

# Smoking: Is it a Risk Factor for Common Warts?

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**ABSTRACT:** Introduction: Common warts are one of the most prevalent infections affecting the skin. Common warts are caused by human papillomaviruses (HPV), which are ubiquitous in our environment. Most HPV infections are directly controlled and cleared by host immune system, although each case has the potential to persist and transform into a recalcitrant form. It is not exactly clear why certain populations are more susceptible to common warts. Aim: To investigate factors affecting the occurrence and outcome of common warts. Material and methods: A total of 188 consecutive patients with common warts (106 men, 82 women) and 188 controls were prospectively enrolled. Demographic and clinical characteristics were recorded. The Chi-square, Mann-Whitney U and Kruskal-Wallis tests were used for statistical analysis, with a significance threshold of  $p < 0.05$ . Results: There were not any significant associations between cigarette smoking, alcohol consumption, accompanying diseases, medications, family history of warts and the duration of warts ( $p=0.102$ ,  $p=0.317$ ,  $p=0.535$ ,  $p=0.535$ ,  $p=0.535$ , respectively). There were not any significant associations between cigarette smoking, alcohol consumption, accompanying diseases, medications, family history of warts and the number of warts ( $p=0.232$ ,  $p=0.762$ ,  $p=0.389$ ,  $p=0.389$ ,  $p=0.824$ , respectively). Conclusions: Our study has revealed that smoking is not a risk factor for common warts. However, we suspect the lack of statistical differences are likely due to small sample size of the study. Further studies with larger sample sizes are needed.

**KEYWORDS:** Common warts, human papillomavirus, smoking, risk factors.

## Introduction

Common warts are one of the most prevailing reasons for dermatology consultations.

Common warts are skin coloured hyperkeratotic lesions caused by human papillomavirus (HPV), which is a small, double-stranded DNA virus that infects the epithelia of skin or mucous membranes.

More than 120 genotypes of HPV have been identified so far. Having tropism for epithelial cells, HPVs cause pathologies varying from warts to mucocutaneous neoplasias.

The clinical manifestations of HPV infections depend on both the viral subtype and the immune status of the patient.

HPVs are well-known to have developed immune evasion strategies that interfere with host immunity.

Many HPVs reduce the risk of immune clearance by causing persistent asymptomatic infections [1-5].

Common warts are usually self-limiting and in patients with an intact immune response common warts generally regress within months to years without treatment.

However, there is a disparity between individuals in terms of resolution rates of the warts. It is believed that cell mediated immune deficiency to HPV is the key factor responsible for the disparity. Smoking is well-known for its negative impact on immune system [1-5]

Here, in this study we aimed to investigate the role of smoking and other factors on common warts.

## Material and Methods

188 consecutive patients with common warts and 188 age- and sex-matched controls were prospectively enrolled in the present study over a period of 12 months.

The study was conducted according to the guidelines laid down in the Declaration of Helsinki and was approved by the local ethical committee.

Written informed consent was obtained from all participants prior to study inclusion.

A thorough history regarding educational attainment, marital status, occupation, smoking habits, alcohol consumption, accompanying diseases, current medications, duration of warts, previous treatments for warts and family history of warts was obtained.

Individuals who were current smokers or had a smoking history were asked to report smoking years and number of cigarettes smoked per day.

Accordingly, 'packyears' (PY) measurement (the product of the number of packs smoked per day by years of smoking) calculated and smoking habits of the participants were rated on a 4-point scale as: 1=' $PY < 5$ ', 2=' $5 \leq P < 20$ ', 3=' $20 \leq PY < 40$ ' and 4=' $PY \geq 40$ '.

For those who were drinkers, alcohol consumption was ranked on a 3-point scale as: 'daily', 'several times a week', 'rarer than once a month'.

Occupations of the participants were classified according to International Standard Classification of Occupations (ISCO)-08 [6].

For each patient a complete dermatological examination was performed and the number and the localization of warts were recorded.

### Statistical analysis

The statistical analysis was performed using SPSS software (version 20; SPSS Inc., Chicago IL, USA).

Categorical variables were expressed by numbers and percentages, while continuous variables were reported as means±standard deviations and ranges.

The Chi-square test and Mann-Whitney U tests were performed on categorical and non-parametric continuous data, respectively.

The Kruskal-Wallis test was conducted to compare the amount and duration of warts among different educational and occupational groups.

A *p*-value of <0.05 was considered to be statistically significant.

### Results

A total of 188 patients [106 men and 82 women; mean age, 27.1±9.8 years (range: 18-60 years)] were recruited in the study.

Accompanying diseases and medication history were recorded in 28 of 188 patients (14.9%). 15.4% of the patients (n=29) were graduates of compulsory school, 12.8% (n=24) were secondary school-educated, 45.7% (n=86) were high school-educated and 26.1% (n=49) were graduates of a university (Figure 1).

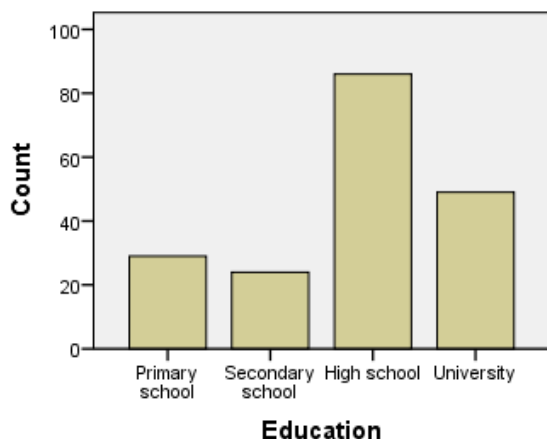


Figure 1. Educational attainment of the study group.

65 of 188 patients (34.6%) were married. 34% of the patients (n=64) were students, 16% (n=30) were unemployed.

Table 1 shows the distribution of occupations among the individuals in the study (Table 1).

Table 1. The distribution of occupations among patients and controls.

Major occupation groups	Patient group		Control group	
	n	%	n	%
Professionals	12	6.4	8	4.3
Technicians and associate professionals	12	6.4	17	9
Clerical support workers	13	6.9	14	7.4
Services and sales workers	10	5.3	15	8
Skilled agricultural, forestry and fishery workers	7	3.7	13	6.9
Craft and related trades workers	7	3.7	10	5.3
Plant and machine operators and assemblers	7	3.7	9	4.8
Elementary occupations	21	11.2	19	10.1
Armed forces occupations	6	3.2	2	1.1

53 of 188 patients (28.2%) were current smokers or had a smoking history. According to smoking habits 4-point scale, 13.8% of the patients (n=26) were in the group 1 (PY<5), 11.2% (n=21) were in the group 2 (5≤PY<20), 3.2% (n=6) were in the group 3 (20≤PY<40) (Figure 2).

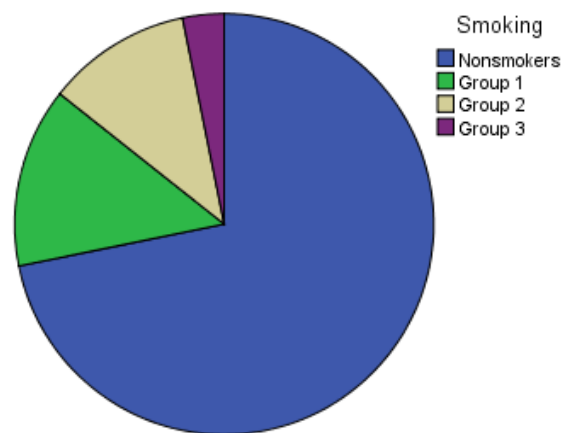
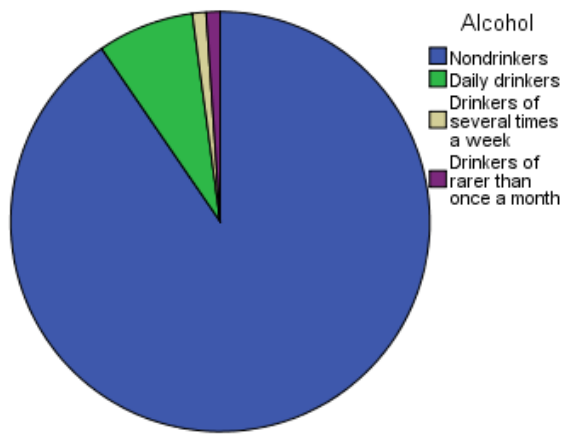


Figure 2. Smoking habits of the study group.

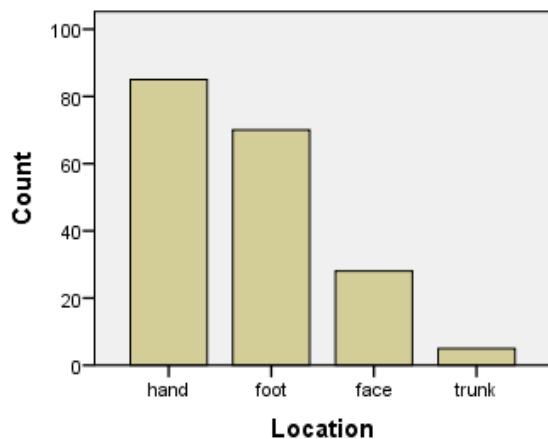
90.4% of the patients (n=170) never had drunk alcohol. 18 of 188 patients (9.6%) were current drinkers, 2 of 18 patients (1.1%) were daily drinkers, 2 patients (1.1%) were drinkers of 'several times a week' and 14 patients (7.4%) were drinkers of 'rarer than once a month' (Figure 3).



**Figure 3. Alcohol consumption habits of the study group.**

21 of 188 of patients (11.2%) had a family history of common warts.

Warts were localized on hands in 45.2% (n=85), on feet in 37.2% (n=70), on face in 14.9% (n=28), on trunk in 2.7% (n=5) of the patients (Figure 4).

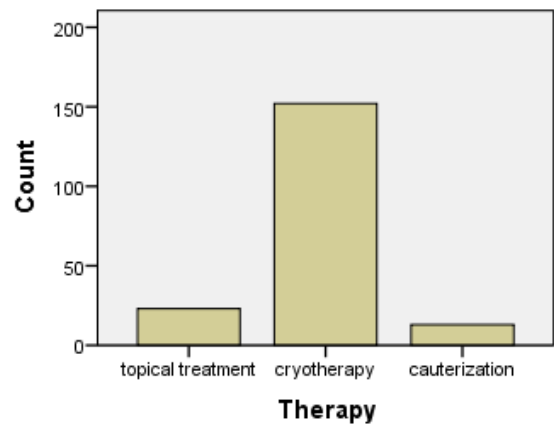


**Figure 4. Localization of warts in the study group.**

7 of 188 patients (3.7%) had two different localizations for warts.

The duration of warts ranged from 1 to 89 months (mean±SD: 13.2±17.1).

The total number of warts ranged from 1 to 20 (mean±SD: 4.1±3.7). 11.2% (n=23) of the patients had received topical treatments for warts previously, while the treatment of choice had been cryotherapy for 80.9% (n=152) and cauterization for 6.9% (n=13) of the patients (Figure 5).



**Figure 5. Past wart-treatment history of the study group.**

The age of the control group ranged from 18 to 60 years (mean: 27±9.8).

There was no significant difference between the genders of the patient and control groups. 88 of 188 controls (44.7%) were married. 31.4% (n=59) were students and 11.7% (n=22) of the controls were unemployed. 21.3% (n=40) of the controls were graduates of compulsory school, 5.3% (n=10) were secondary school-educated, 50% (n=94) were high school-educated, 23.4% (n=44) were graduates of a university. 45 of 188 controls (23.9%) were current smokers or had a smoking history.

According to smoking habits 4-point scale, 18.1% of the controls (n=34) were in the group 1 (PY<5), 4.8% (n=9) were in the group 2 (5≤P<20), 1.1% (n=2) were in the group 3 (20≤PY<40). 7.4% (n=14) of the controls (7.4%) were current drinkers. 1.6% (n=3) were drinkers of ‘several times a week’ and 5.9% (n=11) were drinkers of ‘rarer than once a month’.

Accompanying diseases and medication history were detected in 21 of 188 controls (11.2%).

There weren’t any statistically significant differences in education, occupational status, presence of accompanying diseases, prevalence rates of smokers and drinkers between patient and control groups (Mann-Whitney U test; p=0.637, p=0.391, p=0.284, p=0.348, p=0.859, respectively).

There were not significant associations between cigarette smoking, alcohol consumption, accompanying diseases, medications, family history of warts and the duration of warts (Mann-Whitney U test; p=0.102, p=0.317, p=0.535, p=0.535, p=0.535, respectively).

The median of the duration of warts was 5 months in smokers while it was 7 months in nonsmokers [interquartile range (IQR), 9 vs. 14].

Likewise, there were not any significant associations between cigarette smoking, alcohol consumption, accompanying diseases, medications, family history of warts and the number of warts (Mann-Whitney U test;  $p=0.232$ ,  $p=0.762$ ,  $p=0.389$ ,  $p=0.389$ ,  $p=0.824$ , respectively).

The median number of warts was 3 both in smokers and nonsmokers (IQR, 4).

There were not any significant differences neither in duration [men vs. women, median (IQR) 6 (14) vs. 7 (10),  $p=0.335$ ] nor in number of warts [men vs. women, median (IQR) 3 (4) vs. 3 (4),  $p=0.673$ ] between genders.

Moreover, no significant differences were detected in the duration and the number of warts between different educational groups (Kruskal-Wallis test;  $p=0.788$ ,  $p=0.099$ , respectively).

The statistical analysis did not reveal any significant difference in the number of warts among different occupational groups (Kruskal-Wallis test;  $p=0.843$ ).

However, it was found out that clerical support workers and services/ sales workers had significantly longer duration of warts than patients with other occupations (Kruskal-Wallis test;  $p=0.016$ ,  $p=0.014$ , respectively).

## Discussion

The effects of smoking on common warts in adult populations have not been investigated up to now.

To the best of our knowledge, our study is among the first to review the effects of smoking and other social and economic factors, such as education and employment on the occurrence and outcome of common warts in adults.

Few studies have conducted to explore the association between smoking and the reported clinical diagnosis of anogenital warts [7-12].

Wiley et. al. demonstrated that genital warts were associated with smoking as in their study smokers were 23% more likely than non-smokers to have shown clinical incidence of genital warts [10].

Hansen et. al. proved smokers to experience a moderately increased risk of being diagnosed with genital warts [9].

Likewise results of another study, although did not demonstrate the association between the size of anal warts and current smoking status, showed that at baseline women who smoked had

much larger anal warts than those who did not smoke [11].

Smoking is an established risk factor for numerous diseases.

The immunomodulatory effects of smoking has been proposed as being the underlying reason for most of its adverse effects. Smoking influences both innate and adaptive immune system.

Cigarette smoke is a complex mixture of thousands of chemicals, including tar and nicotine, which are known to have immunosuppressive effects on the immune system.

Studies have shown that nicotine causes a significant loss of antibody responses and T-cell proliferation.

After binding an antigen, T cells from nicotine-treated animals cannot normally transmit the antigen-receptor-mediated signals.

Adaptive immune cells affected by smoking mainly include T helper cells, CD4+CD25+regulatory T cells, CD8+T cells, B cells and memory T/B lymphocytes.

Smoking induces production of many immune and inflammatory mediators, including pro-inflammatory cytokines, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 (IL-1), IL-6, IL-8 and granulocyte-macrophage colony-stimulating factor (GM-CSF).

Smoking has dual effects on immune system, by either exacerbation of pathogenic immune responses or attenuation of defensive immunity.

Thus, other than pro-inflammatory effects, immunosuppressive effects of smoking have been shown as to decrease IL-6, IL-8, and IL-10 production and suppress Th1 and Th17 responses with corresponding switch towards the Th2 lineage.

Moreover, smoking decreases neutrophils phagocytic activity, affects chemotaxis and inhibits the release of reactive oxygen species.

Therefore, despite the amplification of inflammation, neutrophils exposed to cigarette smoke lose their ability to produce respiratory bursts, thus becoming less effective in attacking microorganisms [13-16].

HPV infections are among the most prevalent persistent infections affecting humans.

HPV have developed strategies to evade the host immune system, which allows their persistence within the host.

Indeed, HPV are known to have a unique ability to prevail in the host's epithelium by creating a complex and localized immune suppressive milieu. Immune response evasion is

one of the most important feature of HPV perseverance.

Most HPV infections are cleared by an effective cell mediated immune response, however at different intracellular levels HPV manage to stay undetected by the host.

HPV alters gene expression of chemokines, adhesion molecules and TLRs creating a noninflammatory environment for enhanced virus replication, assembly and release.

Overall, there is a vast amount of literature signifying HPV induced immune dysfunction at the site of infection shaped by modulation of immune cells, receptors, cytokines, chemokines, transcription factors and other immune mediators [17-20].

According to results of our study, smoking do not increase the risk of HPV infection in adults.

As far as we know, our study is the first in the literature to investigate the relationship between smoking and common warts, thus interpretation of the results with that of similar studies is unlikely.

However we would have expected an increased incidence of persistent infection among smokers, since the immunosuppressive effects of smoking has been proved [13-16] and recalcitrant HPV infections are associated with greater immunological deficit [17-20].

The human organism is a very intricate biological system, composed of varied systems, substructures, confined in order to function as a whole.

There are puzzling mysteries of the human body that are to be solved.

Although current data indicate that smoking is related with increased risk of genital warts [7-12], there might not be an indicative relationship between smoking and common warts.

On the contrary, further studies might prove this relation.

We also did not detect any effect of neither alcohol consumption nor education level on the severity of warts.

Likewise, major occupational groups and the amount of warts were not related.

We have only detected a significant relationship between occupation and the duration of warts, as clerical support workers and services/sales workers had significantly longer duration of warts than patients with other occupations.

It has been shown that high alcohol consumption [21,22] and a low socioeconomic

status are associated with increased risk of genital warts [12].

There is not enough data in the literature about the prevalence and risk factors of common warts in adult populations.

In one of the studies investigating epidemiology and clinical profile of cutaneous warts in children, the prevalence of cutaneous warts has been shown to be higher in patients from rural areas than those from urban areas [23].

Likewise, in another study of children, risk factors were shown to be male sex, attending a public school, having a large family size, being a smoker and working.

On the contrary, having a highly-educated father appeared to reduce the overall risk of common warts [24].

Although there is a growing evidence that smoking is associated with higher prevalence rates of genital warts, the current data does not provide a full picture for the association of smoking and other risk factors with the overall HPV infection risk.

The likelihood of behaving in a high-risk manner in term of sexual practices is well-known among addicts.

Smoking and alcohol addiction increase the tendency of high-risk sexual behaviour [12,25].

Therefore, it is not clear whether the increased incidence and prevalence rates of anogenital warts among smokers and drinkers is related with the potential relationship among risky sexual behaviour and addiction or with the possible effect of smoking on HPV infection.

We conclude that the relationship between smoking and HPV infections is still unclear and current data is limited.

Further studies should be conducted to figure out whether the lack of statistical significance observed here is a result of sample size, or reflects a true lack of association.

## Conflict of interests

None to declare.

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