Prognostic models predicting clinical outcomes in patients diagnosed with visceral leishmaniasis: a systematic review

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Introduction

Visceral leishmaniasis (VL) is a neglected tropical disease prevalent in populations affected by poverty, war, and famine. Without effective treatment, death is the norm. Prognostic models, as used by Médecins Sans Frontières (MSF) in East Africa, are used to identify high-risk patients for intensive management, including hospital admission, treatment with liposomal amphotericin B, broad-spectrum antibiotics, and blood transfusions. We provide a comprehensive and objective resource for policymakers, healthcare providers, and investigators, by identifying, summarising, and appraising the available prognostic models predicting clinical outcomes in patients with VL.

Methods

We performed a systematic review of published studies that developed, validated, or updated models predicting future clinical outcomes in patients diagnosed with VL. We searched five bibliographic databases (Ovid Embase, Ovid MEDLINE, Web of Science Core Collection, SciELO, and LILACS) on March 1, 2023, for papers published from database inception, with no language restriction. Screening, data extraction, and risk of bias assessment were performed in duplicate. This study is registered with PROSPERO (ID: CRD42023417226).

Ethics

This study is a systematic review of published studies and therefore does not require ethics review.

Results

Eight prognostic model studies, published between 2003 and 2021, were identified describing 12 prognostic model developments and 19 external validations. Nine models were developed in Brazil and three in East Africa by MSF investigators (two developed in South Sudan and one in Ethiopia). In-hospital mortality was the outcome for all but two Brazilian models, which predicted registry-reported mortality. Three models were developed exclusively in adolescents or children. Risk of bias was assessed as high for all model evaluations. Model overfitting due to small sample sizes, leading to optimistic model performance measures and exaggerated risk estimates, was identified for all but one model development. Only half of the presented risk scores were reproducible by following the authors' methodology.

Conclusion

A poorly developed model can result in inaccurate risk estimation, potentially leading to harmful and inequitable decision making. With half of all risk scores incorrectly calculated, and a high risk of bias identified across all model evaluations, caution must be exercised when using these models to guide patient management. In the first systematic review of VL prognostic models, we show that no models predicted treatment failure and relapse, and despite South Asia representing the highest VL burden before 2010, no models were developed in this population. These represent important evidence gaps, which should be prioritised when developing new models. Using the Infectious Diseases Data Observatory repository of VL individual patient data from clinical trials, we are currently building a prognostic model for VL relapse in South Asia, which we hope to serve the ongoing elimination campaign.

Conflicts of interest

All authors declare no competing interests.