SINET: Ethiop. J. Sci., 44(1):119–128, 2021 ISSN: 0379–2897 (PRINT)
 eISSN: 2520–7997

DOI: https://dx.doi.org/10.4314/sinet.v44i1.11

Association of human papilloma Virus infection other than cervical cancer: Systematic Review and Meta Analysis

Habtamu Molla [1,*], Habtamu Temesgen [2] and Dereje Beyene [3]

[1] Lecturer in Medical Laboratory Department, Health Science College, Addis Ababa University, Addis Ababa, Ethiopia. E-mail: habtamu.molla@aau.edu.et,

[2] Lecturer in Department of Human Nutrition and Food Sciences, College of Health Science, Debre Markos University, Debre Markos, Ethiopia. E-mail: habtamutem@gmail.com

[3] Assisstance Professor in Molecular Genetics/Functional Genomics at Microbial, Cellular and Molecular Biology Department, Addis Ababa University, Addis Ababa, Ethiopia. E-ail: dereje.beyene@aau.edu.et

ABSTRACT: Human Papilloma Virus (HPV) infection causes different cancer diseases. Cervical cancer is the most common HPV related disease. HPV infection also causes cancer of anus, vulva, vagina, penis, skin, bladder, prostate, breast, oral and others because the HPV virus is epithelium-tropic. But the association of HPV infection other than cervical cancer, for example breast cancer, bladder cancer, prostate cancer etc is still inconclusive. Thus, the objective of this review was to collect published information on HPV infection other than cervix to explore the pooled prevalence of HPV infection as well as related types of cancers. Publish research articles of HPV infection and cancer risks other than cervical cancer were systematically searched through Internet. The preferred reporting items for systematic review and meta-analysis guidelines were followed. Joanna Brigg's Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) adapted for cross sectional/case control study design was used for quality assessment of each individual study. A total of 22 studies were extracted and analyzed using STATA 14. The random effect model was used to estimate the pooled prevalence; whereas subgroup analysis and meta-regression was performed to identify the probable source of heterogeneity. Both Egger's and Begg's tests were used to check publication bias. The totals of 486 studies were retrieved and 22 studies were included in this meta- analysis. The meta-analysis result showed that the pooled prevalence of HPV infection other than cervix was 34.36% (95% CI: 23.75, 44.97) with severe heterogeneity (I^2 = 99.5%; p<0.001) with no publication bias. The highest pooled prevalence of HPV infection other than cervix was related to genital cancer which is 58.63% (95% CI: 51.86, 65.39), followed by oral cancer (47.15% with 95% CI: 19.67, 74.63). Although cervical cancer is primarily HPV induced cancer which well articulated with so many researches, other cancer types (based on the location of the HPV infection) are also increasing across the world based on this systematic and meta-analysis study. HPV infection increases the risk of developing cancers other than cervical cancer.

Key words/phrases: HPV infection, HPV related cancers, Review

INTRODUCTION

Human Papillomavirus (HPV) is a group of viruses that are extremely common globally. HPV is a non-enveloped small (8000bp) DNA virus with circular double stranded DNA, mainly infects epithelia cells of skin and mucosal membrane (Münger, Baldwin *et al*. 2004, Asiaf, Ahmad *et al*. 2014).

There are more than 200 types HPV identified, of which many do not caused problems (Woodman, Collins *et al*. 2007). Based on the association between cancers, HPV types can be classified as high risk HPV and low risk HPV (Muñoz, Bosch *et al*. 2003). Infections with low risk HPV types like HPV 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 etc does not cause symptoms and disappear when the body builds immunity to the virus (Tadlaoui, Hassou *et al*. 2020). But infections with high risk HPV types like HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82 etc cause different cancers (Yete, D'Souza *et al*. 2018).

HPV infection causes different cancer diseases and cervical cancer is the most common HPV related disease (Serrano, Brotons *et al*. 2018). HPV infection also causes cancer of anus, vulva, vagina, penis, skin, bladder, prostate, breast, oral and others because the HPV virus is epithelium-tropic (Parkin 2006). But the association of HPV infection other than cervical cancers, for example

*Author to whom correspondence should be addressed.

breast cancer, bladder cancer, prostate cancer etc is still inconclusive.

Cervical cancer is the fourth most common cancer in women (Small, Bacon *et al*. 2017). 70% of cervical cancer is caused by HPV type 16 & 18 (Bryan 2007). About 4.5% of all cancers worldwide (630,000 new cancer cases per year) are attributable to HPV: 8.6% in women and 0.8% in men (de Martel, Plummer *et al*. 2017). HPV infection and cervical cancer relations were well studied and already awareness was created about the risk. But HPV infection related cancers other than cervical cancer did not get attention among researchers, policy makers or in different charity organizations. Thus, the objective of this review was to collect published information on HPV infection other than cervix to explore the pooled prevalence of HPV infection as well as related types of cancers. This systematic analysis could directly help future research.

METHODS

Searching strategies

This systematic review and meta-analysis designed to estimate the pooled prevalence of HPV infection and related types of cancer risk. Initially systematic review and meta-analysis, including registered protocols were searched to avoid duplications and it was confirmed that there was no any review and meta-analysis was conducted to HPV infection and cancer risk other than cervix. Published research reports of HPV infection and cancer risks other than cervical cancer were searched. We systematically reviewed and analyzed published research articles to determine the pooled prevalence of HPV infection and its related cancer type. To identify published articles, major databases such as Pub med/Medline, Cochrane library, Goggle and Google scholar were used. In addition, reference lists were used. The key used in search was "prevalence" or "infection" *and* "HPV" and "risk cancer" and "HPV type". The search was conducted from September 1, 2020 to October 1, 2020. I followed the preferred reporting item for systematic review and meta-analysis (PRISMA) guideline during the systematic review (Liberati, Altman *et al*. 2009).

Eligibility criteria

All studies which report the prevalence of HPV infection and cancer risk, and case control and cross sectional study designs were included under this systematic review and meta-analysis. Articles published in English language and studies conducted worldwide were included. Published articles until September 1/2020 were eligible for this review. But studies difficult to access full text, not English language, studies which do not report specific outcome of HPV infection and studies done on cervical cancer were excluded from this systematic review and meta-analysis.

Data abstraction

Data were extracted using a standardized data extraction spreadsheet. In data extraction sheet study characteristics such as authors name, country, publication year, study design, sample size; prevalence of HPV infection; type of cancer were included.

Quality Assessment of studies

The Database search results were combined and duplicate articles were removed manually using Endnote (version X7). Joanna Briggs Institute meta-analysis of Statistics Assessment and Review Instrument (JBT-MAStARI) adapted for both cross sectional and case control study design was used (Schultz and Florence 2007). Three independent reviewers critically evaluated each individual paper. Discrepancies between those reviewers were solved by discussion. If not, a third reviewer was involved to resolve inconsistencies in between the two independent reviewers. Studies which score five and above from a total of 9 score were included in the final systematic review and meta-analysis.

Outcome measurement

This review and meta-analysis has two main outcomes. The primary outcome was prevalence of HPV infection and the second outcome was HPV infection related cancer types.

Data analysis

The extracted data were entered into an excel sheet and imported to STATA version 14 for meta-analysis. Heterogenicity among reported prevalence was assessed by using the inverse variance (I^2) with Cochran Q statistic of 25%, 50% and 75% as low, moderate and sever heterogenicity respectively with p-value less than 0.05 (Tate and Brown 1970). Random effect meta-analysis model was used to estimate the pooled prevalence of HPV infection. The forest plot was also used to visualize the presence of heterogenicity graphically. Possible differences

between the studies were explored by sub-group analysis and meta-regression. The finding was presented using forest plot with respective odds ratio and 95% confidence intervals. Evidence of publication bias was assesses using both Egger's and Begg's tests with p-value of less than 0.05 as a cutoff point to declare the presence of publication bias (Sutton, Abrams *et al*. 2000, Kontopantelis and Reeves 2010).

RESULTS

Selection of studies

A total of 486 articles searched through the electronic search of which 156 duplicate articles were excluded. From the remaining 330 articles, 306 articles were excluded after reading of titles and abstracts. Finally, 24 full text articles were assessed for eligibility criteria. Based on the pre-defined criteria and after criteria appraisal (two articles excluded) (Ammatuna, Giovannelli *et al*. 2008, Siegler, Shiner *et al*. 2017), 22 articles were included in the final analysis (Figure 1).

Characteristics of included studies

The total 22 articles were included in this meta-analysis and systematic review that meets the inclusion criteria. All the included studies were published from 2000 up to 2019. All included studies used either cross sectional or case control study design. A total of 8967cancer suspected individuals participated in these studies using an estimated sample size range from 30 (Makiyama, Hirai *et al*. 2013) up to 3393 (Zhao, Wu *et al*. 2018) to estimate the pooled prevalence of HPV infection and cancer risk other than cervix. From the total of 22 articles, 5 studies in USA; 3 study in India; 3 study in Iran; 1 study conducted in China; 1 study in Denmark; 1 study in England; 1 study in Germany; 1 study in Iraq; 1 study in Japan; 1 study in Mexico; 1 study in Netherland; 1 study in Oman; 1 study in Sweden and 1 study in Spain. The results were tabulated according to publication year (Table 1).

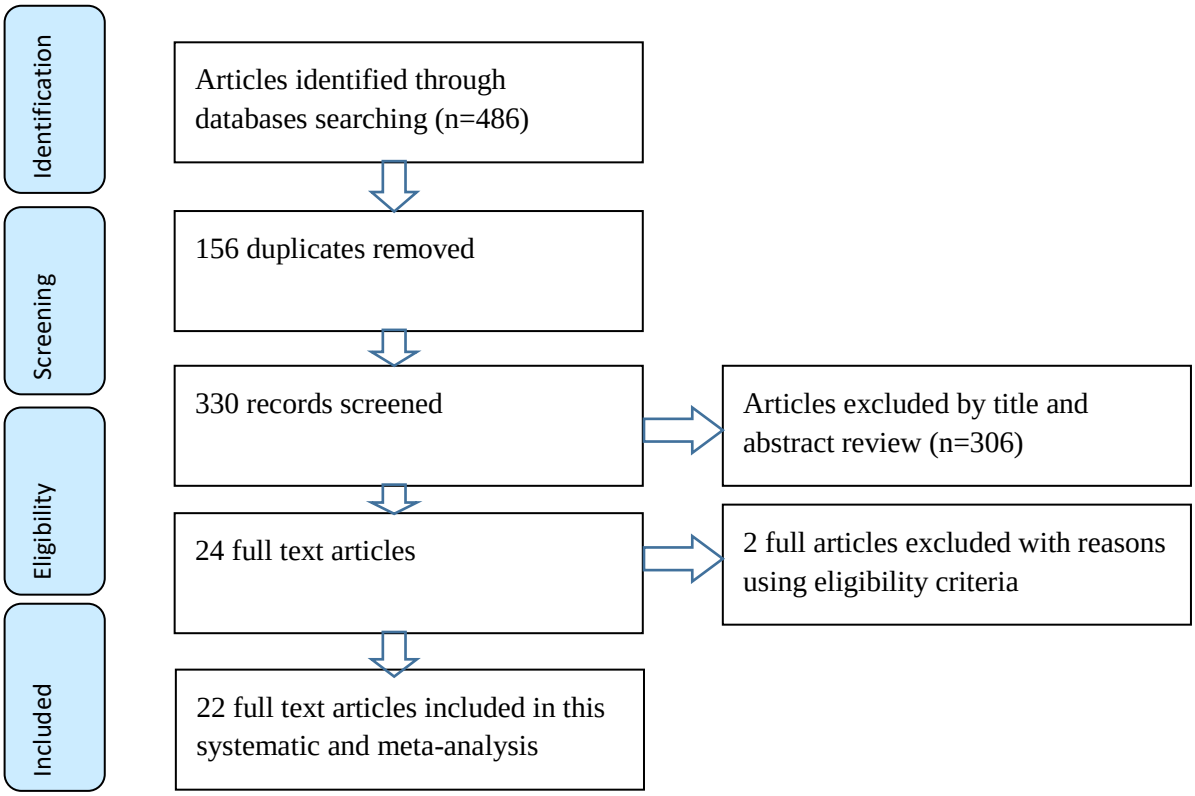

Figure 1. PRISMA flow diagram of included studies to estimate the pooled prevalence of HPV infection and cancer risk other than cervix.

Pooled prevalence of HPV infection other than cervix (Meta-analysis)

The pooled prevalence of HPV infection other than cervix was 34.36% (95% CI: 23.75, 44.97) (Figure 2). As shown in the forest plot below, statistically significant heterogeneity was identified (I^2 = 99.5%; p<0.001) indicating that the use of random effect models for estimating the pooled estimate is applicable. The significant magnitude of the heterogeneity also suggests the need to conduct subgroup analysis to identify the source of heterogeneity (Figure 2).

Subgroup analysis

Subgroup analysis was done based on study country (Figure 3), study design, publication year and cancer type to identify the possible source of heterogeneity across the studies (Table 2). The subgroup analysis result directed that the source of heterogeneity was not due to study country, publication year, cancer type and detection methods (the overall p-value for each subgroup is less than 0.001).

Table 1. Characteristics of 22 included studies to estimate the pooled prevalence of HPV infection and cancer risk other than cervix.

ID	Authors	Publication year	Country	Study design	Detection method	Sample size	Prevalence (%)	Cancer type
1	Gillison *et al*	2000	USA	case control	PCR	253	25	Head and neck cancer
2	Jatin *et al*	2002	India	cross sectional	PCR	110	33.6	Oral cancer
3	Harwood *et al*	2004	England	case control	PCR	124	62.9	Skin cancer
4	Smith *et al*	2004	USA	case control	PCR	201	22.9	Head and neck cancer
5	Katiyar *et al*	2005	India	cross sectional	PCR	101	44	Oral cancer
6	Moonen *et al* l	2006	Netherland	cross sectional	PCR	107	15.2	Bladder cancer
7	Krustrup *et al*	2008	Denmark	cross sectional	PCR	145	61	Genital cancer
8	Patel *et al*	2008	Germany	case control	PCR	239	20	Skin cancer
9	Escutia *et al*	2010	Spain	case control	PCR	142	21.2	Skin cancer
10	Larsson *et al*	2012	Sweden	cross sectional	PCR	69	53.6	Genital cancer
11	Kiyoshi *et al*	2012	Japan	case control	Hybrid	30	69.2	Oral cancer
12	Michuad *et al*	2015	USA	cross sectional	PCR	1069	14.8	Oral cancer
13	Hussein *et al*	2016	Iraq	cross sectional	PCR	104	12.5	Any type
14	Fatemeh *et al*	2016	Iran	cross sectional	PCR	200	20	Prostate cancer
15	Doosti *et al*	2016	Iran	cross sectional	PCR	47	22.9	Breast cancer
16	Gheit *et al*	2017	India	cross sectional	PCR	364	13.7	Head and neck cancer
17	Luna-Aguirre *et al*	2017	Mexico	cross sectional	PCR	724	87	Any type
18	Fu Xi *et al*	2018	USA	cross sectional	PCR	1090	5	Skin cancer
19	Zhao *et al*	2018	China	cross sectional	PCR	3393	15.1	Any type
20	Agalliu *et al*	2019	USA	case control	PCR	125	75.7	Oral cancer
21	Al-lawati *et al*	2019	Oman	cross sectional	PCR	258	17.8	Any type
22	Niloofar *et al*	2019	Iran	case control	PCR	72	48.6	Breast cancer

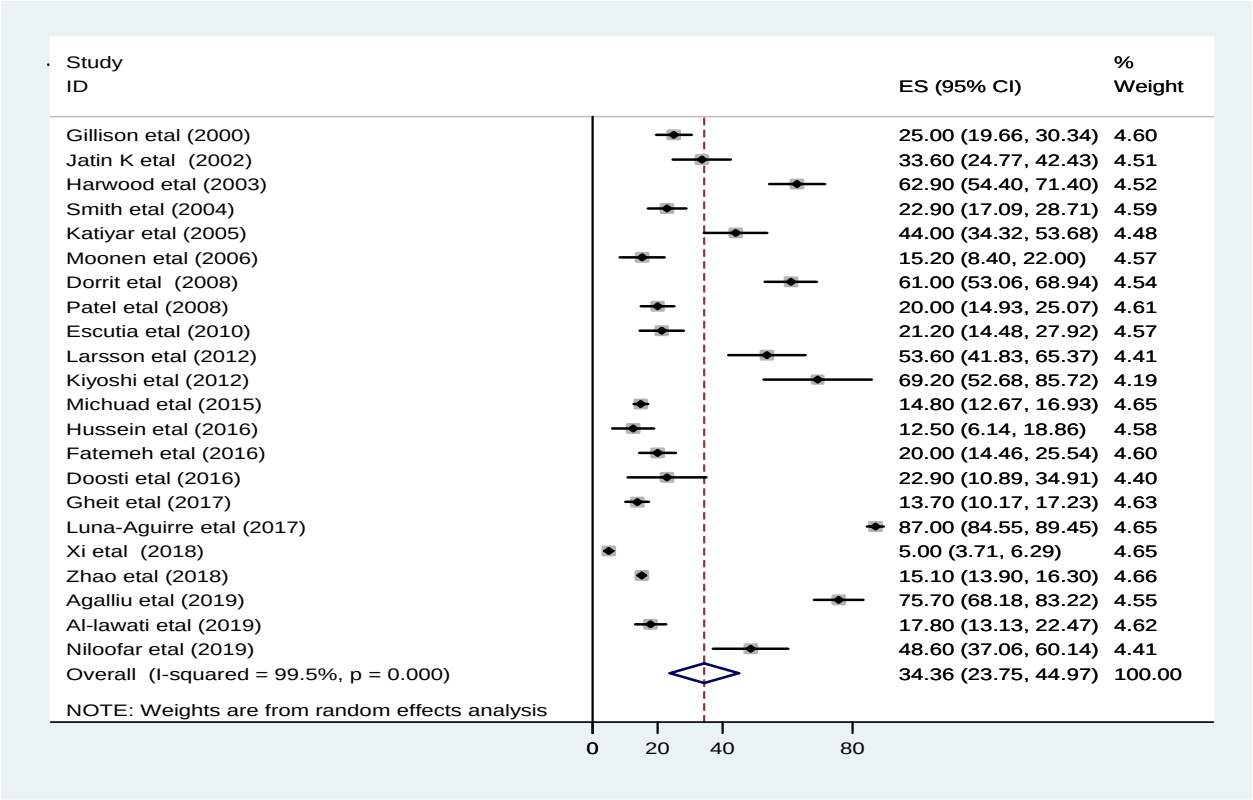

Figure 2. Forest plots showing the pooled prevalence of HPV infection other than cervix.

The lowest pooled prevalence of HPV infection other than cervix was indicated in usa [28.21% (95% CI: 14.41, 42.02)] (Figure 3). There was decrement of HPV infection other than cervix starting from 2015 (30.19% (95% CI: 14.56, 45.82)) (Table 2). The highest pooled prevalence of HPV infection other than cervix was related to genital cancer, secondly oral cancer is the highest prevalence and breast cancer is in the third rank (Table 2 and Figure 4).

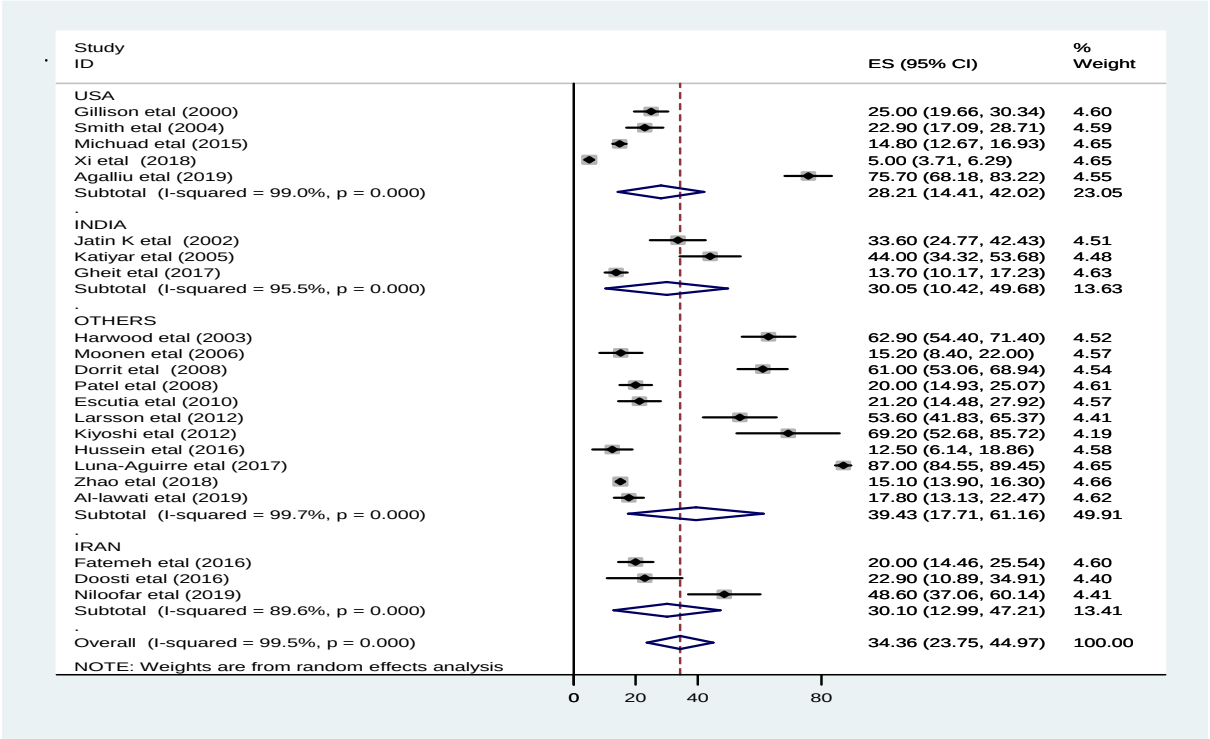

Figure 3. Forest plot shows subgroup analysis of HPV infection other than cervix by country.

Table 2. Subgroup analysis which indicates the pooled prevalence of HPV infection other than cervix.

Subgroups		No. of studies	Prevalence (95% CI)	Heterogeneity statistics	P - value	I^2 (%)
Cancer type	Head and Neck cancer	3	20.29(12.65,27.94)	14.98	0.001	86.6
	Oral cancer	5	47.15(19.67,74.63)	297.64	<0.001	98.7
	Skin cancer	4	26.95(7.05,46.84)	216.70	<0.001	98.6
	Genital cancer	2	58.63(51.86,65.39)	1.04	0.307	4.2
	Breast cancer	2	35.80(10.62,60.99)	9.14	0.003	89.1
	Others	6	27.97(-3.39,59.34)	2730.78	<0.001	99.8
Detection method	PCR	21	32.84(22.03,43.65)	4000.01	<0.001	99.5
	Hybridization	1	69.2(52.68,85.72)	0	<0.001	99.5
Study design	Cross sectional	14	29.62(16.12,43.11)	3656.49	<0.001	99.6
	Case control	8	42.65(27.49,57.80)	254.07	<0.001	97.2
Publication year	Before 2015	11	38.22(27.98,48.46)	210.15	<0.001	95.2
	2015 and above	11	30.19(14.56,45.82)	3722.16	<0.001	99.7

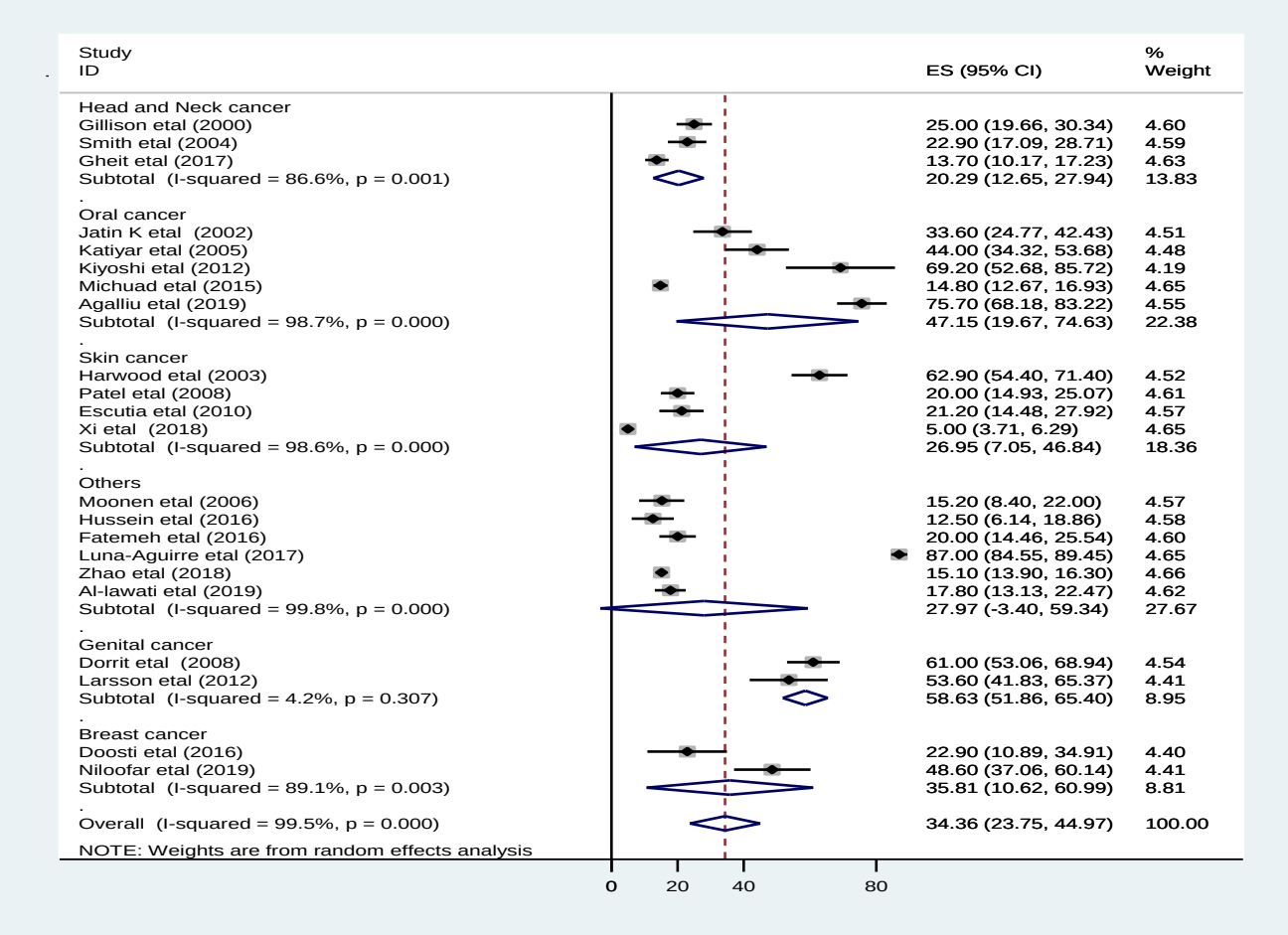

Figure 4. Forest plot shows subgroup analysis of HPV infection other than cervix by cancer type.

Publication bias

In addition to subgroup analysis, publication bias as source of heterogeneity was also checked using both Begg's and Egger's tests using STATA version 14. The result of Begg and Egger tests were not identified as the source of heterogeneity pooled prevalence of HPV infection other than cervix at p-value of (p=0.003) and (p=0.104) respectively.

Meta regression

Besides subgroup analysis and publication bias, meta regression was also assumed by considering both continuous and categorical data

to identify associated factor of heterogeneity for the pooled prevalence of HPV infection other than cervix. Study country, sample size, publication year and study design were considered in meta-regression. However, the Meta regression indicated that the pooled prevalence of HPV infection other than cervix was not associated with study country, sample size, publication year and study design (Table 3).

Table 3. Meta regression to identify the source of heterogeneity for the prevalence of HPV infection other than cervix.

Variables		Number	Coefficients	P –value
Study country	Iran	3	Reference	Reference
	USA	5	-1.8704	0.921
	India	3	-0.1106	0.996
	Others	11	8.9016	0.598
Sample	Sample size	22	-0.0083	0.249
Publication year	Before 2015	11	8.3976	0.424
	2015 and above	11	Reference	Reference
Study design	Case control	8	Reference	Reference
	Cross sectional	14	-13.1325	0.225

DISCUSSION

This systematic review and meta-analysis was conducted to estimate the pooled prevalence of HPV infection other than cervix and related types of cancers from 2000 to 2019. According to this systematic review and meta-analysis, more than one third (34.36%) of participants were infected with HPV other than cervix. Genital cancers and oral cancers were more frequent related diseases with HPV infection other than cervix. The prevalence of HPV infection other than cervix is decreasing after 2015 based on the meat-analysis result of this study. In this meta- analysis low prevalence of HPV infection other than cervix have been seen in USA compared to India and Iran.

The prevalence of HPV infection other than cervix in this systematic review and meta-analysis is lower than with study done by (Ortiz, Tamayo *et al*. 2017), (Fernandes, Meissner Rde *et al*. 2009), (So, Lee *et al*. 2019) and (Ghosh, Shetty *et al*. 2019). But it is higher than the study done by (Shrivastava, Agrawal *et al*. 2015), (Chikandiwa, Pisa *et al*. 2019), (Guan, Howell-Jones *et al*. 2012) and (Ferré, Ekouevi *et al*. 2019). (de Martel, Plummer *et al*. 2017) reported than the prevalence of HPV infection was <3% in USA and >20% India. In this meta-analysis also the prevalence was higher in India than USA. But it is lower than the overall prevalence of HPV in USA and India summarized in this meta-analysis. These disparities may be due to sample size and study methodologies difference between this meta-analysis and other studies.

Regarding the issue HPV infection induced cancers; it is obvious that many research finding reported than cervical cancer primarily associated cancer type. But there are also other cancer types related with HPV infection. A study by (Mirghani, Sturgis *et al*. 2017) showed that there is an increasing risk tongue or tonsil cancers (oral cancers) which could be an indication of HPV infection in different anatomical locations cause cancers both in men and women.

This meta-analysis study has certain limitations which includes only articles publish in English language and there are also research articles which didn't included to this review due to limitation of access to papers.

CONCLUSION

Although cervical cancer is primarily HPV induced cancer, other cancer types (based on the location of HPV infection) are also increasing across the world. More than 34.36% of participants included in this study were infected with HPV other than the cervical region. This increases the risk of development of cancers other than cervix induced by HPV infection. Therefore, countries and health organizations should also give attention to risk of other cancers induced by HPV infection in parallel to cervical cancer.

ACKNOWLEDGMENT

We would like to thank all authors of studies included in this systematic review and meta-analysis.

REFERENCES

1. Agalliu, I., Chen, T., Wang, R., Hayes, N., Freedman, S., Gapstur, M and Burk, D (2018). "Oral Alpha, Beta, and Gamma HPV Types and Risk of Incident Esophageal Cancer." *Cancer Epidemiol Biomarkers Prev* **27**: 1168-1175.

2. Al-Lawati, Z., Khamis, F., Al-Hamdani, A., Al-Kalbani, M., Ramadhan, F., Al-Rawahi, T and Al-Kobaisi, M (2020). "Prevalence of human papilloma virus in Oman: Genotypes 82 and 68 are dominating." *Int J Infect Dis* **93**: 22-27.

3. Ammatuna, P., Giovannelli, L., Matranga, D., Ciriminna, S. and Perino, A (2008). "Prevalence of genital human papilloma virus infection and genotypes among young women in Sicily, South Italy." *Cancer Epidemiol Biomarkers Prev* **17**: 2002-2006.

4. Asiaf, A., Ahmad, S., Mohammad M., Zargar, A (2014). "Review of the current knowledge on the epidemiology, pathogenesis, and prevention of human papillomavirus infection." *European Journal of Cancer Prevention* **23**: 206-224.

5. Atashafrooz, F. and Rokhbakhsh-Zamin, F. (2016). "Frequency and Type Distribution of Human Papilloma Virus in Patients with Prostate Cancer, Kerman, Southeast of Iran." *Asian Pac J Cancer Prev* **17**: 3953-3958.

6. Bryan, J. (2007). "Developing an HPV vaccine to prevent cervical cancer and genital warts." *Vaccine* **25**: 3001-3006.

7. Chikandiwa, A., Pisa, P., Sengayi, M., Singh, E and Delany-Moretlwe, S (2019). "Patterns and trends of HPV-related cancers other than cervix in South Africa from 1994-2013." *Cancer Epidemiol* **58**: 121-129.

8. de Martel, C., Plummer, Vignat, V and Franceschi, S (2017). "Worldwide burden of cancer attributable to HPV by site, country and HPV type." *Int J Cancer* **141**: 664-670.

9. Doosti, M., Bakhshesh, M, Zahir, S., Shayestehpour, M and Karimi-Zarchi, M. (2016). "Lack of Evidence for a Relationship between High Risk Human Papillomaviruses and Breast Cancer in Iranian Patients." *Asian Pac J Cancer Prev* **17**: 4357-4361.

10. Escutia, Ledesma, B., Serra-Guillen, Gimeno, C., Vilata, J., Guillén, C. and Nagore, E. (2011). "Detection of human papilloma virus in normal skin and in superficial and nodular basal cell carcinomas in immunocompetent subjects." *J Eur Acad Dermatol Venereol* **25**: 832-838.

11. Fernandes, J., Meissner Rde, V., Carvalho, M., Fernandes, de Azevedo, T. and Villa, L. (2009). "Prevalence of HPV infection by cervical cytologic status in Brazil." *Int J Gynaecol Obstet* **105**: 21-24.

12. Ferré, V., Ekouevi, D., Gbeasor-Komlanvi, F., Collin, G., Le Hingrat, Q., Tchounga, B., Salou, M., Descamps, D., Charpentier, C. and Dagnra, A. (2019). "Prevalence of human papillomavirus, human immunodeficiency virus and other sexually transmitted infections among female sex workers in Togo: a national cross-sectional survey." *Clin Microbiol Infect* **25**: 1560.e1561-1560.e1567.

13. Fu Xi, L., Schiffman, M., Ke, Y., Hughes, J., Galloway, D., He, D., Hulbert, H., Winer, R., Koutsky, L. and Kiviat, N. (2017). "Type-dependent association between risk of cervical intraepithelial neoplasia and viral load of oncogenic human papillomavirus types other than types 16 and 18." *Int J Cancer* **140**: 1747-1756.

14. Gheit, T., Anantharaman, D., Holzinger, D., Alemany, L., Tous, S., Lucas, E., Prabhu, P., Pawlita, M., Ridder, R., Rehm, S., Bogers, J., Maffini, F., Chiocca, S., Lloveras, B., Kumar, R., Somanathan, T., de Sanjosé, S., Castellsagué, X., Arbyn, M., Brennan, P.,. Sankaranarayanan, R., Pillai, Gangane, M. and Tommasino, M. (2017). "Role of mucosal high-risk human papillomavirus types in head and neck cancers in central India." *Int J Cancer* **141**: 143-151.

15. Ghosh, S., Shetty, R., Pattanshetty, S., Mallya, S., Pandey, D., Kabekkodu, S., Kamath, V., Prabhu, N., D'Souza, J. and Satyamoorthy, K (2019). "Human papilloma and other DNA virus infections of the cervix: A population based comparative study among tribal and general population in India." *PLoS One* **14**: e0219173.

16. Gillison, M., Koch, W., Capone, R., Spafford, M., Westra, W., Wu, L., Zahurak, M., Daniel, R., Viglione, M., Symer, D., Shah, K. and Sidransky, D. (2000). "Evidence for a causal association between human papillomavirus and a subset of head and neck cancers." *J Natl Cancer Inst* **92**: 709-720.

17. Guan, P., Howell-Jones, R., Bruni, N,. de Sanjosé, S., Franceschi, S. and Clifford, G. (2012). "Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer." *Int J Cancer* **131**: 2349-2359.

18. Harwood, C. , Surentheran, T., Sasieni, P., Proby, C., Bordea, C., Leigh, I., Wojnarowska, F., Breuer, J. and McGregor, J. (2004). "Increased risk of skin cancer associated with the presence of epidermodysplasia verruciformis human papillomavirus types in normal skin." *Br J Dermatol* **150**: 949-957.

19. Hussein, N., Balatay, A., Assafi, M. and AlMufty, T. (2016). "High Risk Human Papilloma Virus Genotypes in Kurdistan Region in Patients with Vaginal Discharge." *Asian Pac J Cancer Prev* **17**: 3191-3193.

20. Katiyar, S., Hedau, S., Jain, N., Kar, P., Khuroo, M., Mohanta, J., Kumar, S., Gopalkrishna, V., Kumar, N. and Das, B. (2005). "p53 gene mutation and human papillomavirus (HPV) infection in esophageal carcinoma from three different endemic geographic regions of India." *Cancer Lett* **218**: 69-79.

21. Khodabandehlou, N., Mostafaei, S., Etemadi, A., Ghasemi, A., Payandeh, M., Hadifar, S., Norooznezhad, A., Kazemnejad, A. and

Moghoofei, M. (2019). "Human papilloma virus and breast cancer: the role of inflammation and viral expressed proteins." *BMC Cancer* **19**: 61.

22. Kontopantelis, E. and Reeves, D. (2010). "metaan: Random-effects meta-analysis." *The STATA Journal* **10**(3): 395-407.
23. Krustrup, D., Jensen, H., van den, Brule, A. and Frisch, M. (2009). "Histological characteristics of human papilloma-virus-positive and -negative invasive and in situ squamous cell tumours of the penis." *Int J Exp Pathol* **90**: 182-189.
24. Larsson, G., Helenius, L., Andersson, S., Sorbe, B. and Karlsson, M. (2013). "Prognostic impact of human papilloma virus (HPV) genotyping and HPV-16 subtyping in vaginal carcinoma." *Gynecol Oncol* **129**: 406-411.
25. Liberati, A., Altman, D., Tetzlaff, J., Mulrow, C., . Gøtzsche, P., Ioannidis, J., Clarke, M., Devereaux P., Kleijnen, J. and Moher, D. (2009). "The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration." *Bmj* **339**: b2700.
26. Luna-Aguirre, C., Reyes-Cortés, L., Torres-Grimaldo, A., Karr-de-León, S., Cerda-Flores, R., Melo-Nava, B., Aizpuru-Akel, V. and Barrera-Saldaña, H. (2018). "Prevalence of human papillomavirus types in North and Central regions of Mexico." *Epidemiol Infect* **146**: 1724-1730.
27. Makiyama, K., Hirai, R., Matsuzaki, H. and Ikeda, M. (2013). "Assessment of human papilloma virus infection in adult laryngeal papilloma using a screening test." *J Voice* **27**: 230-235.
28. Michaud, D., Langevin, S., Eliot, M., Nelson, H., Pawlita, M., McClean, M. and Kelsey, K. (2014). "High-risk HPV types and head and neck cancer." *Int J Cancer* **135**: 1653-1661.
29. Mirghani, H., Sturgis, E., Aupérin, A., Monsonego, J. and Blanchard, P. (2017). "Is there an increased risk of cancer among spouses of patients with an HPV-related cancer: A systematic review." *Oral Oncol* **67**: 138-145.
30. Moonen, P., Bakkers, J., Kiemeney, L., Schalken, J., Melchers, W. and Witjes, J. (2007). "Human papilloma virus DNA and p53 mutation analysis on bladder washes in relation to clinical outcome of bladder cancer." *Eur Urol* **52**(2): 464-468.
31. Münger, K., Baldwin, A., Edwards, K., Hayakawa, H., Nguyen, C., Owens, M., Grace,.M. and Huh, K. (2004). "Mechanisms of human papillomavirus-induced oncogenesis." *Journal of virology* **78**(21): 11451-11460.
32. Muñoz, N., Bosch, F., De Sanjosé, S., Herrero, R., Castellsagué, X, Shah, K., Snijders, P. and Meijer, C (2003). "Epidemiologic classification of human papillomavirus types associated with cervical cancer." New England journal of medicine **348**: 518-527.
33. Nagpal, J., Patnaik, S and Das, B. (2002). "Prevalence of high-risk human papilloma virus types and its association with P53 codon 72 polymorphism in tobacco addicted oral squamous cell carcinoma (OSCC) patients of Eastern India." *Int J Cancer* **97**: 649-653.
34. Ortiz, A., Tamayo, V., Scorsone, A., Soto-Salgado, M., Febo, I., Piovanetti, P., Venegas-Ríos, H., Yamamura, Y. and Zorrilla, C. (2017). "Prevalence and correlates of cervical HPV infection in a clinic-based sample of HIV-positive Hispanic women." *Papillomavirus Res* **4**: 39-44.
35. Parkin, D. (2006). "The global health burden of infection-associated cancers in the year 2002." *International journal of cancer* **118**: 3030-3044.
36. Patel, A., Karagas, M., Pawlita, M., Waterboer, T. and Nelson, H. (2008). "Cutaneous human papillomavirus infection, the EVER2 gene and incidence of squamous cell carcinoma: a case-control study." *Int J Cancer* **122**: 2377-2379.
37. Schultz, T. and Florence, Z. (2007). Joanna Briggs institute meta-analysis of statistics assessment and review instrument, Adelaide: Joanna Briggs Institute.
38. Serrano, B., Brotons, M., Bosch, F. and Bruni, L. (2018). "Epidemiology and burden of HPV-related disease." *Best practice & research Clinical obstetrics & gynaecology* **47**: 14-26.
39. Shrivastava, S. B., G. Agrawal, M. Mittal and P. Mishra (2015). "Management of Vaginal Cancer." *Rev Recent Clin Trials* **10**: 289-297.
40. Siegler, E., Shiner, M., Segev, Y., Mackuli, L., Lahat, N. and Lavie, O. (2017). "Prevalence and Genotype Distribution of HPV Types in Women at Risk for Cervical Neoplasia in Israel." *Isr Med Assoc* J **19**: 635-639.
41. Small, W., Bacon, M., Bajaj, A., Chuang, L., Fisher, B., Harkenrider, M., Jhingran, A., Kitchener, H., Mileshkin, L., Viswanathan., A. and Gaffney, D. (2017). "Cervical cancer: A global health crisis." *Cancer* **123**: 2404-2412.
42. Smith, E., Ritchie, J., Summersgill, K., Hoffman, H., Wang, D., Haugen, T. and Turek, L. (2004). "Human papillomavirus in oral exfoliated cells and risk of head and neck cancer." *J Natl Cancer Inst* **96**: 449-455.
43. So, K. A., Lee, I., K. H. Lee, K., Hong, S., Kim, Y., Seo, H. and Kim, T. (2019). "Human papillomavirus genotype-specific risk in cervical carcinogenesis." *J Gynecol Oncol* **30**: e52.
44. Sutton, A., Abrams, K., Jones, D., Jones, D., Sheldon, T. and Song, F. (2000). Methods for meta-analysis in medical research, Wiley Chichester.

45. Tadlaoui, K., Hassou, N., Bennani, B. and Ennaji, M. (2020). Emergence of Oncogenic High-Risk Human Papillomavirus Types and Cervical Cancer. Emerging and Reemerging Viral Pathogens, *Elsevier***:** 539-570.

46. Tate, M. and Brown, S. (1970). "Note on the Cochran Q test." *Journal of the American Statistical Association* **65**: 155-160.

47. Woodman, C., Collins, S. and Young, L. (2007). "The natural history of cervical HPV infection: unresolved issues." *Nature Reviews Cancer* **7**: 11-22.

48. Yete, S., D'Souza, W. and Saranath, D. (2018). "High-Risk Human Papillomavirus in Oral Cancer: Clinical Implications." *Oncology* **94**: 133-141.

49. Zhao, Y., Wu, K., Tong, H., Liu, Y., Zha, H., H. Yue, H., Zhang, J. and X. Liu, X (2018). "Genotype patterns and prevalence of human papilloma virus in non-vaccinated women in Zunyi, China." *Saudi Med J* **39**: 572-578.