Prevalence of genital warts in reproductive-aged Turkish women presenting at gynecology outpatient clinics for any reason

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Summary

The objective of this multicenter descriptive study was to calculate the frequency of genital warts among Turkish women aged 15-49 years, who visited outpatient gynecology clinics for a variety of reasons. The study was conducted in February 2011 to collect data for a minimum of 154 patients at each center, and the total sample size reached 2,967 women (95.1% completion rate). Oral informed consents were obtained. A questionnaire including data on socio-demographic characteristics and reasons for admission was administered, and a pelvic examination was performed. The overall point prevalence was 3.5% (95% CI = 3.1%-4.0%), correcting for sampling design, with the highest rates observed in the 15 to 19-year-old group. The odds of having a genital wart was 1.82 times (95% CI = 0.99-3.33) higher among non-pregnant participants than in pregnant women (p = 0.051). The overall point prevalence of genital warts among reproductive-aged women attending gynecology outpatient clinics for any reason in Turkey was 3.5%.

Key words: Genital warts; Prevalence rates; Turkish women.

Introduction

Human papillomavirus (HPV), a cause of cervical cancer, is also known to be responsible for *condylomata accuminata*, or genital warts [1-3]. There are approximately 40 molecularly identified HPV types, and all types can infect the anogenital tract, cause visual disturbances, and lead to psychosexual sequelae [4-6]. HPV genotypes 6 and 11 are responsible for more than 90% of genital warts [7].

Although genital warts are among the most common sexually-transmitted diseases (STDs) worldwide, quite a few articles have been published on its incidence and prevalence. The source populations, sampling techniques, sociodemographic and health-related characteristics of study participants, diagnostic methods used, data sources, and calculated indices vary across these studies, but overall, they suggest that occurrence rates of genital warts differ across populations.

Neither the prevalence of genital warts nor the associated economic cost, are known in Turkey. Some estimate of the overall prevalence rates is necessary, along with the dynamics of genital wart development across different birth cohorts, in order to investigate whether routine HPV vaccination is needed at the national level. Given the low feasibility of population-based prevalence studies of genital warts and the unavailability of a usable medical recording system in Turkey, clinically-based studies currently seem to be the best alternative to investigate the frequency of genital warts in the population to roughly estimate the percentage of reproductive-aged Turkish women with genital warts. This information, in turn, may be used to guide health policy makers in decisions of whether to incorporate HPV vaccination into the routine vaccination schedule.

The objective of the study was to calculate the frequency of genital warts among Turkish women aged 15-49 years, who visited outpatient gynecology clinics for a variety of reasons. Using the proportion of reproductive-aged women with genital warts, it was possible to estimate point prevalence rates by age group.

Materials and Methods

A multicenter descriptive study was planned to estimate the prevalence of genital warts in reproductive-aged women (15-49 years) attending selected gynecology outpatient clinics (in universities, public hospitals, and private healthcare units) across ten cities in Turkey; namely, Adana, Ankara, Antalya, Diyarbakir, Erzurum, Istanbul, Izmir, Kayseri, Samsun, and Trabzon. The cities and individual outpatient clinics were selected by convenience, based on the heterogeneity of subjects in terms of sociodemographic characteristics, healthcare-seeking behaviors, geographic regions of residence, and cooperation of the attending physicians. None of the centers selected provided any special service for genital warts, nor were they known to be referral centers for genital warts.

Sample size was enlarged for an expected design effect of two. Each participating center was requested to collect data for a minimum of 154 patients.

The study was conducted in February 2011. In each city, the study aimed to collect data in at least one university hospital, one public hospital, and one private gynecology clinic. At each center, data collection was terminated at the end of 30 days, even if the intended sample size was not reached, and the total sample size reached 2,967 women (i.e., 95.1% completion rate).

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A standardized questionnaire was administered to all participants in each center. The questionnaire aimed to collect data on age, current occupation, current marital status, main reason for visiting the gynecology outpatient clinic, whether and if so where the patient had attended before with the same complaint, and type of contraceptive method currently used. The questionnaire was administered during a face-to-face interview and a pelvic examination was conducted afterwards. All eligible women presenting at one of the selected gynecology outpatient clinics were approached for the study. Participation was voluntary and oral informed consent was taken from each participant prior to completing the questionnaire. Approval for the study was obtained from the Ethics Committee of Erciyes University. Genital wart diagnosis was made by a participating gynecologist on the basis of a standard pelvic examination. All gynecologists were aware of the main study objective, i.e. assessment of prevalence of genital warts, and were specifically requested to check for and to report presence of genital wart(s) regardless of the admitting diagnosis.

Statistical analysis

Statistical analyses included number and percent distributions and calculation of measures of central tendency and dispersion for continuous variables. Comparison of groups was performed using Student's t-test and Chi-squared test, as appropriate. The alpha value for statistical significance was set at 0.05. The distribution of prevalence rates was calculated for five-year age bands and types of healthcare institutions. Odds ratio estimates were calculated when applicable.

Limitations of the study and measures taken to decrease their potential impact on statistical analysis

I – Data were collected from a selected set of gynecologic outpatient clinics/offices and were not necessarily representative of all healthcare settings in Turkey. In order to derive prevalence estimates that could be valid for women aged 15-49 years attending gynecology clinics throughout Turkey, some assumptions were made:

1) Participants from each selected healthcare setting (e.g. university hospital) were assumed to be representative of all patients attending similar healthcare settings throughout the population, i.e. institution-specific prevalence rates calculated from the sample could be used to estimate institution-specific prevalence rates at the national level.

2) The distribution of participants from the three clinical settings was not proportional to the distribution at the national level, for which a correction needed to be made in estimating the overall prevalence of genital warts among women attending any gynecology clinic at the national level.

Based on the records of the Ministry of Health on the total number of outpatient visits nationwide in 2010, of the total 302,984,218 visits, 235,172,924 (77.6%) were to public institutions, 20,098,754 (6.6%) were to university clinics, and 47,712,540 (15.7%) were to private clinics [8]. Of the total participants in this study, 419 (13%) visited public institutions, 1,744 (54%) visited university clinics, and the remaining 1,044 (33%) attended private clinics/offices. Therefore, the distribution of sampling from the three main types of healthcare institutions was not proportional to overall attendance patterns in the general population, and this, in turn, necessitated some adjustments in calculating overall estimates. In order to adjust for the sampling design used, sampling weights, calculated as the inverse of the "assumed" sampling proportions, were used.

Upon comparison of the five-year age bands (15-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49), the percentages of study participants in 15-19 and 25-34 year age groups were found to be significantly different compared to those of the general population of Turkish women in the year 2010 [9]. Gynecology clinic attendance rates were not expected to be similar across five-year age bands, and would be expected to be less common among 15 to 19-year-old women and women over the age of 40. The present findings were in line with this expectation and, thus, the authors preferred not to use any post-survey weighting adjustments. Robustness analysis was conducted using a set of 21 post-adjustment weights for adjustment to population-specific distribution of age bands. The overall outcome rate of 3.8% and 95% confidence interval of 3.4% to 4.3% were very close to the final estimates, without post-survey weighting adjustments.

II - Descriptive and disease-related characteristics of patients attending a specific healthcare setting may vary for several reasons. Given that the study centers provided no special care for genital warts, the authors would expect a non-differential selection bias, if any. On the other hand, if genital warts co-exist with certain gynecologic diseases, which may cause differential rates of attendance in certain settings, such a situation could have caused a differential selection bias in the study. However, neither the authors' literature search, nor expert opinions supported this.

III - The objective of the study was to make some estimations, based on clinical data, for the prevalence of genital warts in the general population of 15 to 49-year-old women residing in the community. In a survey study performed in Turkey in 2011, data from 72 hospitals of women visiting a gynecologist were collected, and the prevalence of genital warts among women aged 30-65 years was found to be 154 per 100,000 [10]. In the STD literature, authors have restricted analyses to pregnant women, as surrogates for the general population. However, studies suggest that rates calculated solely on the basis of pregnant women may either underestimate or overestimate the true risk in the population, although the final estimates for point prevalence of genital warts in the general population have been predicted based on calculations restricted to pregnant study participants who visit the clinic for routine pregnancy follow-up [11-15].

In this study population, the prevalence of genital warts among non-pregnant women was about twice as high as that among pregnant women, even after age adjustment. Therefore, prevalence in pregnant women was not deemed a good surrogate measure for prevalence in the whole female population.

Also, it was understood that this data set, even when combined with available health records, was not sufficient to estimate the prevalence of genital warts in the general population. The findings can only be considered representative of reproductive-aged Turkish women attending gynecology outpatient clinics for "any" reason.

Statistical Package for the Social Sciences (SPSS) for Windows, the Complex Samples module, was used for statistical analysis and weighted analyses, using city (n = 10) and healthcare setting type (n = 3) as "strata", and the individual clinics where data were collected (e.g. hospital A) as "clusters". Weights were used, as necessary.

Results

Data were collected for 2,967 women aged 15-49 years, attending 23 centers in ten cities. Table 1 presents the distribution of women included in the study by city, at the end of the 30-day study period. Not all centers were able to provide the minimum number of participants (n = 154 women). The highest completion rate was achieved in Izmir (n = 546) and Istanbul had the lowest completion rate (n =

Table 1. — *Distribution of study participants by city and type of healthcare setting attended.*

City	Type of gynecology outpatient clinic			
	Public hospital	University hospital	Private clinic/hospital	Total number of participants completing the study
Adana	–	147	106	253
Ankara	144	–	113	257
Antalya	–	154	70	224
Diyarbakır	–	180	182	362
Erzurum	–	157	139	296
Istanbul	66	–	38	104
Izmir	175	307	64	546
Kayseri	–	341	173	513
Samsun	–	131	114	245
Trabzon	–	166	–	165
Total N	385	1,583	999	2,967

Data are presented as numbers.

104). It is also important to note that not all healthcare units were represented in each city; for example, no data were collected for women attending public institutions in Adana and Istanbul, and none were collected for women attending university hospitals in Istanbul (Table 1).

The distribution of selected descriptive characteristics of study participants according to type of healthcare setting is provided in Table 2. The mean age of study participants was 32.60 years, with a standard deviation of 8.46 years. The ages ranged from 15 to 49 years, with a median age of 32 years (25% under 26 years of age, and 75% over 40 years of age). Age distributions for the three different clinical settings were similar: the mean ages were 33.31 ± 8.50, 33.30 ± 9.05, and 31.50 ± 7.25 years for those attending public institutions, university hospitals, and private care units, respectively.

The occupational classification of women was established according to the frequency and potential effect of a particular occupation on awareness of genital warts and/or related healthcare seeking behavior. The majority of the study participants were housewives, with a lower percentage among those attending private clinics/offices. The percentages of professional women working in healthcare and education sectors were quite small, yet significantly higher in private healthcare settings ($p < 0.001$).

At the time of the study, 80% of the participants were married, about ten percent were single, and two to four percent were divorced or separated. The marital status distribution did not change significantly according to the type of healthcare setting to which women were admitted (p = 0.850).

The most common reason for attending a gynecology clinic was menstrual dysfunction (11.1%), followed by vaginal discharge (2.9%), bleeding (2.8%), and pain (0.6%). It was notable that patients rarely mentioned genital warts as the reason for attending a gynecology clinic. Overall, 0.2% of all women (ranging from 0.2% in private hospitals to 3.2% in university hospitals) attending a gynecology clinic reported genital warts as their main reason for attendance (Table 2). Pregnancy-related reasons accounted for about one-fifth of all motivations for attending private clinics, but

Table 2. — *Distribution of selected descriptive characteristics by type of healthcare center.*

Characteristics studied	Public hospital (n = 385) n (%)	University hospital (n = 1,583) n (%)	Private clinic/hospital (n = 999) n (%)	Total (n = 2,967) n (%)
Occupation				
Housewife	299 (77.7)	1,239 (78.3)	542 (54.3)	2,080 (70.1)
Student	8 (2.1)	92 (5.8)	22 (2.2)	122 (4.1)
Healthcare sector worker*	9 (2.3)	38 (2.4)	40 (4.0)	87 (2.9)
Educational sector worker†	4 (1.0)	54 (3.4)	58 (5.8)	116 (3.9)
Others	65 (16.9)	160 (10.1)	337 (33.7)	562 (19.0)
Marital Status				
Married	329 (86.1)	1,368 (86.9)	879 (88.7)	2,576 (87.4)
Single	38 (9.9)	176 (11.2)	93 (9.4)	307 (10.4)
Separated/ Divorced	15 (3.9)	31 (2.0)	19 (1.9)	65 (2.2)
Reason for attending the gynecology clinic				
Menstrual dysfunction	41 (10.6	222 (14.0)	66 (6.6)	329 (11.1)
Discharge of any type	36 (9.4)	19 (1.2)	32 (3.29	87 (2.9)
Bleeding	16 (4.2)	54 (3.4)	12 (1.2)	82 (2.8)
Pain	3 (0.8)	9 (0.6)	7 (0.7)	19 (0.6)
Control/check-up	23 (6.0)	121 (7.6)	131 (13.1)	275 (9.3)
Contraception	30 (7.8)	271 (17.2)	213 (21.3)	514 (17.3)
Genital warts	1 (0.3)	5 (3.2)	2 (0.2)	8 (0.2)
Infertility	–	66 (4.2)	49 (4.9)	115 (3.9)
Counseling for intended pregnancy	18 (4.7)	18 (2.3)	8 (0.8)	44 (1.5)
Pap smear	17 (4.4)	28 (1.8)	–	45 (1.5)
Other reasons‡	200 (51.9)	920 (51.0)	472 (47.3)	2,113 (71.2)
Any previous consultation for the complaints detailed above?				
None	241 (62.6)	532 (33.6)	584 (59.5)	1,357 (46.0)
Yes, to:				
same physician	35 (9.1)	214 (13.5)	195 (19.9)	444 (15.1)
family medicine	14 (3.6)	41 (2.6)	20 (2.0)	75 (2.5)
public hospital	74 (19.2)	474 (29.9)	51 (5.2)	599 (20.3)
private hospital/doctor	15 (3.9)	275 (17.4)	121 (12.3)	411 (13.9)
other	6 (1.6)	47 (3.0)	10 (1.0)	63 (2.1)
Contraceptive method¥				
None	194 (50.5)	1,050 (66.6)	675 (69.5)	1,919 (65.5)
Any	190 (49.5)	526 (33.4)	296 (30.5)	1,012 (34.5)

Column percentages are presented. Some column totals may not be equal due to rounding. * Includes physician, nurse, midwife, dentist, medical biologist, medical technician, and laboratory technician. † Includes teachers and instructors. ‡ A total of 656 different types of entries were present in the data set as admitting diagnosis, most of which had frequencies of 1 or 2. Given that physicians were not specifically trained for grouping the admitting diagnosis, the same diagnosis could have been entered under different headings, such as, bleeding, vaginal bleeding, abnormal bleeding, frequent bleeding, menorrhagia, etc. and it was very difficult to distinguish whether meanings differed or were essentially the same. The Table presents the ten most common diagnoses. Those diagnoses with scarce frequencies are grouped under the "other" category. ¥ Data were available for 2,931 women for this question.

were less common in public health settings (7.8%). Although data were not specific enough to distinguish "admissions for routine examination" and "admissions for a previously diagnosed disease", these two together constituted about 6.0%, 7.6%, and 13.1% of women attending public institutions, university facilities, and private institutions/clinics, respectively (Table 2).

When participants were asked whether they had visited another physician previously for the same reason stated at the time of study, the distributions varied by the type of healthcare unit, as expected. Among those who were admitted to a university outpatient clinic, two-thirds mentioned that they had previously visited a healthcare setting for the same reason. Of those, about half had a previous

visit to a public hospital. Among those attending a public institution, about 40% had had a previous visit, and half of those attended another public institution. Among the participants attending private clinics/offices, more than half had previously visited a physician for the same reason, and more than half of these previous visits were either to the same physician or to another private clinic/office. It was observed that attendance patterns according to type of healthcare unit might vary for different reasons, including social security coverage, socio-economic status, type of disease/problem, severity of symptoms, women's expectations of the healthcare settings, and even place of residence. Unfortunately, there was no question in the data set to investigate which reasons could have played a role in differences in preferences.

It is interesting that the proportion of pregnant women changed significantly according to type of clinical setting. Women visiting for reasons related to pregnancy made up 5.8%, 52.7%, and 41.1% of patients attending public hospitals, university clinics, and private healthcare units, respectively ($p < 0.001$).

It is not surprising to see that about 65.5% of all participants were not using any contraceptive method at the time of the study; 17.3% were pregnant, with higher rates in private sector units and in university hospitals ($p < 0.001$). The most commonly used method was condom (9.3%), followed by intrauterine device (8.6%), pills (8.6%), tubal ligation (3.6%), injection (0.3%), calendar method (0.1%), implant (< 0.1%), and vasectomy (< 0.1%).

Table 3 presents the distribution of patients in whom any genital wart was detected by the physician at the time of the study. Study participants with at least one genital wart detected at the time of pelvic exam (n = 114) had a similar age distribution (average age = 33.5 ± 8.5 years) compared with their counterparts with no genital warts (average age = 32.7 ± 8.5 years) (t-test p = 0.304). The distribution of major occupation types was not significantly different across the two groups (p = 0.395). Similarly, the distribution of marital status was similar for patients with or without genital warts: the majority of the group was reportedly married (p = 0.146). Among women with genital warts, the percentage of women who used a contraceptive method was statistically significantly higher (5.2%) than that of those who did not (3.2%) (p = 0.008).

Compared with the 514 pregnant women, the odds of having a genital wart were 1.82 times (95% CI = 0.99-3.33) higher among non-pregnant participants (Chi-squared *p* value = 0.051) (Table 3).

As summarized in Table 4, the prevalence of genital warts among reproductive-aged women attending gynecology clinics/offices for "any" reason ranged from 3.4% (public institutions) to 4.1% (private offices/clinics), with an overall point prevalence of 3.5% (95% CI = 3.1-4.0%).

It is noteworthy that point prevalence of genital warts varied by age among the study participants. Table 5 presents age-specific prevalence rates for genital warts. The highest rates were observed in the 15 to 19-year-old group.

Table 3. — *Distribution of descriptive characteristics by the presence of any genital wart in pelvic exam.*

Characteristics studied	Women with warts (n = 114) n (%)	Women without genital warts (n = 2,853) n (%)	*p* value
Occupation (n = 2,967)			
Housewife	76 (66.6)	2,004 (70.2)	0.395[1]
Student	3 (2.6)	119 (4.2)	
Healthcare sector worker[2]	2 (1.8)	85 (3.0)	
Educational sector worker[3]	4 (3.5)	112 (4.0)	
Others	29 (25.4)	533 (18.7)	
Marital Status (n = 2,948)			
Married	92 (81.4)	2,484 (87.6)	0.146[1]
Single	17 (15.0)	290 (10.2)	
Separated/Divorced	4 (3.5)	61 (2.2)	
Reason for attending the gynecology clinic			
Menstrual dysfunction	7 (6.1)	322 (11.3)	n/a
Discharge of any type	-	87 (3.0)	
Bleeding	-	82 (2.9)	
Pain	-	19 (0.7)	
Control/check-up	-	275 (9.6)	
Contraception	12 (10.5)	502 (17.6)	
Genital warts	5 (4.4)	3 (0.19	
Infertility	1 (0.9)	114 (4.0)	
Counseling for intended pregnancy	2 (1.8)	42 (1.5)	
Pap smear	-	45 (1.6)	
Other reasons[4]	87 (76.3)	2,026 (71.0)	
Any previous consultation for the reason described above (n = 2,949)?			
None	50 (46.3)	1,307 (46.0)	0.036[1]
Yes:			
same physician	7 (6.5)	437 (15.4)	
family medicine	1 (0.9)	74 (2.6)	
public hospital	31 (28.7)	568 (20.0)	
private hospital/doctor	18 (16.7)	393 (13.8)	
other	1 (0.9)	62 (2.2)	
Contraceptive method use (n = 2,922)			
None	61 (3.2)	1,858 (96.89	0.0081
Any	113 (5.2)	2,809 (94.8)	

Column percentages are presented. Some column totals may not be equal due to rounding. Data were not complete for all variables, thus, percentages were calculated out of total number of answers for each question. [1] Chi-squared test *p* value is presented. [2] Includes physician, nurse, midwife, dentist, medical biologist, medical technician, and laboratory technician. [3] Includes teachers and instructors. [4] The table presents the ten most common diagnoses, and those diagnoses with scarce frequencies are grouped under the "other" category.

Discussion

The lifetime rate of HPV infection among 15 to 49-year-old women in U.S.A. is up to 75% [16]. However, the majority of women infected with HPV eliminate the virus without developing clinical symptoms [4, 17], and clinically apparent genital warts reportedly affect about one percent of reproductively active women [17]. Genital warts are reported as the most commonly diagnosed STD in the U.S.A. [18]. In the United Kingdom (2003), ten percent of women visiting all genitourinary medicine clinics were "newly-diagnosed cases" of genital warts [15], and the incidence of genital warts increased to 4.2% over a one-year period [19]. In a study of 69,147 women aged 18-45 years, residing in Denmark, Norway, Iceland, and Sweden, the self-reported prevalence of "ever" having a genital wart was 10.6%, and 1.3% reported having experienced genital warts within the 12 months preceding the survey. This same study found that the likelihood of genital warts increased along with number of lifetime sexual partners, history of

Table 4. — *Distribution of selected descriptive characteristics by type of healthcare center.*

Detected genital warts	Public hospital (n = 385)	University hospital (n = 1,583)	Private clinic/hospital (n = 999)	Overall
Raw numbers of genital wart cases detected during pelvic exam in the study group	13	60	40	114
Prevalence estimates % (95% CI)[1,2,3]	3.4 (3.4-3.4)	3.8 (2.2-6.5)	4.1 (2.0-8.1)	3.5* (3.1-4.0)

[1]Weights were used to adjust for non-proportional sampling fractions with respect to healthcare setting. [2]Point prevalence with 95% confidence intervals. [3]Represents women attending a gynecology outpatient clinic for "any" reason, with or without genital warts. *Adjusted for the sampling design used in the study.

Table 5. — *Age-group-specific point prevalence for physician-diagnosed genital warts and odds ratios for the association between genital warts diagnosis and age.*

Age groups	Number of women examined	Age-group-specific prevalence estimates % (95% CI)	Odds ratio (95% CI)
15-19 years	115	6.6 (6.3-6.8)	1.71 (1.46-2.01)
20-24 years	470	3.4 (2.5-4.6)	0.85 (0.72-1.00)
25-29 years	606	3.4 (3.2-3.5)	0.86 (0.75-0.99)
30-34 years	579	3.1 (2.5-3.9)	0.79 (0.74-0.84)
35-39 years	450	1.0 (0.9-1.1)	0.25 (0.22-0.29)
40-44 years	366	5.9 (5.7-6.2)	1.54 (1.31-1.81)
45-49 years	381	4.0 (3.3-4.7)	1.00 (reference)

STD, use of hormonal contraceptives, use of condoms, smoking, and higher educational attainment [20]. The cumulative incidence of genital warts in different birth cohorts, estimated on the basis of age at first diagnosis, has been found to be increased with younger age ($p < 0.001$), suggesting that the burden of genital warts will be increasing in upcoming years [20]. However, the cross-sectional nature of the given study restricted its ability to assess the temporality and several potential confounders (such as self-awareness, access to healthcare, diagnostic accuracy, and validity of self-reporting) which could limit the validity of the interpretations. In contrast, the study had distinct strengths, including large sample size, random selection of study participants, inclusion of participants from four different Nordic countries, and high response rates [20]. Overall, their findings suggested that the prevalence of genital warts is not low, and the associated disease burden is likely to increase in future years.

In a recent literature review of incidence/prevalence studies on genital warts, Singhal *et al*. [21] identified a total of 25 peer-reviewed studies and classified them into four groups according to data collection method: 1) retrospective administrative claims database or medical chart reviews (n = 10); 2) prospective physician reports (n = 4); 3) gynecological or pelvic exams (n = 5); and 4) patient self-reports (n = 6).

In countries like Turkey, where routine surveillance systems and medical record systems do not include data about disease burden, research-based calculations are important for estimating the overall burden of disease in the general population. This is also valid for investigating the overall disease burden and economic cost associated with genital warts among women in Turkey. Various methods, having particular strengths and limitations, have been used for research-based estimates of genital warts in different countries.

Research based on data collected in clinical settings represents the prevalence of warts among women visiting healthcare facilities. These findings are therefore valid only for a subgroup of women in the population, and thus will be of limited generalizability, depending on how representative the study participants are of women who have not visited a similar healthcare setting. Singhal *et al*. [21] reported ten peer-reviewed publications on annual incidence and prevalence of genital warts among women, based on retrospective administrative claims database or medical chart review studies, and determined that annual incidence rates ranged from 120-231 per 100,000 and prevalence rates ranged from 128-165 per 100,000. It is important to note that this type of study provides evidence limited to data recorded in the database/medical charts, and can underestimate the true prevalence of disease in several situations, for example when two or more diseases coexist and only one diagnosis (for major symptoms) is recorded. Centripetal- and referral-filtered biases could also be a problem if not all hospitals/care centers are included in the data collection process. All of these factors may lead to information bias, most likely resulting in an underestimation of the "true" risk. Prospective studies of genital warts are less prone to information bias, if standard diagnostic tools are used and if all physicians are equally aware of the purposes of the study.

Warts often cause annoying symptoms such as burning, itching, bleeding, and pain, and psychosocial stress may result in negative self-perception, low self-esteem, embarrassment, and anxiety [22]. Despite this, not all women with warts seek medical attention for this condition. This issue is of special concern in self-report based studies. The review by Singhal *et al*. [21] reported the results of six peer-reviewed publications in which the rates of genital warts were based on self-reported history of physician-diagnosed genital warts. The 12-month prevalence rates were 300-1,900 per 100,000 and the corresponding lifetime prevalence was 356-12,000 per 100,000. The wide range of occurrence rates can be at least partially explained by reporting and recall bias.

Singhal *et al*. [21] also reviewed a total of five peer-reviewed journal articles published between 2000 and 2010, which attempted to estimate the prevalence of genital warts among women based on genital examinations, and stated that the estimated prevalence was found to be between 200 and 4,030 per 100,000. The wide range of rates suggests population-based differences in occurrence, or simply, differences in rates of availability, accessibility, and acceptability of gynecological care services provided for different populations. It is also possible that those visiting a gynecology clinic for "any" reason are more likely to have a genital wart compared with their counterparts who have not attended such a clinic. Thus, generalizability of the findings to the overall female population could be low. Also, given that patients with warts may choose to admit to several different outpatient clinics dealing with warts, includ-

ing gynecology, urology, and dermatology, all such clinics' patients should be recruited for a comprehensive analysis of prevalence rates of genital warts. Subsequently, studies of genital warts based on outpatient clinic visits often underestimate the true prevalence of warts in the general population.

It is important to note that all studies set up on clinically-collected data will be limited in terms of generalizability and are prone to several sources of biases, such as Berkson's fallacy, hospital access bias, ascertainment bias, and diagnostic access bias.

In contrast, population-based prevalence studies set up on "random" samples of reproductive-aged women are limited by poor response rates, given privacy concerns, and low acceptance rates for genital examination [22]. Distinct privacy concerns in the identification of genital warts in the general population have led to a scarcity in the number of such studies in the literature [23, 24], but are sufficient to deduce that rates differ widely across regions and countries, ranging from 1.4% in Spain to 25.6% in Nigeria [25, 26]. Poor awareness and recall might also lead to underestimation of the true rates of occurrence.

Despite these limitations in coverage and generalizability, most studies on frequency of genital warts have been conducted in selected populations, such as, STD clinic attendees, university students, or individuals insured through private health plans [17, 20, 27, 28].

It is important to note that, regardless of the study designs and sample populations, sole use of point prevalence rates will serve to further underestimate the annual genital wart-associated disease burden, given that some of the warts disappear spontaneously. This is of special concern in disease-associated cost estimations.

In the present study, the prevalence of genital warts among reproductive-aged women attending gynecology clinics/offices for "any" reason ranged from 3.4% to 4.1%, with an overall point prevalence of 3.5%, which corresponds well with other studies in different countries [29-33]. This finding is in line with findings of Hillemanns *et al*. [34], who reported a prevalence of 148 per 100,000 (new: 114/100,000 and recurrent: 35/100,000) among females aged 14-65 years who were consulting gynecologists for genital warts.

Based on genital examination, rates ranged from 200-4,030 per 100,000. Nyári *et al*. [32] studied 397 asymptomatic women, with a mean age of 35.5 years, attending gynecology clinics in Hungary, and found point prevalence of genital warts to be 4,030 per 100,000.

In the present study, the overall point prevalence of genital warts among reproductive-aged women attending gynecology outpatient clinics for any reason was calculated as 3.5%. It is worth noting that point prevalence of genital warts varied by age among women attending a gynecology clinic. The highest rates were observed in the 15 to 19 year-old group. Kjaer *et al*. [20], in their study of prevalence in Nordic countries, reported that the average age at first diagnosis of genital warts ranged around 21-22 years; the minimum age for first diagnosis of genital warts ranged from three years in Norway to 14 years in Iceland and Sweden. In the same study, self-reported history of genital warts in the 12 months preceding the study was highest for ages < 20 years and in the 21 to 24-year-old group, with rates decreasing with increasing age. The present findings are in parallel with those of Kjaer *et al*. [20], other than our observation of an increase in genital warts in the 40 to 44-year-old group (5.9%).

This study is a pioneer in Turkish literature, with a specific aim to investigate genital warts in a heterogeneous group of reproductive-aged women. Given this, the study has several intrinsic limitations, analyses were conducted with extreme caution to avoid bias in the interpretation of the study findings, and issues of concern are summarized below:

1. The convenience sample, with data from ten selected cities and a total of 23 healthcare facilities enhanced the heterogeneity of women participating in the study. Yet, sampling design still limits the generalizability of the results to the whole Turkish female population of similar age. It is important to note that data were neither representative of all cities in Turkey, nor of all types of healthcare settings. Data collection based on visits to specific healthcare settings, rather than on a random sample of the general population, further restricts the ability to generalize the study findings.

Study findings can be generalized to reproductive-aged women visiting a gynecology clinic for any reason, but not to the general female population. Given the scarcity of available evidence on national attendance rates and reasons, it is difficult to validly discuss the direction of bias in generalizing results to all women.

2. The refusal rate cannot be validly estimated and those women refusing to participate in the study might be different than those who took part in the study. However, given this, women were not informed of the main aim of "studying genital warts", and that none had been examined differently from the others, there is no reason to believe that refusal by some participants was non-random with regard to the presence of genital warts.

3. Data cannot be used to distinguish "new" vs "existing" (either "persistent" or "recurrent") genital warts. The frequency of lifetime ("ever") genital warts cannot be estimated, either. As such distinction would be of value in economic evaluations, further studies should include specific questions, enabling such distinctions.

4. The descriptive nature of the study design, with no follow-up, restricts the ability of the study to evaluate causality, and to calculate incidence rates.

5. Although the study aimed to reach an equal number of women at each participating center, this goal could not be realized. The authors' daily observations and data from previously-published studies reveal that women attending public institutions, universities, and private clinics may differ in terms of educational attainment, health-related awareness, socio-economic status, and even the type of health problems they suffer from. Weights were used in the study to minimize selection bias-related interpretation errors. Weights were calculated as the inverse of sampling fractions, assuming that: 1) the distribution of healthcare visits

for "all" reasons is similar to that for "genital warts" across public health institutions, universities, and private sector clinics; 2) the characteristics of women attending study centers are similar to those attending corresponding types of healthcare settings (namely, public health institutions, universities, and private sector clinics) in the general population.

It is noteworthy to mention that women with warts might have been admitted to other outpatient clinics (such as, dermatology and/or urology clinics), and therefore the present estimates might be an underestimate of the "true" attending-based prevalence rate.

6. One of the main objectives of the study, investigation of the validity of self-report for genital warts, could not be established because the two related questions were misunderstood by participants.

Future studies should prepare more specific questions to further investigate the validity of self-report in identifying genital warts, and questions should be pre-tested in large numbers of eligible women prior to the data collection phase.

7. The non-systematic coding attending diagnosis hindered the authors' ability to use this variable effectively in the study. In future studies, standard training of physicians and data collectors could improve the quality of the data.

Conclusion

This kind of study was conducted for the first time in Turkey. Estimation on national burden of the disease was facilitated by weighted analyses. The overall point prevalence of genital warts being 3.5 suggests that it is common in the population; and thus, effective prevention methods are required.

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