Impact of Visceral Leishmaniasis on Liver Function in Gadaref State - Sudan

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Abstract:

Introduction: Leishmaniasis is a neglected vector-borne tropical infection that is considered to be a disease of the poor. Leishmaniasis has three types; VL (visceral leishmaniasis) is a systemic disease is the most important one as it is fatal if left untreated; cutaneous, the most common; and mucocutaneous. In Gadaref stat, in eastern Sudan VL is endemic affecting wide range of ages. So this study conducted to evaluate VL’s effects on liver by measuring different parameters.

Material and methods: one hundred subjects selected to fulfillment this study, 50 were VL infected individuals and 50 were healthy ones all were alcohol free. Chemical analysis for Albumin, TB, DB, AST, ALT and ALP by means of Biosystem’s

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device and reagents in medical laboratory section of Kala-azar hospital in Gadaref state.

Result: parameters measured were albumin, total and direct bilirubin, AST, ALT) and ALP. Albumin brought decreased significant difference with P=0.000 but other parameters brought increased significant difference.

Conclusion: VL infection has an effect on liver function test (LFT) measured for those VL.

Key words: leishmaniasis, VL, TB, DB, AST, ALT, ALP and LFT.

INTRODUCTION

The liver is a large, complex organ that is well designed for its central role in carbohydrate, protein and fat metabolism. It is the site where waste products of metabolism are detoxified through processes such as amino acid deamination, which produces urea. In conjunction with the spleen it is involved in the destruction of spent red blood cells and the reclamation of their constituents. It is responsible for synthesizing and secreting bile and synthesizing lipoproteins and plasma proteins, including clotting factors. Liver disease is often reflected by biochemical abnormalities of 1 of 2 different hepatic systems or of liver function. Although tests that measure the level of serum liver enzymes are commonly referred to as liver function tests, they usually reflect hepatocyte integrity or cholestasis rather than liver function. A change in serum albumin level may be associated with a decrease in liver functioning mass, although it is not specific for liver disease. Alterations in liver enzyme levels that are encountered in hospital centers may vary by the geographical location of the hospital and the ethnicity of the patients, while the timing of liver enzyme abnormalities in relation to the age of the patient, comorbid conditions and ingestion of medications provides valuable information, and
the most common alterations in enzyme levels encountered in clinical practice can be divided into 2 major subgroups: hepatocellular predominant and cholestatic predominant. Although certain liver diseases may display a mixed biochemical picture — usually elevated AST and ALT levels with mild abnormalities of alkaline phosphatase (ALP)\textsuperscript{2,6}.

Leishmaniasis is a neglected vector-borne tropical infection that is considered to be a disease of the poor\textsuperscript{2} that is caused by obligate intra-macrophage protozoa; the disease is characterized by both diversity and complexity\textsuperscript{8}. Concentrated in poverty-stricken countries within Southeast Asia, East Africa, and Latin America, it is also endemic in several Mediterranean countries\textsuperscript{8}. On a global scale, \textasciitilde{}350 million people live in areas characterized by active transmission of Leishmania, with 14 million people directly affected by the disease\textsuperscript{3}. There are three main types of leishmaniasis: visceral (kala-azar), the most important disease; cutaneous, the most common; and mucocutaneous. Among parasitic diseases, mortality from leishmaniasis is second only to malaria and, in terms of disability-adjusted life years (DALYs), the third most common cause of morbidity after malaria and schistosomiasis, with children under 15 years of age suffering most of the disease burden. International traveling has caused an increase of leishmaniasis cases in non-endemic countries, making the recognition of this parasitic infection important\textsuperscript{10}. The lifecycle of \textit{L. donovani} has two distinct forms: a promastigote flagella form found in the gut of the arthropod vector and an amastigote form, which develops intracellularly in the mammalian host. Only female phlebotomine sandflies transmit the disease, by inoculation of the promastigote form into the skin. The parasites are internalized by dendritic cells and macrophages in the dermis and transform into amastigotes by losing their flagella. They multiply and survive in phagolysosomes through a complex parasite–host interaction\textsuperscript{11-12}.
VL (visceral leishmaniasis) is a systemic disease that is fatal if left untreated and is caused by the Leishmania donovani complex — L. donovani sensu stricto in East Africa and the Indian subcontinent and Leishmania infantum in Europe, North Africa and Latin America\textsuperscript{13-14}. Following an incubation period that generally lasts between 2 and 6 months, VL patients present symptoms and signs of persistent systemic infection (including fever, fatigue, weakness, loss of appetite and weight loss) and parasitic invasion of the blood and reticulo-endothelial system (that is, the general phagocytic system), such as enlarged lymph nodes, spleen and liver. Fever is usually associated with rigor and chills and can be intermittent. Fatigue and weakness are worsened by anemia, which is caused by the persistent inflammatory state, hypersplenism (the peripheral destruction of erythrocytes in the enlarged spleen) and sometimes by bleeding. The clinical presentation of VL is similar in the various endemic areas but there are some differences. For example, enlarged lymph nodes are rarely found in Indian VL patients but are frequent in Sudanese VL patients\textsuperscript{15,16}.

Hypoalbuminemia seen in VL is associated with edema and other features of malnutrition. Diarrhea may occur as a result of intestinal parasitization and ulceration. Liver function may be normal or altered and loss of leucocytes eventually makes VL patients generally immunosuppressed, and bacterial infections are a common cause of death in lethal cases of VL\textsuperscript{17}.

**MATERIAL AND METHOD**

Hospital based case control study, targeted well known diagnosis subjects with visceral leishmaniasis in East of Sudan, Gadaref state-Sudan where as remote areas are familiar with visceral leishmaniasis infections. Ethical approval and Formal consent obtained from hospital administration and patients respectively before the startup of sample collection. Fifty (50)
hospitalized non-alcoholic VL patients in addition to another fifty (50) healthy individuals considered as control group, they selected as no formal hepatic disease neither visceral leishmaniasis and non-alcoholic, they enrolled in this study to evaluate the state of liver function test among patients. After formal consent from the Kala-azar hospital administration and subjects involved in the study blood collection started under hygienic condition, every one donated 5ml of whole blood collected in heparinized container, separation of plasma by centrifugation for subsequent chemical measurement, which conducted via Biosystem’s spectrophotometer with Biosystem’s reagents for bilirubin (direct and total), albumin, ALT, AST and ALP.

RESULT

One hundred free alcohol subjects involved in this study. 50% were hospitalized patients with VL were involved in this study, their mean’s age was 42.1 years, they were 56% males and 44% females (case group) and other 50% were healthy subjects (control group), mean’s age was 35.5 years, 84% males and 16% females. Albumin, bilirubin (direct and total), AST, ALT and ALP were measured for both. All measured parameters were high among case group except the albumin, which was low considering normal subject readings. Statistical analysis with SPSS version 21 via (independent T-test) for the two groups brought significant difference for all parameters, albumin was decreased one as P =0.00, while others were increased, for enzymes more significant difference for AST, then ALP and last ALT, bilirubin (direct and total) were lesser than enzymes but still increased as in table 1.
Table 1 shows mean±SD for LFT and age for both genders

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case (Mean±SD)</th>
<th>Control (Mean±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42.14±18.36</td>
<td>35.5±15.64</td>
<td>0.07</td>
</tr>
<tr>
<td>Male</td>
<td>56%</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>44%</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>albumin</td>
<td>3.60±0.51</td>
<td>4.30±0.67</td>
<td>0.000</td>
</tr>
<tr>
<td>Indirect</td>
<td>1.81±0.48</td>
<td>0.92±0.32</td>
<td>0.036</td>
</tr>
<tr>
<td>Bibirubin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct Bibirubin</td>
<td>0.72±0.17</td>
<td>0.29±0.14</td>
<td>0.017</td>
</tr>
<tr>
<td>AST</td>
<td>198.3±29.2</td>
<td>30.16±9.95</td>
<td>0.000</td>
</tr>
<tr>
<td>ALT</td>
<td>62.64±10.7</td>
<td>39.50±18.70</td>
<td>0.006</td>
</tr>
<tr>
<td>ALP</td>
<td>126.2±60.9</td>
<td>71.86±17.59</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Significant difference P value <0.05

Difference in control group and case group measured parameters shown in figure 1 and 2 comparisons.

Figure 1 compared albumin Total bilirubin (T.B) and direct bilirubin (D.B) in between control and case groups

Figure 2 compared albumin AST, ALT and ALP in between control and case groups
DISCUSSION

The life cycle of Leishmania is initiated when the infected female Sand fly injects metacyclic promastigotes into the host during a regular blood meal. Within minutes, the promastigotes are rapidly taken up by phagocytic cells, including macrophages and neutrophils. Since neutrophils have a very short life span, macrophages are the final host cells for proliferation of Leishmania parasites. Leishmania parasites are obligatory intracellular pathogens; macrophages are indispensable for parasite survival, replication, and differentiation. After initial infection, both neutrophils and macrophages are recruited to the infection site and their interactions with the parasites significantly influence the outcome of infection. Sudan known to be one of the harboring residency for VL, Gadaref state is part of these areas, as typical situations for chronic infection and reinfection with VL are present, so that huge center to hospitalize patients infected with it is located there. Our finding consistent with damage occurrence in liver function, Hypoalbuminemia among VL gave a significant difference and that in agreement with several studies, one of them was found low albumin in nearly half of VL patients involved in that study, and microalbuminiuria detected in their urine sample, that confirming the concept of renal involvement in chronic VL. Also same finding in other study detected hematuria, proteinuria and microabuminuria with extra finding was proliferative glomerulonephritis among part of subjects. Liver enzymes and bilirubin (direct and total) in this study were high among VL patients more than control group, that in agreement with an Iranian study, many parameters were analyzed included liver enzymes, AST, ALT and ALP beside TB & DB all were significantly high and accompanied with hypalbuminemia as well.
CONCLUSION

Our study unfortunately revealed what bad status patients with visceral leishmaniasis are going toward. High liver function tests indicated liver damage occurrence and low albumin level indicated renal dysfunction on.

RECOMMENDATION

To eliminate a disease the source should be considered first, and easy, cheap routine detection method and vaccination should be supplied in order to decrease rate of morbidity and mortality.

REFERENCES


