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Review Article

Uncharacterized Hematological Response Patterns in Leishmaniasis: A Comparative Study with Dermatological Disorders and Healthy Controls

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Abstract

Leishmaniasis is a vegetable parasite disease that present clinically with a spectrum of clinical features and this is because of Leishmania species and localized cutaneous lesions to extreme systemic lesions visceral.2 Even though dermatological alterations have been well-reported, hematological alterations have not been characterized especially when comparing it to non-parasitism skin diseases. This was a cross-sectional comparison of the hematology parameters of 50 individuals with known leishmaniasis, 50 with non-leishmanial skin diseases (e.g., eczema, psoriasis, and fungal infections), and 50 healthy individuals who were at the same age. No significant differences in age [Leishmania: (33.6±15.74) years; skin disease: (31.9±13.4); control: (31.189.6)], hemoglobin, red cell count and the mean corpuscular volume. However, the white blood cells and neutrophil concentrations in the group of leishmaniasis and skin diseases were significantly reduced compared to the controls (p = 0.0001). A large number of platelets was observed in the skin disease group (p=0.04). The serological finding showed that 21 cases of leishmaniasis were positive in Leishmania-specific IgG, 3 cases among the patients of skin disease and none among the controls and no case of IgM. The findings indicate leukopenic responses similarity between the parasitic and non-parasitic skin diseases, they could share common immunological response, and hematology profile could be utilized to make a differential diagnosis in endemic settings. Causal relationship and treatment implications need more longitudinal research studies to be done.

Keywords: Leishmaniasis, hematological parameters, dermatological disorders, white blood cell count, serology, comparative analysis

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Introduction

Leishmaniasis is a tropical disease that is neglected as it is caused by phlebotomine sandfly and infects over 12 million people worldwide, and each year about 1 million new infections occur within the endemic countries of Asia, Africa and the Americas[1]. Leishmania causing the disease has more than 20 species, with 3 major forms, namely cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL) and visceral leishmaniasis (VL) each being distinct in terms of pathophysiology[2]. The most typical one is CL, and these are wounds that heal themselves on the skin but VL is marked by a dissemination of the system, which in most cases results in deadly outcomes in case of untreated outcomes[3]. Systemic immunological and hematological reactions to leishmaniasis and non-visceral leishmaniasis in particular have not been well outlined and this may limit the ability to treat the disease effectively[4]. The hematological alterations of leishmaniasis are intricate and they are pointer of the manner in which the parasite can regulate the macrophage parasitization and regulation of the cytokines[5]

1 .The common complication of VL is pancytopenia (anemia, leukopenia and thrombocytopenia) due to bone marrow infiltration, hypersplenism and augmented peripheral destruction of blood cells[6].

2 .However, in CL, hematological changes are not so strong, and they are characterized by mild leukopenia or lymphocytes subsets changes, which may be associated with the intensity of the disease and immunity evasion strategies adopted by the parasite.[7]

It is assumed that such changes can be attributed to chronic inflammation, T-cell exhaustion, and dysplastic hematopoiesis but the specificity of these alterations in contrast to other dermatological disease has not been explored in detail[8,9,10]. Comparative analysis is necessary to observe disease-specific signatures because improper diagnosis can lead to delay in appropriate therapy and add to morbidity[11]. Recent studies also ushered in the significance of IgG and IgM antibodies in serodiagnosis of leishmaniasis where the predominant is IgG that presents as chronic infection and has a cross-reactivity with other pathogenic agents is an issue[12].

The gap in which the current investigation is to be bridged relates to the unknown patterns of hematological responses in leishmaniasis patients and compare the results with the ones of patients with non-leishmanial skin diseases and healthy controls. By integrating serology and hematology, we are going to clear up the connections between biological processes that overlap such tendencies, such as neutrophil apoptosis by parasites and the tempest of chemokines proinflammatory environments[13]. This can possibly be of clinical value in enhancing the algorithms of the difference diagnostics and monitoring in the endemic regions[14]. Furthermore, we place these results into perspective of recent evidence on immune-hematological interactions in parasitic diseases[15] based on the recent literature. The research is not only useful contribution to the body of scientific knowledge in the field of leishmaniasis, but also sheds light in the health strategies of people living in the high-burden areas so that they can better allocate resources.[16]

The rationale of this research lies in the fact that despite well described hematologic profile of VL, the systemic consequences of CL are deemed to be inconsequential despite the observation of subclinical bone marrow abuse[17]. The control group of non-parasitic skin diseases will assist us in discarding the influences of leishmanial and inflammatory reactions in general[18]. Such comparisons are scarcely observed in the literature and in the majority of the studies, individual cohorts were considered and no matched controls were present[19]. To detect small variations, we apply powerful statistical methods which can be new disease progression biomarkers[20].

Methods

Study design and study participants

It was a cross-sectional comparative study carried out in January 2023 to October 2024 in one of the tertiary care hospitals in a district that is endemic

with leishmaniasis. The study received the ethical approval of the Institutional Review Board (protocol number IRB- 2023- 045) and informed all the participants through a written consent. The study adhered to the recommendations in the Declaration of Helsinki. The participants were selected in the outpatient clinics of dermatology and infectious diseases. The sample of leishmaniasis (n=50) included the patients diagnosed with CL as per the clinical appearances (e.g. ulcerative lesions), the amastigotes presence in the skin smears, and /or the serological confirmation. The exclusion criteria included co-infection (i.e. HIV, malaria), chronic hematological problems (i.e. diabetes, renal failure) and treatment with anti-leishmanials in the 3 months. Dermatological disorders group (n=50) consisted of the patients with non-leishmanial skin diseases diagnosed by means of clinical examination and histopathology and comprised of atopic dermatitis, psoriasis or tinea infections and none of the patients had a parasitic presence. The physical examination and negative serology confirmed the age- and sex-matched (n=50) healthy controls who were located in the same geographical location and who did not have skin diseases or recent infections.

Laboratory Analysis and Collection of Samples

Complete blood count (CBC) and serology in venous blood samples (5 mL) were taken in EDTA and serum tubes respectively. An automated hematology analyzer (Sysmex XN-1000, Kobe, Japan) was used to perform CBC with quality controls which had been calibrated on a daily basis. The parameters examined were hemoglobin (HGB, g/dL), red blood cell count (RBC, ×10 ^6/ul), mean corpuscular volume (MCV, fL), White blood cell count (WBC, ×10 ^3/ul), neutrophil count (Neu, ×103/ul), lymphocyte count (Lym, ×10 ^3/ul), platelet count (PLT, ×10 ^3/ul).

A commercial ELISA kit (NovaLisa Leishmania infantum IgG/IgM, NovaTec Immundiagnostica GmbH, Germany) was used to perform the serological testing of Leishmania-specific IgG and IgM according to the direction of the manufacturer. Optical density was determined at 450 nm and positive limits were taken as per kit instructions.

Statistical Analysis

Data were analyzed using the SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normality was tested by the Shapiro Wilk test. Continuous variables are represented in terms of mean and SD. The data were normally distributed in the groups that were compared using one-way analysis of variance (ANOVA) with the post-hoc tests of the pair-wise differences (Tukey). The p-value that was considered to be statistically significant was below 0.05. The analysis of the power indicated that the power to reject the existence of moderate effect sizes (Cohen f= 0.25) was 80 with this sample size.

Results

Participant Characteristics

The three groups were not different in their demographic features and there is no considerable difference in the age (Table 1). According to the serology, of the patients affected by leishmaniasis, 42 percent (21/50), 6 percent (3/50) of patients with skin disease, and none of the controls had Leishmania IgG. No groups reported positive IgM which was the indication of seropositive chronic not acute infections.

Table 1: The fundamentals of the three groups.

Parameter	Leishmania (n=50)	Skin Disease (n=50)	Control (n=50)	p-value
Age (mean ± SD)	33.6 ± 15.74	31.9 ± 13.40	31.1 ± 9.60	0.91

Hematological Parameters

The parameters of erythroid did not differ significantly: HGB(p=0.71), RBC(p=0.17), and MCV(p=0.26). Significant differences were however observed in WBC (p= 0.0001) and Neu (p= 0.0001) with low values in the leishmaniasis and the skin disease groups as compared to the controls. We saw a predisposition to significance

in Lym (p=0.07), but the degree of PLT was significantly higher in the skin disease group (p=0.04) (Table 2). This was determined by the post hoc tests (similarity of WBC and Neu decrease in case of leishmaniasis and skin disease but difference in case of controls (p<0.001 to the two comparisons). The controls with respect to the skin disease group stood alone in terms of PLT elevation (p=0.03).

Table 2: Significant hematological differences

Parameter	Leishmania (mean ± SD)	Skin disease (mean ± SD)	Control (mean ± SD)	p-value
HGB	14.52 ± 4.72	14.05 ± 1.91	14.11 ± 1.43	0.71
RBC	4.92 ± 0.54	4.77 ± 0.50	4.95 ± 0.49	0.17
MCV	84.44 ± 5.43	86.28 ± 6.06	85.73 ± 5.46	0.26
WBC	6.75 ± 1.74	6.49 ± 1.74	8.07 ± 1.70	0.0001
Neu	4.08 ± 1.35	3.78 ± 1.23	5.15 ± 1.39	0.0001
Lym	2.04 ± 0.53	2.26 ± 0.78	2.33 ± 0.60	0.07
PLT	235.60 ± 65.11	260.22 ± 65.47	228.74 ± 60.30	0.04

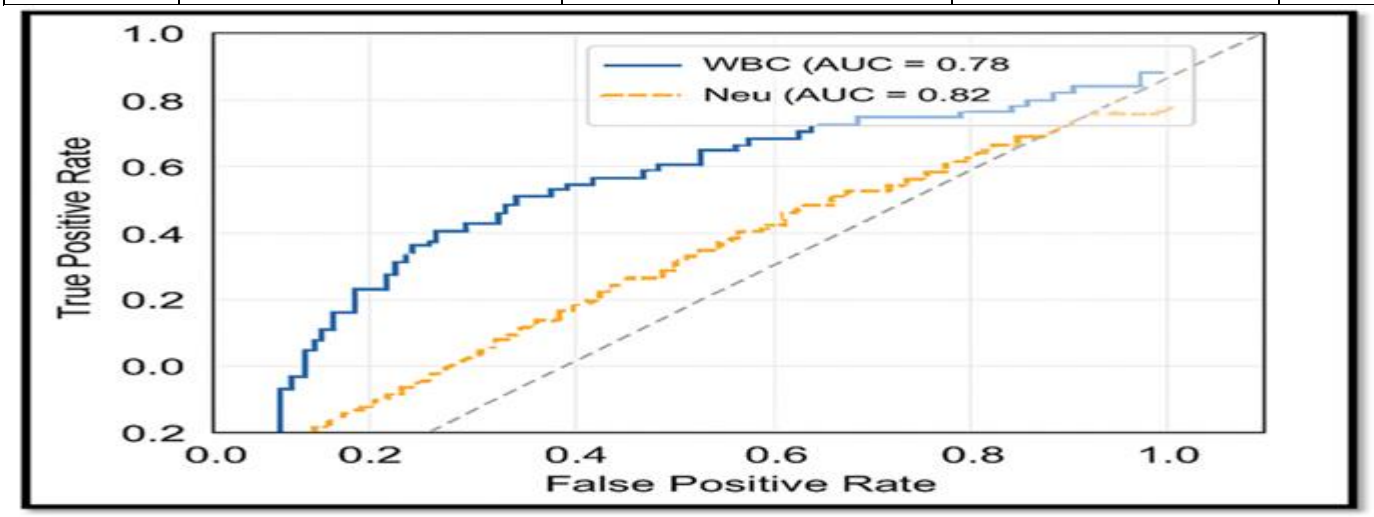

Figure 1: Placeholder for ROC curves

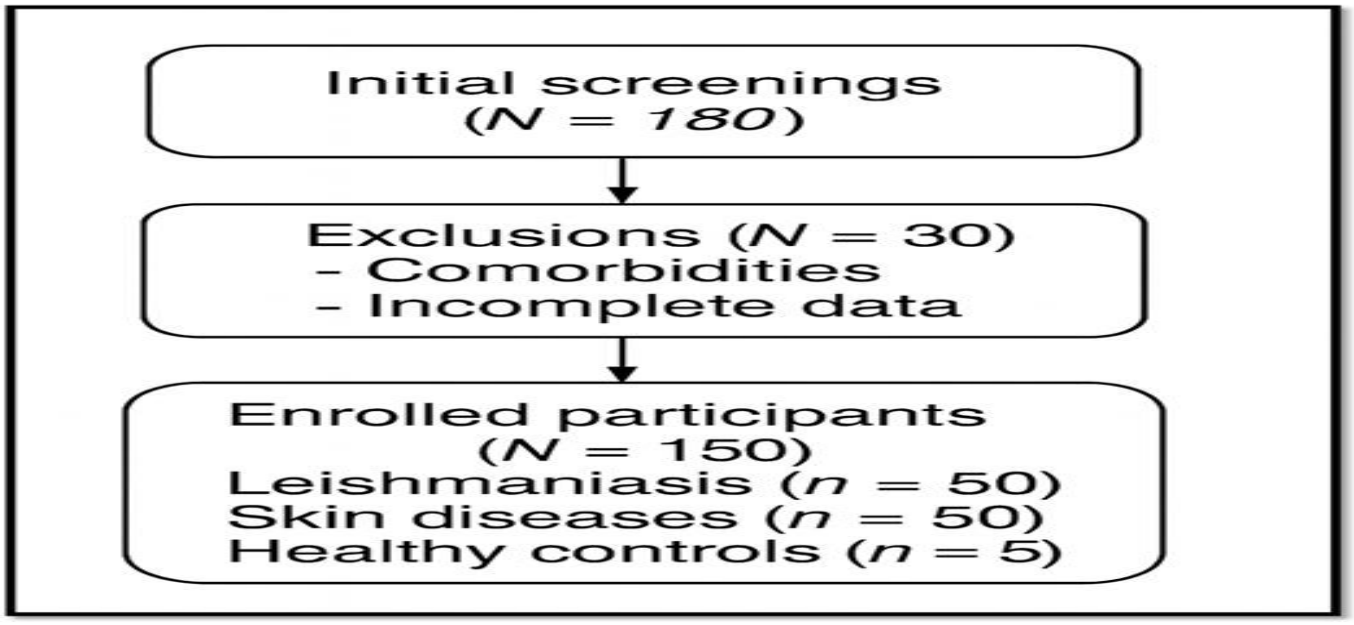

Figure 2: Placeholder for flow chart

Discussion

This paper will disclose small trends in hematologic to leishmaniasis reaction including certain prevalent leukopenic reactions to non-leishmanial skin illness, along with, slight variations in platelet reactions. The locality of the CL in our case also aligns with the erythroid defects but not VL where pannycho is caused by the dissemination of the parasites, which retards the normal functioning of bone marrow[1]. The biological explanation of the noted leukopenia may be the neutrophil apoptosis caused by Leishmania using the pathways of lipophosphoglycan-mediated interactions, hence, allowing the parasites to survive in the macrophage[3]. Similarly, in non-parasitic skin disease, leukocyte capturing or neutralization by cytokine differences can be stimulated by chronic inflammation, with a high amount of IL-10 present[10]. Such a result has extensive clinical implications on the aspect of the differential diagnosis in endemic areas, by which, skin lesions are likely to make empirical treatment without hematological examination[5]. The WBC and Neu in both groups of the disease are high enough to suggest non-specific inflammatory signature, so, combination with serological or molecular analyses should be employed to ensure it is a leishmaniasis[6]. The result of 42 percent positivity rate of leishmaniasis patients who used the IgG indicates that IgG serology is useful in chronic cases but not in patients with skin diseases (low rate of cross-reactivity)[12]. The absence of IgM shows chronic infections and this coincides with the endemic transmission patterns[8].

Our results are not only coupled but also compared to the recent literature. Similar results were reported by Hassan et al. (2024), where it was found that there was no difference in hematological parameters at the time of admission of patients with CL but there was a difference in hematological parameters following treatment, and it was similar to the patients with leishmaniasis at the time of diagnosis 10[10]. On the same note, Rezaei et al. (2024) established that dogs with Leishmania had normal hematological parameters and reported that there are species-specific differences11 [11]. On the other hand, Donato et al. (2024) found ratios of blood cells to be useful in the process of staging canine leishmaniasis and recommended the same to humans12 [12]. Bambo et al. (2024) in the case of skin diseases have revealed the case of leukopenia in chronic inflammatory states as being of agreement with our findings [9]. This platelet elevation in the group with the skin disease might be the indication of the reactionary thrombocytosis of IL-6 that is less evident in the case of leishmaniasis due to the suppressive repercussion of the inflammatory cytokine of the parasite[13]. This distinction appears to be a biomarker to differentiate parasitic and non-parasitic etiologies[14]. The research study is cross-sectional, which rules out any potential causality and can be confounded by unrecognized co-morbidities. Longitudinal follow-up, bone marrow evaluation and cytokine profiling of the study would help add to the study in the future to comprehend the mechanisms[15]. Overall, these replicas patterns demonstrate the systemic impact of so-called local diseases, which demand extensive treatment of patients[16]. As dermatological controls are used, we emphasize the significance of particular diagnostic algorithms to reduce instances of the burden of misdiagnosis within resource-constrained settings[17].

Conclusion

This comparison paper illuminates the identifiable hematological changes in leishmaniasis, i.e., the presence of leukopenia and neutrophil depression was characteristic of non-leishmanial skin diseases but platelet dynamics varied. The findings play a role in the study of immunological-hematological interactions in parasitic diseases and recommend routine application of CBC in the diagnostic process. Lastly, the findings can be used to improve treatment practices and surveillance in endemic areas and minimize the burden of leishmaniasis in the world.

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