Characterization of Visceral leishmaniasis Outbreak, Marsabit County, Kenya, 2014

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Abstract

Background: Visceral leishmaniasis (VL) is caused by protozoa of the Leishmania donovani complex. Annually, an estimated 500,000 cases of VL are reported globally posing a public health challenge. The objectives of our study were to confirm and determine the magnitude of VL outbreak, characterize the outbreak clinically and epidemiologically and evaluate the county preparedness and response in Marsabit County, Kenya.

Methods: A retrospective review of laboratory registers and patients’ clinical notes was done at Marsabit County Hospital. Cases were persons with confirmed VL diagnosis either by microscopy, serology or molecular technique coming from Marsabit County from May to October 2014. Cases were interviewed using structured questionnaire to collect clinical and epidemiologic information. Blood samples were collected from cases for laboratory confirmation.

Results: A total of 136 cases were confirmed of which 77% (105) were male with a median age of 17 (IQR: 22) years and 9.6% (13) case fatality rate. All cases were admitted at Marsabit County Referral Hospital, Kenya. Medical records of 133 cases were retrieved. Of the 133 cases, 102 (77%) presented with fever, 43 (32%) with splenomegaly, 26 (20%) with hepatomegaly and 96 (72%) were managed with Sodium stibogluconate (SSG) monotherapy. Thirty four cases (26%) received Full haemogram (FHG) test and none had more than one Liver Function Tests (LFTs) in a span of six months. No VL case management training had been conducted nor VL treatment guidelines distributed among health care workers (HCWs) in the last one year.

Conclusions: VL cases were confirmed. Inadequate case monitoring and management was evident. VL case management sensitization training was conducted. The County health department should put in place VL surveillance and facilitate periodic case management trainings.

Background

Visceral leishmaniasis (VL), also known as Kala-azar, still remains a public health problem. Globally, an estimated 500,000 cases of visceral leishmaniasis occurs annually. In Kenya, it is estimated that about 4,000 cases occur annually while 5 million people are at risk of infection (Technical guidelines for Integrated Disease Surveillance and Response in Kenya (2012). Though Kala-azar is curable, it still
causes high morbidity and sometime death due to its low index of suspicion by health care providers, late diagnosis and poor cases management. If left untreated, it has a high mortality rate (over 95%) (Alvar et al., 2012). In May 2014, reports of 18 laboratory (rK39) confirmed Kala-azar cases in Marsabit County from 10th to 21st May 2014 were received at the Ministry of Health through Disease Surveillance and Response Unit (DSRU). This prompted the Ministry of Health to conduct an investigation in Marsabit County, to confirm and determine the magnitude of an outbreak, describe the epidemiology, clinical characteristics and treatment outcomes of rK39 confirmed VL cases, and evaluate the county preparedness and response to the outbreak.

Methods
Study design and setting:
This study characterizes VL outbreak cases in Marsabit County referral Hospital, Marsabit County about 550 km North of Nairobi, Kenya. Marsabit is the largest county in Kenya covering 70,961 square Kilometres. It is divided into 7 Sub-Counties: Marsabit, Laisamis, North Horr, Loiyangalani, Sololo, Moyale and Chalbi. Marsabit borders three counties; Wajir to the east where VL is endemic, Turkana to the west and Isiolo to the south. It also borders the country of Ethiopia to the north. The people of Marsabit County are mainly nomadic pastoralists rearing cattle, goats, sheep and camels. Herding is usually done by men; boys, youths and adults. During the dry period, pastoralists move from one area to another and settle in areas called Fora in search of pasture and water for their livestock. A fora is a forestry and swampy grazing areas where the pastoralists stay with their animals for months before returning to their households. In the fora’s, they sleep in open areas next to the animals without use of mosquito nets.

Characteristics of participants:
All VL cases in the County were referred to this health facility for management. A case of VL was defined as any person living in or has traveled to Marsabit County and complains of fever ≥38°C (or history of fever) or headache for more than two weeks and/or splenomegaly, lymphadenopathy, general weight loss, anorexia with VL diagnosis either by microscopy, serology or molecular technique from May to October 2014.

Data collection:
Retrospective record review was conducted from May 2013 to May 2014 to determine the period when the outbreak could have started. All health care facilities which had reported at least one suspected VL case were selected for the investigation; Marsabit Sub-County Hospital, Logologo Health Centre and Mountain Clinic. This was followed by prospective record review of medical and laboratory records of VL confirmed cases in Marsabit County Referral Hospital from May 2014 to October 2014. Interviews and data abstraction from medical and laboratory records were conducted using a structured questionnaire (Additional file 1) to collect clinical and epidemiologic information. Variables of interest were epidemiological characteristics: Age, gender, residence, occupation, date seen at the facility, date of admission, date of referral, place of referral and hospitalization days; clinical characteristics: fever ≥38°c (or history of fever), headache, splenomegaly, lymphadenopathy, general weight loss, anorexia, vomiting, poor appetite, anaemia, intermittent respiratory infections and epistaxis; treatment regimen: Sodium stibogluconate (SSG), paramonycin (PM) and liposomal amphotericin B (Ambisome) drugs; biological markers for monitoring treatment: total blood count, kidney and liver function test and treatment outcome: dead or alive.

Approximately 4–6 milliliters of blood was obtained from consenting or assenting suspected and confirmed cases and stored in a refrigerator at 2–8°C at Marsabit Sub-County Hospital Laboratory. Assent was sought from all study participants below 18 years before study participation. Samples were centrifuged within 6 hours of sample collection. The refrigerator’s temperature was monitored with a thermometer to ensure the temperature stayed within 2–8 °C. Samples were later triple packaged in a cooler box and transported to National Public Health Laboratory services (NPHLs), Nairobi, Kenya by air (Mission Aviation Fellowship) for further differential analysis using Polymerase Chain Reaction (PCR) and Enzyme-Linked Immune-sorbent Assay (ELISA). The results were E-mailed from NPHLs to Marsabit Sub-County Hospital at the completion of testing of all the samples for patient notification and optimal case management. Preparedness and response to VL outbreak was assessed by administering a structured questionnaire (Additional file 2) to the members of the Sub-County and County Health Management Teams through face to face interview. The questionnaire addressed the
following areas; information on outbreak preparedness and response, management of information, case management, laboratory surveillance, vector control activities, documentation and data utilization. Verification of responses, where necessary, was made by observation.

Data analysis:
Data generated was entered and analysed using Microsoft Excel 2010. Descriptive statistics were determined.

Results
Descriptive investigation of Kala-azar:
A total of 433 VL cases were identified of which 136 (31.4%) were laboratory (rK39) confirmed during the period of the record review (Figure 1). Of the 136 confirmed cases, 105 (77%) were male and the median age was 17 (IQR: 22) years (Table 1). All cases were admitted at Marsabit County Referral Hospital for management. Thirteen deaths were reported (CFR: 9.6%). Two thirds of the confirmed cases came from Bubisa (29%, 40 of 136), Logologo (24%, 33 of 136) and Shurr (13%, 18 of 136) villages. Clinical notes of three confirmed cases diagnosed in November 2013 were missing. Of the 133 confirmed cases with clinical notes, 102 (77%) presented with fever, 72 (54%) with vomiting, 65 (49%) with cough, 63 (47%) with headache, 58 (44%) with abdominal pain, 43 (32%) with splenomegaly and 26 (20%) with hepatomegaly (Figure 2).

Of the 133 cases admitted, 96 (72%) were treated with Sodium stibogluconate (SSG) monotherapy and 37 (28%) with combine regimen; sodium stibogluconate and paromomycin. Various biomarkers; Full Haemogram (FHG), kidney function test (creatinine levels) and Liver function test, were used to monitor cases' progress during treatment. Upon admission, 84 (63%) cases had FHG test, 20 (15%) had creatinine levels estimated and six (5%) had liver function test conducted. One week after treatment initiation, 34 (26%) cases had FHG test, six (5%) had creatinine levels estimated and three (2%) had liver function test conducted (Figure 3). Of the monitoring biomarkers, 34 (26%) cases had at least two Full Haemogram (FHG) tests, seven (5%) cases had at least two creatinine tests and none had more than one Liver Function Tests (LFTs) by the third week of treatment. Ten (8%) cases were transfused with blood.

Of the 13 death reported, 12 (92%) were male with a median age of 40 (IQR: 20) years. Cases
presented with fever (85%), headache (77%), vomiting (69%), abdominal pain (62%), cough (54%), splenomegaly (46%), hepatomegaly (46%), jaundice (23%), epistaxis (15%), loss of appetite (8%) and abdominal distention (8%). Ten (77%) were treated with Sodium stibogluconate monotherapy and three (23%) were on the combined regimen of sodium stibogluconate and paromomycin. On admission, 10 (77%) cases had FHG test, five (38%) had creatinine levels estimated and two (15%) had liver function test conducted (Figure 4). A significant number did not receive any form of monitoring; three (23%) had zero FHG test, eight (62%) had zero creatinine test and 11 (85%) had zero LFT test. One (8%) case had blood transfusion.

**Laboratory analysis:**
A total of 18 blood specimen were drawn from the laboratory confirmed (rK39 diagnostic kit antigen-based dipstick, IT-Leish, DiaMed AG, Switzerland) cases. Enzyme-linked immune-sorbent Assay (ELISA) and PCR testing techniques were used for differential diagnosis to rule out other febrile illness. Of the two test employed, all (100%) samples were negative for Yellow Fever, Dengue Fever, West Nile, Chikungunya and Rift Valley viruses by IgM ELISA; Flavi, Alpha, Orthobunya, Yellow Fever, West Nile, Dengue, Rift valley fever and Chikungunya viruses by PCR; Rickettsia Spp., Leptospira Spp. and Salmonella Spp. bacteria and Plasmodium Spp. parasites by PCR.

**Evaluation of outbreak preparedness and response:**
A total of seven face to face interviews were conducted among health facility in-charges and Health Management Team (HMT) members. Of the three heath facilities which reported VL cases, one (33%) was a private health care facility, two (66%) had surveillance focal persons, one (33%) had analyzed their data and two (66%) submitted monthly feedback to HMT. All (100%) HMT members and facility in-charges from both private and public facilities were aware of Kala-azar outbreak in Marsabit County. However, VL outbreak and case management sensitization had not been done in all health facilities. Two (66%) health care facility had been involved in active case finding in the community.

Mass screening was conducted on 21st May 2014 at Shurr village where VL confirmed cases were clustered.

Information, Education and Communication (IEC) materials on Kala-azar were not available in all
facilities. None of the sampled health facilities had surveillance guidelines for kala-azar, kala-azar standard case definition, emergence and environmental control plan. Only the private health facility (Mountain Clinic) had stocked rK39 diagnosis kit for the last one year. None of the health facilities had stocked Kala-azar medication (Sodium stibogluconate (SSG) and paramomycin) in the last one year. None of the health care worker in Marsabit County had been trained on Kala-azar case and specimen management in the last one year.

Discussion

One hundred and thirty six VL cases were confirmed using rK36 rapid diagnostic test (RDT) kit. Blood samples taken for differential diagnosis were negative for several viral, bacterial and parasitic microorganisms analyzed; Yellow Fever, Dengue Fever, West Nile, Chikungunya, Rift Valley Fever, Flavi, Alpha, and Orthobunya viruses; Rickettsia Spp., Leptospira Spp. and Salmonella Spp. bacteria and Plasmodium Spp. parasites.

The first cases (72%) during this outbreak were treated with the Sodium stibogluconate (SSG) monotherapy; the available treatment option at the time of diagnosis. Though efficacious, SSG monotherapy treatment requires a longer hospitalization period (30 days) (Reithinger et al., 2007; Ritmeijer et al., 2006 and Rijal et al., 2003) compared to stibogluconate and paromomycin combined therapy (17 days) (Musa et al., 2012). However at the tail end of the outbreak, a combine regimen of sodium stibogluconate and paromomycin was administered. This is the recommended VL first line treatment in Eastern African countries (Musa et al., 2012 and Melaku et al., 2007).

Male were more affected than female. Although all age categories were affected, majority of the cases were older male between 15 and 44 years. This is inconsistent with a study conducted among the Ugandan and Kenyan Pokot community where the most affected age group were male between 5 and 14 years (Mueller et al., 2014). This can be attributed to culturally defined duties in these nomadic communities where men of different age groups are involved in cattle herding while women are left at home to conduct household chores. The age group shift from 5—14 years to 15—44 years can be attributed to the introduction of free primary education in Kenya. The primary school eligible age group seems to have abandoned herding to schooling. Majority (30%) of the cases were 15—29
years old which is similar to cases reported at Metema Hospital, Ethiopia from 2008 to 2012 (Shiferaw et al., 2016).

The clinical picture of VL patient in Marsabit differed from those presented among the Pokot communities despite the fact that they share similar Manyatta lifestyle. In the current study, more than a third of the cases presented with fever and a third presented with splenomegaly. This is inconsistent with Mueller et al. (2014) study among the Pokot community where all the cases presented with fever and more than two third of the cases presented with splenomegaly.

Visceral leishmaniasis patients’ response to treatment can be clinically evaluated by monitoring reduction of spleen/liver size and examining the normalization of blood cell counts through Full Haemogram test which serves as an indicator of bone marrow recovery (Kip et al., 2015). Assessment of the Kidney function (Creatinine levels) is used to monitor toxicity associated with sodium stibogluconate-SSG treatment (ZijlstraEE and el-HassanAM, 2001). In this study no spleen/liver size reduction assessment was conducted while liver function and blood cell count were inconsistently monitored. This is suggestive of poor VL case management.

Conclusions

The study documents new VL endemic Foci in Marsabit County, where the disease is a big burden to the currently devolved health care department. Cases were inadequately managed. The County outbreak preparedness was inadequate.

Recommendations

The County health department should initiate VL surveillance and carry out periodic VL case management training to assure optimal case management.

List Of Abbreviations

AFENET Africa Field Epidemiology Network
BSc Bachelors of Science
DSRU Disease Surveillance and Response Unit (DSRU)
ELISA Enzyme-Linked Immunosorbert Assay
FELTP Field Epidemiology and Laboratory Training Program
FHG Full haemogram
HCWs Health care workers
HMT Health Management Team
IEC Information, Education and Communication
IgM Immuno-globulin M
Declarations

Ethical approval and consent to participate:
This being a public health response by the Kenya Ministry of Health, no review by an institutional ethics review board was sought. However, all study participants gave an informed consent or assent before study participation. Assent was sought from parent or guardian of all participants less than 18 years. Additionally personal identifiers (name, identification number and in-patient number) were removed from the participants’ data. The data were then stored in a computer which could only be accessed by authorized persons through a password to avoid a breach in confidentiality.

Consent for publication:
Not applicable

Availability of data and materials:
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. The data will also be deposited in publicly available repositories after manuscript publication.

Competing interests:
The authors declare that they have no competing interests.

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Author contributions:
EWK was responsible for overall study design, protocol preparation, data collection, specimen collection and analysis, data analysis, report and manuscript writing.

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Table

Table 1: Age distribution of visceral leishmaniasis cases, Marsabit County Referral Hospital, Kenya,
2014 n=145

| Age in Years | Frequency | Percentage |
|--------------|-----------|------------|
| Under 5      | 32        | 22         |
| 5 to 14      | 36        | 25         |
| 15 to 29     | 43        | 30         |
| 30 to 44     | 18        | 12         |
| 45 and above | 16        | 11         |
| Total        | 145       | 100        |
Figures

Figure 1

Epicurve of visceral leishmaniasis cases, Marsabit County Referral Hospital, Kenya, 2014

n=136
Figure 2

Clinical presentation of visceral leishmaniasis cases, Marsabit County Referral Hospital, Kenya, 2014 n=133

Figure 3

Biomarkers monitored in visceral leishmaniasis cases management, Marsabit County Referral Hospital, Kenya, 2014 n=133
Figure 4

Biomarkers monitored among diseased visceral leishmaniasis cases, Marsabit County Referral Hospital, Kenya, 2014 n=13

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
Additinal file 1 - Kala-azar Case investigation form.doc
Additional file 2 - Kala-azar outbreak preparedness form.doc