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Highlights

- GWs prevalence rate of 5.8 % in the Czech population aged 16-55 years
- GWs incidence increased to 442 per 100,000 person-years in 2010-2013
- An infected sexual partner was the strongest risk factor for GWs acquisition
- Almost 23% patients reported spontaneous GWs disappearance
- 4HPV immunisation was protective factor reducing GWs acquisition by more than 90%

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Rates and predictors of genital warts burden in the Czech population

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Abstract

Background. To describe the burden and the predictors of genital warts in Czech men and women.

Methods. A population-based cross-sectional study was conducted with 32,974 randomly selected health clinics attendees from all 14 regions of the Czech Republic. Information on genital warts and lifestyle behaviour was collected using a questionnaire.

Results. Results revealed a 5.8% prevalence rate of self-reported genital warts (GWs) in the Czech population aged 16-55 years. There was an increase of GWs incidence in the years 2010-2013 when compared with lifetime incidence rates, going from 205.4 (95% CI 191.0 to 219.7) to 441.8 (95% CI 393.1 to 490.6) per 100,000 person-years. No significant differences were observed between genders. The strongest risk factors found for GWs were an infected sexual partner (adjusted OR 114.3; 95% CI 78.9 to 165.4) and high number of lifetime sexual partners (adjusted OR 3.36; 95% CI 2.72 to 4.17 for > 14 partners vs. 1 partner). New finding was 22.7 % (95% CI 20.9 to 24.6%) of participants with claiming that the pathology spontaneously disappeared without medical assistance.

Conclusions. The results provide baseline information for the development and monitoring of prevention strategies against genital warts in the Czech Republic.

Keywords: human papillomavirus, genital warts, incidence, prevalence, risk predictors

Text: 2911 words

INTRODUCTION

Genital human papillomavirus (HPV) causes broad morbidity among men and women, ranging from cancer to genital warts. Although the disease is not life-threatening, the lesions can cause not only clinical symptoms, such as burning, itching, bleeding, and pain, but also psychosocial stress, embarrassment, and anxiety^{1,2}. Two HPV types (HPV6 and 11) cause up to 90% of all GWs cases³. A link between genital warts and various health-related behaviours and lifestyle factors have been suggested by other studies, and there is now widespread concern on the growing problem of genital warts^{4,5,6}. Despite the existence of several works on the prevalence and incidence of genital warts, only a few have provided data on the general population^{5,7,8}. As such, new knowledge on the overall rates and dynamic acquisition of genital warts in the general population is crucial to be able to develop national strategies to control and prevent HPV infection. This has become even more relevant since a prophylactic quadrivalent vaccine (4HPV) against HPV6, 11, 16 and 18 is now available⁹. The same prevention of genital warts is expected from new 9-valent HPV vaccine including the HPV types in the 4HPV vaccine and five additional oncogenic types (31, 33, 45, 52 and 58)¹⁰. In fact, the absence of a response against antigen HPV6 and 11 meant that the bivalent vaccine (2HPV) against HPV16 and 18 could never fully control genital warts. Therefore the routine HPV vaccination in the United Kingdom was switched from the bivalent to the quadrivalent vaccine.

The objective of this study was to describe the prevalence and incidence rates of genital warts in the Czech Republic using a questionnaire survey that captures a larger cross-section of the general population than clinic-based data. The study also sought to identify and evaluate predictors for the pathology.

SUBJECTS, MATERIALS, AND METHODS

Study population

A cross-sectional survey on genital warts was conducted in all 14 regions of the Czech Republic; volunteers were randomly recruited from people attending outpatient's health clinics, and offered a paper-based self-administered questionnaire. To guarantee confidentiality, participants were asked to, once the questionnaire was completed, seal it in the envelope supplied.

Physicians or parents could fill the survey for children or adolescents younger than 18 years old. The goal was to include at least 1,500 participants from each region.

Between January 2013 and March 2014, valid data was collected for 32,974 attendees from the 268 outpatients clinics that agreed to engage in the survey. There were 166 paediatricians, 57 gynaecologists and 45 other specialists, including dermatologists and allergists, involved as well as immunisation and transfusion centres. The percentage of subjects in each region ranged from 5% to 11%. The study was approved by Executive Committee of Preventive Medicine at Charles University in Prague.

Data collection

The questionnaire enquired on several lifestyle factors, including residence (rural or urban), education, smoking (age when first started smoking and number of cigarettes per day), number of lifetime sexual partners and HPV immunisation status (also type of commercial HPV vaccine received, year of last dose, and if they have received all 3 doses), as well as date of birth and gender.

Information on genital warts was obtained from the question, 'Have you ever had genital warts?' Study participants were also asked for the year of their first outbreak of GWs, and of recurrent episodes if any occurred, treatments received, as well as GWs status of their sexual partner. The questionnaire also contained six illustrative pictures representing three different types of genital warts for men and women, from which the respondents had to choose the one more similar to theirs.

Statistical analysis

Overall and age-specific lifetime prevalence of self-reported genital warts was estimated with a 95% confidence interval (CI). Associations between the various lifestyle factors and GWs were examined using univariate and multiple logistic regression, by which odds ratios (ORs) and the corresponding 95% CIs were estimated. The multivariate analysis of different lifestyle factors effect on GWs prevalence was initially performed separately for both genders but later pooled together, after no statistically significant differences were found between the two groups

Incidence rates were calculated as the number of genital warts claims divided by the total person-years at risk (reported per 100,000 person-years). Person-time began accumulating after birth and ended or at the date of the first genital warts episode, or, if none occurred, at the survey date.

Analyses were performed using StatsDirect Statistical Software, version 3.0.117 (StatsDirect Ltd, UK).

RESULTS

Study participants had a mean age of 35,8 years (95% CI 35.7 to 35.9 years), with only 1.0% (95% CI 0.9 to 1.1%) 15 years of age or younger, and less than 6% older than 56 years of age (up to 80 years of age). Most of the participants were in the age group 16-55 years, i.e. 93.1% (95% CI 92.9 to 93.4%). Subjects were studied in 5-year age groups. The study population consisted predominantly of women, i.e. 81.4% (95% CI 81.0 to 81.8%).

Current smoking was 25.2% (95% CI 24.7 to 25.6 %), more frequent in men than women (age adjusted OR 1.4; 95% CI 1.3 to 1.5). More than 90% of adults aged 23 years or older had, at least, basic schooling of 13 years (high school). The median lifetime number of sexual partners was 3 for both genders, with a mean of 11.1 (95% CI 6.0 to 16.2) for men and 4.3 (95% CI 4.2 to 4.3) for women. While the majority of the study population lived in urban areas (77.7%; 95% CI 77.2 to 78.2%), there was no difference in age distribution between urban and rural residents i.e. age adjusted OR 1.0 (95% CI 0.97 to 1.03).

Interestingly, despite the low HPV vaccination rate in the study population (7.2%; 95% CI 6.9 to 7.5%), 29.4% (95% CI 28.1 to 30.7%) of girls and young women aged 11-25 years have been immunised. Although the HPV vaccination rate of men was submarginal, i.e. 0.8% (95% CI 0.6 to 1.1%), no man reported GWs acquisition after immunisation.

Overall, 1968 participants (6.0%; 95% CI 5.7 to 6.2%) reported one or more episodes of genital warts. Lifetime prevalence of self-reported genital warts was independent of gender, with rates of 5.7% (95% CI 5.2 to 6.3%) for men and 6.0 % (95% CI 5.7 to 6.3%) for women. Prevalence rate was not different between men and women with regard to their age, number of sexual partners or sexual partner having ever had GWs, residence and smoking (Table 1).

From participants with clinically diagnosed genital warts, 76.2% (74.3 to 78.1%) reported to have required treatment with topical cytotoxic agents and/or ablative techniques, while ~~only~~ 22.7 % (95% CI 20.9 to 24.6%) claimed that the pathology disappeared without medical assistance.

The prevalence of self-reported genital warts increased with age peaking at 7.6% (95% CI 6.9 to 8.4%) in the age group 26-30, after which declined to 4.9% (95% CI; 4.0% to 6.0%) at the oldest age group. The sex-, age- and region-standardised GWs prevalence rate reached 5.8% (95% CI 5.4 to 6.2%) in the Czech population aged 16-55 years.

The lifetime incidence rate of genital warts per 100,000 persons-years was 165.7 (95% CI 158.4 to 173.1) for the study participants, and 141.6 (95% CI 158.4 to 173.1) for the Czech population. This rate increased to 291.6 (95% CI 278.7 to 305.1) in the study, and 205.4 (95% CI 191.0 to 219.7) in the Czech population when we only considered individuals aged 16-55 years.. A slightly lower incidence was found in men than in women, but this was not statistically significant, i.e. OR 1.11 (95% CI 0.99 to 1.26) for study participants and 1.12 (95% CI 0.97 to 1.28) for the Czech population.

The sex- and age-standardised incidence rate between the years 2010-2013 was 441.8 (95% CI 393.1 to 490.6) per 100,000 persons-years at risk, revealing a increasing tendency for genital warts infection among the population aged 16-55 years during this period, when compared with lifetime

rates. This observation was further supported by the rise, in 2013, of GWs first infections: up to 0.83% (95% CI 0.67 to 1.03%) among subjects aged 16-35 years, and 0.58% (95% CI 0.47 to 0.70%) among those between 16-55 years of age.

Figure 1 shows the lifetime incidence rate of self-reported GWs by gender and age. The highest incidence in attendees with a history of genital warts was found in the age group 21-25 (459.2; 95% CI 424.9 to 495.6 per 100,000 person-years). No significant differences were observed between men and women, except in two age groups: the group of those between 16-20 years of age, where more women than men reported a first episode of GWs, and those of 31-35 years of age where the exact opposite occurred.

Risk factors were estimated for both genders independently because no significant differences of GWs prevalence between men and women were observed (Table 1).

A sexual partner with GWs was identified as the strongest risk factor for infection acquisition (Table 2). The percentage of subjects reporting genital warts in both members of the couple was 87.6% (83.2-91.3%), and the mutually adjusted odds ratio, independently of gender, achieved 114.3 (95% CI 78.9 to 165.4) when compared to participants whose sexual partners never had the infection.

The second most important GWs predictor was lifetime number of sexual partners; risk of infection increases with the number of partners. The highest GWs prevalence (13.2%; 95% CI 11.5 to 15.1%) was among subjects with more than 14 sex partners, i.e. adjusted OR 3.36 (95% CI 2.72 to 4.17) compared to those with just one sex partner.

Other risk factors were being in the age group 21-30 years old, smoking more than 10 cigarettes a day, and living in urban areas. Data also seemed to indicate a link between lifestyle and health-related behaviour and lifetime number of sexual partners. In fact, the percentage of heavy smokers with 5 or more lifetime sexual partners (40.6%; 95% CI 38.4 to 42.9%), was 1.7 times higher than the non-smokers with the same number of partners 24.2%; 95% CI 23.6 to 24.7). The odds ratio

between them achieved 2.14 (95% CI 1.95 to 2.36). Reports of at least 5 lifetime sexual partners were also more frequent among participants from urban areas (28.2%; 95% CI 28.2 to 29.4%) than in those from rural locations (21.7%; 95% CI 20.6 to 22.8 %), i.e. OR 1.5 (95% CI 1.4 to 1.6).

An immunisation with 4HPV vaccine, on the other hand, substantially decreases GWs prevalence, especially among young women. The percentage of 4HPV-immunised women that went to develop genital warts was reduced by 91.2% (95% CI 81.8 to 96.7%) and 91.8% (95% CI 83.0 to 96.9%) when compared to unvaccinated and 2HPV vaccinated, respectively. In conclusion, only 4HPV immunisation can be considered a protective factor against genital warts acquisition.

Although only 0.6% (95% CI 0.5 to 0.7%) of all individuals reported recurrent disease, their percentage inside the affected group increased to 9.5% (95% CI 8.2 to 10.9). In fact, it was also found that the risk of recurrence was higher than that of a first infection, i.e. age adjusted OR 1.60 (95% CI 1.37 to 1.88), and it was not influenced by gender, i.e. age adjusted OR 0.99 (95% CI 0.66 to 1.46).

Discussion

This is the first representative study of genital warts of the general population in the Czech Republic. Overall, 6.1% of the sexually active persons aged 16 to 55 years reported genital warts.

Other self-reported studies have already found lifetime GWs prevalence ranging from 4.0% or 4.4% in Australian men or women aged 16-59 years old¹¹, and 5.6% in US nationals aged 18-59 years¹².

A slightly higher prevalence of 10.6% and 7.9% was found among Danishes women and men aged 18-45 years^{13,14}, as well as among women of the same age in Iceland (12.0%), Norway (9.5%) and Sweden (11.3%). The estimation in the present study of 5.8% for GWs prevalence rates in Czech men, and 6.1% for Czech women, is close to the midpoint of previously published values.

The GWs incidence rate of 0.83% in our study participants aged 16-35 years who had a first GWs episode in the year 2013, was similar to that documented in 2010 for Czech women¹⁵. These numbers are slightly higher than the annual incidence rates per 100,000 sexually active persons reported in the United Kingdom¹⁶, France¹⁷, Spain¹⁸ or Germany¹⁹, but still lower than the

percentages of newly acquired genital warts per year reported in women of the Nordic countries, i.e. 1.3% in Denmark, 1.9% in Iceland, 1.1% in Norway and 1.0% in Sweden¹⁴.

In agreement with results from others studies^{12,20}, the peak GWs occurrence in men seen in our study occurs slightly later in life than in women. Like in the US study we see no statistically significant differences in GWs prevalence or incidence rates between adult men and women²¹. However, results from other surveys have already suggested higher incidence rate in men than women^{18,20}, as well as also the opposite^{12,19}.

Besides methodological differences in study design, differences in the epidemiology of genital warts between countries can be explained by geographical and cultural variation in sexual behaviour. In addition, the epidemiological knowledge across the world shows an increasing trend for GWs occurrence in the last 30-40 years^{14,20,22}, this could also contribute to the different rates estimated in distinct years of the last 15 years.

Sexual behaviour was found to be the strongest risk predictor for genital warts burden in both men and women. This is the first study that estimated the risk of acquiring GWs when having an infected sexual partner. The probability of contracting GWs in these circumstances is almost 17 times higher than with a non-infected partner. In fact, there was a 87.6% chance of becoming infected as well, independently of the gender.

Increased risk was also observed in men or women who reported at least 2-4 lifetime sex partners in comparison with those who had one or no sexual partner. Consistent with other studies, GWs risk was found to grow with increasing numbers of sexual partners^{12,13,14}. Individuals with a prior GWs history were identified as being 1.8 times more susceptible to a new infection than those with no previous episodes.

It was also discovered that the frequency of genital warts correlated with health-related behaviours (heavy smoking) and demographic variables (urban residence). Although both predictors appeared to be risk factors for GWs acquisition, heavy smokers or those living in urban areas also reported 5 or more lifetime sex partners more frequently than other participants. Therefore it is uncertain

whether smoking and residence are confounding or risk factors for genital warts. This could also explain why the association between smoking and GWs incidence has been inconsistent across studies, with some reporting a positive correlation between smoking and genital warts burden^{13,14,23,24}, while the others saw none^{25,26}.

To our knowledge, this is the first published survey, which includes immunisation with HPV quadrivalent vaccine as a protective predictor. And it is clear that this vaccine contributes to a substantial reduction in GWs burden^{28,29,30}; at least 90% more individuals were protected against the disease after the vaccination, in comparison with those not vaccinated or immunised with the bivalent HPV vaccine.

A potential limitation of our survey was the lack of a system to routinely register sexually transmitted infections, like the one existing in the United Kingdom²⁷, to confirm the self-reported sexual behaviour. Despite a high participation rate, the existence of bias pertaining to non-attendance or interviewed bias cannot be excluded. Another limitation was an absence of information on other health-related or demographic variables cited in other studies, such as marriage status, other sexually transmitted infections, pregnancy history, contraceptives use, alcohol drinking, contact with a prostitute, etc.

Nevertheless, our epidemiological survey still has much relevance. First, it is the largest study so far to assess GWs occurrence in Czech men and women. Second, it is a nationwide investigation with randomised data from the general population in all 14 regions of the Czech Republic. Third, HPV immunisation only recently was established as a predictor for the disease, and had not been studied. Fourth, the survey, contrary to most studies, was not limited to individuals with clinically diagnosed genital warts, this enabled attendees to self-diagnose using the pictures included in the questionnaire.

Interestingly, while the treatment was refused by only 10% of the infected in the US and 7.4% in Australia^{31,32}, in our study almost 23% of attendees did not require genital warts treatment, most likely because they were not aware of the infection.

In conclusion, our study showed that the overall prevalence of genital warts in Czech population aged 16-55 years is 5.8%, but incidences rate are rising fast as demonstrated by the growing number of cases per year, going from an average of 205.4 lifetime cases to 441.8 cases per 100,000 person-years between 2010-2013.

As such vaccination, against HPV type 6 and 11 together with type 16 and 18 or eventually with additional type 31, 33, 45, 52 and 58 (and not just HPV16 and 18) must become widespread, because it is the only highly effective instrument against what is an increasingly problematic situation. Because genital warts are not restricted to women the absence of routine immunisation for boys, and routine immunisation of 13 years old Czech girls with any type of HPV vaccine will no longer be sufficiently efficient to control this disease.

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Competing interests statement

M.P. has received lecture fees from Merck. V.A. has no potential conflicts.

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Table 1. Prevalence rates of self-reported genital warts in men and women related to predictors

Category, parameter	Men		Women		OR ^a
	No	% with GWs	No	% with GWs	
GWs status of sexual partner					
Negative	6089	5.0 (4.5-5.6)	26610	5.3 (5.1-5.6)	0.95 (0.83-1.07)
Positive	48	93.8 (82.8-98.7)	227	86.3 (81.2-90.5)	2.47 (0.82-7.39)
Age					
≤15 years	64	3.1 (0.4-10.8)	255	1.2 (0.2-3.4)	0.96 (0.85-1.08)
16-20 years	463	2.6 (1.3-4.5)	1794	5.1 (4.1-6.2)	
21-25 years	529	6.8 (4.8-9.3)	2647	7.5 (6.5-8.6)	
26-30 years	807	7.1 (5.4-9.1)	3781	7.7 (6.9-8.6)	
31-35 years	1105	5.9 (4.6-7.4)	5672	6.1 (5.5-6.7)	
36-40 years	1228	5.9 (4.7-7.4)	5549	5.6 (5.0-6.2)	
41-45 years	799	6.4 (4.8-8.3)	3009	5.7 (4.9-6.6)	
46-50 years	465	4.1 (2.5-6.3)	1634	5.8 (4.7-7.1)	
51-55 years	271	5.9 (3.4-9.4)	961	3.6 (2.5-5.0)	
≥56 years	406	4.9 (3.0-7.5)	1535	5.0 (3.9-6.2)	
Lifetime no. of sexual partners					
0	139	1.4 (0.2-5.1)	411	1.7 (0.7-3.5)	0.84 (0.24-2.90)
1	1402	3.1 (2.2-4.1)	6429	3.5 (3.1-4.0)	0.87 (0.63-1.21)
2-4	1097	5.4 (4.1-6.9)	7143	5.1 (4.6-5.7)	1.05 (0.79-1.39)

Category, parameter	Men		Women		OR ^a
	No	% with GWs	No	% with GWs	
5-9	901	7.8 (6.1-9.7)	4572	7.6 (6.8-8.4)	1.02 (0.78-1.33)
10-14	458	7.0 (4.8-9.7)	1429	9.4 (8.0-11.1)	0.76 (0.51-1.13)
≥15	548	10.6 (8.1-13.5)	834	15.0 (12.6-17.6)	0.69 (0.48-1.01)
Smoking (cigarettes-day)					
never or 1	4335	5.1 (4.5-5.8)	20558	5.4 (5.1-5.8)	0.96 (0.83-1.11)
2-10	890	6.7 (5.2-8.6)	4255	7.4 (6.6-8.2)	0.92 (0.69-1.22)
more than 10	726	7.2 (5.4-9.3)	1203	10.4 (8.7-12.3)	0.69 (0.47-1.02)
Residence					
Rural	956	5.3 (4.0-7.0)	4917	4.9 (4.3-5.5)	1.14 (0.83-1.55)
Urban	3701	5.6 (4.9-6.4)	16722	6.0 (5.7-6.4)	0.93 (0.80-1.09)
HPV immunisation					
no	6091	5.8 (5.2-6.4)	24711	6.3 (6.0-6.6)	0.92 (0.82-1.04)
2HPV	9	0.0 (0.0-33.6)	816	6.7 (5.1-8.7)	NA
4HPV	19	0.0 (0.0-17.7)	1113	0.6 (0.3-1.3)	NA

a) age-adjusted odds ratio between men and women

b) NA ... not applicable

Table 2. Predictors associated with self-reported genital warts

Category, parameter	No	% with GWs	OR ^a	OR ^b
GWs status of sexual partner				
Negative	32699	5.3 (5.0-5.5)	1.0	1.0
Positive	275	87.6 (83.2-91.3)	127.58 (88.3-184.2)	114.25 (78.9-165.4)
Age				
≤ 15 years	319	1.6 (0.5-3.6)	0.33 (0.13-0.82)	0.55 (0.22-1.38)
16-20 years	2257	4.6 (3.7-5.5)	1.0	1.0
21-25 years	3176	7.4 (6.5-8.4)	1.67 (1.32-2.12)	1.33 (1.03-1.72)
26-30 years	4588	7.6 (6.9-8.4)	1.72 (1.37-2.16)	1.29 (1.01-1.65)
31-35 years	6777	6.0 (5.5-6.6)	1.34 (1.08-1.68)	0.99 (0.78-1.26)
36-40 years	6777	5.7 (5.1-6.2)	1.26 (1.01-1.57)	0.97 (0.76-1.23)
41-45 years	3808	5.8 (5.1-6.6)	1.29 (1.02-1.65)	0.98 (0.75-1.26)
46-50 years	2099	5.4 (4.5-6.5)	1.20 (0.91-1.58)	0.98 (0.73-1.31)
51-55 years	1232	4.1 (3.1-5.4)	0.90 (0.64-1.27)	0.72 (0.50-1.03)
≥ 56 years	1941	4.9 (4.0-6.0)	1.09 (0.82-1.45)	0.98 (0.73-1.33)
Lifetime no. of sexual partners				
0	550	1.6 (0.8-3.1)	0.61 (0.30-1.26)	0.64 (0.32-1.28)
1	7831	3.5 (3.1-3.9)	1.0	1.0
2-4	8240	5.1 (4.7-5.6)	1.50 (1.28-1.75)	1.37 (1.17-1.62)

Category, parameter	No	% with GWs	OR ^a	OR ^b
5-9	5473	7.6 (6.9-8.3)	2.24 (1.91-2.63)	2.04 (1.73-2.41)
10-14	1887	8.9 (7.6-10.2)	2.41 (2.13-3.20)	2.34 (1.89-2.89)
≥ 15	1382	13.2 (11.5-15.1)	4.13 (3.39-5.05)	3.36 (2.72-4.17)
Smoking (cigarettes-day)				
never or 1	24893	5.4 (5.1-5.7)	1.0	1.0
2-10	5145	7.3 (6.6-8.0)	1.35 (1.19-1.52)	1.14 (1.00-1.29)
more than 10	1929	9.2 (7.9-10.6)	1.74 (1.48-2.05)	1.33 (1.11-1.59)
Residence				
Rural	5874	5.0 (4.4-5.6)	1.0	1.0
Urban	20425	6.0 (5.6-6.3)	1.22 (1.07-1.39)	1.19 (1.03-1.36)
HPV immunisation				
no	30802	6.2 (5.9-6.5)	1.0	1.0
2HPV	825	6.7 (5.1-8.6)	1.01 (0.76-1.35)	1.17 (0.86-1.58)
4HPV	1132	0.6 (0.2-1.3)	0.10 (0.05-0.20)	0.09 (0.04-0.20)

NOTE. Missing values were excluded from the analysis, CI, confidential interval, OR, odds ratio

a) Adjusted for age

b) All factors mutually adjusted

Figure 1. Lifetime incidence rate of self-reported genital warts by gender and age

33.

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Figure 1

