

Epidemiological characteristics and factors associated with Visceral Leishmaniasis in Marsabit County, Northern Kenya

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Abstract

Introduction: Visceral Leishmaniasis (VL) is endemic in 14 of the 47 counties in Kenya. An upsurge of VL cases started in March 2017, the number of cases continued rising and by June 2017, 104 cases and 3 deaths had been reported. We conducted an investigation to describe the magnitude and pattern of the outbreak and to assess factors associated with VL infection among the cases. **Methods:** We conducted a secondary data analysis of VL data from 1st January 2014 to 11th July 2017 obtained from Marsabit county referral hospital and Laisamis Mission Hospitals, with a VL case being defined as any entry with a clinical or laboratory diagnosis of VL. We also conducted a frequency matched case-control study among 76 case-patients and 152 controls. A confirmed case was a person with positive rK39 serology for VL from 1st April 2017 through 11th July 2017; whereas a control was a person within a defined age-category as a case, without signs/symptoms of VL since 1st January 2017, and negative on serology. We calculated attack rates (AR) and case fatality rates (CFR) over the study period. In the case control study, we conducted unconditional logistic regression with adjusted odds ratio (AOR) and 95% confidence interval (CI). **Results:** A total of 383 records were reviewed, out of which 308(80%) were rK39 positive. Of the 308 confirmed cases. 256 (83%) were males. The overall AR was 169/1000 while AR among children <5 was 149 cases/100000. Overall CFR was 4.2% (13/308). History of travel to VL endemic areas (AOR =3.23, 95% CI 1.63-6.40), being a male (AOR=2.49, 95% CI 1.29-4.81), presence of termites mounds around homesteads (AOR=2.29, 95% CI 1.17-4.47), and residing in rural sub-counties (AOR=2.99, 95% CI 1.26-7.13) were factors independently associated with the VL infection. **Conclusion:** The burden of Visceral Leishmaniasis is high affecting males and children < 5 years of age. We recommended health education, increase community awareness on Leishmaniasis, indoor residual spraying and intensifying the use of insecticide impregnated bed nets targeting children < 5 years.

KEYWORDS

Visceral Leishmaniasis, Northern Kenya, Outbreak, Laboratory diagnosis

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Introduction

Visceral leishmaniasis (VL), also known as Kala-azar, is a vector borne parasitic disease caused by *Leishmania* which mainly affects poor rural communities in the tropics [1]. The causative agents, *Leishmania donovani* complex in East Africa and Indian Subcontinent; and *Leishmania infantum* in Europe, North Africa and Latin America, are transmitted from an infected animal or human to a susceptible person through an infective bite of the phlebotomine sandflies [2,3]. In Kenya the vectors implicated are *Phlebotomus martini* and *P. orientalis* [4]. VL is systemic disease that results in deaths if left untreated [5].

VL is endemic in 75 (38%) countries of the world with 50,000-90,000 new cases reported annually [6]. Of the VL cases reported in 2015, over 90% came from seven endemic countries, five of which are in the Eastern Africa region [6]. However, due to weak surveillance systems and under-reporting the burden of VL in endemic countries is underestimated [5,7].

VL is a neglected tropical disease that mostly affects impoverished communities [8]. A study in North Sudan estimated median cost at US\$450 with over 75% of the households reporting catastrophic out-of-pocket expenditures [9]. Similarly, VL illness has been found to pose a huge economic burden with average VL treatment cost; exceeding the annual household per capita income in the Indian sub-continent [9,10]. The costs included both direct VL treatment costs and indirect costs which were mainly as a result of loss of income and productivity due to VL illness [11].

Although important differences in terms of reservoir, ecology, parasites and vectors exists across different continents, attempts have been made to define various determinants of VL transmission. In Eastern Sudan where VL is transmitted by *P. orientalis*, the population of the vectors are concentrated in areas in close proximity to *Acacia seyal* and *Balanites aegyptica* trees that commonly grows on black cotton soil [12]. *P. orientalis* sandflies are known to bite outdoors, mostly during evening and early morning [12]. In East African countries, proximity to dogs, sleeping outside under acacia trees or in thatched houses, low socio-economic status, termites mounds within or around homesteads and treating livestock with insecticide appeared to be associated with VL infections [13-17]. Having animals in the

homesteads, having a mosquito net in the household, and having some knowledge about symptoms of VL were reported as possible protective factors in Kenya [17].

In Kenya, VL is endemic in 14 of the 47 counties in the country [4,18]. Nearly 4000 new cases occur in Kenya annually [19]. Northern Kenya has experienced multiple outbreaks of VL in the last 10 years with several counties being affected. In July 2006, a VL outbreak was reported in Isiolo County recording more than 60 cases. Wajir County experienced a large outbreak in March 2018 where more than 180 cases were admitted, case fatality rate (CFR) of 7.6% [20]. In 2014, a VL outbreak was reported in Marsabit County for the first time [19]. In March 2017, the Disease Surveillance and Response was notified of an upsurge in VL cases. The number of cases continued rising and as of June 2017, 104 cases were reported with 3 deaths. Diagnosis of VL was done using rK39 serologic tests. We investigated the outbreak to describe the magnitude and pattern of the outbreak and to assess factors associated with VL infection.

Methods

Investigation site

We conducted the investigation at Marsabit County in Northern Kenya. The county lies between latitude 02°45' North and 04° 27' North and longitude 37° 57' East and 39° 21' East. The county has a mostly rural population of 291,166. Marsabit County has a tropical climate which is mainly hot and dry with frequent droughts. The county is divided into four sub-counties: Laisamis and North Horr sub-counties mostly rural and predominantly inhabited by nomadic population while Moyale and Sakuu are semi-urban areas with commercial centres. Most of the areas inhabited by the pastoralists are arid and semi-arid land predominately covered by acacia trees and dry grass. (Figure 1)

Review of records at health facilities

We conducted a secondary data analysis of VL data from 1st January 2014 to 11th July 2017 obtained from Marsabit county referral hospital and Laisamis Mission Hospitals. We reviewed medical records, health facility registers and outbreak line lists, at the hospitals and extracted variables on socio-

demographics, clinical signs and laboratory findings. The two hospitals were the only facilities offering Kala-azar treatment in Marsabit County.

A VL case was defined as any entry into health facility records of any patient with a clinical or laboratory diagnosis (serology using rK39 test) of VL from 1st January 2014 to 11th July 2017.

Case control study

Based on retrospective data analysis, we hypothesized that the environment and the pastoralist lifestyle of the communities could have a relationship with exposure to the sand fly vectors. To test these hypotheses and understand other factors associated with visceral leishmaniasis infection in the region, we conducted a case control study using VL cases from 2017 outbreak.

A VL case was defined as a serology confirmed case being treated at Marsabit County referral hospital or Laisamis Mission hospital from 1st April 2017 to 11th July 2017 or who had successfully completed treatment and was discharged since 1st April 2017. The discharged VL cases were enrolled with the assistance of community health volunteers (CHVs) to achieve the required number of cases. We excluded children <6 months of age from the study.

We frequency matched cases with community controls by age groups (<5, 5-14, 15-24, 25-40 and 40+). We defined controls as rK39 negative individuals without clinical signs and symptoms of VL disease since 1st January 2017, and without prior history of treatment for VL or post-kala-azar dermal lesions (PKDL), and has been a resident of Marsabit for at least 6 months.

For each selected village, a reference point of entry was identified using a common landmark and a bottle was tossed to identify the first household from the direction where the bottle was pointing. Subsequent households were selected systematically until all controls for that particular location were achieved. One person matching the age group of a case was randomly selected from each household from a list of all the eligible household members within that age group. Households where there were no respondents or where consent was not provided would prompt selecting the next household. This was done until the required number of controls in

each location was attained. All eligible controls were screened using rk39 test t and those found positive were dropped as controls and enrolled as cases instead.

Sample size determination was done using Fleiss formula to detect an Odds Ratio (OR) of 2.22 at significance level of 95%, power of 80% and precision of 5%, where proportion of exposure among controls was 43.5% for presence of acacia nilotica in the controls' house compound [21,22].

We interviewed both cases and controls using a structured questionnaire which had sections on demographics information (age, sex, occupation, level of education and marital status), risk factors and protective factors for VL. The factors were grouped into the following sections: household and environmental factors (presence of termite hills, the nature, number and the condition of the house/roof/floor, acacia tree nearby, the type of sleeping area and sleep proximity to the animal house), behavioral factors (sleeping habits), use of a mosquito net). Interviews were conducted by trained assistants using hand-held electronic open data collection kit (ODK).

Serology testing was performed using rapid rK39-based immune-chromatographic test (ICT) that qualitatively detects antibodies specific for the recombinant Leishmania antigen rK39 for all cases and controls to ensure that controls did not have VL [9]. The rapid test was performed according to the manufacturer's instructions [23].

Data management and analysis

Data analysis was done using Epi info 7.2 software. We calculated VL case fatality rates (CFR) and Attack Rates (AR) based on the projected population of 2017 from 2009 national census. We computed adjusted Odds ratio (aOR) and 95% confidence interval (CI) to test for associations between cases and control based on various factors. We performed unconditional logistic regression for variables with p-value ≤ 0.25 at the bivariate analysis. Only factors with p-value ≤ 0.05 in the final model were retained.

Ethical consideration

Verbal consent was obtained from all participants, and from guardians for children <15 years old before

the interviews and laboratory testing. The investigation being a response to a public health emergency did not require an approval from an ethical review board (ERB) and therefore the protocol was cleared by the Ministry of Health.

Results

Description of Line Listed VL cases, 2014-2017

We reviewed 383 records of suspected VL cases between 2014 and July 2017; 80.4% (308/383) were serologically confirmed using rK39. The median age of the confirmed cases was 13 years (IQR: 3-25 years). The majority of the confirmed cases were, 83% (256/308), male.

The overall attack rate for VL since 2014 was 83 cases/100,000 population using the projected population of the county and was highest among children aged <5 years and the residents of Laisamis. There were 13 deaths (case fatality rate, CFR =4.2%) reported between 2014 and July 2017. The CFR declined from 8 (6%) in 2014 to 1 (4%) in 2015 and 4 (2.8%) in 2017. Residents of Laisamis sub county (CFR=6.3%), females (CFR=5.8%) and adults aged 40 year and above (CFR=17.4%) had higher CFR. (Table 1).

The index patient presented to the health facility on 4th January 2017 and the number of cases increased steadily in the months of March and April 2017 when the outbreak was declared. The outbreak peaked in June 2017 and started declining from mid-July 2017. (Figure 2).

Of the confirmed cases, 43% (132/308) were reported in 2014; 8% (25/308) in 2015; 3% (8/308) in 2016 and 46% (143/308) in 2017. VL cases were present throughout the years with two peaks being seen in 2014 and 2017 pointing to the two reported outbreaks. (Figure 3).

Case Control

A total of 77 cases and 154 controls were recruited. The proportion of participants with formal schooling was low among both cases 13.0% (10/77) and controls 14.4% (22/154). Herding animals was the main occupation among both cases 48.1% (37/77) and controls 42.2% (65/154). (Table 2).

Table 3 summarizes associations between various demographic, household, behavioral and environmental factors and visceral leishmaniasis infection. Three demographic factors i.e. male gender (OR=2.70 95% CI 1.50-4.86), living in the rural sub counties (OR=2.64 95% CI 1.28-5.44) and having a family with > 5 members (OR=2.03 95% CI 1.00-4.13), and two environmental and behavioral factors comprising presence of termite hills around homesteads (OR=2.14 95% CI 1.19-3.85), and having a history of travel outside the usual village of residence in the past 6 months (OR=2.83 95% CI 1.61-4.97) were significantly associated with having VL infection (Table 3).

The unconditional multivariate analysis identified four independent risk factors for VL in Marsabit County after adjusting for age groups. History of travel to areas where VL (AOR =3.23 95% CI 1.63-6.40) was the most important risk factor identified. Other significant risk factors identified were: Male gender (AOR=2.49 95% CI 1.29-4.81), presence of termites mounds within or near homestead (AOR=2.29 95% CI 1.17-4.47), and residing in the rural sub counties of Laisamis and North Horr (AOR=2.99 95% CI 1.26-7.13). (Table 4)

Discussion

Our study highlights a high burden of VL disease among the rural communities where children <5 year and the men within the productive age groups who traditionally travel with and take care of animals are most affected. Our study with the case control component attempts to assess factors associated with Kala-azar outbreaks in arid and semi-arid regions of Kenya.

Our retrospective data suggests that Kala-azar infections occurs throughout the year with new cases emerging during rainy seasons (March-April) and peaking after the start of the dry season (June-July). Low number of cases being seen in 2015 and 2016 may represent endemicity in the county [24]. However, under detection which may occur during months without outbreaks may have affected numbers of cases being reported in 2015 and 2016.

The male gender has been demonstrated as an independent risk factor for VL in various parts of the

world including Ethiopia, Kenya and Sudan where disproportionate risk was associated with their occupational activities which involves being outdoor or sleeping in the fields which exposes them to sandflies [13,25,26]. In pastoralist communities living in rural parts of Marsabit County, the men traditionally take care of and move with animals in search of pasture and water. Detection of more clinical diseases in males than in females could be due to more frequent exposure of men than women, but it could also be due to under detection of the disease in women in culturally male-dominated communities [3].

The significant burden of disease among <5 children is consistent with other studies in Somalia and South Sudan where children <5 of age carried the most burden of VL [6,27]. Contrary to our findings was an observation in a study done in Bangladesh where older children (3-14 years) accounted for the highest proportion of cases of VL although association between VL and age groups was demonstrated similar to our study [28]. This higher susceptibility of younger children could be attributed to malnutrition secondary to the drought and famine which has affected the county since early 2017. Lack of or under developed immunity could be another possible explanation for the age based predominance of VL among the younger children [29].

In addition, our study demonstrates that the risk of VL is dependent on increased potential exposure to sand flies and evidence suggests that transmission occurs both in the household setting and outdoor setting. Evidence for indoor transmission is shown by trapping of sand flies indoors using CDC light traps and castor oil sticky papers by the entomology team involved in the 2017 outbreak. The high burden of disease among the under 5 year children who are not involved in occupational or school activities which involve spending a lot of their time outdoors also points to a possible indoor transmission.

In addition, presence of termites mounds in proximity to the living areas or the homestead was significantly associated with clinical disease. Termites mounds and acacia trees are considered ideal breeding grounds for sandflies especially in East Africa where VL is associated with ecological settings with Acacia-Balanites and termites mounds[3]. Our finding is consistent with findings from a study by Bantie et al in North West Ethiopia

who demonstrated that sleeping in proximity to termite hills was associated with three times risk of getting VL [29]. The finding from current study is also consistent with a study done in Turkana, Kenya where spending time or sleeping near termite mounds was significantly associated with higher risk of VL [26]. Although our study did not show a significant association between presence of acacia trees around the homestead and VL, the study in North West Ethiopia showed acacia trees as an independent risk factor for Kala-azar (OR=3.19, 95% CI=1.70,5.99) [29]. Similarity between cases and controls in terms of exposure to the acacia trees may explain why we failed to detect significant relationship between VL and the acacia trees.

Evidence of outdoor transmission was demonstrated by the fact that history of travelling outside their usual area of residence, which mostly involved moving with animals in search of pasture was significantly associated with VL among the residents, implying that exposure occurred during the time spent in the field. The fact that more males were affected than their female counterparts especially among the people within the productive age groups reinforced our hypothesis that the exposure is occurring in the field. Increased risk of VL has been demonstrated among nomadic men who spent a lot of time sleeping outside or on the ground during the time in the field with their animals [30]. Movement of susceptible population into an endemic area or infected persons moving into a non-endemic areas and leading to outbreaks has long been established [3,23]. Historically, Kala-azar was brought to Central Kenya by infected soldiers who were returning from serving in VL endemic regions in Ethiopia and Sudan and local vectors were able to sustain transmission in the region and cause outbreaks in Kenya [31].

Some of the potential limitations for this study may include the fact that the cases and controls were not matched with their area of residence. The other potential limitation was the omission of immunosuppressive conditions like malnutrition and HIV status from our assessment as potential factors associated with VL.

Conclusion

The burden of Visceral Leishmaniasis is high, affecting males and children < 5 years of age. We recommended health education, increase community awareness on Leishmaniasis, indoor residual spraying and intensifying the use of insecticide impregnated bed nets targeting children < 5 years. Environmental modification in terms of clearing of termite mounds around areas of residence may be helpful where applicable.

What is known about this topic

- Causative agents, signs and symptoms, risk factors and various drugs that have been proven effective in treatment of visceral leishmaniasis
- Though the main risk factors behind visceral leishmaniasis are known, these factors vary across environmental and ecological settings

What this study adds

- The study attempted to identify risk factors associated with the outbreak in Marsabit County and we found that movement with animals in VL endemic areas was the main risk associated with VL infection.

Competing interests

The authors declare no competing interest.

Authors' contributions

DD, MO, SM, PL, KN, HB, AL, WM, ZI designed the study, carried out the investigations and collected data while FO and DN performed the laboratory component of the study. DD, MOO and MO analyzed the data, prepared and reviewed the manuscript. GK evaluated county preparedness and response to the outbreak while TW and DM helped with the vector component of the study.

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Figure 3: Distribution of confirmed VL cases and deaths by Month and Year seen at Health facilities in Marsabit County, 2014-2017

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Table 1: Attack rates (AR) and Case fatality rate (CFR) by demographic characteristics among VL cases seen in Marsabit County, 2014 – 2017

Variable	Projected population 2017	Cases (n)	Percent (%)	AR/100,000 population	Deaths (n)	Percent (%)	CFR (%)
Age groups							
<5	58,451	87	28.2	149	3	23.1	3.4
5-9	59,975	36	11.7	60	1	7.7	2.8
10-14	55,814	37	12.0	66	1	7.7	2.7
15-19	45,766	27	8.8	59	1	7.7	3.7
20-24	32,639	42	13.6	129	1	7.7	2.4
25-29	24,060	30	9.7	125	0	0.0	0.0
30-34	19,908	19	6.2	95	1	7.7	5.3
35-39	15,018	7	2.3	47	1	7.7	14.3
≥40	61,300	23	75	38	4	30.8	17.4
Median (IQR)	13 (3-25) years						
Sex							
Female	179,384	52	16.9	29	3	23.1	5.8
Male	193, 547	256	93.1	132	10	76.9	3.9
Sub-county							
Laisamis	84,111	142	46.1	169	9	69.2	6.3
North Horr	96,312	128	41.6	133	4	30.8	3.1
Sakuu	59,560	27	8.8	40	0	0.0	0.0
Moyale	132,948	15	4.9	11	0	0.0	0.0

Table 2: Socio-demographic characteristics of Case Control study participants in Marsabit County, 2017

Factors	Category	Cases (n)	Percent (%)	Controls (n)	Percent (%)
Gender	Male	55	71.4	74	48.0
	Female	22	28.6	80	52.0
Residence	Laisamis	49	63.6	77	50.0
	North Horr	21	27.3	34	22.1
	Sakuu	6	7.8	43	27.9
	Moyale	1	1.3	0	0.0
Family size	Less than 5	12	15.6	42	27.3
	More than 5	65	84.4	112	72.7
Participant's education	No formal education	42	54.6	84	54.6
	Primary school, completed	1	1.3	4	2.6
	Primary school, uncompleted	7	9.1	16	10.4
	Secondary/tertiary education	2	2.6	2	1.4
	Too young	25	32.5	48	31.2
Participant's occupation	Student	12	15.6	20	13.0
	Herding	37	48.1	65	42.2
	Salaried worker	0	0.0	1	0.7
	Housewife/unemployed	2	2.6	12	7.8
	Young children	26	33.8	56	36.4
Sex of head of the family	Male	70	90.9	110	71.4
	Female	7	9.1	44	28.6
Education level of head of family	No formal education	70	90.9	133	86.4
	Primary school	6	7.8	13	8.4
	Secondary/tertiary education	1	1.3	8	5.2

Table 3: Bivariate analysis of various factors associated with VL in Marsabit County, 2017						
Factors	Category	Cases (n)	Percent (%)	Controls (n)	Percent (%)	OR (95% CI)
Demographic factors						
Sex	Male	55	71.4	74	48.0	2.70 (1.50-4.86)
	Female	22	28.6	80	52.0	ref
Residence	Rural sub counties	66	85.7	107	69.5	2.64 (1.28-5.44)
	Urban sub counties	11	14.3	47	30.5	ref
Family size	>5 members	65	84.4	42	27.3	2.03 (1.00-4.13)
	<5 members	12	15.6	112	72.7	ref
Education	No formal education	67	87.0	22	85.7	1.12 (0.50-2.49)
	Formal education	10	13.0	22	14.3	ref
Household/Behavioral/Environmental factors						
Occupation	Herding	37	48.1	65	42.2	ref
	Housewife/Children/salaried	40	51.9	89	57.8	1.27 (0.73-2.20)
History of travel outside village past 6 months	Yes	46	59.7	53	34.4	2.83 (1.61-4.97)
	No	31	40.3	101	65.6	ref
Place of stay from sunset to sleep time	Indoor	23	29.9	42	27.3	ref
	Outdoor	10	13.0	13	8.4	1.41 (0.53-3.70)
	Both indoor and outdoor	44	57.1	99	64.3	0.81 (0.44-1.51)
Type of house	Hut/Manyatta	75	97.4	15	9.7	4.05 (0.90-18.17)
	Other house type	2	2.6	139	90.3	
Factors	Category	Cases (n)	Percent (%)	Controls (n)	Percent (%)	OR (95% CI)
Acacia trees in homestead/surrounding	Yes	67	78.0	123	79.9	1.69 (0.78-3.66)
	No	10	13.0	31	20.1	ref
Termites hills in homestead/surrounding	Yes	55	71.4	83	53.9	2.14 (1.19-3.85)
	No	22	28.6	71	46.1	ref
Where for toilet purposes at night	Outside house yard	60	77.9	127	82.5	0.75 (0.38-1.48)
	Within house yard	17	22.1	27	17.5	ref
Cracked walls	Yes	4	50.0	13	59.1	0.69 (0.14-3.52)
	No	4	50.0	9	40.9	ref
House sprayed with insecticide	Yes	15	19.5	37	24.0	0.77 (0.39-1.51)
	No	62	80.5	117	76.0	ref
Termites in sleeping room	Yes	42	55.3	88	58.7	0.87 (0.50-1.52)
	No	34	44.7	62	41.3	ref
Sleeping on the floor	Yes	70	90.9	130	84.4	1.85 (0.76-4.45)
	No	7	9.1	24	15.6	ref
Animals in homestead at night	Yes	56	72.7	114	74.0	0.94 (0.50-1.74)
	No	21	27.3	40	26.0	ref
Use of insect repellants on animals	Yes	33	42.9	66	42.9	1.00 (0.58-1.74)
	No	44	57.1	88	57.1	ref

Table 4: Results of multivariate logistic regression for the factors associated with VL in Marsabit County, 2017

Variable	Category	AOR (95% CI)
Sex	Male	2.49 (1.29-4.81)
	Female	1
Residence	Rural sub counties	2.99 (1.26-7.13)
	Urban sub counties	1
History of travel outside their village past 6 months	Yes	3.23 (1.63-6.40)
	No	1
Presence of termites hills in homestead/surrounding	Yes	2.29 (1.17-4.47)
	No	1
Presence of acacia trees in homestead/surrounding	Yes	1.40 (0.57-3.46)
	No	1
Type of house	Hut/Manyatta	2.12 (0.37-12.09)
	Other house type	1
Family size	>5 members	2.19 (0.95-5.01)
	<5 members	1

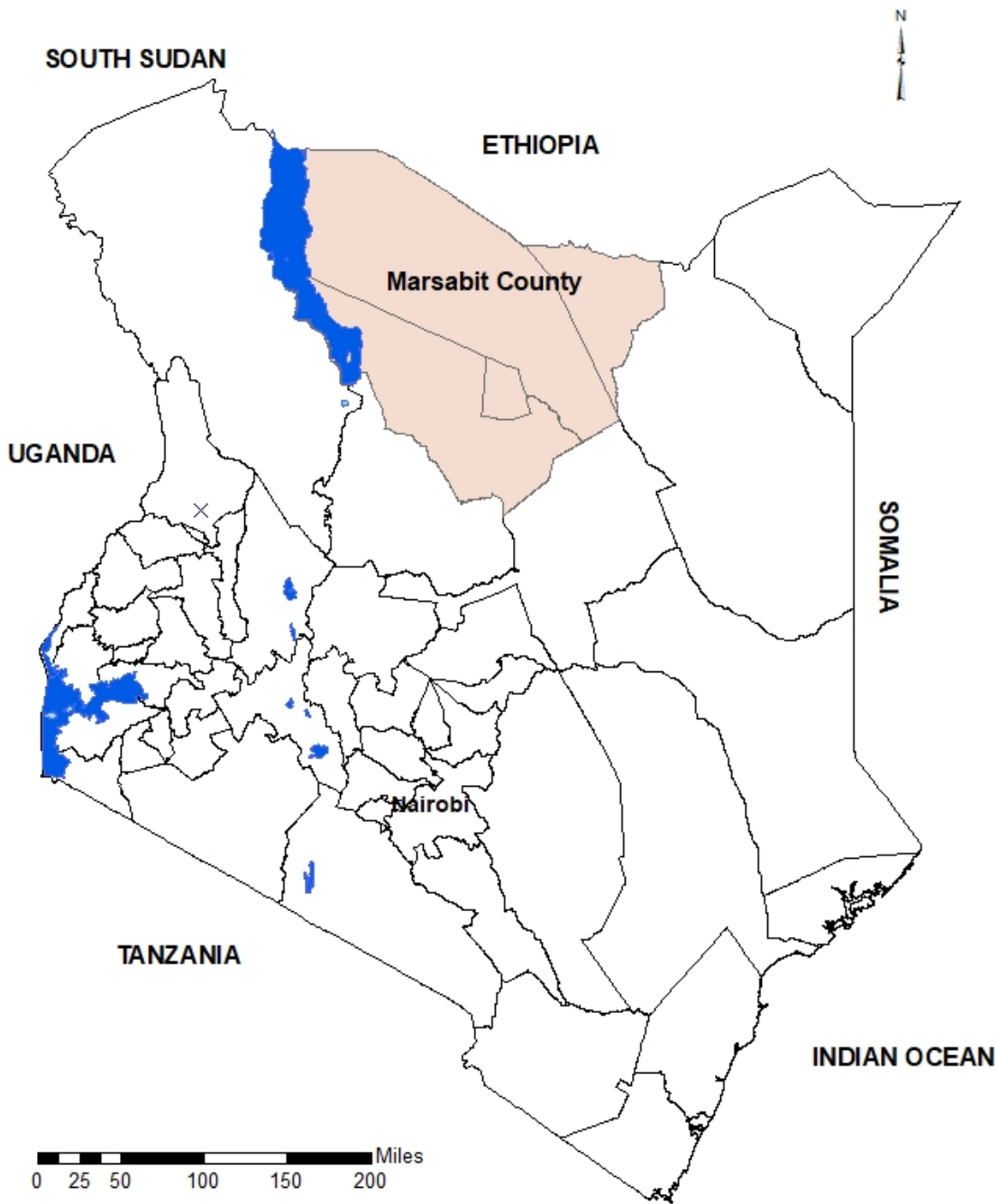


Figure 1: A map of Kenya showing Marsabit County

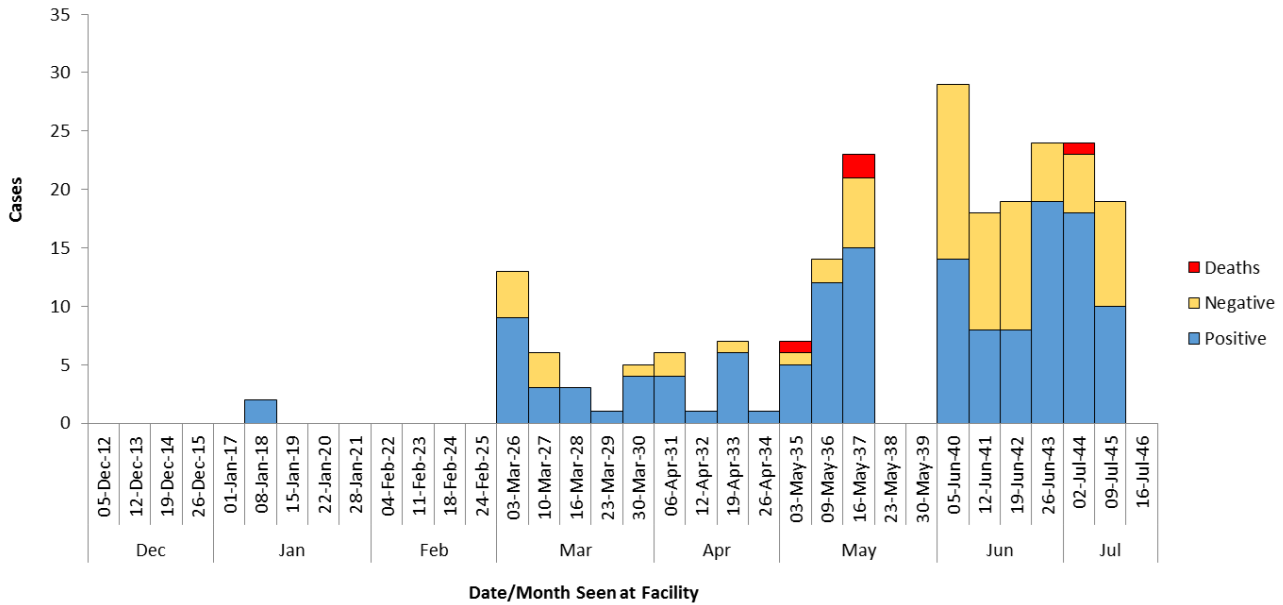


Figure 2: Epidemiologic curve of VL cases by month and date seen at Health facilities, Marsabit County January-July 2017

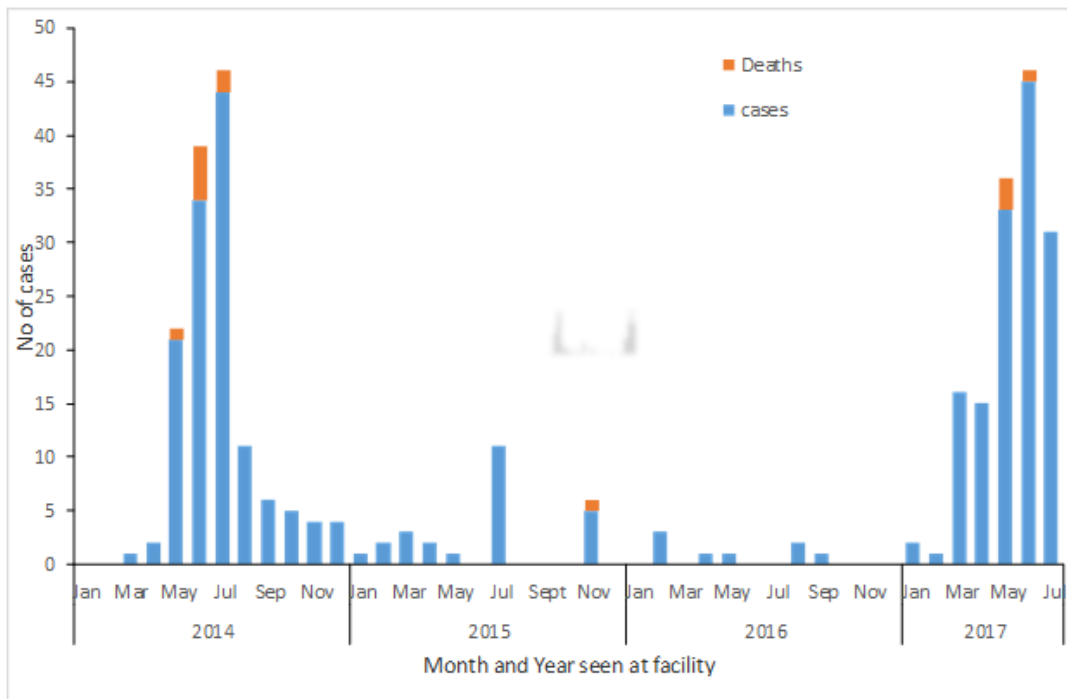


Figure 3: Distribution of confirmed VL cases and deaths by Month and Year seen at Health facilities in Marsabit County, 2014-2017