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Challenges of addressing neglected tropical diseases amidst the COVID-19 pandemic in Africa: A case of Chagas Disease

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ABSTRACT

Chagas Disease (CD) is an infectious, neglected tropical disease (NTD) that has affected over 1.7 billion people worldwide. Unfortunately, most countries usually put little effort into mitigating the spread of NTDs, having weak public health approaches, diagnostic delays, and ineffective clinical management guidelines and resources. However, the ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by the coronavirus SARS-CoV-2, exacerbates the impact of NTDs. In this review, we examine the subsequent changes that have been imposed on CD prevention and treatment. Articles from Google Scholar and PubMed were extracted which satisfied our inclusion criteria. From our data, we gather that COVID-19 has — from preventive measures to treating patients — greatly affected every stage in the fight against CD. For instance, co-infection of CD and COVID-19 puts patients at higher risk for cardiomyopathy (i.e., atrial fibrillation, chronic heart failure), yet no clinical guidelines were established for co-infected patients. To mitigate the spread of CD during the COVID-19 pandemic, further investigations on the impacts of co-infections and vaccines that can be developed to treat such conditions are warranted.

1. Introduction

According to the World Health Organization (WHO), neglected tropical diseases (NTDs) comprise a group of 20 diseases affecting more than 1.7 billion people worldwide. These are found mainly in the venerable communities of tropical and subtropical regions [1]. Among these diseases is Chagas Disease (CD), also referred to as American trypanosomiasis, an illness caused by *Trypanosomiasis cruzi* which affects the cardiovascular system. With 6–7 million infections globally, most cases of CD are found in rural Latin America, with others found in the United States of America, Canada, Europe, and Africa.

Before the surge of novel SARS-CoV-2, the aetiological pathogen causing the coronavirus disease 2019 (COVID-19) pandemic, most NTDs were paid little to no attention by various healthcare systems, having weak public health approaches, diagnostic delays, and ineffective clinical management guidelines and resources. Therefore, the recent emergence of the COVID-19 pandemic has exacerbated the impact of NTDs, bringing numerous social, economic, epidemiological, and health challenges to daily lives [2,3]. Currently, very little emphasis is put on CD as most healthcare systems and governments are focused on mitigating the spread of COVID-19 [4]. Subsequently, many cases of CD are undiagnosed and compound the devastating impacts and comorbidities of COVID-19 [4].

In this review, we will evaluate the challenges and changes in CD management, brought on by the COVID-19 pandemic. Consequently, we will then discuss future implications in mitigating the spread of CD with SARS-CoV-2.

1.1. Phases of chagas diseases

Being responsible for 70% of cases, *Trypanosomiasis cruzi* (*T. cruzi*) is

mainly transmitted via contact with the urine or faeces of an infected triatomine ‘kissing’ bug. However, other modes of transmission include vertical, organ transplantation, and blood transfusions from infected individuals. CD is, unfortunately, one of the most prevalent diseases in the field of healthcare, being responsible for more morbidities and mortalities than any other parasitic disease [5].

Once a human host is infected, CD presents through two phases: chronic and acute. The acute phase may last up to two months, with less than 50% of infected individuals presenting nonspecific symptoms of fever, headache, lymphadenopathy, abdomen or chest pain, dyspnoea, and angioedema. In chronic phases, parasites reside in solid organs like the heart, leading to cardiomyopathies in 30% of cases, and gastrointestinal structures such as the oesophagus and colon in 10% of cases. Patients with CD are also at higher risk of contracting COVID-19, which may lead to increased co-morbidities [5,13–18].

Cases of CD may be diagnosed with serological testing and treatment can be initiated, whether symptomatic or not. With efficiencies close to 100%, both benznidazole (BZN) and nifurtimox (NFX) are effective treatments for CD, if administered in the acute phase. However, both medications are highly toxic and contraindicated for pregnant women due to potential teratogenicity. Both may cross the placental barrier and disrupt gestational development. That said, CD is still treatable post-partum if no other options are available.

While treatments for CD exist, complete eradication of the disease is arduous as wild animals are the largest reservoir of *T. cruzi* parasites. Although, vector control has been considered the most effective method so far.

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2. The current status of chagas disease amidst the COVID-19 pandemic

The upsurge of COVID-19 cases has led to very little emphasis on CD. As a result, many cases of CD went undiagnosed, complicating the health status of those who were also simultaneously infected with COVID-19 [4].

In addition to the usual symptoms of CD (i.e., fever, fatigue, body ache, headache), co-infection with COVID-19 contributed to dysregulated immunothrombosis, triggering a considerable change in management as anticoagulants were now included [6,15]. Some studies also suggested possible cardiovascular involvement as a complication in co-infected patients, putting individuals at greater risk of prolonged hospitalisation and increased mortality [2].

Additionally, research conducted in Brazil demonstrated that with co-infection of COVID-19 and chagas, patients had an increased prevalence of complications such as atrial fibrillation (AF) and chronic heart failure compared with patients without CD. However, there were no significant differences in inpatient outcomes [7].

3. Challenges facing responses to chagas disease during COVID-19 pandemic and efforts to overcome them

CD and the COVID-19 pandemic are both multi-systemic diseases that can impact various internal organs, including the cardiovascular, central nervous [13–18], and digestive systems [4].

Populations infected with CD are economically disadvantaged and have limited access to healthcare services. Additionally, many CD cases in this population have gone untreated due to a lack of healthcare facilities [4].

In 2005, the WHO recognized CD as an NTD [5]. As with other NTDs, resource allocation for CD has been invested in fighting the COVID-19 pandemic. This, alongside the limited knowledge of COVID-Chagas co-infection, has posed great challenges to counteracting multiple pandemics at once. Prevention programs for CD have been impaired to such an extent that there may be a reversal in progress [10]. COVID-19 and CD share more in terms of biological processes and pathophysiology. Chronic phases of pathogenesis are characterised by various disorders, such as fibrosis, inflammation, autoimmunity, and macrovascular changes.

In contrast, SARS-CoV-2 can cause endothelial and microvascular dysfunction, myocardial injury, myocardial infarction, and plaque instability [8].

Patients with CD already have comorbid conditions, making them more susceptible to other illnesses like COVID-19 and in danger of developing a severe version of the condition.

One study examined the outcome of CD and COVID-19 co-infections and concluded that even though co-infection by *T. cruzi* and COVID-19 pose a great risk of complications, the pathogenic relationship may result in a worse prognosis. In their studies, no significant difference in terms of clinical signs and co-infected patient outcomes compared to patients in the control group except for increased rates of heart failure and AF [9].

And their study cannot be generalized due to the small number (31) of patients. A need for extended study and political will to allocate resources for neglected diseases is needed. CD is no longer confirmed in Latin America, the epidemiology has shifted to global.

Current drugs used to treat CD involve Benznidazole (BZN) and Nifurtimox (NFX). However, caution should be taken when these drugs are used in SARS-CoV-2 patients. Due to the hepatic metabolism of BZN (95%) and NFX (>99%), the hepatotoxicity of these drugs should be monitored when used in conjunction with medications used to treat COVID-19 (Tables 1 and 2).

Table 1

Treatment guides for Chagas Disease and COVID-19 co-infection.

Chagas disease (CD) status	SARS-CoV-2 (COVID-19) status	Guides on treatment with BZN and NFX
Chronic CD or indeterminate CD.	Negative	Delay treatment
Chronic CD or indeterminate CD	Positive either with symptoms or not	Delay treatment until patients free of COVID-19
Acute cases or clinical evidence of changes in diseases	Whether positive or negative	Start treatment
Chronic CD or indeterminate CD on treatment	Positive and have symptoms	Postpone treatments especially if immunosuppressive drugs are used in the treatment of COVID-19 and if CD reactivation occurs. Start treatment
Chronic CD or indeterminate CD on treatment	Positive without symptoms	Keep treatment

4. Summarizing the impact of COVID-19 on chagas diseases

5. Future FOCUS to eliminate chagas disease

The core for eliminating CD lies in multiple strategies, including multisector collaboration, political will, finance allocation, clinical guidelines, and task force training. Urgent testing is still relevant for pregnant women, newborn to seropositive mothers and individuals to receive immunosuppression. Screening before blood product transfusion, organ transplantation, and vector control remains relevant to mitigate transmission [4,5].

While multiple treatment methods exist, gauging the benefits and disadvantages of each method is important to consider. Treating patients who are already infected with *T. cruzi* with approved drugs can mitigate the transmission and chronicity of the disease. However, patients may lose compliance with treatment as it can last up to two months.

Minimizing vector transmission is another option to consider. Residual insecticides may be used to target the domestic and/or peridomestic habitats formed by Triatominae parasites. Practicing good hygiene by hand-washing and clean food preparation is especially in areas endemic to CD.

The development of a vaccine may also reduce the prevalence rates of CD. However, vaccine testing will be met with ethical implications and will require early detection of CD in test subjects, which has not yet proven to be applicable [11,19–21].

Table 2

Impact of COVID-19 on different intervention programs.

Area impacted	Impact imposed by COVID-19
Diagnosis	- Reduced frequency of visits to healthcare settings not in contact with COVID-19 - Laboratory diverted to COVID-19 testing
Treatment	- Lack of necessary skills on drug interaction in co-infection management - Lack of clinical guidelines on co-infection
Psychosocial	- Increasing poverty - Isolation from support networks out of fear to contact COVID-19
Prevention	- Reduced interest and commitment by governments agencies to allocate resources to the CD program - Clinical research diverted to COVID-19 - Lower media interest in neglected diseases - Reduced preventive methods such as campaigns, and community events

Population in the rural areas often has difficulty accessing and utilizing the health care system for control and treatment of Chagas disease. One reason for this is the dearth of media attention on this condition for a long time, creating a lack of awareness. Thus, many patients tend to avoid seeking medical help, which can also be attributed to the fear of stigmatization. This barrier can be countered by designing and strengthening the system by involving social workers, support groups and psychological support. Transport facilities to medical centers also helps the rural communities to access health care easily [12,22–26].

6. Discussions

We have thoroughly reviewed articles published in accredited journals, 12 papers met our inclusion criteria and others were excluded from the study. We found that covid19 impacted many aspects of society such as the global economy and health care sector. A little emphasis was put on already neglected diseases such as Chagas, as the whole world focused on the pandemic. As a result, many cases of Chagas disease were undiagnosed even as COVID-19 contributed to the co-morbidities among these patients [4].

COVID-19 has diverted resource allocation for Chagas diseases to fight the pandemic, patient uncertainty to contract COVID-19 when visiting health facilities has been a great challenge to testing and following up on patients with Chagas. Limited knowledge for health practitioners on co-infection of Chagas diseases and covid19 and treatment plan as well as drug interactions [6].

Chronic phases of pathogenesis are characterized by various disorders, such as fibrosis, inflammation, autoimmunity, and macrovascular changes.

On the other hand, SARS-CoV-2 can cause endothelial and microvascular dysfunction, myocardial injury, and myocardial infarction plaque instability. Therefore, there is a similarity in pathogenesis which exacerbates chronicity and poor prognosis [6]. One study was done to examine the outcome of Chagas and covid19 co-infections and concluded that even though co-infection by *T.cruzi* and covid19 pose a great risk of complications it can result in a worse prognosis. In their studies, they didn't find any significant difference in clinical signs and hospital outcomes with co-infection compared to controls except increased rate of heart failure and atrial fibrillation.

COVID-19 pandemic has impaired progress in the Chagas diseases prevention program, as much needed financial and human resources have been diverted. One might even anticipate a reversal in progress achieved in elimination efforts [9]. BZN and NFX (a drug used to treat Chagas) used together with common drugs used in SARS-2 management, hepatic toxicity should be monitored [4]. We have also observed reduced commitment from governments in terms of allocation of resources, policies and research diverted to covid19. Decreased visits to health settings out of fear of contacting covid19 and laboratory functionality diverted to covid19. In line with eliminating Chagas diseases, we suggest that developing vaccines will dramatically reduce the diseases, so further research and vaccine development is still relevant. Designing and strengthening the health care system for marginalized people in the rural area to access Chagas control and treatment programs where access to routine healthcare can contribute a lot. And again large cohort or retrospective studies are necessary to conclude the clear impact of covid19 and Chagas co-infection.

7. Conclusion

The global focus has moved from reducing the spread of NTDs to reducing COVID-19 rates since the start of the COVID-19 pandemic. Due to immunological suppression, which increases the likelihood that the disease will develop to the chronic form, which affects the heart, oesophagus, and intestines, CD is more common in marginalized communities. By examining novel therapeutic options, it's critical to refocus some attention on CD. For instance, early use of anti-parasitic

medications in the disease's acute phase has shown to be successful. Due to the high risks of hepatotoxicity, medications like BZN or NFX can be used in co-infected patients with the correct monitoring. Additionally, the most effective method of preventing CD infection is vector control. Future studies must concentrate on the development of vaccines and the care of individuals who have both CD and COVID-19 infections.

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Author contribution

Olivier Uwishema: Conceptualization, Project administration, Writing-review and Designing. Philemon Nisingizwe: 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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Declaration of competing interest

No conflicts of interest declared.

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