

## RESEARCH COMMUNICATION

# Estimating Prevalence of Genital Warts in Turkey: Survey among KETEM-affiliated Gynecologists across Turkey

Nejat Ozgul\*, Murat Tuncer, Melike Abacioglu, Murat Gultekin

## Abstract

**Background & Purpose:** In order to develop cost effective health strategies regarding HPV screening and prevention methods, determining the incidence and prevalence of HPV as well as the diseases it gives rise to such as cervical cancer and genital warts is essential. This study is a first step in determining nationwide annual prevalence of genital warts in Turkey. **Patients & Methods:** Through the survey sent to gynecologists in each city in Turkey, a record number of data for 4,013,084 patients, out of which 5511 diagnosed with genital warts were collected from 81 cities. The survey was sent in May 2011 and recollected in July 2011. The data belonged to patients consulted in 2010. Patients ranged between women 30-65 years old. The prevalence per city was projected using population per city as presented in Turkish Statistical Institute (TUIK). The treatment types prescribed and conducted for each patient and number of referrals were also collected. **Results:** The annual prevalence of 154 per 100,000 women aged 30-65 was found as the Turkey average. Given 15-37% recurrence rate estimates based on distribution of treatments provided in Turkey, an annual incidence of 97-131 per 100,000 women is estimated. Wide regional differences were observed across regions, with Aegean Region having the highest and the Southern Eastern regions having the lowest annual prevalence rates in Turkey. **Conclusion:** The annual prevalence rates and extrapolated incidence rates are comparable to incidences in European countries where intensive research into treatment of HPV and national health strategies are developed. Turkey should deepen its research in this area. This study contributes to these efforts as a first step in determining cost effective national health strategies.

**Keywords:** Turkey - genital warts - prevalence - gynecologists - regions - treatment

*Asian Pacific J Cancer Prev*, 12, 2397-2440

## Introduction

In order to determine effective national health strategy regarding the human papillomavirus and develop relevant prevention and screening programs, it is essential to understand the national burden of the virus across all major diseases it gives rise to. HPV is the known cause of cervical cancer (Schiffman et al., 1993; Liaw et al., 1999; Walboomers et al., 1999; Tuncer et al., 2010). Similarly HPV is also the cause of benign condylomata acuminata, known as genital warts. The first step in estimating the national burden of a disease involves establishing prevalence of the disease in the given population. Therefore, this article shares the first findings regarding prevalence of genital warts in Turkey.

In the US, it is estimated that 27% of women between ages of 14 and 59 are infected with different types of HPV at a given point in time (Dunne et al., 2007). Studies indicated that the prevalence of HPV tends to reach its peak among women aged 20-24 at 20%, subsequently declining to 8-10% among women over 30 years old (von Krogh G et al., 2000). There are about 100 HPV types, which depending on their properties, are classified as high risk and low risk for causing cervical cancer. High risk

HPV types, particularly HPV 16 & 18 are held responsible for the occurrence of cervical cancer. On the other hand, particularly low-risk HPV types 6 & 11 are known to result in around 90% of genital warts (von Krogh et al., 2000). Although genital warts are not life threatening, they still generate a sizable financial burden on the countries and highly impact the quality of the patient's everyday life. In the US, it is estimated that more than 200 million US dollars are spend each year on the management of this disease (Markowitz et al., 2007).

As part of disease prevention, national vaccination programs are often established against many communicable diseases. Many countries try to estimate the cost effectiveness of such a national vaccination program. Today there are two types of HPV vaccines on the market. Although both vaccines, Gardasil and Cervarix provide protection against the high risk HPV 16 and 18, Gardasil also provides protection against Types 6 and 11. Therefore, in order to determine the most cost effective vaccination strategy it is also extremely important to understand the significance of the genital warts and their burden on the nation. The largest cost benefit of Cervarix was found to be reduced abnormal pap test results, colposcopies and excisional treatments (Harper and Vierthaler, 2012).

Cancer Control Department, Turkish Ministry of Health, Ankara, Turkey \*For correspondence: nozgul@gmail.com

Many countries such as US, Spain and UK have conducted similar studies to estimate the prevalence and incidence of this disease. This study aims to establish the annual prevalence of genital warts in Turkey. This study is unique as it also tries to shed light to any regional differences observed in the prevalence across each city in Turkey. Moreover, the study gives a first baseline of the types of treatments most commonly applied in Turkey.

In this study, a first step towards understanding the applicability of the genital warts risk factors to Turkish population was examined. Several studies thus far have indicated that a women's life time number of sex partners is associated to genital HPV acquisition (Baseman and Koutsky, 2005). This study also tries to explore this risk factor in Turkey by determining if any correlation exists between a proxy for the number of sex partners and the annual prevalence of the disease.

## Materials and Methods

A survey is prepared by the Department of Cancer Control in Turkish Ministry of Health. This survey is sent to the Gynecology Department of hospitals selected in each city across Turkey in May 2011 and recollected in July 2011. Due to convenience of data tracking, these selected hospitals are those which are affiliated with the Cancer Early Screening & Diagnosis Centers (KETEM) in each given city. Where there were no hospitals affiliated with KETEM in a given city, surveys were forwarded to university hospitals in that city. KETEM affiliated hospitals included 3 hospitals in Istanbul, 2 in Ankara, 2 in Kahramanmaraş and 1 in each remaining city. Sixty-eight cities participated in the study. The Gynecology Departments were asked to report the number of patients who sought consultation during the period January 1, 2010- December 31, 2010. The departments were asked to report the number of patients identified with genital warts during consultation, number of patients treated, referred and the type of treatment prescribed. The treatment options included conization, cauterization, cryotherapy, excision, imiquimod and other optional field. The diagnosis was conducted through visual inspection. This data was consolidated by the Department of Cancer Control.

The patients included those female adults between 30 and 65 years old who visited a gynecologist during 2010 for any given reason. This study does not include teenagers and male patients with genital warts disease. Within the scope of this study, data is obtained from gynecologists and no data is estimated from dermatologists or urologists, as per authors' primary research such data represents minority in Turkey. Similar study in France also found incidence rates with data from gynecologists only to be highly reflective of prevalence rates (Monsonégo et al., 2007). Another study in Germany involved data from urologists but determined the data was not statistically significant to yield reliable incidence rates for males (Arbyn et al., 2007).

The raw data regarding identified number of cases per each city was then extrapolated with the population in each city. The population estimates per age, gender and city for 2010 from Turkish National Statistics Institute

(TUIK) were used (Turkish Statistical Institution).

A comparison of prevalence among different regions in Turkey was made and the correlation of prevalence to number of sex partners was explored per each region. As no comprehensive data was available for number of sex partners Turkish women have in their lives, a proxy was determined. The difference between average age at first marriage and average age for marriage overall was used as proxy. Thereby, potential proxy for number of sex partners was correlated with prevalence across regions. It was assumed that a larger difference between age at first marriage and the average marriage age per city was due to potential divorces and second marriages and indicated a longer period of sexual freedom between two marriages. Therefore this difference was used as a proxy for the number of sexual partners. For this analysis the data reported by TUIK for 2010 was used (Turkish Statistical Institution).

## Results

### Prevalence

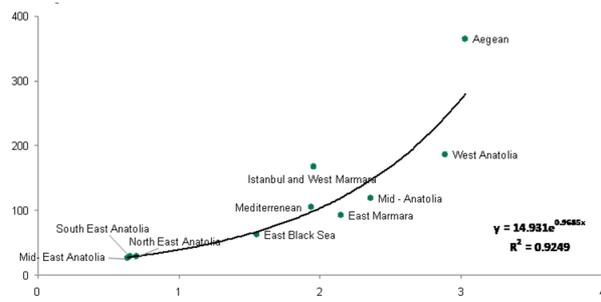
Data from 72 hospitals indicated a total of 4,013,084 women aged 30-65 sought consultation of a gynecologist. Among these women, 5,511 were diagnosed to have genital warts at the time of the visit. Given a population of 14,054,135 women across the 68 cities where the participating hospitals were located and the respective rates for each city were gathered, it is estimated that 21,684 patients have had genital warts in Turkey in 2010. This indicates an annual prevalence of 154 women per 100,000. This result includes both the newly diagnosed and recurring genital warts observed during the consultation. Wide regional differences were observed in the prevalence rates across Turkey. The highest prevalence was observed in Western part of Turkey in the Aegean region with 326 per 100,000, about twice the rate for Turkey average. The lowest rate was observed in the Eastern Turkey with 26 per 100,000 followed by 29 per 100,000 in Southeastern Turkey. The raw data and the projected data are presented in Table 1 respectively.

On the other hand prevalence across cities differed even more: Kirsehir is with highest prevalence at 3054 per 100,000 followed by Kutahya at 1639 per 100,000. Some other cities which have prevalence twice as great as the Turkey average include: Artvin, Bilecik, Edirne, Eskisehir, Edirne, Usak, Tunceli and Osmaniye.

**Table 1. Number of Patients, Raw and Projected Data for Genital Warts**

Regions	Patients	Patients with GW	Population aged 30-65	Projected number
Black Sea	686,199	248	1,336,927	681
Mid- Anatolia	699,518	1,995	2,327,376	5,863
Marmara	525,396	586	4,642,991	5,267
South East	532,364	174	713,988	207
Aegean	484,352	1,866	2,328,019	7,583
Mediterranean	536,549	456	1,970,427	1,894
East Anatolia	548,706	186	734,407	189

The projection was conducted per each city and data were later grouped into regions



**Figure 1. Regional Difference between Age at Marriage and Prevalence of Genital Warts**

We have also observed differences across regions regarding marriage age as reported by TUIK. We have found a strong correlation between annual prevalence of genital warts and the difference between age at first marriage and average marriage age, a potential proxy for number of sexual partners. As the difference between the two marriage ages increase, prevalence of genital warts followed an exponential increase. This correlation is therefore a first proxy in Turkey to correlate increasing number of sex partners to increased chances of genital warts. The results can be seen in Figure 1. The highest age difference, therefore the highest prevalence was observed in Aegean region, whereas lowest prevalence and lowest age differences were observed in the Northern Eastern and Southern Eastern Turkey. The only region that did not follow this pattern was found to be Western Black Sea with high age difference and relatively low prevalence rates.

#### Treatments

The most common treatment was observed to be cryotherapy with 41% of all treatments prescribed. The second most common was cauterization at 30%. Prescription of medicine only accounted for 14%, with Aldara for 11%. Excision accounted for 15% and conization for only 1%. The most commonly used treatment method also varied across the regions (see Table 2). In Black Sea Region the most common treatment was Aldara, whereas in Mid-Anatolia and Aegean it was cryotherapy, in Marmara and Eastern regions excision, Southeastern and Mediterranean regions cauterization.

About 2% of all patients diagnosed with genital warts were not able to be treated at the place of diagnosis and were referred out. This number is predominantly due to Antalya which has reported to have referred out around 83% of all women it diagnosed with genital warts.

**Table 2. Distribution of Treatment Modalities for Genital Warts across Regions**

	Cauterisation		Excision	Other*	
	Cryotherapy		Imiquimod		
Black Sea	30%	14%	15%	38%	3%
Mid- Anatolia	35%	45%	15%	5%	1%
Marmara	25%	3%	31%	18%	24%
South East	90%	1%	6%	3%	0%
Aegean	16%	69%	5%	10%	1%
Mediterranean	49%	10%	16%	24%	2%
East Anatolia	20%	0%	47%	22%	11%
Average	30%	41%	15%	11%	4%

\*Include Podophylin, TCA & conization.

## Discussion

Arbyn et al. estimates that Turkey experiences 3.5 per 100,000 crude cervical cancer incidence rate vs. Germany at 10.6 and France at 7.1, more than twice the rate in Turkey (Turkish Statistical Institution). Even though the estimated incidence of cervical cancer in Turkey compared with the rates in other European countries and the US, is found to be much less, the genital warts data still indicate comparable levels. Previous studies in the US indicate an annual prevalence of 170-205 cases per 100,000 adults in 2000 and 2001 respectively (Insinga et al., 2003; Koshiol et al., 2004). A more recent study from Spain indicates 182.1 per 100,000 cases in 2008 (Castellsague et al., 2008). In this study the annual prevalence for genital warts for Turkey is found comparable to these rates.

Given the distribution of treatments in Turkey found in the study and the respective recurrence rates of treatments (Beutner and Ferenczy 1997; Edwards et al., 1998; Tying et al., 1998; French et al., 2002; Wiley 2003), average recurrence rate in Turkey can be estimated to be between 15% - 37%. This indicates an annual incidence of 97-131 per 100,000. Assuming 1/4 recurrent to new genital warts ratio or 1/3 as in the case in Hillemanns et. al. study, the annual incidence of new cases of genital warts in Turkey can also be roughly estimated to be 103-116 per 100,000. This is also comparable to Germany where the incidence of new cases of genital warts is at 113.7 per 100,000 and recurrent cases is at 34.7 per 100,000 (Hillemanns et al., 2008). This indicates that genital warts present a sizable problem in Turkey and respective health strategies should be developed as is done in other European countries.

In similar studies where incidence of genital warts is tried to be estimated, data were also collected from dermatologists for men and women and urologists for men. In Spain, 20% of all genital warts among women were estimated to be diagnosed during a visit to a dermatologist (Castellsague et al., 2008). This ratio is also close to 17% in Germany (Hillemanns et al., 2008). According to author's primary research, the health behavior of women regarding genital warts indicates that a visit to a gynecologist is much more likely in Turkey. However, for future studies clinical data from dermatologists and urologists can be obtained for further verification.

The treatments observed in the patient population indicate that surgical treatment of genital warts in Turkey is preferred to medical treatment. Given that 70% of 5511 patients in the study are treated with cauterization or cryotherapy may also indicate that the patients at the time of consultation experienced relatively large size warts and visited the gynecologist at an advanced stage of the wart. The treatment through medicine with Aldara 5% imiquimod costs in Turkey 130.75 TL for 12 x 0.25 g; Compared to US online drug store price at 118.99 USD, the price in Turkey is not particularly different. However, given that the cost of cauterization and cryotherapy is at 29.7 TL indicates that surgical preferences also reflect a concern for cost effectiveness. Black Sea region is particularly an exception regarding use of medical treatment such that 38% of all treatments is through Aldara vs. Turkey average (excluding Black Sea

Region) of Aldara treatment at 9.8%. Given that Black Sea Region also has a relatively low annual prevalence of genital warts, it might indicate that the size of genital warts observed in Black Sea Region was relatively small at the time of consultation.

In this study an interesting finding is the differences in annual prevalence of genital warts across different cities and regions in Turkey. The rate in Western Turkey is found to be higher than it is in Eastern Turkey. Moreover, the number of gynecologists per 1000 population of women between ages 20-65 has a standard deviation of 1.25 gynecologists per 1000 across Turkey indicating a low variance in access to such services across different regions (Turkish Ministry of Health, 2011). Even though access levels are similar, there might be still issues regarding health care behavior observed among women across regions, where some cultures might not allow for regular visits. Yet the regional differences observed beg the question whether risk factors observed across regions differ. Risk factors for HPV infection include sexual activity at early ages and multiple sex partners over a women's lifetime (Baseman and Koutsky, 2005). The parameter used in this study, the difference between the age at first marriage and the average age at marriage is only a first step and a proxy for determining the number of partners. This proxy is only relevant to the extent that the patient population experiences first sexual activity within marriages. This proxy would be less relevant in time as younger populations might be engaging in sexual activity outside marriage. However, despite the big assumptions given the analysis indicate that the higher potential number of sexual partners in marriages the higher the prevalence of genital warts in the regions across Turkey. This proxy presents an initial hypothesis to be tested for Turkey in future studies. Further data should be collected and number of sexual partners in life time and self reported cases of ever having been diagnosed with genital warts should be incorporated in the surveys for future studies.

Initial estimate for annual prevalence of genital warts is found to be comparable to other European countries where extensive research on cost effectiveness of health strategies is conducted. Even though not life threatening, it is highly recommended that Turkey takes steps towards more in depth clinical studies in order to better understand the prevalence of genital warts, a disease that causes much discomfort and often quoted shame in everyday life of its people.

## References

- Arbyn M, Bruni L, de Sanjosé S, et al (2011). Prevalence of human papillomavirus infection and burden of cervical cancer in Europe in 2008. In: Ayhan A, Reed N, Gultekin M, Dursun P, eds. 2nd edition. Textbook of Gynecological Oncology. Ankara, Turkey: Gunes Publishing; 89-98.
- Baseman JG, Koutsky LA (2005). The epidemiology of human papillomavirus infections. *J Clin Virol*, **32 Suppl**, S16-24.
- Beutner KR, Ferenczy A (1997). Therapeutic approaches to genital warts. *Am J Med*, **102**, 28-37.
- Castellsague X, Cohet C, Puig-Tintore LM, et al (2008). Epidemiology and cost of treatment of genital warts in Spain. *Eur J Public Health*, **19**, 106-10.
- Dunne EF, Unger ER, Sternberg M, et al (2007). Prevalence of HPV infection among females in the United States. *JAMA* **297**, 813-19.
- Edwards L, Ferenczy A, Eron L, et al (1998). Self-administered topical 5% imiquimod cream for external anogenital warts. HPV Study Group. Human Papillomavirus. *Arch Dermatol*, **134**, 25-30.
- French L, Nashelsky J, White D (2002). What is the most effective treatment for external genital warts? *J Fam Pract*. 51:313.
- Harper DM, Vierthaler SL (2012). Bivalent HPV Vaccine Approved for 6 Cervical Cancer Prevention in Females. In: Ayhan A, Reed N, Gultekin M, Dursun P, eds. 2nd edition. Textbook of Gynecological Oncology. Ankara, Turkey: Gunes Publishing; 127-45.
- Hillemanns P, Breugelmans JG, Giesecking F, et al (2008). Estimation of the incidence of genital warts and the cost of illness in Germany: A cross-sectional study. *BMC Infectious Diseases*, **8**, 76.
- Insinga RP, Dasbach EJ, Myers ER (2003). The health and economic burden of genital warts in a set of private health plans in the United States. *Clin Infect Dis*, **36**, 1397-403.
- Koshiol JE, Laurent SA, Pimenta JM (2004). Rate and predictors of new genital warts claims and genital warts-related healthcare utilization among privately insured patients in the United States. *Sex Transm Dis*, **31**, 748-52.
- Liaw KL, Glass AG, Manos MM, et al (1999). Detection of human papillomavirus DNA in cytologically normal women and subsequent cervical squamous intraepithelial lesions. *J Natl Cancer Inst*, **91**, 954-60.
- Markowitz LE, Dunne EF, Saraiya M, et al (2007). Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*, **56 (RR-2)**, 1-24.
- Monsonégo J., Breugelman JG, Bouée S. et al (2007). Anogenital warts incidence, medical management and costs in women consulting gynaecologists in France. *Gynécologie Obstétrique Fertilité*, **35**, 107-13.
- Schiffman MH, Bauer HM, Hoover RN, et al (1993). Epidemiologic evidence showing that human papillomavirus infection causes most cervical intraepithelial neoplasia. *J Natl Cancer Inst*, **85**, 958-64.
- Tuncer AM, Moore M, Qiao YL, et al (2010). Asian Pacific Organization for Cancer Prevention Cancer Report 2010. Ankara, Turkey: SUVAK – New Hope in Health Foundation; 2010; 215-21.
- Turkish Ministry of Health (2011). Online state database. 15 July 2011. Number of gynecologists in private, state and university hospitals.
- Turkish Statistical Institution (2011). Population projections based on age and gender. [http://tuik.gov.tr/VeriBilgi.do?tb\\_id=39&ust\\_id=11](http://tuik.gov.tr/VeriBilgi.do?tb_id=39&ust_id=11)
- Turkish Statistical Institution (2011). Average age at marriage and mean age at first marriage by Classification of Statistical Region Units, January-March 2010. [http://www.tuik.gov.tr/PreHaberBultenleri.do?id=6280&tb\\_id=2](http://www.tuik.gov.tr/PreHaberBultenleri.do?id=6280&tb_id=2)
- Tyring S, Edwards L, Cherry LK, et al (1998). Safety and efficacy of 0.5% podofilox gel in the treatment of anogenital warts. *Arch Dermatol*, **134**, 33-8.
- von Krogh G, Lacey CJ, Gross G, et al (2000). European course on HPV associated pathology: guidelines for primary care physicians for the diagnosis and management of anogenital warts. *Sex Transm Infect*, **76**, 162-8.
- Walboomers JM, Jacobs MV, Manos MM et al (1999). Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*, **189**, 12-9.
- Wiley DJ (2003). Genital warts. *Clin Evid*, **9**, 1741-53.