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**ORIGINAL RESEARCH**

# Comparative Study of Safety and Efficacy of Intralesional BCG and Intralesional Vitamin D3 in Cutaneous Wart

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## ABSTRACT

**Background:** Cutaneous warts are a common dermatological condition caused by the human papillomavirus (HPV). They are often challenging to treat due to their persistence and tendency to recur. Multiple treatment options exist, but none are universally effective, and many have limitations, such as pain, side effects, or high recurrence rates. Immunotherapy has emerged as a promising approach, utilizing agents like Bacillus Calmette-Guérin (BCG) vaccine and vitamin D3 to modulate the immune response against warts. The intralesional route is particularly attractive, as it can stimulate a localized immune response, potentially improving treatment efficacy and reducing systemic side effects. This study aims to compare the efficacy and safety of intralesional BCG vaccine versus intralesional vitamin D3 in the treatment of cutaneous warts, with a focus on evaluating clinical response, adverse effects, and recurrence rates. **Objective:** To compare the efficacy and safety of intralesional Bacillus Calmette-Guérin (BCG) vaccine versus intralesional vitamin D3 in the treatment of cutaneous warts. **Methods:** A randomized comparative prospective study was conducted involving 112 patients with cutaneous warts. Patients were divided into two groups: Group A received intralesional BCG vaccine (0.1 ml) and Group B received intralesional vitamin D3 (0.2 ml, 15 mg/ml). Treatments were administered at 2-week intervals for a total of 4 sessions. Efficacy was assessed based on reduction in wart size, complete clearance, and grading of response. **Results:** At the final follow-up (8th week), complete response was observed in 37.5% of patients in the BCG group and 42.86% in the vitamin D3 group. Palmoplantar warts showed the best response to both treatments. Vitamin D3 demonstrated superior efficacy in clearing all types of warts compared to BCG vaccine. The vitamin D3 group experienced fewer side effects, with pain at the injection site being the most common (71.43%). The BCG group reported more diverse side effects, including erythema (67.86%), swelling (60.71%), and ulceration (53.57%). **Conclusion:** Intralesional vitamin D3 showed superior efficacy and a better safety profile compared to intralesional BCG vaccine in the treatment of cutaneous warts. Vitamin D3 demonstrated particular effectiveness in clearing palmoplantar warts and resulted in higher patient satisfaction due to its lasting clinical effects and reduced recurrence rate.

**Keywords:** Cutaneous warts, Bacillus Calmette-Guérin (BCG) vaccine, Vitamin D3, Intralesional immunotherapy, Palmoplantar warts, Efficacy, Safety, Randomized comparative study.

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## INTRODUCTION

Viral warts are a prevalent dermatological disease. They are benign tumours resulting from the infection of keratinocytes by the Human Papillomavirus, appearing as well-defined hyperkeratotic protrusions. Human Papillomavirus are diminutive, epitheliotropic, non-enveloped viruses characterised by icosahedral symmetry and possessing circular double-stranded DNA (ds-DNA). HPV can infect and induce illness at any location within stratified squamous epithelium, whether keratinising (skin) or non-keratinizing (mucosa). Over 100 HPV subtypes have been sequenced,[1] resulting in diverse manifestations such as common warts, palmoplantar



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warts, filiform warts, plane warts, genital warts, and the rare genetic condition epidermolysis bullosa verruciformis. Despite appearing innocuous, they significantly affect the patient's quality of life by inducing discomfort, shame, and considerable irritation owing to their persistence and/or recurrence.Moderate to severe discomfort is observed in 51.7% of patients, while social or leisure activities are impacted to a moderate to severe extent in 38.8%.[2]

Despite a spontaneous resolution rate of 65-78% for warts within two years, the potential for aesthetic deformity, propensity for dissemination, and related decline in quality of life necessitate prompt intervention. [3]They are infamous for their infectious, recurring, and obstinate characteristics and can disseminate by direct touch or autoinoculation. The compromise of epithelial barrier function due to trauma (even minor abrasion), maceration, or both, predisposes individuals to HPV inoculation [4]. Individuals with compromised cell-mediated immunity are more susceptible.

Despite several therapeutic techniques, the treatment of warts remains a persistent difficulty, and there is no universal opinion on the ideal approach. The absence of optimal treatment has prompted extensive study and studies in this subject recently.Warts are predominantly addressed with destructive therapies, including topical keratolytics, electrofulguration, radiofrequency ablation, liquid nitrogen cryotherapy, and laser vaporisation utilising either pulsed dye laser or CO2 laser.[5-8] All these treatment approaches can be uncomfortable and may result in scarring and repeated recurrences. Moreover, destructive methods are ineffective for the treatment of numerous and resistant warts, as they only eliminate the lesions that are directly treated, leaving distant lesions unaffected[9]. Recurrence rates of warts of 30% have been documented using cryotherapy, perhaps attributable to an insufficient immune response. Multiple factors have been identified, including insufficient formation of memory T cells to combat human papillomavirus (HPV) infection, inadequate clonal growth of lymphocytes in response to stimulation, impaired trafficking of T lymphocytes to infection sites, and a diminished effector response mechanism.[10] [2]Consequently, immunotherapy is being explored for the treatment of warts to achieve improved outcomes. The precise mechanism of action of intralesional immunotherapy remains ambiguous. The proposed mechanism involves the activation of a robust non-specific inflammatory response targeting HPV-infected cells. The injection of antigens may correlate with the growth of peripheral blood mononuclear cells that enhance Th1 cytokine responses, including IL-2, IFN-gamma, and TNF-alpha. These then stimulate cytotoxic T-cells and natural killer cells to eliminate HPV-infected cells. This induced immune response could subsequently eradicate all lesions on the body rather than just those that are locally treated. [10]

The immunotherapies under investigation include bivalent and quadrivalent HPV vaccines, topical contact sensitisers such as DNCP, DPCP, and SADBE, immune modifiers like imiquimod, and antigens like BCG, PPD, candida, trichophyton, mumps, MMR, mycobacterium w vaccine, vitamin D3, and interferons. The current indications for immunotherapy encompass recurring warts, resistant warts, numerous warts, and challenging treatment regions, namely periungual and palmoplantar sites.[11]

The operational mechanism of both the BCG vaccine and vitamin D3 is based on the notion of immunotherapy. The precise mechanism of intralesional vitamin D3 in wart treatment is not fully elucidated; nonetheless, it regulates cell proliferation, differentiation, and has immunoregulatory properties.[12] Intralesional immunotherapy harnesses the immune system's capacity to elicit a delayed-type hypersensitivity response to certain viral, bacterial, fungal antigens, and HPV. The BCG vaccine, due to its low cost, could serve as an effective treatment option for warts in impoverished and developing nations. [13]In several studies, the notable response to BCG may be attributed to the utilisation of living antigens (live vaccine) and their enhanced antigenic potency (vaccines exhibit greater antigenicity than skin test antigens).[14]

## MATERIAL AND METHODS

A randomized comparative prospective study was conducted in the Department of Dermatology, Venereology, and Leprology at Nalanda Medical College and Hospital, Patna.The study involve a total of 112 patients and over a period of 18 months.

### Patient Selection

The study population will include patients attending the indoor and outpatient departments of dermatology at Nalanda Medical College and Hospital with a diagnosis of cutaneous warts. Patients will be selected based on the inclusion and exclusion criteria.

### Ethical Approval and Consent

Ethical approval for the study will be obtained from the Ethical Committee of Nalanda Medical College and Hospital. Written informed consent will be obtained from all patients or their parents/guardians (in the case of minors) after the nature of the study is explained in their local language.

The study will include both male and female patients who consent to participate, have not received prior treatment for warts in the past 6 months, and have 15 or fewer warts. Exclusion criteria will include patients unwilling to participate, those under 12 or over 70 years old, those with fever or signs of systemic/local inflammation or infection, pregnant or lactating women, individuals with immunosuppression (HIV,



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asthma, meningitis, convulsions, or on immunosuppressive drugs), those with contraindications to BCG vaccine or vitamin D3, and patients with more than 15 warts.

**Study Procedure**

Patients will be randomly allocated into two groups:

**Group A** will receive intralesional injections of 0.1 ml BCG vaccine, administered at 2-week intervals for a total of 4 sessions.

**Group B** will receive intralesional injections of vitamin D3 (0.2 ml, 15 mg/ml), administered at 2-week intervals for a total of 4 sessions.In cases of multiple warts, injections will be administered to fewer than 5 warts, prioritizing larger lesions. Clinical photographs will be taken at each visit for both groups.

Data collection will involve taking personal and medical histories, including present and past history of warts, systemic diseases (HIV, diabetes, renal/hepatic conditions), and drug use. Clinical examinations will confirm the diagnosis of cutaneous warts, noting wart type, duration, number, and location. Investigations will screen for hepatitis B, C, and HIV before treatment. Patients will be randomly allocated into Group A (receiving 0.1 ml intralesional BCG vaccine) or Group B (receiving 0.2 ml intralesional vitamin D3), with treatments repeated every 2 weeks for 4 sessions, followed by an 8-week assessment for efficacy and recurrence. Outcome measures will include reduction in the number of warts, complete clearance, and grading of response.

**The response was assessed as**

a. Complete response: responders who show 100% outcome
b. Marked response: responders who show 75 to 99% outcome
c. Moderate response: partial responders 50 to 75% outcome
d. Inadequate response: those who show less than 50% outcome.

Adverse events will be recorded, and patients with earlier clearance will be checked for recurrence during follow-up.

**RESULTS**

The study included 112 patients, with 56 in both the BCG and Vitamin D3 groups. The types of warts observed were palmoplantar warts (37.5% in the BCG group, 35.71% in the Vitamin D3 group), verruca vulgaris (35.71% in the BCG group, 32.14% in the Vitamin D3 group), and periungual warts (26.79% in the BCG group, 32.14% in the Vitamin D3 group). The mean age of patients was 31.0892 years in the BCG group and 31.2678 years in the Vitamin D3 group, with a significant p-value of less than 0.001. Regarding sex distribution, 57.14% of patients in the BCG group and 55.36% in the Vitamin D3 group were male, while females accounted for 42.86% and 44.64%, respectively. Occupation-wise, students made up 23.2% of the BCG group and 32.14% of the Vitamin D3 group, while homemakers were 19.64% in both groups. Agricultural workers constituted 12.5% of the BCG group and 10.71% of the Vitamin D3 group. Non-agricultural indoor workers were more prevalent in the BCG group (30.35%) compared to 17.85% in the Vitamin D3 group, while non-agricultural outdoor workers made up 14.29% and 19.64%, respectively. In terms of literacy, 33.92% of the BCG group were illiterate compared to 28.57% in the Vitamin D3 group, while the majority were literate (66.07% in the BCG group and 71.42% in the Vitamin D3 group). Socioeconomic status showed that 67.8% of BCG group patients and 71.4% of Vitamin D3 group patients were above the poverty line, while 32.14% and 28.57% were below it, respectively. Lastly, 44.64% of the BCG group and 41.07% of the Vitamin D3 group were from rural areas, while 55.35% and 58.93% were from urban areas, respectively.

**Table- 1 Demographic and Clincal Profile of Study Participants**

| Category | BCG Group | Vit D3 Group | Total |
|---|---|---|---|
| Type of Warts | | | |
| Palmoplantar wart | 21 (37.5%) | 20 (35.71%) | 41 |
| Verruca vulgaris | 20 (35.71%) | 18 (32.14%) | 38 |
| Periungual wart | 15 (26.79%) | 18 (32.14%) | 33 |
| Total (Type of Warts) | 56 | 56 | 112 |
| Mean Age ± SD (years) | | | |
| Number | 56 | 56 | - |
| Mean | 31.0892 | 31.2678 | - |
| SD | 10.0432 | 11.1795 | - |
| Minimum | 18 | 16 | - |
| Maximum | 56 | 57 | - |
| Median | 28 | 29 | - |
| p-value | < 0.001 | | - |
| Sex Distribution | | | |



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| | | | |
|---|---|---|---|
| Male | 32 (57.14%) | 31 (55.36%) | 63 |
| Female | 24 (42.86%) | 25 (44.64%) | 49 |
| Occupation | | | |
| Student | 13 (23.2%) | 18 (32.14%) | 31 |
| Homemaker | 11 (19.64%) | 11 (19.64%) | 22 |
| Agricultural worker | 7 (12.5%) | 6 (10.71%) | 13 |
| Non-agricultural indoor worker | 17 (30.35%) | 10 (17.85%) | 27 |
| Non-agricultural outdoor worker | 8 (14.29%) | 11 (19.64%) | 19 |
| Literacy Status | | | |
| Illiterate | 19 (33.92%) | 16 (28.57%) | - |
| Literate | 37 (66.07%) | 40 (71.42%) | - |
| Socioeconomic Status | | | |
| Above Poverty Line (APL) | 38 (67.8%) | 40 (71.4%) | 78 |
| Below Poverty Line (BPL) | 18 (32.14%) | 16 (28.57%) | 34 |
| Residence | | | |
| Rural | 25 (44.64%) | 23 (41.07%) | 48 |
| Urban | 31 (55.35%) | 33 (58.93%) | 64 |

In this study, the duration of warts averaged 6.5 months in the BCG group and 6.36 months in the Vitamin D3 group, with a standard deviation of 3.968 and 3.313, respectively. The minimum duration was 1 month, with a maximum of 18 months in the BCG group and 15 months in the Vitamin D3 group, and a median of 6 months for both groups. The initial site of warts varied, with fingers affected in 14.28% of the BCG group and 17.85% of the Vitamin D3 group, hands in 16.07% and 14.28%, palms in 16.07% for both groups, legs in 19.64% and 17.85%, toes in 12.5% and 14.28%, and soles in 21.42% of the BCG group and 19.64% of the Vitamin D3 group. Koebnerization was present in 32.14% of the BCG group and 28.57% of the Vitamin D3 group, with the majority in both groups not experiencing it (67.85% and 71.42%, respectively). Regarding family history, 25% of patients in the BCG group and 32.14% in the Vitamin D3 group had a positive family history of warts, while 75% and 67.85% did not.

**Table- 2 Comparison of Wart Characteristics and Treatment Outcomes Between BCG and Vitamin D3 Groups**

| Category | BCG Group | Vit D3 Group | Total |
|---|---|---|---|
| Duration of Warts (in months) | | | |
| Number | 56 | 56 | - |
| Mean | 6.5 | 6.36 | - |
| SD | 3.968 | 3.313 | - |
| Minimum | 1 | 1 | - |
| Maximum | 18 | 15 | - |
| Median | 6 | 6 | - |
| p-value | <0.001 | <0.001 | - |
| Initial Site of Wart | | | |
| Finger | 8 (14.28%) | 10 (17.85%) | - |
| Hand | 9 (16.07%) | 8 (14.28%) | - |
| Palm | 9 (16.07%) | 9 (16.07%) | - |
| Leg | 11 (19.64%) | 10 (17.85%) | - |
| Toes | 7 (12.5%) | 8 (14.28%) | - |
| Sole | 12 (21.42%) | 11 (19.64%) | - |
| Koebnerization | | | |
| Present | 18 (32.14%) | 16 (28.57%) | 34 |
| Absent | 38 (67.85%) | 40 (71.42%) | 78 |
| Family History | | | |
| Present | 14 (25%) | 18 (32.14%) | 32 |
| Absent | **42 (75%)** | **38 (67.85%)** | **80** |

At the 1st follow-up (2nd week), in the BCG group, 46.43% of patients showed no response, 41.07% had an inadequate response, 10.71% had a moderate response, 1.79% showed a marked response, and none achieved a complete response. In the Vitamin D3 group, 42.86% had no response, 39.29% showed an inadequate response, 14.29% had a moderate response, 3.57% showed a marked response, and none



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had a complete response. At the 2nd follow-up (4th week), the BCG group had 26.79% showing no response, 28.57% with an inadequate response, 19.64% with a moderate response, 17.86% with a marked response, and 7.14% achieving complete response. In comparison, the Vitamin D3 group had 21.43% showing no response, 17.86% with an inadequate response, 23.21% with a moderate response, 25% with a marked response, and 12.5% achieving a complete response. At the 3rd follow-up (6th week), the BCG group showed 12.5% with no response, 14.29% with inadequate response, 21.43% with moderate response, 25% with marked response, and 26.79% with complete response, while the Vitamin D3 group had 10.71% with no response, 10.71% with inadequate response, 16.07% with moderate response, 30.36% with marked response, and 32.14% with complete response. By the 4th follow-up (8th week), the BCG group showed 7.14% with no response, 10.71% with inadequate response, 14.29% with moderate response, 30.35% with marked response, and 37.5% with complete response, while the Vitamin D3 group had 5.36% with no response, 5.36% with inadequate response, 12.50% with moderate response, 33.93% with marked response, and 42.86% with complete response. In patients with common warts at the 4th follow-up, 10% in the BCG group and 11.1% in the Vitamin D3 group showed no response, 15% in the BCG group and 5.6% in the Vitamin D3 group had an inadequate response, 15% in the BCG group and 11.1% in the Vitamin D3 group had a moderate response, 25% in the BCG group and 33.3% in the Vitamin D3 group had a marked response, and 35% in the BCG group and 38.9% in the Vitamin D3 group achieved a complete response.

**Table-3 Treatment Response Over Time in BCG and Vitamin D3 Groups for Different Types of Warts**

| Category | BCG Group (CW, PPW, PW) | Total (%) BCG | Vit D3 Group (CW, PPW, PW) | Total (%) Vit D3 | p-value |
|---|---|---|---|---|---|
| 1st Follow-Up (2nd Week) | | | | | **< 0.0001** |
| No Response | 10, 9, 7 | 26 (46.43%) | 9, 7, 8 | 24 (42.86%) | |
| Inadequate Response | 8, 8, 7 | 23 (41.07%) | 7, 7, 8 | 22 (39.29%) | |
| Moderate Response | 2, 3, 1 | 6 (10.71%) | 2, 4, 2 | 8 (14.29%) | |
| Marked Response | 0, 1, 0 | 1 (1.79%) | 0, 2, 0 | 2 (3.57%) | |
| Complete Response | 0, 0, 0 | 0 (0%) | 0, 0, 0 | 0 (0%) | |
| 2nd Follow-Up (4th Week) | | | | | < 0.0001 |
| No Response | 7, 4, 4 | 15 (26.79%) | 4, 2, 3 | 9 (21.43%) | |
| Inadequate Response | 5, 6, 5 | 16 (28.57%) | 3, 4, 3 | 10 (17.86%) | |
| Moderate Response | 4, 5, 2 | 11 (19.64%) | 5, 6, 5 | 16 (23.21%) | |
| Marked Response | 3, 4, 3 | 10 (17.86%) | 4, 5, 5 | 14 (25%) | |
| Complete Response | 1, 2, 1 | 4 (7.14%) | 2, 3, 2 | 7 (12.5%) | |
| 3rd Follow-Up (6th Week) | | | | | |
| No Response | 3, 2, 2 | 7 (12.5%) | 3, 1, 2 | 6 (10.71%) | |
| Inadequate Response | 2, 3, 3 | 8 (14.29%) | 3, 1, 2 | 6 (10.71%) | |
| Moderate Response | 5, 4, 3 | 12 (21.43%) | 3, 4, 2 | 9 (16.07%) | |
| Marked Response | 5, 6, 3 | 14 (25%) | 4, 7, 6 | 17 (30.36%) | |
| Complete Response | 5, 6, 4 | 15 (26.79%) | 5, 7, 6 | 18 (32.14%) | |
| 4th Follow-Up (8th Week) | | | | | < 0.001 |
| No Response | 2, 1, 1 | 4 (7.14%) | 2, 0, 1 | 3 (5.36%) | |
| Inadequate Response | 3, 2, 1 | 6 (10.71%) | 1, 1, 1 | 3 (5.36%) | |
| Moderate Response | 3, 3, 2 | 8 (14.29%) | 2, 3, 2 | 7 (12.50%) | |
| Marked Response | 5, 7, 5 | 17 (30.35%) | 6, 7, 6 | 19 (33.93%) | |
| Complete Response | 7, 8, 6 | 21 (37.5%) | 7, 9, 8 | 24 (42.86%) | |
| Result for Common Wart (4th Follow-Up) | | | | | < 0.0001 |
| No Response | 2 (10%) | 2 (11.1%) | | | |
| Inadequate Response | 3 (15%) | 1 (5.6%) | | | |
| Moderate Response | 3 (15%) | 2 (11.1%) | | | |
| Marked Response | 5 (25%) | 6 (33.3%) | | | |
| Complete Response | 7 (35%) | 7 (38.9%) | | | |
| Total (Common Wart) | 20 | | 18 | | |



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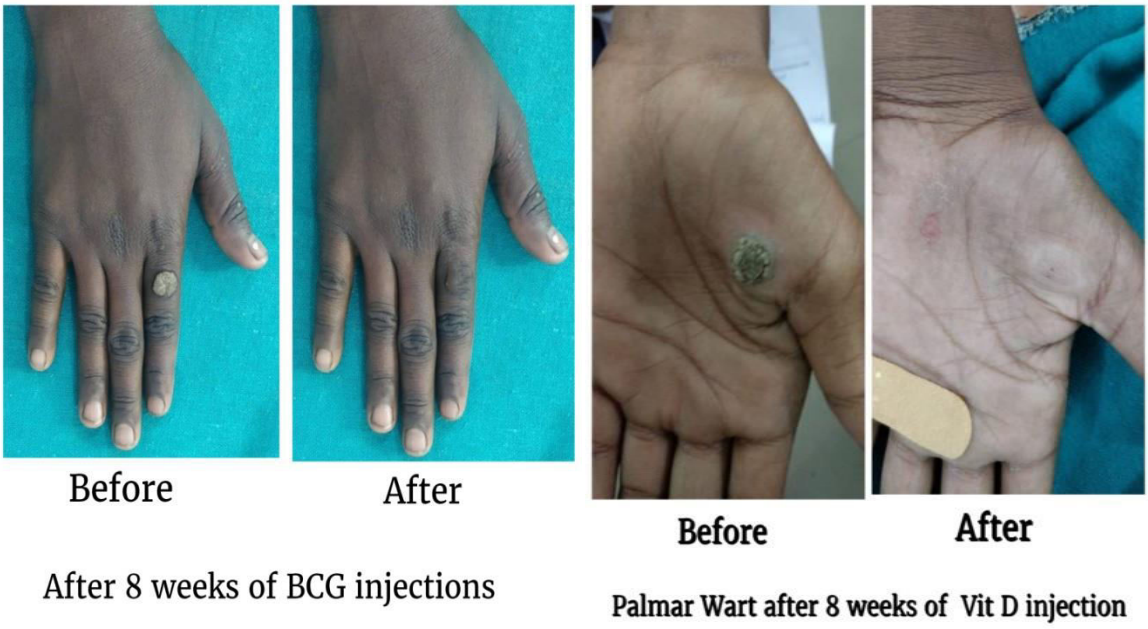


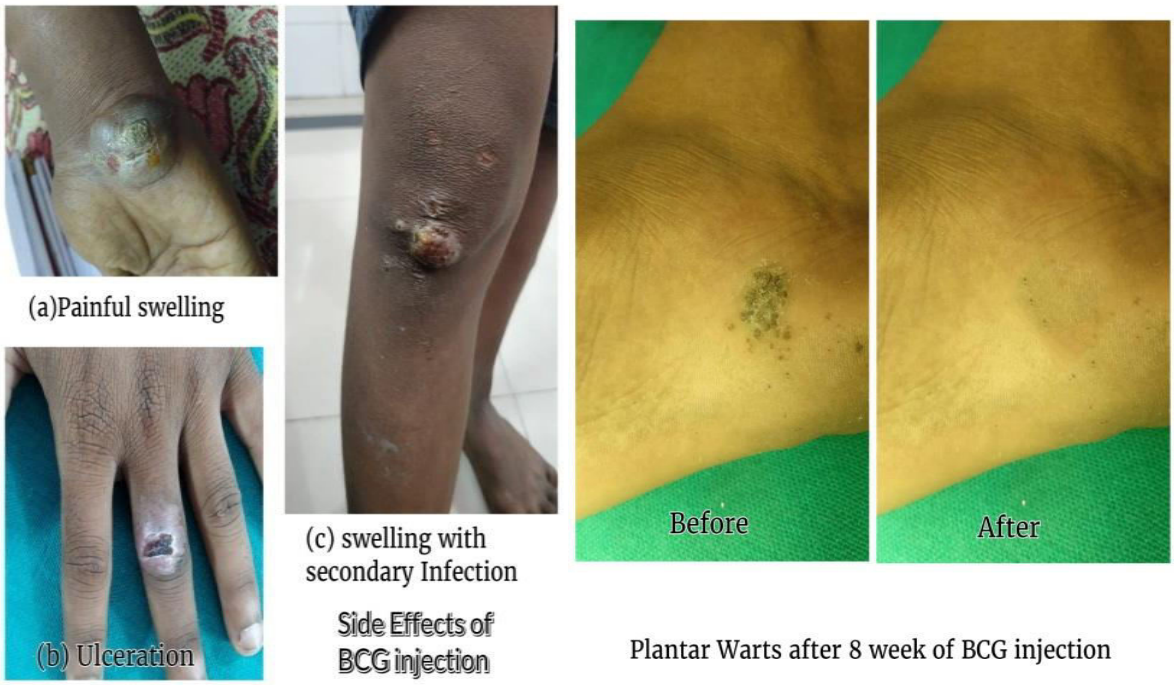


At the 4th-week follow-up for palmoplantar warts (PPW), in the BCG group, 4.76% of patients showed no response, 9.52% had an inadequate response, 14.28% showed a moderate response, 33.33% had a marked response, and 38.09% achieved a complete response. In comparison, the Vitamin D3 group had 0% showing no response, 5% with an inadequate response, 15% with a moderate response, 35% with a marked response, and 45% achieving a complete response. For periungual warts (PW) at the 4th week, the BCG group had 6.67% showing no response, 6.67% with an inadequate response, 13.33% with a moderate response, 33.33% with a marked response, and 40% achieving a complete response. In the Vitamin D3 group, 5.56% showed no response, 5.56% had an inadequate response, 11.11% showed a moderate response, 33.33% had a marked response, and 44.44% achieved a complete response. Regarding treatment-emergent side effects, pain during injection occurred in 44.64% of the BCG group and 71.43% of the Vitamin D3 group. Erythema was noted in 67.86% of the BCG group and 14.29% of the Vitamin D3 group, while ulceration occurred in 53.57% of the BCG group and 3.57% of the Vitamin D3 group. Swelling was observed in 60.71% of the BCG group and 28.57% of the Vitamin D3 group. Hyperpigmentation was seen in 32.14% of the BCG group and 10.71% of the Vitamin D3 group, and flu-like symptoms were reported in 17.86% of the BCG group but were absent in the Vitamin D3 group.



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**Table- 4 Response to Treatment for Palmoplantar and Periungual Warts, and Treatment Emergent Side Effects in BCG and Vitamin D3 Groups**

| Category | BCG Group (PPW, PW) | Total (%) BCG | Vit D3 Group (PPW, PW) | Total (%) Vit D3 | p-value |
|---|---|---|---|---|---|
| Result for Palmoplantar Wart (4th Week) | | | | | **< 0.001** |
| No Response | **1 (4.76%)** | | **0 (0%)** | | |
| Inadequate Response | **2 (9.52%)** | | **1 (5%)** | | |
| Moderate Response | **3 (14.28%)** | | **3 (15%)** | | |
| Marked Response | **7 (33.33%)** | | **7 (35%)** | | |
| Complete Response | **8 (38.09%)** | **21** | **9 (45%)** | **20** | |
| Result for Periungual Wart (4th Week) | | | | | **< 0.0001** |
| No Response | **1 (6.67%)** | | **1 (5.56%)** | | |
| Inadequate Response | **1 (6.67%)** | | **1 (5.56%)** | | |
| Moderate Response | **2 (13.33%)** | | **2 (11.11%)** | | |
| Marked Response | **5 (33.33%)** | | **6 (33.33%)** | | |
| Complete Response | **6 (40%)** | **15** | **8 (44.44%)** | **18** | |
| Treatment Emergent Side Effects | | | | | |
| Pain during injection | **25 (44.64%)** | | **40 (71.43%)** | | |
| Erythema | **38 (67.86%)** | | **8 (14.29%)** | | |
| Ulceration | **30 (53.57%)** | | **2 (3.57%)** | | |
| Swelling | **34 (60.71%)** | | **16 (28.57%)** | | |
| Hyperpigmentation | **18 (32.14%)** | | **6 (10.71%)** | | |
| Flu-like symptoms | **10 (17.86%)** | **25** | **0 (0%)** | **40** | |

## DISCUSSION

From 30th October 2018 to 30th April 2020, a total of 84,948 patients sought outpatient consultations in the Department of Dermatology, Venereology, and Leprosy at NMCH, Patna. Among these, 989 patients were diagnosed with cutaneous warts, constituting 1.16% of the total outpatient attendees.

A total of 130 patients were chosen for the study according to the established exclusion and inclusion criteria. Eleven patients did not complete the research and did not attend the follow-up.

In this study, among 56 patients in the BCG group, 21, 20, and 15 patients presented with palmoplantar warts, verruca vulgaris, and periungual warts, respectively. In the Vitamin D3 group, 20, 18, and 18 patients presented with palmoplantar warts, verruca vulgaris, and periungual warts, respectively.

The mean age of participants in the BCG group was 31.08 ± 10.04 years, with an age range of 18 to 56 years, while the mean age in the vitamin D3 group was 31.26 ± 11.17 years, with an age range of 16 to 57 years. The study primarily comprised people in their late twenties and early thirties. Prior research in several regions worldwide has also identified a higher prevalence of viral warts in the young adult demographic.[112,113] among the 56 patients in the BCG group, 32 were male and 24 were female, resulting in a male-to-female ratio of 1.3:1. In the Vitamin D3 group, there were 31 males and 25 females, resulting in a ratio of 1.24:1. In the research conducted by Chandrashekhar et al., the male to female ratio was 1.8:1. [17]

The occupational distribution in the BCG group indicated that there were 13 students, 17 non-agricultural indoor workers, and 11 homemakers. The remainder were either agricultural workers or non-agricultural outdoor workers. In the Vitamin D3 group, there were 18 students, 10 non-agricultural indoor workers, and 11 homemakers. The remainder were either agricultural workers or non-agricultural outdoor workers. the BCG group, 37 patients were literate and 19 were illiterate, while in the VIT D3 group, 40 patients were literate and 16 were illiterate.

Furthermore, as illustrated in Figure 7, 67.8% of the BCG group were above the poverty level (APL), whereas 32.14% were below the poverty line (BPL). In the Vitamin D3 group, 71.4% were above the poverty line (APL) and 28.57% were below the poverty line (BPL).

In the BCG group, 31 patients resided in urban areas and 25 in rural areas, while in the Vit D3 group, 33 patients were from urban areas and 23 from rural areas.

Among the 56 patients in the BCG group, the average duration of warts was 6.5 ± 3.968 months, with a range from 1 month to 18 months. The mean duration of the trial in the vitamin D3 group was 6.36 ± 3.313 months, with a range of 1 to 15 months. A study conducted by Saini et al. revealed that 74.4% of patients had a mean disease duration of less than one year [18]. In the study conducted by Chandrashekhar et al., the length at presentation was 1-2 months for 39.6% of participants, followed by less than 1 month for 30.15%, and 2-3 months for 20.6% [17].

Family history was observed in 14 out of 56 participants in the BCG group. In the VIT D3 cohort, 18 out of 56 individuals had a positive family history . This finding parallels the research conducted by Chandrashekhar et al. [17] and Sait et al. [18]. Koebnerization occurred in 18 cases and was absent



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in 38 patients within the BCG group. In the VIT D3 group, Koebnerization was observed in 16 patients and not observed in the BCG group, warts were distributed as follows: on the fingers in 8 subjects, on the hand in 9 subjects, on the palm in 9 patients, on the leg in 11 patients, on the toes in 7 patients, and on the sole in 12 patients. In the VIT D3 group, warts were observed on the fingers of 10 patients, on the hands of 8 patients, on the palms of 9 patients, on the legs of 10 patients, on the toes of 8 patients, and on the soles of 11 patients. The study's efficacy parameters included the evaluation of wart size reduction and total clearance, with grading conducted accordingly. In the initial follow-up of patients in the BCG group, no significant improvement was observed in 26 patients (46.43%), comprising 10 with common warts, 9 with palmoplantar warts, and 7 with periungual warts. Insufficient progress was observed in 23 patients (41.07%); 8 patients presented with common warts, 8 with palmoplantar warts, and 7 with periungual warts. Six patients (10.71%) had moderate improvement; two patients had common warts, three had palmoplantar warts, and one had a periungual wart. A notable response was observed in one patient (1.79%), specifically with a single case of palmoplantar wart. No patients exhibited complete clearance. In the Vitamin D3 group, no substantial improvement was observed in 24 patients (42.86%), comprising 9 patients with common warts, 7 with palmoplantar warts, and 8 with periungual warts. Insufficient progress was observed in 22 patients (39.29%); 7 patients presented with common warts, 7 with palmoplantar warts, and 8 with periungual warts. Moderate improvement was observed in 8 patients (14.29%); 2 patients had common warts, 4 had palmoplantar warts, and 2 had periungual warts. Two patients (3.75%) had considerable improvement in their palmoplantar warts, however none achieved complete resolution. In the second follow-up, among the patients in the BCG group, no improvement was observed in 15 patients (26.79%), comprising 7 with common warts, 4 with palmoplantar warts, and 4 with periungual warts. Insufficient progress was observed in 16 patients (28.57%), comprising 5 with common warts, 6 with palmoplantar warts, and 5 with periungual warts. Moderate improvement was observed in 11 patients (19.64%), comprising 4 with common warts, 5 with palmoplantar warts, and 2 with periungual warts. A notable response was observed in 10 patients (17.86%); 3 patients presented with common warts, 4 with palmoplantar warts, and 3 with periungual warts. Complete clearance was observed in 4 patients (7.14%): 1 patient had a common wart, 2 patients had palmoplantar warts, and 1 patient had a periungual wart. In the Vitamin D3 group, no improvement was observed in 9 patients (21.43%), comprising 4 patients with common warts, 2 with palmoplantar warts, and 3 with periungual warts. Insufficient progress was observed in 10 patients (17.86%); 3 patients presented with common warts, 4 with palmoplantar warts, and 3 with periungual warts. Sixteen patients (23.21%) had moderate improvement; five patients had common warts, six had palmoplantar warts, and five had periungual warts. A notable response was observed in 14 patients (25%), comprising 4 patients with common warts, 5 patients with palmoplantar warts, and 5 patients with periungual warts. Complete improvement was observed in 7 patients (12.5%), comprising 2 with common warts, 3 with palmoplantar warts, and 2 with periungual warts.

In the third follow-up, no improvement was observed in 7 patients (12.50%) within the BCG group, comprising 3 patients with common warts, 2 with palmoplantar warts, and 2 with periungual warts. Eight patients (14.29%) exhibited an inadequate response; two patients had common warts, three had palmoplantar warts, and three had periungual warts.Moderate improvement was observed in 12 patients (21.43%); 5 had common warts, 4 had palmoplantar warts, and 3 had periungual warts. A marked reaction was observed in 14 patients (25%); 5 had common warts, 6 had palmoplantar warts, and 3 had periungual warts. A complete response was observed in 15 patients (26.79%); 5 patients had common warts, 6 had palmoplantar warts, and 4 had periungual warts. In the Vitamin D3 group, no improvement was observed in 6 patients (10.71%), comprising 3 patients with common warts, 1 patient with palmoplantar warts, and 2 patients with periungual warts. Insufficient progress was observed in 6 patients (10.71%); 3 patients presented with common warts, 1 with palmoplantar wart, and 2 with periungual warts. Nine patients (16.07%) exhibited moderate improvement; three had common warts, four had palmoplantar warts, and two had periungual warts. A notable response was observed in 17 patients (30.36%); 4 had common warts, 7 had palmoplantar warts, and 6 presented with periungual warts. Complete removal was observed in 18 patients (32.14%); 5 patients had common warts, 7 had palmoplantar warts, and 6 had periungual warts.

In the fourth follow-up among the patients in the BCG group, no improvement was observed in 4 patients (7.14%); 2 patients had common warts, 1 had palmoplantar wart, and 1 patient had periungual wart. Six patients (8.93%) exhibited an inadequate response; three had common warts, two had palmoplantar warts, and one had a periungual wart. Eight patients (12.50%) had moderate improvement; three patients had common warts, three had palmoplantar warts, and two had periungual warts. A notable response was observed in 17 patients (32.14%); 5 patients had common warts, 7 presented with palmoplantar warts, and 5 had periungual warts. Complete elimination was observed in 21 patients (39.29%), comprising 7 with common warts, 8 with palmoplantar warts, and 6 with periungual warts. In the Vitamin D3 group, no improvement was observed in 3 patients (5.36%), comprising 2 patients with



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common warts and 1 patient with periungual wart. Insufficient improvement was observed in 3 cases (5.36%). One patient presented with a common wart, one with a palmoplantar wart, and one with a periungual wart. Moderate improvement was observed in 7 patients (12.50%); 2 patients had common warts, 3 had palmoplantar warts, and 2 had periungual warts.Nineteen patients (33.93%) shown considerable improvement; six patients had common warts, seven had palmoplantar warts, and six had periungual warts. Complete improvement was observed in 24 patients (42.86%), comprising 7 patients with common warts, 9 with palmoplantar warts, and 8 with periungual warts.Numerous open-label studies have been conducted utilising various immunotherapeutic drugs for wart therapy. Singh et al. and Meena et al. reported a complete response of 54.5% and 83% in patients receiving the Mw vaccination, respectively, combined with a response in remote warts of 86.3% and 70%, respectively. Horn et al. observed no significant variation in reaction across the individual antigens (candida, 59%; mumps, 51%; trichophyton, 62%; p=0.48).

In the analysis of outcomes observed in both groups concerning various types of warts after the eighth week, among the 20 patients with common warts in the BCG group, no response was noted in 10% of cases, inadequate response in 15%, moderate response in 15%, marked response in 25%, and complete response in 35% of cases. In the VIT D3 group, among 18 patients with common warts, 11.1% exhibited no reaction, 5.6% shown an inadequate response, 11.1% showed a moderate response, 33.3% had a notable response, and 38.9% achieved a complete response.

After the eighth week of treatment for palmoplanter warts, among 21 patients in the BCG Group, no response was observed in 4.76% of cases, inadequate response in 9.52%, moderate response in 14.28%, marked response in 33.33%, and full response in 38.09% of cases. In the VIT D3 group, among 20 cases with palmoplantar warts, 5% exhibited inadequate response, 15% shown moderate response, 35% showed notable response, and 45% achieved complete response.

In the context of periungual warts after the eighth week, among 15 patients in the BCG group, 6.67% exhibited no response, 6.67% demonstrated inadequate response, 13.33% showed moderate response, 33.33% experienced marked response, and 40% achieved complete response. In the VIT D3 group, among 18 patients, 5.56% exhibited no reaction, 5.56% demonstrated inadequate response, 11.11% showed moderate response, 33.33% experienced marked response, and 44.44% achieved complete response.

In the BCG group, 44.64% of patients reported pain at the injection site as a treatment-emergent adverse event. Other notable side events were injection site reactions such as erythema and oedema, found in 67.86% and 60.71% of patients, respectively. These adverse effects persisted for up to 24 hours in the majority of instances. Ulceration was observed in 53.57% of individuals. Nonetheless, 32.14% of patients experienced post-inflammatory hyperpigmentation that remained despite the resolution of warts. 17.86% of patients exhibited influenza-like symptoms. In the Vitamin D3 group, 71.43% of patients reported pain at the injection site, much higher than in the BCG group. Erythema was observed in 14.29% of patients, while oedema was noted in 28.57% of patients, both of which were comparatively lower than in the BCG group. Ulceration was observed in 3.57% of individuals. Post-inflammatory hyperpigmentation was observed in 10.71% of individuals. None of the patients exhibited influenza-like symptoms.In terms of efficacy, Vitamin D3 demonstrated superior performance relative to the BCG vaccine and shown considerable advantages in the treatment of cutaneous warts compared to the BCG vaccine. The patients with palmoplantar warts in both groups had a significant response; however, Vitamin D3 demonstrated superior clearance efficiency compared to the BCG vaccine for this type of wart. The patients with common warts exhibited minimal response to both modalities, with VIT D3 demonstrating a slightly superior clearing rate for common warts. In this trial, Vitamin D3 had a superior side-effect profile compared to the BCG vaccine. The primary side effect observed with Vitamin D3 was injection pain, whereas the BCG vaccine exhibited other side effects, including ulceration and oedema, leading to the withdrawal of numerous participants from the research. The limitations of the current trial include the recruitment of the research sample from a single site and the attrition of several patients due to the burdensome and multiple-session procedures.

## CONCLUSION

Intralesional Vitamin D3 demonstrates superior efficiency in the eradication of all varieties of cutaneous warts compared to intralesional BCG vaccine. Palmoplantar warts exhibited the most significant response to all treatment modalities; however, vitamin D3 demonstrated superior efficacy compared to the BCG vaccine in the eradication of palmoplantar warts. Vitamin D3 demonstrates superior efficacy in eliminating the other two forms of warts in comparison to the BCG vaccine. Intralesional Vitamin D3 exhibits a reduced adverse effect profile compared to intralesional BCG vaccination. Vitamin D3 is a safe therapeutic option for the treatment of cutaneous warts, offering the significant benefit of reduced recurrence due to its enduring clinical effects beyond the treatment regimen, in contrast to the BCG vaccine. There is a notable degree of patient satisfaction with Vitamin D3 in comparison to the BCG vaccine.



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