

Systematic Review

The Prevalence of Human Papilloma Virus Infection and Its High Risk Genotypes among Healthy Women in 28 Provinces in Iran: A Systematic Review and Meta-AnalysisMojgan Akbarzadeh-Jahromi^{1,2}, Negar Taheri¹, Babak Dashtdar³, Nasim Taheri⁴, Fatemeh Abiri¹, Marjan Zare^{2*}¹Department of Pathology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.²Maternal-Fetal Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.³Department of Orthopedic Surgery, School of Medicine, Fasa University of Medical Sciences, Fasa, Iran.⁴Department of Physiology, College of Sciences, Shiraz Branch, Islamic Azad University, Shiraz, Iran.

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ABSTRACT

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Key words:Women's health;
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Iran.

Introduction: Human Papilloma Virus infection (HPV) high-risk genotypes are responsible for up to 70% of invasive cervical cancers. It was aimed to determine the national and provincial prevalence of the total HPV and its high-risk genotypes including HPV genotype 16 (HPV16) and HPV genotype 18 (HPV18), and HPV genotypes other than genotypes of 16 and 18 (HPV other genotypes) among Iranian healthy women.

Methods: Iran with 28 provinces locates at latitude and longitude of 32° 00' north and 53° 00' east. All Persian and English studies reporting HPV infection based on cervical specimens were selected through searching the PubMed, Magiran, Scopus, Irandoc databases, and Google Scholar research search engine. Sample size and event rates were used to compute the overall event rates and 95% confidence interval (95% C.I); Fixed or random effects model, heterogeneity indices including Q-statistics (p-value), and degree of heterogeneity (I²) were reported. The search was done up to February 29, 2022. Comprehensive Meta-analysis 2.2.064 and ArcGIS 10.8.2 software tools were used at a significance level of <0.05.

Results: The meta-analysis included nineteen studies with 258839 participants. The national meta-analysis resulted in a total HPV prevalence of 0.025 (95% C.I 0.016, 0.039); those of HPV16, HPV18, and HPV other genotypes were 0.032 (95% C.I 0.019, 0.051), 0.028 (95% C.I 0.019, 0.040), and 0.048 (95% C.I 0.033, 0.069), respectively. The provincial meta-analysis showed that the total HPV prevalence was highest in Zanjan and Kerman (0.323 and 0.240, respectively); that of HPV16 was highest in Boushehr and Khozestan (0.298 and 0.253, respectively); that of HPV18 was highest in Tehran (0.089) and that of HPV other genotypes was highest in Khozestan (0.542).

Conclusion: The current results would help policymakers and health managers accentuate on further implementation of screening strategies and health services in needier areas such as Zanjan, Kerma, Khozestan, and Tehran.

Introduction

Human Papilloma Viruses infection (HPV) are

from Papilloma viridian family with more than 200 identified types according to phylogenic position and biological characteristics. Its

*.Corresponding Author: marjan.zare@gmail.com

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prevalence is estimated 31% nationwide; also, developing countries have higher rate compared with developed countries (42.2% vs. 22.6%).¹ Alpha papilloma virus genus, which are commonly detected in the genital tract, are sub classified into high-risk (HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73 and 82) and low-risk (HPV-6, 11, 34, 40, 42, 43, 44, 54, 61, 70, 72, 81, and 89) HPV genotypes.^{2,3} Cervical cancers are the fourth most frequent type of gynecological cancer with more than 270000 annual deaths from which ~ 85% happen in developing countries.⁴ High-risk HPV genotype 16 (HPV16) and 18 (HPV18) are responsible for up to 70% of invasive cervical cancers.⁵ Despite the global usage of HPV vaccines, vaccination against HPV has been very limited in Iran.⁶

Published data on national and provincial HPV prevalence and its' high-risk HPV16 and HPV18 genotypes in Iranian healthy women are scarce. A systematic approach to combine different smaller studies in a bigger one in a meta-analysis study would enhance the accuracy of HPV prevalence especially by each province. Consequently, the load of disease, vaccine coverage, medical facilities, and the infection control guidelines would be implemented in more at risk areas.

The present study aimed to determine the national and the provincial prevalence of total HPV and its high-risk genotypes including HPV16, HPV18, and HPV genotypes other than genotypes of 16 and 18 (HPV other genotypes) among Iranian healthy women

Methods

Study area

Iran is located in western Asia covering 1.64

million square kilometers with the population of 86.8 million. Its latitude and longitude are 32° 00' north and 53° 00' east. It include 28 provinces including Azarbayjan Sharghi, Boushehr, Esfahan, Fars, Gilan, Golestan, Kerman, Khorasan, Mazandaran, Sistan, Tehran, Zanjan, Ardabil, Azarbayjan Gharbi, Charmahal, Qazvin, Hamedan, Hormozgan, Ilam, Khozestan, Kermanshah, Kohgiluyeh, Kordestan, Lorestan, Markazi, Qom, Semnan, and Yazd (with Tehran as the capital). Using Google-Earth online system (US Department of State Geographer 2016), all 28 provinces of Iran got their latitude/longitude coordinate systems.

Study design

Doing a systematic review and meta-analysis, HPV infection prevalence and its high-risk genotypes HPV16 and HPV18, and HPV other genotypes were estimated in 28 provinces of Iran. It should be noted that provinces that were reported in more than one article had entered in the meta-analysis; however, the generic single point was reported for provinces reported in one study.

Search strategy

National (Magiran and Irandoc) and international (PubMed and Scopus databases as well as Google Scholar research search engine) were reviewed to find the published studies with no time limit. The following key words with their Farsi equivalents were applied in the systematic search process:

“human papillomavirus”, “HPV”, “HPV16”, “HPV18”, “high-risk genotype”, “frequency”, “rate”, “prevalence”, “seroprevalence”,

“seroepidemiology”, “pap smear”, “PCR”, “polymerase chain reaction”, “cervical cancer”, “Iran”, and “Persia”.

The search was done up to February 29, 2022. To enhance the sensitivity of our search, two researchers got involved doing the systematic search.

Study selection

We assessed each title of articles and read their abstracts. Primarily, we excluded all duplicates. Then, irrelevant studies were eliminated after reviewing titles, abstracts, and full texts. The study selection flowchart is depicted in Figure 1.

Eligibility criteria

After evaluation process and quality assessment, all Persian and English cross sectional studies reporting HPV infection prevalence, HPV16, HPV18, and HPV other genotypes among healthy Iranian women based on cervical specimens were selected.

The studies which did not report the prevalence and sample size, those done on men, cancerous women, duplicates, congress or meeting abstracts, and no full text articles were excluded from the meta-analysis. In addition, the grey literatures were excluded due to the absence of peer-review procedure in the academic journals; in addition, books

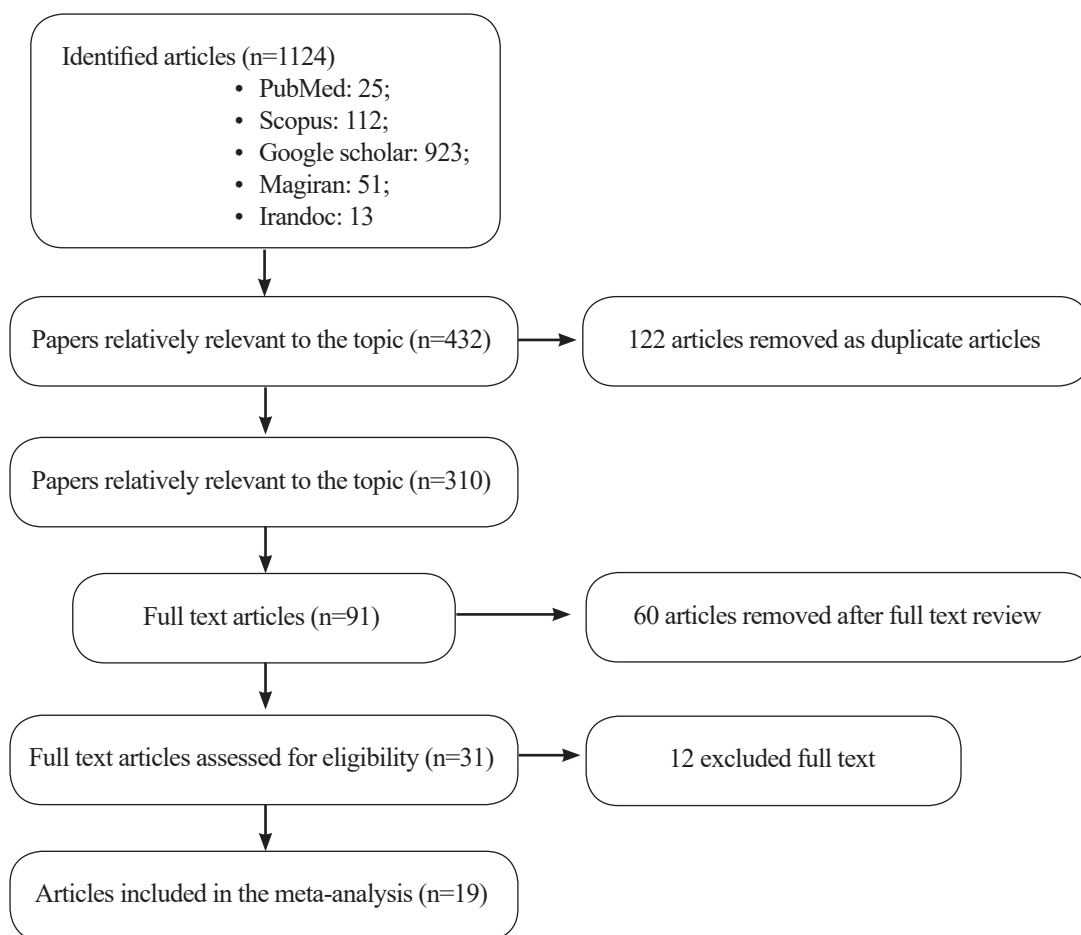


Figure 1. Study selection flowchart

and book chapters were viewed as nearly grey literature, because though they were produced and distributed commercially by publishers and might be widely available, studies located in them are often difficult to identify through typical search procedures.

Quality assessment

After selection of the articles based on their relevance to be included in the meta-analysis, their quality was assessed using Newcastle - Ottawa Quality Assessment Scale adapted for cross-sectional studies checklist.⁷ It contains ten questions defined in four domains regarding selection of cases (maximum five scores), comparability (maximum one score), outcome (maximum three scores), and statistical tests (maximum one score). The farther the final score from ten, the lower the quality of the study.

Data extraction

Author's name, study location, type of study, publication year, sample size, total HPV prevalence, HPV16 prevalence, HPV18 prevalence, and HPV other genotypes were extracted from the studies.

Statistical analysis

Sample size and event rates were used to compute the overall event rates and 95% confidence interval (95% C.I). The heterogeneity indices including Q-statistics and p-value as well as degree of heterogeneity, I², were reported. Fixed and random effects models were used to estimate the pooled effect sizes. In studies with a fixed effects model, it

was assumed that all studies measure the same parameter derived from the same population, and the existing difference between the effect sizes was due to the random sampling error. However, in studies with random effects model, it was assumed that they were derived from different populations and the difference was due to the either random sampling error or heterogeneity. When the number of studies was small or heterogeneity was significantly ruled out, the fixed effect model was used.⁸ The assessment for publication bias by funnel plots was planned but not performed for meta-analysis with small number of included studies.⁹ Instead, Begg and Mazumdar's test for rank correlation was used to test the null hypothesis of "symmetry exists in the funnel plot (no publication bias)"; Sensitivity analysis removing one article at each step was done to test the validity of the results. If there were information on several districts of a province, the summary effect size was provided for the capital only. Finally, the prevalence of total HPV, HPV16, HPV18, and HPV other genotypes were depicted on the map. All statistical analyses were performed using Comprehensive Meta-analysis 2.2.064 and ArcGIS 10.8.2 software tools at the significance level < 0.05.

Results

The meta-analysis included nineteen articles with 258839 participants. The total HPV prevalence was reported for all 28 provinces; however, some provinces did not report the HPV16, HPV18, and HPV other genotypes; in addition, the nineteen articles were from high-quality articles. The characteristics of nineteen articles and their quality assessment have been

Table 1. The characteristics and quality assessment of nineteen articles entered in the systematic review and meta-analysis

ID	Author [Ref]	Study location	Type of study	Publication year	Sample size	Event rate				Newcastle - Ottawa Quality score
						Total	HPV16	HPV18	HPV other genotypes	
1	Kesheh ¹⁵	Ardabil	Cross sectional	2013	377	0.048	0.073	0.028	0.210	10
2	Kesheh ¹⁵	Azarbayjan sharghi	Cross sectional	2013	125	0.04	0.060	0.021	0.116	
3	Kesheh ¹⁵	Esfehan	Cross sectional	2013	274	0.022	0.021	0.002	0.045	
4	Kesheh ¹⁵	Qazvin	Cross sectional	2013	232	0.03	0.016	NR	0.026	
5	Kesheh ¹⁵	Gilan	Cross sectional	2013	257	0.054	0.017	NR	0.005	
6	Kesheh ¹⁵	Hormozgan	Cross sectional	2013	232	0.095	0.004	NR	0.018	
7	Kesheh ¹⁵	Kerman	Cross sectional	2013	171	0.023	0.000	NR	0.030	
8	Kesheh ¹⁵	Khozestan	Cross sectional	2013	308	0.042	0.253	0.036	0.542	
9	Kesheh ¹⁵	Kordestan	Cross sectional	2013	205	0.024	NR	NR	NR	
10	Kesheh ¹⁵	Yazd	Cross sectional	2013	226	0.031	NR	NR	NR	
11	Kesheh ¹⁶	Azarbayjan gharbi	Cross sectional	2019	10266	0.006	0.018	0.012	0.003	9
12	Kesheh ¹⁶	Azarbayjan sharghi	Cross sectional	2019	10266	0.007	0.039	0.033	NR	
13	Kesheh ¹⁶	Boushehr	Cross sectional	2019	10266	0.004	0.298	0.064	NR	
14	Kesheh ¹⁶	Charmahal	Cross sectional	2019	10266	0.003	0.000	0.000	0.090	
15	Kesheh ¹⁶	Esfehan	Cross sectional	2019	10266	0.007	0.101	0.055	NR	
16	Kesheh ¹⁶	Fars	Cross sectional	2019	10266	0.007	0.016	NR	0.032	
17	Kesheh ¹⁶	Gilan	Cross sectional	2019	10266	0.08	0.013	NR	0.018	
18	Kesheh ¹⁶	Golestan	Cross sectional	2019	10266	0.002	0.009	NR	0.021	
19	Kesheh ¹⁶	Hamedan	Cross sectional	2019	10266	0.001	0.008	NR	0.032	
20	Kesheh ¹⁶	Ilam	Cross sectional	2019	10266	0.000	0.004	NR	0.091	
21	Kesheh ¹⁶	Kerman	Cross sectional	2019	10266	0.003	NR	NR	NR	
22	Kesheh ¹⁶	Kermanshah	Cross sectional	2019	10266	0.006	0.058	0.048	0.103	
23	Kesheh ¹⁶	Khorasan	Cross sectional	2019	10266	0.001	0.020	NR	NR	
24	Kesheh ¹⁶	Khorasan	Cross sectional	2019	10266	0.008	0.090	0.094	0.150	
25	Kesheh ¹⁶	Khorasan	Cross sectional	2019	10266	0.006	NR	NR	NR	
26	Kesheh ¹⁶	Khorasan	Cross sectional	2019	10266	0.004	0.030	0.007	0.082	
27	Kesheh ¹⁶	Kohgiluyeh	Cross sectional	2019	10266	0.000	0.120	0.000	0.010	
28	Kesheh ¹⁶	Lorestan	Cross sectional	2019	10266	0.007	NR	NR	NR	
29	Kesheh ¹⁶	Markazi	Cross sectional	2019	10266	0.014	NR	NR	NR	
30	Kesheh ¹⁶	Mazandaran	Cross sectional	2019	10266	0.028	NR	NR	NR	
31	Kesheh ¹⁶	Qom	Cross sectional	2019	10266	0.020	NR	NR	NR	
32	Kesheh ¹⁵	Semnan	Cross sectional	2013	231	0.030	NR	NR	NR	
33	Kesheh ¹⁶	Sistan	Cross sectional	2019	10266	0.004	NR	NR	NR	
34	Kesheh ¹⁶	Tehran	Cross sectional	2019	10266	0.202	NR	NR	NR	
35	Kesheh ¹⁶	Zanjan	Cross sectional	2019	10266	0.001	NR	NR	NR	
36	Moeinzadeh ¹⁷	Zanjan	Cross sectional	2020	546	0.447	0.073	0.028	NR	9
37	Eghbali ⁶	Boushehr	Cross sectional	2012	799	0.006	NR	NR	NR	9
38	Eghbali ⁶	Mazandaran	Cross sectional	2013	47	0.362	NR	NR	NR	
39	Farahmand ¹⁸	Tehran	Cross sectional	2020	571	0.240	NR	NR	NR	10
40	Ghaffari ¹⁹	Tehran	Cross sectional	2006	77	0.130	NR	NR	NR	9
41	Jamali ²⁰	Tehran	Cross sectional	2008	600	0.057	NR	NR	NR	9
42	Jamdar ²¹	Tehran	Cross sectional	2018	2453	0.103	NR	NR	NR	9
43	Khodakarami ²²	Tehran	Cross sectional	2012	825	0.078	0.191	0.089	NR	9
44	Makiani ²³	Tehran	Cross sectional	2017	400	0.383	NR	NR	NR	10

Table 1 (continued)

ID	Author [Ref.]	Study location	Type of study	Publication year	Sample size	Event rate				Newcastle - Ottawa Quality score
						Total	HPV16	HPV18	HPV other genotypes	
45	Shafaghi ²⁴	Tehran	Cross sectional	2013	851	0.311	NR	NR	NR	8
46	Yousefzadeh ²⁵	Tehran	Cross sectional	2014	851	0.311	NR	NR	NR	9
47	Shahramian ²⁶	Sistan	Cross sectional	2011	265	0.325	NR	NR	NR	8
48	Hamkar ²⁷	Mazandaran	Cross sectional	2002	44	0.091	NR	NR	NR	10
49	Afshar ²⁸	Kerman	Cross sectional	2013	410	0.263	NR	NR	NR	10
50	Moradi ²⁹	Golestan	Cross sectional	2011	378	0.201	NR	NR	NR	10
51	Mehran ³⁰	Gilan	Cross sectional	2015	98	0.041	NR	NR	NR	10
52	Safaei ³¹	Fars	Cross sectional	2010	402	0.055	NR	NR	NR	10
53	Zandi ³²	Boushehr	Cross sectional	2010	200	0.055	NR	NR	NR	9

HPV, Human Papilloma Virus; HPV16, Human Papilloma Virus genotype 16; HPV18, Human Papilloma Virus genotype 18; HPV other genotypes, Human Papilloma Virus genotypes other than 16 & 18; NR, Not Reported.

described in Table 1.

National HPV prevalence

The meta-analysis including 53 studies with 258839 participants, 25 studies with 157370 participants, 15 studies with 94882 participants, and 19 studies with 115107 participants resulted in the estimated prevalence of the total HPV, HPV16, HPV18, and HPV other genotypes equal to 0.025 (95% C.I 0.016, 0.039), 0.032 (95% C.I 0.019, 0.051), 0.028 (95% C.I 0.019, 0.040), and 0.048 (95% C.I 0.033, 0.069); related studies were statistically heterogeneous (p-value<0.05 for all) with no publication bias (p-value>0.05 for all). Meta-analysis results for the total HPV, HPV16, HPV18, and HPV other genotypes accompanied by the forest plots have been presented in Figure 2 & Table 2.

Provincial HPV prevalence

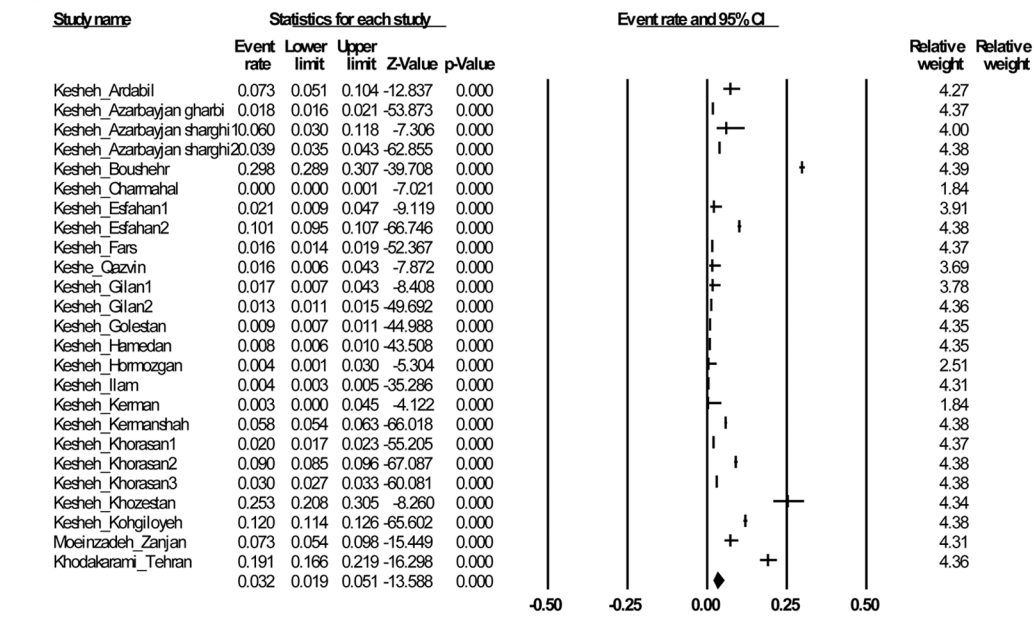
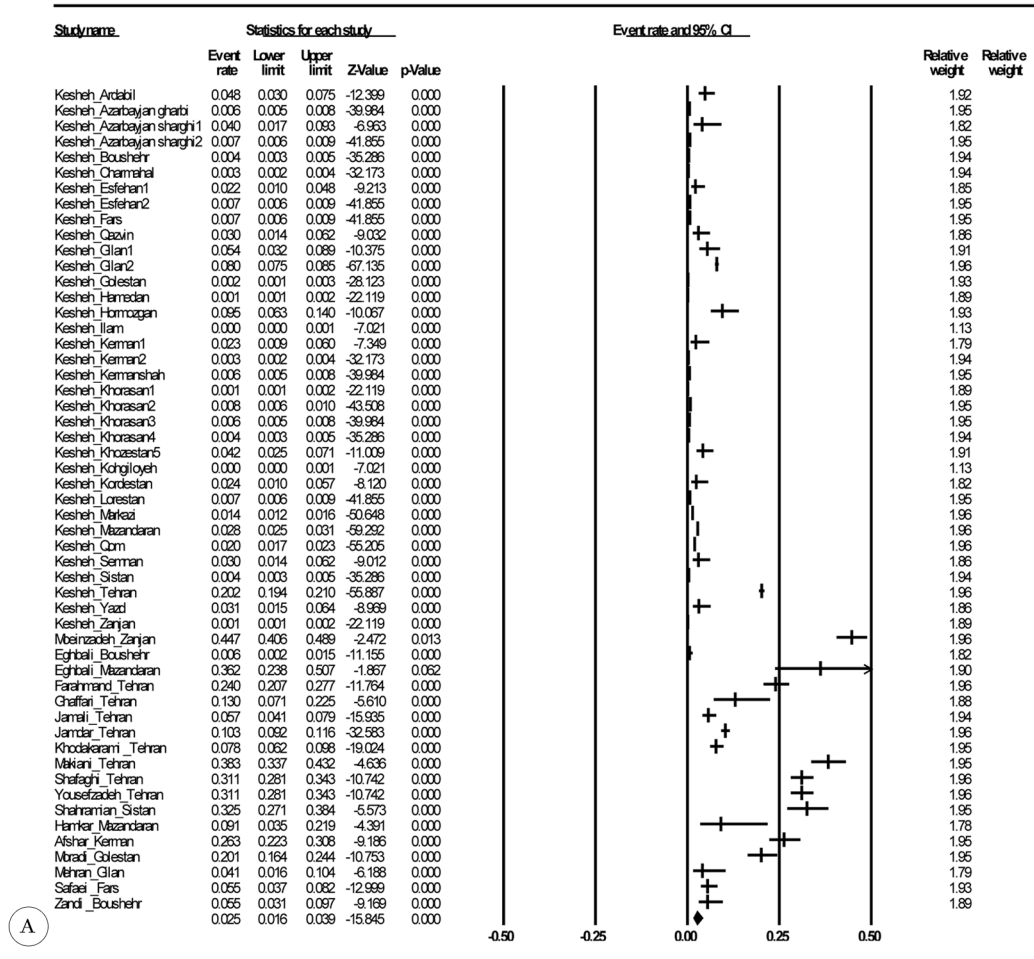
No heterogeneity were seen estimating the

total HPV, HPV16, and HPV other genotypes for Gilan, HPV 16 for Azarbayjan sharghi, and HPV 18 for Azarbayjan gharbi (p-value>0.05 for all); however, heterogeneity was observed for other provinces (p-value<0.05 for all). In addition, there were no publication bias for all provinces (p-value>0.05 for all). The provincial meta-analysis results of the total HPV, HPV16, HPV18, and HPV other genotypes have been presented in Table 3.

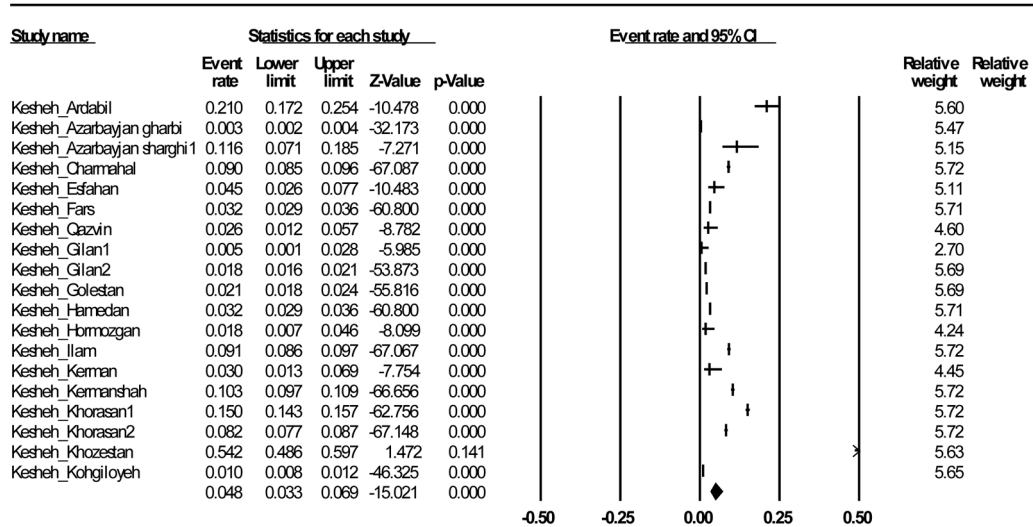
The total HPV prevalence was highest in Zanjan and Kerman (0.323 and 0.240, respectively); HPV16 prevalence were highest in Boushehr and Khuzestan (0.298 and 0.253, respectively). HPV18 was highest in Tehran (0.089), and HPV other genotypes were highest in Khuzestan (0.542).

The meta-analysis results of the pooled estimated prevalence accompanied by the single reported prevalence for total HPV, HPV16, HPV18, and HPV other genotypes in healthy women by provinces have been displayed in Figure 3.

The Prevalence of Human Papilloma Virus Infection ...

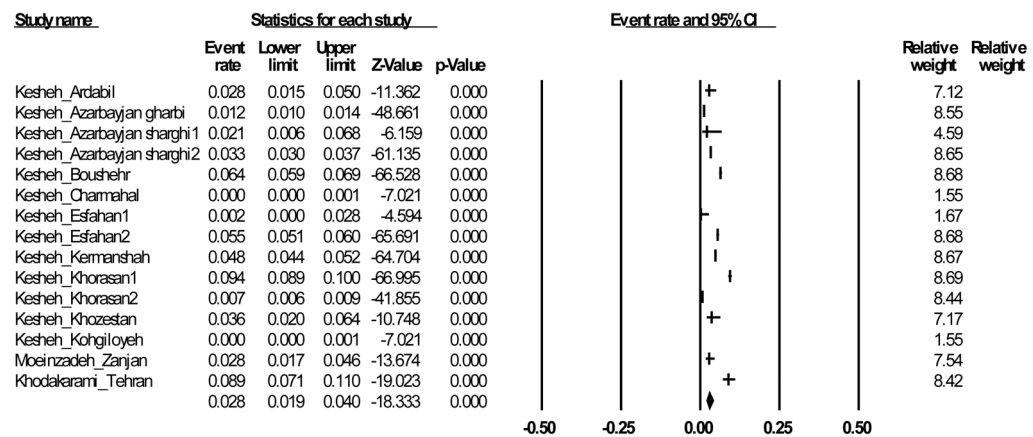


B Meta Analysis



Meta Analysis

(C)



Meta Analysis

(D)

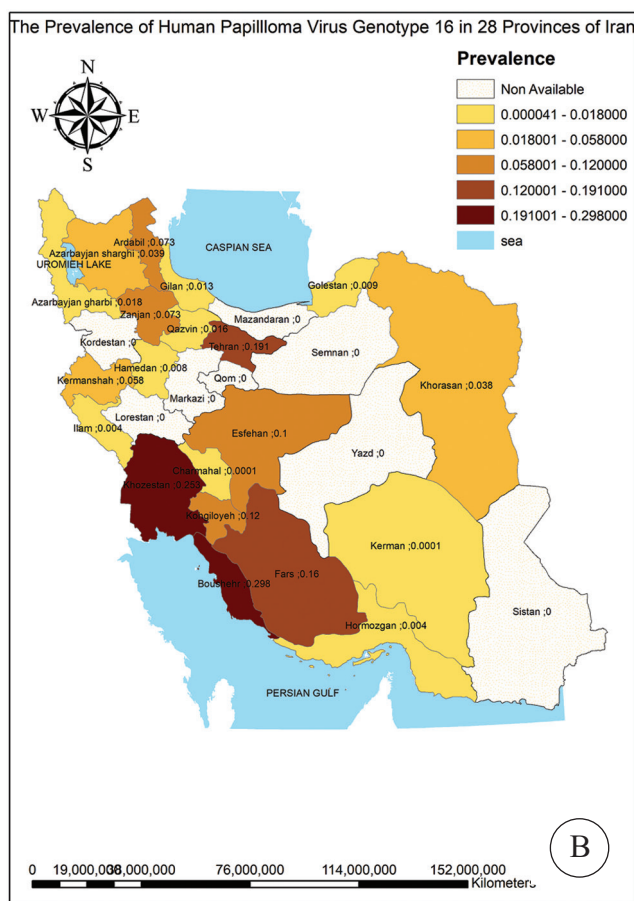
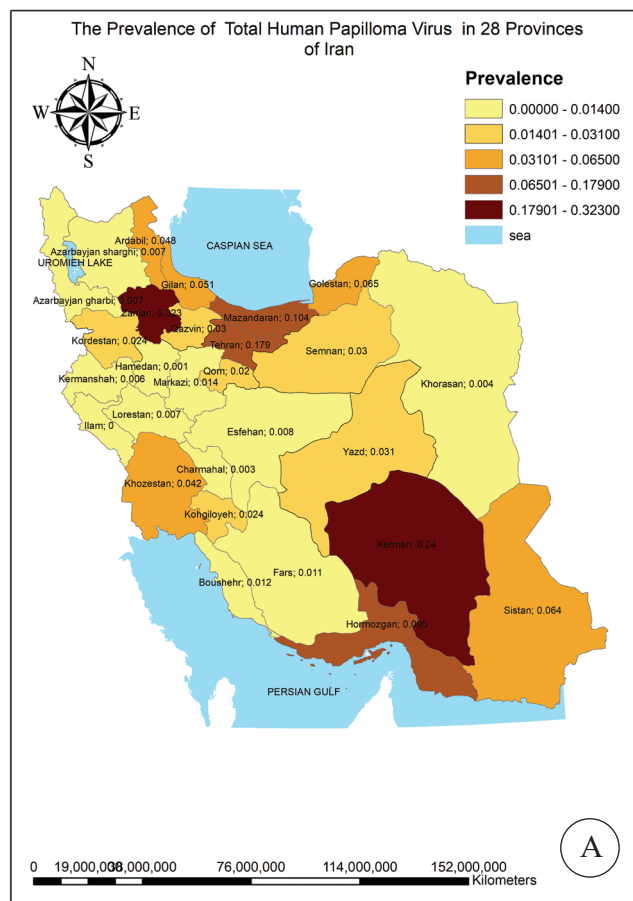
Figure 2. The forest plots of the total HPV (A), HPV16 (B), HPV other genotypes (C), and HPV18 (D) in Iranian healthy women.

The Prevalence of Human Papilloma Virus Infection ...

Table 2. National meta-analysis results of the total human papilloma virus, human papilloma virus genotype 16, human papilloma virus 18, and other genotypes human papilloma virus in Iranian healthy women

HPV Genotype	Number of studies	Sample size	Model	Event rate (95% C.I)	ANOVA table for heterogeneity			Publication bias test	
					Heterogeneity statistic		Heterogeneity severity	Begg and Mazumdar's test for rank correlation	
					Q-statistic	p-value	I ² (%)	Kendall's Tau	p-value
Total HPV	53	258839	Random effects	0.025 (0.016, 0.039)	12259.144	<0.001	99.57	0.031	0.753
HPV16	25	157370	Random effects	0.032 (0.019, 0.051)	9178.84	<0.001	99.74	0.010	0.944
HPV18	15	94882	Random effects	0.028 (0.019, 0.040)	1119.31	<0.001	98.75	-0.298	0.125
HPV other genotypes	19	115107	Random effects	0.048 (0.033, 0.069)	3661.89	<0.001	99.51	-0.300	0.073

E.S (95% C.I), Effect size (95% confidence interval); HPV, Human Papilloma Virus; HPV16, Human Papilloma Virus genotype 16; HPV18, Human Papilloma Virus genotype 18; HPV other genotypes, Human Papilloma Virus genotypes other than 16 & 18.



The Prevalence of Human Papilloma Virus Infection ...

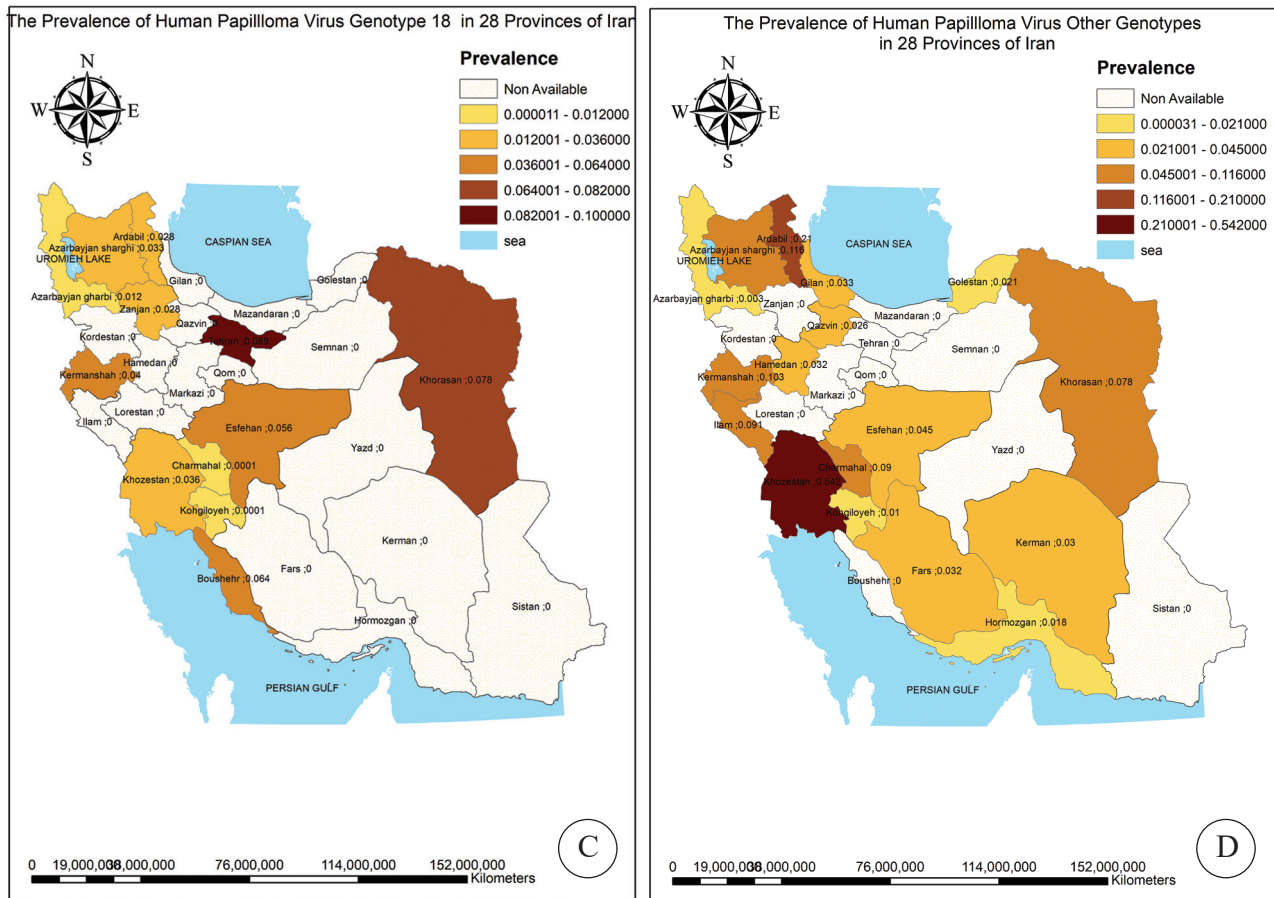


Figure 3. The prevalence of total human papilloma virus (A), human papilloma virus genotype 16 (B), human papilloma virus genotype 18 (C), and human papilloma virus other genotypes (D) in 28 provinces of Iran

Table 3. Provincial meta-analysis results of the total human papilloma virus, human papilloma virus genotype 16, human papilloma virus 18, and other genotypes of human papilloma virus in Iranian healthy women

HPV Genotype	Number of studies	Province, n	Author's name; year	Model	Event rate (95% C.I)	ANOVA table for heterogeneity			Publication bias test	
						Heterogeneity statistic		Heterogeneity severity	Begg and Mazumdar's test for rank correlation	
						Q-statistic	p-value	I ² (%)	Kendall's Tau	p-value
Total HPV	2	Zanjan, n=10511	Moeinzadeh; 2020	Fixed	0.322 (0.313, 0.331)	740.44	<0.001	99.78	NC	NC
			Kesheh; 2019							
	2	Kerman, n=581	Afshar; 2013	Fixed	0.240 (0.206, 0.278)	27.21	<0.001	96.32	NC	NC
			Kesheh; 2013							
	8	Tehran, n=16894	Makiani; 2017	Random	0.179 (0.173, 0.185)	489.05	<0.001	98.36	-0.288	0.404
			Shafaghi; 2013							
			Yousefzadeh; 2014							
			Farahmand; 2020							
		Kesheh; 2019								
		Ghaffari; 2006								

Table 3. (continued)

HPV Genotype	Number of studies	Province, n	Author's name; year	Model	Event rate (95% C.I)	ANOVA table for heterogeneity			Publication bias test	
						Heterogeneity statistic		Heterogeneity severity	Begg and Mazumdar's test for rank correlation	
						Q-statistic	p-value	I ² (%)	Kendall's Tau	p-value
Total HPV	8	Tehran, n=16894	Jamdar; 2018 Khodakarimi; 2012 Jamali; 2008	Random	0.179 (0.173, 0.185)	489.05	<0.001	98.36	-0.288	0.404
	3	Mazandaran, n=10357	Eghbali; 2013 Hamkar; 2002 Kesheh; 2019	Random	0.104 (0.098, 0.112)	97.66	<0.001	97.95	0.666	0.296
	2	Golestan, n=355	Kesheh; 2019 Moradi; 2011	Fixed	0.065 (0.043, 0.098)	370.89	<0.001	99.73	NC	NC
	2	Sistan, n=19531	Shahramian; 2011 Kesheh; 2019	Fixed	0.064 (0.060, 0.072)	546.96	<0.001	99.81	NC	NC
	2	Gilan, n=355	Kesheh; 2013 Mehran; 2015	Fixed	0.051 (0.030, 0.081)	0.27	0.610	0.00	NC	NC
	3	Boushehr, n=11265	Zandi; 2010 Eghbali; 2012 Kesheh; 2019	Random	0.012 (0.010, 0.021)	56.31	<0.001	96.44	0.001	>0.999
	2	Fars, n=10668	Kesheh; 2019 Safae; 2010	Fixed	0.011 (0.010, 0.012)	75.04	<0.001	98.66	NC	NC
	2	Esfahan, n=10540	Kesheh; 2013 Kesheh; 2019	fixed	0.008 (0.006, 0.010)	7.21	0.007	86.14	NC	NC
	2	Azərbayjan sharghi, n=10391	Kesheh; 2013 Kesheh; 2019	fixed	0.007 (0.005, 0.091)	54.34	<0.001	87.87	NC	NC
	4	Khorasan*, n=41064	Kesheh; 2019 Kesheh; 2019 Kesheh; 2019 Kesheh; 2019	Random	0.004 (0.003, 0.005)	53.2	<0.001	87.45	-0.176	0.734
HPV16	3	Gilan, n=10621	Kesheh; 2013 Kesheh; 2019 Mehran; 2015	fixed	0.013 (0.011, 0.015)	0.27	0.610	0.00	0.001	>0.999
	2	Esfahan, n=10540	Kesheh; 2013 Kesheh; 2019	fixed	0.100 (0.094, 0.106)	0.308	0.579	0	NC	NC
	2	Azərbayjan sharghi, n=10391	Kesheh; 2013 Kesheh; 2019	fixed	0.039 (0.036, 0.430)	1.42	0.233	29.574	NC	NC
	3	Khorasan*, n=30798	Kesheh; 2019 Kesheh; 2019 Kesheh; 2019	fixed	0.038 (0.014, 0.099)	575.86	<0.001	99.652	-0.666	0.296
HPV18	2	Azərbayjan sharghi, n=10391	Kesheh; 2013 Kesheh; 2019	fixed	0.033 (0.030, 0.036)	0.55	0.458	0	NC	NC
	2	Esfahan, n=10540	Kesheh; 2013 Kesheh; 2019	fixed	0.056 (0.051, 0.590)	6.2	0.013	83.87	NC	NC
	2	Khorasan*, n=20532	Kesheh; 2019 Kesheh; 2019	fixed	0.078 (0.074, 0.083)	477.06	<0.001	99.79	NC	NC

Table 3. (continued)

HPV Genotype	Number of studies	Province, n	Author's name; year	Model	Event rate (95% C.I)	ANOVA table for heterogeneity			Publication bias test	
						Heterogeneity statistic		Heterogeneity severity	Begg and Mazumdar's test for rank correlation	
						Q-statistic	p-value	I ² (%)	Kendall's Tau	p-value
HPV other genotypes	3	Gilan, n=10523	Kesheh; 2013 Kesheh; 2019 Mehran; 2015	fixed	0.033 (0.030, 0.036)	0.55	0.458	0	0.001	>0.999
	2	Khorasan*, n=20532	Kesheh; 2019 Kesheh; 2019	fixed	0.078 (0.074, 0.083)	477.06	<0.001	99.79	NC	NC

*Four different prevalence were provided for four districts of Khorasan; HPV, Human Papilloma Virus; HPV16, Human Papilloma Virus genotype 16; HPV18, Human Papilloma Virus genotype 18; HPV other genotypes, Human Papilloma Virus genotypes other than 16 & 18; NC, Not Computed.

Discussion

The national HPV prevalence in healthy women was estimated almost low and this could be due to influential factors including socioeconomic status, education, HPV screening practices, and the support systems for female sex workers; in addition, the provincial total HPV prevalence was highest in Zanjan and Kerman; HPV16 prevalence were highest in Boushehr and Khuzestan; also, HPV18 was highest in Tehran, and HPV other genotypes were highest in Khuzestan; although our study found a higher HPV prevalence in some regions of Iran, these variations between different provinces could be attributed to differences in the sociodemographic and behavioral characteristics of their population in addition to the preventive programs such as primary cervical cancer screening and condom promotion.

A previous study done on healthy women in the Middle East has reported that the prevalence of total HPV ranging from 0.0062 to 0.25,¹⁰ which covers the estimated prevalence of 0.025 in the current work. However, a systematic review and meta-analysis done in Iran in 2016 including 7655 healthy Iranian women resulted in the total HPV prevalence of 0.94 which was

higher than the current estimated total HPV prevalence of 0.025.¹¹

It was shown in a study similar to our society in terms of culture and social behavior that the total HPV prevalence on 899 Pakistani married women aged between 15 and 59 years was reported 0.28,¹² which is higher than the current estimate of 0.025. Also, in a Turkish study conducted on 2161 cervical specimens, total HPV prevalence was revealed 0.126, which is higher than the current estimation of 0.025, and the prevalence of HPV18 (0.029) which is almost the same as 0.028 in the current study, and HPV16 (0.024%) which is less than 0.032 in the current work.¹³

Previous systematic review and meta-analysis conducted by Sabeena et al. showed that rural women and those referring to cervical cancer screening programs featured higher genital HPV prevalence compared to their urban counterparts.¹⁴

Conclusion

Our study showed that the national HPV prevalence in healthy women was estimated almost low. In addition, the provincial total HPV prevalence was highest in Zanjan and Kerman; HPV16 prevalence were highest in

Boushehr and Khozestan; also, HPV18 was highest in Tehran, and HPV other genotypes were highest in Khozestan. More surveillance system on total HPV, HPV16, HPV18, and HPV other genotypes were expected in areas with higher estimated prevalence, and there would be an urgent to set up more health care efforts including infection control guideline, vaccine coverage, and medical facilities. The reported prevalence of HPVs by places will persuade policymakers and health managers to dedicate more health care and services in needier areas.

Strength and limitations

The current work revealed the epidemiology of HPV infection and used the largest number of studies; it, also, demonstrated the prevalence of the HPV infection in each province separately. The heterogeneity noticed between the outcomes of the studies was one of the limitations of this systematic review and meta analysis. Many studies did not determine the mean age of the study population. Another obstacle of our study is that most of the included studies did not report the risk factors associated with this type of infection such as characteristics of the sexual partners, frequency of sexual contact, and alcohol and drug abuse. In addition, most of the studies included in this systematic review were from urban areas.

Conflict of interest

The authors declared no conflict of interest.

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