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The prevalence of *Leishmania* RNA virus in cutaneous leishmaniasis: a meta-analysis and systematic review

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Abstract

Background While numerous studies have investigated the role and presence of RNA viruses within Leishmania parasites, the existing literature presents a fragmented view of *Leishmania* RNA virus (*LRV*) prevalence in parasites associated with cutaneous leishmaniasis (CL). Therefore, the present study aimed to elucidate the prevalence of *LRV* in parasites obtained from patients with CL.

Methods To achieve this aim, we conducted a systematic literature search across international databases, specifically Web of Science, PubMed, Embase, and Scopus. We extracted relevant studies reporting the prevalence of *LRV* in parasites obtained from patients with CL, utilizing predefined keywords and covering the period from December 1988 to August 2024. The extracted data underwent meta-analysis using a random-effects model, with statistical analyses performed in STATA version 14.

Results Our search yielded 44 studies that fulfilled the eligibility criteria, representing a total sample size of 2,276 participants. *LRV* detection was performed on biopsied lesion fragments and cultured isolates derived from these lesions. Among the 2,276 CL patients, 647 tested positive for *LRV*. We observed regional variations in *LRV* prevalence, with 45.16% in the New World (NW) and 30.00% in the Old World (OW). The majority of included studies examined *Leishmania (Viannia) guyanensis*, *L. (V.) braziliensis*, *L. (Leishmania) major*, *and Leishmania* (*L.*) *tropica. LRV* prevalence was 32.26% in lesion biopsies and 30.96% in cultured isolates. Notably, *LRV* exhibited a high prevalence in *Leishmania* species obtained from mucocutaneous leishmaniasis (MCL), suggesting a strong association between *LRV1* and this clinical manifestation in the NW.

Conclusion This study demonstrated a substantial prevalence of *LRV* in CL. *LRV* was identified in both lesion biopsies and cultured isolates, revealing significant regional variations with higher prevalence in the NW compared to the OW. Furthermore, a strong association was observed between *LRV1* and MCL in the NW.

Keywords *Leishmania* RNA virus, Cutaneous leishmaniasis, Prevalence

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particularly involving larger sample sizes and cross-species comparisons, is warranted to elucidate the complex role of *LRV*s in leishmaniasis.

Paranaiba et al. (2018) [63] reported that *L. (L.) major*, which exhibited a 38.5% *LRV* prevalence in our study, typically induces self-healing lesions, whereas *L. (L.) tropica* (20.6% prevalence) is more frequently associated with chronic cutaneous leishmaniasis (CCL), a condition characterized by persistent and recurrent lesions.

The increased pathogenicity of NW *Leishmania* species may be attributed to their capacity to modulate the host immune system through TLR3 and type I interferon (IFN-I) signaling pathways. This observation aligns with our findings, which revealed a significantly higher *LRV* prevalence in metastatic cases (30.6%) compared with non-metastatic cases (25.34%). Atayde et al. (2019) [14] and Ives et al. (2011) [17] have linked this inflammatory response to treatment resistance, particularly in *LRV1*-bearing parasites, which exhibit reduced clearance following standard pentavalent antimonial (SbV) therapy.

LRV1 exhibits a strong association with mucosal involvement and disease dissemination [64, 65]. Our study further investigated *LRV* prevalence across distinct clinical forms of CL, revealing rates of 36.0% in CL, 22.36% in ML/MCL, and 2.88% in DCL/DL. Hartley et al. (2014) [66] have previously documented lower cure rates for *LRV1*-positive *L. (V) guyanensis* and *L. (V) braziliensis* infections treated with SbV therapy, which corroborates our data demonstrating higher *LRV* prevalence in severe disease forms.

Conclusion

Our findings are consistent with previous research indicating that *LRV1* is frequently associated with metastatic and severe forms of CL, potentially contributing to immune modulation and treatment resistance. However, the role of *LRV*2 in exacerbating CL remains unclear. The variability in findings across studies suggests that the mere presence of *LRV* may not reliably predict disease severity. Instead, host-related factors, environmental influences, and migration patterns likely contribute to *LRV* distribution and its impact on clinical outcomes.

Given the observed regional variations and the complex interactions between *LRV*s, *Leishmania* species, and host immune responses, further large-scale studies are essential. Future research should prioritize broader geographical coverage, standardized methodologies, and in-depth investigations into the mechanisms underlying *LRV*-associated pathogenesis. A comprehensive understanding of these factors will be critical for refining disease management strategies and developing targeted therapeutic interventions.

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Authors' contributions
N.Y. and GH.H. wrote the main manuscript text, and M.D. prepared Figs. 1, 2, 3, 4, 5 and 6. All authors reviewed the manuscript.

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Data availability
The data that support the findings of this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
Not Applicable.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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