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High prevalence of Papillomavirus (HPV) infection in asymptomatic male partners of females with genital warts: An underestimated condition

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Introduction

Human Papillomavirus (HPV) infection is one of the most common sexually transmitted condition in both genders and is responsible for penile, oral, neck and anal cancers in men [1-2]. However, seminal HPV infection may contribute to the risk of male infertility [3].

HPV comprises a family of over 200 genotypes, which can be loosely categorized based on oncogenicity into low risk (LR) and high-risk (HR) genotypes. LR genotypes, such as 6 and 11, preferentially infect cutaneous sites to cause skin warts and condyloma acuminata [4-5]. HR genotypes, such as 16, 18, 31, 33, 45, 52 and 58, among others, preferentially infect mucosal sites and are associated with the development of certain vaginal, vulvar, cervical, penile, anal and oropharyngeal cancers [4-5].

If, on one side, the presence of HPV infection in women is associated with genital warts in a high percentage of cases, on the other side in men HPV infection is often asymptomatic. In particular, Bartoletti and co-workers' reported a 27% prevalence of HPV infection in asymptomatic men [6]. However, the course of naturally acquired HPV infection in men is less studied than that of women with cervical HPV infection [4]. The HPV Infection in Men (HIM) study followed-up 4085 men for a median of 48.6 months and concluded that men remain susceptible to HPV infection throughout their lifespan, highlighting the need for prevention efforts with long-lasting duration [7]. Furthermore, in non-vaccinated asymptomatic heterosexual men whose female partners were positive for HPV DNA test, HR genotypes were more likely to persist over time when compared with other HPV genotypes [1].

So, in this study, we assess the prevalence of HPV genital infection in a group of asymptomatic men whose partners were positive for genital warts.

Materials and methods

Study design and population

This is an observational study. The population consisted of all consecutive asymptomatic heterosexual men attending a single medical institution dealing with couple pathologies, from January 2017 to December 2019, whose female partners were positive for genital warts. All female partners performed a biopsy indicative of the presence of acuminata condyloma.

Inclusion criteria

Men were eligible to participate in the study if they were: (i) Older than 18 years of age, (ii) Partners of women positive for acuminata condyloma or cervical squamous intra-epithelial lesions associated to HPV infection, (iii) With a stable relationship for at least two years.

Exclusion criteria

Men affected by major concomitant diseases, with known anatomical abnormalities of the urinary tract or with evidence of others urological diseases, diagnosed with genital or anal warts, with burning during urination or ejaculation, or participating in an HPV vaccine study or programme were excluded from the present study. Men having sex with men were also excluded due to the increased risk of exposure to HPV infection in this population.

Sample collection

All men underwent andrological visit with high magnification lens and with particular attention to preputial groove, anal region and urethral meatus, anatomical site frequently involved in HPV lesions [8]. After provided informed consent, all men were screened for HPV infection. Genital samples were obtained for preputial groove with a cytobrush by a specialist doctor (M.G.); samples were collected by swabbing the shaft skin of penis for at least ten minutes. Then urethral swabs sample were also collected, instead of urine sample specimens due to increased sensitivity in identifying the presence of HPV-DNA [9].

Laboratory procedures

All collected samples were kept at room temperature before analysis. A rapid kit was used for identification and typing of HPV DNA with polymerase chain reaction (PCR) single step and Reverse Line Blot. We classified the following genotypes as high-risk HPV: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 (HR-HPV) and as *low risk HPV*: 6, 11, 26, 40, 42, 43, 44, 53, 54, 55, 61, 62, 64, 66, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, 87, 89 and 90 (LR-HPV). HPV types not listed are still positive at an HPV Universal Sequence. DNA amplification is complete with a dUTP/UNG system for the prevention of carry over contamination. On the strip there is also a probe for the detection of the amplified TST gene, used as amplifiability control of the extracted DNA. The kit includes a single PCR master mix ready to use: once aliquoted, just add the DNA, co-amplification of an "housekeeping" gene as an internal reaction control, HPV plasmid DNA 61 (as a kit positive control), the strips and all the reagents for the visualization of the amplicons (ampliquality).

HPV-positive samples which did not hybridise with any of the type-specific probes were referred to as positive non-genotypeable HPV (PNG-HPV) [1, 10].

Samples with insufficient human beta-globin DNA were considered invalid regardless of HPV reads.

Ethics statements

Collection of biological samples were conducted following written informed consent from studied individuals. Nevertheless, our study was conducted in line with the Good Clinical Practice (GCP) guidelines and with the ethical principles laid down in the latest version of the Declaration of Helsinki. This was deemed a service evaluation by ethics committee and, thus, did not require approval, due to all procedures being performed according to routine standards, with no data collection additional to routine care in our medical institution.

Results

A total of 145 subjects were enrolled in the present study. 141 men performed preputial groove swab: 9 samples were considered invalid as specified above. The HPV genotype distribution in the remaining 132 men was: only HR-HPV n= 14 (10.6%), only LR-HPV n=13 (9.8%), both HR-HPV and LR-HPV n=5 (3.8%) and PNG-HPV n=2 (1.5%). In total 34/132 male subjects (25.7%) tested positive for any HPV genotype at the preputial groove swab. In particular HPV genotypes more represented was: HPV 18 (7/34; 20.5%), HPV 16 (5/34; 14.7%), HPV 31 (5/34; 14.7%). In 12 men infection with multiple HPV genotypes has been reported; in particular in a man six different HPV types (both HR-HPV and LR-HPV) was reported.

90 men performed urethral swab sample, none of which were considered invalid. The HPV genotype distribution was: only HR-HPV n=2 (2.2%), only LR-HPV n=16 (17.8%), both HR-HPV and LR-HPV n=3 (3.3%) and PNG-HPV n=2 (2.2%). In total 23/90 male subjects (25.5%) tested positive for any HPV genotype at the urethral swab. HPV genotypes more represented was: HPV 53 (5/23; 21.7%), HPV 42 (4/23; 17.4%), HPV 66 (2/23; 8.7%). Interestingly in a man five different HPV genotypes (both HR-HPV and LR-HPV) was reported simultaneously.

87 men performed both preputial and urethral swab: 8 men resulted HPV positive in both sites with concordance of HPV genotypes in only 3 men.

Considering the entire population of male subjects who has undergone at least one swab sample (n=132), 49 men resulted positive for at least one HPV genotype (49/132; 37.1%).

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Discussion

HPV infection is one of the most common sexually transmitted conditions in both genders and men play a key role in the transmission of HPV to women [1]. The majority of studies conducted to address the prevalence of HPV infection in males have been performed on specific male populations, such as men have sex with men, infertile or human immunodeficiency virus-infected men [1, 3, 11]. Instead, few studies have been performed to search the prevalence of HPV infection in healthy males and in particular in males of heterosexual couples with documented HPV infection in female partner.

In a Czech Republic healthy population, Jaworek and others reported a 31.3% of HR-HPV genotypes positivity in penile swabs with a prevalence of HPV 16 (6.67%) [12]. In a community-based Malaysian-men, the HR-HPV prevalence in anogenital samples was 27.1% [13].

The high prevalence of HPV infection in free-clinical partners of women with cervical intraepithelial neoplasia (CIN) is well understood and a systematic review was recently done [14]. The total HPV prevalence in this kind of male population was 49.1% (range 12.9%-86%) and in six studies the HPV 16 was the most frequent [14]. Despite these significant data, to our knowledge, studies with focus on prevalence of HPV infection in male partners of heterosexual couples with female partners affected by acuminata condyloma, are missing. It is, however, worrying the burden of HPV infection and associated disease not only for associated cancer but also for benign associated HPV disease such as mucocutaneous warts in particular cervical, vaginal, vulvar [5, 15].

So, in this study we have searched the prevalence of HPV infection in asymptomatic males of partners with genital confirmed warts. Results are very similar to prevalence in heterosexual couples with female partners affected by CIN (37.1% vs 49.1%). The prevalence of HPV 16 infection in preputial groove swab (14.7%) without association with genital male warts is of particular importance because HPV 16 infection could represent a risk factor for prostate cancer, also in young adults [16].

This high prevalence of genital HPV infection in asymptomatic males acquires even more importance since mean time to infection clearance (the time necessary to determine a complete regression in at least 50% of infected subjects) occur within 12 months in non-vaccinated males, independently of the HPV genotype considered [1, 17].

Then, HPV vaccination can represent a valid weapon to lead to increased numbers of cancers and warts prevented, as recommended by The American Cancer Society and The Advisory Committee on Immunization Practices [18]. However, in Italy both organizational and educational strategy have to be implemented to improve vaccine coverage, especially in young males [19].

This study has also some limitations. We have not collected some epidemiological, anamnestic and clinical data of male partners especially their circumcision status and cigarette smoking habits, conditions that may play a role in increasing HPV prevalence.

Conclusions

In conclusion, we found a high prevalence of HPV infection in asymptomatic male, partners of female with ascertained genital warts, highlighting the need for considering the implementation of screening of HPV and of male vaccination programmes.

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References

1. Cai T, Perletti G, Meacci F, Magri V, Verze P, Palmieri A, Mazzoli S, Santi R, Nesi G, Mirone V, Bartoletti R. Natural history of human papillomavirus infection in non-vaccinated young males: low clearance probability in high-risk genotypes. *Eur J Clin Microbiol Infect Dis 2016; 35: 463-469.*

2. Forman D, de Martel C, Lacey CJ. Global burden of human papillomavirus and related diseases. *Vaccine 2012; 30(suppl 5): F12-F23.*

3. Lyu Z, Feng X, Li N, Zhao W, Wei L, Chen Y, Yang W, Ma H, Yao B, Zhang K, Hu Z, Shen H, Hang D, Dai M. Human papillomavirus in semen and the risk for male infertility: a systematic review and meta-analysis. *BMC Inf Dis 2017; 17: 714.*

4. Lieblong BJ, Montgomery BEE, Su LJ, Nakagawa M. Natural history of human papillomavirus and vaccinations in men: a literature review. *Health Sci Rep, 2019; 2: e118.*

5. Serrano B, Brotons M, Bosch FX, Bruni L. Epidemiology and burden of HPV-related disease. *Best Pract Res Clin Obstet Gynaecol 2018; 47: 14-26.*

6. Bartoletti R, Cai T, Meliani E. Human papilloma-

Ghezzi M, Cescato A, Bisonni G, Albertin E, Pecorari V, et al. High prevalence of Papillomavirus (HPV) infection in asymptomatic male partners of females with genital warts: An underestimated condition. G Med Sci. 2021; 2(3): 042-045. https://www.doi.org/10.46766/thegms.virology.21053106

virus infection is not related with prostatitis-related symptoms: results from a case-control study. *Int Braz J Urol, 2014; 40(2): 247-256.*

7. Ingles DJ, Lin HY, Fulp WJ, Sudenga SL, Lu B, Schabath MB, Papenfuss MR, Abrahamsen ME, Salmeron J, Villa LL, Ponce EL, Giuliano AR. An analysis of HPV infection incidence and clearance by genotype and age in men: the HPV Infection in Men (HIM) study. *Papillomavirus Res 2015; 1: 126-135.*

8. Tsikis S, Hoefer L, Charnot-Katsikas A, Schneider JA. Human papillomavirus infection by anatomical site among Greek men and women: a systematic review. *Eur J Cancer Prev 2016; 25(6): 558-571.*

9. Lazcano-Ponce E, Herrero R, Munoz N, Hernandez-Avila M, Salmeron J, Leyva A, Meijer CJ, Walboomers JM. High prevalence of human papillomavirus infection in Mexican males: comparative study of penile-urethral swabs and urine samples. Sex Transm Dis 2001; 28(5): 277-280.

10. Munoz N, Xavier Bosch F, de Sanjose S, Herrero R, Castellsaguè X, Shah KV, Snijders PJF, Meijer CJLM. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med, 2003; 348(6): 518-527.*

11. Parisi SG, Cruciani M, Scaggiante R. Anal and oral human papillomavirus (HPV) infection in HIV-infected subjects in northern Italy: a longitudinal cohort study among men who have sex with men. *BMC Infect Dis 2011; 11: 150.*

12. Jaworek H, Koudelakova V, Oborna I, Zborilova B, Brezinova J, Ruzickova D, Vrbkova J, Kourilova P, Hajduch M. Prevalence and genotype distribution of human papillomavirus in Czech non-vaccinated heterosexual couples. *Virol J 2021; 18: 80.*

13. Khoo SP, Shafii MKA, Bhoo-Pathy N, Yap SH, Subramaniam S, Nasir NH, Lin Z, Belinson J, Goh PP, Qu X, Gravitt P, Woo YL. Prevalence and sociodemographic correlates of anogenital Human Papillomavirus (HPV) carriage in a cross-sectional, multi-ethnic, community-based Asian male population. *PloS One 2021; 16(1): e0245731.*

14. Skoulakis A, Fountas S, Mantzana-Peteinelli M, Pantelidi K, Petinaki E. Prevalence of human papillomavirus and subtype distribution in male partners of women with cervical intraepithelial neoplasia (CIN): a systematic review. *BMC Inf Dis 2019; 19: 192.*

15. Park IU, Introcaso C, Dunne EF. Human Papillomavirus and Genital Warts: a review of the evidence for the 2015 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. *Clin Inf Dis 2015; 61(S8): S849-855.*

16. Russo GI, Calogero AE, Condorelli R, Scalia G, Morgia G, La Vignera S. Human papillomavirus and risk of prostate cancer: a systematic review and meta-analysis. *The Aging Male 2018.*

17. Giuliano AR, Lee JH, Fulp W. Incidence and clearance of genital human papillomavirus infection in men (HIM): a cohort study. *Lancet 2011; 377(9769): 932-940.*

18. Saslow D, Andrews KS, Manassaram-Baptiste D, Smith RA, Fontham ETH. Human Papillomavirus Vaccination 2020 Guideline Update: American Cancer Society Guideline Adaptation. *Cancer J Clin, 2020.*

19. Trucchi C, Costantino C, Restivo V, Bertoncello C, Fortunato F, Tafuri S, Amicizia D, Martinelli D, Paganino C, Piazza MF, Tassinari F, Tisa V, Stefanizzi P, Baldo V, Casuccio A, Prato R, Ansaldi F, Icardi G. Immunization campaigns and strategies against human papillomavirus in Italy: the results of a survey to regional and local health units' representatives. *BioMed Res Int 2019.*

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