



Original Article

Re-emergence of chikungunya as a public health problem in North India: A dermatologist's perspective on the mucocutaneous manifestations — An observational cross-sectional study

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Received: 04 October 2025

Accepted: 19 November 2025

Published: 15 January 2026

DOI

10.25259/CSDM_181_2025

Quick Response Code:



ABSTRACT

Objectives: Chikungunya fever is an Aedes mosquito-borne arboviral illness with significant morbidity. Recognizing and understanding a plethora of these mucocutaneous manifestations is essential for early diagnosis and timely intervention. Hence, the aim was to establish the role of dermatologists in public health problems in viral epidemics on the basis of mucocutaneous manifestations, as there is an upsurge of viral exanthems in recent years.

Materials and Methods: A hospital-based descriptive cross-sectional study was conducted in patients who attended the outpatient department from June 2023 to December 2023 according to the case definition. Immunoglobulin M enzyme-linked immunosorbent assay was used for serological confirmation of chikungunya.

Results: Of 164 patients, 157 patients satisfied the suspected case definition criteria and were screened for chikungunya; the positive serological reactivity was noted in 43% of the cases. The male-to-female ratio was 1:1.37. The most common age group affected was 20–40 years with a mean age of 37.27 ± 17.3 years. The most common mucocutaneous manifestations observed were maculopapular rash (43.9%), followed by facial hyperpigmentation (13.3%) and CHIK sign (5.7%). Lichenoid hyperpigmentation and arthralgia formed the most important post-febrile sequelae during the follow-up period.

Conclusion: Dermatologists are playing a pivotal role in the detection and surveillance of neglected tropical diseases. Mucocutaneous manifestations of viral exanthems provide an early clinical clue for their detection, and this study reinforces the findings of previous studies. Therefore, awareness regarding these cutaneous manifestations becomes essential for their detection and also helps in halting the spread and re-emergence of viral infection.

Keywords: Chikungunya, Maculopapular, Mucocutaneous, Outbreaks, Public health problem

INTRODUCTION

Chikungunya, a neglected tropical disease transmitted by the *alphavirus* genus in the *Togaviridae* family, has gained importance globally due to frequent outbreaks. Being a vector-borne disease (*Aedes* spp. Mosquitoes), it predominantly affects the musculoskeletal system in the form of joint pains and dermatological rash.

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The first outbreak of chikungunya (CHIK) was documented in Tanzania in 1952, and India recorded its first outbreak in 1963. This was followed by cyclic and regular epidemics in Tamil Nadu, Maharashtra, and Andhra Pradesh till 1973. After the quiescent period of almost 3 decades, India saw a re-emergence of CHIK virus infection in 2006. Since then, regular outbreaks have been recorded in North and South India.^[1]

Muco-cutaneous involvement is prominent and a significant finding that may help in distinguishing this viral infection from other viral febrile exanthems. Generalized maculopapular rash has been the most common manifestation in 30–50% of the cases.^[1] The febrile episodes and maculopapular rash may be a coincidental feature during recurrent bouts of viremia. Systemic involvement has also been described.^[1,2]

Diagnosis of CHIKV (Chikungunya virus) infection is mainly clinical, as there are no pathognomonic findings. However, there are three specific tests for the detection of CHIKV infection: virus isolation, reverse transcriptase polymerase chain reaction (RT-PCR), and serological tests for identifying CHIKV-specific antibodies (Immunoglobulin M antibody capture (MAC-Ig) enzyme-linked immunosorbent assay [ELISA]).^[3] Viral isolation remains the gold standard to confirm the diagnosis.^[4] However, a definitive diagnosis can be established earlier in the acute phase of infection by RT-PCR in less than 5 days of infection and by Immunoglobulin M (IgM) antibody detection in the sera using ELISA in more than 5 days.^[3] Serological diagnosis is made by demonstrating a fourfold rise of CHIKV IgG titer in acute and convalescent sera, as these CHIKV-specific IgM antibodies persist for several 3-months of infection.^[3] RT-PCR test has been developed using primer pairs amplifying specific components of the gene regions: capsid C, envelope E-2, and part of E-1 of CHIKV.^[4,5]

Communicable and neglected diseases pose a challenge to the healthcare sector. The impact on productivity, quality of life, and physical and mental well-being can be substantial.^[6] The present study is being conducted to establish the role of dermatologists in public health problems in viral epidemics on the basis of mucocutaneous manifestations.

MATERIAL AND METHODS

An observational, descriptive, hospital-based study was conducted in a tertiary care institute from North India through its fever clinic during the outbreak of Chikungunya from July 2023 to December 2023 after obtaining approval from the Institutional Ethics Committee. (IEC/RTR/23/34027) Patients who attended the outpatient department in dermatology were prospectively enrolled according to the case definition of the “suspect cases” of Chikungunya infection^[7,8] [Figure 1].

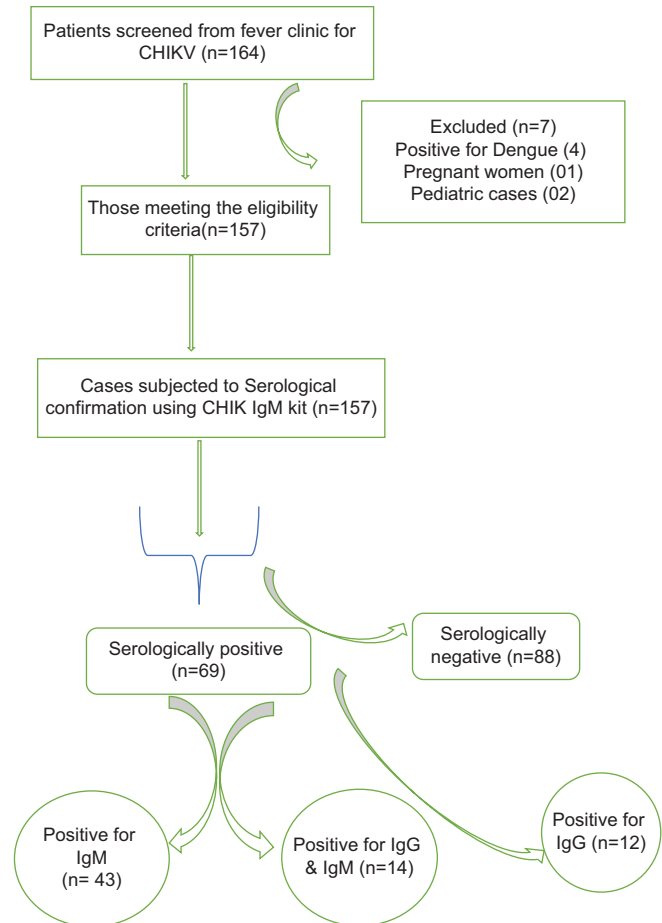


Figure 1: The protocol of the study conducted.

The criteria for a suspected new case were sudden onset of fever associated with skin rash, myalgia, headache, and swelling of the joints^[7] [Table 1].^[7,9] Detailed history, clinical examination, and relevant investigations were conducted after obtaining written informed consent from each patient. Diagnosis was made clinically, and serological confirmation was performed using IgM ELISA.

Patients who refused to participate in the study, those having concomitant co-infection with dengue, having a seroreactivity to other viral illnesses, those suspected to have an autoimmune disease or suspected to have drug reaction, human immunodeficiency virus seroreactivity or immunocompromised status, with pre-existing dermatosis, pregnancy, lactation, and having seroreactivity to chikungunya before enrollment, were all excluded from the study.

Data were collected by authors (MM and TK) on a day-to-day basis for study variables, and then they were entered into a predesigned pro forma. Mean and standard deviation were used for descriptive statistics, and proportion/percentage for categorical variables. Pearson correlation was used for

Table 1: Diagnostic criteria for chikungunya fever.

Suspected case
<ul style="list-style-type: none"> • A patient presenting with an acute onset of fever, usually with chills/rigors • Which lasts for 3–5 days • With multiple joint pains/swellings of extremities that may continue for weeks to months
Probable case
A suspected case above with any one of the following: <ul style="list-style-type: none"> • History of travel or residence in the area reporting outbreaks • Ability to exclude malaria, dengue, and any known cause of fever with joint pains.
Confirmed case
Any patient who meets one or more of the following findings, irrespective of clinical presentation <ul style="list-style-type: none"> • Virus isolation in cell culture or animal inoculation from acute-phase sera. • Presence of viral RNA in acute-phase sera by RT-PCR • Presence of viral-specific IgM antibodies in a single serum sample in the acute or convalescent stage. • Fourfold increase in virus-specific IgG antibody titer in samples collected at least 3 weeks apart.
RNA: Ribonucleic acid, RT-PCR: Reverse transcriptase polymerase chain reaction, IgM: Immunoglobulin M, IgG: Immunoglobulin G

leukocyte, platelet, and C-reactive protein (CRP). Analysis of data was done using the Statistical Package for the Social Sciences version 23.

RESULTS

Of 164 patients screened from the fever clinic for new cases of suspected chikungunya, 157 were found eligible for enrollment. Of these, 66 were male, and 91 were female. The mean age was 37.27 ± 17.3 years with a range of 36.2–38.1 \pm 16.1–19 years. The male-to-female ratio was 1:1.37. The most common age group affected was 20–40 years. The mean duration of the fever with rash was 3 days \pm 2 days. Clinicodemographic profile and comorbid conditions are summarized in Table 2. Mucocutaneous lesions observed during the 1st week of the disease presentation are summarized in Table 3. These manifestations were further divided into the following groups:

- The most common cutaneous manifestation was erythematous maculopapular rash with pruritus in 43.9% ($n = 69$) of the patients [Figure 2a].
- The second common mucocutaneous manifestation in our study was pigmentary changes seen in 23.4% ($n = 37$) [Figure 2b-d].
- Oral ulceration and desquamation of palms and soles [Figure 2e and f] were observed in 5.0% ($n = 8$) each, while genital ulceration [Figure 3a] was present in

Table 2: Clinicodemographic profile of study population ($n=157$).

Age group (in years)	No of cases
11–20	22
21–40	75
41–60	42
>60	18
Gender	
Male	66
Female	91
Socioeconomic status	
Low-income group	90
Middle-income group	40
High-income group	27
Residential status	
Rural	58
Urban	99
Clinical features	
Symptoms	
Fever	100% ($n=157$)
Myalgia	96% ($n=150$)
Headache	82.8% ($n=130$)
Arthralgia	66.8% ($n=105$)
Chills	44.5% ($n=70$)
Vomiting	38.2% ($n=60$)
Joint involved	($n=105$) 66%
Interphalangeal+metacarpophalangeal joints	38% ($n=40$)
Elbow+shoulder	21.9% ($n=23$)
Knee and Ankle joint	15.2% ($n=16$)
Wrist joint	6.3% ($n=26$)
Laboratory abnormalities	
Leukopenia	12.5%
Thrombocytopenia	5%
Transaminitis (>2 times)	3%

3.1% ($n = 5$) over the scrotum and groin in the acute phase.

- Palmar erythema and urticaria [Figure 3b] were present in 3.8% and 3.1% of the cases, respectively.
- Scrotal dermatitis and edema of the hands and feet occurred in 2.5% ($n = 4$) of the cases each. [Figure 3c].
- Miscellaneous: Vesico-bullous lesions 2.5% ($n = 4$) [Figure 3d], Milan's sign of erysipelas in 1.9% ($n = 3$), purpuric lesions in 1.8% ($n = 2$), [Figure 3e and f] conjunctivitis exacerbation of the pre-existing dermatosis in 0.6% ($n = 1$) of the cases, respectively.

CRP is significantly negatively correlated with leukocytes ($r = -0.255$) and platelets ($r = -5.40$) at $P = 0.001$ [Figure 4a-c].



Figure 2: (a) Maculopapular rash involving the trunk during the acute phase. (b) Melasma-like pigmentation on face; (c) Melasma-like pigmentation on face (Lateral view); (d) Centro-facial region hyperpigmentation (Post chikungunya); (e) Desquamation of hands in acute phase; (f) Desquamation of feet during post-febrile phase.

Table 3: Types of cutaneous manifestations in Chikungunya patients.

S.no	Manifestations	Number of patients affected (%) <i>n</i> =157
1.	Maculopapular rash	69 (43.9)
2.	Centro Facial hyperpigmentation	21 (13.3)
3.	Chik sign	09 (5.7)
4.	Desquamation of palms and soles	08 (5.0)
5.	Oral ulcerations	08 (5.0)
6.	Lichenoid pigmentation	07 (4.4)
7.	Palmar erythema	06 (3.8)
8.	Urticarial rash	05 (3.1)
9.	Genital ulcerations	05 (3.1)
10.	Scrotal dermatitis	04 (2.5)
11.	Edema of hands and feet	04 (2.5)
12.	Vesiculobullous disorders	04 (2.5)
13.	Localized erythema and swelling of the pinnae	03 (1.9)
14.	Purpuric lesions	02 (1.8)
15.	Conjunctivitis and Uveitis	01 (0.6)
16.	Exacerbation of pre-existing dermatosis	01 (0.6)

DISCUSSION

After a gap of 29 years, an urban epidemic of CHIKV was reported in the Democratic Republic of Congo. Similar outbreaks were reported in India during 2005–2006 after a period of 32 years. These outbreaks are usually associated with multiple risk factors such as heavy rainfalls, absence of herd immunity, poor vector control, globalization, viral mutations, and increased international travel.^[9] CHIKV infection can present with varied mucocutaneous manifestations. Recognizing and understanding a plethora of these mucocutaneous manifestations is, therefore, essential for early diagnosis and timely intervention.

The present study is in accordance with that of Mohan^[9] where females outnumbered males, but was in contrast to previous studies of Riyaz *et al.*^[10] and Inamadar *et al.*^[1] where males outnumbered females.

Generalized maculopapular rash (43%, *n* = 69) was the most common observation of our study; presenting on day 3–5 with fever and resolved by day 4. The rash showed preference for the trunk, face, and extremities along with pruritus. These findings were consistent with earlier studies of Inamadar *et al.*,^[1] Gulanikar and Abrol.^[11] Other



Figure 3: (a) Punched out scrotal ulceration during the acute phase; (b) Urticarial lesions over the forearm during the acute phase; (c) Edema of hands during the acute phase; (d) Multiple vesicular eruptions seen over the thigh in an adult patient during the acute phase, (e) Purpuric lesions over the forearm; (f) Pinpoint hemorrhagic lesions over the anterior aspect of the legs during the acute phase.

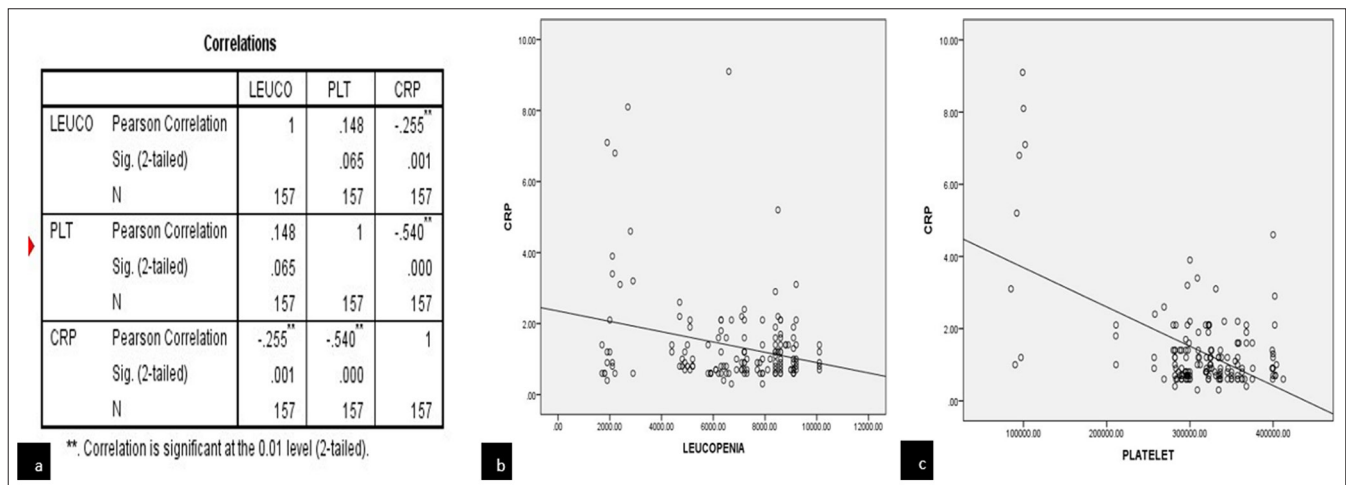


Figure 4: (a) Correlation between C-reactive protein (CRP), Leukopenia, and thrombocytopenia; (b) Scatter plot diagram (Leukopenia and CRP); (c) Scatter plot diagram (Thrombocytopenia and CRP).

researchers like Rueda *et al.* and Kumari *et al.*^[12,13] observed them in 40–50% of the cases. While Bhat *et al.*,^[14] Chatterjee *et al.*^[15] and Kumar *et al.*^[16] observed them in 53.5–80%

of their patients. This may be due to the cytopathic and immunological factors directly leading to endothelial capillary injury.

Centro-facial hyperpigmentation was present in 13.3% ($n = 21$), Lichenoid rash in 4.4% ($n = 7$), while Chik sign [Figure 2a-c] was observed in 5.7% ($n = 9$) of the patients in our study. Centro-facial pigmentation (30.3%) was the commonest finding present in the study of Inamadar *et al.*,^[1] and while it was seen in 27% in Raju *et al.*^[17] The most common site involved was the nose and cheek. This may be due to increased intraepidermal retention and dispersion of melanin triggered by bouts of viremia or post-inflammatory hyperpigmentation.^[1,18]

Desquamation of palms and soles was present in 15% of the patients. This was in contrast to Riyaz *et al.*^[10] who observed them in only 5% of the cases, which is attributed to subsiding inflammation in this area.

In our study, oral mucosal involvement was seen in 8.1% ($n = 13$) of the patients, while Riyaz *et al.*^[10] observed them in 13.6% ($n = 22$), and Rueda *et al.*^[12] in 2.6% ($n = 14$) of the cases.

Penoscrotal ulceration was seen in the studies of Prashant *et al.*,^[19] Gulanikar and Abrol^[11] who observed them in 23.7% ($n = 27$) and 30% ($n = 15$) cases, respectively, while we observed them in 3.1% ($n = 5$). These ulcers were observed after 3–4 days of fever onset and healed without any sequelae in 2 weeks. All other relevant investigations pertaining to ulceration were negative (Herpes simplex virus (HSV) antibodies, viral markers, VDRL, Gram staining, and Tzanck smear).

Vesicubullous lesions appeared on day 2 after fever and disappeared in 2 weeks. Similar lesions were reported by Gulanikar and Abrol^[11] and Kumari *et al.*^[13] in their study. These vesicular eruptions were due to viral replication leading to focal necrosis and ballooning degeneration.^[16]

Joint involvement was a prominent finding in our study, being present in 66% of the patients. This was in accordance with

Table 4: Characteristics of Cutaneous Manifestations of Chikungunya in the literature.

Author name and year	Place of study	Sample size (n=)	Muco-cutaneous Manifestations on first visit in %age	Site involved	Serological confirmation (IgM ELISA)	Systemic and mucosal involvement	Post-fever sequelae
Inamadar <i>et al.</i> 2008 ^[1]	Karnataka	145	42% hyperpigmentation	Face, trunk	NA	ND	Yes
Riyaz <i>et al.</i> 2010 ^[10]	Kerala	162	33.95% Maculopapular rash	Trunk, limbs, and face	97%	yes	ND
Gulanikar and Anuradha 2019 ^[11]	Maharashtra	50	40% Maculopapular rash	Face and neck, trunk, limbs	% age Not reported	Yes	Asymptomatic
Rueda <i>et al.</i> 2019 ^[12]	Colombia	548	44.7% ($n=132$) Maculopapular rash	Face and limbs	53.8%	Yes	yes
Kumari <i>et al.</i> 2024 ^[13]	Bihar	50	40%	Trunk, face, and limbs	NA	ND	ND
Bhat <i>et al.</i> 2011 ^[14]	Karnataka	75	52% Maculopapular rash	Face and neck, trunk, limbs	ND	yes	yes
Chatterjee <i>et al.</i> 2024 ^[15]	Eastern India	20	60% maculopapular eruptions	Face and neck, trunk, limbs	% age Not reported	ND	yes
Kumar <i>et al.</i> 2017 ^[16]	Rajasthan	112	80% Maculopapular rash	Trunk, face, and extremities	67.8%	yes	Without any sequelae
Raju <i>et al.</i> (2018) ^[17]	Karnataka	200	35% Maculopapular rash	Extremities, trunk, neck and ear lobe	ND	Yes	Yes
Prashant <i>et al.</i> ^[19]	Andhra Pradesh	41	35.56% Maculopapular rash	Trunk, extremities & face	ND	ND	Without any sequelae
Suryawanshi <i>et al.</i> 2009 ^[22]	Maharashtra	318	31% Maculopapular rash	NA	52.4%	Yes	Yes
Reshma <i>et al.</i> , 2021 ^[24]	Kerala	148	0 in hospital-based and 25.7% in survey	NA	90% PCR/IgM ELISA	ND	Yes
Present study, 2024	Punjab	157	43% Maculopapular rash	Face and neck, trunk, limbs	43%	Yes	Yes

ND: Not detected

the studies by Simon *et al.*^[4] and Pialoux *et al.*^[3] Small joints of the hand, wrist, and ankles were involved in accordance with the study of Borgherini *et al.*^[20] and Mizuno *et al.*^[21]

Hematological abnormalities such as Leukopenia and thrombocytopenia were observed in 12.7% ($n = 20$) and 5.0% ($n = 8$) of the patients in our study, while Suryawanshi *et al.*^[22] observed thrombocytopenia in their study. These findings were variable in various studies, consisting of Leukopenia, thrombocytopenia, lymphocytosis, or lymphopenia.^[4]

Hemorrhagic manifestations like purpura were present in 1.8% in contrast to Kumar *et al.*^[23] who found them in 3.5% of the cases. This can be attributed to thrombocytopenia induced by the viral replication in capillary endothelium, leading to vascular damage. The immune mechanism is another possibility causing vascular damage by type-3 immune reaction.^[16]

Mucocutaneous manifestations of chikungunya provides an early clinical clue for their detection.^[24-26] Table 4 summarizes the characteristics of cutaneous manifestations of chikungunya in the literature.

Exacerbation of pre-existing diseases has been reported in the studies of Bhat *et al.*^[14] and Inamadar *et al.*^[1] which is in accordance with our study.

Systemic involvement was reported by Pialoux *et al.*^[3] in the form of central nervous system and hepatic involvement, while Rueda *et al.*^[12] found gastrointestinal findings to be an important finding in their cases.

All patients were managed symptomatically. Protective clothing was emphasized along with vector control measures. The quest for a leap forward for safe and effective vaccine is the demand of the present time.^[27-29]

Limitations: Being a single-center study, it included only those cases that reported to the tertiary care institute and hence represents the tip of the iceberg. Small sample size study, selection bias, lack of gene sequencing, and non-availability of RT-PCR were some limitations.

CONCLUSION

Dermatologists are playing a pivotal role in detecting neglected tropical diseases. Therefore, awareness regarding a plethora of these cutaneous manifestations by dermatologists not only becomes essential for their detection, rather they also help in halting the spread and re-emergence of viral infection. Further, the re-emergence of chikungunya has opened doors for ample opportunities in the field of viral replication, genomic coding, diagnostic, and field research.

There are currently two approved chikungunya vaccines: IXCHIQ (Valneva, Vienna, Austria; live-attenuated, single dose) and VIMKUNYA (Bavarian Nordic, Hellerup,

Denmark; virus-like particle, single dose). VIMKUNYA is currently only licensed for those aged 12 years and older, and IXCHIQ for adults aged 18 years and older. However, these are not widely available and are licensed in few regions (European union, UK and U.S.A.) for travellers to high risk areas and should be given after careful consideration of the benefits and risks.

Ethical approval: The research/study was approved by the Institutional Review Board at GOVERNMENT MEDICAL COLLEGE AMRITSAR, number IEC/RTR/23/34027, dated 2023.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship: Nil.

Conflict of interest: There are no conflict of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Kaur T, Mahajan M, Raj RT. Re-emergence of chikungunya as a public health problem in North India: A dermatologist's perspective on the mucocutaneous manifestations — An observational cross-sectional study. *CosmoDerma*. 2026;6:9. doi: 10.25259/CSDM_181_2025