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Impact of Climate Change on Parasitic liver Diseases in Africa

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ABSTRACT

Climate change is already a reality in Africa. Many countries across Africa are classified as Least-Developed Countries (LDCs) with poor socio-economic conditions and by implication are faced with particular challenges in responding to the impacts of climate change. African countries have the least efficient public health systems in the world. Infectious disease burdens, which are sensitive to climate impacts, are highest in the sub-Saharan African region. Changes in climate will affect the spread of infectious agents as well as alter people's disposition to these infections Climate change has the capability to drive parasitic disease incidence and prevalence worldwide. There are both direct and indirect implications of climate change on the scope and distribution of parasitic organisms and their associated vectors and host species. Currently there is lack of reviews in the literature addressing comprehensively the impact of climate change on the prevalence of parasitic liver disease in Africa.

The aim of the current review is to discuss the impact of climate change on parasitic liver disease in Africa, and to detect the gaps in the research done in this field.

This review is discussing the impact of climate change on some common parasitic liver diseases in Africa regarding the spread of infectious agents and the liver diseases caused by them.

***Conclusion:** Evidences showed that climate change; including rise in ambient temperature, disturbance of rainfall, water safety, and ecological changes, leads to change in the expansion of vectors or reservoirs of infection and the burden of parasitic infections in endemic areas in Africa. In addition to the effect of man-made construction of irrigation schemes are also responsible for continued transmission of some parasitic diseases in African countries.*

Keywords
Africa, Climate Change, Schistosomiasis, Malaria, Human Fascioliasis, Visceral Leishmaniasis, Human Echinococcosis, Amoebic Liver Disease.

Introduction
Climate change is already a reality in Africa, as it is elsewhere in the world. According to the Intergovernmental Panel on Climate Change, the vulnerability of Africa to climate change is driven by a range of factors that include weak adaptive capacity, high dependence on ecosystem goods for livelihoods, and less developed agricultural production systems [1]. Many countries across Africa are classified as Least-Developed Countries (LDCs) with poor socio-economic conditions, and by implication are faced with particular challenges in responding to the impacts of climate change [2].

African countries have the least efficient public health systems in the world. Infectious disease burdens, which are sensitive to climate impacts, are highest in the sub-Saharan African region. Changes in climate will affect the spread of infectious agents as well as alter people's disposition to these infections [3]. Climate change has the capability to drive parasitic disease incidence and prevalence worldwide. There are both direct and indirect implications of climate change on the scope and distribution of parasitic organisms and their associated vectors and host species [4].

Climate change has the potential to alter or extend the natural ranges of these organisms and make regions of our globe that were previously uninhabitable for parasites habitable. Increases in temperature affect the life cycles of parasites, which can directly affect how prevalent the organism is within the area, considering many parasitic organisms have a temperature-dependent developmental baseline, either within their host or in the environment [5].

Currently there is lack of reviews in the literature addressing comprehensively the impact of climate change on the prevalence of parasitic liver disease in Africa.

The African Middle East Association for Gastroenterology (AMAGE) and the Clinical Research Committee of the World Gastroenterology Organization (WGO) had established a joint research group called Climate African Group (CAG) to study the impact of climate change on the Gut and the liver health. Among the points that were studied by the group was the impact of climate change in African countries on the parasitic liver diseases.

Aim of the Work
The aim of the current review is to discuss the impact of climate change on parasitic liver disease in Africa, and to detect the gaps in the research done in this field.

Methodology
Search was done on Embase® data base for articles in English language published in the last 10 years and containing the following words ('climate change'/exp OR 'climate change') AND ('africa'/exp OR 'africa' OR 'middle east'/exp). Searches were done for other words (parasitic liver disease, schistosomiasis, malaria, human fascioliasis, visceral leishmaniasis, human echinococcosis, amoebic liver disease. The search result was reviewed by two independent researchers of the group to retrieve the relevant articles. Data extraction was done by other 2 researchers. References included in the originally retrieved articles were retrieved and searching for full text was done on the PubMed Central® data base to increase the extracted data. Editing Committee of the group had prepared the preliminary draft of the review that was circulated to other members of the group to get their feedback that was included into the final version of the review manuscript.

Discussion
The current review is discussing the impact of climate change on some common parasitic liver diseases in Africa, and highlighting the gaps in the published research work.

Human schistosomiasis
Human schistosomiasis otherwise called bilharzia, is a fresh- water snail transmitted intravascular debilitating disease resulting from infection by the parasitic dimorphic Schistosoma trematode worms, which lives in the blood stream of humans [6]. The World Health Organization (WHO) regards the disease as a neglected tropical disease, with an estimated 732 million persons being vulnerable to infection worldwide in renowned transmission areas [7]. The WHO further estimated that schistosome infections and geohelminths accounts for over 40% of the world tropical disease burden with the exclusion of malaria [8]. Prevalence of schistosomiasis, at present, is still high in sub-Saharan Africa. In 2008, 17.5 million people were treated globally for schistosomiasis, 11.7 million of those from sub-Saharan Africa only [7]. Approximately 120 million individuals in sub-Saharan Africa have schistosomiasis-related symptoms while about 20 million undergo hardship as a result of chronic presentations of the disease [9].

The exact impact of climate change on schistosomiasis is currently unknown, but likely to vary with the snail-parasite species, specific ecologies and the spatio-temporal scale of investigation. Stensgaard et al. [10] conducted a systematic review to identify studies reporting on impacts of climate change on schistosomiasis. They found that, despite a recent increase in scientific studies that discuss the potential impact of climate change on schistosomiasis, only a handful of reports have applied modelling and predictive forecasting that provide a quantitative estimate of potential outcomes. The volume and type of evidence associated with climate change responses were found to be variable across geographical regions and snail-parasite taxonomic groups. Some evidence is available from eastern Africa, mainly for *Schistosoma mansoni*. While studies focused on the northern and southern range margins for schistosomiasis indicate an increase in transmission range as the most likely outcome, there was less agreement about the direction of outcomes from the central and eastern parts of

Africa. The current lack of consensus suggests that climate change is more likely to *shift* than to *expand* the geographic ranges of schistosomiasis. A comparison between the current geographical distributions and the thermo-physiological limitations of the two mains African schistosome species (*Schistosoma haematobium* and *S. mansoni*) offered additional insights, and showed that both species already exist near their thermo-physiological niche boundaries. The African species both stand to move considerably out of their "thermal comfort zone" in a future, warmer Africa, but *S. haematobium* in particular is likely to experience less favourable climatic temperatures. The consequences for schistosomiasis transmission will, to a large extent, depend on the parasites and snails' ability to adapt or move.

McCreesh et al. [11] developed an agent-based model of the temperature-sensitive stages of the Schistosoma mansoni and intermediate host snail lifecycles. The model was run using low, moderate and high warming climate projections over eastern Africa. For each climate projection, eight model scenarios were used to determine the sensitivity of predictions to different relationships between air and water temperature, and different snail mortality rates. Maps were produced showing predicted changes in risk as a result of increasing temperatures over the next 20 and 50 years.

Baseline model output compared to prevalence data indicates suitable temperatures are necessary but not sufficient for both *S. mansoni* transmission and high infection prevalences. All else being equal, infection risk may increase by up to 20% over most of eastern Africa over the next 20 and 50 years. Increases may be higher in Rwanda, Burundi, south-west Kenya and eastern Zambia, and *S. mansoni* may become newly endemic in some areas. Results for 20-year projections are robust to changes in simulated intermediate host snail habitat conditions. There is greater uncertainty about the effects of different habitats on changes in risk in 50 years' time.

They concluded that temperatures are likely to become suitable for increased *S. mansoni* transmission over much of eastern Africa. This may reduce the impact of control and elimination programmes. *S. mansoni* may also spread to new areas outside existing control programmes. They called for increased surveillance in areas defined as potentially suitable for emergent transmission.
Mangal and co-workers showed that a rise in ambient temperature from 20°C to 30°C will lead to over ten-fold increase in the mean burden of *S. mansoni* infection in endemic areas. Nonetheless, at temperatures above 30°C a decrease in the disease burden was observed, probably due to higher death rate of the intermediate snail host. They observed that although an increase in disease burden leads to increased morbidity and mortality, there might be a negligible increase in prevalence of the disease [12]. Rainfall patterns also have an effect on the transmission of schistosomiasis; in Senegal, the snail species Biomphalaria pfeifferi is responsible for *S. mansoni* transmission during the raining season, while during the dry season S. haematobium infection is transmitted by Bilunus globosus [13].

Ecological changes due to man-made construction of irrigation schemes, reservoirs and dams for agricultural purposes and electricity generation are also responsible for continued transmission of schistosomiasis in some sub-Saharan African countries [14]. An analysis by Esrey and co-workers reported on the role of improved water supply and hygiene on disease transmission and incidence. They concluded that availability of safe water and sanitation are necessary for reducing the incidence and prevalence of schistosomiasis and some other water related diseases [15]. Many inhabitants of sub-Saharan countries have limited access to potable water for domestic use, leaving them with the option of using natural water bodies such as lakes, rivers, ponds, and other water sources contaminated with developmental stages of the schistosome parasite. A study carried out in northern Nigeria showed the link between safe water and intensity of urinary schistosomiasis. A higher rate of infection (88.57%) was recorded in a community that only had a pond as source of water for domestic use in comparison with 0.59% in a neighboring community with borehole [16].

Occupational activities such as fishing and farming are also risk factors for transmission of the disease. Contact with infected water is a vital factor in transmission of infection; women and children get exposed to infection during activities such as laundry, plate washing, water fetching for domestic use and bathing. Recreational activities such as swimming and diving also expose an individual to infection [7].

Malaria

In 2010 there were an estimated 216 million episodes of malaria worldwide, mostly among children younger than 5 years in the African Region [17]. The number of global malaria deaths was estimated to be 1,238,000 in 2010 [18].

The influence of temperature on malaria development appears to be nonlinear, and is vector specific [19] Increased variations in temperature, when the maximum is close to the upper limit for vector and pathogen, tend to reduce transmission, while increased variations of mean daily temperature near the minimum boundary increase transmission [20]. Analysis of environmental factors associated with the malaria vectors Anopheles gambiae and A. funestus in Kenya found that abundance, distribution, and disease transmission are affected in different ways by precipitation and temperature [21].

The strongly nonlinear response to temperature means that even modest warming may drive large increases in transmission of malaria, if conditions are otherwise suitable [19].

On the other hand, at relatively high temperatures modest warming may reduce the potential of malaria transmission [22]. Another review [23] reported that decadal temperature changes have played a role in changing malaria incidence in East Africa. But malaria is very sensitive also to socioeconomic factors and health interventions, and the generally more conducive climate

conditions have been offset by more effective disease control activities. The incidence of malaria has reduced over much of East African countries [24], although increased variability in disease rates has been observed in some high-altitude areas [25].

At the turn of the century, a clear decrease in malaria incidence was observed in East Africa. This decline could be simply the result of disease control measures, or could reflect the temporary slowdown in increase in global mean surface temperature, a phenomenon that was observed between 1998 and 2005.

To answer this question, Rodó and colleagues [26] focused on the region of Oromia in Ethiopia, a densely populated highland between 1,600 and 2,500 m above sea level. This region presents the advantage of having complete records of annual cases of malaria caused by both *P. falciparum* and *P. vivax* parasites between 1968 and 2007, and that public health interventions to control the disease were not reinforced in the region until 2004. This allows to separate the effect of climate from the effect of disease control measures.

Using mathematical modelling, the research team analysed the association between malaria cases, regional climate (local temperatures and rainfall) and global climate (in particular the effect of El Niño and the Pacific Decadal Oscillation on the Pacific Ocean). The results show that the variation in malaria cases correlates extremely well with changes in regional temperatures: the regional decline in temperatures linked to the slowdown in climate change coincided with the reduction in malaria cases observed from 2000, five years before disease control measures were reinforced. This decline in cases coincided with the slowdown in the increase of global surface temperature, as a result of the El Niño and the Pacific Decadal Oscillation. The analysis shows there is a "chain of effects" from global climate variability to regional temperature variations in East Africa, which translates into new malaria cases in the Ethiopian highlands. The coupling between disease dynamics and climate conditions is so strong that it is evident at multiple temporal scales, from seasonality to multiannual cycles to decadal trends.

Human Fascioliasis

Fascioliasis is a disease of ruminants caused by two major parasitic trematodes, Fasciola hepatica and Fasciola gigantica. Over the past two decades human fascioliasis has gained notice as a disease of primary importance. Human fascioliasis is currently classified as a plant/food-borne trematode infection, commonly acquired by eating metacercaria encysted on leaves that are eaten as vegetables [27].

Estimates suggest that up to 2.4 million or even up to 17 million people are infected with Fasciola hepatica in the world. The major associated health problems in cases of fascioliasis are found in Andean countries of South America, northern Africa, Iran, and Western Europe [28]. Fasciola hepatica is a zoonotic re-emerging neglected tropical parasite which infects mainly grazing sheep and cattle. The global warming increases the survival and expansion of the free-living cercaria and snail vector and at the same time, the increase of grazing season increases the exposure of the grazing animals to the parasite. Therefore, and as expected, the prevalence of Fascioliasis increased in the last decade in endemic countries [29].

Hyperendemicity of human fascioliasis has been noted in the Middle East and North African (MENA) region [30,31] particularly in Egypt [32,33] and Ethiopia [34].

Surveys done in the hyperendemic Nile Delta valley in Egypt [33], and river Tana basin in Ethiopia [34] found a high association between fascioliasis and schistosomiasis as well as myriad other intestinal parasites. A gender distribution skewed in both intensity and prevalence towards girls in the age group of 9–11 years among a young key population was also noted. The coinfection and childhood distribution raise a further differential in the clinical presentation and etiology of parasitic illnesses on the continent especially in rural, animal rearing areas [34,35].

Other African countries reporting scattered cases of human fascioliasis include Cameroon [36], Chad [37], Senegal [38], South Africa [39] and Zimbabwe [40]. Animal fascioliasis on the other hand has been extensively reported in almost all countries in the African equatorial belt [34] and east, central, west, and southern Africa [35,41-44]. A favorable climatic and environmental picture further presents for easy human transmission.

A typical complicating infection control scenario of zoonotic infections including fascioliasis in sub-Saharan Africa includes: (a) global warming and civil unrest, (b) close proximity to domestic animals, (c) rural-urban migration with poor personal, water, and food hygiene, and (d) lax biosafety and surveillance systems. Therefore, control programs of human fascioliasis should have an integrated approach whereby all factors that contribute to the presence of the disease are considered [45,46].

Visceral Leishmaniasis

Over the last few decades, some previously considered “tropical infectious diseases” are now seen in non-endemic settings such as leishmaniasis and others [47,48].

Mansueto et al. [49] published an epidemiologic and clinical review of the impact of dynamic environmental factors such as human mobility, increasing migration of human populations into niches of leishmaniasis transmission, and climate changes leading to expansion of vectors or reservoirs of infection as prominent factors in the increasing prevalence of leishmaniasis. The spectrum of disease by this protozoal infection depends on host factors and exposure to specific sandflies and particular Leishmania species. From a clinical perspective, leishmaniasis infection in both endemic and non-endemic settings can be divided into visceral, viscerotropic, cutaneous, and mucocutaneous types [47]. There are over 20 species of Leishmania, with each species having the potential to cause more than one clinical syndrome. An estimated 12 million people worldwide suffer from some form of this disease,

and over 350 million people live in areas with potential exposure to these organisms [48].

Visceral leishmaniasis is predominantly caused by Leishmania donovani or Leishmania infantum/ Leishmania chagasi, and the vast majority of cases of visceral disease are found in India, Bangladesh, Sudan, and Brazil. Manifestations of visceral forms of Leishmaniasis may include fever, weakness, weight loss, and hepatosplenomegaly. In addition, anemia, pancytopenia and hypergammaglobulinemia may also be present [47]. Coinfection with HIV seem to be also an increasing association among travelers visiting at risk areas in the Mediterranean [49]. Differential diagnosis of visceral leishmaniasis among those with HIV is mainly with disseminated histoplasmosis.

Human Echinococcosis

Echinococcus granulosus remains a clinical problem in sheep and subsistence farming communities. Human cystic echinococcosis caused by *E. granulosus* is the most common presentation and probably accounts for more than 95% of the estimated 2−3 million annual worldwide cases. The liver (70−80%) and lungs (15−25%) are the most frequent locations for echinococcal cysts [50].

Cystic echinococcosis occurs in most regions of sub-Saharan Africa, but the frequency of this zoonosis differs considerably among and within countries. Especially human cases seem to be focally distributed. A number of environmental and behavioural factors partially explain this pattern, i.e. density of livestock, presence of dogs, uncontrolled slaughter, and hygiene. In addition, the various taxa of Echinococcus spp. are known to differ considerably in infectivity to different host species including humans. Genetic characterizations of isolates, which are necessary to evaluate the impact of this factor - so far done in only a few countries - indicate that the diversity of Echinococcus spp. in Sub-Saharan Africa is greater than on any other continent. The very incomplete data which are available show that some taxa may infect different hosts, others may be geographically restricted, some life cycles involve livestock while others infect wild animals [51].

Few prevalence studies on echinococcosis have been conducted in humans in Southern Africa Development Community (SADC) countries [52]. All of them were based on retrospective cases of hospital records and the disease was not primarily suspected due to the similarity of clinical manifestation with other conditions. High cost of reliable diagnostic tests (imaging tests and surgery) could be one of the reasons why this disease has been underdiagnosed in many of the SADC countries [53]. In Turkana area of Kenya, besides of keeping the herds, young dogs are acquired by farmers to clean children and food utensils as a way of saving water [54,55] constituting an important source for human infection.

Amoebic liver disease

Amoebiasis, or amoebic dysentery, is a term used to describe an infection caused by the protozoan Entamoeba histolytica (*E. histolytica*). Most infections are asymptomatic, but invasive intestinal disease may occur manifesting with several weeks of cramping, abdominal pain, watery or bloody diarrhea, and weight loss [56]. Disseminated, extra intestinal disease such as liver abscess, pneumonia, purulent pericarditis, and even cerebral amoebiasis has been described [57]. Worldwide, it has been estimated that up to 50 million people are affected by E. histolytica, primarily in developing countries, and it is responsible for over 100,000 deaths a year [58,59]. Transmission generally occurs by the ingestion of infected water or food due to fecal excretion of cysts, and even fecal-oral transmission within household and during male homosexual activity [56].

Amebic liver abscess, which is the most common extra-intestinal manifestation, develops when trophozoites disseminate to the liver. For poorly understood reasons, amebic liver abscesses are 10 times more common in men than women, often presenting between the ages of 20 and 40 years. Onset can be acute, subacute, or subtle. Hepatic amebiasis has been reported over 20 years after the last visit to an endemic area, so any travel history may be important in this diagnosis. The majority will present with fever and right upper quadrant pain, typically without concurrent dysentery or gastrointestinal symptoms [60]. Hepatomegaly with point tenderness over the liver can often be detected. Cough and respiratory symptoms, including pleuritic right-sided chest pain, may occur, or even referred pain to the shoulder. Elevated alkaline phosphatase and peripheral leukocytosis, usually in the range of 12 000–20 000/ mm^3, is seen, though typically without eosinophilia. Imaging more often reveals right lobe lesions, usually solitary, but left lobe or multiple lesions may be less commonly seen [60]. Amebic liver abscess may be difficult to clinically distinguish from pyogenic liver abscess. Echinococcal cysts of the liver are another important differential, but they tend to appear as multiple clustered fluid collections without surrounding enhancement on imaging. Peripheral eosinophilia is rare with amebic liver abscess and is more commonly associated with echinococcosis and hepatic fascioliasis (liver fluke). Detection of bacteremia by blood culture, stool studies, and serology will also help to narrow the differential diagnosis. Occasionally, diagnostic or therapeutic aspiration is required. Aspiration of the amebic liver abscess reveals “anchovy paste,” chocolate-colored fluid consisting of necrotic hepatocytes.

In conclusion, Migration, globalization and climate change lead to a) expansion of endemic areas and b) emerging cases outside endemic areas (e.g. for cystic echinooccosis and schistosomiasis), resulting in delayed diagnosis and mismanagement [61].

Parasitic diseases may not always cause high mortality rates, but they can be very debilitating, preventing economic growth and advancement and keeping the communities affected in a positive feedback loop of poverty [62].

The areas of the world likely to be most affected by climate change are those still developing, with inadequate waste management systems [63], medical supplies, and education to effectively subdue parasitic diseases. Climate change has the potential to further

ramp up, in a negative way, the issues already faced because of parasitic diseases. It is therefore crucial and imperative that we consider these possibilities and begin to prepare for these changes that are already underway, planning for methods to limit epidemic eruptions and prevalence and incidence of parasitic diseases in Africa.

Conclusion

In conclusion, evidence showed that a rise in ambient temperature in the upcoming years will lead to an increase in the mean burden of Schistosoma mansoni infection in endemic areas in Africa. Rainfall patterns also have an effect on the transmission of schistosomiasis. Water safety and ecological changes due to man-made construction of irrigation schemes are also responsible for continued transmission of schistosomiasis in some sub-Saharan African countries. Analysis of environmental factors associated with the malaria vectors in African countries found that abundance, distribution, and disease transmission are affected in different ways by precipitation and temperature. The global warming and civil unrest impact the infection control scenario of zoonotic infections including fascioliasis in sub-Saharan Africa with increased burden of human fascioliasis. Climate changes lead to expansion of vectors or reservoirs of infection as prominent factors in the increasing prevalence of visceral leishmaniasis due to the impact of dynamic environmental factors such as human mobility, increasing migration of human populations into niches of leishmaniasis. The prevalence of other parasitic liver diseases in Africa, as human echinococcosis and amebic liver abscess, is impacted by climate changes and other environmental factors.

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