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Hematological and Biochemical Alterations in Visceral Leishmaniasis (Kala-Azar) Patients Treated with Sodium Stibogluconate (SSG) and Ambisome

Andrea Lafleur[1], Stephane Daffis[2], Charles Mowbray[2], Byron Arana[2*]

[1]Doctoral Training Centre, University of Oxford, Oxford OX1 3NP, UK.
[2]Drugs for Neglected Diseases initiative (DNDi), 1202 Geneva, Switzerland.

***E-mail** ✉ barana@dndi.org

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ABSTRACT

Visceral leishmaniasis (VL) is a major public health threat due to its high morbidity and mortality rates in untreated cases. The purpose of this study was to evaluate the hematological and biochemical parameters in patients with VL in ElGadarif State, Sudan. Blood samples were collected from 39 VL patients for the analysis of complete blood count (CBC) and clinical chemical tests. The CBC was analyzed, and clinical chemistry tests were performed using a Biosystem analyzer with relevant reagents. Statistical analysis was done using SPSS version 22 software. The results showed a significant decrease in levels of hemoglobin (Hb), packed cell volume (PCV), mean cell hemoglobin (MCH), white blood cells (WBCs), and platelets (PLT) in the VL group compared to the control group, while mean corpuscular hemoglobin concentration (MCHC) was elevated in the VL group. The mean corpuscular volume (MCV) showed no significant difference between the two groups. Liver and renal function tests showed that urea, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were significantly higher in VL patients than in the control group, while creatinine and alkaline phosphatase (ALP) showed only mild increases. Furthermore, a comparison between ambisome and sodium stibogluconate (SSG) treatments showed a non-significant increase in urea, creatinine, ALT, AST, and ALP in the Ambisome group. VL patients showed anemia, leukopenia, and thrombocytopenia, alongside slight increases in urea, creatinine, and liver enzymes. Ambisome treatment was associated with a more significant increase in urea and a mild elevation in creatinine and AST compared to SSG treatment.

Keywords: Ambisome, Visceral leishmaniasis, Hematological parameters, Sodium Stibogluconate (SSG)

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Introduction

Leishmaniasis, a disease strongly associated with poverty, is caused by the intracellular Leishmania parasite, which infects mammalian hosts. It manifests primarily in two forms: visceral and cutaneous leishmaniasis [1, 2]. Globally, approximately 0.7 to 1 million cases are reported annually, with an estimated 350 million people at risk. Leishmaniasis is endemic in 98 countries, including Sudan [3]. While there has been a notable decline in visceral leishmaniasis cases due to better healthcare access, prognosis improvements, and enhanced vector control programs, the disease remains a serious issue, especially in East Africa. In Sudan, regions such as Blue Nile, Upper Nile, Al-Qadarif, Jonglei, Kassala, and areas north of Khartoum are most affected [4, 5].

In Africa, South America, and parts of Asia like Bangladesh, Nepal, and India, the treatment of leishmaniasis has traditionally relied on Pentavalent antimonial compounds (Sbv), which inhibit amastigote glycogen synthesis and oxidative fatty acid pathways. However, resistance to Sbv has led to the consideration of Amphotericin B deoxycholate as a first-line treatment, although logistical and infrastructural barriers have hindered its widespread implementation [6, 7].

Visceral leishmaniasis (VL) is often associated with significant hematological and biochemical disturbances, which can contribute to high morbidity and mortality rates [8]. Commonly observed clinical and laboratory symptoms include anemia, leukopenia, thrombocytopenia, and pancytopenia. These hematological alterations, such as neutropenia, are linked to an increased risk of bleeding and a heightened vulnerability to secondary bacterial infections [9, 10]. Anemia is often the result of RBC hemolysis, poor nutrition, and various coexisting conditions, including chronic diseases and opportunistic infections, as the amastigote proliferates in the mononuclear phagocytic system. This can lead to an enlargement of the spleen and the development of hematological defects, which are often reflected in the course of the illness. Additionally, liver dysfunction is common in VL patients, marked by elevated levels of ALT, AST, and ALP, along with hypertriglyceridemia and decreased cholesterol levels. The disease also affects renal function, contributing to acute kidney injury and the associated glomerular damage due to immune complex deposition [11-16].

In the eastern Sudanese state of Al-Qadarif, there has been an alarming increase in mortality rates despite the implementation of established treatment protocols. Patients in this region continue to experience severe symptoms even during treatment, raising concerns about the efficacy of the current drug regimen. This study aims to assess hematological and biochemical parameters among Sudanese patients with visceral leishmaniasis to provide insight into the effectiveness of current treatment protocols and inform public health authorities.

Materials and Methods

Study design

This research was conducted as a descriptive cross-sectional study in Al-Qadarif State, Eastern Sudan, from April to December 2021. The study involved patients diagnosed with visceral leishmaniasis (VL), who were categorized as the case group. A control group was composed of healthy subjects. Patients suffering from malaria or other conditions that could potentially affect hematological and chemical parameters were excluded from the study. Ethical approval was granted by the Alzaeim Alazhary University ethics committee and the local government hospital administration. All participants were informed about the study and its objectives before sample collection.

Sampling collection

Whole blood samples were gathered from 39 VL patients between April and December 2021 under sterile conditions. Blood was collected into Ethylenediaminetetraacetic acid (EDTA) tubes for complete blood count (CBC) analysis and into heparinized tubes for clinical chemistry tests.

Method

CBC analysis was performed using a Mindray BC3000 Plus hematology analyzer (China), which utilized appropriate reagents. Clinical chemistry tests were carried out using a biosystem chemical analyzer (Germany), also equipped with the necessary reagents to measure various analytical parameters.

Data analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 22. An independent t-test was used to calculate p-values, with a p-value of less than 0.05 considered statistically significant. Additionally, the chi-square test was employed to assess the associations between different parameters.

Results and Discussion

This research was based on the El-Gadarif state, a region affected by Kala-Azar. A total of 39 professionally diagnosed VL patients were included, with a mean age of 21.2 ± 14.3 years. Among the patients, 21 (53.80%) were male, and 18 (46.20%) were female. Additionally, 39 healthy individuals were included as the control group.

Hematological parameters results

The study revealed a significant decrease in hemoglobin (Hb), packed cell volume (PCV), mean cell hemoglobin (MCH), white blood cells (WBCs), and platelets in the case group compared to the control group, with p-values less than 0.05 for each. However, the mean corpuscular hemoglobin concentration (MCHC) was significantly higher in the case group. There was no significant difference between the groups in terms of mean corpuscular volume (MCV), with a P-value > 0.05.

When comparing the results by gender, a significant decrease in Hb was observed, with lower levels in females than in males, yielding a P-value of < 0.05. Other parameters, such as PCV, RBC indices, WBCs, and platelets, showed a decrease in the case group compared to the control group, though the differences were not statistically significant, as indicated by p-values greater than 0.05, as shown in **Table 1**.

Table 1. Comparison of hematological parameters among study groups

Parameters	Case group (n = 39) (Mean ± SD)	Control group (n = 38) (Mean ± SD)	P-value
Hb	9.50 ± 3.60	12.4 ± 2.07	0.000*
PCV	25.50 ± 0.60	37 ± 5.50	0.000*
MCV	74.20 ± 10.30	84.20 ± 13.70	0.731
MCH	28.90 ± 9.06	28.40 ± 2.50	0.001*
MCHC	34.80 ± 3.14	32.80 ± 1.30	0.016
WBCs	4.40 ± 5.20	6.7 ± 2.10	0.000*
Platelet	141.70 ± 77	268.90 ± 105	0.001*

*Significant difference with P-value < 0.05.

Table 2 compares hematological parameters based on treatment. Anemia (Hb < 10 g/dl) was observed in 24 patients (61.5%), and a microcytic hypochromic pattern appeared in 28 patients (71.8%). Thrombocytopenia was found in 18 patients (46.2%), while leukopenia was present in 32 patients (82.1%). Patients were divided into two treatment groups: one group received the Ambisone protocol, consisting of 22 patients, and the other group received the SSG (sodium stiboglyconate) protocol, which included 17 patients. When comparing hematological parameters between the two groups, no significant differences were found, as all parameter levels remained unchanged, with P-values > 0.05.

Table 2. Comparison of hematological parameters based on treatment

Parameters	Ambisone (n = 22) (Mean ± SD)	SSG (n = 17) (Mean ± SD)	P-value
Hb	9.70 ± 4.50	9.20 ± 4.00	0.62
PCV	25.00 ± 7.10	26.30 ± 5.80	0.62
MCV	74.40 ± 8.80	74.10 ± 12.40	0.93
MCH	27.80 ± 5.20	30.30 ± 12.30	0.43
MCHC	35.20 ± 3.60	34.20 ± 2.30	0.32
WBCs	3.70 ± 3.00	5.40 ± 7.20	0.37
Platelet	144.10 ± 81.80	138.70 ± 72.60	0.83

No significant difference between groups with a P-value > 0.05.

Association of hematological parameters with hepatosplenomegaly is presented in **Table 3**.

Table 3. Association of hematological parameters with hepatosplenomegaly

Parameters	Hepatosplenomegaly	Chi-square	P-value
	Yes	No	
Hb	Normal (2, 5.40%)	4 (10.80%)	0.010
	Decreased (11, 29.70%)	20 (54.10%)	
PCV	Normal (2, 5.40%)	4 (10.80%)	0.038
	Decreased (11, 29.70%)	20 (54.10%)	
MCV	Normal (3, 8.10%)	5 (13.50%)	0.025
	Decreased (10, 27%)	19 (51.40%)	
MCH	Normal (8, 22.90%)	7 (20%)	2.9
	Decreased (5, 14.30%)	15 (42.90%)	

MCHC	Normal (13, 36.10%)	21 (58.30%)	1.1
	Decreased (0, 0%)	2 (5.60%)	
WBCs	Normal (3, 8.10%)	4 (10.80%)	0.22
	Decreased (10, 27%)	20 (54.10%)	
Platelet	Normal (4, 10.80%)	14 (37.80%)	2.5
	Decreased (9, 24.30%)	10 (27%)	

No significant association was found with a P-value > 0.05.

Among the patients diagnosed with visceral leishmaniasis, a majority (28 individuals, 71.8%) exhibited microcytic hypochromic anemia, as reflected by decreased hemoglobin (Hb), mean corpuscular volume (MCV), and related red cell indices. In contrast, the remaining 11 patients (28.2%) showed no hematological signs indicative of anemia. The comparison between low Hb and MCV levels demonstrated a statistically significant association (P-value < 0.05).

Biochemical findings

Analysis of renal and liver function parameters revealed a notable rise in urea, aspartate transaminase (AST), and alanine aminotransferase (ALT) levels among VL patients when compared to the control group, with statistical significance (P-value < 0.05). Although creatinine and alkaline phosphatase (ALP) levels were also elevated in the patient group, the differences did not reach statistical significance (P-value > 0.05), as detailed in **Table 4**.

Biochemical parameters

Table 4 summarizes the comparison of liver and renal function test results between VL patients and the control group. Patients showed significantly elevated levels of urea, AST, and ALT compared to controls (P-value < 0.05), indicating liver and kidney involvement. Although creatinine and ALP levels were also higher in the case group, these differences were not statistically significant (P-value > 0.05).

Table 4. Liver and renal function test results in the study groups

Parameters	Case (n = 39) (Mean ± SD)	Control (n = 38) (Mean ± SD)	P-value
Urea	39.30 ± 46.50	23 ± 7.10	0.03*
Creatinine	1.30 ± 1.80	0.93 ± 0.20	0.21
AST	108.80 ± 128.20	36.10 ± 5.20	0.001*
ALT	87.30 ± 114.10	30.18 ± 10.42	0.004*
ALP	88.50 ± 55.20	92.90 ± 46.01	0.65

*Significant at P < 0.05

When evaluating these parameters by treatment type (Ambisone vs. SSG), **Table 5** shows a statistically significant elevation in urea levels among patients treated with Ambisone (P = 0.03). Although creatinine and ALT were also elevated in this group, the differences were not statistically significant (P > 0.05). Interestingly, ALT and ALP levels were slightly lower in the Ambisone group than in the SSG group, though this difference was not statistically meaningful.

Table 5. Comparison of liver and renal parameters by treatment type

Parameters	Ambisone (n = 22) (Mean ± SD)	SSG (n = 17) (Mean ± SD)	P-value
Urea	52.30 ± 58.20	22 ± 8.90	0.03*
Creatinine	1.70 ± 2.30	0.74 ± 0.29	0.11
AST	94.10 ± 125.20	78.80 ± 101.90	0.68
ALT	103.80 ± 134.10	114.60 ± 124.70	0.80
ALP	75.80 ± 44.00	104.70 ± 65.10	0.16

*Significant at P < 0.05

Table 6 presents the comparison of liver and renal parameters between male and female patients. The data show no statistically significant gender-based differences across all parameters (P > 0.05).

Table 6. Liver and renal parameters by gender

Parameters	Male (n = 19) (Mean ± SD)	Female (n = 16) (Mean ± SD)	P-value
Urea	37.40 ± 29.30	41.60 ± 62.10	0.79
Creatinine	1.30 ± 1.70	1.20 ± 1.80	0.76
AST	115.60 ± 146.50	55.80 ± 48.80	0.10
ALT	142.60 ± 158.50	73.00 ± 74.50	0.09
ALP	97.70 ± 69.10	78.00 ± 32.80	0.30

Finally, **Table 7** explores the potential relationship between liver and kidney markers with hepatosplenomegaly. The statistical analysis showed no significant associations between hepatosplenomegaly and any of the biochemical markers examined (P > 0.05).

Table 7. Association between liver/renal parameters and hepatosplenomegaly

Parameters	Hepatosplenomegaly	Chi-square	P-value
	Yes	No	
Urea	Normal: 9 (26.5%)	20 (58.8%)	0.15
	Increased: 2 (5.9%)	3 (8.8%)	
Creatinine	Normal: 6 (18.2%)	15 (45.5%)	0.54
	Increased: 5 (15.2%)	7 (21.2%)	
AST	Normal: 5 (13.9%)	11 (30.6%)	0.05
	Increased: 7 (19.4%)	13 (36.1%)	
ALT	Normal: 4 (11.4%)	10 (28.6%)	0.33
	Increased: 8 (22.9%)	13 (37.1%)	
ALP	Normal: 5 (16.7%)	10 (33.3%)	1.00

Global warming is significantly impacting ecosystems, altering how people interact with one another and how resources are accessed and distributed. These changes have led to an increased risk of zoonotic and communicable disease outbreaks. As climate change progresses, it influences human health, migration patterns, and food security, while also contributing to the expansion of disease-carrying vectors into new environments. The continuous clearance of forests and native habitats for land reuse, industrial development, and water resource management has been associated with the emergence of vector-borne pathogens [17].

Due to the rising number of leishmaniasis cases in Sudan, particularly in eastern regions, this study was initiated to assess hematological and biochemical parameters in Sudanese patients diagnosed with visceral leishmaniasis (VL) and undergoing treatment.

This descriptive case study was carried out in the Kala-azar endemic regions of ElGadarif State. A total of 39 clinically confirmed VL patients were included in the case group, with a mean age of 21.2 ± 14.3 years. Of these, 21 (53.8%) were males and 18 (46.2%) were females. Hepatosplenomegaly was identified in 14 patients (35.9%). Treatment regimens included Sodium Stibogluconate (SSG) for 17 patients (46.2%) and Ambisone for 22 patients (53.8%). Their data were compared with those of healthy individuals serving as a control group.

Notably, similar findings were observed in an Ethiopian institution-based retrospective cross-sectional study involving 141 VL patients. That study reported that males were affected 13 times more frequently than females [12]. Most patients were laborers who traveled to endemic areas during the winter. The study found anemia in 95% of cases, thrombocytopenia in 90%, leukopenia in 86%, and pancytopenia in 79%, with 50% experiencing co-infections. These observations align with findings documented by Bantie *et al.* [18].

Analysis of hematological parameters in the current study revealed significant reductions in hemoglobin (Hb), packed cell volume (PCV), mean corpuscular hemoglobin (MCH), white blood cells (WBCs), and platelets in the case group compared to the control group (P < 0.05). Conversely, mean corpuscular hemoglobin concentration

(MCHC) was significantly elevated in the case group. Mean corpuscular volume (MCV), however, did not differ significantly between the groups ($P > 0.05$).

When evaluating the impact of treatment type, no statistically significant differences were found in hematological parameters between the Ambisone and SSG groups ($P > 0.05$). Gender-based comparisons showed a significant reduction in Hb among female patients ($P < 0.05$), whereas differences in PCV, red blood cell indices, WBCs, and platelet counts between genders were not statistically significant ($P > 0.05$).

Most VL patients exhibited microcytic hypochromic anemia, identified in 28 patients (71.8%) through reduced Hb, MCV, and red blood cell indices, while 11 patients (28.2%) showed no signs of anemia. The significant difference between anemic and non-anemic cases (based on Hb and MCV) was supported by a P-value < 0.05. Anemia (Hb < 10 g/dl) was present in 24 patients (61.5%), microcytic hypochromic anemia in 28 (71.8%), thrombocytopenia in 18 (46.2%), and leukopenia in 32 (82.1%).

The association analysis between hematological parameters and hepatosplenomegaly revealed no statistically significant relationship between these variables.

In terms of liver function tests (LFTs) and renal function tests (RFTs), our findings revealed a significant elevation in the levels of urea, aspartate transaminase (AST), and alanine transaminase (ALT) in the case group when compared to the control group (P-value < 0.05). Although creatinine and alkaline phosphatase (ALP) levels were also higher in the case group, these increases were not statistically significant (P-value > 0.05).

A comparison between treatment subgroups—patients treated with Ambisone and those treated with Sodium Stibogluconate (SSG)—demonstrated a significantly elevated urea level in the Ambisone group (P-value < 0.05). However, although creatinine, ALT, AST, and ALP levels were also higher in the Ambisone group, these differences did not reach statistical significance (P-value > 0.05 for each). Additionally, no statistically significant differences were found in LFT and RFT values based on gender (P-value > 0.05 for all parameters).

When analyzing the association between liver and renal function parameters and hepatosplenomegaly, the study found no significant relationship between these variables. Interestingly, SSG (the antimony-based regimen) showed fewer adverse effects and less liver and kidney toxicity than Ambisone. This observation contradicts existing literature that highlights liposomal amphotericin B (LAB) as a highly effective treatment with minimal toxic side effects due to its efficacy at low doses [19].

Our results align with a study by Tesfanchal *et al.* [14], which reported significantly higher serum levels of AST, ALT, ALP, total bilirubin, and triglycerides in visceral leishmaniasis patients compared to healthy controls. Additionally, that study reached a consensus on hematological changes observed before and after treatment, noting that hemoglobin, white blood cell (WBC), and platelet counts increased post-treatment, except for neutrophil counts, which remained low. Statistical analysis showed a strong negative correlation between parasite load and both WBC and red blood cell indices [15, 20].

The present findings are also partially consistent with another study focusing on pediatric visceral leishmaniasis (PVL). That study found that a substantial proportion of patients presented with mild to severe microcytic hypochromic anemia (67.7% had hemoglobin levels < 8 g/dL), leukopenia (66.7% had WBC counts < $5\times10^3/\mu L$), and thrombocytopenia (24.2%). Additionally, pancytopenia was observed in 18.2% of cases. Low values of MCH, MCV, and MCHC were recorded in 90%, 88%, and 85.1% of the patients, respectively. Furthermore, elevated levels of AST and ALT were detected in 53.33% and 6.66% of cases, respectively [16].

Our findings also align with a study by Sundar *et al.* [19] conducted in India, where diagnostic resources were limited. In that study, the diagnosis of visceral leishmaniasis was confirmed by identifying *Leishmania donovani* (LD) bodies in bone marrow aspirates—a technique still regarded as the gold standard. Patient data included demographic characteristics, clinical signs, complete blood count results, and bone marrow findings. The mean age was 30 months, with a nearly equal distribution of females (33) and males (31). All children experienced periodic fever before diagnosis, with a mean fever duration of 56 days. Hepatomegaly was reported in 84.4% of the patients, and splenomegaly was present in all cases. The average spleen and liver enlargements were 9.3 cm and 3.5 cm, respectively. Mean hemoglobin concentration, WBC count, and platelet count were 6.6 g/dL, 3.58×10^9/L, and 71.7×10^9/L, respectively [21].

An Ethiopian study conducted among VL patients and healthy controls assessed liver function through measurements of AST, ALT, total bilirubin, albumin, and total protein levels. The findings demonstrated a statistically significant elevation in AST, ALT, and total bilirubin levels among VL patients compared to controls (P-value < 0.001) [22].

Visceral leishmaniasis (VL) continues to present a complex clinical challenge. Therefore, newer treatment options—such as liposomal amphotericin B—should be considered as potentially effective regimens with reduced toxicity compared to the current protocols. However, their efficacy and safety must be evaluated in endemic regions like Sudan before widespread implementation. The introduction of new drugs must also be accompanied by strict stewardship to prevent the emergence of drug resistance, forming a crucial part of VL management strategies [23].

Supportive therapies may include the administration of erythropoietin to address anemia. Additional diagnostic investigations, such as bone marrow examination and tests for disseminated intravascular coagulation (DIC), may help identify the underlying causes of leukopenia and thrombocytopenia. Given the rising concern over drug resistance in Sudan, it is essential to continuously monitor the efficacy of existing VL treatment protocols and investigate the resistance patterns of the Leishmania parasite.

Conclusion

This study revealed that the majority of VL patients suffered from thrombocytopenia, leukopenia, and anemia, along with mild but significant increases in urea, creatinine, and liver enzyme levels. Regarding treatment types, no significant differences were observed in hematological parameters. However, Ambisone therapy was associated with a significantly elevated urea level and a modest increase in creatinine and AST levels compared to treatment with Sodium Stibogluconate (SSG).

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