Characteristics of Patients with Anogenital Wart: An Observational and Comparative Study

Marwa A. Shareef, MD* Maryam H. Al Tamimi, MD* Noora Y. Al Ammadi, MD* Noor Y. Janahi, MD** Rola Al Sulaiti, MD, MSc*** Abdulla Darwish, FRCPath**** Hana Al Khayat MD, FRCP(C)*****

ABSTRACT

Background: External genital warts (EGW), also known as condyloma acuminata (CA) is caused by Human Papilloma Virus (HPV) and is the most frequent sexually transmitted viral infection in the world with a worldwide prevalence range of 5% to 20%.

Objective: The aim of the study is to determine the epidemiologic characteristics of the disease and its relation to abnormal pap smear testing and abnormal serologic testing.

Setting and Methodology: a cross sectional retrospective study conducted at Bahrain Force Defence (BDF) Hospital between November 2012 to December 2017 who attended dermatology clinic for CA. A total of 3482 patients' visit were obtained. With inclusion and exclusion criteria only 195 individuals (112 (57%) females and 83 (43%) males) were included in the study.

Results: Epidemiologic characteristics were found as following; majority were between 26-35 years of age 84 (43%), married 136 (70.47%) and having had the wart for months before seeking dermatologist care 93 (47.7%). The two most common sites identified were the groin (31.79%) and labia (22.05%). In female study subjects, 65 underwent pap smear testing of whom 11 tested positives for HPV. Out of 136 study subjects who were serologically tested for HIV, HBsAg, HCV and VDRL/TPHA, 5 males and 1 female showed positive results for either or a combination.

Conclusion: Educating the public and raising awareness about the EGW could potentially help control its spread by emphasizing earlier doctor visits and educating healthcare workers to develop that habit of screening the patient's spouse. Routine screening and serologic testing of patients is recommended to detect high risk sexually transmitted diseases that could be present alongside the EGW.

INTRODUCTION

External genital warts (EGW), also known as condyloma acuminata (CA), is a sexually transmitted disease (STD) caused by Human Papilloma Virus (HPV). It is the most frequent sexually transmitted viral infection in the world[1]. The worldwide annual incidence of condyloma is from 160 to 289 per 100,000 with a recurrence rate as high as 110 per 100,000 among females and 163 per 100,000 among males[1]. The worldwide prevalence of CA ranges from 5% to 20%[2].

It is transmitted through oral, anal and genital sexual contact and a few rare cases reported of vertical transmission[3,4]. They manifest with single or multiple papules on the vulva, perineum, perianal area, vagina, cervix, penis, anus, scrotum and urethra[1]. More than 200 distinct types of HPV have been identified to date[5]. However, ninety percent of cases are caused by HPV 6 and 11[6].

CA represents a major public health problem worldwide especially in developing countries[7]. It is known that if a patient has an STD, he has a risk of having other STDs[2]. There is an increased prevalence of chlamydia and herpes among HPV positive patients due to their similar mode of transmission[8]. Also, persons who are HIV infected are more likely to develop genital warts than persons who are not HIV infected[9]. The burden of HPV infections and HPV associated diseases is high in the HIV infected patients[10].

Many of the researches focus on the association between HPV and cervical cancer. The epidemiology of condyloma is not well characterized[1]. Also, there are a few studies that investigate the relation between CA and other STDs[2]. This research work aims to study the epidemiologic characteristics of CA and the prevalence of abnormal serologic testing in this population.

STUDY SUBJECTS AND METHOD

This is a cross sectional retrospective study (patients' medical record review) conducted at BDF Hospital between November 2012 and December 2017. Samples were collected using the hospital computer-based database system of all patients attending dermatology clinic using the following searches; any encounter note with the dictions viral wart, viral warts, anogenital wart, anogenital warts, genital wart, genital warts, condyloma, condylomata and genital verruca. In addition to, ICD codes A63 and B07 which are diagnostic codes for anogenital (venereal) warts and viral warts respectively.

A total of 3482 patients out of 92514 (the total dermatology clinic visits) were obtained. Out of the 3482 patients; 1428 patients were first visits. And, 2054 were revisits for follow up appointments.

Using patient's medical records, a survey of the following variables was examined: gender, age, marital status, spouse affected or not,

* Resident, Ministry of Health Bahrain, E-mail: marwii@live.com
** Resident, King Hamad University Hospital
*** Chief Resident in Dermatology, BDF Hospital
**** Consultant Histopathologist, BDF Hospital
***** Consultant Dermatologist, BDF Hospital

duration of symptoms, serology (HBsAg, HCV, HIV, VDRL / TPHA), site of genital wart, autoinoculation, and if females whether pregnant or not and pap smear results. The inclusion criteria:

1. Both genders
2. Genital warts
3. Pregnant and non-pregnant females
4. All age groups
5. Any marital status
6. Patients attending dermatology clinic at BDF hospital (first consultation)

Exclusion criteria:

1. Follow up appointments (other visits) – to avoid double entry of the same patient
2. Inpatients with genital warts
3. Patient's attending other clinics with complaint of genital warts (e.g. GP clinic, obstetrics and gynecology clinic etc.)
4. Warts other than anogenital origin

A total of 1428 medical records were retrospectively sought and a total sample of 195 surveys were attained; those who were diagnosed with genital warts. Using the SPSS software data was analyzed.

An ethical approval was obtained from the ethics research committee at BDF Hospital Royal Medical Services.

RESULTS

A total of 195 patients were included in this study. Their characteristics are as follows; 112 (57.4%) were females compared to 83 (42.6%) males (Table 1). The majority were between 26-35 years old 84 (42.86%), followed by 16-25 years old 39 (19.9%), 36-45 years old 31 (16.33%), 46-55 years old 24 (12.24%), 56-65 years old 6 (3.06%), <5 years old 4 (2.05%), 5-10 years old 3 (1.53%) and finally, those aged 11-15 years old and >65 years old were equally affected 2 (1.02%) (Table 2).

Table 1: Gender

Gender	Female	Male
Subjects	112 (57%)	83 (43%)

Table 2: Age Groups

Age	<5	5-10	11-15	16-25	26-35	36-45	46-55	56-65	>65
Subjects	4 (2%)	3 (2%)	2 (1%)	39 (20%)	84 (43%)	31 (16%)	24 (12%)	6 (3%)	2 (1%)

Amongst the subjects, 136 (69.74%) were married, 19 (9.74%) were single, 7 (3.59%) were divorced and 33 (16.92%) unknown marital status. Regarding the pregnancy status, 34 female patients out of 112 were pregnant. The health status of the spouse was unknown in 101 (51.7%), negative (i.e., unaffected) in 55 (28.2%) and positive (i.e., affected) in 39 (20.0%) of the study subjects shown in (Figure 1).

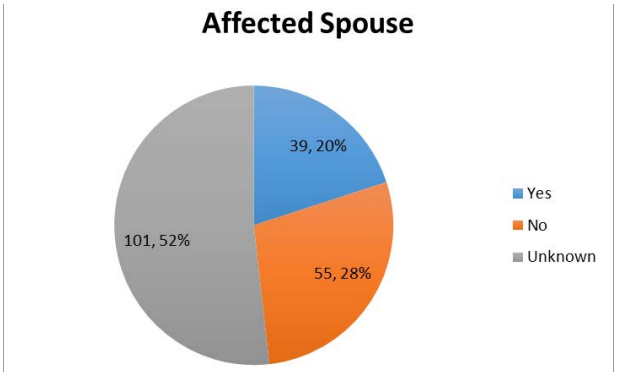

Figure 1: Affected Spouse

With regards to the clinical characteristics of patients with CA; most of the study subjects presented to dermatology clinic months after the onset of their symptoms 93 (47.7%). Followed by weeks 27 (13.8%), years 16 (8.2%) and days 4 (2.04%) shown in (Figure 2). The commonest three sites involved were the groin 62 (31.79%), labia 43 (22.05%) and multiple sites 34 (17.43%) as shown in (Figure 3). The most involved multiple sites were the perianal and labia (55.89%).

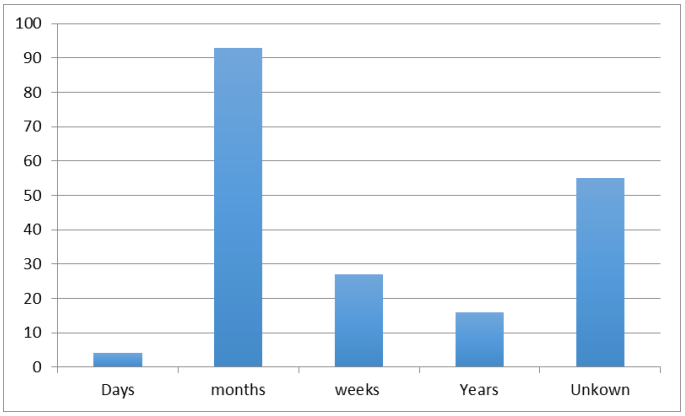

Figure 2: Duration of genital wart

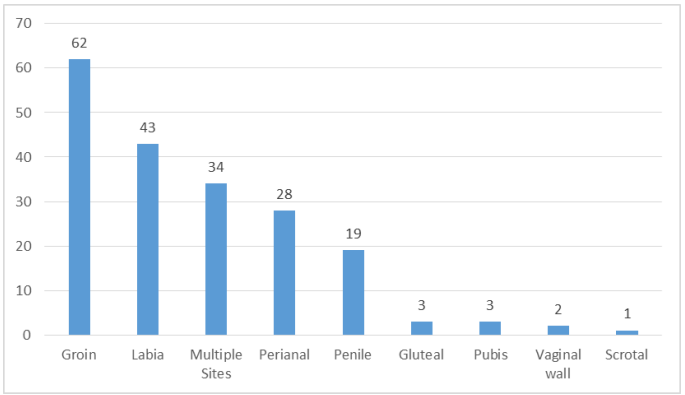

Figure 3: Site of genital wart

The most common site of autoinoculation was the hand 7 (3.6%). Other autoinoculation sites involved the face, chest and lower limbs shown in (Figure 4).

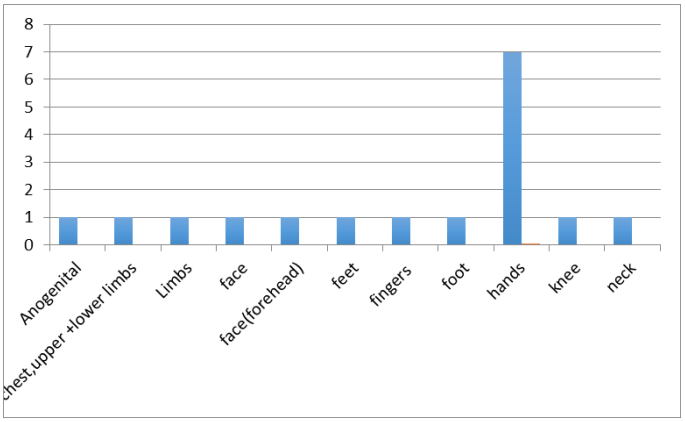

Figure 4: Autoinoculation site

Sixty-five female study subjects underwent pap smear testing, only 14 (21.87%) had an abnormal pap smear result. Of whom, 11 were HPV positive. Other abnormalities found were borderline nuclear changes,

low grade dyskaryosis, bacterial vaginosis and vaginitis. The majority of subjects; 51 (78.46%), had a normal pap smear result, as shown in (Figure 5).

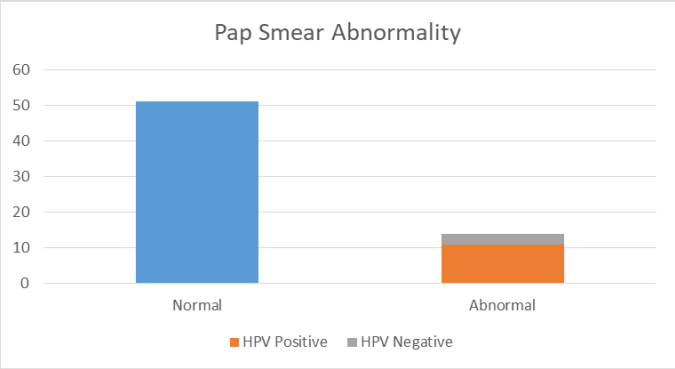

Figure 5: Pap smear abnormality

Table 3: Pap smear and serology results

Pap smear	Serology (VDRL/TPHA) result			
	Positive	Negative	Not done	Total
Abnormal	0 (0.00%)	12 (10.71%)	2 (1.78%)	14 (12.50%)
Normal	1 (0.89%)	45 (40.17%)	5 (4.46%)	51(45.53%)
Not done	0 (0.00%)	37 (33.04%)	10 (8.93%)	47 (41.96%)
Total	1(0.89%)	94 (83.92%)	17 (15.17%)	112 (100.0%)

The relationship between pap smear and serologic results was studied amid the female study subjects. Amongst patients with negative serology results, 12 were found to have abnormal pap smear, 45 had normal pap smear, and pap smear was not done in 37 patients. Only one female had an abnormal serologic test (positive VDRL), and her pap smear result was reported normal as shown in (Table 3).

Table 4: Gender and serology results

Gender	Serology Result		
	Positive	Negative	Total
Female	1	94	95
Male	5	37	42
Total	6	131	137

The relationship between gender and serologic results was also studied. Amongst 95 female patients, only one tested positive for VDRL. And out of 42 male patients who underwent routine serologic testing, only 5 had positive serology result. Two males tested positive only for VDRL and 1 only for HBsAg (Table 4). The remaining 2 patients 1 tested positive for TPHA and HIV while the second tested positive for TPHA, HIV, Anti-HBsAg and Anti-HCV.

DISCUSSION

Our study suggests that viral warts is a major complain patients present with to dermatology clinic. Around 4% of all dermatology clinic visits in our study are patients with viral warts including both first and follow up visits. For the first time visit, 13% of the patients are complaining of genital warts. Infection with human papilloma virus (HPV) is the most common sexually transmitted disease in the world[9]. The prevalence of HPV infection worldwide based on a systematic review is 0.15-0.18%[1]. HPV prevalence in Bahraini women is 9.8%[11].

There are no significant gender differences noted in our study, 57.2% are females compared to 42.6% males. Similar findings are found in a study in Central Mexico, where 50% of the study subjects are female[12] and Czech Republic where no significant differences observed between genders[13]. However, among thirteen studies based on retrospective administrative databases or medical chart reviews, nine reported higher rates in males than females[1]. This finding may be attributed to the diagnostic method, as our study includes patients who self-reported history of genital warts as opposed to incidental finding during genital screening. In agreement to our study, The US National Health and Nutrition Examination Survey found that from 1999 through 2004, a higher percentage of females self-reported a GW diagnosis compared with male patients[14].

The majority of our study sample fall between the ages of 26-35 years (42.86%). Likewise, in Mexico, the average age of patients was 32.8 years (range 18 to 69 years)[12], in Singapore a mean age of 31 years is observed[15] and in Korea, the predominant age for those diagnosed with GW is 25–29 years among male patients and aged 30–34 years in females[16]. Although our study does not compare the age at presentation between genders, both age ranges reported fall between 26 to 35 years which is the majority of patients diagnosed in our study. Other studies found peaks at younger populations, such as in Australia[17] and United States[18]. This may be attributed to differences in sexual behaviors, number of sexual partners, drug abuse or race as these factors have been reportedly associated with genital warts in multivariate analysis[14]. Unlike many studies that exclude children, we included them to appreciate the weight of the disease in younger population. As expected, only 4.5% of our sample size are children and adolescents below the age of 15. Among 1045 examined school students in Egypt for viral warts, genital wart is the least one accounting for only 2.8%[19]. In addition, only 2% of our study sample are preschool children below the age of 5 which goes hand in hand with a study that reports a prevalence of <1% in neonates and primary school children[5].

Unfortunately; although it is reported that the strongest risk factors found for GWs is an infected sexual partner[13], 51.7% of our study subjects are unaware of the health status of their spouse or partner as to whether they are suffering from GW or not. In addition, 70.47% of them are married, compared to 9.84% and 2.63% who are single and divorced respectively. Comparable findings reported in an old study conducted in Bahrain, from the data available from 553 women, 11 women were single, 513 were married 7 were divorced or separated and 20 women were widowed[11]. With these findings, it vital to suggest that all healthcare workers must develop a habit of educating and screening partners of affected patients in order to treat and stop the spread of the disease specially because the majority of these patients are married. It is also important to convey that even if one partner has visible warts, the other may not, although both have likely been exposed in an ongoing sexual relationship[4].

In a comprehensive literature search, it was found that once infected with HPV, the virus typically requires an incubation period from 3 weeks to 8 months prior to clinical manifestation. On average, physical symptoms begin approximately 2 to 3 months after initial contact[11]. Most patients in our study presented to dermatology clinic for the first time with the complain of genital wart months after the onset of the symptoms (47.7%).

Correspondingly, a Canadian study reports that the median delay between the time patients first noticed they had AGWs and their first visit to a healthcare provider was 76 days for men and 30 days for women[1]. This finding attributes to the variety of social and psychological reasons causing delay in self-perception and recognizing the importance of the condition, and therefore delay in seeking healthcare. It is integral to emphasize on earlier doctor visits for early diagnosis and management

to control the spread of the disease especially between sexual contacts.

The commonest three sites involved with genital warts in our study, are the groin, labia and multiple sites. The commonest two sites occurring together were the perianal and labial regions. In literature, it has been reported that in women, the vulva, vestibule, vagina, perineum and perianal regions are the most common sites for condyloma acuminata[5]. In male patients however, the prevalence of HPV among men (penis and urethra) varied from less than 10% to about 50%[5]. Likewise, only 10% of our male study subjects complain of GW over the penile region.

Limited literature is available on the transmission of HPV from one site of the body to another through autoinoculation. Although our study doesn't demonstrate which preceded first. Of the patients who have genital warts, 3.6% also have viral warts on their hands. A study in Hawaii reports that a history of warts on the fingers, arms and trunk (including the back, chest and abdomen) is associated with increased risk of genital HPV infection[20].

Out of the female study subjects who underwent pap smear testing, only 14 reported an abnormal test. Out of which, 11 are HPV positive and only one tested positive for VDRL. In the male study subjects, only 5 out of 42 have an abnormality in the serologic testing. Two males tested positive only for VDRL and 1 only for Anti-HBsAg. The remaining 2 patients 1 tested positive for TPHA and HIV while the second tested positive for TPHA, HIV, Anti-HBsAg and Anti-HCV. A study conducted in Turkey during 2015 found that the rate of positivity of the serological test in patients with CA is similar to that of the control group and general population [2]. Also, a study in Uganda reports a low prevalence of HIV and Syphilis positive tests in patients with positive HPV result on pap smear[21]. On the other hand, a study in Kenya demonstrates a high HIV acquisition in HPV positive men and recommend that HPV infection prevention could potentially be another tool for HIV prevention[22]. These differences could be owing to the dissimilar cultural variation, sexual behavior and religion. Awareness and availability of HPV vaccination in the region might also play a role. Routine serologic screening is requested for every patient presenting with EGW in our center. With the above data; although only a small proportion of patients have a positive serologic testing, we still recommend routine screening since other sexually transmitted diseases are considered high risk and require prompt intervention.

CONCLUSION

To conclude, around 4% of all dermatology clinic visits were patients with viral warts including both first and follow up visits. No significant gender difference was found, and the majority of study subjects were between 26-35 years. Most of the patients were married, however they were unaware of the health status of their spouse or partner as to whether or not they suffer from EGW or not. Educating the public and raising awareness about EGW could potentially help control its spread by emphasizing earlier doctor visits and educating healthcare workers to develop the habit of screening the patient's spouse. Furthermore, routine screening and serologic testing of patients is recommended; although infrequently positive, but to detect high risk sexually transmitted diseases that could be present alongside EGW. Future studies should aim to include higher sample size, study the knowledge of the disease among the population in the kingdom of Bahrain, their awareness about the HPV vaccine and its benefit in order to develop guidelines regarding its inclusion within the routine vaccine schedule.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflict of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 07 June 2021

Ethical Approval and Consent: Ethical Approval was obtained from the Research Ethics Committee of the Royal Medical Services at Bahrain Defence Force Hospital.

REFERENCES

1. Patel H, Wagner M, Singhal P, et al. Systematic review of the incidence and prevalence of genital warts. BMC Infect Dis 2013;13-39.
2. Unal E, Gönül M, Çakmak S, et al. Serological test results of sexually transmitted diseases in patients with condyloma acuminate. Postepy Dermatol Alergol 2015; 32(4):286-9.
3. HPV infection. Mayo Clinic, 2021.
4. Wiley DJ, Douglas J, Beutner K, et al. External Genital Warts: Diagnosis, Treatment and Prevention. Clin Infect Dis 2002; 35(2):210-24.
5. IARC Monographs on the Evaluation of Carcinogenic Risks to Hymans. Human Papillomaviruses, 2019.
6. Moscicki AB, Palefsky JM, et al. HPV in men: an update. J Low Genit Tract Dis 2011; 15(3):231-4.
7. Dochez C, Bogers JJ, Verhelst R, et al. HPV vaccines to prevent cervical caner and genital warts: an update. Vaccine 2014; 32(14):1595-601.
8. RR Finan, Musharrafieh U, Almawi WY. Detection of Chlamydia Tachomatis and Herpes Simplex Virus type 1 or 2 in cervical samples in human papilloma virus (HPV)-positive and HPV-negative women. Clin Microbiol Infect 2006;12(9):927-30.
9. De Camargo CC, Tasca KI, Mendes MB, et al. Prevalence of Anogenital Warts in Men with HIV/AIDS and Associated Factors. Open AIDS J 2014; 8: 25-30.
10. Kojic EM, Rana AI, Cu-Uvin S, et al.; Human Papillomarvirus Vaccination in HIV-infected Women: Need for Increased Coverage. Expert Rev Vaccines 2016; 2016; 15(1): 105-17.
11. Khairya M, Alsayyad AS, Quint W, et al.; An epidemiological study assessing the prevalence of human papillomavirus types in women in the Kingdom of Bahrain. BMC cancer 2014;14: 905.
12. Chang GJ, Welton ML. Human papillomavirus, condylomata acuminata, and anal neoplasia. Clin Colon Rectal Surg 2004;17(4):221-30.
13. Petráš M, Adámková V. Rates and predictors of genital warts burden in the Czech population. Int J Infect Dis 2015; 35:29-33.
14. Dinh TH, Sternberg M, Dunne EF, et al. Genital warts among 18- to 59-year-olds in the United States, national health and nutrition examination survey, 1999--2004. Sex Transm Dis 2008;35(4):357-60.
15. Tan LS, Chio MT, Sen P, et al. Assessment of psychosocial impact of genital warts among patients in Singapore. Sex Health 2014;11(4):313-8.
16. Lee TS, Kothari-Talwar S, Singhal PK, et al. A cross-sectional study estimating the burden of illness related to genital warts in South Korea. BMJ Open 2017;7(6): e014217.
17. Pirotta M, Stein AN, Conway EL, et al. Genital warts incidence and healthcare resource utilisation in Australia. Sex Transm Infect 2010;86(3):181-6.

18. Dunne EF, Sternberg M, Markowitz LE, et al. Human papillomavirus (HPV) 6, 11, 16, and 18 prevalence among females in the United States--National Health and Nutrition Examination Survey, 2003-2006: opportunity to measure HPV vaccine impact? J Infect Dis 2011;204(4):562-5.
19. Essa N, Saleh MA, Mostafa RM, et al. Prevalence and factors associated with warts in primary school children in Tema District, Sohag Governorate, Egypt. J Egypt Public Health Assoc 2019;94(1):6.
20. Hernandez BY, Shvetsov YB, Goodman MT, et al. Genital and extra-genital warts increase the risk of asymptomatic genital human papillomavirus infection in men. Sex Transm Infect 2011;87(5):391-5.
21. Blossom DB, Beigi RH, Farrell JJ, et al. Human papillomavirus genotypes associated with cervical cytologic abnormalities and HIV infection in Ugandan women. J Med Virol 2007; 79(6):758-65.
22. Smith JS, Moses S, Hudgens MG, et al. Increased risk of HIV acquisition among Kenyan men with human papillomavirus infection. J Infect Dis 2010 Jun; 201(11):1677-85.