Thi-Qar Medical Journal (TQMJ):Vol.( 27),No.(1),2024

Web Site: https://jmed.utq.edu Email: utjmed@utq.edu.iq

ISSN (Online): 3006-4791

# Prevalence of Cutaneous Warts Caused by Human Papillomaviruses and the Effect of Vitamin D with it's Distribution Among Patients in Thi-Qar Province

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## Abstract:

**Background**: Cutaneous warts represent prevalent skin lesions resulting from infection with human papillomavirus (HPV) (Sterling et al., 2014). HPV, a diverse group of viruses capable of infecting both skin and mucous membranes, can give rise to various conditions, prominently including the development of warts. With over 100 distinct HPV types identified, the association between specific strains and the manifestation of distinct wart types is well-established (Bernard et al., 2010).

Cutaneous warts are skin infection characterized by skin growths that high and rough. appear in numerous regions of the body, most commonly on the hands, feet, and faces (Shallal et al., 2023). warts caused by Human papillomavirus (HPV). According to previous studies there are possible link between serum vitamin D insufficiency with developing of cutaneous warts (Mahmoud & Ayyash, 2021). investigation of vitamin D aim in verifying the existence of a relationship between vitamin D and the occurrence of cutaneous warts.

**Aim:** The aim of this study is to Investigate the serum levels of vitamin D in patients related to the presence of cutaneous warts caused by human papillomavirus and in compared to healthy individuals.

**Methods:** Between October 2023 and December 2023, this research involved gathering serum samples from 103 individuals diagnosed with cutaneous warts. Additionally, a control group comprising 50 individuals of various ages without warts was included. The determination of serum vitamin D levels was conducted using the electrochemiluminescence (ECL) method.

**Keyword:** Cutaneous warts, HPV (Human Papillomavirus), Cutaneous warts; Vitamin-D.

**Introduction:** Cutaneous warts are common manifestations resulting from HPV infection, appearing in diverse forms like common warts, plantar warts, and flat warts. The prevalence of cutaneous warts exhibits variability among populations and regions. Research, such as that by Sterling et al. (2014), indicates associations between specific HPV genotypes and distinct wart types, with prevalence influenced by factors like age, gender, and geographical location.

Vitamin D, a vital modulator of the immune system, is crucial for preventing various infections, including those caused by HPV, as suggested by studies like that of Chen et al. (2013). The immunomodulatory effects of Vitamin D extend to both innate and adaptive immunity, hinting at a potential role in the persistence or clearance of viral infections. An essential motivation for studying the relationship between serum vitamin D and cutaneous warts is its role in regulating cell proliferation, differentiation, and immunological function, as well as suppressing keratinocyte overgrowth (Mahmoud & Ayyash, 2021). Numerous studies have demonstrated low serum vitamin D levels in individuals with viral warts, underscoring its significance (Shalaby et al., 2022).

Further investigations, such as those by Thappa & Chiramel (2016), have shown successful treatment of cutaneous warts using topical vitamin D3 derivatives and intralesional vitamin D3 injections. The immunoregulatory functions of Vitamin D may impact the host's ability to combat HPV, potentially reducing the likelihood of wart development.

Vitamin D, synthesized in response to sunlight exposure, plays a pivotal role in immune modulation and defense against infections. Its deficiency has been linked to an elevated risk of infections, including those by HPV (Chen et al., 2020; Bikle, 2014). Research by Chen et al. (2013) explores Vitamin D's potential immunomodulatory effects on HPV infections, suggesting a link to variations in cutaneous wart prevalence, particularly in a gender-specific context. Investigations have hinted at gender-specific differences in Vitamin D levels, with some studies indicating a higher susceptibility to deficiency in females (Mirhosseini et al., 2018). Examining whether these variations in Vitamin D status correlate with gender-specific differences in cutaneous wart prevalence could yield valuable insights.

**Study Population and Methods:** The sample collection for this study spanned from October 2023 to December 2023, encompassing individuals aged 8 to 60. Inclusion criteria mandated participants to be free from chronic illnesses and included individuals of both sexes. Exclusion criteria comprised individuals currently receiving vitamin D supplementation, immunosuppressive medications, those with chronic illnesses, pregnant women, and individuals with genital warts. Clinical diagnoses were conducted by attending dermatologists for all participants, and collected data encompassed demographic details such as age and sex.

Both the control group and each study participant underwent blood sample collection, subsequently centrifuged to obtain serum samples. The electrochemiluminescence binding method was employed to detect Vitamin-D levels in the serum samples.

**Statistical Analysis:** Statistical analysis of the data was performed using SPSS version 23 software. The comparison of means was executed through T-tests, while Chi-square "chi 2" tests were employed at a significance level of 0.05 (P value > 0.05).

**Inclusion criteria:** The criteria for patient inclusion have been categorized into groups, and individuals participating in this study have been organized according to the collected data. A questionnaire was employed to gather information about each patient in the sample, encompassing details about their medical history and the type of warts. Demographic information, including age, gender, location, and occupation, was among the data collected.

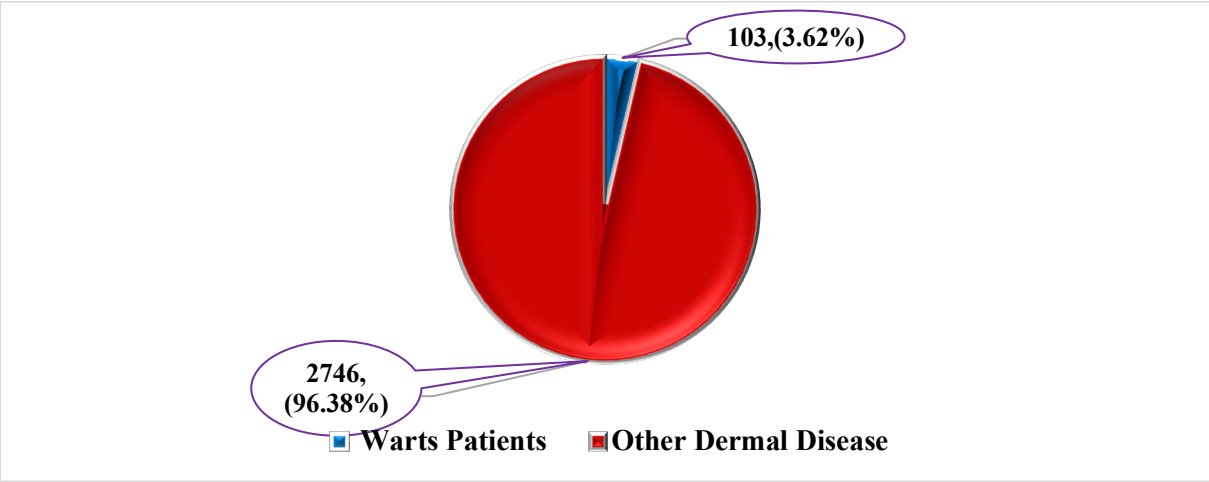
**Exclusion criteria** :The inclusion criteria for the study specify a particular age range for patients, excluding those who are 65 years of age or older and pregnant women. Furthermore, individuals with chronic illnesses or autoimmune conditions are not considered eligible.

**Ethical Consideration:** Enrollment in the study was contingent upon obtaining informed consent from all participants, each of whom presented with cutaneous warts caused by papillomaviruses. The study protocol received approval from the Research Ethics Committee of the Health Office in Thi-Qar Governorate under the ethical number (No. 713 on 22/10/2023). Additionally, the Research Committee, endorsed by a panel of specialized professors in the Department of Health in Thi-Qar Governorate, recommended and sanctioned the protocol (No. 2023/206 on 22/10/2023). All patient samples were collected under the direct supervision of a specialist physician in hospitals.

## Results:

### 1- Prevalence of Warts Disease Among Other Dermal Disease

In the current study, the recorded incidence of warts disease was 103 cases (3.62%) among various dermal diseases, which accounted for 2746 cases (96.38%) during the sample collection period. A statistically significant difference was observed between the two groups, as depicted in Figure 1, with a p-value < 0.05.

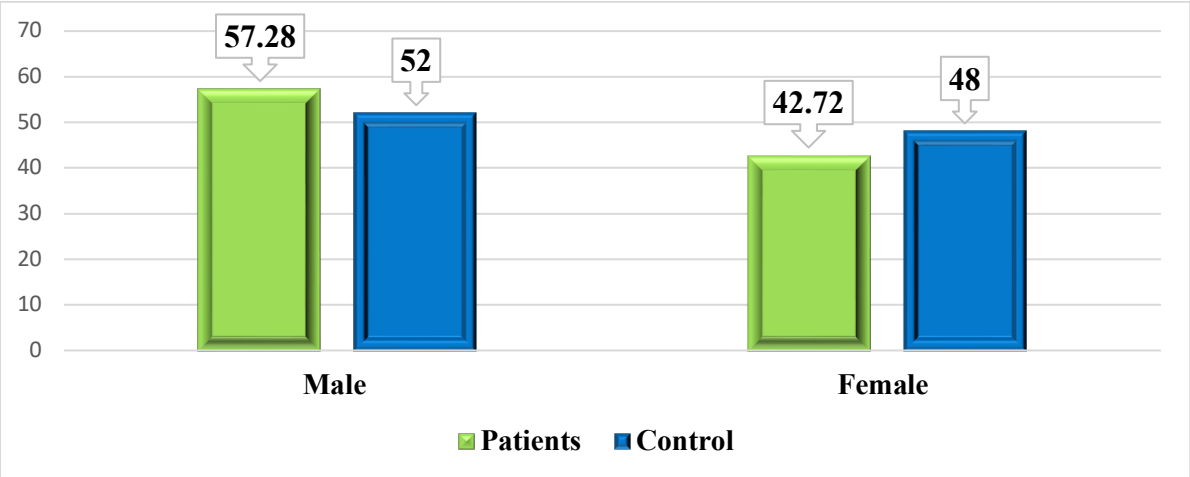



**CalX$^2$= 84.6 TabX$^2$= 3.84 DF=1 p. value < 0.001**

**Figure (1):** Prevalence of warts disease among other dermal disease

### 2- Distribution of Patients and Control Group According to Sex

In the present study, the male group constituted the higher percentage in both the patients (57.28%) and the control group (52.0%). Conversely, the female group comprised the lower percentage at 42.72% for patients and 48.0% for the control group. Notably, the study identified a non-significant difference at a p-value < 0.05 between the patients and the control group based on gender, as illustrated in Figure 2.




**CalX$^2$= 0.504 TabX$^2$= 3.84 DF=1 p. value 0.478**

**OR male/female 1.22 (0.70 – 2.13)**

**Figure (4-2):** Distribution of patients and control group according to sex

### 3-Evaluation of vitamin D in Patients with Warts and Control Group

The current findings indicated a non-significant decrease in the level of Vitamin D3 in patients with warts compared to the control group, with a p-value < 0.05, as presented in Table 1.

**Table (1):** Evaluation of vitamine-D in patients and control group

| Biochemical Parameters | Patients No.103 | Control No. 50 | p. value |
|---|---|---|---|
| | Mean ± S. D | | |
| Vit-$D_3$ | 25.3±9.91 | 28.1±9.59 | 0.112 |

### 4-Evaluation of vitamin D in Patients According to gender

In the current study, the recorded levels of both Vit-D3 did not exhibit a significant difference based on the gender of patients with warts, with a p-value < 0.05, as illustrated in Table 2.

**Table( 2):** Evaluation Of vitamin-D according to sex

| Biochemical Parameters | Male No. 59 | Female No. 44 | p. value |
|---|---|---|---|
| | Mean ± S. D | | |
| Vit-$D_3$ | 23.9±9.48 | 27.3±10.2 | 0.077 |

### 5-Evaluation of vitamin D in Patients According to Age Groups

The current study documented that the levels of Vitamin D3 did not show a significant difference based on age groups, with a p-value < 0.05, as depicted in Table 3.

**Table (3):** Evaluation of vitamin-D according to age groups

| Age groups | Cases No. | $VitD_3$ |
|---|---|---|
| | | Mean ± S. D |
| 10 – 20 | 31 | 26.3±10.8 |
| 21 – 30 | 28 | 26.3±9.90 |
| 31 – 40 | 18 | 23.9±9.17 |
| 41 – 50 | 15 | 23.4±9.67 |
| > 50 | 11 | 25.2±9.89 |
| ANOVA P. Valu | | 0.832 |

### 6-Evaluation of vitamin D in Patients According to Counts of Warts Lesion

The present findings indicate a significant increase in Vitamin D3 levels among patients with three wart lesions and a significant decrease in patients with multiple wart lesions, both at a p-value < 0.05, as demonstrated in Table 4.

**Table (4):** Evaluation of vitamin-D according to counts of warts

| Groups | Cases No. | $VitD_3$ |
|---|---|---|
| | | Mean ± S.D |
| One lesion | 85 | $25.5\pm10.1^{ab}$ |
| Two lesions | 10 | $26.6\pm10.0^{ab}$ |
| Three lesions | 2 | $31.9\pm4.38^{a}$ |
| Multi lesions | 6 | $18.5\pm4.49^{b}$ |
| Control | 50 | $28.1\pm9.59^{a}$ |
| P. Value<br>LSD P. Value | | 0.167<br>$0.018^{3,4}$ , $0.026^{4,5}$ |

*Similar small letters in obove table and othe below tables indicate a non-significant differences between means, while different small letters indicate a significant differences between means.

### 7-Evaluation of vitamin D in Patients According to Size of Warts

The current findings reveal a significant increase in Vitamin D3 levels within the control group and a significant decrease in patients with wart sizes ranging from 6 to 8 mm. Additionally, there was a significant increase in ferritin levels among patients with wart sizes greater than 9 mm, whereas a significant decrease was observed in patients with wart sizes ranging from 3 to 5 mm, all at a p-value < 0.05, as depicted in Table 5.

**Table (5):** Evaluation of vitamin-D according to size of warts

| Groups | Cases No. | $VitD_3$ |
|---|---|---|
| | | Mean ± S. D |
| mm 5 – 3 | 82 | $26.7\pm10.1^{a}$ |
| mm 8 – 6 | 14 | $19.0\pm5.77^{b}$ |
| mm 9 ≤ | 7 | $8.67^{ab}\pm22.0$ |
| Control | 50 | $9.59^{a}\pm28.1$ |
| P. Value<br>LSD P. Value | | 0.013<br>$0.002^{2,5}$ , $0.006^{1,2}$ |

## Discussion:

The current study, conducted at Al-Nassyria Teaching Hospital, recorded a prevalence of warts disease at 3.62% (103 cases) among various dermal diseases, which accounted for 96.38% (2746 cases) during the sample collection period. In the patient group, comprising 103 individuals of both sexes, males represented 57.28%, and females were 42.72%. The study found a non-significant difference at a p-value < 0.05 between patients and the control group concerning gender, aligning with Kasim et al. (2013), who reported no significant sex difference in their study. Conversely, a US study by Johnson & Roberts (1978) observed a significantly higher incidence in males than females, possibly attributed to increased physical activity in men, putting them at higher risk of skin damage, providing an entry point for HPV.

The current results revealed a non-significant decrease in Vitamin D3 levels in patients with warts compared to the control group at a p-value < 0.05, consistent with studies such as Tamer et al. (2020) and a Turkish study by Mertoğlu et al. (2017), which reported no significant difference in serum vitamin D levels between patients with warts and healthy individuals. The study acknowledges the severe vitamin D deficiency in both groups, possibly masking a more apparent relationship. Several international studies, including Kanwal et al. (2023) and Shalaby et al. (2022), have explored the association between vitamin D levels and viral warts, indicating varied outcomes.

The study recorded no significant difference in Vitamin D3 levels based on the gender of patients with warts at a p-value < 0.05. This aligns with Goodarzi et al. (2020), who found no significant association between serum vitamin D levels in males and females with warts. However, an Egyptian study reported lower vitamin D levels in female wart sufferers due to reduced sunlight exposure (Green et al., 2015).

Regarding age groups, the study noted no significant difference in Vitamin D3 levels at a p-value < 0.05. This finding is consistent with Goodarzi et al. (2020), who reported no significant relationship between age groups of patients with warts and serum vitamin D levels, suggesting warts may occur at any age.

The severity scale in the current study, based on wart count and size, demonstrated an increase in severity with larger or a greater number of warts. This underscores the significance of vitamin D in wart development, supported by successful treatments with topical and intralesional vitamin D injections reported in various studies (Aktaş et al., 2016; Jakhar et al., 2019; Kavya et al., 2017; Moscarelli et al., 2011; Raghukumar et al., 2017). However, ERTUĞRUL & AKTAŞ (2022) found no significant difference between serum vitamin D levels and wart severity in their study.

## Conclusions

1- The prevalence of cutaneous warts was identified at 3.62% in relation to the overall number of skin infections.
2- The occurrence of cutaneous warts in individuals with insufficient vitamin D was unaffected by gender or age, as evidenced by the absence of a significant difference.
3- An association between the severity of cutaneous warts, determined by size and number, and vitamin D levels was observed, indicating a correlation.

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