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Introductory Chapter: Malaria Elimination - A Challenge with Multiple Emerging Ecosocial Challenges

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1. Introduction

Malaria has been a major parasitic disease affecting humankind over centuries, with a disproportionate impact among populations, regions of the world and living conditions [1–5]. Caused by five well-accepted species, *Plasmodium falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi* [6] malaria remains a global public health threat due to multiple reasons [7, 8] including biological, social and climatic factors [3, 9–13] influencing the distribution of *Anopheles* vectors, especially *A. darlingi* in the Americas [14, 15]. There is an ongoing debate regarding the potential role of *Plasmodium cynomolgi* as the sixth etiological species of human malaria [16, 17]. The etiological diagnosis and the epidemiological and clinical management of malaria remains a major challenge in many settings, populations, and during specific clinical scenarios including cases of severe malaria in travelers [18–20].

2. Major challenges in malaria elimination: social and economic downturn in Latin America and the role of climate change

Over decades, especially in the 20th century, malaria has been a major cause of morbidity and mortality at national and regional level in Latin America and the Caribbean (LAC) [21, 22]. The epidemiological transition and improvement of social conditions (i.e. social determinants of disease) have concomitantly reduced malaria-associated morbidity and mortality in many countries [1, 5, 23–25]. Since 2000, drastic reductions in the incidence of malaria occurred in countries with the highest burden of disease (i.e., Brazil) [26–28]. Between 1962 and 1973 other countries in the region such as Grenada, Dominica, Barbados, Chile (a country where never was confirmed the occurrence of autochthonous transmission) [29], Saint Lucia, and Trinidad and Tobago received official certification as malaria-free, after the implementation of specific control measures. More recently, Argentina,

Bahamas, Antigua and Barbuda, Paraguay, Saint Kitts and Nevis, Saint Vincent and the Grenadines, Uruguay (another country that never has autochthonous malaria) [30], and lately El Salvador, were added to the list [31]. Experiences in malaria elimination, such as those of El Salvador, have been of significant impact. In other countries of the region, such as Ecuador, malaria had fallen to very low levels between 2000-2009, with transmission increasing again between 2014 and 2020, due to carelessness in the control campaigns in traditional outbreaks, as well as due to the mobilization and immigration from both the northern and southern borders [32, 33]. The starting point was the elimination of foci in each municipality, where active detection was included (searching of malaria cases), considering the DTIR strategy (Detection, Diagnosis, Treatment, Intervention and Response), so that more cases are diagnosed instead of stopping after the index case detection. Specific activities at the local level were monitored and evaluated for an overall impact that led the country to elimination [34].

Unfortunately, factors such as climate change represents a major negative factor that could potentially favor the spread of malaria-to-malaria-free areas [9, 35–40]. Mass deforestation, landscape change, wildfires, and other anthropogenic threats [41] influence the distribution of vector-borne diseases such as malaria [42]. Furthermore, the etiological agents of human malaria have been already detected in non-human primates, especially in Asia [17, 43–50], but also in LAC, particularly in Brazil [51–53] illustrating the risk of humans amplifying the spread of malaria to animal species.

Malaria transmission depends on several weather conditions including rainfall patterns, humidity and temperature (i.e., the ideal environmental characteristics of the malaria transmission are present in the Amazon Basin) and also depends of occurrence of water bodies and associated floating or emerging vegetation, as well as the surrounding forest cover that provides shade on the edges of lagoons. Malaria is associated with climate change [54] because the environmental consequences are linked to specific conditions that would benefit *Anopheles* population, and not only the life and distribution of the vector but the possibility of transmission of malaria too. The influence of climate change is highly relevant as the mosquitoes are ectotherm hosts [55]. To increase the knowledge of what could happen in the future, Intergovernmental Panel on Climate Change (IPCC) Fifth Assessment Report (AR5) provides an interesting review and evaluation of the science of the climate change and their multiple future scenarios (<https://www.ipcc.ch/report/ar5/syr/>). In general, all depends on the real trajectory of the greenhouse gases (GHG) but the development of the global warming is always related with increasing average temperatures and changes in precipitation patterns that has an effect on malaria causal factors [56, 57]. In spite of what acknowledgment we probably want to reach, there are several possible effects as potential scenarios, therefore estimation models are required to approach the most potential situation [58]. To directly associate the increasing of the average temperature with malaria, is known that the distribution of species as *P. falciparum* would expand depending on the increase of the temperatures even in greater latitudes and altitudes [59]. In the case of the changes in precipitation patterns, it is related with the zones where the mosquito breeding proliferates due to water levels decreasing and forming pools after the extreme increase of rivers because of the rain or other reasons like ice melting of the mountains. Nonetheless, species like *Anopheles darlingi* which appears to be directly associated with high levels of precipitation [60], would decrease their population on several scenarios in the future, so the study of climate change and malaria should be specifics owing to the effects of temperature and precipitations could

be different if we evaluate combined possibilities [61]. Even in Europe, some studies have pointed out that climate change is a significant factor associated with reemergence of malaria in southern areas of the continent [62–64].

Two recent initiatives, the World Health Organization (WHO) Strategic Advisory Group on Malaria Eradication and the Lancet Commission on Malaria Eradication, have assessed the feasibility of achieving global malaria eradication and proposed strategies to succeed at it. Both reports (WHO and Lancet Commission) rely on a climate-driven model of malaria transmission to conclude that long-term trends in climate will assist eradication efforts overall and, consequently, neither prioritize strategies to manage the effects of climate variability and change on malaria programming [65]. Climate change associated factors and consequences is key for the consideration of ecosocial and integrative vector control strategies, as has been proposed for decades by the WHO. In the case of Latin America, there is still a long road to improve the associated situation, mitigation, and adaptation on climate change according to the Intergovernmental Panel on Climate Change (IPCC) [66–73]. Then, climate change, is definitively a “stone in the shoe” in the control and elimination of malaria in LAC.

In addition, multiple social factors are still present in the region with a complex interplay, such as uncontrolled mining, poverty, the recent impact of Coronavirus Disease 2019 (COVID-19), political, economic, and social crisis, in countries from different ideological political positions, such as Brazil, Argentina, Peru, Bolivia, but especially Venezuela. The situation in the latter, once considered as the richest in the region, started to fall into a spiral of social devastation since 1998, impacting especially all the health aspects. Malaria control, in the past highlighted as the best program (1930s–1960s), today raises many concerns. Venezuela is the main focus of malaria in LAC, amid a humanitarian crisis, that also impacted Colombia and Brazil, as neighboring countries, but also to distant nations in South and Central America, even generating imported cases to Argentina or Mexico [3, 8, 11–13, 21, 22, 74]. The humanitarian crisis has led to a reemergence of multiple infectious diseases, but also the persistence and increase of multiple endemic diseases including malaria. In this context the forced migration occurring to multiple countries also constitute a challenge in the control of malaria in endemic and even not-endemic countries in LAC. Imported cases may be associated with local transmission by multiples routes, vector and not-vector-borne (e.g., blood transfusion, transplantation, congenital). Unfortunately, such crisis will not be solved in the near future, therefore it lies to the other countries in the region to prioritize the best strategy in managing imported cases, assuring early diagnosis and treatment to avoid potentially associated consequences, and to enhance surveillance and consider the importance of specific programs targeting migrant populations.

Regarding the COVID-19 pandemic, this has posed multiples challenges, including coinfections (SARS-CoV-2/*Plasmodium*), in the efforts of malaria elimination. During 2019–2020, malaria cases increased by 26%, in the countries where malaria is targeted for elimination in the Americas. In particular, there was increased malaria transmission in three countries of Mesoamerica: Nicaragua, Honduras, Panama. With a reduced number of laboratory samples and diagnostic tests, reduced mobility of people and disruption of health services, limited field operations due to social restriction gaps in ensuring personal protective equipment, malaria elimination is facing multiple difficulties. These existing gaps in malaria case detection and treatment may translate into increased chaos by 2021, added to the regional situation above mentioned of Venezuela [75].

3. Conclusions

We face multiple and perennial challenges when controlling tropical infectious diseases, such as malaria [42]. Despite many achievements in malaria control efforts during the last few decades, there are many countries in LAC where malaria transmission remains or revert to being a major public health concern for the region. In other regions of the world, such as Africa and Asia, the recent emergence of zoonotic species of *Plasmodium*, coupled with the impacts of climate change, economic downturn post-COVID-19, and globalization are also causing significant concern. There is an urgent need for local, national, and international health authorities to strengthen surveillance and multisectorial control approaches to advance the noble effort of malaria control and elimination in LAC and other regions.

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