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Research Article

Assessment of Variation in Clinical Presentation of Visceral Leishmaniasis Among Patients Attending the Tropical Diseases Teaching Hospital in Sudan

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Abstract

Background: Visceral leishmaniasis (also known as Kala-azar) is a systemic parasitic infection with many clinical presentations. The present study assesses the variation in presentations among patients who attended the Tropical Diseases Teaching Hospital (TDTH) in Khartoum, Sudan.

Methods: This analytical cross-sectional, hospital-based study was conducted at the TDTH between November 2019 and September 2020. Medical records of patients who presented at the TDTH were reviewed using a structured data extraction checklist. The Chi-square test was used to determine the associations between sociodemographic and clinical presentations of patients. *P*-value < 0.05 was considered as statistically significant.

Results: Out of 195 patients, 79.5% were male and 48.2% were <31 years old. Fever was the main clinical presentation (90.2%) while 53.3% presented with weight loss and 72.3% and 39% presented, respectively, with splenomegaly and hepatomegaly. HIV was detected in 4.6% of the patients. RK39 was the main diagnostic test. We found a significant association between the abdominal distention and the age of the patients ($P < 0.05$) – age groups 11–20 and 41–50 years were more likely to present with abdominal distention than other age groups.

Conclusion: There is no exact clinical presentation or routine laboratory findings that are pathognomonic for visceral leishmaniasis; therefore, it should be considered in the differential diagnosis of any patient with fever, weight loss, and abdominal distention, and among patients with HIV.

Keywords: visceral leishmaniasis, Sudan, clinical presentations

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1. Introduction

Visceral leishmaniasis (VL; also known as Kala-azar) is a systemic parasitic infection caused by *Leishmania donovani*, *L. infatum*, and *L. chagasi* and transmitted via sand fly *Phlebotomus arhentipes* [1]. Clinical presentations include fever, malaise, anemia, weight loss, splenomegaly, hepatomegaly, bleeding tendency, among other [2], with fever often presenting first [3]. The condition may become worse as some patients may develop hepatic dysfunction or concurrent infections due to pancytopenia which is associated with VL, while some patients may develop post-kalazar dermal infection (PKDL) [4]. According to the World health organization (WHO), 55% of Sudanese patients suffered from PKDL [5]. Of note, the severity of the clinical presentations depends on the interaction between the parasite and its host, so some patients can become asymptomatic carriers or develop symptoms with varying severity due to their inability to control the multiplication of the parasite [4]. Moreover, the fatality rate for untreated cases in developing countries can be as high as 100% within two years [6].

Sudan is suffering from VL since the early 1900s, and several epidemics have occurred and claimed the lives of thousands of people [7]. The first epidemic in Sudan was reported in 1936 in the upper Nile Province, wherein about 300 individuals were infected, and the death rate was nearly 80% [8]. Moreover, a recent study disclosed that about 1.3 million new VL cases are reported yearly, with an estimated 20,000–40,000 annual deaths [9]. In addition, about 94% of VL cases are from Sudan, South Sudan, Ethiopia, India, Bangladesh, and Brazil [10]. Furthermore, in 2015, 2902 cases of VL were reported in Sudan [11]. Recent reports confirm that Gedaref State is a known hyper-endemic area for VL, while Western Upper Nile, Kordofan State, Central Sudan, and White Nile State are also considered as endemic areas [12]. Good understanding of the broad spectrum presentation in patients with VL and its relation to certain factors can establish a better outcome, as early diagnosis is the core stone in the management of the disease. Although a number of papers have been published, there is still vagueness due to the diversity of data and classifications, and variation in people from different geographical areas. This study can provide additional information to doctors and decision-makers for improving the management of VL patients.

The present study therefore assesses the variation in presentation among patients presented at the Tropical Diseases Teaching Hospital (TDTH) in Khartoum State, Sudan. Moreover, it describes the sociodemographic characteristics of patients with VL and identifies the association between the presentations of patients diagnosed with VL and the sociodemographic characteristics.

2. Materials and Methods

2.1. Study design and study area

This is analytical, cross-sectional, hospital-based study was conducted to assess the variation in the presentations of VL among Sudanese patients. It was conducted at the TDTH, which is the only tropical hospital in Khartoum State and the biggest in Sudan, between November 2019 and September 2020.

2.2. Study population

Medical records of all Sudanese patients who presented with VL at the TDTH from January 2016 to March 2020 were studied. However, patients whose files were incomplete were excluded.

2.3. Study variables

1. Characteristics of patients: age, gender, education, residence, occupation, income, and marital status

2. Different clinical presentations, past medical history, complications, and treatment

3. Laboratory results (hemoglobin, total white blood cells count, platelet count, albumin)

2.4. Sampling method and sample size

The total coverage method was used for all patients who visited the study center during the study period.

2.5. Data collection

2.6. Secondary data were collected using pretested and structured data extraction checklist from all Sudanese cases reported during the study period and fulfilling the inclusion criteria. Data collectors were the researchers themselves.

2.7. Data analysis

Data were reviewed, coded, entered, and then analyzed using the SPSS (statistical package social science), version 25. Descriptive statistics were computed to determine frequencies and percentages. Chi-square test was used to determine the associations between sociodemographic and clinical presentations of patients diagnosed with VL at the TDTH. *P*-value < 0.05 was considered as statistically significant.

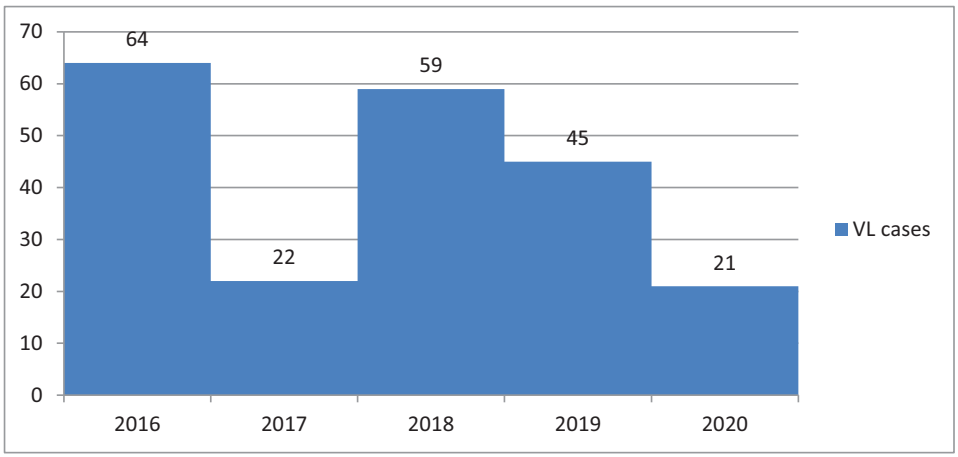

Figure 1: Histogram showing the trend in VL over the 2016–2020 period.

3. Results

3.1. Sociodemographic characteristics

Table 1 presents the sociodemographic characteristics of our participants. A total of 195 patients with VL were identified during the study period. Of them, 155 (79.5%) were male and 140 (71.8%) were aged <41 years. Some of the patients suffered from concurrent chronic disease (Table 2).

3.2. Clinical presentations and hematological findings

Table 3 presents the clinical manifestations of our participants. Out of 195 patients, 177 (90.2%) presented with fever, while 104 (53.3%) presented with weight loss. The mean hemoglobin value was 8.3 g/dl (SD = 2.2), and 177 (90.8%) participants were anemic (hemoglobin level <12 g/dl). While the mean value of the total white blood cells was 3.5 per microliter (SD = 3.4), the mean value of the platelet count was 122 per microliter (SD = 95) and a mean value of 3 g/dl (SD = 1.1) for the albumin.

Table 1: Sociodemographic data of VL patients who were admitted to the TDTH.

Variables		N (%)
Gender	Male	155 (79.5)
	Female	40 (20.5)
Age (yr)	0–10	2 (1.1)
	11–20	42 (21.5)
	21–30	50 (25.6)
	31–40	46 (23.6)
	41–50	29 (14.9)
	15–60	15 (7.7)
	>60	11 (5.6)
Marital status	Child	10 (6.7)
	Single	59 (39.3)
	Married	80(53.3)
	Divorced	1 (0.7)
Residence	Khartoum	51 (26.2)
	Gadarif	26 (13.3)
	White Nile	26 (13.3)
	Blue Nile	8 (4.1)
	North Kordofan	23 (11.8)
	South Kordofan	15 (7.7)
	West Kordofan	5 (2.6)
	North Darfour	3 (1.5)
	South Darfour	6 (3.1)
	West Darfour	4 (2.1)
	Central Darfour	1 (0.5)
	Nile River	1 (0.5)
	Northern State	0
	Kassala State	8 (4.1)
	Aljazeera state	4 (2.1)
	Red sea	1 (0.5)
	Sinnar	5 (2.6)
Occupation	Child	7 (4)
	Unemployed	2 (1.2)
	Farmer	37 (21.4)
	Student	22 (12.7)
	Shepherd	14 (18.1)
	Housewife	25 (14.5)
	Others	66 (38.2)
Income	Low	88 (74.6)
	Average	29 (24.6)
	High	1 (0.8)

Table 2: Chronic diseases often observed in patients with VL admitted to the TDTH.

Chronic diseases	N (%)
Human immunodeficiency virus (HIV)	9 (4.6)
Diabetes mellitus	7 (3.6)
Hypertension	6 (3.1)
Hepatitis B virus	8 (4.1)
Hepatitis C virus	2 (1)

Table 3: Clinical manifestations often observed in patients with VL admitted to the TDTH.

Clinical picture	N (%)	
Symptoms		
Fever	177 (90.2)	
Weight loss	104 (53.3)	
Fatigue	63 (32.3)	
Weakness	3 (1.5)	
Dyspnea	10 (5.1)	
Abdominal pain	90 (46.2)	
Joint pain	11 (5.6)	
Vomiting	21 (10.8)	
Signs		
Hyperpigmentation	7 (3.6)	
Yellow sclera	16 (8.2)	
Abdominal distention	26 (13.3)	
Lower limb edema	23 (11.8)	
Itching	1 (0.5)	
Lymphadenopathy	49 (25.1)	
Splenomegaly	141 (72.3)	
Hepatomegaly	76 (39)	
Pallor	81 (41.5)	
Laboratory findings	**(Mean ± SD)**	
Hemoglobin (gr/dl)	8.2 ± 2.2	
Total white blood cells (per microliter)	3.5 ± 3.4	
Platelet count (per microliter)	122 ± 95	
Albumin (gr/dl)	3 ± 1.1	
	Tested N (%)	**Positive (N)**
RK39	134 (68.7)	119
RK28	3 (1.5)	2
Bone marrow aspiration	70 (35.9)	62
Lymph node aspiration	46 (20.5)	43
DAT	43 (22)	38
Skin biopsy	2 (1)	2

Table 4: Concurrent infections often detected in patients with VL admitted to the TDTH.

Concurrent infections	N (%)
Tuberculosis	7 (3.6)
Gastroenteritis	26 (13.3)
Pneumonia	18 (9.2)
Malaria	11 (5.6)
Otitis media	0
Urinary tract infection	8 (4.1)
Esophageal candidiasis	1 (0.5)

Table 5: The trend in VL admissions to the TDTH from 2016 to 2020.

Year	All hospitalizations	All leishmaniasis	Visceral leishmaniasis	Cumulative # of VL cases
2016	78	66	64	-
2017	61	29	22	86
2018	138	81	59	145
2019	86	66	45	190
2020	54	32	21	211
Total	417	274	211	211

Table 6: Early outcomes for VL patients who were admitted to the TDTH.

Outcomes	N (%)
Death (2016 to 2020)	29 (15)
Discharged after initial improvement	161 (83.4)
Referred (for nonresponse)	1 (0.5)
Discharged against medical advice	2 (1)

3.3. Complications

Concurrent infections were the main complication in our participants (63, 32.3%). Table 4 demonstrates the most common concurrent infections. Other complications were bleeding tendency (34, 17.4%) and PKDL (8, 4.1%).

3.4. Hospitalization rate

Out of 417 admissions to TDTH during the study period, 274 were due to leishmaniasis. This includes only those patients who were admitted to the hospital as inpatient **(**Table 5). Figure **1** demonstrates the trend in VL over the 2016–2020 period.

Table 7: Association between clinical presentations of patients diagnosed with VL at the TDTH and the corresponding age groups.

Clinical picture	Age (yr)							Statistics	
	0–10	11–20	21–30	31–40	41–50	51–60	> 60	Chi-square	P-value
Fever	2	40	46	41	26	11	11	8.046	0.235
Weight loss	1	23	26	21	19	8	6	2.906	0.821
Fatigue	0	18	17	15	8	4	1	6.384	0.382
Weakness	0	0	1	0	0	1	1	8.676	0.193
Dyspnea	0	3	2	2	2	1	0	1.501	0.959
Abdominal pain	1	18	16	22	19	7	7	10.007	0.124
Hyperpigmenta	0	3	2	2	0	0	0	3.755	0.710
Vomiting	0	2	5	6	5	2	1	3..496	0.744
Joint pain	0	4	5	1	0	1	0	6.554	0.364
Yellow sclera	0	3	6	3	1	3	0	5.996	0.424
Abdominal distention	0	8	1	5	8	3	1	13.140	0.041*
Lower limb edema	0	1	8	6	3	4	1	8.089	0.232
Itching	0	0	0	1	0	0	0	3.256	0.776
Lymphadenopa	0	7	12	16	6	3	5	7.511	0.276
Splenomegaly	2	33	39	31	20	7	9	8.537	0.201
Hepatomegaly	2	17	22	18	8	4	5	6.434	0.376
Pallor	0	20	22	16	12	6	5	3.134	0.792

*Significant association

3.5. Diagnosis and treatment

RK39 was the most commonly used diagnostic method, used for 134 (68.7%) of our participants. Other diagnostic methods that were used were bone marrow aspiration (70, 35.9%), lymph node aspiration (46, 23.6%), DAT (33, 22.1%), RK28 (3, 1.5%), and skin biopsy (2, 1%). On the other hand, sodium stibogluconate was the main drug used to treat the patients (103, 52.8%), followed by amphotericin B (93, 47.7%) and paromomycin (66, 33.8%). Some patients received antibiotic therapy (36, 18.5%), 180 (92.3%) received multivitamins, while 41 (21%) required blood transfusion. Early outcomes are presented in Table 6.

Case fatality rate was calculated (Tables 5 & 6) as follows: $29 \div 211 \times 100 = 14.9\%$ (from 2016 to 2020).

Table 8: Association between clinical presentations of patients diagnosed with VL at the TDTH and their gender.

Clinical picture	Gender		Statistics	
	Male	Female	Chi-square	P-value
Fever	141	36	0.036	0.850
Weight loss	79	25	1.699	0.192
Fatigue	51	12	0.123	0.726
Weakness	2	1	0.307	0.579
Dyspnea	8	2	0.002	0.967
Abdominal pain	68	22	1.585	0.208
Hyperpigmentation	6	1	0.173	0.678
Vomiting	17	4	0.031	0.860
Joint pain	10	1	0.933	0.334
Yellow sclera	12	4	0.215	0.643
Abdominal distention	22	4	0.484	0.487
Lower limb edema	21	2	2.233	0.135
Itching	1	0	0.259	0.611
Lymphadenopathy	38	11	0.150	0.698
Splenomegaly	116	25	2.417	0.120
Hepatomegaly	65	11	2.786	0.095
Pallor	65	16	0.049	0.825

3.6. Association between clinical presentations and age groups

Table 7 presents the association between clinical presentations of VL patients at the TDTH and the age groups. A significant association was seen between the abdominal distention and the age of the patients ($P < 0.05$). Age groups 11–20 and 41–50 years were more likely to present with abdominal distention than other age groups.

3.7. Association between clinical presentations and gender

Table 8 presents the association between clinical presentations of VL patients in TDTH and gender. None of the clinical presentations was found to be associated with the gender of the patients.

Table 9: Association between clinical presentations of patients diagnosed with VL at the TDTH and geographic areas.

Clinical picture	Geographic areas										Statistics
	Khartoum state	Gadarif	White Nile	Blue Nile	North Kordofan	South Kordofan	South Darfur	Kassala state	Others	Chi-square	P-value
Fever	48	24	24	8	20	13	6	7	21	5.736	0.766
Weight loss	23	10	16	5	8	11	4	6	16	14.186	0.116
Fatigue	19	8	7	1	6	5	2	6	7	9.767	0.370
Weakness	0	0	0	0	1	0	0	0	1	10.826	0.288
Dyspnea	2	1	2	0	1	1	0	1	2	3.283	0.952
Abdominal pain	23	15	7	1	10	7	4	4	12	15.708	0.073
Hyperpigmentation	2	1	0	0	0	1	0	0	1	13.694	0.134
Vomiting	3	4	4	1	1	2	1	2	3	6.478	0.691
Joint pain	2	0	3	0	1	2	1	0	2	8.408	0.494
Yellow sclera	2	1	5	1	0	1	0	3	3	19.348	0.022*
Abdominal distention	5	5	4	1	3	2	0	1	2	6.924	0.645
Lower limb edema	6	2	2	2	4	0	2	1	4	9.177	0.421
Itching	0	0	1	0	0	0	0	0	0	6.534	0.686
Lymphadenopathy	15	6	5	2	7	2	3	3	4	6.027	0.737
Splenomegaly	41	18	17	5	12	9	5	7	20	12.251	0.200
Hepatomegaly	17	8	9	4	9	6	3	4	10	7.196	0.617
Pallor	20	6	11	4	11	8	3	5	10	6.917	0.646

*Significant association

3.8. Association between clinical presentations and geographical areas

Table 9 presents the association between clinical presentations of VL patients in TDTH and their residence. There was a significant association between the yellow sclera and patients' place of residence ($P < 0.05$). Patients from the White Nile area were more likely to present with yellow sclera than others.

4. Discussion

The clinical features and laboratory findings described here are based on the data from the case files of 195 Sudanese patients diagnosed with VL. We determined that VL is mainly presented by fever, weight loss, splenomegaly, anemia, hepatomegaly, and abdominal pain.

In this study, 155 (95%) patients were male, and 140 (71.8%) of them were younger than 41 years. This finding is in agreement with a previous study conducted in Kenya,

where 105 (77%) patients were male, and 129 (89%) were younger than 45 years [13]. Moreover, a previous study conducted in India concluded that the male gender is a risk factor for VL [14]. Males from a young age are more likely to sleep outside (in yards and farms), so they are more exposed to sand-fly bites [15, 16].

Moreover, a majority of patients in our study presented with fever (90.2%), splenomegaly (72.3%), weight loss (53.3%), or hepatomegaly (39%). In a study conducted in Brazil and Mexico, the patients mainly presented with hepatomegaly (98%), splenomegaly (97.8%), or fever (97.7%) [17]. Moreover, we found that 4.6% of our patients were diagnosed with HIV. This finding is in agreement with another study conducted in Brazil, where 5.5% of VL patients were co-infected with HIV [18]. Owing to the lack of facilities or poor reporting systems, VL/HIV co-infection is underreported in many endemic areas [19]. VL is a common opportunistic infection in HIV patients, as they are more vulnerable to VL infection, and HIV replication is accelerated in VL patients [19].

Most of our patients were treated with sodium stibogluconate (52%), followed by amphotericin B (47.7%) or a combination of paromomycin and sodium stibogluconate. On the other hand, >60% of patients in Brazil and Bulgaria were treated with Meglumine Antimoniate [18, 20]. Due to parasites' drug resistance, liposomal amphotericin B is now the drug of choice for VL [21]. In our study, RK39 was the most used diagnostic test; about 61% of our patients were diagnosed by it. RK39 is a widely used test because it is a simple, sensitive, specific, and economical test [17]. In this study, bone marrow aspiration and lymph node aspiration were done for 70 and 46 patients, respectively, and no patient had undergone splenic aspiration. The splenic aspirate is more sensitive than bone marrow or lymph node aspirate; however, the splenic aspirate is a complicated procedure and associated with a risk of fatal hemorrhage [22, 23].

Regarding limitations of this study, data were available in a paper-based database, this type of database is difficult to deal with, and it can be lost or damaged easily.

5. Conclusion

In conclusion, we found that fever was the main clinical finding, followed by splenomegaly, weight loss, and hepatomegaly. However, there is no exact clinical presentation or routine laboratory findings that are pathognomonic for VL; therefore, it should be considered in the differential diagnosis of any patient presenting with an unusual presentation from the endemic areas or with a history of recent travel. HIV is commonly associated with VL, so VL patients must be investigated for HIV infection.

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Ethical Considerations

Ethical approval was obtained from the Department of Community Medicine at the Faculty of Medicine OIU and the administration of TDTH. Confidentiality was maintained throughout the study.

Competing Interests

Authors declare no conflict of interest.

Availability of Data and Material

Data are available upon request.

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