

Prevalence of Hepatitis B, Hepatitis C, Syphilis and HIV Infections in Patients with Anogenital Warts: A Descriptive Cross-Sectional Study

Anogenital Siğilli Hastalarda Hepatit B, Hepatit C, Sifiliz ve HIV Enfeksiyonlarının Sıklığı: Tanımlayıcı Kesitsel Bir Çalışma

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ABSTRACT Objective: There are limited studies on the frequency of other sexually transmitted diseases in patients with anogenital warts (AGWs). In this study, we aimed to evaluate the frequency of hepatitis B, hepatitis C, syphilis and human immunodeficiency virus (HIV) infections in patients with AGWs. **Material and Methods:** The data of the patients with AGWs, who applied to our dermatology outpatient clinic between January 2015 and December 2021, were analyzed retrospectively. Serological test results for hepatitis B, hepatitis C, syphilis and HIV infections of patients with AGWs were evaluated. **Results:** Of 765 patients with AGWs, 541 were male and 224 were female. Among 313 patients who underwent hepatitis B surface antigen (HBsAg) testing, HBsAg positivity was detected in 5 (1.6%) patients. Hepatitis C virus antibody (anti-HCV) positivity was detected in 4 (1.2%) of 324 patients who underwent anti-HCV testing. Four (1.3%) of 298 patients who underwent rapid plasma reagin (RPR) for syphilis were positive (RPR titers 1/2, 1/4, 1/16, and 1/128). Treponema pallidum hemagglutination assay (TPHA) test was negative in 2 patients. The diagnosis of syphilis was confirmed by TPHA test in 2 patients whose RPR titers were 1/16 and 1/128. Among 344 patients who underwent HIV antibody (anti-HIV) testing, anti-HIV positivity was detected in 16 (4.7%) patients. It was later uncovered that 13 of 16 patients were HIV-infected patients who had been already followed by infectious diseases specialists. Confirmation test for HIV infection was negative in 2 patients and positive in 1 patient. As a result, 14 HIV-positive patients were detected. **Conclusion:** The patients with AGWs should be evaluated for other sexually transmitted diseases, especially syphilis and HIV infection.

Keywords: Genital warts; hepatitis; human immunodeficiency virus; sexually transmitted diseases; syphilis

ÖZET Amaç: Anogenital siğilli hastalarda eşlik eden diğer cinsel yolla bulaşan enfeksiyonların sıklığı hakkında çalışmalar sınırlıdır. Bu çalışmada, anogenital siğilli hastalarda hepatit B, hepatit C, sifiliz ve insan immün yetmezlik virüsü [human immunodeficiency virus (HIV)] enfeksiyonu sıklığının değerlendirilmesi amaçlanmıştır. **Gereç ve Yöntemler:** Ocak 2015-Aralık 2021 tarihleri arasında dermatoloji polikliniğimize başvuran anogenital siğilli hastaların verileri retrospektif olarak incelendi. Hastaların hepatit B, hepatit C, sifiliz ve HIV enfeksiyonuna yönelik yapılmış serolojik test sonuçları değerlendirildi. **Bulgular:** Anogenital siğil tanılı 765 hastanın 541'i erkek, 224'ü kadındı. Hepatit B yüzey antijen tetkiki yapılmış 313 hastanın 5'inin (%1,6) testi pozitif olarak sonuçlandı. Hepatit C virüsü antikoru tetkiki yapılmış olan 324 hastanın 4'ünün (%1,2) testi pozitif olarak saptandı. Sifiliz için hızlı plazma kazanımı [rapid plasma reagin (RPR)] bakılan 298 hastanın 4'ünde (%1,3) pozitiflik (1/2, 1/4, 1/16 ve 1/128 titrelerde) bulundu. RPR titrasyonu 1/2 ve 1/4 gelen 2 hastanın treponema pallidum hemagglütinasyon testi [treponema pallidum hemagglutination assay (TPHA)] negatif olarak sonuçlandı. RPR titrasyonu 1/16 ve 1/128 gelen 2 hastanın TPHA ile sifiliz tanısı doğrulandı. HIV antikoru [HIV antibody (anti-HIV)] testi yapılan 344 hastanın 16'sının (%4,7) testi pozitif. Anti-HIV testi pozitif çıkan 16 hastanın 13'ünün enfeksiyon hastalıklarından takipli HIV pozitif hastalar olduğu ortaya çıktı. Diğer 3 hastanın ise 2'sinin doğrulama testi negatif olarak sonuçlandı. Bir hasta ise doğrulama testinin pozitif sonuçlanması ile HIV enfeksiyonu tanısı aldı. Sonuç olarak 14 HIV pozitif hasta tespit edildi. **Sonuç:** Anogenital siğilli olan hastalar, özellikle sifiliz ve HIV gibi cinsel yolla bulaşan diğer hastalıklar açısından değerlendirilmelidir.

Anahtar Kelimeler: Genital siğiller; hepatit; insan immün yetmezlik virüsü; cinsel yolla bulaşan hastalıklar; sifiliz

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Anogenital warts (AGWs), also known as condylomata acuminata or genital warts, are sexually transmitted diseases caused mostly by human papillomavirus types 6 and 11.¹ AGWs cause a widespread public health problem affecting young women and men.² Reported annual incidence rates of AGWs range between 100 and 200 new cases per 100,000 general adult population.¹

An increased number of sexual partners during lifetime, a new sexual partner in the past 12 months, immunosuppression and smoking have been associated with increased risk of AGWs. Data on association of the presence of other sexually transmitted diseases with the appearance of AGWs are conflicting.³ Since AGWs are usually sexually transmitted, it is recommended that individuals with AGWs be screened for other sexually transmitted diseases.^{4,5}

There are limited number of studies on the frequency of other sexually transmitted diseases in patients with AGWs. Knowing the frequency of other sexually transmitted diseases in patients with AGWs may contribute to the prevention of the spread of the diseases in the society by providing early diagnosis to patients. In this study, it was aimed to evaluate the frequency of hepatitis B, hepatitis C, syphilis and human immunodeficiency virus (HIV) infections in patients diagnosed with AGWs.

MATERIAL AND METHODS

This study was performed in accordance with the ethical principles of the declaration of Helsinki. Approval for this retrospective study was obtained from Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine (date: January 13, 2022; number: 2022/04).

The data of the patients with AGWs, who applied to the dermatology outpatient clinic of Aydın Adnan Menderes University Hospital between January 1, 2015 and December 31, 2021, were analyzed retrospectively using the hospital database.

Demographic features and clinical findings of the patients with AGWs were collected. Their serological tests including hepatitis B surface antigen (HbsAg), hepatitis B surface antibody (anti-HBs),

hepatitis C virus antibody (anti-HCV), HIV antibody (anti-HIV) and rapid plasma reagin (RPR) were reviewed. If the RPR, anti-HCV or anti-HIV were positive, confirmatory tests of syphilis, hepatitis C, and HIV infections were examined.

Data analysis was conducted using IBM SPSS Statistics 25.0 (IBM Corp., Armonk, New York). Categorical variables were presented as numbers and percentages, while continuous variables were shown as mean and standard deviation. Chi-square test was used to compare categorical variables. A p value less than 0.05 was considered statistically significant.

RESULTS

Of the 765 patients with AGWs included in the study, 541 (70.7%) were male, 224 (29.3%) were female. The mean age of the patients with AGWs was 34.3±13.4 years with a range of 1 to 82 years. Thirty-three of the patients with AGWs were younger than 18 years of age. The majority of patients were below 40 years of age (68.1%).

Among 313 patients who underwent HBsAg testing, HBsAg positivity was detected in 5 (1.6%) patients. Of the 5 patients, 3 had previous hepatitis B infection and 2 were newly diagnosed. All 5 patients with hepatitis B infection were male. Anti-HBs test was performed in 255 patients and anti-HBs positivity was found in 125 (49%) patients. Anti-HCV positivity was detected in 4 (1.2%) of 324 patients who were tested for anti-HCV. Confirmation test for hepatitis C virus infection was negative in 2 patients and positive in 1 patient. The patient with positive confirmatory test was female. One patient did not have a confirmatory test for hepatitis C virus infection.

RPR test was performed in 298 (38.9%) of 765 patients. Four (1.3%) of 298 patients who underwent RPR for syphilis were positive [RPR titers 1/2 (male), 1/4 (female), 1/16 (male), and 1/128 (male)]. Treponema pallidum hemagglutination assay (TPHA) test was negative in two patients with RPR titer 1/2 and 1/4. The diagnosis of syphilis was confirmed by TPHA test in 2 (0.7%) patients whose RPR titers were 1/16 and 1/128. Two patients with diagnoses of secondary syphilis and latent syphilis were treated with benzathine penicillin G. In addition, 2 patients

diagnosed with syphilis and the patient whose RPR test was false positive (titer 1/2) were found to be HIV positive.

Anti-HIV test was performed in 344 (44.9%) of 765 patients. We observed anti-HIV positivity in 16 (%4.7) patients. It was later uncovered that 13 of 16 patients were HIV-infected patients who had been already followed by infectious diseases specialists. The confirmatory tests of 2 patients were negative. Confirmation test for HIV infection was positive in 1 patient. As a result, 14 (4%) HIV-positive patients were detected. All HIV-positive patients were male.

The frequency of testing and diagnosis for hepatitis B, hepatitis C, syphilis and HIV infection in patients with AGWs is shown in Table 1.

The localizations of AGWs were defined in 750 patients. AGWs were genital in 600 (80%) patients, perianal in 105 (14%) patients, and both genital and

perianal in 45 (6%) patients. There was a significant difference between women and men in terms of localization of AGWs ($p<0.001$) (Table 2).

Perianal region (78.6%) was the most common site of AGWs in HIV-positive male. There was a significant difference between HIV-positive males and HIV-negative males in terms of localization of AGWs ($p<0.001$) (Table 3).

Additionally, genital molluscum contagiosum in 10 patients, tinea inguinalis in 10 patients, scabies in 7 patients and herpes genitalis in 2 patients were detected in the examinations of patients with AGWs.

DISCUSSION

AGWs are common sexually transmitted diseases, particularly affecting young women and men.² It is reported that the incidence of new AGWs ranged from 103 to 168 per 100,000 in men and from 76 to

TABLE 1: Frequency of testing and diagnosis for hepatitis B, hepatitis C, syphilis and HIV infection in patients with anogenital warts.

| | Number and percentage of all patients screened (n=765) | | Number and percentage of diagnosed patients among screened patients | |
|--------------|--|------|---|------|
| | n | % | n | % |
| Hepatitis B | 313 | 40.9 | 5 | 1.59 |
| Hepatitis C | 324 | 42.3 | 1* | 0.3 |
| Syphilis | 298 | 38.9 | 2 | 0.67 |
| HIV-positive | 344 | 44.9 | 14 | 4.0 |

*Anti-HCV positivity was detected in 4 (1.2%). Confirmation test for hepatitis C virus infection was negative in 2 patients and positive in 1 patient. One patient did not have a confirmation test for hepatitis C virus; HIV: Human immunodeficiency virus.

TABLE 2: Localization of anogenital warts according to gender.

| | Localization of anogenital warts | | | p value |
|----------------|----------------------------------|----------------|------------------------|---------|
| | Genital n (%) | Perianal n (%) | Genital+perianal n (%) | |
| Male (n=530) | 460 (86.8) | 49 (9.2) | 21 (4) | <0.001 |
| Female (n=220) | 140 (63.6) | 56 (25.5) | 24 (10.9) | |

TABLE 3: Localization of anogenital warts in male patients according to infections with HIV.

| | Localization of anogenital warts | | | p value |
|----------------------|----------------------------------|----------------|------------------------|---------|
| | Genital n (%) | Perianal n (%) | Genital+perianal n (%) | |
| HIV-negative (n=235) | 203 (86.4) | 21 (8.9) | 11 (4.7) | <0.001 |
| HIV-positive (n=14) | 2 (14.3) | 11 (78.6) | 1 (7.1) | |

HIV: Human immunodeficiency virus.

191 per 100,000 in women.¹ Previous studies showed that the majority of patients with AGWs who applied to the dermatology outpatient clinic are male patients (ranged 58.5%-88.8%).⁶⁻¹² In our study, the number of male patients (70.7%) was higher than female patients, consistent with the literature.

In studies conducted in our country (Türkiye), the mean age of patients with AGWs varies between 30.8 and 35.2 years.^{9,10} In our study, the mean age of the patients was 34.3 years, which is consistent with the literature.

Various studies conducted outside of Türkiye have reported that HBsAg positivity in patients with AGWs varies between 0% and 2.6%.^{11,13,14} In studies conducted in our country, it was found that HBsAg positivity in patients with AGWs ranged from 0% to 3.2%.^{7,9,10} According to studies reported from different regions of Türkiye, HBsAg positivity rate in blood donors varies between 0.5% and 3.17%.¹⁵ The findings of population-based studies in Türkiye revealed that 4% of the adult population has HBsAg positivity.¹⁶ It is also reported that the estimated prevalence of hepatitis B in Türkiye was 4.57%.¹⁷ HBsAg positivity in our study is not higher than HBsAg positivity rates in Türkiye.

Previous studies conducted outside of Türkiye reported that anti-HCV positivity in patients with AGWs varies between 0.6% and 5.6%.^{11,13,14} In studies conducted in our country, it was found that anti-HCV positivity in patients with AGWs ranged from 0% to 0.9%.^{7,9,10,18} According to studies reported from different regions of Türkiye, anti-HCV positivity rate in blood donors varies between 0.15% and 0.92%.¹⁵ In a study conducted in Aydın (the province where our study took place), anti-HCV positivity in blood donors was reported as 0.16%.¹⁹ A fieldwork study in Türkiye revealed that 1% of the adult population has anti-HCV positivity.¹⁶ In our study, 4 (1.2%) of patients with AGWs had anti-HCV positivity. As a result, anti-HCV positivity in our study was slightly higher than anti-HCV positivity rates in Türkiye. However, only 1 patient was diagnosed with hepatitis C virus infection by confirmation testing. It has been revealed that blood transfusion and nosocomial risk factors are responsible for the majority of hep-

atitis C cases in Türkiye; on the other hand sexual transmission does not play a major role of hepatitis C cases.¹⁶ We think that performing anti-HCV screening test in patients with AGWs may be beneficial for public health via providing early diagnosis of patients with hepatitis C virus infection.

According to the data of the Türkiye Ministry of Health, the number of syphilis cases started to increase in our country as of 2016. While 502 syphilis cases were detected in 2015, 3,533 syphilis cases were detected in 2022 in our country. In 2022, 4.14 syphilis cases per 100,000 were reported.²⁰ While no syphilis was detected in patients with AGWs in the studies of Aktaş et al. and Tamer et al.; Kaymak et al. found syphilis in 2 (4%) patients and Ünal et al. found syphilis in 3 (3.2%) patients.⁶⁻⁹ We found 2 (0.7%) syphilis cases among patients with AGWs. Considering both the fact that the prevalence of syphilis in our country has increased in recent years and 2 syphilis cases were detected in our study, we think that patients with AGWs should be tested for syphilis.

In many previous studies conducted in our country, HIV infection was not detected in patients with AGWs.^{6,7,9,10,18} However, Tamer et al. (Türkiye) reported that 1 (0.5%) of 200 patients with AGWs had HIV infection.⁸ According to studies reported from different regions of Türkiye, anti-HIV positive rate in blood donors varies between 0% and 1.06%.¹⁵ In the study where the seroprevalence of anti-HIV was 1.06%, the prevalence of HIV infection was found to be 0.002% after HIV confirmation testing was performed.²¹ In our study, HIV infection was found in 14 (4%) of 344 patients with AGWs. This is a surprisingly high rate when compared to the studies conducted with individuals who displayed AGWs or who are blood donors. In our country, it has been reported that the number of people with newly diagnosed HIV-positive increased in recent years.²² In addition, AGWs are much more frequent in HIV-positive individuals compared to HIV-negative individuals.²³ HIV infection has been reported to be a risk factor for AGWs in both genders.²⁴ It is also known that AGWs may facilitate HIV transmission.²⁵ We think that the high rate of HIV positive individuals in our study may be related to the increased prevalence of

HIV in our country in recent years and also the higher frequency of AGWs in HIV-positive individuals.

According to data from Türkiye Ministry of Health, 39,437 HIV positive people and 2,295 acquired immunodeficiency syndrome (AIDS) cases were reported since 1985 until November 8, 2023. Among these 41,732 HIV/AIDS cases in Türkiye, 34,028 (81.5%) were reported to be men and 7,704 (18.5%) were women.²² In our study, all HIV positive patients were male.

Although AGWs can occur in any part of the anogenital skin, they are usually observed in areas exposed to trauma during sexual intercourse.⁵ Mueller et al. reported that AGWs were most commonly localized on the genital region (63.8%), followed by anal (20.9%), both genital and anal (14.8%), and lips (0.5%).¹¹ Jiamton et al. found that AGWs in men were most commonly localized on the penile shaft (56.9%), followed by perianal area (13.8%), multiple sites (10.5%), scrotum (6.1%), intraanal area (5.5%) and intraurethral area (5.5%).¹³ Similar to previous studies, we found that the most common area of AGWs in both genders was genital region. However, perianal region localization was higher in women than in men. The localization of AGWs may be associated with sexual intercourse route (anal, vaginal). Unfortunately, we did not have information about the sexual intercourse route of the patients in our study.

AGWs were most common in the genital region in HIV-negative men, while they were most common in the perianal region in HIV-positive men. We think that the difference in the localization of AGWs between HIV-positive and HIV-negative men may be related to sexual orientation and sexual intercourse route. HIV displays many different routes of transmission. It is reported that the most common mode of transmission of HIV in our country is heterosexual transmission. However, it was reported that the frequency of transmission through men who have sex with men has increased recently in our country.^{26,27} The fact that the most common region of AGWs in

HIV-positive men in our study is the perianal region may be related to the increased mode of homosexual transmission in HIV-positive men in our country in recent years. Prospective further studies on this subject are needed in order to reach definitive conclusions.

One of the limitations of this study is that some data are missing due to its retrospective nature. The second limitation of our study is that conditions such as sexual orientation and sexual intercourse route (anal, vaginal) that may affect the localization of the AGWs could not be evaluated.

CONCLUSION

The patients with AGWs should be evaluated for other sexually transmitted diseases such as syphilis and HIV infection which shown increased prevalence in our country in recent years.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Münevver Güven; **Design:** Münevver Güven, Gizem Çetinkaya; **Control/Supervision:** Münevver Güven; **Data Collection and/or Processing:** Münevver Güven, Gizem Çetinkaya; **Analysis and/or Interpretation:** Münevver Güven, Gizem Çetinkaya; **Literature Review:** Münevver Güven, Gizem Çetinkaya; **Writing the Article:** Münevver Güven; **Critical Review:** Münevver Güven; **References and Fundings:** Münevver Güven, Gizem Çetinkaya; **Materials:** Münevver Güven, Gizem Çetinkaya.

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