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Human papillomavirus infection and its correlates with clinically relevant gynecological and obstetric conditions: A cross-sectional study☆

Daniel López-Hernández[a,b,*], Luis Beltrán-Lagunes[b], Leticia Brito-Aranda[a], Maria de la Luz López-Hernández[a]

[a] Centro de Investigación y de Educación Continua (CENINVEC), Ciudad Nezahualcóyotl, Estado de México, Mexico
[b] Clínica de Medicina Familiar Gustavo A. Madero, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Mexico City, Mexico

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ABSTRACT

Background and objective: To analyze the prevalence of human papillomavirus (HPV) infection and the possible epidemiological association with conditions of clinical relevance in women.
Materials and methods: A cross-sectional study from Mexico City was conducted from January 2012 to December 2014. HPV molecular detection was performed on cervical samples. Data were analyzed with appropriated statistic tests.
Results: A total of 1604 females (median 47, interquartile range 38–54) were analyzed. Global prevalence of infection for any HPV is 9.91% (95% CI 8.6–11.3). An association between infection with 16-HPV and number of abortions (NA) (OR = 1.427; 95% CI 1.091–1.866), by univariate regression model (UVRM) was estimated. Moreover, menarche (OR = 1.566; 95% CI 1.079–2.272), NA (OR = 1.570; 95% CI 1.106–2.227) and number of pregnancies (NP) (OR = 0.461; 95% CI 0.260–0.818) have a direct and inverse association with infection by genotype 18 of HPV, respectively. Also, infection with HR-HPV genotypes has an inverse association with NP (OR = 0.791; 95% CI 0.707–0.884) by normal labor (OR = 0.867; 95% CI 0.767–0.979) and NA (OR = 0.715; 95% CI 0.534–0.959) (UVRM), and a direct association with number of sexual partners (OR = 1.082; 95% CI 1.015–1.154). Onset of sexual activity has an inverse association with infection by genotype 16- (UVRM: OR = 0.814; 95% CI 0.715–0.926; multinomial regression model (MNRM): OR = 0.803; 95% CI 0.702–0.918) and HR-HPV (UVRM: OR = 0.933; 95% CI 0.889–0.980, and MNRM: OR = 0.912; 95% CI 0.867–0.959), all *p* values were lower than .03.
Conclusions: Prevalence of HPV cervical infection is different according to age and it is associated with several medical conditions of clinical relevance in women.

Infección por el virus del papiloma humano y su correlación con situaciones ginecológicas u obstétricas de relevancia clínica: estudio transversal

Palabras clave:
Infección por el virus del papiloma humano
Cáncer cervical
Embarazo
Aborto

RESUMEN

Antecedentes y objetivo: Analizar la prevalencia de la infección por el virus del papiloma humano (VPH) y la posible asociación epidemiológica con las situaciones de relevancia clínica en las mujeres.
Material y métodos: Se llevó a cabo un estudio transversal en la ciudad de México desde enero de 2012 a diciembre de 2014. Se realizó la detección molecular del VPH sobre muestras cervicales. Los datos se analizaron utilizando las pruebas estadísticas adecuadas.

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* Corresponding author.
E-mail address: ceninvec@gmail.com (D. López-Hernández).

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Resultados: Se analizó a un total de 1.604 mujeres (mediana 47, rango intercuartílico 38-54). La prevalencia global de infección para cualquier VPH fue del 9,91% (IC 95% 8,6-11,3). Se calculó la asociación entre la infección por VPH-16 y el número de abortos (NA) (OR = 1,427; IC 95% 1,091-1,866) mediante el *univariate regression model* (UVRM, «modelo de regresión univariada»). Además, la menarquia (OR = 1,566; IC 95% 1,079-2,272), el NA (OR = 1,570; IC 95% 1,106-2,227) y el número de embarazos (NE) (OR = 0,461; IC 95% 0,260-0,818) tienen una asociación directa e inversa con la infección con el genotipo 18 del VPH, respectivamente. También, la infección por los genotipos VPH-HR tiene una asociación inversa con el NE (OR = 0,791; IC 95% 0,707-0,884), los partos normales (OR = 0,867; IC 95% 0,767-0,979) y el NA (OR = 0,715; IC 95% 0,534-0,959) (UVRM), y una asociación directa con el número de parejas sexuales (OR = 1,082; IC 95% 1,015-1,154). El inicio de la actividad sexual tiene una asociación inversa con la infección por el genotipo 16 (UVRM: OR = 0,814; IC 95% 0,715-0,926; *multinomial regression model* (MNRM, «modelo de regresión multinomial»): OR = 0,803; IC 95% 0,702-0,918) y VPH-HR (UVRM: OR = 0,933; IC 95% 0,889-0,980; y MNRM: OR = 0,912; IC 95% 0,867-0,959). Todos los valores de p fueron inferiores a 0,03.
Conclusiones: La prevalencia de la infección cervical por VPH es diferente en relación con la edad, y está asociada a diversas situaciones médicas de relevancia clínica en las mujeres.

History

There is little experimental information linking human papillomavirus (HPV) infection with pregnancy loss; besides, the epidemiological information is inconsistent. Conde-Ferráez et al. reported that cervical HPV infection was not associated with spontaneous abortions in 2 hospitals of the Social Security in Merida, Mexico, concluding that more studies were needed.[1]

HPV is a sexually transmitted virus with a more frequent association with cervical cancer (CC) around the world.[2] This virus is related to a reduced rate of clinical pregnancies, being able to double the rate of spontaneous abortions compared to uninfected women after in vitro fertilization and embryo transfer.[3] Furthermore, experimental studies suggest that HPV infection could be involved in abnormal placentation and impaired endometrial adhesion.[4–6]

In the 90s, Hermonat et al. and Malhomme et al. reported that it is possible to detect HPV in the trophoblastic tissue, and that this virus is more prevalent in spontaneous abortions specimens compared with elective abortions[4–9]; however, Sifakis et al. reported that no HPV genomes were observed in samples from 102 women with spontaneous abortions.[10] In addition, murine models support the hypothesis: HPV infection may affect embryo survival and apoptosis.[11] Therefore, we conducted a cross-sectional study to analyse the prevalence of HPV infection and co-infection, and possible epidemiological association with clinically relevant conditions in women.

Materials and methods

Study design

A cross-sectional study was performed. The present study includes women from Clinic of Family Medicine (CFM) "Gustavo A. Madero" belonging to Institute of Security and Social Services for State Workers (ISSSTE: Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, for its acronym in Spanish) at Mexico City, Mexico. The data collection was according to a retrospective research design.

Patient enrollment and study population

We included all women who were enrolled from screening programme for HPV at CFM "Gustavo A. Madero". Patients were monitored through outpatient family medicine consultations. Exclusion criteria were lack of medical history and to have an incomplete record within database. A total of 1814 women were recruited since 2012–2014 and 210 women were excluded.

Ethical considerations

This study was conducted in accordance with Good Clinical Practices of our laws and the Helsinki Declaration. The protocol was approved by the appropriate ethics committee from CFM "Gustavo A. Madero".

Molecular, Pap smear and sampling procedures for detection of human papillomavirus infection

Cervical samples were collected in PCR cell collection media (COBAS®, Roche Molecular Systems, Inc.) and solution media (PRESERVCYT®, Cytyc Corp.). Samples were kept at room temperature during transportation (according to manufacturer's recommendations) to the Centro de Apoyo Diagnóstico (CAD) San Rafael belonging to ISSSTE for further analysis. Samples were processed with appropriate supplies and trained personnel.

The molecular detection of HPV DNA was performed using an automated sample preparation system (COBAS® 4800 System HPV Test). The system utilizes amplification of target DNA by the technics of Polymerase Chain Reaction (PCR) and nucleic acid hybridization, for detect 14 high-risk (HR) HPV-genotypes in a single analysis. The genotypes of HPV identified are the genotypes 16 and 18 (HPV-16 and HPV-18), and a pool of other HR-HPV genotypes: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.

Study variables

The personal medical history of gynecological and obstetric conditions such as pregnancy, cesarean, abortion, hysterectomy, cryotherapy, hormone replacement therapy (HRT), cervical cone biopsy (CCB), abnormal bleeding (AB), pluritus vulvae (PV), vaginal discharge (VD), vaginal burning (VB), characteristics of the cervix (normal cervix; NC, abnormal cervix; AC, cervix not observed; CNO, and cervical ectropion; CE), abnormal bleeding during gynecological exploration (ABGE); background of Pap smear and PCR test, lifestyles habits such as tobacco smoking, and sexual history were obtained using a structure questionnaire.

Database and statistical analysis

All information and laboratory results were included in a database. Categorical variables were described by both the absolute frequency and percentage with the corresponding 95% confidence interval (CI). All 95% CI, for categorical variables, were obtained using a bootstrap sample of 1000 replications. All categorical variables were compared using chi square test. The specific prevalence and correlation analysis and interquartile range (IQR) were