Social determinants of visceral leishmaniasis elimination in Eastern Africa

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ABSTRACT

Visceral leishmaniasis is a vector-borne, protozoan disease with severe public health implications. Following the successful implementation of an elimination programme in South Asia, there is now a concerted endeavour to replicate these efforts in Eastern Africa based on the five essential elimination pillars of case management, integrated vector management, effective surveillance, social mobilisation and operational research. This article highlights how key social determinants (SD) of health (poverty, sociocultural factors and gender, housing and clustering, migration and the healthcare system) operate at five different levels (socioeconomic context and position, differential exposure, differential vulnerability, differential outcomes and differential consequences). These SD should be considered within the context of increasing the success of the five-pillar elimination programme and reducing inequity in health.

INTRODUCTION

Leishmaniasis elimination

Visceral leishmaniasis (VL or kala-azar) is a protozoan disease grouped within the neglected tropical diseases (NTDs) transmitted by sandflies.

VL, which is present in 80 countries, is deeply linked with poverty and fatal if untreated.1 2 The VL incidence peaks every 10–15 years, most likely due to declining herd semi-immunity.3 4 Poor environmental sanitation, temperature, rainfall, humidity, soil type and vegetation coverage are the most important environmental determinants of sandfly distribution.5 6 Post-kala-azar dermal leishmaniasis (PKDL) is a non-painful, non-itching skin condition that appears in a high proportion of patients with properly treated VL.7 PKDL incidence rates vary widely between countries (15% in Sudan and less in other Eastern African countries).

Studies in South Asia have shown that PKDL serves as the main parasitic reservoir for transmission, threatening the elimination of VL. Due to this fact, the WHO has recognised the detection and treatment of PKDL as one of the indicators for VL elimination in South Asia.8–10

In 2005, when oral miltefosine was proven to be highly efficacious, health policymakers in Bangladesh, India and Nepal launched the Kala-azar Elimination Programme (KAEP) which aimed to achieve fewer than 1 case per 10 000 people at risk in intervention areas by 2015.11 Despite challenges, by 2021 the KAEP achieved said target in 98.8% of the intervention areas.

Presently, 12% of the world’s VL case burden is in the Indian subcontinent meanwhile Eastern Africa harbourrs 66% of the cases, out of which 53% are children less than 15 years old, and one-third of cases occurring in women.12 However, in outbreaks, all age groups are equally susceptible.13 Although there are multiple differences between the two regions, WHO and partners are developing a strategy for a similar elimination programme in Eastern Africa using existing tools and lessons learnt from Asia.14
countries specificities, has identified the most vulnerable groups and the constrains for elimination, always in the frame of the NTD road map for 2030, the Sustainable Development Goals and the Universal Health Coverage. Moreover, the representatives from the ministries of health of Chad, Eritrea, Ethiopia, Kenya, Somalia, South Sudan, Sudan and Uganda, and main stakeholders in the region (End Fund, Drugs for Neglected Diseases initiative (DNDi), Médecine Sans Frontière (MSF), African Union, Bill and Melinda Gates Foundation (BMGF), Special Program for Research and Training in Tropical Diseases-TDR/World Health Organization/WHO, Africa Centers for Disease Control and Prevention-Africa CDC) launched the Nairobi Declaration on the 27 January 2023 to join efforts on elimination of VL as a public health problem from the Eastern African countries, countries included either at the WHO Africa or Eastern Mediterranean Regions (publication in preparation). The cross-border collaboration will be an integral part of the VL elimination strategy in East Africa.

WHO has aligned clearly with Sustainable Development Goal 3.3; its roadmap for NTDs calls for action to eliminate VL as a public health problem in 56 countries by 2025 and in 64 by 2030. The strategy for VL elimination in Eastern Africa comprises five elements:

► **Case management** including early detection and treatment of VL as well as complicated forms such as PKDL and HIV/VL coinfection. Meanwhile *Leishmania donovani* is the parasite in both regions, the intraspecies variability makes that the response to treatment in East Africa is much lower than in Asia. Short course regimens do not work, although it has been clearly shown the efficacy and safety of combining miltefosine and liposomal amphotericin B to treat primary attacks, relapses, HIV/VL coinfection and PKDL.

► **Integrated vector management** including various means to reduce contact between sandflies and humans such as environmental sanitation, insecticide impregnated bed nets, repellents and, eventually, peri-domestic residual spraying.

► **Effective surveillance** to monitor the effectiveness of the programme such as case fatality rate, incidence and the delay in time between symptom onset and treatment.

► **Social mobilisation** to ensure population participation such as awareness campaigns and the involvement of local health activists.

► **Operational research** to ensure the efficacy of each of the previous four pillars of the elimination programme.

Our paper aims to support the plan for VL elimination in Eastern Africa by identifying the main social determinants (SD) of health which influence the five key elements of the elimination strategy.

### Social determinants of health

WHO defined health determinants as the non-medical factors that influence health outcomes. They are the circumstances in which people are born, grow, live and age, in the context of economic and political systems, all of which influence health inequities. A preparatory WHO report outlined the diverse theoretical foundations of the conceptual framework, including so-called structural determinants such as income, gender and ethnicity, as well as intermediary determinants including material and psychosocial circumstances. An analysis was also conducted on the SD of importance to NTDs. Graham previously pointed out the importance of distinguishing between determinants of health and determinants of health inequities; this article focuses on the former.

The Commission on Social Determinants of Health report (CSDH-2008) applied an analytical framework for causal pathways for health action which included five levels. It differentiated between individuals, population groups and society, and identified causal links between them. In this article, a simplified version of the analytical framework will be applied to understand how SD operate in relation to the pillars of VL elimination, using the five levels:

- **Socioeconomic context and position** signify how a society is organised and how entitlements are distributed at the macro level, for example, models of healthcare funding or discrimination against certain social groups.
- **Differential exposure** pertains to the likelihood of getting infected by sandflies, for example, due to housing, occupation or other practices.
- **Differential vulnerability** focuses on whether individuals or groups are more likely to get infected due to biomedical factors (eg, comorbidity or malnutrition), rather than the social meaning of the term.
- **Differential outcomes** pertain to the level of success of various actions taken, for example, the cure rate of healthcare services.
- **Differential consequences** focus on the outcomes of certain actions, for example, the economic impact of treatment expenses.

### SOCIAL DETERMINANTS IN RELATION TO VL ELIMINATION

The significance of SD of health has been analysed specifically in relation to NTDs, including leishmaniasis. Below we address those of particular importance to VL.

#### Poverty

Poverty, here defined as low income with the inability to acquire the basic goods and services necessary for survival with dignity, is the most important structural SD of leishmaniasis morbidity and mortality, establishing a root cause for the intermediary determinants mentioned below. For poor patients depending on a daily income, financial support is needed to seek early diagnosis and treatment, but also to address poverty-related risks such as housing conditions, environmental sanitation, nutrition, personal protective measures, healthcare services and preventive strategies. If not provided, these patients...
will need to delay attendance, risking life and allowing parasite transmission. In the KAEP, a wage loss compensation of US$89 is given in India to patients with VL and US$54 to patients with PKDL, paid by the government. In Africa, hospitalisation for medical treatment lasts 17 days versus 2–4 days in Asia, and therefore indirect costs to the patient are higher.\textsuperscript{24} Wage loss compensation may not be feasible in East Africa but other patient incentives such as reimbursement of travel or transport costs, meal support or free provision for patients and caretakers, free treatments, waiver of hospital stay fees, and other locally feasible incentives can be considered.

**Sociocultural factors and gender**

*Phlebotomus orientalis*, the main vector in East Africa, is primarily exophilic biting at sunset and night in the peridomestic space where people interact and men and children frequently sleep.\textsuperscript{25} 26 Other outdoor activities in this region like herding cattle are predominantly conducted by young men.\textsuperscript{27}

In Africa, anaemia affects an estimated 40.4\% of women of reproductive age (15–49 years). This factor, combined with malnutrition, HIV, tuberculosis (TB) and other co-infections or comorbidities will increase vulnerability among women,\textsuperscript{28} as is the case in highly endemic rural areas for VL, such as Tigray, Ethiopia.\textsuperscript{29}

In general, people tend to seek healthcare with local but unqualified health practitioners first, only going to the formal healthcare system (HCS) when the disease becomes serious.\textsuperscript{30} After a decade of this practice, KAEP finally initiated a collaboration with private practitioners and traditional healers. In addition, the Ministries of Health (MoHs) engaged local female practitioners and traditional healers. In the KAEP, a wage loss compensation of US$89 is given in India to patients with VL and US$54 to patients with PKDL, paid by the government. In Africa, hospitalisation for medical treatment lasts 17 days versus 2–4 days in Asia, and therefore indirect costs to the patient are higher.\textsuperscript{24} Wage loss compensation may not be feasible in East Africa but other patient incentives such as reimbursement of travel or transport costs, meal support or free provision for patients and caretakers, free treatments, waiver of hospital stay fees, and other locally feasible incentives can be considered.

**Housing and clustering**

House structures in rural East Africa consist of a compound with small huts and a barn surrounded by a fence. In the hot season, sandflies can be abundant in peridomestic areas and people tend to sleep outside of their houses, within the compound, where they are at high risk of being bitten. If there are breeding conditions and resting sites for sandflies (eg, environmental degradation, cracked black cotton-clay soil or termite hills) in proximity, the transmission conditions for the vector of the disease are given.\textsuperscript{25} Considering that sandflies fly less than 100 metres, in anthropogenic foci where infected humans are the reservoir, there are frequently cluster transmissions with micro-epidemics within the same family and their neighbours.\textsuperscript{10} 35

As poverty is a root cause for poor housing, the Indian Prime Minister’s Housing Scheme (Pradhan Mantri Awas Yojana) enabled the most marginalised citizens to acquire reasonable houses, though this possibility was not accessible to the lowest castes.\textsuperscript{36} Alternative factors may apply to the African context, but surveillance and vector control in all endemic areas could lead to VL control as a public health problem.

**Migration**

Migration is of particular importance for VL, including refugees from natural or political disasters, migrant workers or nomads.\textsuperscript{39} 37 It has been reviewed that military or civil unrest events between 1995 and 2010 and estimated a sixfold increase in the incidence of VL, primarily attributed to the dismantling of the HCS and displacement of people.\textsuperscript{38}

Migrant populations may be vulnerable due to their lack of immunity when entering VL endemic areas, and the local HCSs should be designed to address the specific needs of these groups. The intertribal war in South Sudan in the 1980s resulted in displacements of immunologically naïve and malnourished populations into VL transmission areas causing an overwhelming outbreak with over 100 000 deaths, possibly surpassing the toll of the civil war itself.\textsuperscript{39} 40 When the situation stabilised, people returned home, introducing the disease to new areas.\textsuperscript{41}

An additional factor for the spread of VL in Africa is labour-mediated migration, which was thoroughly studied during the outbreak in the Libo Kemkem highlands of Ethiopia. These areas were initially free of VL until the return of seasonal workers who were infected harvesting crops in the fertile but highly endemic lowlands of Humera-Tigray.\textsuperscript{37} 42 It was not a significant problem in Asia, but it is a problem caused by population movement for different reasons in Africa. Preventive interventions including surveillance and early detection with (mobile) clinics next to the farms when harvesting, followed by accessible free of charge treatment are also necessary VL control measures in this population.
Healthcare system

The HCS has been identified as SD of health and deserves particular attention in VL elimination in Eastern Africa. Effective case management and positive treatment outcomes depend on the quality of HCSs. Building on existing literature, we have highlighted the following key aspects: availability (do the necessary resources such as manpower, facilities and drugs exist?), accessibility (are the services within reasonable reach?), affordability, acceptability (are the services in accordance with the patients’ culture?) and adherence (are the patients able to follow the prescribed treatment?). With the existing drugs, patients will be treated following the national guidelines at the hospital level to ensure compliance. Only when a new oral chemical entity is ready, decentralisation at the house level can be considered. Meanwhile, expansion of the coverage of current diagnosis and treatment services in all areas and scaling up of all preventive interventions including early detection, surveillance and vector control in all endemic areas could lead to achievement of the VL elimination as a public health problem.

Diagnostic provisions are made under KAEP in 100% of health facilities in endemic areas in India, where in most of the places, despite the free provision of VL rapid tests and treatment, additional indirect costs such as from hospitals pose financial burdens. As a result, families must take loans and sell assets to pay for care. Some patients have been reported to undergo forms of financial exploitation prior to receiving the VL treatment without charge. The absence of trust within the community towards the HCS may lead many patients to use private services, incurring high direct and indirect costs. In Eastern Africa as well as in Asia, the availability of diagnosis and treatment free of charge is very important for adherence as well as campaigns carried out by local leaders. The direct relationship between villagers and health activists (the Accredited Social Health Activists or ASHAs in the KAEP), will be critical for a prompt advise in case of prolonged fever.

SOCIAL DETERMINANTS AND VL ELIMINATION IN AFRICA

The action plan for VL elimination in Eastern Africa comprises five elements: case management, integrated vector management, effective surveillance, social mobilisation and operational research. Below each of the elements are analysed based on key SD and pathways.

Case management

The VL elimination initiative in South Asia started with 28 days of treatment. Although it was oral and ambulatory, the treatment took relatively long and faced challenges of adherence due to both side effects and the availability of supplies as they originated from a single manufacturer. However, in subsequent stages, the primary treatment was modified to a single dose of liposomal amphotericin B and diagnoses could be reliably conducted with a rapid test. The tools for diagnosis and treatment of VL in Africa are less effective than in Asia. The current treatment regimen requires 17 days of hospital-administered intramuscular injections with two drugs. Improved diagnostic tests and safer oral drugs would accelerate the elimination strategy. In addition, challenges related to drugs and diagnostics, supplier limitations, fragile supply chains, in-kind compensation and patient acceptability persist in the context of weak HCSs in poor communities.

Surveillance, early detection, with equitable and affordable universal access to current diagnosis and treatment in remote areas are key to VL control as a public health problem. At the socioeconomic level, there is a need to raise awareness among MoHs about the importance of VL elimination, maintaining adequate human resources, acquiring and registering diagnostics and drugs, implementing quality assurance measures and ensuring proper storage and distribution for availability and accessibility. This may include supranational/regional partnerships. Furthermore, MoHs should ensure the affordability of curative and preventive VL services for those in need.

Information campaigns targeting relevant population segments, including vulnerable groups (comorbidities with HIV or TB, seasonal workers, pastoralists) should be initiated by health authorities, following the example of Southeast Asia where several awareness campaigns have been conducted using banners, posters and wall paintings in health facilities. Accessible and acceptable curative healthcare services are essential to VL elimination, ensuring adherence and good quality outcomes, even for migratory populations. Failure to provide affordable healthcare services may result in catastrophic expenditures for patients, which can have negative consequences.

Integrated vector management

At the socioeconomic level there is a need for strengthening national vector management programmes in all endemic areas, including trained personnel, entomology research centres, insectaries, insecticides and preventive measures such as bed nets and other equipment. Integrated vector management for VL in Africa presents unique challenges compared with Asia due to factors such as the geographical dispersion of foci, the presence of three species of sandflies (as opposed to one), limited investigation into one of the species and the complexity of their peridomestic and sylvatic habitats.

Vector management should consider how sociocultural and gender-related variations influence exposure, for example, due to differential work tasks, social mobility or sleeping places and patterns. Vector management should also address housing structures and clustering, impregnated bed nets or peridomestic spraying, possible animal reservoirs and environmental deterioration facilitating breeding sites. Awareness is also needed on how migration patterns expose vulnerable non-immune population segments to infection. A vector control programme taking these diverse local factors into consideration will lead to better outcomes and consequences.
Effective surveillance
At the socioeconomic level the MoHs should ensure that an adequate surveillance system is in place for VL management including relapses, outbreaks, HIV-co-infection, PKDL, and vector and human migration patterns.

Effective communication between the central decision-making level and regional/local authorities is essential. In KAEP, the communication chain was often interrupted downstream, with field practitioners not receiving feedback after feeding data to the surveillance system, which discouraged the bidirectional collaboration.\(^36\)

At the exposure level, there are two elements: (1) monitoring human migration patterns (e.g., flows of refugees) that may expose new population segments; (2) fluctuations in sandfly populations related to seasonal and climatic changes including effectiveness of vector control programmes.

Early VL and PKDL case detection and adequate reporting of VL outbreaks is essential within and outside known endemic areas. The incentive strategy and the reporting of VL outbreaks is essential within and outside programmes.

Table 1 Cross-tabulation of the five elements of the visceral leishmaniasis elimination programme and the five mechanisms through which social determinants may play a role, highlighting which social determinants of health are of importance

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<th>Socioeconomic context and position</th>
<th>Case management</th>
<th>Integrated vector management</th>
<th>Effective surveillance</th>
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<td>Differential healthcare outcomes</td>
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Social mobilisation
At the socioeconomic level, MoH policies should align with national frameworks and guidelines to empower and engage citizens (including patients) in supporting curative services and vector control in endemic areas.

To circumvent the social bias among health workers towards the most marginalised and vulnerable groups, effective coordination between stakeholders and HCSs should be ensured, involving community leaders and local groups.

Engaging communities in endemic areas through targeted vector control programmes can increase their acceptability and reduce exposure for the sedentary population as well as migrants where relevant.

Where applicable, communities should support local initiatives in their efforts to provide effective health outcomes for all (including vulnerable groups such as the immunosuppressed) and ensure vector control measures based on the principles of availability, accessibility, affordability, acceptability and adherence\(^45\) for even the poorest households. The consequence of
insufficient social mobilisation will be diminished community activism and the reduced effectiveness of local vector control.

Operational research
At the socioeconomic level, MoHs should ensure that a functional and appropriate cross-disciplinary operational research capacity is in place, either at national research institutions or within the MoHs themselves, to conduct relevant VL-related research, with a stable financial provision for the research units during all phases of elimination programme.

Specific aspects of exposure that should be explored include long-distance and local patterns of human migration, as well as local variations in sandfly populations and habitats, including potential variations in housing providing breeding and resting sites for sandflies. The influence of climate change on vector distribution and density, exposing new populations to infection, should be considered as well. Reducing exposure through innovative vector control strategies will affect epidemiological outcomes.

The vulnerability caused by malnutrition and poverty-related consequences such as the lack of access to HCSs, can greatly hinder the achievement of elimination programmes. Targeted studies on treatment-seeking practices among various ethnic groups may be conducted to shape VL information campaigns and increase adherence and outcomes of conventional healthcare services.

Furthermore, there is a need for targeted studies on the economic consequences of a lack of curative services, including catastrophic health expenditures disaggregated according to gender, ethnic groups, and migrant status. At the preparatory phase of the elimination programme, we urge policymakers and public health planners to consider these determinants in their formulation of elimination strategies for VL, as understanding them leads to more effective strategies and increased equity in health.

CONCLUSION
This article explores the inter-relationship between key social determinants of health (such as poverty, sociocultural factors and gender, housing and clustering, migration and the HCS) and the five pillars of the VL elimination programme in the pipeline for Eastern Africa: case management, vector control, surveillance, social mobilisation and operational research. Table 1 demonstrates how these social determinants operate on five levels: (1) socioeconomic context and position, (2) differentials of exposure, (3) vulnerability, (4) outcomes and (5) consequences.

Scaling up of all preventive interventions including active surveillance, vector control and early case detection, with universal access to current diagnosis and treatment services in all endemic as well as migration and cross-border areas, can lead to the achievement of VL elimination as a public health problem. Country-specific community awareness campaigns and other mechanisms such as wage loss compensation have been shown to help control the disease. At the preparatory phase of the elimination programme, we urge policymakers and public health planners to consider these determinants in their formulation of elimination strategies for VL, as understanding them leads to more effective strategies and increased equity in health.

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