

## Original Research Article

# Clinico-epidemiological profile of condylomata acuminata with special emphasis on HPV typing

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## ABSTRACT

**Background:** Condylomata acuminata (CA) or genital wart is a sexually transmitted infection (STI) caused by human papilloma virus (HPV). As there was little information about the HPV types commonly causing CA in our state, we decided to study the clinico-epidemiological profile of CA with special emphasis on HPV typing.

**Methods:** We did HPV typing in 25 clinically diagnosed cases of CA. The biopsied specimens were sent for HPV typing using Polymerase chain reaction (PCR) and those with high risk HPV types were histologically analyzed for any dysplastic change. We also evaluated for other STIs which can coexist with CA.

**Results:** Out of the 25 cases, 18 (72%) were males and 7 (28%) females. Majority of our patients belonged to 21-40 year age group (64%). Clinical types of CA were the classical fleshy exuberant type in 22 patients (88%), flat type in 2 (8%) and keratotic type in 1 (4%). HPV positivity was obtained in 21 (84%). The most common type was HPV 6 in 10 cases (40%) and HPV 11 in 8 (32%) patients. HPV 16 alone was isolated in 1 (4%) case. HPV types 6 and 16 and 11 & 18 were isolated in one case each. Dysplastic changes were observed in two cases with HPV 16 and 18. VDRL and TPHA positivity was found in 2 (8%) males and HBsAg positivity was seen in 1 (4%) male patient.

**Conclusions:** This study highlights the importance of HPV typing for identifying the high risk types and to assess the efficacy of HPV vaccines.

**Keywords:** Condylomata acuminata, HPV types, PCR, Dysplasia

## INTRODUCTION

Condylomata acuminata (CA) caused by human papilloma virus (HPV) constitute one of the common sexually transmitted infections. CA can manifest as cauliflower-like (classical), flat, papular or keratotic lesions on sites like vulva, penis, groin, perineum, perianal skin or other mucosal surfaces and may be associated with symptoms like pruritus, burning pain or may remain asymptomatic. Atypical lesions, unresponsiveness to treatment and immunocompromised

individuals may need further investigations like biopsy.<sup>1</sup> Though HPV typing is not routinely recommended, it may help to determine the prevalence of different genotypes and also to assess the efficacy of the quadrivalent vaccination in the population under study.<sup>2</sup>

We did HPV typing from biopsied specimens of genital warts using Polymerase chain reaction (PCR). Preponderance for malignancy is seen associated with genital warts caused by HPV 16, 18. Early detection of the cases help to check the transmission and recognize

the cases at risk for malignant transformation as incidence of genital HPV infections is on the rise. As genital HPV is often associated with other STIs, a thorough evaluation for other STIs needs to be done.<sup>3</sup>

## METHODS

The study was conducted among 25 consecutive patients who were clinically diagnosed to have genital warts at the outpatient clinic of the Department of Dermatology and Venereology, Government Medical College Hospital, Thiruvananthapuram from April 2003 to March 2004, after informed written consent and clearance from institutional ethical committee. Those who were not willing to participate in the study were excluded.

The clinical types of condylomata acuminata were studied and the types of HPV causing it were also ascertained using PCR. The presence of other STIs was assessed using clinical evaluation as well as biochemical and serological studies. Detailed history with specific focus on their sexual history was taken emphasizing the number of sexual contacts, frequency of contact and presence of genital warts in partners. A thorough clinical examination was done in which the distribution of warts, their morphology, evidence of malignant change and presence of features of other STIs were noted. Blood was collected from all patients and their partners and serum was separated for tests such as VDRL, TPHA, and ELISA for HIV and HBsAg. Urine deposit was examined for Gram stain, wet film with potassium hydroxide and normal saline. Genital warts were biopsied. It was collected in normal saline, snap frozen in liquid nitrogen and stored at -80°C till PCR was done. It was taken to the division of cancer research, Regional cancer centre, Thiruvananthapuram where HPV typing (types 6, 11, 16, 18) using PCR was done using consensus primers first and if found positive was subtyped using HPV type specific PCR primers. Steps involved were DNA extraction, quantitation followed by polymerase chain reaction which utilizes a DNA polymerase and two oligonucleotide primers to synthesise and amplify a specific DNA fragment of interest from a single str and template sequence. In this study, PCR was used to amplify the integrated viral DNA of HPV in the tissue specimen. Biopsy specimens of lesions associated with high risk HPV types were sent for histopathological analysis to assess for any dysplastic changes or malignancy.

Data were entered in MS excel and statistical analysis was done using SPSS version 22. Categorical variables were expressed as proportions and percentage.

## RESULTS

18 (72%) out of 25 patients were males and the rest (28%) were females. Male to female ratio is 2.57:1. The demographic profile of the patients is given in Table 1.

Of the 376 STI patients, 25 were having CA forming 6.64% of new STI cases. Majority of the patients belonged to 21-30 years (36%). Sixteen out of eighteen males (88.9%) had either pre or extramarital contacts. All females had marital contacts only but male partners of 5 of them gave history of extramarital contacts. 4 out of our 7 female patients (57%) were pregnant. 7 males out of 18 (39%) had 5 or more partners and 8 males had contact with 2-4 partners. Of the female patients, two gave history of presence of genital warts in their marital partners. 16 (64%) of patients were asymptomatic. Of the 9 symptomatic patients, 5 were males and 4 females. In males, commonest symptom was itching followed by burning sensation and pain and in females it was vaginal discharge followed by itching. Predominant site in males was perianal area (38.8%) followed by prepuce (22.2%). In females, multiple sites were involved in 4 out of 7 patients (57.15%). Most common type of CA found in males was the classical fleshy exuberant type which was observed in 15 patients (83.3%). Two males had flat type and one had keratotic type. All females in the study were having lesions of classical fleshy exuberant type. VDRL and TPHA positivity was found in 2 (8%) males and HBsAg positivity was seen in one male (4%) patient.

**Table 1: Age, occupation and sexual behavioural in patients with condylomata acuminata.**

Characteristics	N=25 (%)
<b>Age group</b>	
11-20	2 (8)
21-30	9 (36)
31-40	7 (28)
41-50	5 (20)
>50	2 (8)
<b>Occupation</b>	
Manual labourer	6 (24)
White collar job	5 (20)
Skilled labourer	6 (24)
House wives	6 (24)
Drivers	2 (8)
<b>Behavioral pattern</b>	
Heterosexual unprotected	12 (48)
Heterosexual protected	1 (4)
Inconsistent condom usage	6 (24)
Homosexual	2 (8)
Bisexual	4 (16)

The results of HPV typing are given in Table 3. HPV positivity was found in 21 out of 25 cases (84%). It was negative in 1 female and 3 males. The most common type detected was HPV 6 (40%) followed by HPV 11 (32%). The types of HPV present in lesions obtained from different sites in males and females are shown in Table 4 and 5 respectively.

The most common type isolated in those having a single partner was HPV 6 followed by HPV 11. In those having

multiple partners, HPV 11 was the commonest type. Dysplastic changes were observed in the histopathology of the two cases with HPV 16 and 18. More than one

HPV was found in those having multiple partners. An increase in the number of genital warts was associated with increasing HPV positivity.

**Table 2: Type of condylomata and HPV types.**

Clinical types	HPV not isolated	HPV 6	HPV 11	HPV 16	HPV 6 and 16	HPV 11 and 18	Total
<b>Classical</b>	3	8	8	1	1	1	22
<b>Keratotic</b>	0	1	0	0	0	0	1
<b>Flat</b>	1	1	0	0	0	0	2

**Table 3: HPV typing.**

Types	Number of patients	Percentage (%)
<b>HPV-6</b>	10	40
<b>HPV 11</b>	8	32
<b>HPV 16</b>	1	4
<b>HPV 6 and 16</b>	1	4
<b>HPV 11 and 18</b>	1	4

**Table 4: HPV types in males.**

Site	HPV types					
	6	11	16	18	6 and 16	11 and 18
<b>Frenum</b>	0	0	0	0	0	0
<b>Coronal sulcus</b>	1	1	0	0	0	0
<b>Prepuce</b>	2	1	0	0	0	0
<b>Perianal area</b>	3	4	0	0	0	0
<b>Multiple sites</b>	0	0	1	0	1	1

**Table 5: HPV types in females.**

Site	HPV types	
	6	11
<b>Introitus</b>	2	0
<b>Labia majora</b>	0	1
<b>Multiple sites</b>	2	1

## DISCUSSION

In our study, the mean age of patients was 33.4 years and there was a male preponderance with a male to female ratio of 2.57:1. It agrees to the statement that overt HPV disease is more in young adults with male preponderance.<sup>4</sup> 4 out of our 7 female patients (57%) were pregnant. Similar observation of HPV in pregnancy has been reported by previous workers.<sup>5,6</sup>

Though majority of patients were asymptomatic, the commonest symptoms in males were itching in genitalia (in 5 out of 18) and in females, it was discharge per vaginum (in 4 out of 7). This observation agrees with that of previous studies.<sup>3,7</sup>

7 males out of 18 (39%) had 5 or more partners, and 8 males had 2-4 partners. Increase in the number of

partners has been described as the major risk factor for HPV infection.<sup>4,8</sup>

Perianal area was the commonest site of involvement in males followed by prepuce, which was not reported in previous studies. Introitus was the commonest site of involvement in females. The commonest clinical type in both males and females was the fleshy exuberant type as observed in most of the studies.<sup>3,7</sup>

Knowledge about of HPV prevalence and genotype distribution is important. It may help to assess the impact of cervical cancer screening and HPV vaccination on the incidence of HPV associated diseases. In our study HPV positivity was found in 84% of cases. The most common HPV type isolated was HPV 6 (40%) followed by HPV 11 (32%) which is similar to the observation in many other studies. A study of type specific HPV prevalence in

Czech women and men with anogenital diseases showed HPV 6 (72%) as the commonest type in benign lesions.<sup>9</sup> HPV prevalence can vary significantly with age and region. In a study conducted at Jiangxi province, China the prevalence and HPV typing was investigated among 71,435 individuals ranging in age from 16 to 77 years by collecting cervical swabs.<sup>10</sup> The most frequently detected genotypes were HPV-6 (low risk) and HPV-16, 18, 33, 52 and 58 (high risk). A multicentre survey in France to assess the prevalence of HPV genotypes in condylomata acuminata showed that the most prevalent genotypes were 6 (69%) and 11 (16%) followed by 16 (9%), 51 (8%), 52 (7%), 66 (6%), 53 (5%), 31 (3%), and 18 (3%).<sup>11</sup>

In a study conducted among men attending a Swedish STI clinic, the predominant low risk type was HPV 6 and high risk type HPV 16. There was a significant association of low risk HPV types with acuminata lesions and high risk type with macular lesions. However in our study the high risk types were associated with the classical acuminata type. High risk types were more located over fore skin while low risk types on penile shaft and pubis.<sup>12</sup> We did not notice any site predilection for high risk types. The high risk HPV types were present only in males. A study done at the Centre for Sexual Health in Malmö, Sweden showed that high risk HPV types were more common in females than males.<sup>13</sup>

The association between high risk HPV types and malignancy is well established. 2 of our cases showing infection with high risk HPVs (16 and 18) showed dysplastic changes. A similar observation is seen in the study by Baydar et al where there was a significant association of dysplasia with high risk HPV types in males.<sup>14</sup> Hence they recommend careful follow up and counselling in patients with oncogenic HPV infection. In a study of the epidemiological, clinical and virological features of women with genital warts in Greece, concurrent cervical intra epithelial neoplasia was present in 11.1% which underlines the importance of cytology and colposcopy for all women with genital warts.<sup>15</sup>

2 patients showed more than one type of HPV. There is a proven coexistence of more than one type of HPV in the same patient.<sup>9-11</sup>

Seropositivity for other STDs such as blood VDRL and TPHA positivity was found in 2 male patients and HBsAg positivity was observed in another male patient. This may be explained by the exposure to multiple sexual partners. A study by Ünal, et al. found an increased incidence of syphilis sero positivity among patients with CA while that of HBsAg was comparable to that of general population.<sup>16</sup> HIV positivity was significantly absent in our study but HIV-1 infection, not syphilis or HBV infection, was identified as a strong risk for anorectal condyloma in the study by Nishijima et al.<sup>17</sup>

This study highlights the importance of HPV typing for identifying the high risk types which can be associated with dysplasia. Furthermore, knowledge about the HPV types in a region will help to assess the efficacy of bivalent /quadrivalent vaccines in prevention of CA. The limitation of our study was the inability to do HPV typing for genotypes other than 6, 11, 16 and 18 due to financial constraints.

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