The Philippine Journal of Orthopaedics

ORIGINAL ARTICLE

Evaluation of the Efficacy of Intramuscular Immunoglobulin in Treating Post-Chikungunya Arthralgia

Suraj Sudarshan Doshi, Santosh Shridhar Borkar, Shubham Ramdas Sanap, Shivraj Konde, Rhythm Tahilramaney, Vipul Pise, Animesh Gunjal

Maharashtra Institute of Medical Education and Research Medical College and Dr. Bhausaheb Sardesai Talegaon Rural Hospital, Maharashtra, India

ABSTRACT

Background. Chikungunya virus (CHIKV) infection may be followed by persistent musculoskeletal symptoms, particularly chronic arthralgia and arthritis, causing pain, impairing mobility and function, and reducing quality of life. Conventional management is primarily symptomatic and may include analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, selected disease-modifying antirheumatic drugs (DMARDs), and rehabilitation, which often provide incomplete relief and are associated with long-term adverse effects. The evidence supporting specific therapies for persistent chikungunya-related rheumatic disease remains limited. Intramuscular immunoglobulin (IMIG), because of its immunomodulatory properties, may represent a potential therapeutic option.

Objectives. To evaluate the association of intramuscular immunoglobulin (IMIG) therapy with changes in pain, joint arthralgia severity, and joint mobility in patients with post-chikungunya arthralgia, and to document treatment-related adverse effects.

Methodology. This prospective observational study was conducted in a tertiary care hospital over 18 months. Sixty adults with post-chikungunya arthralgia of at least one-month duration were included. IMIG was administered as part of clinical management, and outcomes were prospectively observed before and after treatment. No additional investigational drug was administered. Pain intensity was assessed using the Visual Analogue Scale (VAS), arthralgia severity using the Patient-Reported Arthralgia Inventory (PRAI), and joint mobility by clinical range-of-motion assessment at baseline, one week, one month, and six months. Descriptive statistics, paired comparisons, Repeated measures ANOVA, and multivariable regression were used.

Results. Mean VAS decreased from 7.6 ± 1.1 at baseline to 4.9 ± 1.2 at one week, 3.1 ± 1.0 at one month, and 2.5 ± 0.8 at six months (p <0.001). Mean PRAI score decreased from 6.2 ± 1.0 at baseline to 3.8 ± 1.1 at one week, 2.4 ± 0.9 at one month, and 1.9 ± 0.7 at six months (p <0.001). At baseline, 70.0% of participants had moderate-to-severe restrictions of joint movement; at six months, 80.0% had normal or near-normal mobility. Overall functional improvement was reported by 85.0% of participants. Mild injection-site pain occurred in six patients (10.0%) and transient low-grade fever in four (6.7%); no serious adverse events or allergic reactions were observed. In multivariable analysis, a higher baseline VAS was associated with greater pain reduction, whereas increasing age and longer duration of arthralgia were associated with smaller reductions.

Conclusion. IMIG administration was associated with improvements in pain, arthralgia severity, and joint mobility in this prospective observational cohort. Controlled randomized studies are required to establish efficacy, comparative effectiveness, and safety.

Keywords. chikungunya virus, post-chikungunya arthralgia, intramuscular immunoglobulin, patient-reported arthralgia inventory, immunomodulatory therapy, visual analogue scale

ISSN 0118-3362 (Print)
eISSN 2012-3264 (Online)
Printed in the Philippines.
Copyright© 2026 by Doshi et al.
Received: August 10, 2026
Accepted: October 14, 2026
Published Online: November 12, 2026
https://doi.org/10.69472/poai.2026.18100

Corresponding author: Shubham Ramdas Sanap, MD
Maharashtra Institute of Medical Education and Research Medical College and
Dr. Bhausaheb Sardesai Talegaon Rural Hospital,
Talegaon Dabhade, Taluka Maval,
Pune, Maharashtra, India 410507
E-mail: info@mitmimer.com
ORCiD: https://orcid.org/0009-0008-5478-9760

INTRODUCTION

Chikungunya virus (CHIKV) infection is an arthropod-borne viral illness transmitted primarily by Aedes mosquitoes and is characterized in the acute phase by high-grade fever, polyarthralgia, myalgia, headache, and rash. Although acute illness is usually self-limiting, persistent musculoskeletal manifestations may occur after the acute infection, including arthralgia and inflammatory arthritis. This condition, commonly referred to as post-chikungunya arthralgia, represents the most disabling long-term sequela of CHIKV infection and significantly impairs quality of life, functional capacity, and socioeconomic productivity, particularly among adults in the working-age population.[1-5]

The clinical spectrum of CHIKV infection ranges from uncomplicated febrile illness to atypical and severe manifestations. Severe neurological disease and fatal cases have been reported, particularly in vulnerable populations.[2-4] The chronic rheumatic burden, however, represents an important cause of prolonged morbidity. Prospective and cohort studies have demonstrated persistent arthralgia, arthritis, and rheumatoid-like polyarthritis after CHIKV infection, with disease persistence influenced by factors such as age and severity of the acute illness. [6-11]

The pathophysiology of post-chikungunya arthralgia is complex and involves both persistent viral components and host immune-mediated mechanisms. Clinical and experimental studies have demonstrated evidence of viral persistence in joint tissues together with sustained inflammatory and immune responses.[12,13] In patients with post-chikungunya arthritis, altered cytokine profiles and changes in T-cell subsets have also been reported, including associations between disease activity and inflammatory cytokines such as IL-6 and TNF.[14] These findings support a multifactorial model in which viral persistence, tissue inflammation, and dysregulated host immune responses may contribute to chronic symptoms.

Conventional management of chikungunya is primarily supportive and symptomatic, as no specific antiviral therapy is currently available. Depending on the phase and severity of disease, treatment may include analgesics, antipyretics, and NSAIDs. After excluding dengue, short courses of corticosteroids can be given for selected inflammatory or refractory presentations, and physical therapy or rehabilitation may be initiated. In selected cases of persistent or chronic chikungunya arthritis, disease-modifying antirheumatic drugs (DMARDs), including hydroxychloroquine or methotrexate, may be considered. However, persistent musculoskeletal disease can remain disabling despite commonly used symptomatic treatments, and the evidence supporting specific pharmacological interventions remains limited and heterogeneous.[15-19] Rehabilitation approaches, including kinesiotherapy, may improve pain, mobility, function, and quality of life, although the evidence base remains limited.[20]

Human normal immunoglobulin has immunomodulatory effects and is used in a range of immune-mediated and inflammatory disorders. Proposed mechanisms include modulation of pathogenic antibodies, cytokine networks, complement activation, and immune-cell function.[21] Passive immunotherapy with human antibodies has also been investigated in severe manifestations of CHIKV infection, including neurological complications, with case reports describing clinical responses to immunoglobulin therapy. [22,23] Intravenous immunoglobulin (IVIG), such as Flebogamma®, is a plasma-derived product prepared from pooled human serum and contains immunoglobulin G subclasses in proportions similar to normal human plasma (IgG1 66.6%, IgG2 28.5%, IgG3 2.7%, IgG4 2.2%). While IVIG is primarily indicated for antibody deficiency syndromes at replacement doses, higher doses exert significant immunomodulatory effects and have been successfully employed in various inflammatory and autoimmune conditions, including dermatological and neurological disorders.[21]

Despite its therapeutic potential, its use is limited by high cost, requirement for hospital-based administration, and risk of systemic adverse reactions. In this context, intramuscular immunoglobulin (IMIG) represents a practical and potentially cost-effective alternative, offering ease of administration, better feasibility in outpatient settings, and a lower risk of systemic side effects. Preliminary clinical observations suggest that IMIG may be beneficial in chronic inflammatory and post-viral arthralgia by modulating aberrant immune responses and reducing inflammatory joint symptoms. However, robust clinical evidence evaluating efficacy in post-chikungunya arthralgia remains scarce.

Given the persistent morbidity associated with post-chikungunya musculoskeletal disease, the limitations of the existing evidence for conventional therapies, and the potential immunomodulatory effects of immunoglobulin therapy, the present study was undertaken to prospectively observe changes in pain, arthralgia severity, and joint mobility following IMIG administration in patients with post-chikungunya arthralgia.

METHODOLOGY

Study design and setting

This was a prospective observational study with pre- and post-treatment assessment conducted in the Department of Orthopaedics at MIMER Medical College and Dr. BSTR Hospital over a period of 18 months. The study was designed to prospectively observe outcomes among patients receiving IMIG as part of their clinical management. It was not a randomized controlled clinical trial and did not include a parallel control group.

The decision to use IMIG was made in the context of clinical management, and the study did not administer any additional investigational drug. Patients were counselled regarding the

available treatment options and the potential benefits and risks of immunoglobulin therapy. The study protocol was reviewed and approved by the Institutional Ethics Committee.

Participants

A total of 60 adult patients diagnosed with post-chikungunya arthralgia were enrolled. Sample size was determined using a prevalence-based approach incorporating the anticipated change in pain scores and feasibility within the study period.

Sample size formula

The sample size was calculated using the formula:
$n = [(Z\alpha/2 + Z\beta)^2 \times \sigma^2] / \delta^2$
$Z\alpha/2 = 1.96$,
$Z\beta = 0.84$
$\sigma = 1.5$
$\delta = 2.0$ points.
The calculated sample size was adjusted to 60.
N – 72 were screened
N – 60 were enrolled and completed six-month follow-up with 0% attrition.

Inclusion criteria

- Age ≥18 years.
- History of chikungunya infection confirmed clinically and/or serologically, defined as positive IgM anti-CHIKV ELISA or RT-PCR during acute phase.
- Persistence of joint pain for at least one month following acute chikungunya infection with mono-, oligo- or poly-articular symptoms
- Previous use of analgesic medication with inadequate relief, defined as persistent VAS ≥5 despite ≥4 weeks of optimized NSAIDs.
- Willingness to participate and provision of written informed consent.

Exclusion criteria

- Known autoimmune diseases such as systemic lupus erythematosus.
- Established rheumatoid arthritis, osteoarthritis, or seronegative inflammatory arthritis.
- Arthralgia attributable to active or recent (≤3 months) concurrent dengue, malaria, or COVID-19 confirmed by serology/PCR.
- History of hypersensitivity to immunoglobulin preparations.
- Immunoglobulin therapy within the preceding 6 months.

Intervention

BHARGLOB, a human normal immunoglobulin preparation derived from pooled plasma, was administered intramuscularly under standard aseptic precautions according to the treating physician's clinical protocol.

The specified BHARGLOB dosage was 0.75 mL/kg (total volume, 2.5–5.0 mL) via deep IM injection into the gluteal muscle. The half-life of immunoglobulin is approximately 21–28 days, which justified the 6-month exclusion window.

No additional investigational drug was administered as part of the study.

Primary outcome measures

Change in pain intensity measured using the Visual Analogue Scale (VAS) at baseline, one week, one month, and six months.

Secondary outcome measures

- Change in arthralgia severity measured using the Patient-Reported Arthralgia Inventory (PRAI)[24]
- Improvement in joint mobility evaluated via goniometric range-of-motion (ROM) measurement
- Functional improvement cross-validated using the validated Health Assessment Questionnaire–Disability Index (HAQ-DI).

Data collection

Baseline assessment included demographic characteristics, clinical history, duration of symptoms, pain severity, arthralgia severity, and joint mobility. Follow-up assessments were conducted at 1 week, 1 month, and 6 months after treatment. At each visit, VAS, PRAI, and joint mobility were recorded.

Statistical analysis

Data was entered into Microsoft Excel and analyzed using SPSS version 26. Descriptive statistics were used to summarize demographic and clinical characteristics.

- Paired t-tests were used for pre- and post-treatment continuous variables.
- Repeated measures ANOVA with post-hoc analysis was used to evaluate changes across multiple time points.
- Multivariable linear regression was performed to explore associations between patient characteristics and reduction in VAS score at six months. A p-value <0.05 was considered statistically significant.

Ethical considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Paper-based records were stored in a secured and restricted-access location and were accessible only to authorized study personnel. Electronic study files were password protected and secured against unauthorized access. Direct patient identifiers were removed from study datasets whenever feasible and were not included in the analytical dataset. Patients were informed about the nature of the treatment, its potential benefits and risks, and their

right to participate voluntarily and withdraw from the study without affecting their clinical care.

The immunoglobulin used was a commercially available preparation used in clinical practice. No additional payment was made to participants specifically for research participation; patients receiving the medicine bore the relevant treatment cost as part of their clinical care. Clinical consultation and counselling related to the study were provided without additional research-related charges. The study did not administer treatment solely for research purposes; rather, outcomes of patients receiving the treatment as part of clinical management were prospectively observed.

RESULTS

Baseline characteristics

The study included 60 participants with a mean age of 42.6 ± 11.8 years. There were 26 males (43.3%) and 34 females (56.7%). The mean duration of arthralgia before enrolment was 2.8 ± 1.3 months. Fourteen patients (23.3%) had monoarticular involvement, 19 (31.7%) had oligoarticular involvement, and 27 (45.0%) had polyarticular involvement. The knee, ankle, and wrist were the most commonly involved joints (Table 1).

Pain outcomes

The mean VAS score decreased from 7.6 ± 1.1 at baseline to 4.9 ± 1.2 at one week, 3.1 ± 1.0 at one month, and 2.5 ± 0.8 at six months (Table 2). The overall change across time points was statistically significant (p <0.001). The maximum clinical improvement occurred within the first week.

Table 1. Baseline demographic and clinical characteristics

Variable	Value
Age, mean ± SD (years)	42.6 ± 11.8
Male, n (%)	26 (43.3%)
Female, n (%)	34 (56.7%)
Duration of arthralgia, mean ± SD (months)	2.8 ± 1.3
Monoarticular, n (%)	14 (23.3%)
Oligoarticular, n (%)	19 (31.7%)
Polyarticular, n (%)	27 (45.0%)
Most commonly involved joints	Knee (78.3%) Ankle (65.0%) Wrist (51.7%) PIP/MCP (38.3%)

Table 2. Comparison of VAS pain scores

Time point	Mean VAS ± SD	*p* value*
Baseline	7.6 ± 1.1	—
1 week	4.9 ± 1.2	<0.001
1 month	3.1 ± 1.0	<0.001
6 months	2.5 ± 0.8	<0.001

* Repeated measures ANOVA with post-hoc analysis. The largest absolute reduction occurred during the first week (ΔVAS −2.7 points), followed by further gradual improvement through one month and six months.

Arthralgia severity

Mean PRAI score decreased from 6.2 ± 1.0 at baseline to 3.8 ± 1.1 at one week, 2.4 ± 0.9 at one month, and 1.9 ± 0.7 at six months (Table 3). The change across follow-up was statistically significant (p <0.001). Delta PRAI within the first week was 2.4 points.

Joint mobility and functional outcome

At baseline, 12 patients (20.0%) had normal or near-normal mobility, 18 (30.0%) had mild restriction, 21 (35.0%) had moderate restriction, and nine (15.0%) had severe restriction (Table 4). At six months, 48 patients (80.0%) had normal or near-normal mobility, eight (13.3%) had mild restrictions, three (5.0%) had moderate restrictions, and one (1.7%) had severe restrictions. Overall functional improvement was reported by 85.0% of participants in six months.

Adverse effects

IMIG was generally well tolerated. Mild local injection-site pain was reported in six patients (10.0%), and transient low-grade fever occurred in four patients (6.7%). No serious adverse events or allergic reactions were observed during the study period.

Multivariable regression analysis

A higher baseline VAS was independently associated with greater pain reduction at 6 months (β = 0.58, p <0.001) (Table 5). Increasing age (β = −0.07, p = 0.031) and longer

Table 3. Changes in PRAI scores

Time point	Mean PRAI ± SD	*p* value*
Baseline	6.2 ± 1.0	—
1 week	3.8 ± 1.1	<0.001
1 month	2.4 ± 0.9	<0.001
6 months	1.9 ± 0.7	<0.001

*Repeated measures ANOVA
PRAI – Patient-Reported Arthralgia Inventory

Table 4. Distribution of joint mobility status

Joint mobility status	Baseline, n (%)	6 months, n (%)
Normal / near normal	12 (20.0%)	48 (80.0%)
Mild restriction	18 (30.0%)	8 (13.3%)
Moderate restriction	21 (35.0%)	3 (5.0%)
Severe restriction	9 (15.0%)	1 (1.7%)

Table 5. Multivariable linear regression for reduction in VAS at 6 months

Predictor	β	SE	95% CI	*p* value
Age (years)	−0.07	0.03	−0.14 to −0.01	0.031
Duration of arthralgia (months)	−0.19	0.07	−0.33 to −0.06	0.006
Baseline VAS	0.58	0.09	0.41 to 0.75	<0.001
Female vs male	−0.04	0.17	−0.38 to 0.30	0.801

duration of arthralgia before treatment ($\beta = -0.17$, $p = 0.006$) were associated with smaller reductions in pain. Sex was not significantly associated with treatment response ($p = 0.801$). The regression model was statistically significant ($F = 15.4$, $p < 0.001$) and explained approximately 52% of the variance in pain reduction ($R^2 = 0.52$; adjusted $R^2 = 0.49$).

Model statistics

- $R^2 = 0.52$
- Adjusted $R^2 = 0.49$
- $F = 15.4$
- $p < 0.001$

DISCUSSION

In this prospective observational study of 60 patients with post-chikungunya arthralgia, we observed clinically significant reductions in pain and stiffness following administration of intramuscular immunoglobulin (IMIG). Mean Visual Analogue Scale (VAS) pain scores decreased from 7.6 ± 1.1 at baseline to 4.9 ± 1.2 at one week, 3.1 ± 1.0 at one month, and 2.5 ± 0.8 at six months ($p < 0.001$). Similarly, mean PRAI stiffness scores reduced from 6.2 ± 1.0 to 2.4 ± 0.9 at one month and 1.9 ± 0.7 at six months ($p < 0.001$) (Tables 2 and 3). These findings suggest that IMIG may provide a rapid and sustained improvement in symptom severity among patients with chronic arthralgia following chikungunya infection. Chronic musculoskeletal manifestations, including arthralgia and arthritis, are well-recognized sequelae of chikungunya virus (CHIKV) infection. Nearly 40–60% of patients develop lingering joint symptoms lasting three or more months after acute illness, a condition often described as chronic chikungunya arthritis (CCA) or post-chikungunya arthralgia. In a narrative review, more than 40% of infected individuals had arthritic manifestations >3 months post-infection, with patterns ranging from polyarthritis to nonspecific arthralgia consistent with post-viral arthralgia.[25]

The natural history of chikungunya includes a spectrum of persistent rheumatic manifestations. Previous studies have documented persistent arthralgia and arthritis months to years after acute infection, with substantial effects on function and quality of life.[6-11] The burden is clinically important because persistent joint symptoms may interfere with activities of daily living and may require prolonged treatment and rehabilitation.

The pathogenesis of chronic chikungunya musculoskeletal disease is multifactorial. Persistent viral material has been demonstrated in joint tissues in experimental and human studies, while chronic disease is also associated with sustained inflammatory and adaptive immune responses.[12,13] A cross-sectional study of patients with post-chikungunya arthritis found associations between disease activity and inflammatory cytokines, including IL-6 and TNF, together with alterations in regulatory T-cell populations.[14] These findings provide biological plausibility for investigating therapies that may modify immune pathways, although they do not establish that immune dysregulation is the sole cause of chronic symptoms. These immunological patterns may partly explain why conventional analgesics or NSAIDs often provide only partial or transient relief; they primarily target symptomatic inflammation rather than the underlying immune imbalance.

Conventional management remains largely symptomatic and phase-dependent. National and international guidance describes the use of analgesics, NSAIDs, corticosteroids, selected DMARDs, and physical rehabilitation according to disease severity and chronicity.[15,17] The systematic review by Martí-Carvajal et al. identified randomized trials evaluating chloroquine, NSAIDs, corticosteroids, and DMARDs, but concluded that the overall evidence was of very low quality because of small samples, heterogeneity, and risk of bias.[16] More recent observational data also suggest that DMARD-based treatment may benefit selected patients with chikungunya arthritis, although these data do not establish a standardized treatment regimen.[26]

Published studies on therapeutic strategies for chronic CHIKV-related arthralgia have primarily evaluated symptomatic treatments or repurposed disease-modifying antirheumatic drugs (DMARDs) rather than immunomodulatory therapies. Methotrexate (MTX), a DMARD commonly used in rheumatoid arthritis, has been investigated in some cohorts with chronic chikungunya arthritis and was found to improve pain and disease activity when combined with corticosteroids over four weeks, as measured by VAS and composite disease activity scores.[26] In these cohorts, combination pharmacotherapy produced measurable reductions in pain, though the variability in outcome measures and lack of standardized trials limit direct quantification.

Compared to these published trends, the magnitude of pain reduction observed in our study with IMIG (mean VAS reduction of ~4.5 points at one month) compares favorably with outcomes reported with pharmacologic DMARD-based regimens, where clinical improvements were documented but often required several weeks of therapy.[26] Additionally, IMIG demonstrated rapid onset of benefit, with statistically significant symptom relief by the first week post-treatment. This contrasts with many DMARD regimens, which typically exhibit slower onset of effect due to their mechanisms of action requiring weeks to months to reach maximal immunomodulatory effect.

Non-pharmacologic approaches such as physiotherapy and neuromodulation (e.g., transcranial direct current stimulation) have also shown potential in reducing pain and improving functional outcomes in chronic chikungunya arthralgia, indicating the multifactorial nature of chronic musculoskeletal symptoms and the potential role of multidisciplinary treatment strategies.[20] However, most of these studies did not use standardized immunomodulatory agents like immunoglobulin and were limited by small sample sizes or pilot designs.

Physical therapy and musculoskeletal rehabilitation are important components of management for persistent symptoms. A 2023 systematic review found that rehabilita-

tion approaches, particularly kinesiotherapy with or without electrothermophototherapy and other functional rehabilitation strategies, may improve pain, quality of life, and functional outcomes, although the evidence remains limited.[20]

Against this background, immunoglobulin therapy represents a biologically plausible but insufficiently studied therapeutic approach. Human immunoglobulin has multiple immunomodulatory actions, including effects on antibody-mediated inflammation, cytokine networks, complement activation, and immune-cell function.[21] Human immunoglobulin has also been reported in severe CHIKV-associated neurological disease, including chikungunya encephalitis and Guillain-Barré syndrome.[22,23,27]

Immunoglobulin therapy has long been used in immune-mediated and inflammatory disorders for its multimodal immunomodulatory effects, including neutralization of pathogenic autoantibodies, modulation of cytokine networks, Fc receptor blockade, and regulatory effects on immune cell function. Although intravenous immunoglobulin (IVIG) has been more extensively studied, its use is limited by cost, accessibility, and systemic adverse effects. IMIG, as used in the present study, offers a practical outpatient-friendly alternative that demonstrated symptomatic improvement with a favorable safety profile.

The significant reductions in VAS and PRAI scores observed in our cohort suggest that IMIG may act on underlying immune pathways that contribute to chronic pain and stiffness in post-CHIKV arthralgia. Unlike purely symptomatic treatments (e.g., NSAIDs), the immunomodulatory effects of IMIG may contribute to more durable symptom relief. This is particularly relevant given the lack of standardized, high-quality randomized trials on immunomodulatory therapies in this condition, as noted in previous literature reviews where no consensus exists on optimal chronic treatment strategies for CCA.[20] In contrast to published studies that primarily emphasize DMARDs like MTX and supportive measures, the results from our study suggest an additional therapeutic avenue that merits further investigation. Importantly, IMIG was well tolerated; no serious adverse events were reported, and minor local reactions were the only side effects observed. This safety profile is favorable compared to potential systemic adverse effects associated with long-term steroid or DMARD therapy. The regression analysis showed that patients with higher baseline pain scores experienced greater reductions in VAS, whereas increasing age and longer duration of arthralgia were associated with smaller improvements. These associations may help identify clinical factors related to recovery, but they should not be interpreted as predictors of IMIG efficacy without validation in controlled studies.

The favorable short-term safety profile observed in this cohort is encouraging. Only mild injection-site pain and transient low-grade fever were reported, and no serious adverse events or allergic reactions were observed. However, the sample size was small, and the absence of serious adverse events in this cohort does not establish the overall safety profile of IMIG. Larger studies with systematic adverse-event surveillance are necessary.

The present findings therefore support further investigation rather than definitive therapeutic recommendations. In particular, randomized controlled trials comparing IMIG with conventional management or placebo, with standardized diagnostic criteria, validated outcomes, adequate sample size, and longer follow-up are required.

Strengths and limitations

The strengths of this study include its prospective design, predefined follow-up intervals, repeated assessment of pain and arthralgia severity, assessment of joint mobility, and prospective recording of adverse effects. The use of multivariable regression also allowed exploration of factors associated with change in pain.

The principal limitation is the absence of a randomized control group. Therefore, causal efficacy of IMIG cannot be established. Additional limitations include the relatively small sample size, single-center design, potential selection bias, possible confounding by the natural history of post-chikungunya disease and concurrent care, and follow-up limited to six months. The observational pre-post design may overestimate treatment-associated improvement. The study also did not compare IMIG directly with NSAIDs, corticosteroids, DMARDs, or rehabilitation alone. Future studies should address these limitations through randomized controlled designs with adequate sample size and longer follow-up.

CONCLUSION

In this prospective observational cohort, intramuscular immunoglobulin administration was associated with significant reductions in pain and arthralgia severity and improvement in joint mobility among patients with post-chikungunya arthralgia. The treatment was generally well tolerated, with no serious adverse events observed in this cohort. However, because the study lacked a randomized control group, the observed improvements cannot be attributed definitively to IMIG. The findings should therefore be regarded as preliminary and hypothesis-generating. Well-designed randomized controlled trials are required to determine the efficacy, comparative effectiveness, optimal dosing strategy, and long-term safety of IMIG in post-chikungunya arthralgia.

STATEMENT OF AUTHORSHIP

All authors certified fulfilment of ICMJE authorship criteria.

CREDIT AUTHOR STATEMENT

SSD: Conceptualization, Investigation, Data curation, Writing – original draft preparation, Writing – review and editing, Visualization, Project administration; **SSB:** Methodology, Resources, Writing – original draft preparation, Writing –

review and editing, Visualization; **SRS:** Conceptualization, Formal analysis, Investigation, Data curation, Visualization, Writing – original draft preparation, Writing – review and editing; **SK:** Validation, Supervision, Project administration; **RT:** Software, Resources; **VP:** Formal analysis, Investigation, Supervision, Project administration; **AG:** Investigation, Supervision, Project administration.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed in this study are included in the published article.

FUNDING SOURCE

None.

REFERENCES

1. Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. J Gen Virol. 2007;88(Pt 9): 2363-77. PMID: 17698645 DOI:10.1099/vir.0.82858-0
2. Lemant J, Boisson V, Winer A, et al. Serious acute chikungunya virus infection requiring intensive care during the Reunion Island outbreak in 2005–2006. Crit Care Med. 2008;36(9):2536-41. PMID: 18679124 DOI:10.1097/CCM.0b013e318183f2d2
3. Economopoulou A, Dominguez M, Helynck B, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005-2006 outbreak on Réunion. Epidemiol Infect. 2009;137(4):534-41. PMID: 18694529 DOI:10.1017/S0950268808001167
4. Sá PKO, Nunes MM, Leite IR, et al. Chikungunya virus infection with severe neurologic manifestations: report of four fatal cases. Rev Soc Bras Med Trop. 2017;50(2):265-8. PMID: 28562768 DOI:10.1590/0037-8682-0375-2016
5. Duarte M do CMB, Oliveira Neto AF de, Bezerra PG de M, et al. Chikungunya infection in infants. Rev Bras Saúde Matern Infant. 2016;16(Suppl 1):S63-71. DOI:10.1590/1806-9304201600s100006
6. Imad HA, Matsee W, Kludkleeb S, et al. Post-Chikungunya virus infection musculoskeletal disorders: syndromic sequelae after an outbreak. Trop Med Infect Dis. 2021;6(2):52. PMID: 33921055 PMCID: PMC8167736 DOI:10.3390/tropicalmed6020052
7. Chopra A, Anuradha V, Ghorpade R, Saluja M. Acute Chikungunya and persistent musculoskeletal pain following the 2006 Indian epidemic: a 2-year prospective rural community study. Epidemiol Infect. 2012;140(5):842-50. PMID: 21767452 DOI:10.1017/S0950268811001300
8. Borgherini G, Poubeau P, Jossaume A, et al. Persistent arthralgia associated with chikungunya virus: a study of 88 adult patients on Reunion island. Clin Infect Dis. 2008;47(4):469-75. PMID: 18611153 DOI:10.1086/590003
9. Sissoko D, Malvy D, Ezzedine K, et al. Post-epidemic Chikungunya disease on Reunion Island: course of rheumatic manifestations and associated factors over a 15-month period. PLoS Negl Trop Dis. 2009;3(3):e389. PMID: 19274071 PMCID: PMC2647734 DOI:10.1371/journal.pntd.0000389
10. Essackjee K, Goorah S, Ramchurn SK, Cheeneebash J, Walker-Bone K. Prevalence of and risk factors for chronic arthralgia and rheumatoid-like polyarthritis more than 2 years after infection with chikungunya virus. Postgrad Med J. 2013;89(1054):440-7. PMID: 23645664 DOI:10.1136/postgradmedj-2012-131477
11. Gérardin P, Fianu A, Michault A, et al. Predictors of Chikungunya rheumatism: a prognostic survey ancillary to the TELECHIK cohort study. Arthritis Res Ther. 2013;15(1):R9. PMID: 23302155 PMCID: PMC3672753 DOI:10.1186/ar4137
12. Hoarau JJ, Jaffar Bandjee MC, Krejbich Trotot P, et al. Persistent chronic inflammation and infection by Chikungunya arthritogenic alphavirus in spite of a robust host immune response. J Immunol. 2010;184(10):5914-27. PMID: 20404278 DOI:10.4049/jimmunol.0900255
13. Hawman DW, Stoermer KA, Montgomery SA, et al. Chronic joint disease caused by persistent Chikungunya virus infection is controlled by the adaptive immune response. J Virol. 2013;87(24):13878-88. PMID: 24131709 PMCID: PMC3838294 DOI:10.1128/JVI.02666-13
14. Chang AY, Tritsch SR, Herrera Gomez CA, et al. Cytokine and T cell responses in post-chikungunya viral arthritis: a cross-sectional study. PLoS One. 2024;19(3):e0299521. PMID: 38507338 PMCID: PMC10954186 DOI:10.1371/journal.pone.0299521
15. National Center for Vector Borne Diseases Control. National guidelines for clinical management of chikungunya fever. New Delhi: Ministry of Health and Family Welfare, Government of India; 2023. https://ncvbdc.mohfw.gov.in/Doc/National-Guidelines-for-Clinical-Management-of-Chikungunya-Fever-2023.pdf
16. Martí-Carvajal A, Ramon-Pardo P, Javelle E, et al. Interventions for treating patients with chikungunya virus infection-related rheumatic and musculoskeletal disorders: a systematic review. PLoS One. 2017;12(6):e0179028. PMID: 28609439 PMCID: PMC5469465 DOI:10.1371/journal.pone.0179028
17. Simon F, Javelle E, Cabie A, et al; Société de pathologie infectieuse de langue française. French guidelines for the management of chikungunya (acute and persistent presentations). November 2014. Med Mal Infect. 2015;45(7):243-63. PMID: 26119684 DOI:10.1016/j.medmal.2015.05.007
18. Natesan SK, Chandrasekar PH. Chikungunya virus. Medscape. Accessed September 13, 2026.
19. Pathak H, Mohan MC, Ravindran V. Chikungunya arthritis. Clin Med (Lond). 2019;19(5):381-5. PMID: 31530685 PMCID: PMC6771335 DOI:10.7861/clinmed.2019-0035
20. Sales WB, Leite DG, Truta Ramalho CS, Macêdo SGGF, de Souza GF, Cavalcanti Maciel ÁC. Contributions of musculoskeletal rehabilitation in patients after chikungunya fever: a systematic review. BMC Musculoskelet Disord. 2023;24(1):347. PMID: 37143009 PMCID: PMC10157903 DOI:10.1186/s12891-023-06450-6
21. Jolles S, Hughes J, Whittaker S. Dermatological uses of high-dose intravenous immunoglobulin. Arch Dermatol. 1998;134(1):80-6. PMID: 9449914 DOI:10.1001/archderm.134.1.80
22. Chusri S, Siripaitoon P, Hirunpat S, Silpapojakul K. Case reports of neuro-Chikungunya in southern Thailand. Am J Trop Med Hyg. 2011;85(2):386-9. PMID: 21813863 PMCID: PMC3144841 DOI:10.4269/ajtmh.2011.10-0725
23. Scott SSO, Braga-Neto P, Pereira LP, et al. Immunoglobulin-responsive chikungunya encephalitis: two case reports. J Neurovirol. 2017;23(4):625-31. PMID: 28577289 DOI:10.1007/s13365-017-0535-y
24. Castel LD, Wallston KA, Saville BR, et al. Validity and reliability of the Patient-Reported Arthralgia Inventory: validation of a newly-developed survey instrument to measure arthralgia. Patient Relat Outcome Meas. 2015;6:205-14. PMID: 26251635 PMCID: PMC4524452 DOI:10.2147/PROM.S47997
25. Amaral JK, Bilsborrow JB, Schoen RT. Chronic Chikungunya arthritis and rheumatoid arthritis: what they have in common. Am J Med. 2020;133(3):e91-7. PMID: 31705850 PMCID: PMC7385732 DOI:10.1016/j.amjmed.2019.10.005
26. Amaral JK, Bingham CO, Taylor PC, Vilá LM, Weinblatt ME, Schoen RT. Therapy for Chikungunya arthritis: a study of 133 Brazilian patients. Am J Trop Med Hyg. 2023;109(3):542-7. PMID: 37549898 PMCID: PMC10484246 DOI:10.4269/ajtmh.23-0205
27. Balavoine S, Pircher M, Hoen B, et al. Guillain-Barré syndrome and chikungunya: description of all cases diagnosed during the 2014 outbreak in the French West Indies. Am J Trop Med Hyg. 2017;97(2):356-60. PMID: 28722564 PMCID: PMC5544060 DOI:10.4269/ajtmh.15-0753

Disclaimer. All articles and materials published in PJO are solely those of the authors. Statements and opinions expressed by authors do not represent those of the editor/s of the Philippine Journal of Orthopaedics or of its publisher, the Philippine Orthopaedic Association.