

Reactivation of Old World Tegumentary Leishmaniasis Following Iatrogenic Immunosuppression: Occurrence and Role for Secondary Prophylaxis

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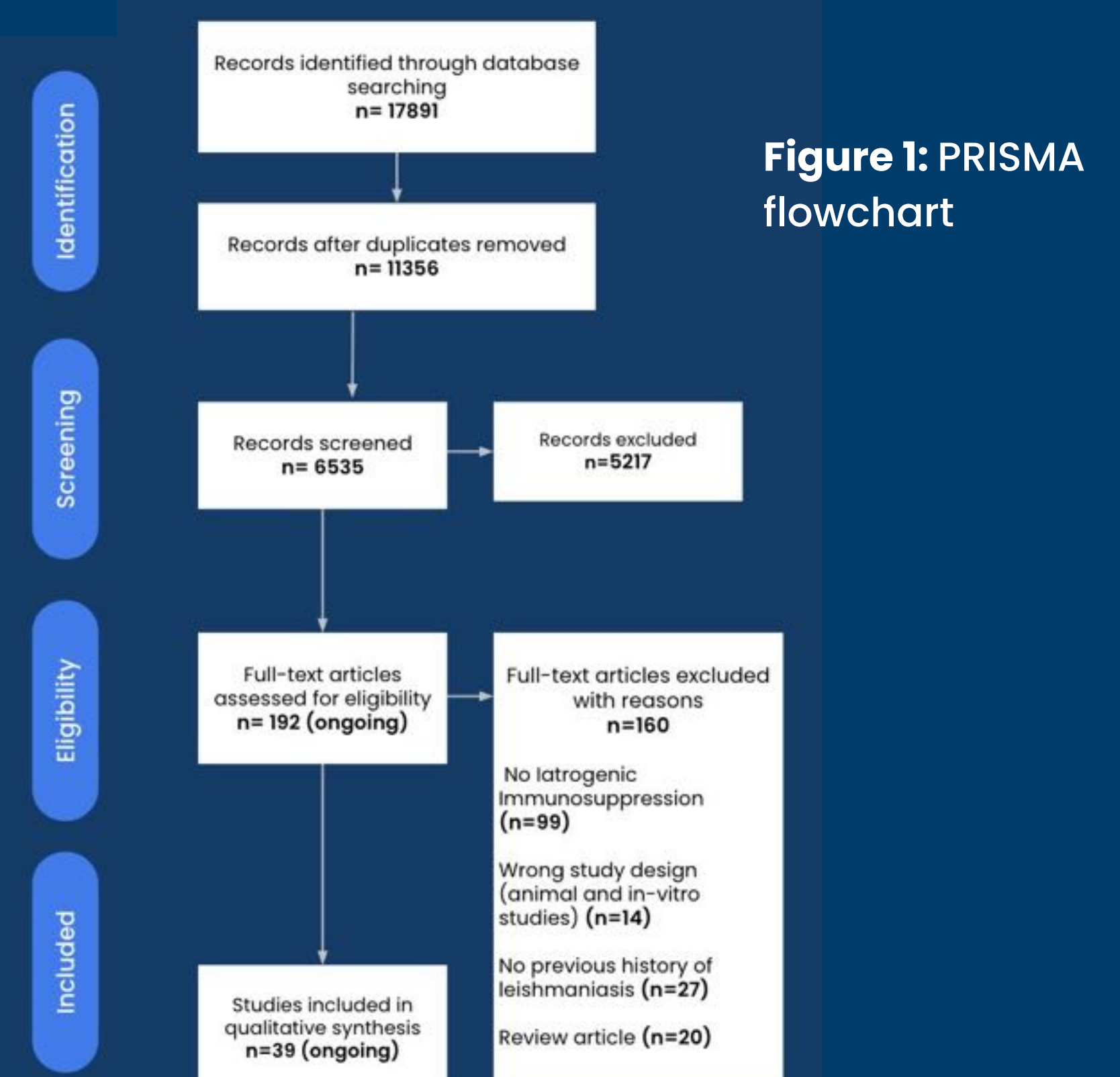
Introduction

- Old world tegumentary leishmaniasis (OWTL) is a neglected tropical disease caused mainly by the species *L. donovani*, *L. aethiopica*, *L. tropica*, *L. major* and *L. infantum*.
- Recent increases in global migration, travel, and climate change contribute to the growing burden of OWTL¹.
- Iatrogenic immunosuppression can increase the risk of reactivation and severe disease manifestations due to weakened immunological control².
- Currently, the role for secondary prophylaxis in preventing such outcomes is unknown.

Objective: We aim to synthesize the available data surrounding leishmaniasis reactivation and corresponding immunosuppressive regimens as well as the potential role of secondary prophylaxis in order to guide healthcare providers on the clinical management of this patient population.

Methods

- PubMed (NCBI), Medline (OVID), Embase (OVID), Web of Science (BioSIS) and LILACS (VHL) were searched for between inception to February 27, 2023 with combinations of the search terms "Leishmania reactivation", "Leishmaniasis" and "secondary prophylaxis".
- Case series, case reports, cohort studies, clinical trials and relevant systematic reviews and meta-analyses of all languages are being included in this systematic review.
- Screening is being independently performed by two reviewers with conflicts resolved by a third reviewer.
- Quality assessment of studies reporting therapeutic interventions will be conducted using the GRADE approach³.



Results

First Author, Year	Country	Species	Manifestations (primary → reactivations)	Iatrogenic Immunosuppression	Primary Treatment	Treatment for Reactivations	Secondary Prophylaxis Regimen	Outcomes
Richter, 2011	Germany (history of travel to Spain)	<i>L. infantum</i>	ML → ML	Treatment for systemic lupus erythematosus	L-AmB	Miltefosine	Extended Miltefosine	Success. No recurrence.
Perez-Jacoi ste Asin, 2017	Spain	Unspecified	VL → ML → VL	Kidney Transplant Regimen: Prednisone, tacro, MPA (mycophenolic acid)	L-AmB	Reactivation 1: L-AmB Reactivation 2: Miltefosine	L-AmB for 12 months	Success. No third recurrence.
Darcis, 2017	Belgium (history of travel to Spain)	<i>L. infantum</i>	VL → CL → CL → CL + ML	1. EBV-negative classical Hodgkin lymphoma Treatment: C-MOPP + radiation therapy for EBV-negative 2. Rheumatoid arthritis: Entanercept (later switched to Rituximab), ciclosporin, methylprednisolone	L-AmB	L-AmB	Monthly AmB	Implementation after primary infection and reactivation 1 resulted in failure. Secondary prophylaxis was not used after reactivation 2 and 3.
Micallef, 2014	Malta	<i>L. donovani</i>	CL (no recurrence to date)	Treatment for seronegative arthritis: Adalimumab, anti-TNF, methotrexate	Sodium stibogluconate	n/a	Monthly sodium stibogluconate	No recurrence to date.
Nieto Gomez, 2019	Spain	not specified	CL (no recurrence to date)	Treatment for psoriatic arthritis: Infliximab and methotrexate	L-AmB	n/a	Monthly L-AmB	No recurrence to date but patient is still being followed up.

Table 1: Summary of preliminary data on cases of OWTL reactivation and outcomes of secondary prophylaxis.

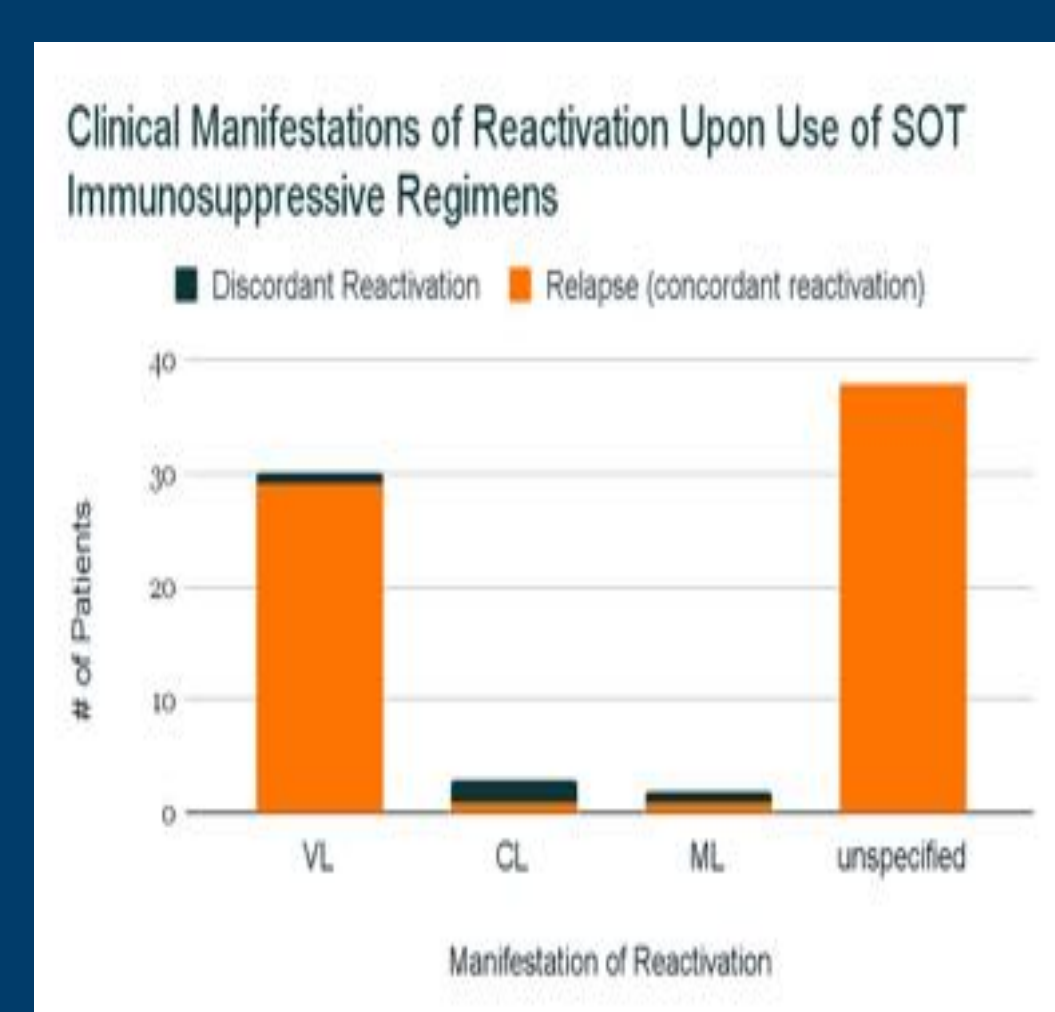


Figure 2. Clinical manifestations of reactivation in solid organ transplant (SOT) recipients upon use of immunosuppressive regimens.

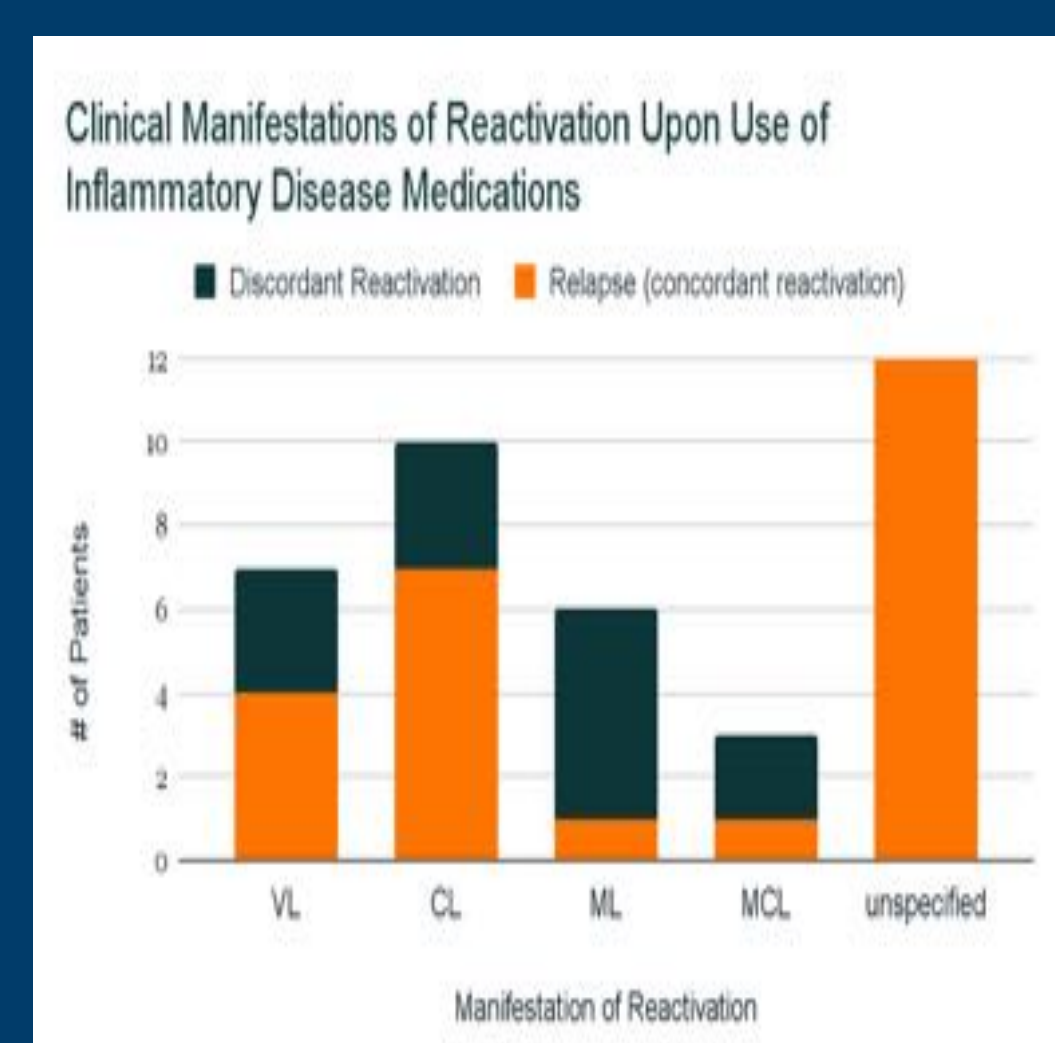


Figure 3. Clinical manifestations of reactivation upon use of immunosuppressive treatments for inflammatory diseases.

Discussion

- VL and CL were shown to be the most common forms of reactivation in transplant recipients and inflammatory disease patients, respectively.
- Currently, numerous review papers support the use of secondary prophylaxis in preventing relapse of VL, but the same confidence does not exist for OWTL.
- The role of secondary prophylaxis in the context of OWTL remains inconclusive due to the dearth of data around this topic. Thus, this systematic review aims to further investigate its role in order to guide the clinical management of this patient population.

References

