stratification on the risk of HPV infection in pregnant women*

Variable	Studies, *n*	No. of subjects		I^2 for heterogeneity (%)	*P* for heterogeneity	Model selected	OR (95% CI)
		Pregnant	Non-pregnant				
Total	14	3455	7190	81·8	<0·001	Random	**1·42 (1·25–1·61)**
Age (yr)							
<25	2	314	300	11·8	0·287	Fixed	**1·79 (1·22–2·63)**
25~29	10	2229	6234	86·5	<0·001	Random	**1·40 (1·21–1·62)**
⩾30	2	912	656	44·8	0·178	Fixed	1·27 (0·93–1·74)
Region							
Asia	1	308	308	—	—	—	0·87 (0·52–1·46)
Europe	9	2451	5330	62·2	0·007	Random	1·16 (0·99–1·36)
North America	4	696	1552	83·6	<0·001	Random	**2·35 (1·88–2·93)**
No. of detection types							
<5	4	614	709	72	0·013	Random	1·29 (0·95–1·74)
5–10	5	1799	4663	43·5	0·131	Fixed	1·04 (0·86–1·26)
>10	5	1042	1818	85·4	<0·001	Random	**2·05 (1·68–2·50)**
Detection method							
PCR	5	1545	4773	30·9	0·216	Fixed	0·94 (0·78–1·14)
FISH	2	267	192	0	0·434	Fixed	**1·76 (1·09–2·85)**
SH	2	200	288	78·4	0·031	Random	1·50 (0·92–2·43)
VP	4	1169	877	49·1	0·117	Fixed	**1·79 (1·16–1·93)**
HC2	1	274	1060	—	—	—	**3·57 (2·65–4·82)**
Publication date							
1987–1999	9	2492	5534	68	0·002	Random	**1·19 (1·02–1·38)**
2000–2012	5	963	1656	86	<0·001	Random	**2·01 (1·62–2·50)**

HPV, Human papillomavirus; OR, odds ratio; CI, confidence interval; PCR, polymerase chain reaction; FISH, fluorescence *in situ* hybridization; SH, Southern hybridization; VP, ViraPap; HC2, Hybrid Capture System II.

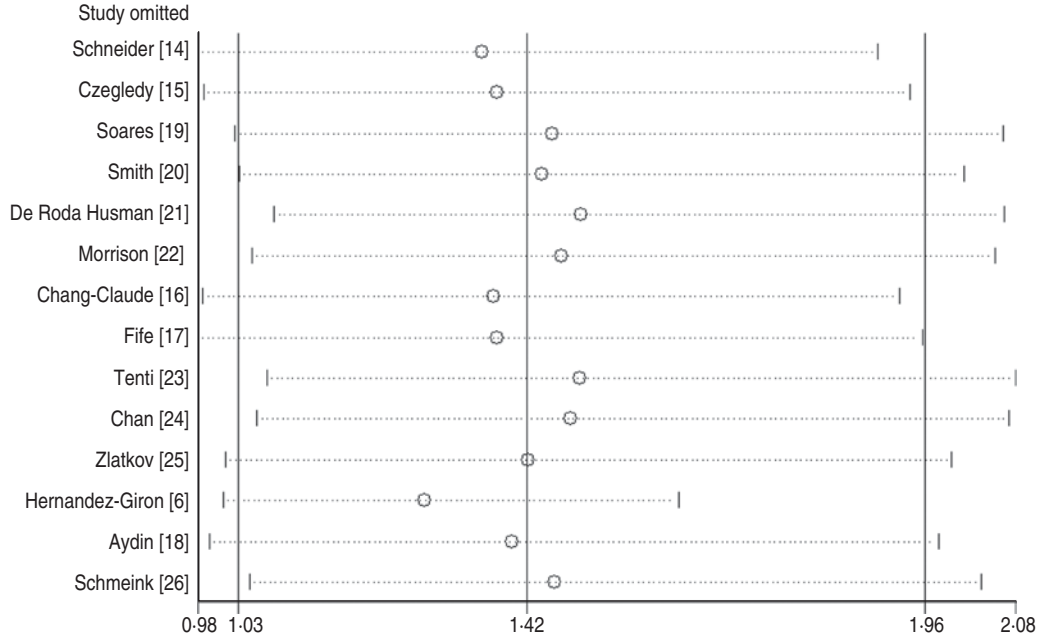

Fig. 3. Sensitivity analysis of meta-analysis for HPV infection in pregnant women.

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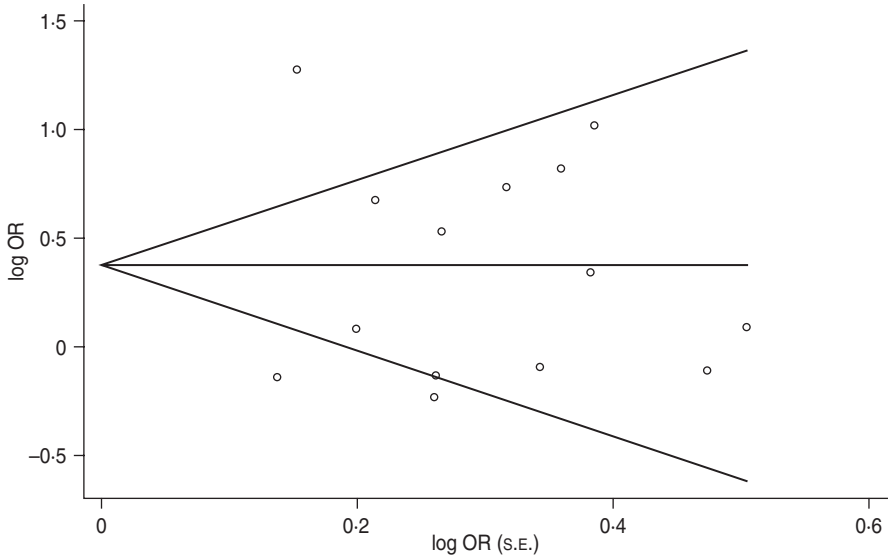

Fig. 4. Begg's funnel plots for assessing the publication bias.

PGMY09/11, GP5/6(+) and (PG)MY09/11 combined, SPF10, HPV DNA chip, and other PCR [45]. The specificity and sensitivity within PCR-based methods vary greatly, aside from built-in changes due to the development of techniques over time [45]. Women from the same population tested with different techniques may double or even triple the estimated HPV prevalence [45]. PCR with GP5+/6+ and PGMY09/11 showed intermediate analytical sensitivity, and PCR with SPF10 showed the highest sensitivity [52, 53], particularly at very low concentrations of HPV, which is common in normal cytological findings [54]. Another source of variability is the differential sensitivity of PCR primer sets to specific HPV types [55], especially with the less frequent types. The type-specific performance of the assays depends not only on the technique but also on the laboratory and the processing of the specimen [53]. Therefore, the standardization of protocols and techniques in population-based genotyping characterizations is crucial for HPV vaccine surveillance and comparisons globally.

Although the incidence of cervical cancer in pregnancy is low, about 0·02–0·4%, it is the most common tumour in pregnant women [56]. Moreover, the published articles reported that the detection rate of infectious disease was high in pregnant women. For example, statistical data showed there was a significantly greater proportion of bacterial vaginosis (BV) in pregnant women with HPV infection compared to those without HPV infection [57]. At the same time, research carried by Merckx *et al*. [12] showed there was a significantly higher risk of HPV infection in children born to HPV-positive mothers. Therefore, our results showed pregnant women had a higher risk of HPV infection, and because of the existence of maternal–neonatal transmission, we inferred that the prevalence of HPV infection in infants would be increased as well. Therefore, we suggest that pregnant women should pay more attention to limit their HPV exposure (e.g, condom use during pregnancy), in order to reduce HPV prevalence in infants.

It is necessary to consider the limitations of the present meta-analysis. First, only studies published in English and Chinese were included, which might limit the results. Second, not all pregnant women came for routine antenatal visits which made the results prone to selection bias. Third, some studies just provided the prevalence of HPV infection in one trimester, which might be higher or lower than others. This would lead to the summarized prevalence values in our review being higher or lower than the actual values. Moreover, evident heterogeneity was observed between the included studies. The results of multivariate meta-regression and stratified analyses showed that variables were not the source of heterogeneity, so further studies providing detailed information about HPV prevalence are needed to verify the current findings.

In summary, our meta-analysis suggested a significantly increased risk of HPV infection in pregnant women, especially those aged <25 years. Since potential biases and confounders could not be ruled out completely in this meta-analysis, these results need to be verified by further studies.

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APPENDIX. *Quality assessment of observational studies (total 10 points)*

1. Selection of participants (1/0)
Cohort studies (1/0)
Selected cohort was representative of the general population (population-based studies) or target catchment population (hospital-based studies) (1)
Cohort was a selected unrepresentative group (0)
Case-control studies (1/0)
Cases and controls drawn from the same population (1)
Cases and controls drawn from different sources or the selection of groups (0)

2. Comparability of groups (2/0)
No significant differences between the groups reported in terms of age, plurality, smoking, history of preterm birth, pre-eclampsia or gestational diabetes, pre-existing medical conditions were explicitly reported, or these differences were adjusted for (2)
Differences between groups were not examined (1)
Groups differed and no adjustment results provided (0)

3. Definition of outcomes (2/0)
Definition of outcomes
Referenced or standard definition (2)
Explicit non-standard definition (1)
Unspecified or unacceptable definition (0)

4. Ascertainment of outcomes (2/0)
How the diagnosis was made
Prospectively diagnosed or review of notes/hospital discharge records (2)
Retrospective chart review or database coding (1)
Process not described (0)

5. Sample size (1/0)†
>100 participants in each group (1)
<100 participants in each group (0)

6. Study design (2/0)
Prospective cohort or nested case-control within a prospective cohort (2)
Cross-sectional, case-control or retrospective cohort (1)
Not described or poorly designed (0)

Exclusion: a total score <7 out of 10 maximum points.
* A score-based quality assessment criteria for non-randomized observational studies adapted from Duckitt & Harrington and Wei *et al*. [27, 28].
† In the original document, i.e. ⩾200 participants in a cohort study; ⩾50 participants in either group (case/control) (1). 100 ⩽participants <200 in a cohort; 25⩽ participants <50 in either group (case/control) (0·5). <100 Participants or total number of events <10 in a cohort; <25 participants in either group (case/control) (0).

DECLARATION OF INTEREST

None.

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