Original Research Article

Outbreak of kala azar: our experience in South Sudan

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ABSTRACT

Background: Worldwide kala azar affects around 500,000 people every year with at least 50,000 deaths annually. Gedaref state in east Sudan is the epicentre of visceral leishmaniasis in east Africa. Objectives of this study were to describe the outbreak of kala azar in South Sudan, from August 2009 to July 2010, in terms of person and time distribution and to describe the outbreak of kala azar in South Sudan, from August 2009 to Jul 2010, in terms of frequency of various clinical features and outcome

Methods: A prospective cross-sectional descriptive study conducted at South Sudan with cases of kala azar affected during an outbreak in South Sudan from August 2009 to July 2010. Statistical analysis was percentage.

Results: This outbreak indicates the emergence or re-emergence of kala azar in South Sudan. Within the restrictions on movement because of the civil war, further research is needed to investigate the extent of the transmission zone and whether other populations in South Sudan have been infected and have no access to treatment.

Conclusions: There is lack of awareness regarding dog bite and its management among the rural population.

Keywords: Kala azar, Outbreak, South Sudan, Splenomegaly

INTRODUCTION

Visceral leishmaniasis (kala azar) is a deadly disease caused by the protozoa Leishmania and transmitted through the bite of sandflies. Worldwide kala azar affects around 500 000 people every year.1 Without prompt appropriate treatment, it has a mortality rate as high as 95%, resulting in at least 50,000 deaths annually worldwide.2 Among parasitic diseases, only malaria is more deadly. The northeastern Indian state of Bihar is home to some 90% of patients with kala azar in India and nearly 50% of patients worldwide.3 Two thirds of patients are in southeast Asia. East Africa, suffering from an increasing burden of kala azar over the last two decades, is the second largest focus; and contributes to perhaps as many as 40000 cases every year.1,2

In the Horn of Africa, kala azar has a focal distribution in two distinct ecologic settings; the semi-arid regions in the north where Phlebotomus orientalis breeds in cracks in the black cotton clay soil; and the savanna and forest areas in the south where the vectors P. martini and P. celiae are found in association with Macrotermes termite mounds. In Ethiopia, long recognized kala azar endemic foci are situated in Metema and Humera along the border with Sudan in the northwest, reflecting the first ecologic pattern, and in the regions of Lake Abaya, Omo river, and the Aba Roba plains in the south, following the second, with an estimated country wide incidence of 2,000 cases/year. In Ethiopia, recent years have seen the disease spread to previously nonendemic districts such as Libo Kemkem, whereas commonly occurs with kala azar it was initially misdiagnosed as malaria.1
Data for visceral leishmaniasis are scarce: most endemic countries have not established effective surveillance systems. In Sudan the disease exhibits wave behaviour; the last few years have seen an increase in incidence in eastern Sudan. Gedaref state in east Sudan is the epicentre of visceral leishmaniasis in east Africa. Outbreaks of new epidemic cycles always start in eastern Sudan; and from there spread into South Sudan and Ethiopia”. This is the main kala azar belt in east Africa.¹

In Sudan, visceral leishmaniasis is endemic in the area extending from north of Malakal and the Sobat river (upper Nile province) up to Kasala province, along the White Nile and Blue Nile. Another important endemic area is in the Kapoeta region, near the border with Kenya. Smaller foci described in some villages in central and northern Sudan, show strong evidence of northwards spread.⁴

Médecins Sans Frontières (MSF) has warned that a new outbreak of kala-azar, could wreak havoc among the population of southern Sudan, whose nutritional status is severely compromised by 20 years of war and famine.⁵

Objectives

Objectives of the study were to describe the outbreak of kala azar in South Sudan, from August 2009 to July 2010, in terms of person and time distribution and the outbreak of kala azar in South Sudan, from August 2009 to July 2010, in terms of frequency of various clinical features and outcome.

METHODS

General settings and population

Malakal County in Upper Nile State in South Sudan consists of 5 payams with a total estimated population of 126583. The Malakal Teaching Hospital, serves as the primary provider of medical and health care for the population. The WHO staff augments the meagre resources available to the Ministry of Health, Government of South Sudan. The population described in this report included all patients diagnosed with kala azar at the Malakal Teaching Hospital between August 2009 and July 2010. All patients with kala azar were treated as inpatients in the kala azar ward of this health facility.

Study design

The study design was a prospective cohort.

Data collection

The town of Malakal and surrounding areas were visited frequently during the period August 2009 to July 2010. All patients clinically suspected of kala azar and those already under treatment for kala azar in the local health facilities were examined. The total number of admissions was obtained from the main registration book of the health facility. Demographic and clinical information were collected from individual patient cards. Parasitological isolation was made by aspiration of bone marrow, lymph node and spleen. Culture was attempted of bone marrow and splenic aspirates. Since the patients under treatment had been diagnosed only clinically by the local medical officers and medical assistants a sample of fingertip blood was taken on a filter paper. This was examined for antibodies against Leishmania by ELISA using a water-soluble lysate antigen of L donovani; (DIAMED IT LEISH, manufactured by Diamed AG, Diagnostic and medical products, 1785 Cressier s/Morat, Switzerland.

The number of cases of kala azar detected over time, by age, sex, and geographical origin was analysed. Data from all sources was validated, compiled and analysed statistically using standard statistical tests.⁶ The analysis was carried out in terms of percentage of various categories.

Ethical issues

Only data collected routinely in the process of monitoring a treatment program was used. Confidentiality of clinical and laboratory patient information was maintained; patients were explained the reason for taking additional blood samples and were asked for oral consent.

RESULTS

Patients

Majority of the patients were local ethnic Sudanese. Travel histories of these patients could not reveal any specific focus of transmission. Of 553 clinically suspected cases assessed by DAT up to July 2010, 497 were serologically confirmed and 56 were confirmed parasitologically. Study did not see a clear epidemic curve, possibly because the variation in duration of symptoms was wide.

Week wise admissions of fresh cases of kala azar, discharge, cases in treatment and deaths due to kala azar for the period of study is depicted in Figure 1. Age wise and sex wise distribution of cases is presented in Figures 2 and 3, respectively.

Clinical features

Out of 553, 527 patients (95.30%) were primary kala azar; while 26 (4.70%) were relapse/Post kala azar dermal leishmaniasis i.e., PKDL. Out of 553 patients, 197 (35.63%) were <5 years, 244 (44.12%) were 5-17 years; and 112 (20.25%) were >17 years. The incidence of disease was only slightly greater in males (57%) as compared to females (43%). The male:female ratio of the DAT-positive and spleen aspirate-positive cases was 1.33:1. Out of 553, 83 (15.01%) patients had symptoms...
for less than 1 month, 397 (71.79%) between 6 months and 2 years, and 73 (13.20%) reported their symptoms since more than a year. In this study treatment centre the mean duration of symptoms was 11 months. The distribution of various clinical symptoms was as follows; fever/prolonged fever 553 (100%), splenomegaly 459 (83%), anaemia 210 (37.98%), hepatomegaly 177 (32.01%), and severe lymphadenopathy 47 (8.50%). Blood and other microbiological specimens were negative for malaria, tuberculosis, and typhoid fever.

**Figure 1: Week wise admissions of fresh cases of kala azar, discharge, cases in treatment and deaths due to kala azar.**

**Figure 2: Age wise distribution of cases of kala azar.**

**Treatment**

All patients were treated with sodium stibogluconate (Pentostam®, GlaxoSmithKline, Greenford, UK) 20 mg Sb/kg per day for 30 days, with a maximum dose of 900 mgSb.

**Outcome**

A total 503 (90.96%) cases responded well, clinically, to treatment; and were discharged on completion of complete course of treatment. Discharge criteria were defined as: no fever in the last week of treatment, regression of spleen size, and improved general well-being. No routine parasitological test of cure was done. Forty-seven (8.5%) patients had their treatment prolonged by 1 to 2 weeks because they failed to meet the discharge criterion of no fever. Fifty (9.04%) patients succumbed to the disease despite intensive treatment. Estimating the number of patients who died before they presented to our health facility is beyond the scope of this study, due to resource constraints.

**DISCUSSION**

The disease was first reported from Southern Sudan in 1904, and the first epidemic was documented in 1940 with a death rate of 80%.

Satti, in 1962, reported an epidemic of kala azar in East Africa, dating back to the 1950s, which occurred among the JumJum tribe of Southern Blue Nile district which was severe enough to have wiped out almost the entire tribe. Subsequent epidemics had similar consequences in terms of devastation and mortality. Beginning in 1984, an epidemic (unrecognized until 1988) devastated the western part of upper Nile state, ultimately causing ≈100,000 deaths in a population of 280,000 over a 10-year period. In 1988, El Hassan et al reported an outbreak of kala azar amongst the Nuer tribe in Khartoum, killing an estimated 40000 people. The Nuer tribe had migrated from Bentiu, located in Western upper Nile to the north, due to war, famine and disease in their homeland. These are in sharp contrast to our study with a mortality rate of 9.04%.
Passive case-detection data on kala-azar in Southern Sudan, collected by the World Health Organization (WHO) since 1989, indicate a cyclical pattern of kala-azar with considerable variation in the caseload from year to year.\(^1\) Médecins Sans Frontièr es–Holland (MSFH) has been running KA treatment centers since 1989, and 120,000 patients were treated by MSFH in southern Sudan between 1989 and February 2002.\(^9\)

Blackwell et al reported the epidemic of kala azar in eastern and southern Sudan as one of the greatest epidemics of the 20\(^{th}\) century. Longitudinal studies revealed marked differences in the incidence of clinical disease between villages inhabited by different ethnic groups. MSF reported 100,000 deaths due to the disease in Western upper Nile in the early 1990s, wiping out a third of the population living in that region. Insecurity, malnutrition, population migration and poor access to health care lowered the natural resistance of the population, creating an environment conducive for outbreaks to occur. Throughout the 20\(^{th}\) century, kala azar has been reported in southern Sudan, and major outbreaks have followed population movement, flooding, food shortages, and conflict. The worst recorded epidemic probably killed 1100,000 people in the Western upper Nile area of southern Sudan from 1984-1994, a loss of one-third of the population of that area.\(^9\)\(^10\)

Mercer et al reported an outbreak of kala azar from five remote villages in Nasir county in Eastern upper Nile in October 1994.\(^11\)

Since 2002, the case-fatality rate recorded at healthcare facilities has been 4%-6%. Southern Sudan is currently between epidemics and provides a warning that cases may rise dramatically in coming years. In 2006, a total of 1,117 cases were reported, 65.4% of which were primary cases; the remainder were either relapses or cases of post-kala-azar dermal leishmaniasis. The findings of the above study differ from that of our study. From January through June 2007, a total of 492 cases were reported, of which 88.2% were primary cases. These findings are similar to those of the present study. The 5 locations accounting for 74.2% of the primary cases in 2007 were Malakal (n=83), Ulang (n=72), Nasir (n=63), and Kiechkuon (n=25) in upper Nile state and Lankien (n=79) in Northern Jonglei state.\(^1\)

Collin et al, conducted a study of adult patients with kala azar who were admitted to an MSFH treatment center in Dur, western upper Nile, between August 1990 and July 1991, during the epidemic. They linked young and old age, long duration of illness, anemia, malnutrition, splenomegaly, high parasite density, and vomiting with a higher risk of death. However, the cause of subsequent fluctuations in death rates at MSFH treatment centers by year, month, and location remained unclear and could not be determined from the routine statistics. In addition, new drug treatments and MSFH’s desire to provide optimal care for the most severely ill patients required further investigation of risk factors for death.\(^9\)

Herrero et al found that young children and older patients were much more likely to die than older children or young adults. Expectedly other predictors of mortality were, severe anemia, severe malnutrition, edema, HIV status, and the presence of pneumonia or tuberculosis. Severe malnutrition, anemia, and immunosuppression from HIV all intensify kala azar morbidity. Bacterial pneumonia has been recognized as an indicator of poor prognosis. Jaundice has also been recognized as an indicator of poor prognosis.\(^12\)

Limitations of this study were the data presented here primarily relies on patients who could have access to a primary medical and health care facility, the limitations of which are apparent. It is quite probable, that many more cases could have been missed out due to failure to report to the health facility. Entomological studies could not be carried out due to resource constraints.

**CONCLUSION**

This outbreak indicates the emergence or re-emergence of kala azar in South Sudan. Within the restrictions on movement because of the civil war, further research is needed to investigate the extent of the transmission zone and whether other populations in South Sudan have been infected and have no access to treatment.

**Recommendations**

Based on the findings of the study the following recommendations are submitted. Areas at risk for epidemics through the influx of infected people should be identified to avoid or control epidemics. Particular attention should be paid to urban areas, given the ongoing trend towards uncontrolled urbanization. Surveillance should be strengthened, which would help to prevent the reintroduction of kala azar transmission, in areas of low endemicity. The burden of hidden cases can also be detected by strengthening surveillance.

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**REFERENCES**

1. World Report. East African countries struggle with visceral leishmaniasis. Lancet. 2009;374:371-2.
2. Kolaczinski JH, Hope A, Ruiz AJ, Rumunu J, Richer M, Seaman J. Kala-azar Epidemiology and Control, Southern Sudan. Emerg Infect Dis. 2008;14(4):664-6.
3. Sundar S, Chakravarty J, Agarwal D, Rai M, Murray HW. Single-dose liposomal amphotericin B for
visceral leishmaniasis in India. N Engl J Med. 2010;362:504-12.
4. Perea AW, Moren A, Ancelle T, Sondorp E. Epidemic visceral leishmaniasis in Southern Sudan letter. The Lancet. 1989:1222-3.
5. Moszynski P. Health organisation warns that kala-azar has returned to South Sudan. The Lancet. 2002;360:1672.
6. Knapp RG, Miller MC. Clinical epidemiology and biostatistics. The national medical series for independent study. Malvern, Pa.: Harwal Publishing Company; 1992.
7. Ibrahim EM. Population genetics. The epidemiology of visceral leishmaniasis. The epidemiology of visceral leishmaniasis in East Africa: hints and molecular revelations. Trans The Royal Soci Trop Med Hyg. 2002;96 (1 Suppl):258-298.
8. Hassan AE, Hashim FA, Ali MS, Ghalib HW And Zijlstra EE. Kala azar in western upper nile province in the southern sudan and its spread to a nomadic tribe in the north. Trans The Royal Soci Trop Med Hyg. 1993;87:395-8.
9. Collin S, Davidson R, Ritmeijer K, Keus K, Melaku Y, Kipngetich S, Davies C. Conflict and kala-azar: determinants of adverse outcomes of kala-azar among patients in Southern Sudan. Clin Infect Dis. 2004;38:612-9.
10. Blackwell JM, Mohamed HS, Ibrahim ME. Genetics and visceral leishmaniasis in the Sudan: seeking a link. Trends Parasitol. 2004;20(6):268-74.
11. Mercer A, Seaman J and Sondorp E. Kala azar in eastern upper nile province, Southern Sudan letter. The Lancet. 1995;345:187-8.
12. Herrero M, Orfanos G, Argaw D, Mulugeta A, Aparicio P, Parreno F, et al. Natural History of a Visceral Leishmaniasis Outbreak in Highland Ethiopia. Am J Trop Med Hyg, 2009;81(3):373-7.