Helminths and COVID-19 Co-Infections: A Neglected Critical Challenge

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ABSTRACT: Helminth infections are among the most common infectious diseases in underdeveloped countries. Helminths suppress the host immune responses and consequently mitigate vaccine efficacy and increase severity of other infectious diseases. Helminth co-infections might suppress the efficient immune response against SARS-CoV-2 at the early stage of the infection and may increase morbidity and mortality of COVID-19.

KEYWORDS: SARS-CoV-2, COVID-19, helminth, coinfection, type 2 immunity, immunoregulation

It late 2019, a pneumonia due to coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, and immediately spread worldwide to become a pandemic problem. The disease has diverse sequels among older individuals (>60 years old) and patients who have co-morbidities or co-infections, such as pulmonary diseases, chronic kidney diseases, diabetes, hypertension, and cardiovascular diseases.¹

Helminth infections are among the most common infectious diseases, particularly in underdeveloped countries.² Schistosomiasis and soil-transmitted helminths (STHs) (known as ascariasis, hookworm, and trichuriasis) are the most common helminth infections worldwide (Table 1).² In 2016, the global burden of STH was accounted to be above 3 million disability-adjusted life-years (DALYs).³ Typically, most STH result in a chronic manifestation with minor clinical symptoms.² It is well-documented that chronic infection alters the immune system toward type 2 immunity (e.g., interleukin (IL)-4, IL-5, IL-9, and IL-13).⁴ The consequence of this immune modulation is suppression of the essential immune response against intracellular pathogens.^{5,6} Therefore, in individuals with helminth infections, the susceptibility and severity to infectious diseases, such as HIV/AIDS, tuberculosis, and malaria, have increased.⁵ As reviewed elsewhere, helminth infections are more common among developing or underdeveloped regions of the world, such as sub-Saharan Africa, East Asia, and the Indian subcontinent.^{2,5} In these regions, the prevalence of major infectious diseases, including HIV/AIDS, malaria, and tuberculosis, are higher than that in other parts of the world.^{2,5} Studies indicate that helminth co-infection can increase morbidity and mortality of these infections and that de-worming can revert this phenomenon.^{5,7–9} Hence, the concurrence of SARS-CoV-2 and helminths in a population with either HIV/AIDS, malaria, and tuberculosis can lead to more severe outcomes than single infections.

Development of an efficient vaccine is one of the main preventive strategies against SARS-CoV-2 infection. However, the immunomodulatory effects of helminth infections can mitigate vaccination efficacy.¹⁰ For example, the poor

immunogenicity of BCG vaccination was detected in a helminth-infected Ethiopian population.¹¹ It is notable that BCG vaccination could protect against severe SARS-CoV-2 infection by mechanisms related to trained immunity.¹² In a murine model, efficacy of flu vaccination declined in helminth-infected animals via an IL-10-dependent manner. Interestingly, previous helminth infections also impaired vaccination efficacy.¹³ The results of a recent meta-analysis regarding parasite infections and immunization revealed that chronic helminthiasis has more negative impact on immunization than acute disease.¹⁴ As such, infections with parasites at the time of vaccination led to worse immunization outcomes.¹⁴

Older individuals, people with comorbidities, or patients with immunocompromising conditions are at higher risk of severe SARS-CoV-2 infection.¹ Vaccination is more challenging in these populations because the immunogenicity of vaccines is diminished overall in these groups.¹⁰ Therefore, in these populations, either vaccines against SARS-CoV-2 or other diseases may have less immunogenicity when concomitant with helminth infections.

Pregnant women are a population vulnerable to congenital infections due to modulation of their immunological responses that occurs over the three trimesters of pregnancy.⁶ Pregnancy also increases susceptibility to helminth infections.⁶ As such, the synergistic immunoregulatory effects of helminth infections and pregnancy can increase susceptibility to congenital infectious diseases.⁶ Although limited data are available about congenital transmission of SARS-CoV-2, an increase in susceptibility and severity of SARS-CoV-2 infection as well as congenital transmission is plausible in pregnant women with helminth

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Table 1. Worldwide Prevalence of the Most Common Human Helminth Infections^a

helminth species	disease or condition in humans	estimate prevalence worldwide	habitat of adult worm in humans
Nematodes			
<i>Ascaris lumbricoides</i> and <i>A. suum</i>	ascariasis	804 million	small intestine
<i>Trichuris trichiura</i>	trichuriasis	477 million	large intestine
<i>Enterobius vermicularis</i>	enterobiasis (oxyuriasis)	>200 million	
<i>Toxocara canis</i>	visceral or ocular larva migrans	unknown	N/A
<i>Necator americanus</i>	necatoriasis		
<i>Ancylostoma duodenale</i>	ancylostomiasis	472 million	small intestine
<i>Ancylostoma ceylanicum</i>			
<i>Strongyloides stercoralis</i>	strongyloidiasis	30–100 million	
<i>Wuchereria bancrofti</i>	lymphatic filariasis	44 million	lymphatic vessels
<i>Brugia malayi</i> or <i>Brugia timori</i>			
<i>Onchocerca volvulus</i>	onchocerciasis (river blindness)	17 million	subcutaneous tissue
<i>Trichinella spiralis</i>	trichinellosis	0.066 million	small intestine
Trematodes			
<i>Schistosoma mansoni</i>	intestinal schistosomiasis		mesenteric veins
<i>Schistosoma hematobium</i>	urogenital schistosomiasis	206 million	venous plexus of urinary bladder
<i>Schistosoma japonicum</i>	intestinal schistosomiasis		mesenteric veins
<i>Fasciola hepatica</i>	fascioliasis		bile ducts
<i>Clonorchis sinensis</i>	clonorchiasis	80 million	bile ducts and gall bladder
<i>Opisthorchis spp.</i>	opisthorchiasis		
<i>Paragonimus spp.</i>	paragonimiasis		lungs
Cestodes			
<i>Echinococcus granulosus</i>	hydatid disease	0.8 million	N/A
<i>Echinococcus multilocularis</i>	alveolar echinococcosis	0.019 million	N/A
<i>Cysticercus cellulosae</i> (<i>Taenia solium</i> larva)	cysticercosis and neurocysticercosis	1 million	N/A
<i>Taenia solium</i>	intestinal taeniasis	0.38 million	small intestine

^aN/A, not applicable. There is no development of adult worms in humans. Reproduced from ref 2. Copyright 2020 Gazzinelli-Guimaraes and Nutman.

infections. Helminth infections are also linked with malnourishment, which reduced efficient immune response against pathogens.⁶ Therefore, co-infection with SARS-CoV-2 and helminths may have more hidden outcomes than predictable ones.¹⁵ It should be noted that another recent hypothesis proposed that helminth co-infection may also have a mitigating effect in COVID-19 severity.¹⁶ Hence, more research in animal models and clinical studies are needed to clarify the interaction between helminth and SARS-CoV-2 co-infection.

CONCLUSIONS

Our conclusions are as follows: (1) Helminth co-infection may suppress the efficient immune response against SARS-CoV-2 in the early stage of the infection, and thereby may increase morbidity and mortality of COVID-19. (2) Helminth infections

can suppress the immune responses and can mitigate SARS-CoV-2 vaccine efficacy. (3) The synergistic immunoregulatory effects of helminth infection and pregnancy may increase susceptibility to congenital transmission of COVID-19. (4) Treatment and prevention of helminth infections in endemic regions might decrease the morbidity and mortality of COVID-19.

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Notes

The author declares no competing financial interest.

ABBREVIATIONS

COVID-19: coronavirus disease 2019

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

STHs: soil-transmitted helminths

DALYs: disability-adjusted life-years

IL: interleukin

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