

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* & *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
- The role for secondary prophylaxis in preventing such outcomes is currently unknown

- Objective:** We aim to synthesize available data surrounding leishmaniasis reactivation and immunosuppressive regimens as well as the potential role of secondary prophylaxis to guide healthcare providers on clinical management

Methods

- Five databases were searched from database inception to March 2024
- Conducted in accordance with PRISMA guidelines
- Certainty & quality of evidence evaluated via the GRADE framework³

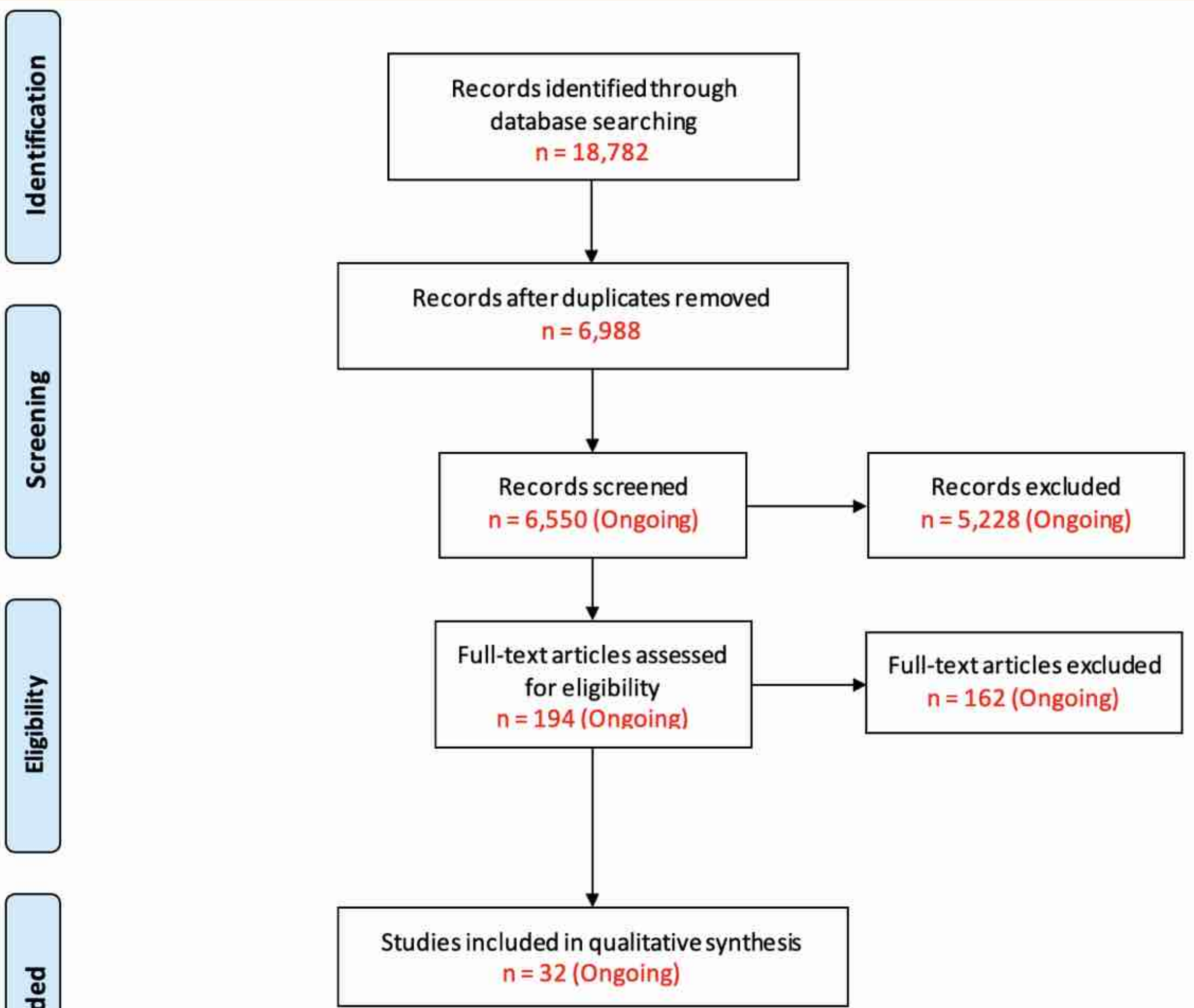


Figure 1. PRISMA Flowchart

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-Jacoste Asin, 2017	Spain	Unspecified	VL → ML → VL	Kidney Transplant Regimen: Prednisone, tacro, MPA	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. Abbreviations: Cutaneous leishmaniasis (CL), Epstein-Barr virus (EBV), Liposomal amphotericin B (L-AmB), Mucocutaneous leishmaniasis (ML), Mycophenolic acid (MPA), Tacrolimus (tacro), Tumor necrosis factor inhibitor (anti-TNF), Visceral leishmaniasis (VL); *Chemotherapy regimen: Cyclophosphamide, Vincristine (Oncovin), Procarbazine, Prednisone

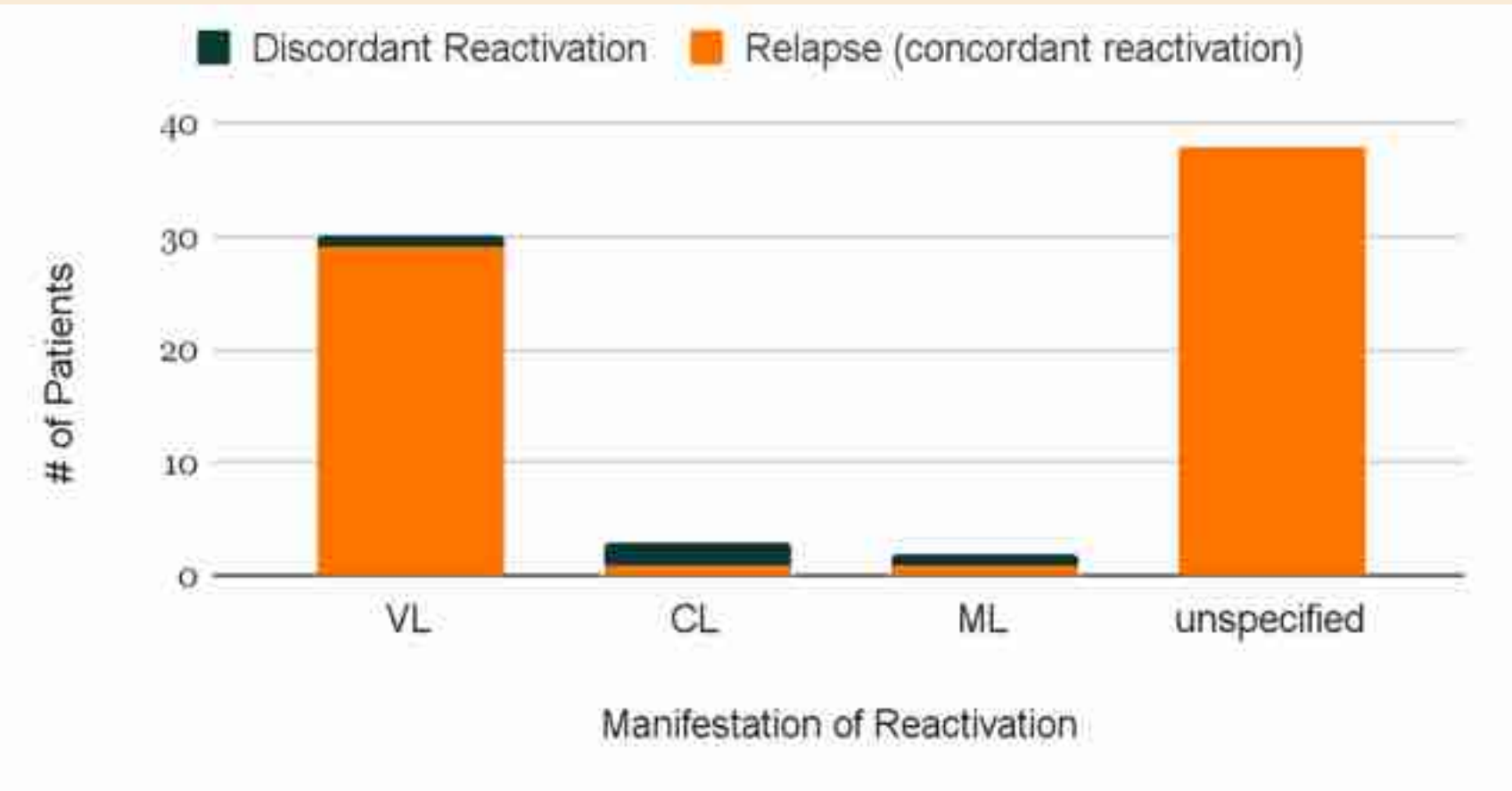


Figure 2. Clinical manifestations of reactivation in solid organ transplant (SOT) recipients upon use of immunosuppressive regimens. Abbreviations: Cutaneous leishmaniasis (CL), Mucocutaneous leishmaniasis (ML), Visceral leishmaniasis (VL)

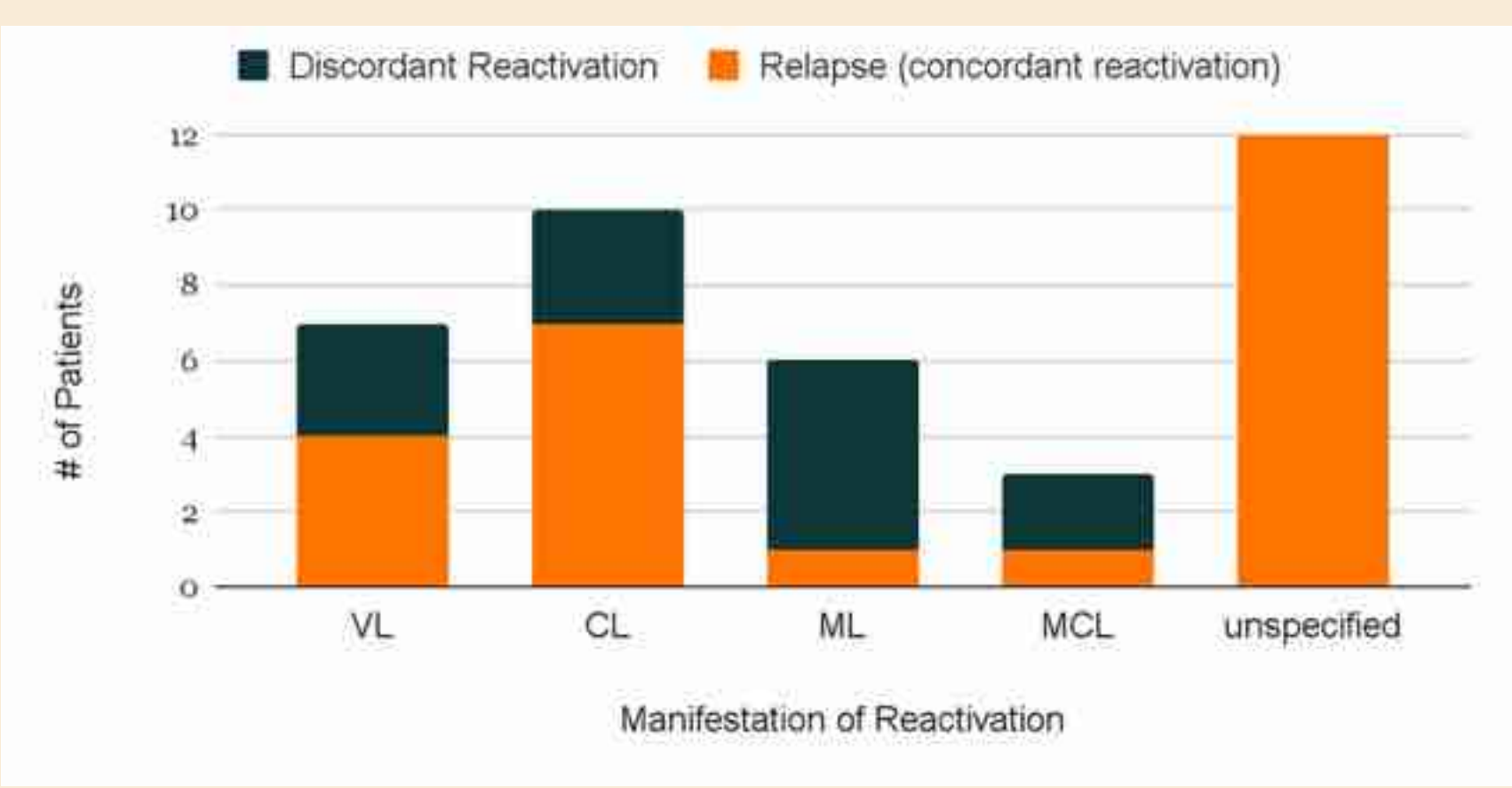


Figure 3. Clinical manifestations of reactivation upon use of immunosuppressive treatments for inflammatory diseases. Abbreviations: Cutaneous leishmaniasis (CL), Mucocutaneous leishmaniasis (MCL/ML *per original reporting), Visceral leishmaniasis (VL)

Discussion

- VL and CL were shown to be the most common forms of reactivation in transplant recipients and inflammatory disease patients, respectively (Figure 2 & 3)
- 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
- This systematic review aims to further investigate the role of prophylaxis to guide clinical management in this patient population

References

