



Short Communication

Leishmaniasis control in the light of the COVID-19 pandemic in Africa



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ABSTRACT

Leishmaniasis is a parasitic disease, endemic to Africa, Asia, and South America due to inadequate access to medication and underreporting of leishmaniasis cases. Leishmaniasis has two forms: cutaneous and visceral. The fight against leishmaniasis has been greatly affected by the coronavirus disease 2019 (COVID-19) pandemic that impacted resource distribution and access to medication. Continuous effort in vaccine development and affordable therapeutics are necessary to eliminate leishmaniasis in low-income countries. Further research is necessary to determine molecular drug resistance markers in leishmaniasis patients. In this analysis, we focus on the effect of COVID-19 on leishmaniasis in Africa.

1. Introduction

Coronavirus disease 2019 (COVID-19) is an atypical pulmonary infection that emerged in Wuhan city, China, in early December 2019, and was officially classified as a pandemic by the World Health Organisation (WHO) by March 2020. COVID-19 infection begins as viral particles are transmitted through respiratory droplets and gain access to bronchial epithelial cells exhibiting ACE-2 receptors in the lower respiratory tract, leading to respiratory distress syndrome. There is no medical treatment that can be used to eliminate the physiological effects of COVID-19 after infection immediately and supportive management remains essential to treat the condition [1].

Leishmaniasis is an endemic neglected tropical disease in Africa, Asia, and South America. It has two main forms, cutaneous and visceral. Leishmaniasis has an incidence of approximately 400 000 cases per year, with the majority residing in Asia and Africa. Africa has its main distribution in the African horn, including Sudan, Ethiopia, Somalia, and Kenya (Fig. 1). Countries with risk factors dominant — poverty, migration, poor hygiene, and malnutrition — are associated with the development of visceral leishmaniasis and happen to be very

characteristic of communities in these regions. *Leishmania* parasite is transmitted by sandflies of the genera *Phlebotomus* and *Lutzomyia* of the Old and New Worlds, respectively. *Leishmania* mainly affects the reticuloendothelial system through its amastigote forms, causing non-specific symptoms of fever, weight loss, hepatosplenomegaly, and low blood cell counts in visceral form, and mucocutaneous lesions in the cutaneous form [2]. This article inspects the battle against leishmaniasis in Africa before the COVID-19 pandemic. It also compares the efforts and challenges facing the response to the disease during the pandemic (Fig. 1).

2. The situation of fighting leishmaniasis pre-COVID-19 pandemic in Africa

Before the COVID-19 pandemic, the fight against both visceral and cutaneous leishmaniasis was focused on North Africa and East Africa due to the high prevalence of the disease among those countries [3]. However, the disease is also present in epidemic proportions in West Africa.

The variant of leishmaniasis, its related pathologies, and the

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Fig. 1. Map showing the distribution of leishmaniasis in Africa (countries in grey: Sudan, Ethiopia, Somalia, and Kenya).

geographic locations play a vital role in the treatment of leishmaniasis [5]. Besides the need for an immunocompetent status, medications can help to eradicate the organism from the human system. Thus, the risk of relapse of the disease is high in immunosuppressed patients [5].

Moreover, the prevention and control of leishmaniasis are primarily based on an aggregate of intervention strategies as transmission takes place in a complicated biological system concerning the human host, parasite, sand-fly vector, and, in some instances, an animal reservoir host [5]. Important strategies consist of early diagnosis and effective case and vector control, powerful disease surveillance, management of animal reservoir hosts, social mobilization, and strengthening organizations [5].

As mentioned previously, the fight against leishmaniasis differs between the African countries. Apart from Eritrea which employed Meglumine antimoniate, Kenya, South Sudan, Somalia, Northern Sudan, and Uganda use Stibogluconate (SSG) as the first-line treatment regimen. All countries use Amphotericin B, Ambisome, and paromomycin as second-line treatments [3].

Due to less preference for treating leishmaniasis in West Africa, the disease is managed only during outbreaks. Chemotherapeutic drugs are provided to those patients found symptomatic which is inadequate for eradicating the disease [4].

An effective way of reducing disease incidence is vector control with insecticides against the sand-fly vectors. However, West African countries have not been applying this technique.

This unequal fight is nevertheless intensified by the work of the World Health Organisation (WHO) on leishmaniasis control. Such measures include aiding national leishmaniasis control programs and creating awareness regarding the worldwide burden of leishmaniasis. This has allowed reasonable admittance to health services for disease prevention and case management. In addition, evidence-based policy guidelines, strategies, and standards are also developing. Moreover, collaborations among stakeholders have been strengthened that contributed to diagnostic tests and antileishmanial medicines provision, promoting effective research on leishmaniasis and aiding in the dissemination of its discoveries [5].

Unfortunately, no authorized vaccine is available for cutaneous or

visceral leishmaniasis. However, some were designed and developed by the Infectious Disease Research Institute (IDRI), based on the organism's antigenic epitome. These vaccines, named F1, F2, and F3-lesh alongside recombinant protein and DNA-based vaccines, are still in clinical trials. The vaccine is believed to facilitate long-term immunity and even limit chemotherapy use [6].

The battle against Leishmaniasis has been well fought so far. However further work is still warranted to successfully eliminate leishmaniasis from the African Population.

3. Burden and status of leishmaniasis in Africa during the COVID-19 pandemic

Compared to the global incidence rate, a moderate number of COVID-19 cases have been reported in Africa. However, due to inadequate testing and reporting, leishmaniasis continues to be an endemic public health problem in Africa. Even though leishmaniasis and COVID-19 follow different pathophysiology, the overlapping clinical features present an issue, particularly for timely diagnosis and treatment. Immunocompromised individuals are vulnerable subgroups for both infections, and dual infection, unfortunately, increases the risk of mortality (Table 1).

Table 1 Shows a summary of the salient features for both infections [7,8,16–21].

General features	Leishmaniasis	COVID-19
Transmission	Bite of the female <i>Phlebotomus</i> sandfly	Respiratory droplets and/or aerosols
Diagnosis	<p>Immunological</p> <p>Rapid immunochromatographic test for recombinant rK39 antigen</p> <p>Immunofluorescence (IF) enzyme</p> <p>Immunoassay (ELISA)</p> <p>Parasitological:</p> <p>Direct and in vitro examination of parasites in infected tissue, particularly bone marrow.</p> <p>Molecular test:</p> <p>PCR test for Leishmania DNA</p>	<p>For active infection:</p> <p>PCR tests for mRNA of SARS-CoV-2 virus</p> <p>Lateral flow tests (LFTs)</p> <p>For the previous infection:</p> <p>Serology tests</p>
Clinical signs and symptoms	<p>MILD</p> <p>VL</p> <p>Prolonged fever</p> <p>Weight loss</p> <p>Pallor</p> <p>Leukopenia</p> <p>Splenomegaly</p> <p>Hepatomegaly</p> <p>CL</p> <p>Disfiguring lesions of the nose, mouth, and throat mucous membranes.</p> <p>SEVERE:</p> <p>Malnutrition</p> <p>Lower-limb oedema</p> <p>Anasarca</p> <p>Bleeding from the nose or mouth</p> <p>Jaundice</p> <p>Ascites</p>	<p>MILD</p> <p>Fever</p> <p>Cough</p> <p>Rigours</p> <p>Fatigue</p> <p>Diarrhoea</p> <p>Loss of taste or smell</p> <p>SEVERE</p> <p>Difficulty breathing or shortness of breath</p> <p>Loss of speech or mobility, or confusion</p> <p>Chest pain</p> <p>Lymphopenia</p> <p>Elevated liver enzymes</p>

4. Current efforts and challenges facing responses to leishmaniasis in Africa during the COVID-19 pandemic

4.1. Challenges

Since the WHO declared COVID-19 as a public health emergency [27], the consideration of the global community has been grossly disrupted and turned regarding interventions and endeavours to restrain the pandemic [28]. Therefore, the advance of COVID-19 is exacerbating leishmaniasis by diverting all the required materialistic and human resources. Consequently, the number of infections and deaths from leishmaniasis is still increasing yearly [8].

The number of infections and deaths from leishmaniasis is rising, with more than 1 million new cases and additional 30 000 deaths occurring annually [5].

The emergence of the COVID-19 pandemic has concealed Africa with demanding situations, particularly in the healthcare system. These include delayed admission of patients with leishmaniasis due to limited bed spaces. Additionally, the suspensions of some drug distributions and the stakeholders have been negatively impacted by drug suspension, leading to financial losses [9].

In the matter of decreasing community transmission of the virus, lockdown methods that have been executed in Africa have altered access to healthcare services [9]. East Africa, where sandflies are endemic to the poorest rural areas, is facing a plethora of challenges. These comprise lack of access to diagnosis and treatment, misdiagnosis of visceral leishmaniasis with fatal consequences due to the disease's non-specific symptoms, and lack of awareness [10].

Canine visceral leishmaniasis (CVL) plays a vital role in the continuance of transmission levels and the dissemination of the disease, particularly in urban areas [8,22–25]. Therefore, successful control of this disease is an onerous task.

Both zoonoses face common challenges, from vaccine and drug development to improved animal health surveillance to increasing knowledge of the animal reservoir. Leishmaniasis is additionally facing extra challenges including proper implementation and monitoring of the vector control programs [8].

4.2. Efforts

The international consortium funded by the UK government, "Tackling Visceral Leishmaniasis in South Asia and East Africa" (KalaCORE), played a major role in the fight against VL by providing education, tutelage, adjudication of cases, operation research, and surveillance in countries like Ethiopia, Sudan, and South Sudan. KalaCORE also worked on improving access to prompt diagnosis and effective treatment, training health workers, equipping health centres, raising community awareness, and bolstering national surveillance systems and vector control methods for protection against sandflies [11].

When it comes to training health workers, advocacy is one of the main targets of the KalaCORE story. Health workers have attended regular policy dialogues with the health departments to negotiate strategies to reduce the economic burden on patients [10]. Additionally, they have also attended several pieces of training and been granted access to enriching online resources. Therefore, the accurate diagnosis of patients with rapid testing followed by the administration of an effective single-dose injectable drug for treatment (AmBisome) results in a clinical and parasitological cure in most cases, occurring in a matter of days [10,11].

Meanwhile, despite civil war and mass displacement in East Africa, Interchurch Medical Assistance World Health mobile teams, defended by KalaCORE, have shown a remarkable commitment to contacting, acknowledging, and limiting disease outbreaks in remote communities, especially in tough circumstances [10]. KalaCORE also provided online resources to help practitioners fight against VL. At the same time, the

London School of Hygiene and Tropical Medicine launched a MOOC (massive open online course) intending to guide health practitioners in the fight against VL. Such a MOOC aimed to enlarge understanding regarding the spread of VL and gain extra-practical tools to control and combat it in different settings [10].

Finally, several important issues, such as comorbidities, drug resistance/treatment failure, and the population-ecology nexus, somehow influence efforts for VL elimination and control [7].

4.3. Future possibilities and recommendations

When fighting zoonoses, there are many fields of mitigation between COVID-19 and leishmaniasis to synergize efforts and control the disease. We can state the following opportunities: in general surveillance, potentiality strengthened in COVID-19 including supervision sites, policymakers, and private stakeholders, risk communications developed in favour of epidemic-prone diseases, media information dissemination, information technology capabilities strengthened in COVID-19, and the field logistics [8,29,30].

Not only do health authorities and sectors oversee fighting both zoonoses fairly and equitably, but non-health sectors also pose as equally important in this group. Only wide harmonious teamwork can synergize such effects [8,31,32].

Many areas could advance significantly in the perspective of diagnosis and management of leishmaniasis. Currently, limited methods of evaluation and unfamiliarity of physicians with endemic leishmaniasis are major barriers to the prompt and precise detection of this disease. Diagnosing leishmaniasis is incommensurate; therefore, strengthening serological testing could forefront timely identification and treatment. In addition, informing local, national, and international health officials should be required when making the diagnosis [33,34].

A better understanding of the disease's characteristics, risk factors, and geographic variation's contribution to leishmaniasis can be made only if health authorities provide the reports to all states and the nation.

In terms of therapeutic approach, the cost of medicine, its resistance and toxicity are emerging concerns that can limit the antiparasitic treatment arsenal. Unfortunately, no identifiable mediators are available to detect medicine resistance for Leishmaniasis. One of the historical standards of care was pentavalent antimony, but there is likely increased drug resistance due to insufficient treatment and proper drug dosing [6]. Even the resistance to miltefosine is increasing, and the price of the medicine can be unaffordable [12]. Directly Observed Therapy in recent treatment dominions along with drug development campaigns may facilitate maintenance of treatment accomplishment and combat resistance. In addition, no-cost treatment of leishmaniasis from structured drug aid projects (and restrictions on without drugs prescriptions) would promote the suitable prescription application. It could avoid the development of any resistance [26,35,36].

Vaccination can be the best method to control leishmaniasis as there are many limitations to the treatment regimens. The vaccine should aim to be harmless, efficient, reasonable, and extensively accessible. Unfortunately, no vaccine exists for leishmaniasis despite years of study [6, 12]. Recombinant vaccines like Leishmune, and CaniLeish have proven their effectiveness in the dog and might assist in preventing leishmaniasis [13]. The IDRI, Washington, Seattle, invented a candidate immunization (LEISHF3 + GLA SE) using recombinant antigen proteins from *L. donovani* and *L. infantum* and is presently evaluating volunteers in phase I clinical studies [14]. Similarly, the Sabin Vaccine Institute Product Development Association (Sabin PDP) is effective in an immunization that uses the protein of recombinant *L. donovani* with antigens from sandfly saliva [15]. Lately, a third-generation leishmaniasis vaccine, ChAd63KH, is considered to produce CD8⁺ T cells against leishmaniasis and is in phase 1 clinical trials [15]. With the support of the European Commission, Bill and Melinda Gates Foundation, the Carlos Slim Foundation, the Ministry of Federal Research and Education NIH, and the Wellcome Trust the vaccine against human visceral leishmaniasis

(MeLeVaClin) is under preclinical trials [6]. It is hoped that this study resolves the inadequacy of an effective prophylactic vaccine and amends the immunization that can help those in endemic areas. Further, an effective vaccine to lessen the threat of carriers of leishmania parasites should be addressed soon.

5. Conclusion

This commentary shows that leishmaniasis, specifically VL, is a major disease to be contended with. It remains a threat to the African population, who still suffer from a high increase in the numbers of infections and deaths yearly due to inadequate testing and lack of awareness. It continues to be an endemic public health problem in Africa. Before the COVID-19 pandemic, some preventive measures involved controlling parasites, hosts, and vectors. Despite effective medicines for visceral leishmaniasis, it is still hard for disadvantaged people to get adequate access to them. The flare-up of COVID-19 has been a double-edged weapon in the leishmaniasis fight in Africa. COVID-19 has led to a rapid scarcity of AmBisome injections used to treat VL patients. Travel restrictions have also made effective control of diseases. Surely, to combat emerging drug resistance that limits the antiparasitic treatment, further research is necessary to look for resistance markers and avail medications and vaccines for poor countries.

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Author contribution

Olivier Uwishema: Conceptualization, Project administration, Writing-review and Designing, **Suhail Sapkota:** Collection and assembly of data, **Olivier Uwishema:** Reviewed and edited the first draft, supervisor, **Jack Wellington MSc (LSHTM) FGMS:** Reviewed and edited the second draft, **Helen Onyeaka:** Reviewed and edited the final draft, Supervisor, **Manuscript writing:** All authors, **Final approval of manuscript:** All authors.

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List of Abbreviations

COVID-19	Coronavirus Infectious Disease
WHO	World Health Organization
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
ACE-2	angiotensin-converting enzyme-2
SSG	Sodium stibogluconate
DNA	Deoxyribonucleic acid
NIH	National Institute of health
VL	Visceral Leishmaniasis
CVL	Canine Visceral Leishmaniasis
MeLeVaClin	European Multivalent Vaccine for Human Visceral Leishmaniasis
DOT	Directly Observed Therapy
IDRI	Infectious Diseases Research Institute
MeLeVaClin	a multivalent vaccine for human visceral leishmaniasis
KalaCORE	Kalazar control and elimination
MOOC	a massive open online course
IT	Information technology
CaniLeish	canine leishmaniasis vaccine

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