



# Strongyloidiasis Hyperinfection Syndrome in COVID-19 Positive Migrants Treated with Corticosteroids

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## Abstract

The aim of this study is to highlight the potentially fatal risk of Strongyloidiasis Hyperinfection Syndrome for hospitalized immigrant patients with moderate to severe COVID-19 disease and undiagnosed Strongyloidiasis. We reviewed electronic medical records of immigrants from 2010 to 2022 and extracted the number of patients with eosinophilia, strongyloidiasis and COVID-19 infection, outpatient and hospitalized. While 885 outpatients were diagnosed with eosinophilia, only 356 (40.2%) were tested for strongyloidiasis and 160 (44.9%) yielded a reactive serology. COVID-19 infection was reported in 6,412 patients. 1135 (17.7%) of these patients sought hospital care. Patients with undiagnosed strongyloidiasis are at risk for a potentially fatal parasitosis if treated with systemic corticosteroids for COVID-19. This supports clinical guidelines in hospital settings for those with severe COVID-19. Strongyloidiasis should be considered by taking a thorough travel or migration history and testing before giving immunosuppressive drugs.

**Keywords** Strongyloides · Hyperinfection · Eosinophilia · Corticosteroids

## Introduction

In this third year of the most significant health crisis in the past 100 years, the COVID-19 pandemic, it is clear that not only has this disease caused tremendous devastation worldwide, but has posed great challenges for treating those who become severely ill, with only a limited number of effective chemotherapies. Trials such as the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial conducted by the University of Oxford showed the beneficial effect of dexamethasone and the National Institutes of Health COVID-19 Treatment Panel recommendations have outlined the use of systemic corticosteroids such as dexamethasone in patients that require hospitalization and supplemental oxygen [1, 2].

Dexamethasone is generally safe for short term use and even at high doses it is mostly without adverse effects. Most clinicians are well-versed on the risks of hyperglycemia and increased infection risks with short term use of this potent steroid; however many clinicians may not be aware of the significant risk of dexamethasone use in individuals with untreated (and often undiagnosed) strongyloides infection, which can lead to disseminated infection or Strongyloides Hyperinfection Syndrome (SHS).

Strongyloidiasis, caused by the nematode *Strongyloides Stercoralis*, is commonly seen throughout the world, both in tropical and sub-tropical areas. It is predominantly transmitted through soil that is contaminated with larvae that penetrate the skin and migrate to the small intestines where eggs are laid. The eggs can hatch into filariform larvae in the intestines and directly auto-inoculate, there can be an autoinfection, perpetuating chronic infection. This chronic infection can last for years and remain subclinical or asymptomatic.

The global prevalence of strongyloidiasis is significant with a recent analysis indicating over 600 million people worldwide affected. [3]. A recent meta-analysis found strongyloidiasis seroprevalence among migrants worldwide to average 12.2% and a seroprevalence of 11.4% among those from Latin America and the Caribbean [4].

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These intestinal parasites can be present in immigrant populations in the United States and often go undiagnosed. Diagnosis can be made following serologic testing for strongyloidiasis antibodies (IgG). This is often performed in a primary care setting upon finding eosinophilia (absolute eosinophil count > 450 cells/microliter). In populations infected with this parasite, Strongyloides Hyperinfection Syndrome can occur with immunosuppression, including with the use of systemic corticosteroids such as dexamethasone. This can cause an uncontrolled multiplication of the parasite (hyperinfection) and potential life-threatening dissemination of larvae, with mortality rates of untreated Strongyloides hyperinfection syndrome from 85 to 100% [5]. This potentially fatal iatrogenic complication can occur regardless of dose, duration (including short-term), or route of treatment [6].

Since hyperinfection involves an increased larval migration, clinically the hallmark of SHS is a significant increase of larvae in stool and/or sputum and an exacerbation of both gastrointestinal and pulmonary symptoms.<sup>6</sup> There is a wide array of symptoms of SHS, including fatigue, weakness, body pain and both gastrointestinal and cardiopulmonary symptoms. Chest imaging often demonstrates bilateral or focal interstitial infiltrates [7]. Blood counts at this time can demonstrate a suppressed eosinophil count [8]. The clinical presentation of SHS might mimic the manifestations of severe COVID-19 infection, and therefore may contribute to missing a potentially fatal diagnosis that requires an alternative treatment.

There are two published case reports of SHS in COVID-19 patients who were given immunosuppressive medications (dexamethasone and tocilizumab) as well as four additional case reports of symptomatic strongyloidiasis after hospitalization and steroid treatment for COVID-19 [9, 10]. It is likely, however, that this occurrence is an underreported event due to the clinical presentation similarities of severe COVID-19 and SHS.

## Methods

This retrospective study was done at Sun River Health, a federally qualified health center (FQHC) located in New York State. The network is made up of 41 health centers in rural, suburban, and urban counties. The center provides comprehensive primary care to approximately 275,000 patients, including a large migrant population. 30% of our patients were born outside of the United States and are considered immigrants to this country. Many of those who were born outside of the USA originate from Central and South America.

In this study, we used Cognos, a web-based business intelligence software that organizes patient data from our electronic medical record (EMR), eClinicalWorks (eCW), and extracted the number of immigrants accessing care among our population of patients. We similarly ascertained the number of patients with eosinophilia, strongyloidiasis, and COVID-19 within the immigrant population from 1/25/2011 to 1/01/2022. The number of patients COVID-19 and strongyloidiasis infection as well as the number who had both COVID-19 and eosinophilia (as a proxy marker for strongyloidiasis given low rates of testing for strongyloidiasis) within the specified period was assessed. The proportion of patients with COVID-19 that accessed hospital care was determined and considered as a marker of COVID-19 severity and potential for receiving steroid treatment however this number is believed to be underreported due to inaccessibility of all hospital records. Furthermore, the proportion of patients who received corticosteroid treatment could not be determined due to the inability to access hospital records.

The study underwent review and was approved by the Clinical Directors Network (CDN) Institutional Review Board (IRB).

## Results

At Sun River Health, 106,132 out of 245,520 patients (43.2%) were identified as being born outside the USA. Eosinophilia was diagnosed in 885 patients over the past eleven years. Strongyloidiasis testing by serology for IgG was conducted for 356 of the migrant patients, and of those, 160 were IgG reactive for a 44.9% positivity. COVID-19 disease was reported for 6,412 immigrant patients. 1,135 of these patients accessed hospital care for COVID-19 infection, with 341 (30%) of those patients admitted to hospital. Among the 6,412 outpatient migrants with COVID-19 infection, 68 (1%) had documented eosinophilia and 19 (0.3%) were serology positive by IgG for Strongyloidiasis.

## Discussion

Strongyloidiasis, a chronic but easily treatable parasitic infection can lead to SHS when the immune system is suppressed, including after administration of a course of steroid therapy, a mainstay treatment in severe COVID-19. In outpatient settings such as our health center, healthcare providers initiating steroid therapy in migrant patients from Strongyloides endemic countries should ensure that Strongyloidiasis is not present. These guidelines were adapted in some settings for patients who were candidates for corticosteroid therapy before the era of COVID-19 [11].

In this era of the Coronavirus Disease 2019 (COVID-19) pandemic, having an approach to reducing the risk for SHS is paramount, especially in lieu of possible hospitalization in patients with COVID-19. Strategies have been proposed and adapted as best practices in both the outpatient and hospital settings to screen and treat for Strongyloides [12].

FQHCs such as Sun River Health provide comprehensive primary care and preventive care services to individuals regardless of their ability to pay or their health insurance status. They are therefore a critical component of the health care safety net. These centers welcome patients from around the world, and many centers have significant numbers of migrants who seek their services. When immigrants migrate to the USA through the immigration processes, they benefit from screening which includes, in addition to vaccines, screening for infectious diseases such as tuberculosis, hepatitis, STIs, HIV and parasitic infections. Migrants who come into the country undocumented have not been screened for these infections, and it is therefore important for healthcare providers to be mindful of potential infections. Eosinophilia can indicate parasitic infections that may indicate the need for screening in an outpatient setting.

In this FQHC, almost 44% of patients identified as coming from another country, accounting for a significant proportion of the population. To deliver appropriate health care, it is imperative that primary care clinicians understand unique health needs of their patient population, including infections that are endemic in their countries of origin such as Strongyloidiasis. From the 885 migrants diagnosed with eosinophilia, only 356 were tested for Strongyloidiasis infection. The 44.9% positivity rate of those tested further highlights the need for universal screening of migrant patients. This demonstrates how common this often-asymptomatic condition is in this population as well as how many patients could be at risk for SHS if they require steroid therapy.

Additionally, we identified 68 migrant COVID-19 patients who had eosinophilia and 29 who had confirmed Strongyloidiasis infection. These represented very small proportions of the migrant patients with COVID-19 infection (1.0% and 0.5%, respectively), however this is likely a significant underestimate due to the lack of testing for Strongyloidiasis serology and access to hospital laboratory results. Given the significant number of patients accessing hospital care for COVID-19, there are presumably those who would have received systemic steroid therapy and thus risking this potentially fatal outcome.

Even for migrant patients not screened for Strongyloidiasis on their first contact with the healthcare system, it is important for providers to be aware of eosinophilia as an indication of possible Strongyloidiasis and to perform Strongyloides serology testing. This is an important consideration before the initiation of steroid therapies, however,

in emergency situations such as severe COVID-19 infection, there may not be sufficient time for Strongyloidiasis serology testing. This further highlights the importance of screening by primary care providers, especially in the case of migrants with eosinophilia.

In a hospital setting, the presence of eosinophilia cannot be the sole indicator of a potential helminth infection such as Strongyloides. In fact in the case of hyperinfection, there may be eosinopenia, as eosinophilia is usually not seen due to steroid use as a precipitating factor of the hyperinfection syndrome. [4] In this setting, diagnosis can be made by the identification of larvae in bodily fluids (such as sputum or bronchoalveolar lavage) as well as positive serology [13].

This study was limited by common problems with data sharing between different healthcare systems. Patients who were diagnosed with COVID-19 at outside testing sites or clinical settings may not have been reported to our center. Further, we were only able to capture data on the COVID-19 hospitalizations, eosinophilia, and Strongyloidiasis serology testing that were reported to our clinic. These numbers are undoubtedly underestimated. Furthermore, we did not have access to data on COVID-19 mortality.

This pandemic has highlighted once again the disparities in medical care in this country. We must ensure that the primary care clinicians who serve migrant and immigrant populations are aware of additional medical risks of those with untreated strongyloidiasis infection, and they implement universal screening and treatment for this often-asymptomatic infection.

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## Declarations

**Conflict of interest** Nancy Piper Jenks, none declared. Brendan Driscoll, none declared. Tiffany Locke, none declared.

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