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Forum

The impact of COVID-19 on neglected parasitic diseases: what to expect?

Danilo C. Miguel [1,*], Mariana B.C. Brioschi [1], Leticia B. Rosa [1], Karen Minori [1] and Nathalia Grazzia [1]

Here we highlight coinfections of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with ectoparasites, helminths, and protozoa, described in the literature, and the urgent need to understand the conditions of these associated pathologies. We emphasize the notion that such information is crucial for the continuity of measures that have been used for decades to control neglected parasitic diseases.

COVID-19 meets parasitic neglected tropical diseases (NTDs)

On 11 March 2020, concerned by the alarming levels of spread and severity, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic[i]. Since then, much has been speculated regarding forms of transmission that could effectively explain the dispersion of the SARS-CoV-2. One year later, the scientific community recognized the relevance of SARS-CoV-2 airborne transmission, setting aside the viral dissemination through objects and surfaces[ii].

The spread of the virus has spared no segment of the globe, but the impact on developing/poor countries, which have the highest prevalence rates for NTDs, is likely to be much more severe and prolonged. COVID-19 infections are not only expected to hinder social and economic development directly but have also been responsible for stopping NTD control programs, especially those related to mass drug administration (MDA) [1]. This widespread therapeutic intervention is highly dependent on public–private partnership investments and direct contact between health/surveillance professionals and the affected population. Regrettably, MDA is expected to face long-term challenges regarding its successful continuity once measures of social distancing, isolation, and monetary crisis become our new reality.

Developing/poor countries are endemic for NTDs caused by ectoparasites, helminths, and protozoa – classically referred to as parasites – which represent a heavy burden on malnourished populations that live in unsanitary conditions. The impact of parasitic NTDs in the context of COVID-19 is yet to be determined while literature emerges describing new cases of coinfections.

COVID-19 and ectoparasitosis

Ectoparasites live on the outside of their hosts. In some underdeveloped countries most ectoparasites – such as bedbugs, scabies, jigger, and myiasis-causing flies – are highly endemic, but additional infestations could be introduced by tourists; as traveling has been directly reduced by COVID-19, cases linked to tourists are expected to decrease. However, in terms of poor areas that are affected by ectoparasites, a Turkish study reported an increase in cases of scabies in national hospitals in March 2020. This rise in cases may be explained by COVID-19-imposed restrictions which exacerbated the poor-hygiene conditions of families that were forced to live in close quarters in rural areas which favor infestations of *Sarcoptes scabiei* [2].

Conversely, an interesting study by Galassi and colleagues demonstrated the impact of the current pandemic on cases of pediculosis in Latin America. This study was carried out during a strict lockdown period (March–July, 2020) in Argentina. Data from 1118 school-aged children showed a decrease in head-lice infestation from 70% (before lockdown) to 43% (during lockdown) [3]. As this disease depends on physical contact, it is not surprising that there was a significant reduction in the prevalence of head lice during the imposed lockdown due to the restricted movement of children outside their homes and the absence of regular classes.

Together, these examples shed light on the different effects that social distancing and lockdowns can have on infestations by ectoparasites. While other parasites remain to be studied (e.g., bedbugs, fleas), it is expected that lockdowns in unsanitary conditions would favor the development of previously controlled infestations.

COVID-19 and helminthiasis

The control of helminth infections is based on the collective effort aimed at effectively preventing parasite–host transmission, promoting MDA, and encouraging initiatives for promoting public health campaigns. There is a high expectation that NTDs caused by helminths will be eradicated, or massively controlled, by 2030 in affected tropical and subtropical regions; however, the chances of global control are threatened by the SARS-CoV-2 circulation [1,4].

Most African countries, for example, have faced countless NTDs for many decades; these NTDs include schistosomiasis, for which ideal preventive measures rely on basic sanitation systems. Unfortunately, endemic areas have also been drastically affected by COVID-19 cases among the vulnerable population. Oyeyemi and coauthors found that the occurrence of active cases of COVID-19 was higher in areas endemic for schistosomiasis. Concomitantly, in regions where praziquantel treatment coverage is high, a significant reduction in

COVID-19 active cases is expected, followed by an improvement in recovery rates [5]. Additionally, the continuity of control and prevention programs for schistosomiasis proved to be threatened after the establishment of the pandemic in 12 schistosomiasis-endemic provinces in China. Guo *et al*. observed a dramatic reduction of ~1/4 of the gross funds allocated to these programs from January to March, 2020, pointing out that a short-term impact on the schistosomiasis-monitoring program had been seen due to COVID-19 [6].

With regard to treatment, there should be a constant concern for patients receiving high doses of corticosteroids for COVID-19 in NTD-endemic areas. There are reports in the literature pointing to the development of disseminated strongyloidiasis after immunosuppressant therapy, an expected event given that corticosteroids promote moulting of the larvae, leading to severe hyperinfection cases. Therefore, it is essential to consider screening for *Strongyloides* infections in individuals with COVID-19 from endemic regions before the administration of immunosuppressants [7].

A curious recent report reinforces another example of coinfection that may require attention from health professionals. In this case, a blood smear sample was collected from a 37-year-old south Asian man with COVID-19 pneumonia; he had no symptoms of filariasis despite the presence of *Wuchereria bancrofti* microfilaria. It is important to emphasize in such cases that mixed infections should be suspected during clinical examinations, and that routine laboratory tests should be carried out in order to allow proper disease monitoring in endemic regions [8].

COVID-19 and protozoan infections

Protozoan infections represent a major public health concern. Several routes of transmission are responsible for the maintenance of different life cycles, essentially among vulnerable populations.

Intestinal infections caused by *Giardia duodenalis* can be found worldwide. Recently, a 66-year-old patient with COVID-19 was diagnosed with giardiasis. In this case, CD4 lymphocytopenia was observed during lung infection, which may have contributed to *Giardia* infection. Thus, reactivation of latent parasites should be considered during infections by SARS-CoV-2 [9]. Conversely, several measures adopted to control COVID-19 may be favorable for giardiasis control, taking into account the relevance of fecal–oral cyst transmission. Thus, with day-care and schools closure, and with social distancing measures, it is plausible to expect a reduction in cases of *Giardia* infection. Moreover, individual behavioral changes related to basic hygiene measures, including continuous hand washing and the use of hand sanitizers, are also expected to play an important role in relation to other diarrhea-causing parasites.

The current pandemic scenario has generated several studies focused on early detection of SARS-CoV-2, a strategy that could help to predict outbreaks. As one of the symptoms of COVID-19 is related to gastrointestinal distress, it is relevant to search for SARS-CoV-2 particles in wastewater, reinforcing the relevance of wastewater-based epidemiology research. However, when performing this analysis, other pathogens, such as *Cryptosporidium* spp. and *G. duodenalis*, can be detected, allowing the prediction of new outbreaks. In fact, these pathogens were responsible for all protozoan outbreaks transmitted by water consumption in the world from 2011 to 2016. These are usually underreported diseases since outbreaks are discovered through clinical tests of symptomatic patients and the majority of infected individuals remain asymptomatic [10].

In addition, the role of ventilation systems in the transmission of the virus has recently gained relevance. Siddiqui and colleagues proposed the coating of air-conditioning filters with antimicrobial material, in addition to the use of smaller pores in the filters and the use of ultraviolet irradiation to prevent transmission of SARS-CoV-2 and, additionally, other pathogens, such as *Acanthamoeba* and *Legionella pneumophila*-infected *Acanthamoeba* [11].

Vector-borne protozoan infections caused by *Trypanosoma cruzi* (Chagas' disease, CD) and *Leishmania* spp. (cutaneous and visceral leishmaniasis, CL and VL) may also be impacted by COVID-19. Considering that the population with CD (>6 million people worldwilde) is socioeconomically vulnerable, and presents many comorbidities, the spread of the pandemic becomes a concern. Zaidel and coauthors pointed out that chronic medical conditions, such as diabetes, chronic obstructive pulmonary disease, and other cardiovascular diseases, increase the risk of death from the new coronavirus. Besides, there is scientific evidence that elderly people with chronic Chagas' cardiomyopathy (CCC) have a higher risk of death from COVID-19 when compared to seronegative patients of the same age [12].

Alberca *et al*. reported fatal cases of elderly Brazilian patients coinfected with CD and COVID-19 [13]. The case of a Brazilian woman with concomitant leprosy, CD, and cutaneous/mucosal manifestations of the coronavirus infection has been reported and the authors speculate that, although the patient had borderline leprosy and CCC, she did not show any recrudescence of leprosy symptoms, worsening of cardiac symptoms, or severe COVID-19, a fact possibly explained by immunomodulatory properties of the leprosy treatment she had previously undergone [14]. Although CD cases in the Brazilian Southeast region comprise less than 5% of the total prevalence in Brazil, COVID-19–CD cases may

be an important cause of uninvestigated death in endemic regions. Parasitic disease also presents itself as an important risk factor for the development of the severe form of COVID-19 since some patients have respiratory and systemic impairment, especially in areas endemic for both diseases [12].

Box 1. Key points to be considered in the context of COVID-19 and parasitic NTD coinfections

- Certain NTDs may have their control programs affected by the COVID-19 pandemic, requiring urgent attention from governmental and nongovernmental institutions.
- It is important that medical and scientific communities recognize the particularities of different parasitic diseases and the impact that coinfection with SARS-CoV-2 may have on the progression in each case.
- Parasitic NTDs in endemic areas should be considered when diagnosing COVID-19. In nonendemic areas, attention should be given to immigrants, refugees, and tourists.
- The effects of immunosuppressive therapies must be monitored as their use may allow some parasites to find favorable conditions for uncontrolled proliferation.

Leishmaniasis also deserves attention. The incidence of CL cases can increase substantially in areas with migratory movements due to the poverty scenario that can be accentuated by COVID-19. This is extremely relevant when added to the fact that several reports have shown that middle Eastern countries facing civil conflicts are experiencing a massive displacement of refugees. As a consequence, *Leishmania* parasites show the potential to be transmitted by permissive vectors present in other territories[iii]. In terms of *Leishmania*–SARS-CoV-2 pathogenesis modulation, Carvalho and collaborators speculated that COVID-19 may be aggravated in VL-endemic areas due to ineffective immune control against viral infections in VL patients [15]. In truth, it illustrates the complexity of SARS-CoV-2 coinfections – for which risks and the severity of clinical symptoms interfere with the course of each disease, perhaps due to immune modulation.

Concluding remarks

Unfortunately, countries with a high prevalence of parasitic NTDs have demonstrated the inability to adopt effective control measures to curb the spread of COVID-19; such countries include African, Caribbean, and Middle Eastern countries, Brazil, and India[iv]. Therefore, cases of coinfection should be more frequent in these areas. Examples presented reveal the short-term impact of coinfections at the individual level. No less important is the idea that SARS-CoV-2 coinfections may lead to serious long-term consequences for entire communities, especially those requiring basic resources to guarantee their survival. The imminent possibility of resource scarcity in settings where MDA control and health surveillance programs have been used to control NTDs is threatening.

Still in the pandemic scenario, where consequences must be prolonged for months/years, new cases of coinfection must be reported, bringing to light examples that need to be well understood, biologically and epidemiologically, so that the conditions of the associated pathologies are known (Box 1). Such information may provide clues to government and health professionals, enabling them to establish effective parasitic disease control and surveillance policies in endemic and nonendemic regions. As urgent measures, we emphasize the need for intragovernmental and global health agency alliances to base their efforts on mass vaccination against COVID-19, essentially in poor/developing countries, and emphasize the importance of measures to restrain the spread of SARS-CoV-2 in order to lessen negative impacts on control programs for parasitic NTDs.

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Declaration of interests

The authors declare no competing interests.

Resources

[i]www.who.int/news/item/27-04-2020-who-timeline—covid-19

[ii]www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html

[iii]www.natureasia.com/en/nmiddleeast/article/10.1038/nmiddleeast.2019.74

[iv]https://graphics.reuters.com/world-coronavirus-tracker-and-maps/

[1]Department of Animal Biology, Parasitology Section, Biology Institute, University of Campinas – UNICAMP, Campinas, São Paulo, Brazil

*Correspondence:
dcmiguel@unicamp.br (D.C. Miguel).

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