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Review Article

One Health Approach Prospect for Integrated Control and Elimination of Visceral Leishmaniasis in Ethiopia: A Narrative Review Article

Tadesse HAILU

Department of Microbiology, Immunology and Parasitology, College of Medicine and Health Science, Bahir Dar University, P.O.Box 79, Bahir Dar, Ethiopia

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***Correspondence**
Email:
tadesshailu89@gmail.com

Abstract

Background: Leishmaniasis is an obligate intercellular protozoon that affects animals and human. It has zoonosis and/or anthroponosis transmission. Human and veterinary medicine, environmental science and wildlife conservation specialists have many commonalities in case of visceral leishmaniasis. Still the above disciplines respond against leishmaniasis in a separate way. The aim of this review is to indicate inter- and intra- sectoral collaboration for planning future control strategies.

Methods: literatures written on visceral leishmaniasis and one health approach were systematically reviewed from the year 1969 to 2014 from Pub Med, Scopus, Medline and Google scholar sources.

Result: Such a one health approach would enhance biomedical progress; improve medical and veterinary serves, entomological control and wildlife conservation for Visceral Leishmaniasis especially in endemic areas.

Conclusion: Inter- and intra – sectoral collaboration in the leishmaniasis control is limited in Ethiopia. Therefore, incorporating one health approach or integrated inter- and intra – sectoral collaboration for visceral leishmaniasis control is an effective control strategy in endemic areas.

Introduction

Leishmaniasis is an obligate intracellular protozoon of the genus *Leishmania* that has zoonotic and anthroponotic transmission. It is endemic in 98 countries and territories with 350 million people at risk (1), 1.3 million estimated infected cases, 20,000 – 30, 000 estimated deaths, 200,000 - 400,000 estimated new Visceral leishmaniasis (VL) case

annually (2) around the world. Of which, more than 90% of VL human cases occur in six countries, namely Bangladesh, Brazil, Ethiopia, India, South Sudan, and Sudan (2). The highest numbers of VL cases are also recorded in Eastern Africa including Eritrea, Ethiopia, Kenya, Somalia, Sudan, South Sudan, and Uganda (3). More than 4,000 VL cases were recorded in the lowland and arid areas of Ethiopia (4).

There are four main clinical spectrums of leishmaniasis: VL, Cutaneous leishmaniasis (CL), Mcocutaneous leishmaniasis (MCL),) and Post Kalaza dermal leishmaniasis (PKDL) (5). VL is one of the most severe forms of leishmaniasis which affects the reticulo-endothelial systems (2). It is vector-borne disease transmitted by the bite of the female Phlebotomus in the old and Lutzomyiain the new worlds (6, 7). It is transmitted from human to human (anthroponosis) (8) and from animal to human (zoonosis) (9).

The epidemiology of the leishmaniases is dynamic and the conditions of transmission are continually changing depending on change in environment, demography, human behavior, socioeconomic status, and immunogenic profile of affected human populations (10-12). These factors affect the prevention and control measures done against leishmaniasis especially in resource poor countries like Ethiopia.

VL is not only a human disease rather it affects domestic and wild animals. The disease can easily transmit from human to human, human to animal, animals to animals or animal to human through the vector (13). According to ministry of health (MOH) strategic plan in Ethiopia, outreach teams have been deployed in high VL endemic regions to strengthen early case detection, outbreak identification and response, community awareness and surveillance (14). These teams focus on prevention and control of VL in Ethiopia only through treatment of infected human cases. But this may not effective unless we could address the health of animal reservoir hosts and launch effective vector control strategy.

The major objective of this review is to indicate the power of inter- and intra- sectoral collaboration in VL prevention and control for planning future control strategies in the country.

Therefore, inter- and intra- sectorial collaboration between human and animal medicine, environmental science and wild life conservation disciplines should be formulated in VL endemic areas where the bond of animal-human relationship is strong.

Considering VL recent up surging, I systematically reviewed how the above four disciplines worked so far in Ethiopia. Here below the responsibilities of the above four disciplines and how they cooperate and work together under one health concept is discussed and reviewed.

Methods

The narrative review covers all information about VL prevention and control approaches. Scientific information written on VL and one health approach was systematically reviewed. Literatures written about leishmaniasis burden, prevention and control and one health approach from the year 1969 to 2014 were systematically reviewed using Pub Med, Scopus, Medline and Google scholar sources.

Wildlife conservation

Wildlife's are potential sources for emerging infectious diseases in humans and domestic animals (15). They are important sources, reservoirs and amplifiers of emerging human and domestic livestock pathogens (16). Currently, domestic dogs are the main reservoir for VL. However, some wild animal can also serve as reservoirs hosts (17-19). The magnitude of leishmaniasis combined with the complexity of its epidemiology and the links in transmission net should be clear to develop effective control strategies (20). During VL transmission, dogs may be infected from wildlife source by consuming infected wild animals or vectors. Human being may also be infected

from the wildlife source or from dogs through sandfly bite. Unless the health of wild life is maintained, the human population may be at risk due to close relationships between the human population and animals. In this aspect the wild life conservation specialists should be concerned to protect the health of the community by preserving wild animals which are potential source for emerging infectious diseases like VL (21).

Veterinary medicine

Treatment and prevention of animal cases from VL infection is one basic component in the prevention of human infection. Animal reservoir hosts should be identified, diagnosis and treated in areas where human cases live. Veterinarians find themselves on the front lines in recognizing, diagnosing and responding to VL (22).

According to some reports, the domestic dogs (23), rodents and carnivores (17-18) are reservoir host for VL in East Africa. The presence of un plastered house wall and previous cases of canine are the major risk factors for domestic dogs (24). The animal reservoir hosts vary from place to place in east Africa. For instance, domastic dogs (25) and some wild animals like grass rat, Spinus mouse, Serval, Genet (17) and Jackal (26) are incriminated as a reservoir host in Sudan.

Limited studies have been conducted in finding the reservoirs of VL in Ethiopia but still the *L. donovani* is not found by parasitological investigation. According to Kenubih et al., 2014, some domestic animals showing the existence of *Leishmania* antibody in their serum and the highest seropositivity was found among cattle and dogs in Ethiopia but the organism was not confirmed by parasitological test (27). The most important and possible reservoir hosts are the human, and dogs (27-28).

Most of the people live in VL endemic areas of Ethiopia are farmers who have close relationships with dogs. Incrimination of dogs and other wild animals which act as a reservoir host in eastern Africa are not confirmed in Ethiopia. In addition, there is no diagnosis and treatment center for VL infected animal cases. Beside, unclear animal reservoir host in the environment and limited diagnostic and treatment practice for the human cases may aggravate the disease burden in Ethiopia. Therefore, Veterinarians should engage themselves in clearly identifying the possible VL reservoir hosts, detecting and treating of animal cases to break zoonotic transmission.

Environmental science

Based on entomological studies, there are two distinctive ecologic settings of VL endemic areas in Ethiopia due to suitable breeding sites. In northwestern foci, *P. orientalis* is found in association with black cotton-clay soils and acacia forests (29). In southern foci, *P. martini* and *P. celiae* are believed to transmit VL and termite hills are possibly their breeding sites (30). The vector transmits VL from human or animals to human since it feeds on the human and animals blood. The main means of transmission of VL in Ethiopia is via anthroponotically (31).

Through VL is mainly transmitted from human to human, there is no single prevention methods adopted for VL prevention in Ethiopia. This may lay its own contribution to high prevalence of VL in the country. The entomologists should engage themselves in identification of the vectors, discovery of the possible sites where the vectors live and breed. They also assess the ecological factors associated with the pre-existence of the vector. In addition, they should study about vector-human interaction and finding effective prevention strategies which help for proper vector control done in the country (32).

Human medicine

Human medicine is concerned in management of VL infected individuals. VL is a systemic disease caused by the *L. donovani* in East Africa and the Indian subcontinent (33) and *L. infantum* in Europe, North Africa and Latin

America (34). In east African countries namely Sudan, Ethiopia, Kenya and Somalia, *L. donovani* is the cause of VL which has zoonotic and anthroponotic transmission (31).

VL is prevalent in Ethiopia mainly in the lowlands of the country (35). An estimated 3.2 million people are at risk of VL (36) and 3,700-7400 cases occur annually (37) in Ethiopia. The highest number of VL cases was reported in Humera and Metema in the northern (36, 38) and Lake Abaya, Omo River, and lower Omo, Segen and Woyto valleys in the Southern part of Ethiopia (39). Outbreak of VL was recorded in Libo Kemkem district; the highlands of Northwest Ethiopia (40). *L. donovani* is transmitted from human reservior to human (anthroponotic) or from animal reservoir host to human (zoonotic) by the vectors (27-28).

Risk model of VL for Ethiopia based on soil type, altitude, mean annual rainfall, surface temperature and slope vis-à-vis GPS data on clinical VL presence and absence predicted that 33 % of the total land mass is at high and very high risk of VL endemicity and over 3.2 million people live in areas at risk (Fig. 1) (41, 42). Considering the large scale immigration of temporary labourers and settlers to these areas might be an underestimation.

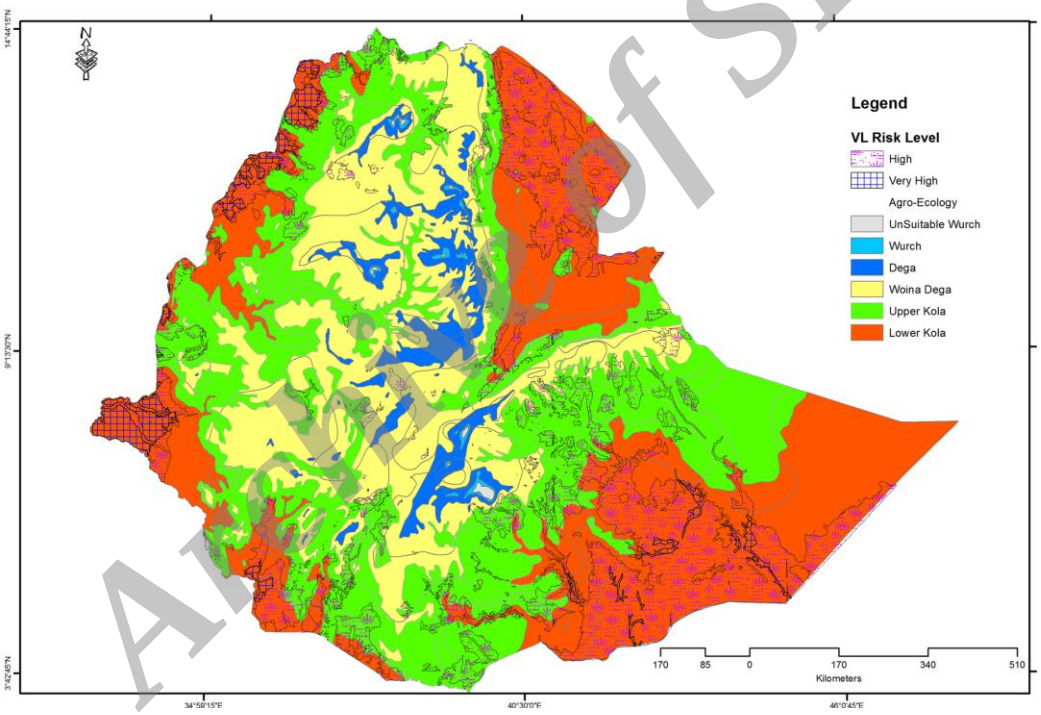

Fig. 1: The distribution of VL in Ethiopia

The clinical manifestation of VL patients includes: fever (more than two weeks), fatigue, and weakness, loss of appetite, weight loss, enlarged lymph nodes, hepatosplinomegally and sometimes bleeding (33). *L donovani* multiplies and survives in phagolysosomes through a complex parasite–host interaction with in the macrophages (43). The parasites disseminate through the lymphatic and vascular systems and infect other monocytes and macrophages in the reticulo-endothelial system, resulting in infiltration of the bone marrow, hepatosplenomegaly and lymphadenopathy (33).

Post Kala-azar Dermal Leishmaniasis (PKDL) is a sequel of VL that appears as

macular, papular or nodular rash usually on face, upper arms, trunks and other parts of the body. People with PKDL are considered to be a potential source of kala-azar infection (44). The prevalence of PKDL in Ethiopia is higher in people co-infected with Human Immunodeficiency Virus (HIV) and VL. However, during the Libo Kemkem VL outbreak, the incidence of PKDL was higher than seen routinely in Ethiopia (45).

Several factors are associated for the high prevalence of VL in the Southern and Northern parts of Ethiopia. Marked increase in VL cases is particularly associated with migration of non-immune labourers from the surrounding highlands to the extensive agricultural farm lands of the Humera and Metema lowlands in the northwestern (18, 46). On the other hand, the unique human adaptation and settlement patterns of the communities in Aba Roba focus and the very focal nature of sandfly habitats are believed to be the major factors VL burden in southwestern parts of the country (47).

Recent studies conducted in the Northwest parts of the countries indicated that the highest prevalence of VL in Humera and Metema is associated with the highest prevalence of HIV-VL co-infection (48-49). When high labour demand *Leishmania*-nonimmune highlanders go to the VL-endemic regions, they become exposed and infected. People infected with HIV will develop VL more rapidly than those who are not infected (4).

Co-infection of VL with HIV intensifies the burden of VL by causing severe forms and more difficult to manage (50). Up to 30% of VL cases are co-infected with HIV in North West Ethiopia (51). Leishmania-HIV co-infected people have high chance of developing the full blown clinical disease, high relapses and mortality rates (44).

There are also other risk factors for high prevalence of VL in Ethiopia. For instance, family size, housing condition, cracked black soil near houses, close relation with animals such as dogs, dumping animal dung near houses, sleeping outside near animal shelters, under *Balanites* and *Acacia* trees and in the farm field overnight are the major risk factors for VL (52).

L. donovani infected cases should be properly identified from the other febrile cases, and diagnostic with highly sensitive and specific laboratory tests. The confirmatory diagnosis of leishmaniasis relies on either the microscopically demonstration of *Leishmania* amastigotes in tissues aspirates or biopsies, smears after staining with Giemsa's stain solution (53). However, in general, both microscopic detection and culture should be performed since smears negative lesion can be cultured positive and culture negative lesion can be smear positive (54). Direct agglutination test (DAT) has a better sensitive test to diagnosis VL both in human and canine cases (55) but it is not applied all health institutions in endemic areas of Ethiopia due to limited resource.

There is a definite need for continued investment in diagnostics VL. The rK39 ICTs perform well for the primary diagnosis of VL, but further high performance test development and evaluation is required in Ethiopia, with specific attention to the diagnostic accuracy in HIV co-infected patients. Early detection of VL using serological tests and timely treatment of cases could decrease the mortality and morbidity rates of VL successfully in Iran (56) but absence of early detection of cases, limited diagnostic test kits and drugs in endemic areas of Ethiopia worsen the disease.

Treatment should be given based on the country drug line regimen. There are several drug treatments available including oral, parenteral, and topical medications (57). Pentavalent antimonials such as stibogluconate and meglumine antimoniate, have been the main drugs, but are complicated by adverse side effects, resistance and cost. Liposomal amphotericin B is more favorable in regions where resistance is common (33). Here in human medicine, Parasitologists, and physicians should work together in proper VL case iden-

tification, diagnosis and treatment for the proper management of VL cases. Integration of VL into health surveillance system and inter- and intra – sectoral collaboration would be a priority for planning future control strategies.

One Health Approach and interdisciplinary collaboration

In order to address the challenges of leishmaniasis prevention and control in Ethiopia, one health approach may be an ideal model. It is a holistic view of the previously distinct disciplines of human medicine, veterinary medicine, environmental science and wildlife conservation. One Health recognizes the fundamental links between these areas of scientific Endeavour (58). Each discipline has its own key roles in the prevention of leishmaniasis. The sum of these disciplines data produces one complete data which help in eradication of the disease. Therefore, the above disciplines must work together as one team for the proper management of leishmaniasis especially in VL endemic areas.

Though, MOH made efforts so far to control VL through treatment of VL infected cases, the diseases increases from time to time. Hence, VL is developing both on a spatial distribution and the burden increases year after year (59).

In Ethiopia, the collaboration between veterinarians and their counterparts in human medicine, environmental science and wildlife conservation contributing to an enhanced multidisciplinary approach is weak. In addition, the overall level of collaboration and communication between veterinary and human medicine has been limited and often neglected.

Therefore, in order to get a healthy environment from VL infection, all the four disciplines must collaborate, share their knowledge and work together hand in hand. MOH should adopt one health approach to prevent emerging diseases like VL and recruit specialists from the above disciplines. In addition, MOH should revise the strategic plan of VL control programs through addressing reservoir hosts and vector control, effective diagnosis and treatment of cases and minimizing the risk factors for VL infections especially in endemic parts of country.

The purpose of this review was to collect all available information on one health approach and VL control strategies including those, which have been published in scientific journals and not usually usable for researchers and other people who are interested in the issue. Here I discuss the current VL prevention and control strategies and future perspectives in Ethiopia.

Conclusion

In order to identify, characterize and undertake surveillance for VL, and to develop integrated strategies for the control and prevention of the associated diseases, one health approach becomes imperative. Therefore, integrated inter- and intra – sectoral collaboration for visceral leishmaniasis control is an effective control strategy in endemic areas. In such situations, it is essential that interdisciplinary teams of medical, veterinary and environmental and wild life specialists work together in one office to alleviate the disease burden especially in endemic parts of the country.

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