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Research Article

Prevalence of Hepatitis B, Hepatitis C, HIV and Malaria Co Infection among Patients Infected with Visceral Leishmaniasis in Gedarif, Eastern Sudan

Abstract

Background: Concomitant infections with HBV, HCV, HIV and Malaria among VL patients are not uncommon, thus this study conducted to describe the prevalence of HBV, HCV, HIV and Malaria co-infection with VL among patients admitted to Gedarif teaching hospital in Eastern Sudan.

Methods: This was a retrospective, hospital-based study, carried out on data collected from the Medical records of confirmed VL patients at Gedarif Teaching Hospital between January 2013 and June 2014. Sera samples were tested for HBSAg, anti- HCV and HIV antibodies using enzyme-link immunosorbant assay (ELISA). Thick blood films were examined for malaria.

Results: A total of 313 confirmed VL cases were enrolled in the study with mean age 31.4± (11.9) years. The majority of patients were male 237(75.7%). farmers 176 (56.2%) and rural residents 233(74.4%). Antibodies for HIV, HCV and HBV were detected in 14(4.4%), 5(1.6%) and 6(1.9%) cases respectively. Blood film positive for malaria was found in 29(9.1%). VL/HIV co-infection was noted in 12 (3.8%) patients, VL/HSV co-infection was observed in 6(1.9%), VL/HCV co-infection was detected in four patients (1.3%), VL/ Malaria co-infection was accounted for 29(9.3%) and VL/HIV/ HBV/HCV/ Malaria co-infection was identified in 6(1.9%). 27(8.5%) patients were died of whom 18(62, 1%) patients had VL/ Malaria co-infection and 2 (33.3%) patients had VL/HIV/HSV/HCV/ Malaria co-infection, 5(1.9%) patients had pure VL and 2(16.7%) had VL/HIV co- infection. Although there was no significant difference in age, Gender, residence, and occupation among different groups, there was a high proportion of deaths among VL/ Malaria co-infected cases 18(62.1%) vs. 5(1.9%) $p < .001$.

Conclusion: Concurrency of VL/HIV/HCV/HSV and Malaria is an existing entity in Eastern Sudan. Therefore, it is recommended to perform routine screening of VL infected patients for simultaneous infection with HIV, HBV, HCV and Malaria.

Introduction

Leishmaniasis continues to be an important public health problem worldwide. Visceral Leishmaniasis (VL) is severe form of the disease, Where if it is not treated result in 90% mortality [1]. VL is caused by *Leishmania donovani* (*L. donovani*) complex and transmitted by infected sand fly mosquito. The global annual incidence was estimated by 200,000 to 400,000 cases. Fever, weight loss, Hepato-Splenomegaly and anemia were the predominant clinical manifestations [2]. More than 90% of VL cases were reported from Bangladesh, Nepal, India, Brazil, and Sudan [3]. VL has been reported in Eastern region of Sudan since 1904 and Around 15,700 to 30,300 VL patients were reported annually from different endemic foci in Sudan [4,5]. VL has been documented as one of the opportunistic infections among patients with HIV; furthermore, concomitant infection with HIV is associated with more than 100 folds increased risk of acute VL, treatment failure and relapse in endemic areas [6-8]. On the other hand VL has increased the risk of developing AIDS-defining illness [9]. In Sudan, HIV/VL co-infection was reported as 9.4% and 3.6% in central

and eastern Sudan respectively, whereas, in neighboring Ethiopia HIV/VL co-infections ranging between 18- 40 [10]. Worldwide, Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) represent significant public health problems and around 300 million people are infected with HBV and HCV [11,12]. HBV and HCV infections are responsible for the majority of cases of chronic liver diseases namely liver cirrhosis and hepatocellular carcinoma [13]. In Sudan the prevalence of HBV is ranging between 8.4 in Eastern Sudan and 26% in southern region. The sero- prevalence of HCV was documented as 2.2- 4.8 in general population and 26% among haemodialysis patients [14,15]. Hepatotoxicity is a recognized side effect of anti Leishmanial treatment namely sodium stibogluconate (SSG), Co infection of HBV and HCV among patients with VL increased the risk of Hepatotoxicity during treatment with SSG [16]. Since the treatment of VL consists of intramuscular injections of SSG or other anti Leishmanial drugs, patients with VL were at higher risk of contracting dangerous blood-borne infections like HBV, HCV and HIV [17]. Sudan has high endemicity of malaria and visceral Leishmaniasis (VL), therefore, co- infections with both diseases were frequently observed [18].

Likewise, in countries, where visceral Leishmaniasis (VL) and malaria are co-endemic, Concomitant malaria among patients with visceral Leishmaniasis is also noted [19]. In an area characterized by unstable seasonal malaria, in Sudan, the prevalence of VL-Malaria co-infection was reported as 31% [20]. However, in neighboring Uganda, At Amudat Hospital nearly one fifth of VL patients diagnosed as having co-infection with malaria. Furthermore, concomitant infection with malaria increased risk of exacerbating VL symptoms [19]. Studies on prevalence of HBV, HCV and HIV and Malaria among patients with VL are limited, therefore this study was designed to determine the prevalence of HBV, HCV, HIV and Malaria in patients with VL.

Methods

This was a retrospective analysis of consecutive VL patients' records covering the period between January 2013 and June 2014 at Gedarif Teaching Hospital, which is 500 bed tertiary care hospital and provides services for all patients referred from rural hospitals and health centers. Gedarif is located in Eastern Sudan about 400km far from Khartoum, the Capital city. It covers an area of 75263 square kilometers and populated by 1148262 inhabitants. There are ten diagnostic and treatment centers distributed in different localities in Gedarif state. Gedarif Ministry of Health, Leishmaniasis control programme estimated that 2681 cases of VL and 91 (2.8%) deaths from January up to the end of December 2014(unpublished data). Structured questionnaire was filled to gather information on socio-demographic (Age, Gender, residence, occupation) and clinical features.

Diagnosis of VL and HIV, HBV, HCV & Malaria co – infection

The diagnosis of VL was made by the presence of LD bodies obtained from bone marrow, lymph nodes and splenic aspirates of 271 consecutive patients suspected of having VL. Serological tests (Direct agglutination tests (DAT), rK39) were performed for 42 patients. Five ml of venous blood was drawn from each subject, sera was separated and tested for detection of HBV and HCV using immune-chromatographic test (ICT) (Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, United Kingdom). All positive samples were rechecked using, enzyme-link immunosorbant assay (ELISA) (Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, United Kingdom). The diagnosis of HIV was made using the ELISA test according to guidelines of the National AIDS control programme. Peripheral blood smears were prepared (thick film), stained with 10% Giemsa and examined under oil immersion for the detection of malaria. The patients were managed according to the VL programme in collaboration with the Ministry of Health in Gedarif state, when the anti-Leishmanial drugs and the hospital manipulation were offered free of charge for all patients with VL.

Statistical analysis

Data were entered into a computer database using SPSS (SPSS Inc., Chicago, IL, USA, version 16.0) and were double-checked before analysis. The Student's t-test and ANOVA were used to compare means and proportions, respectively. $P < 0.05$ was considered significant.

Ethical approval

The research approved and ethical clearance received from the Health Research board, Ministry of Health at Gedarif State.

Results

Patients' characteristics

The medical records of 313 VL patients admitted to Gedarif teaching Hospital during the study period were reviewed and enrolled in this study. Diagnosis of VL was confirmed by parasitological procedure in 271(86.6%) patients, of these the lymph nodes, bone marrow and splenic aspirates showed positive results for *L. donovani* bodies in 50(15.9%), 212(67.7%), and 9(2.9%) patients respectively. Serological diagnosis was performed in 42(13.4%) patients of whom 35(11.2%) showed positive results for DAT test, while 7(2.2%) were positive for rk39. The mean age of VL patients was $31.4 \pm (11.9)$ years. The majority of patients were male 237(75.7%), farmers 176 (56.2%) and rural residents 233(74.4%) (Table 1). Among the clinical manifestations fever was found in 276 (88.1%), cough in 48(15.3%), vomiting in 48(15.3%), diarrhea in 17(5.4%), Jaundice in 17(5.4%), and anemia in 157(50.1%) (Table 2).

Prevalence of HIV, HBV, HCV and Malaria among the VL patients

Antibodies for HIV HCV, HBV, were detected in 14(4.4%), 5(1.6%), 6(1.9%) respectively. Blood film for malaria was found in 29(9.1%) cases. VL/HIV co-infection was noted in 12 (3.8%) patients, of these 11(91%) patients were male. VL/HBV co-infection was observed in 6(1.9%) and VL/HCV co-infection were detected in four patient (1.3%). VL/ Malaria co-infection was noted in 29(9, 3%) and VL/HIV/HBV/HCV/ Malaria co-infection was observed in 6(1.9%) patients. Deaths were 27(8.5%) of whom 18(62.1%) patients had VL/ Malaria co-infection and 2(33.3%) patients had VL/HIV/HBV/HCV/ Malaria co-infection. 5(1.9%) patients had pure VL and 2(16.7%) had VL/HIV co- infection Despite of no significant difference in age, Gender, residence, and occupation among the different groups, there was a high proportion of death among VL/ Malaria co-infected cases (62.1% vs 1.9%, $p < .001$) (Table 1).

Discussion

To our knowledge this is the first report designed to study the prevalence of VL/HIV/HBV/HCV and Malaria co-infection in Sudan. The prevalence of VL/HIV, VL/HBV, VL/HCV, VL/ Malaria, VL/ HIV/HBV/HCV and Malaria co-infection in this study was estimated by (3.8%), (1.9%), (1.3%), (9.3%) and (1.9%) respectively. The prevalence of VL/HIV co-infection (3.8%) is similar to that reported by Alvar et al., where VL/HIV co-infection accounted for 3.6% [10]. Also in unpublished data conducted by the Médecins Sans Frontières (MSF) in South Sudan between 2010 and 2012, the prevalence of V.L/ HIV co-infection was detected in 2.5% among 2,426 VL patients. In Nepal the prevalence of V.L/HIV co-infection was found in 5.7% [21]. However, the rate of co-infection in the current study was inconsistent with the report from Humera (North-West Ethiopia) where 40% of VL patients co-infected with HIV in 2006 [22]. Although the HIV-infected people are particularly vulnerable to VL, the discrepancy

Table 1: HIV, HBV, HCV and Malaria among the VL patients admitted to Gedarif Teaching hospital, Eastern Sudan (n=313).

variables	VL N=256	VL/ HiV N=12	VL/ HBV	VL/ HcV N=4	VL/Malaria N=29	VL/ HiV / HcV / HBV Malaria N=6	P
Age	31.5(12.3)	36.5(5.2)	29.8(12.8)	29.7(3.2)	27.3(10.1)	31.5 (9.3)	0.337
Sex, male	192(75%)	11(91.%)	3(50.0%)	2(50.0%)	23(79.3%)	6(100%)	0.181
Residence, Rural	70(27.3%)	3(25.0%)	1(16.7%)	2(50.0%)	(6.9%)	2(33.3%)	0.190
Occupation, farmers	145(56.6%)	7(58.3%)	3(50.0%)	2(50.0%)	16(55.2%)	6(50.0%)	0.225
Outcome died	5(1.9%)	2(16.7%)	0(00)	0(00)	18(62, 1%)	2(33.3%)	<.001

Table 2: Clinical characteristic of VL patients admitted to Gedarif teaching hospital, Eastern Sudan (n=313).

Variables	Cases	Percentage of the total cases
Fever	276	88.2.%
Epistaxis	52	16.6%
vomiting	48	15.3%
Diarrhea	17	5.4%
Weight loss	143	45.7%
Cough	48	15.3%
anemia	156	49.8%
Splenomegaly	253	80%
Headache	61	19.5%
Ascites	18	5.8%
Jaundice	17	5.4%
Hepatomegaly	156	49.8%
Lymphadenopathy	62	19.8%

between the results of co-infection in an endemic area like Sudan and Ethiopia may be attributed to under reporting of co-infected cases as well as lack of facilities to diagnose both diseases. Moreover, failure of including the VL as opportunistic infections in the national programs list was also concerned. Interestingly the majorities of the VL/HIV co-infected patients were male that can be explained by an increased male preponderance among VL-infected patients in general. The current study demonstrated the case fatality rates of 16.7% among HIV positive VL cases which is closer to estimates from Ethiopia that showed a mortality rate of 15.5% among VL/HIV co-infected patients treated with SSG [23]. However, it is inconsistent with 39.3% that reported by Mengistu et al., among VL/HIV co-infection [24]. VL/HIV co-infection has important clinical implications, as VL accelerates progression to AIDS by stimulating replication of the HIV. Furthermore, concomitant HIV infection increases the risk of developing active VL and these factors may contribute to death in a significant number of VL/HIV-infected individuals. We found that the seroprevalence of HBV and HCV was 1.9% and 1.3% respectively among VL positive patients. This was slightly lower than HBV and HCV seroprevalence in the general Population in Sudan (HBV (6.8%) and HCV(2.2%)), and much lower than the results obtained in another study performed on VL positive patients in the same study area where the prevalence of HBV and HCV were found in 66.7% and 27% respectively [25,26,16]). Our study showed that VL-hepatitis B co-infection was more preponderance than VL-hepatitis C infection,

which is comparable with the nationwide prevalence of hepatitis B. In contrast Singh et al., in India reported VL/HBV and VL/HCV co-infection as 13.2% and 20.6% respectively. The higher prevalence rate of HCV in VL positive patients in comparison to the rate for HBV positivity in VL infected patients in India could be attributed to reuse of unsterile needles in health care settings, where hepatitis B and C viral infections were found to be common among those who shared use of unsterile injection needles [27]. The VL/ Malaria co-infection rate described in the present study (9.3%) indicating alarming situation among VL positive patients living in areas where both diseases are endemic. Around 10% of the VL patients included in this study were reported to be co-infected with VL and malaria; this is in accordance with study conducted by de Beer et al., among displaced Sudanese population (10.7%). However, it is inconsistent with another study carried out in the same study area in Sudan and showed the rate of co-infection as high as 60%, this variation may be explained by seasonal variation of malarial transmission since more cases anticipated during the rainy season [28,29]. Furthermore, the majority of patients received full anti-malarial prior to their admission to Gedarif tertiary Hospital. The prevalence of VL-Malaria co-infection were also noted in studies from Uganda, India and Bangladesh as (19%, 5.9 and 1.2% respectively) [19,30]. The case-fatality rate was significantly higher among VL/malaria co-infection in this study (62.1%), indicating concomitant malaria as risk factor for poor outcome of VL patients and necessitates urgent call for including Malaria screening program among VL patients particularly in areas where malaria is co-endemic with VL. The High mortality rate among V/Malaria co-infection (11.2%) was also found in the MSF's dataset from Um-el-Kher and Kassab Hospitals [16]. Our results confirmed that VL-infected patients have a high probability of getting malaria, as VL enhanced immunodepression. This series also reports high case fatality rate (33.3%) among VL patients with simultaneous HIV/HBV/HCV/ Malaria co-infection, reflecting that the concurrency of such infections might affect the course of disease or the prognosis. Thus, these findings emphasize an urgent need for early screening of such infections among VL patients, in order to reduce mortality and improve the outcome. The limitations of this study including; retrospective hospital-based which might not reflect that has been happening at the level of the community, risk factors of VLco-infections were not adequately assessed and the sample was relatively of small size.

Conclusion

This study highlights for the first time that concurrent VL/HIV/HCV/HBV and Malaria, is an existing entity in eastern Sudan. Thus,

routine screening of VL infected patients for simultaneous infection with HIV, HBV, HCV and Malaria should be implemented. Further studies involving clinical pattern and risk factors are required to understand the emergence VL/HIV/HCV/HBV and Malaria co-infection.

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