Influence of Host Nutriome on Immunological Control of *Leishmania* Infection

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Introduction

- Immunologic control of parasitic infections arises from a combination of humoral and cellular mechanisms, both of which may be influenced by host nutritional status
- Micronutrient depletion or over-repletion may impair the functioning of the immune system, potentially resulting in increased susceptibility to and poor immunologic control of protozoal infections
- Leishmaniasis is a tissue-dwelling parasitic infection in which disease severity is determined by the host's immune system along with parasitologic factors
- Research suggests that acquired factors such as nutritional inadequacies play a significant role in immunosuppression & pathogenicity
- We aim to synthesize the knowledge surrounding the interplay between host micronutrient status and the tissue-based protozoal infection leishmaniasis

Methods

- Five electronic databases were searched with combinations of search terms such as Parasite* AND (Immunology OR Immunity OR Immune System OR Immune Function OR Immune Impairment OR Immune Response OR Immune Status), from database inception to March 29, 2022
- Screening was performed independently by two reviewers with discrepancies arbitrated by a tertiary reviewer
- Following screening, a comprehensive bias assessment will be carried out using the Grading of Recommendations Assessment, Development, & Evaluation (GRADE) approach

Included	Excluded
Systematic reviews	Review articles
Randomized controlled trials	Case reports
Clinical trials	Case series (n<4)
Cohort studies	Editorials
Observational studies	Conference proceedings
Case-control studies	Animal studies
Case series (n>5)	Trial descriptions only

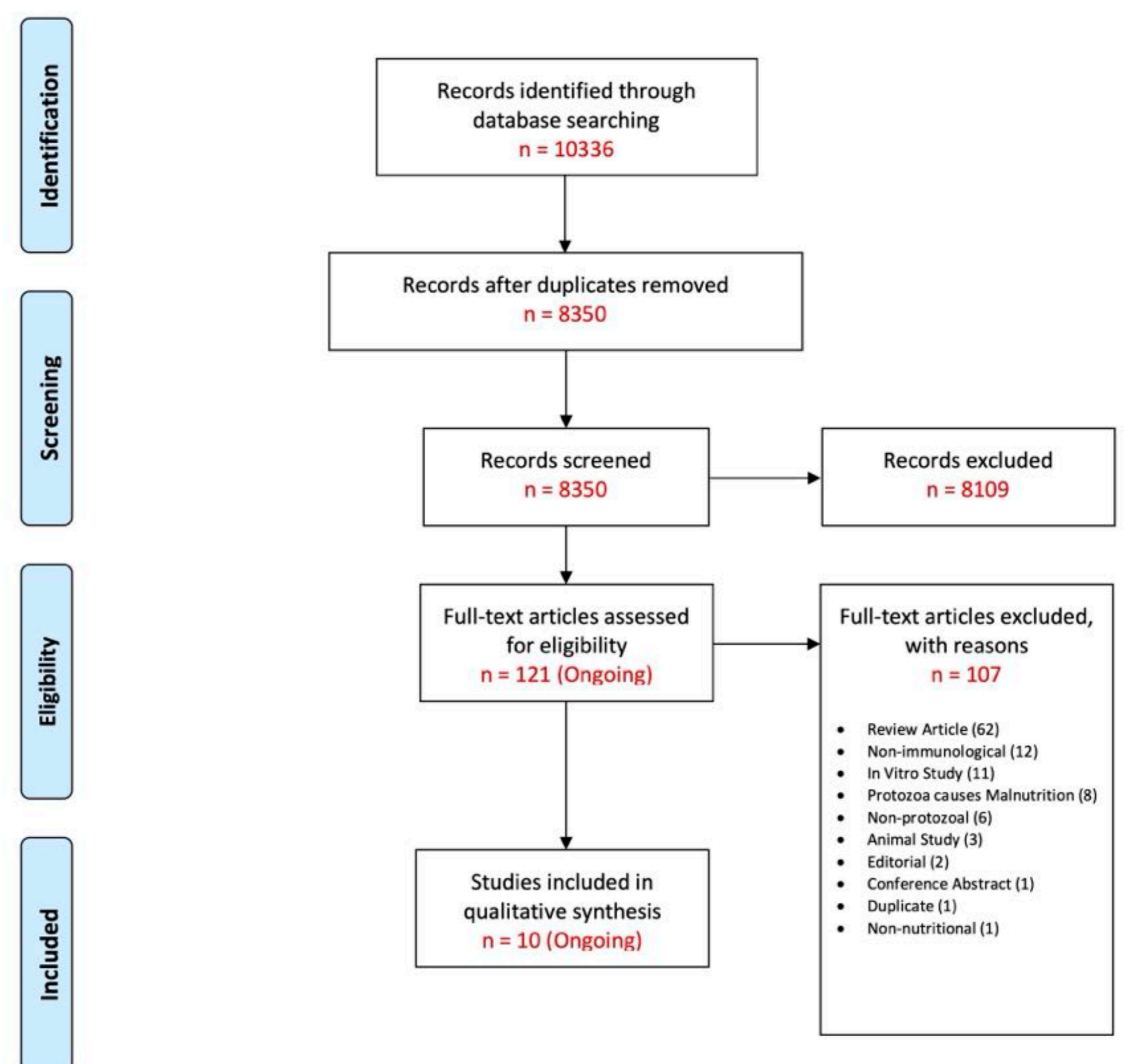**Table 1.** Inclusion and exclusion criteria implemented during title and abstract screening

Figure 1. PRISMA Flowchart

Results

Author, Year	Country	Design	Population	Sample Size	Assessment / Intervention	Mean Age ± SD	Sex (F:M)	Outcomes
[1]Goyonlo, 2020	Iran	Case-Control	Diagnosis of CL confirmed by Geimsa-stained direct smear versus age and sex matched controls	220 Cases (149) Control (71)	Nutritional status and Vitamin A intake via FFQ	21.32 ± 17.62	Cases (82:67) Contorls (45:26)	Daily intake of Vitamin A (p<0.001) was significantly lower among the CL group, as well as energy intake, fiber, Vitamin E, and potassium
[2]Guzman-Rivero, 2014	Bolivia	Case-Control	Patients aged 15-50 with confirmed CL on blood, or microbiological/biochemical analysis.	29 Cases (14) Controls (15)	Zinc gluconate (315mg) vs placebo (315mg cornstarch) for 60 days	Not Reported	Not Reported	A statistically significant biological or clinical effect due to zinc was not found
[3]Maciel, 2014	Brazil	Case-Control	Children with clinical and laboratory confirmed VL versus healthy controls	26 Cases (10) Controls (16)	Serum vitamin A (retinol) status and immune response (CD4+CD24Foxp3+ T cells)	Cases (7.99 ± 7.85) Controls (8.82 ± 6.26)	Cases (7:3) Contorls (5:11)	Vitamin A (retinol) status (p=0.013) and immune cells (p=0.011) were significantly lower in cases versus controls
[4]Maciel, 2008	Brazil	Case-Control	Biochemically confirmed cases of paediatric VL versus healthy controls	149 Cases: Active VL (20) History of VL (33) Antigen Response to VL (40) Controls (56)	Nutritional status via anthropometry, and serum Vitamin A (retinol) level	Cases: Active VL (4.7 ± 3.9) History of VL (10.1 ± 3.3) Antigen Response to VL (11.2 ± 2.4) Controls (8.1 ± 3.4)	Cases: Active VL (11:9) History of VL 19(:14) Antigen Response to VL (20:20) Controls (31:25)	Serum retinol was significantly lower in patients with active VL versus controls (p=0.037)
[5]Cerf, 1987	Brazil	Case-Control	Children aged 0-15 years old with at least 2 consecutive years of anthropometric and serologic data confirming presence of VL	1066	Nutritional status via weight-for-age index	Not Reported	Not Reported	Low weight-for-age was significantly higher In VL children versus controls (p < 0.0001)
[6]Kumar, 2014	India	Case-Control	Patients with confirmed, active, and untreated cases of VL versus healthy controls	40 Cases (20) Controls (20)	Nutrition status via weight-to-height ratios and immune response (including ROS activity, cytokine levels, leishmania antigen) via biochemistry	Not Reported	Not Reported	Patients found to be malnourished had a statistically significant weakened immune response to VL on several accounts as compared to healthy controls: antigen responsiveness, monocytes, & ROS activity (p<0.05), CD62-L (p<0.001)
[7]Kocyigit, 2002	Turkey	Case-Control	Patients with laboratory confirmed CL versus healthy controls	50 Cases (28) Controls (22)	Serum nutrient levels: copper, zinc, and iron and immunoregulatory cytokines: IL-1B, IL-2R, IL-6, IL-8, TNF-a	Cases (27.3 ± 3.8) Controls (28.4 ± 4.1)	Not Reported	Plasma selenium, zinc, iron, and IL-2r levels were significantly lower and plasma copper, IL-1B, IL-8, IL-6, and TNF-a were significantly higher in cases versus controls (p<0.01)
[8]Al-Jurayyan, 1995	Saudi Arabia	Cohort Study	Infants and children undergoing active treatment for Leishmania donovani	94	Haematological findings including nutrition via biochemistry	1.8	39:55	Patients with active infection were found to be immunocompromised and iron deficient
[9]Carbone, 2018	Brazil	Clinical Trial	Patients with parasitologically confirmed presence of VL	67 Intervention: With Zinc (33) Without Zinc (29) Controls (15)	Zinc (2mg/kg/day) plus standard treatment (amphotericin B (0.5-1mg/kg/day) or glucantime (20mg/kg/day)) for 20 days versus standard alone	Intervention: With Zinc (46.20 ± 9.66) Without Zinc (43.76 ± 6.50) Controls (44.60 ± 10.20)	Intervention: With Zinc (12:11) Without Zinc (18:11) Controls (9:6)	Patients who received Zinc supplementation exhibited a more rapid reduction in spleen size compared to controls (p<0.05)
[10]Mengesha, 2014	Ethiopia	Cross-Sectional	Patients age >17 years and non pregnant women with a confirmed diagnosis of VL	403	Nutritional status via BMI	Only Range Provided: 68% 18-27 years old 25.8% 28-37 years old 6.2% >37 years old	6:397	The prevalance of malnutrition and VL infection was 95.5% while presence of intestinal parasitic infection was statistically associated with severe malnutrition in VL patients (p<0.001)

Table 2. Preliminary Data Extraction of Included Studies
Abbreviations: Cutaneous Leishmaniasis (CL), Visceral Leishmaniasis (VL), Food Frequency Questionnaire (FFQ), Reactive Oxygen Species (ROS), Body Mass Index (BMI), Interleukin (IL), Tumor Necrosis Factor (TNF)

Discussion

- Following full-text screening 10 articles remained for absolute inclusion
- Deficiencies reported thus far include malnourishment in general, vitamin A, zinc (n=3 each), iron (n=2), fiber, vitamin E, potassium, selenium, and copper (n=1 each), which variably intersected with clinical disease manifestations and progression
- Disruptions to immune cell count (n=3), and antibody levels (n=1) were also noted
- The data will be summarized to systematically map published literature that will illuminate a number of ways in which nutrient deficiencies or abnormal micronutrient status alter and impair immune function in persons with leishmaniasis
- This synthesized body of information will ultimately inform adjunctive therapeutic decisions in the context of leishmaniasis, which has the potential to improve patient prognosis

References