ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 05 | May - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFICACY AND SAFETY OF INTRALESIONAL MMR VACCINE IN RECURRENT CUTANEOUS AND PERIUNGUAL WARTS

Dermatology

Dr Radhika S R
Department of Dermatology, Venereology and Leprosy,East Point College of Medical Sciences & Research Centre, Bengaluru – 560049, Karnataka, India

ABSTRACT

Background and Objective: Cutaneous warts are common dermatological lesions caused by Human Papillomavirus (HPV). Recurrent and periungual warts are often difficult to treat because conventional destructive modalities are painful, may cause scarring, and are associated with recurrence. Intralesional immunotherapy with the Measles, Mumps, and Rubella (MMR) vaccine has emerged as a promising alternative. This study evaluated the efficacy and safety of intralesional MMR vaccine in recurrent cutaneous and periungual warts.**Materials and Methods:**This prospective, open-label, single-arm interventional study enrolled 75 patients aged 12–60 years presenting with recurrent cutaneous warts and/or periungual warts. MMR vaccine (Tresivac, Serum Institute of India) 0.2–0.5 ml was injected intralesionally into the base of the largest wart every two weeks for a maximum of five sessions. Response was classified as complete (100% clearance), partial (50–99% reduction), or no response (0–49% reduction) at both the injected and distant (un-injected) sites. Side effects and recurrence at two months post-treatment were also assessed.
Results: The mean age was 38.66 ± 12.43 years with male preponderance (58.67%). Periungual warts were the most common type (32%), followed by palmar warts (26.67%). Overall, 61.33% of patients achieved complete response, 20% partial response, and 18.67% no response. Plantar warts showed the highest complete response rate (100%), followed by periungual warts (83.33%) and palmar warts (70%). Both injected-site (Chi-square = 88.63, p = 0.0023) and distant-site responses (Chi-square = 73.25, p = 0.0168) were statistically significant. Significant responses were observed from the 3rd follow-up visit onwards. Adverse effects included pain (42.67%), post-inflammatory hyperpigmentation – PIH (25.33%), and flu-like symptoms (6.66%). No recurrence was observed at two months post-treatment.**Conclusion:** Intralesional MMR vaccine is a safe, effective, and economical treatment for recurrent cutaneous and periungual warts.

KEYWORDS

Cutaneous Warts, Human Papillomavirus, Immunotherapy, Intralesional Injection, Mmr Vaccine, Periungual Warts

INTRODUCTION

Cutaneous warts are benign proliferations of skin and mucosa caused by Human Papillomavirus (HPV), a double-stranded DNA virus. Despite their benign nature, warts cause significant psychosocial morbidity: up to 81.2% of patients report embarrassment and 24.7% experience impaired social activities (Ciconte et al., 2003). Conventional modalities including cryotherapy, electrosurgery, and topical salicylic acid focus on physical destruction of lesions and are associated with pain, scarring, and high recurrence rates without addressing distant lesions (Chandrashekar, 2011; Sterling et al., 2014).

Intralesional immunotherapy induces Th1-mediated delayed-type hypersensitivity, generating cytokines including IL-2, TNF-α, and IFN-γ, which activate NK cells and cytotoxic T lymphocytes to clear both injected and un-injected distant warts (El-Khalawany et al., 2015). The Measles, Mumps, and Rubella (MMR) vaccine, a trivalent live attenuated preparation widely available through India's national immunization schedule has demonstrated high response rates and favourable safety in prior studies (Nofal & Nofal, 2010; Gamil et al., 2010). This study evaluated the efficacy and safety of intralesional MMR vaccine in recurrent cutaneous and periungual warts at a tertiary care centre in Bengaluru.

Materials and Methods

This prospective, open-label, single-arm interventional study was conducted at the Department of Dermatology, Venereology and Leprosy, East Point College of Medical Sciences & Research Centre, Bengaluru . Institutional Ethics Committee approval was obtained and written informed consent was taken from all participants.Seventy-five patients aged 12–60 years with clinically diagnosed recurrent cutaneous warts (relapsed after any prior treatment) or periungual warts (≥1 lesion), or multiple warts (>3 lesions), were enrolled. Exclusion criteria included pregnancy, immunocompromised status, genital or infected warts, and co-existing dermatological disorders.

MMR vaccine used was Tresivac (Serum Institute of India Ltd., Pune), containing 1000 $CCID_{50}$ Measles, 5000 $CCID_{50}$ Mumps, and 1000 $CCID_{50}$ Rubella virus. Reconstituted vaccine (0.2–0.5 ml) was injected intralesionally into the base of the largest wart every two weeks for a maximum of five sessions. Responses were graded as: complete (100% clearance), partial (50–99% reduction), or no response (<50% reduction) at both injected and distant sites. Data were analysed using R software; chi-square and multivariate regression were used; significance was set at $p \leq 0.01$.

Results

The cohort comprised 44 males (58.67%) and 31 females (41.33%) (fig 1), mean age 38.66 ± 12.43 years. The 21–30-year age group was most affected (41.33%). Mean duration of illness was 12.22 ± 23 months (Table 1). Periungual warts were the most common type (32%), followed by palmar (26.67%), verruca vulgaris (20%), flat (10.67%), plantar (8%), and filiform warts (2.67%) as shown in Figure 2.

Figure 1: Gender wise distribution of patients

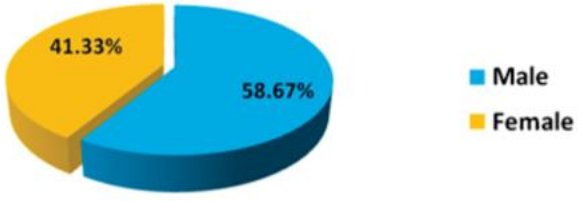

Table 1: Demographic and Clinical Profile of Study Patients (n = 75)

Variable / Category	n	Percentage (%)
Sex:		
Male	44	58.67
Female	31	41.33
Age group (years):		
12–20	16	21.33
21–30	31	41.33
31–40	13	17.33
41–50	09	12.00
51–60	06	8.00
Duration:		
<8m	5	6.67
8m–1yr	29	38.67
1–2yr	18	24
>2yr	23	30.67
Family history:		
Present	26	35
Absent	49	65

Overall, 46 patients (61.33%) achieved complete response, 15 (20%) partial response, and 14 (18.67%) no response (Table 2). Excluding poor-responder types (flat and filiform warts), complete response improved to 69.23%.

Fig 2: Dsitribution of study subjects with respect to Wart types

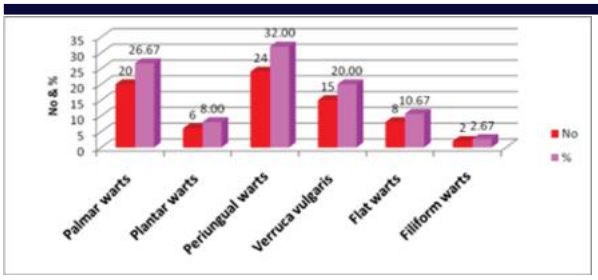

Table 2: Overall Treatment Response to Intralesional MMR Vaccine (n = 75)

Response	Number	Percentage (%)
Complete (100%)	46	61.33
Partial (50–99%)	15	20.00
No Response (0–49%)	14	18.67
Total	75	100.00

By wart type, plantar warts showed 100% complete response, periungual 83.33%, palmar 70%, verruca vulgaris 33.33%, flat warts 12.5%, and filiform warts 0% (Table 3). The injected-site response was statistically significant across follow-up visits ($\chi^2 = 88.63$, $p = 0.0023$), as was the distant-site response ($\chi^2 = 73.25$, $p = 0.0168$) as depicted in Tables 4 and 5, confirming systemic immune-mediated clearance. Significant response emerged at the 3rd to 5th follow-up visits. Shorter disease duration correlated with better outcomes: 80% complete response for <8 months vs. 52.17% for >2 years. Females responded better than males (70.97% vs. 54.54% complete response).

Table 3: Response to Intralesional MMR Vaccine by Wart Type

Wart Type	n	Complete Response	Partial Response	No Response
Plantar	6	6 (100%)	—	—
Periungual	24	20 (83.33%)	4 (16.67%)	—
Palmar	20	14 (70%)	3 (15%)	3 (15%)
Verruca vulgaris	15	5 (33.33%)	5 (33.33%)	5 (33.33%)
Flat warts	8	1 (12.5%)	3 (37.5%)	4 (50%)
Filiform	2	—	—	2 (100%)

Adverse effects were mild and self-limiting (Table 6). Pain was the most common (42.67%), especially in periungual and plantar patients, resolving without analgesics. Post-inflammatory hyperpigmentation (PIH) occurred in 25.33%, mainly in facial and common wart patients. Flu-like symptoms were reported by 6.66%. No patient experienced wart proliferation or serious adverse events, which were found to be statistically significant ($p<0.01$). No recurrence was documented at two-month follow-up.

Table 4: Injected Site Response Rate with Different Follow up Period

Injected site response	1st FU injected	2nd FU injected	3rd FU injected	4th FU injected	5th FU injected
<25 %	53	29	10	03	02
26 - 50%	14	24	22	19	12
51 - 75%	06	09	19	14	14
>75%	02	08	14	22	01
Complete (100%)	00	05	10	17	46

Chi-square-88.63, p-0.0023

Table 5: Distant Site Response Rate with Different Follow up Period

Distant site response	1st FU-distant	2nd FU-distant	3rd FU-distant	4th FU-distant	5th FU-distant
<25% - 21	57	33	13	3	3
26 - 50% - 22	17	23	24	22	14
51 - 75% -23	1	7	18	15	12
>75% -24	0	8	4	19	23
complete (100%) - 25	0	4	16	16	23

Chi-square-73.25, p-0.0168

Table 6: Adverse Effects of Intralesional MMR Vaccine (n = 75)

Adverse Effect	n	%	p-value
Pain at injection site	32	42.67	0.003
Post-inflammatory hyperpigmentation	19	25.33	0.001
Flu-like symptoms	6	6.66	0.0005
Increase in lesions	0	0.00	—
None	19	25.33	0.001

DISCUSSION

The 61.33% complete response rate in this study (81.33% cumulative) is concordant with published literature. Nofal and Nofal (2010) reported 81.4%, Zamanian and Mobasher (2014) reported 75%, Awal and Kaur (2018) reported 68%, Rabia Ali et al. (2017) reported 68.75%, and Riffat Naseem and Aamir (2013) reported 81.3% complete response. The slightly lower rate in our cohort is explained by the inclusion of flat and filiform warts recognised poor responders. Excluding these, our rate of 69.23% is fully concordant with comparable studies. In our study, plantar warts showed 100% complete response rate. Gamil et.al[182] study showed 87% complete response. Nagat Sobhy Mohammad et al.[189] conducted a study on 100 patients with plantar warts which showed 82% complete response.

The significant distant-site response ($p = 0.0168$) confirms the systemic bystander immune effect of intralesional immunotherapy, mediated by TNF-α, IFN-γ, and IL-2 activating NK cells and cytotoxic T lymphocytes (El-Khalawany et al., 2015; Johnson et al., 2001). The trivalent MMR antigen combination generates a broader and more potent immune stimulus than single-antigen preparations (Banatvala & Brown, 2004). Shorter disease duration, younger age, and female sex were associated with better therapeutic outcomes. The favourable side-effect profile, no serious adverse events, no recurrence at two months combined with low cost and the ability to clear distant lesions makes intralesional MMR vaccine a compelling first-line option, particularly for periungual and plantar warts where conventional therapies are least tolerated.

CONCLUSION

Intralesional MMR vaccine is a safe, efficacious, and cost-effective immunotherapeutic modality for recurrent cutaneous and periungual warts. It clears both injected and distant warts through systemic Th1 immune activation, with an excellent safety profile and no recurrence at two months. It should be considered a first-line treatment for multiple recurrent warts and periungual warts. Randomised controlled trials with longer follow-up and pre-treatment MMR sensitivity testing are warranted.

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