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Ali RB Musa
Babylon Health Directorate, Babylon, Iraq

Sabih S Mehdi
College of Medicine, University of Babylon, Iraq

Zainab Khairalla Fakhri
Babylon Health Directorate, Babylon, Iraq

Corresponding Author:
Ali RB Musa
Babylon health directorate, Babylon, Iraq

Clinical and biochemical liver derangements in Patients with Kala azar before starting treatment

Ali RB Musa, Sabih S Mehdi and Zainab Khairalla Fakhri

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Abstract
Background: Kala-azar is an important parasitic disease that affects children of all age groups, it is caused by *Leishmania* species and transmitted by sand fly. The aim of study is to identify the clinical features and biochemical derangements of the liver in patients with kala azar before starting treatment.
Method: A hospital-based cross-sectional research was undertaken on 33 patients with clinical and lab diagnoses of kala azar at Babylon Teaching Hospital for Gynecology and Pediatrics in Hilla from January 2013 to January 2014. A case investigation form collected epidemiological, clinical, and laboratory data. Pre-treatment lab testing assessed liver dysfunction in these individuals. A bone marrow aspiration was utilized to diagnose.
Results: Thirty-three kala azar patients were investigated clinically and laboratory. The majority of 33 patients were under 2 years old. It was 1:1.4, with 19 men and 14 women. Nearly all patients had fever, 91% had splenomegaly, and 70% had hepatomegaly. At diagnosis, half of patients showed biochemical liver function abnormalities and 9% had acute liver failure.
Conclusion: Liver involvement is found in some patients both by clinical and biochemical markers. Some patients presented with features of acute hepatic failure before starting treatment.

Keywords: Clinical, biochemical, liver, derangements, Kala azar, treatment

Introduction
Leishmaniosis is a complex parasitic disease caused by the genus Leishmania, which includes several species that lead to different forms of the disease. Visceral leishmaniasis (VL), also known as kala-azar in India, meaning "black disease" due to skin darkening in patients, is the most severe form of leishmaniasis. This form of the disease is predominantly caused by the intracellular protozoan parasite Leishmania donovani and transmitted through the bite of infected female sandflies, specifically Phlebotomus argentipes. VL is notable for affecting a significant number of children, often leading to severe complications if untreated [1, 2]. The Leishmania donovani complex consists of three main species: *L. donovani*, *L. infantum*, and *L. chagasi*. Each species is associated with distinct clinical features and epidemiological patterns. *L. donovani* primarily causes Old World VL in regions like Kenya, Sudan, and South Asia, while *L. infantum* is responsible for cases in the Mediterranean and Central Asia. In the New World, *L. chagasi* is the main etiological agent, often indistinguishable from *L. infantum* through standard laboratory methods [3, 4, 5]. Historically, the first documented cases of kala-azar in Iraq were reported by Kulz in 1916, who diagnosed the disease in Baghdad. The origin of the disease in Iraq during the First World War is debated; it may have been imported by soldiers or have emerged due to ecological disruptions caused by land reforms and urban development. Currently, VL in Iraq is mostly confined to rural and peri-urban lowland areas, predominantly affecting children [6, 7]. Epidemiologically, transmission of leishmaniasis is heavily influenced by ecological conditions, including proximity to rural areas or certain towns' peripheries, and whether humans intrude into natural zoonotic cycles. Factors that favor VL outbreaks include living in rural regions at altitudes below 600 meters, high humidity, and temperature extremes conducive to sandfly survival. Both zoophilic and anthropophilic sandflies are vectors, with transmission risks increasing when humans and livestock live in close proximity [5]. Globally, VL poses a significant health burden, being the second-highest cause of parasitic disease mortality after malaria. Leishmaniasis remains endemic in 88 countries across tropical and subtropical regions, with high incidences in countries like Afghanistan, Brazil, and India.

In Iraq, the disease is a serious public health concern, especially prevalent in the southern and central regions [8]. Leishmania/HIV co-infection has also emerged as a significant new health challenge, reported in over 35 countries worldwide, complicating the management and outcomes of VL [9]. The lifecycle of Leishmania involves two primary stages: the flagellated promastigote in the sandfly vector and the non-flagellated amastigote within mammalian host cells. The disease is transmitted when infective promastigotes are delivered into the host during a sandfly's feeding, leading to infection of macrophages and other phagocytic cells. The control of infection involves complex interactions between innate and adaptive immune responses, which are critical for the disease's progression and outcome [10, 11]. Risk factors for VL include childhood, malnutrition, and immunocompromised states such as HIV infection. Clinically, VL manifests with symptoms ranging from fever and hepatosplenomegaly to severe anemia and wasting, with potential for fatal outcomes if left untreated. Diagnosis typically involves serologic tests and direct identification of parasites in tissue specimens. Treatment options include antileishmanial drugs like sodium stibogluconate and amphotericin B, with emerging treatments like miltefosine showing promise [12-14]. The aim of study is to identify the clinical features and biochemical derangements of the liver in patients with kala azar before starting treatment.

Method

This study is a cross-sectional analysis conducted at Babylon Maternity and Pediatric Teaching Hospital over a period of 13 months, from January 1, 2013, to January 31, 2014. It involved 33 pediatric patients, ranging in age from 3 months to 9 years, all of whom were admitted with symptoms suggestive of kala azar (visceral leishmaniasis). Data collected for each patient included age, sex, place of residence, and a detailed clinical presentation derived from a complete physical examination. The clinical suspicion of kala azar was based on patient history, physical examination findings, and a series of laboratory tests. These tests comprised a complete blood count, blood film analysis, liver function tests, and abdominal ultrasonography. A definitive diagnosis was confirmed through the detection of Leishman-Donovan (L.D) bodies in bone marrow examinations (BME). Patients with negative BME results, who were initially suspected of having kala azar based on clinical criteria, were excluded from the study. Specific criteria were used to define acute liver failure in the study population: absence of known chronic liver disease, hepatic-based coagulopathy unresponsive to vitamin K (measured by prothrombin time (PT) or international normalized ratio (INR)), and necessary hepatic encephalopathy depending on PT or INR values. Hepatomegaly was defined as a liver edge extending more than 3.5 cm below the right costal margin in newborns and 2 cm in older children. Splenomegaly was indicated by a spleen extending more than 2 cm below the costal margin. Lymphadenopathy (L.A.P.) was defined by lymph node diameters exceeding 1 cm in cervical and axillary regions, and 1.5 cm in inguinal regions. Abnormal laboratory values included a PT greater than 12 seconds, partial thromboplastin time (PTT) over 36 seconds, serum glutamic-pyruvic transaminase (SGPT) above 45 U/L, and total serum bilirubin (TSB) exceeding 1.12 mg/dl. Statistical significance for the study was assessed using the Fisher exact test, with a p-value of less than 0.05 considered statistically significant.

Results

Fig 1 shows the distribution of the patients with Kala-azar by gender. Fifty-eight percent of patients were males and 42% were females, M/F ratio is 1.4:1.

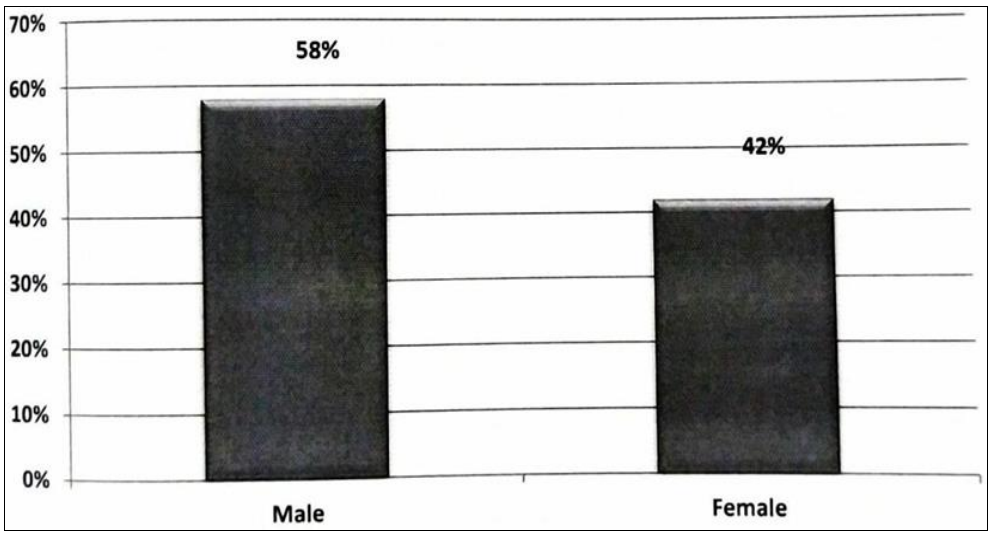

Fig 1: Distribution of patients by gender.

Figure 2 shows the distribution of the patients with kala-azar by dipstick test (immunochromatographic strip assay) results. Majority (76%) of patients presented with positive results.

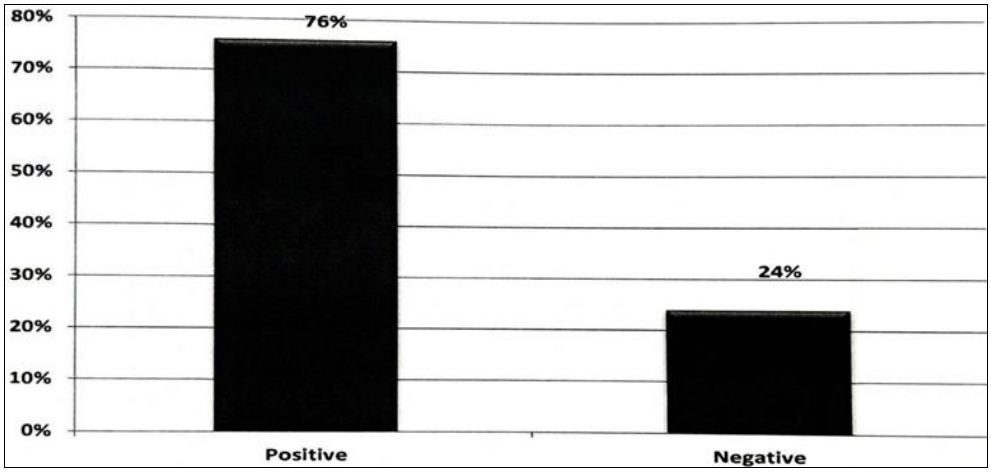

Fig 2: Shows the distribution of the patients with kala-azar by dipstick test

Table 1: shows the distribution of the patients with Kala-azar by clinical signs. Seventy percent of patients presented with hepatomegaly, Majority (91%) of patients presented with splenomegaly, only (18%) of patients presented with lymph node enlargement. All the patients present with fever, and only 18% of the patients with petechiae.

Table 1: Distribution of the patients with Kala-azar by clinical signs.

Sign	No.	%
Hepatomegaly		
Yes	23	70
No	10	30
Splenomegaly		
Yes	30	91
No	3	9
L.A.P		
Yes	6	18
no	27	82
Fever		
Duration	33	100
>=1 month	8	24
> 1 month	25	76
Petechiae		
Yes	6	18
No	27	82

Table 2: shows the distribution of patients with kala-azar by complete blood picture results. Majority (67%) presented with low white blood cell count, (73%) presented with anemia and (52%) presented with thrombocytopenia.

Table 2: Distribution of patients with kala-azar by CBP results

CBP results	Number	%
White blood cells count		
Leukopenia (<4000/mm³) Normal	22	67%
(4000-15000/mm³)	10	30%
Leukocytosis(≥215000/mm³)	1	3%
PCV		
> 33%	24	73%
<= 33%	9	27%
Platelets count		
Thyromocytopenia (< 150000/mm³) Normal or	17	52%
elevated	16	48%

Table 3: Shows distribution of patients with kala-azar by biochemical tests. Thirty percent of the pts presented with elevated total serum bilirubin, (52%) presented with high SGPT (>45) and (46%), and (42%) presented with prolonged PTT and PT respectively.

Table 3: Distribution of patients with kala-azar by biochemical markers.

Liver Function Test Results	Number	%
TSB		
High ≥ 1.12 (mg/dl)	10	30%
Normal <1.12(mg/dl)	23	70%
SGPT		
Elevated (>45U/L)	17	52%
Normal (≤45 U/L)	16	48%
PTT		
Prolonged (>36 seconds)	15	46%
Normal	18	54%
PT		
Prolonged (> 12 seconds)	14	42%
Normal	19	58%

Table 4 shows the association of hepatomegaly and biochemical markers including (TSB, SGPT, PT, and PTT). There was significant association between hepatomegaly with SGPT and PT, meanwhile there was no significant association between hepatomegaly and TSB and PTT. Only (39%) of patients with hepatomegaly presented with elevated total serum bulirubin, (57%) presented with elevated SGPT, (52%) presented with prolonged PTT and (70%) presented with prolonged PT.

Table 4: The association of hepatomegaly and biochemical markers.

Biochemical markers	Hepatomegaly		P-value
	Present	Absent	
TSP			
Hugh ≥ 1.12 (mg/dl)	9(39%)	1 (10%)	0.123 [a]
Normal > 1.12 (mg/dl)	14(61%)	9 (90%)	
SGPT			
Elevated (< 45)	16 (70%).	1 (10%)	0.002** [a]
Normal (≤ 45)	7 (30%)	9 (90%)	
PTT			
Prolong (< 36 seconds)	12 (52%)	3 (30%)	0.283 [a]
Normal	11 (48%)	7 (70%)	
PT			
Prolong (< 12 seconds)	13(57%)	1(10%)	0.021* [a]
Normal	10 (43%)	9(90%)	

*p value ≤ 0.05 was significant
**p value ≤ 0.01 was significant a: Fisher – exact test

A limited number of patients were showing feature of acute hepatic failure which was 6 pt. (18%) as shown in table 5.

Table 5: Show distribution of patients with kala-azar according to liver failure.

State of Liver	**No.**	**%**
Patients with acute liver failure	3	9
Patients without ALF	30	91

Discussion

In this study conducted at Babylon Maternity and Pediatric Teaching Hospital, 33 patients diagnosed with visceral leishmaniasis were analyzed to assess hepatic involvement before treatment initiation, given that screening for liver issues is not commonly prioritized over splenic symptoms in kala-azar cases. The gender distribution was 58% male and 42% female, with a male to female ratio of 1.4:1, aligning with previous studies by Al-Saffar (1.2:1) and slightly lower than Dr. Dhuha Jassim [15]. The majority of the patients were young children, with 52% under one year of age, similar to findings by Abdul Moneim Jamil *et al*. (55%) but higher than those reported in Al-Anbar governorate by Zaid R Al-Ani *et al*. (37%) [16, 17]. Clinical evaluations revealed that 70% of the patients had hepatomegaly, which is comparable to regional studies such as Khlabus (71%) and Hamid (76%), although lower than other findings [18-20]. Splenomegaly was observed in 91% of patients, mirroring results from other studies [18-20]. Lymph node enlargement was noted in 18% of cases, which is consistent with the 20% reported by Hamid [19] but higher than the 6% found by Abdul Moneim Jamil *et al*. [16]. All patients exhibited fever, a common symptom across studies. Bleeding tendency was found in 18% of the patients, comparable to Abdul Moneim Jamil *et al*.'s report of 16%, and higher than the 6% noted by Zaid R Al-Ani *et al*. [16, 17]. Diagnostic results showed 76% of the patients tested positive on the dipstick test, a significant increase compared to the 50% positivity rate found in Dr. Dhuha Jassim's study [15]. Laboratory findings indicated that 67% of patients had a WBC count below 4000 cells/mm³, closely aligning with Zaid R Al-Ani *et al*. (57%). Seventy-three percent had a packed cell volume (PCV) below 33%, which is less than what was found in Zaid R Al-Ani *et al*.'s study (93%) but similar to Khalbus (75%) [17, 20]. Thrombocytopenia was present in 52% of patients, lower than the 78% reported by Zaid R Al-Ani *et al*. [17]. Biochemical tests revealed that 30% of patients had elevated total serum bilirubin (T.S.B.) levels above 1.12 mg/dl, which is similar to Dhuha Jassim's findings (28.5%) and higher than those reported by Hamid (7.8%) [15, 19]. SGPT levels above 45 U/L were found in 52% of cases, and prolonged prothrombin time (P.T.) and partial thromboplastin time (P.T.T.) were noted in 42% and 46%, respectively. This is in line with AKM Mamunur Rashid *et al*., who reported elevated SGPT and jaundice in 56% of their patients [21]. Acute liver failure (ALF) was diagnosed in 9% of the patients, a lower incidence compared to other studies, suggesting that late presentation might influence the development of fulminant hepatitis [22, 23]. This study underscores the need for enhanced screening and management strategies for hepatic involvement in visceral leishmaniasis to improve patient outcomes.

Conclusion

Liver involvement is found in some patients both by clinical and biochemical markers. Some patients presented with features of acute hepatic failure before starting treatment.

Conflict of Interest
Not available

Financial Support
Not available

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