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ROLE OF INTRALESIONAL ACYCLOVIR IN PATIENT WITH PLANTAR WARTS

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Abstract

Introduction: *Warts are the predominant cutaneous manifestation of human papillomavirus (HPV), which infects both dermal and mucosal epithelial tissues. The management of warts is difficult. The viral etiology of warts indicates that acyclovir, an antiviral agent effective against DNA viruses, could serve as a viable therapeutic alternative.*

Objective: *To determine the response of intralesional acyclovir in patient presenting with plantar warts.*

Methodology: *This descriptive study was performed in the Department of Dermatology, Tertiary care hospital, Karachi from July 2024 to Jan 2025. Total 175 male and female patients of age between 18 to 65 years, exhibiting plantar warts, regardless of duration. Informed consent was taken from the patient after explaining risk and benefits of the study. Patients were administered intralesional acyclovir (70 mg/ml; Acyclovir), with 0.1 mL injected into the base of each wart every 02 weekly for a maximum of six sessions (at 0, 2, 4, 6, 8, and 12 weeks). The treatment response was evaluated at 12 weeks and classified as: Complete reaction (total eradication of warts or >75% improvement); Partial response (50-75% decreased quantity/size but not entire elimination); No response (<50% or no diminution of lesions). Statistical analysis was conducted utilizing SPSS version 24.*

Result: *In this study male and female ratio was 1:1; while females were 50.29% (n=88/175) of study population. Cumulative mean age of the study patients was 39.20 ± 11.47 years. 77 (44.0%) patients had complete response, 68 (38.86%) had partial response and 30 (17.14%) had no response. A Statistically significant difference was noticed only for age groups and residential status among all the study confounders.*

Conclusion: *The treatment proved beneficial in the majority of cases, with age and residential status served as strong predictors of response. These findings enhance the existing knowledge on plantar warts care and highlighted the necessity for more studies to refine treatment options.*

INTRODUCTION

Plantar warts are nonmalignant lesions induced by human papillomavirus (HPV) that result in discomfort, hemorrhage, and aesthetic deformity.[i] The acquisition of HPV is influenced by multiple factors, including the type of contact, the viral load, the HPV-specific immunological state of the exposed individual, and the extent and location of lesions.[ii,iii] The recurrence,nature and persistence of warts impact quality of life. The frequency of cutaneous warts is approximately 7-12%.[iv,v] Approximately two-thirds of warts spontaneously disappear; nevertheless, the majority of patients choose treatment due to the fast proliferation, associated discomfort, and unappealing look.[4,5]

Treatment strategies employed include locally destructive therapies such as salicylic acid, surgical curettage, chemical ablation, electrocautery, cryotherapy, hyperthermic therapy, and various laser kinds. All these therapies aim to locally eliminate warts, although they do not influence the host's immunity against HPV. Certain oral drugs, such as H2 receptor antagonists, zinc sulfate, and oral retinoids, have been documented as beneficial in treating cutaneous warts.[vi,vii] Various topical therapeutic alternatives are available, including topical 5-Fluorouracil (5-FU), retinoic acid, vitamin D analogues, topical imiquimod, podophyllin and autoinoculation.[viii] Virucidal agents include glutaraldehyde, formaldehyde, formic acid, and antiviral medications. Anti-mitotic and immunomodulatory drugs represent an alternative. Intralesional injections of Candida antigens and interferon alpha are administered as well.[ix,x]

Acyclovir is a synthetic derivative of a purine nucleoside with antiviral properties against some viruses, including varicella-zoster and herpes simplex. Acyclovir is metabolized into its active form, acyclovir triphosphate, by viral thymidine kinase, which selectively targets viral DNA to impede viral reproduction within the host. Limited studies and case reports have documented the treatment of warts with both topical and oral acyclovir, particularly in cases resistant to earlier therapies.[xi,xii]

The aim of our study is to determine the role of intralesional acyclovir in patient with plantar warts. On extensive literature very limited studies found the role of intralesional acyclovir in patient with plantar warts. Intralesional acyclovir was previous studied for the treatment of various types of cutaneous warts and shows better results. Furthermore, in our local setting there in no consensus on choice of treatment in patient with plantar warts. Findings of our study will help the dermatologist to choose appropriate treatment in order to improve warts early.

MATERIAL AND METHODS

This descriptive study was performed in the Department of Dermatology, Tertiary care hospital, from 2nd July to 2nd Jan 2025. The sample size of 175 patients was determined with the WHO sample size calculator, taking a 33.33% full response rate to intralesional acyclovir for plantar warts,[20] a 7% margin of error, and a 95% confidence level. Non-probability consecutive sampling was utilized to recruit patients aged 18 to 65 years of both sexes exhibiting plantar warts, regardless of duration. Individuals with psychiatric disorders, acute infections necessitating antimicrobial treatment, chronic conditions (including hepatic, renal, hematological dysfunctions, diabetes mellitus, and neoplasia), pregnancy, lactation, or those who underwent wart treatment within the past six months were excluded. Upon receiving approval from the institutional ethical review committee File no 120/2024/Trg/ERC and CPSP, eligible patients from the dermatology outpatient department were included after providing informed written consent subsequent to a detailed explanation of the study. Baseline demographic and clinical data, encompassing age, gender, family monthly income, height, weight, BMI, and the quantity and dimensions of warts, were documented. Plantar warts were clinically identified as firm, granular lesions on the heels or metatarsal regions of the feet. Patients were administered intralesional acyclovir (70 mg/ml; Acyclovir), with 0.1 mL injected into the base of each wart every 2 weekly for a maximum of six sessions (at 0, 2, 4, 6, 8, and 12 weeks). The treatment response was evaluated at 12

weeks and classified as: Complete reaction (>75% total eradication of warts); Partial response (75-50% decreased quantity/size but not entire elimination); No response (<50% no diminution of lesions). Statistical analysis was conducted utilizing SPSS version 24. Qualitative variables were presented as frequencies and percentages, whilst quantitative values were articulated as mean (SD) or median (IQR). Confounding variables (age, gender, income, BMI, wart duration, baseline number, and size) were managed through stratification, followed by the application of the post-stratification *Chi-square/Fisher's Exact* tests considering *p* value ≤ 0.05 as significant.

RESULTS

In this study we enrolled 175 patients presenting with plantar warts. Among 175, male and female ratio was 1:1, while females were 50.29% (n=88/175) of total study population [Figure 1] 55.43% of total study participants belonged to urban area [Figure 2]. The mean age of patient was 39.20 ± 11.47 years. However mean BMI and duration of warts was 25.95 ± 4.60 Kg/m2 and 3.46 ± 1.51 months respectively. Moreover, pre and post treatment number and size of warts were 2.17 ± 0.81 vs 0.80 ± 0.85mm and 6.37 ± 1.63 vs 2.22 ± 2.52 mm respectively. Detailed analysis of various demographic and clinical variables are presented in table 1 and table 2. Furthermore, 77 (44.0%) patients had complete response, 68 (38.86%) had partial response and 30 (17.14%) had no response [Figure 3]. In addition, stratification of treatment response with respect to age, gender, residence, BMI, income, duration of warts, number of warts at baseline and size of warts at baseline shown in table 3.

Table 1: Distribution of Age, income, Height, weight, BMI and duration of warts of study population

Variable	Mean (SD)	Median (IQR)
Age (Years)	39.20 ± 11.47	38 (19.0)
Income (PKR/Month)	53571.43 ± 13526.66	51000 (18000)
Height (m)	1.65 ± 0.08	1.65 (0.11)
Weight (Kg)	70.75 ± 9.27	70 (14.0)
BMI (Kg/m2)	25.95 ± 4.60	25.9 (5.9)
Warts Duration (Months)	3.46 ± 1.51	3 (3.0)

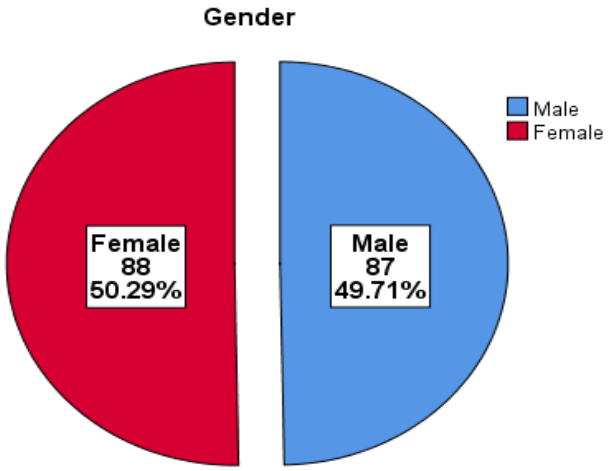

Figure 1: Distribution of Gender in total study population (n=175)

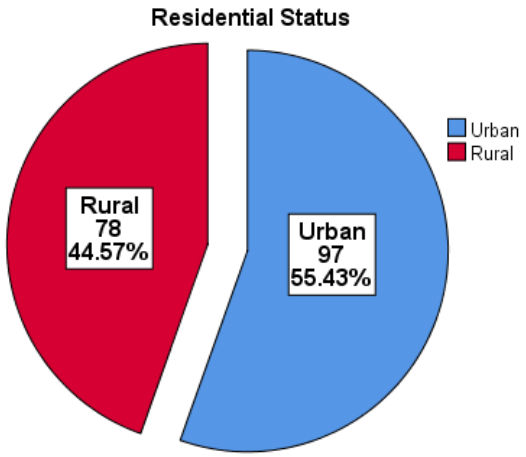

Figure 2: Distribution of place of residence among study participants (n=175)

Table 2: Distribution of number of warts and warts size at baseline and after treatment of study population

Variable	Mean (SD)	Median (IQR)
Number of Warts (Baseline)	2.17 ± 0.81	2.0 (1.0)
Warts Size (Baseline)mm	6.37 ± 1.63	6.0 (2.0)
Number of Warts (after Treatment)	0.80 ± 0.85	1.0 (1.0)
Warts Size (after Treatment)mm	2.22 ± 2.52	2.0 (4.0)

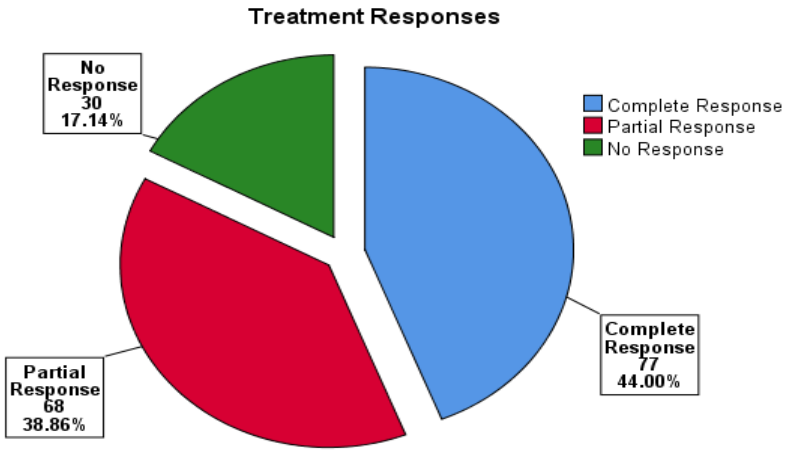

Figure 3: Distribution of responses of intralesional acyclovir in patient presenting with plantar warts.

Table 3: Stratification of treatment response with respect to age, gender, residence, income, BMI, duration of Warts, number of warts and size of warts

Independent Variables		Treatment Response			*p*Value
		Complete Response n (%)	Partial Response n (%)	No Response n (%)	
Age (Years)	<45	54 (70.1%)	44 (64.7%)	12 (40.0%)	0.014
	≥45	23 (29.9%)	24 (35.3%)	18 (60.0%)	

Gender	Male	37 (48.1%)	38 (55.9%)	12 (40.0%)	0.324
	Female	40 (51.9%)	30 (44.1%)	18 (60.0%)	
Residence	Urban	59 (76.6%)	27 (39.7%)	11 (36.7%)	0.000
	Rural	18 (23.4%)	41 (60.3%)	19 (63.3%)	
Income	<50000	36 (46.8%)	25 (36.8%)	13 (43.3%)	0.474
	≥50000	41 (53.2%)	43 (63.2%)	17 (56.7%)	
BMI (Kg/m2)	<30	58 (75.3%)	51 (75.0%)	23 (76.7%)	0.984
	≥30	19 (24.7%)	17 (25.0%)	7 (23.3%)	
Warts Duration (Months)	<4	40 (51.9%)	39 (57.4%)	22 (73.3%)	0.132
	≥4	37 (48.1%)	29 (42.6%)	8 (26.7%)	
Number of Warts	<2	51 (66.2%)	44 (64.7%)	26 (86.7%)	0.072
	≥2	26 (33.8%)	24 (35.3%)	4 (13.3%)	
Warts Size (cm)	≤2	28 (36.4%)	17 (25.0%)	11 (36.7%)	0.286
	>2	49 (63.6%)	51 (75.0%)	19 (63.3%)	

DISCUSSION

Current therapeutic approaches for warts predominantly rely on ablative techniques targeting infected tissue. Physical destruction methods include cryotherapy, electrocautery, surgical excision, and laser therapy, while chemical options involve trichloroacetic acid, salicylic acid, imiquimod, and cytotoxic agents like bleomycin.[9] However, these modalities lack specificity for HPV-infected cells, often resulting in recurrence due to residual latent virus in adjacent tissue. Additionally, ablative therapies can cause pain, scarring, and practical challenges in treating multiple lesions.[xiii,xiv]

A critical limitation of existing treatments is their non-antiviral nature—none selectively eliminate HPV-infected cells. This gap underscores the need for targeted antiviral therapies. Acyclovir, a nucleoside analogue effective against herpesviruses, has shown anecdotal promise in HPV treatment. Its selectivity arises from viral thymidine kinase-mediated phosphorylation, which inhibits viral DNA replication.[12,xv] Case reports describe successful resolution of recalcitrant plantar warts with topical acyclovir cream, while oral valacyclovir coincidentally improved warts during herpes zoster treatment.[11] These observations suggest a potential role for acyclovir in HPV management, warranting further investigation.

Our findings align with several previous studies that have reported a higher prevalence of plantar warts among males. A study by Naheed et al.[xvi] found that men were more likely to develop plantar warts, possibly due to frequent use of communal showers and swimming pools, which are known risk factors for human papillomavirus (HPV) infection. Additionally, the predominance of urban residents in our study is consistent with past research who suggested that higher population density and increased exposure to contaminated surfaces in urban settings contribute to the spread of warts.[xvii]

The mean age of patients in our study (39.20 years) was slightly higher than that reported in previous studies, such as those by Al-Awadhi R et al,[xviii] where the mean age was around 30–35 years. This discrepancy may be attributed to differences in study populations or delayed healthcare-seeking behavior in our cohort. The mean BMI of our patients (25.95 kg/m²) falls within the overweight range, which is noteworthy given that obesity has been linked to impaired immune function and delayed wound healing.[xix] However, our study did not find a statistically significant association between BMI and treatment response (p=0.984).

Regarding treatment efficacy, our study demonstrated a complete response rate of 44.0%, which is comparable to the 50–60% success rates reported in previous studies by Elsayed and Meghana Reddy.[xx,xxi] Study by Meghana Reddy et al reported 60%, and 30% of complete recovery with intralesional acyclovir treatment and intralesional PPD treatment

respectively, in patient with viral warts.Elsayed reported complete clearance of warts was observed in 52.6%, partial response in 36.8%, and no response in 10.5% of the patients in the acyclovir group. The lack of response in our study patients is consistent with previous research indicating that certain individuals exhibit resistance to standard treatments, possibly due to HPV strain variability or host immune factors.[xxii,xxiii]

In 1982, Bauer reported clearance of recalcitrant plantar warts after local application of acyclovir cream in a single case report.[16] A year later, Pechman demonstrated the successful use of acyclovir ointment in a patient with refractory plantar warts.[xxiv] In 2005, Tandeter reported complete resolution of resistant plantar warts after oral intake of valacyclovir 1 gm for coexistent herpes zoster.[12] Similarly, Bagwell et al,[11] described a case of recalcitrant plantar warts that disappeared 10 days after acyclovir therapy for herpes zoster.

The demographics, clinical features, and treatment results of plantar wart patients are well covered in this paper. The results are strengthened by the fairly big sample size including several demographic variables like age, gender, location, and income among others—helps to thoroughly examine treatment responses across different patient populations. The depth of the study is also improved by using stratification to assess therapy response, hence highlighting significant relationships between clinical and demographic factors.

Despite its merits, our research has certain limitations. First, the length of follow-up could not have been adequate to completely evaluate long-term treatment results or recurrence rates. Second, as most of the participants lived in urban areas, the results may not be applicable to rural locations. Third, self-reported data—such as income and other socioeconomic variables—could create reporting bias. The observational character of the study restricts the capacity to determine causation between demographic or clinical variables and treatment responses. Without a control group, we are unable to evaluate the effectiveness of treatment versus placebo or other therapies. Our research did not look at HPV genotypes, which are known to affect treatment resistance and wart persistence. At last, the study was done in one center, which could restrict the generalizability of the results to other populations.

Our results are clinically significant. Though the partial and non-response rates emphasize the necessity for individualized therapeutic approaches, the high complete response rate (44.0%) confirms the efficacy of the treatment technique used. The notable link between younger age, residential status and better treatment outcome implies that early intervention and better life style could enhance prognosis. Furthermore, the statistically insignificant difference between BMI and treatment response suggests that, contrary to certain past ideas, weight control might not be important in wart resolution. Future research should evaluate recurrence rates using HPV genotyping and extended follow-up times. Randomized controlled trials comparing various treatment modalities would help us even more to know the best management techniques for plantar warts.

CONCLUSION

This study demonstrates that plantar warts are more prevalent among females and urban residents. The treatment outcomes were promising, with nearly half of the patients achieving a complete response and more than one-third experiencing partial improvement. Factors such as age, residential status, and baseline clinical characteristics were shown to influence treatment responses. Our findings contribute a valuable knowledge to the field, addressing the identified limitations and implementing the recommendations will be essential for future research to build upon these results and optimize the management of plantar warts.

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