The Egyptian Journal of Internal Medicine

REVIEW

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Strongyloidiasis co-occurrence with tuberculosis and aspergillosis in immunocompromised patients: a global scoping review

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Abstract

Reports on cases of strongyloidiasis and tuberculosis or aspergillosis coinfection are fragmented in the literature and no large-scale reviews are describing its occurrence across the globe. We identified a total of 230 cases of strongyloidiasis and tuberculosis coinfection amongst 2376 participants with tuberculosis disease from eight epidemiological surveys conducted in Ethiopia ($n=4$, 50%); Tanzania ($n=3$, 37.5%) and Malaysia ($n=1$, 12.5%). Clinical outcomes in these studies were not stated as they were largely descriptive. In addition, there were ten individual case reports of strongyloidiasis and tuberculosis coinfection. Of the ten, four were from the USA (40%), two each from India (20%) and Japan (20%), and one each from the UK (10%) and Argentina (10%). Of the ten, six had favourable outcomes, two were fatal and outcomes were unclear in the remainder. Ten cases of strongyloidiasis and aspergillosis coinfection were identified, five were reported from the USA (50%), and one each from the Netherlands (10%), China (10%), Iran (10%), Colombia (10%) and Italy (10%). Five each had favourable and fatal outcomes. Fatal outcomes in strongyloidiasis and tuberculosis or aspergillosis coinfection were associated with steroid therapy ($n=3$), decline for treatment ($n=1$), delayed diagnosis ($n=2$) and delayed presentation ($n=1$). Our findings suggest a significant proportion of individuals living with tuberculosis are also affected with strongyloidiasis, especially in sub-Saharan Africa. However, more studies are required to ascertain the burden of strongyloidiasis and tuberculosis coinfection as few cases were reported from other highly burdened tuberculosis regions. In addition, the role of the attending clinician is critical to reduce morbidities from the coexistence of these clinical entities as a significant number of cases with documented outcomes were fatal.

Keywords Strongyloidiasis, Tuberculosis, Aspergillosis, Immunocompromised, Steroids, Ivermectin, Cancers

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Introduction

Strongyloidiasis is a parasitic infection, mainly caused by the soil-transmitted helminth, *Strongyloides stercoralis* [1]. Sporadic infections with *Strongyloides fuelleborni* also occur in Africa and Papua New Guinea [2]. It is estimated to affect 613.9 million people with a global prevalence of 8.1%, predominantly reported in the South-East Asia region estimated at 237.3 million, followed by the Western Pacific region with 133.2 million, and the African region with 108.1 million [3]. The portal of infection in humans is mainly via the penetration of the skin or mucous membranes by the filariform larvae during autoinfection or via the faecal-oral route. The larvae then migrate through the lymphatics and venules to the lungs and into the alveolar spaces causing inflammatory responses often associated with eosinophilic infiltration and pneumonitis. The parasite enters the gut from the lungs and becomes the parthenogenetic female [2].

The symptomatology of strongyloidiasis is often negligible or without clinical manifestations and can persist for several years in the immunocompetent human host [1]. On the other hand, it can cause a debilitated form of illness in the immunocompromised including cancer patients and following their exposure to chemotherapy, patients on organ transplant, prolonged steroid use, human T-lymphotropic virus (HTLV) infection, rheumatic diseases and HIV/AIDS patients often leading to fatal outcomes [1, 4–6]. The associated factors predisposing to strongyloidiasis hyperinfection or disseminated disease are also critical in setting the stage for tuberculosis (TB) and opportunistic fungal diseases like aspergillosis. The reason for the possible coexistence of these diseases is that they are often associated with impaired immunity. Strongyloidiasis impedes the human immune response to TB and can thus lead to the reactivation of latent TB or worsen an ongoing TB disease [7]. Also, *S. stercoralis* coinfection in pulmonary TB patients is associated with an increased risk of cavitation leading to a greater disease severity and higher bacterial burden [8]. Cavitations on their own are a major risk factor for chronic pulmonary aspergillosis as studies have shown increasing rates amongst post-TB treated patients [9]. Similarly, as the pathogenesis of these diseases involves the lungs, their clinical presentation may mimic each other thus masking an early diagnosis and initiation of appropriate treatment [10–12]. This is besides already existing intricacies in the prompt diagnosis of fungal diseases as they are often misdiagnosed as TB or missed in many cases coexisting with TB thus increasing morbidity and mortality [13–16]. Current estimates show that about 3.8 million individuals die from fungal diseases globally [17], and a total of 1.3 million people are dying from TB as of 2022 (WHO). The attending physician's cognizance of this interrelation is critical to patient management and obtaining favourable outcomes. Clinicians the world over need to be in touch with these trends to improve diagnosis thereby reducing morbidity. This underpins the essence of this review as large-scale reviews on this subject are currently lacking in the literature. We highlight documented studies and case reports of strongyloidiasis coexisting with TB or aspergillosis to drive awareness of early diagnosis and treatment which would invariably improve clinical outcomes.

Methods

We conducted a literature search using PubMed and Google Scholar to identify case reports, case series and observational studies reporting strongyloidiasis coinfection with TB or aspergillosis. The search duration was from inception to February 2024. The search was done using Medical Subject Headings (MeSH) terms and keywords with an appropriate combination using Boolean operators 'AND' and 'OR'. The search algorithm was (('strongyloides' OR 'strongyloidiasis') AND ('tuberculosis')) OR (('strongyloides' OR 'strongyloidiasis') AND ('aspergillosis')). References in all relevant papers were further reviewed for additional publications on studies regarding the subject of this review. We excluded reviews and other articles not relevant to the subject of this review. Data on study authors, location, year of publication, type of study, age, sex, clinical presentation, comorbidities, risk factors, immunosuppressive therapy, method of diagnosis, treatment and outcomes were extracted.

Results

We identified 18 articles reporting strongyloidiasis and TB coinfection. Of the 18, eight (44.4%) were epidemiological surveys and ten (55.6%) were individual case reports. Of the eight surveys, four (50%) were studies conducted in Ethiopia, three (37.5%) were done in Tanzania and one (12.5%) from Malaysia. Five (62.5%) were hospital-based studies, two (25%) were community-based studies and in one (12.5%), participants were recruited from both community and hospital. Overall, a total of 230 cases were reported from 4137 participants. Clinical outcomes in these studies were however not stated as they were largely descriptive (Table 1).

Looking at the case reports, of the ten, four were from the USA (40%), two each from India (20%) and Japan (20%), and one each from the UK (10%) and Argentina (10%). Four were males with a male-to-female ratio of 0.6:1. The mean age (± standard deviation) was 37.7 (± 20.4) and a range of 7 to 73 years. Predominant clinical features were abdominal pain/distention ($n=5$) followed by fever ($n=4$) and weight loss ($n=2$). Associated

Table 1 Epidemiological surveys documenting a co-infection between strongyloidiasis and tuberculosis

Authors/publication year/no. of reference	Location	No. of the population screened	No. of people with TB	No. of people with Ss and MTB coinfection	Survey site	HIV status
Ramos et al., 2006 [18]	[a]Ethiopia	782	100	5	Hospital	Not stated
Abate et al., 2012 [19]	[b]Ethiopia	295	112	3	Community	47% (53/112) of PTB patients were HIV positive
Alemu et al., 2017 [20]	[c]Ethiopia	213	213	2	Hospital	209 were tested for HIV of whom 20 (9.6%) were positive
Sikalengo et al., 2018 [21]	[c]Tanzania	668	668	89	Hospital	25% (167/668) of TB patients were HIV positive
Alemayehu et al., 2014 [22]	[d]Ethiopia	415	72	5	Hospital	Not stated
Mhimbira et al., 2017 [23]	[e]Tanzania	972	597	111	Hospital/community	27.3% (163/597) of TB patients were HIV patient
Wong et al., 2019 [24]	[e]Malaysia	137	82	9	Community	Participants with HIV were excluded
Range et al., 2007 [25]	[f]Tanzania	655	532	6	Hospital	43.6% (232/532) of confirmed TB patients were HIV patients
Total	–	4137	2376	230	-	-

Ss Strongyloides stercoralis, *MTB* Mycobacterium tuberculosis

[a] Participants comprised of patients diagnosed with lower respiratory tract infection, malaria, diarrhoea and TB

[b] Participants included TB patients, community controls and household contacts

[c] All participants were PTB patients

[d] Study population comprised participants with suspected TB

[e] Study population comprised TB patients and healthy TB contacts

[f] Study participants were confirmed or suspected cases of TB

comorbidities and predisposing factors were malnutrition ($n=2$), vitamin B12 deficiency ($n=1$), peptic ulcer ($n=1$), syndrome of inappropriate antidiuretic hormone secretion ($n=1$) and steroid therapy ($n=1$), respectively. Of the ten, six had favourable outcomes, two were fatal and outcomes were unclear in the remainder (Table 2). Of the two fatal cases, a diagnosis of strongyloidiasis coinfection in a TB patient was made, and an anti-TB regimen and ivermectin treatment were initiated. However, the patient still expired probably due to a delayed presentation as symptoms had evolved for a 2-month duration [26]. On the other, a diagnosis of TB was confirmed from sputum culture twelve days after the patient's demise and on autopsy [10].

About strongyloidiasis and aspergillosis coinfection, we found 10 individual case reports. Five were reported from the USA (50%), one each from Iran (10%), China (10%), Italy (10%), Colombia (10%) and the Netherlands (10%). The mean age (± standard deviation) was 65.2 (± 13.5) and a range of 36 to 82. Of the ten, eight (80%) were males with a male:female ratio of 4:1. Clinical features were majorly cough ($n=4$), dyspnoea ($n=4$), fever ($n=3$) and shortness of breath ($n=2$). Commonly encountered comorbidities identified were asthma ($n=3$) and leukaemias ($n=3$) and all the cases were on steroid therapy (Table 3). Of the ten cases highlighted, five each had favourable and fatal outcomes. Of the five with fatal outcomes, antihelminth and antifungal therapy declined in one [35], three were linked with steroid therapy [1, 38, 42] and the remainder due to a delayed diagnosis [12].

Discussion

Strongyloidiasis and tuberculosis coinfection

Expectedly, the reported cases and studies on strongyloidiasis coinfection in TB patients were mainly from endemic regions. Cases reported from non-endemic regions were in immigrants from regions endemic for strongyloidiasis [27–29]. Our review highlights over 200 cases of strongyloidiasis and TB coinfection reported worldwide with a significant proportion from sub-Saharan Africa [18–25]. Paradoxically, despite the endemicity of strongyloidiasis in South-East Asia and the highly burdened TB countries in that region, sparse cases of strongyloidiasis and TB coinfection were reported [26, 28, 31, 33]. This may be linked with the paucity of studies investigating TB patients for strongyloidiasis or perhaps the underdiagnosis and or underreporting of strongyloidiasis and TB coinfection as revealed in this index review. The epidemiological surveys conducted in this regard were all from Africa and none from Asia which suggests missed cases across the globe. Prioritizing research in this area, especially at a global scale will mitigate these gaps.

Table 2 Case reports on *Strongyloides stercoralis* and *Mycobacterium tuberculosis* coinfection

Authors/ publication year/ no of reference	Location	Age	Sex	Clinical presentation	Comorbidities	HIV status	Steroid therapy	Eosinophilia	Diagnosis of strongyloidiasis	Diagnosis of TB	Treatment	Outcomes
Praveena et al., 2022 [26]	India	33	F	Abdominal pain and distention, loose stools, and weight loss	None	Not stated	No	No	Stool wet mount	Ascitic fluid analysis	Anti-TB therapy + Ivermectin	Death
Dwarakanath, et al., 1994 [27]	UK	31	M	Abdominal pain, anorexia, weight loss, diarrhoea	None	Not stated	No	No	Stool microscopy	Sputum culture	Thiabendazole + anti-TB therapy	Favourable
Yamanashi et al., 2017 [28]	Japan	21	F	Swelling in the right supraclavicular region	None	Not stated	No	1348/μL	Serology and stool microscopy	Histopathology, Ziehl–Neelsen staining, culture and a PCR test	Ivermectin, praziquantel and albendazole + anti-TB therapy	Favourable
Kim et al., 2020 [29]	USA	73	M	Syncopal episode, cough	None	No	No	Yes	Serology	BAL analysis	Not stated	Not stated
Rosa et al., 2002 [30]	USA	31	F	Abdominal, pain, nausea, vomiting, diarrhea, fever	None	Positive	No	Not stated	Stool microscopy	Histopathology	Albendazole, Ivermectin + anti-TB therapy	Favourable
Iwashita et al., 2013 [31]	Japan	28	M	Fever, loss of appetite, fatigue	Malnutrition	Not stated	No	No	Stool microscopy	TB Quantiferon assay, Culture of gastric secretions, positive adenosine deaminase test	Ivermectin + anti-TB therapy	Not stated
[a] Saradna et al., 2018 [10]	USA	67	F	Fatigue, abdominal pain, burning sensation in the throat	Vitamin B12 deficiency, peptic ulcer, SIADH	Not stated	No	3%	Histopathology, stool microscopy	Sputum culture	Ivermectin	Death
Terroba et al., 2021 [32]	Argentina	52	F	Aphasia, disorientation, fever	None	Not stated	Yes	38%	Stool microscopy	BAL culture	Anti-TB therapy + Ivermectin	Favourable
Patil et al., 2012 [33]	India	7	M	Abdominal distention, diarrhoea alternating with constipation	Malnutrition	Not stated	No	No	Stool microscopy	Positive Mantoux test	Ivermectin + anti-TB therapy	Favourable
Morales et al., 2019 [34]	Colombia	34	F	Fever, haemoptysis, lower left limb pain	None	Positive	No	Not stated	BAL microscopy	BAL culture	Ivermectin + anti-TB therapy	Favourable

SIADH syndrome of inappropriate antidiuretic secretion, *BAL* bronchoalveolar lavage

[a] Autopsy revealed miliary *Mycobacterium tuberculosis* involving both lungs, para-tracheal and periaortic lymph nodes, the liver, and the pericolic soft tissue

Table 3 Summary of case reports on the co-occurrence of strongyloidiasis and aspergillosis

Authors/ publication year	Location	Age	Sex	Clinical presentation	Comorbidities	Steroid therapy	Eosinophilia	Diagnosis of strongyloidiasis	Diagnosis of aspergillosis	*Aspergillus* species identified	Treatment	Outcomes
Wagenvoort et al., 1994 [35]	Netherlands	72	M	Fever, malaise, vomiting, low blood pressure	Non-Hodgkin's lymphoma	Yes	1%	Wet saline mount of sputum	KOH microscopy, sputum culture	*Aspergillus fumigatus*	Declined	Death
Motamedi et al., 2020 [1]	Iran	55	M	Cough, shortness of breath, wheezing, chest pain, weight loss, weakness, loss of appetite	Chronic pneumonia (two masses in the lung)	Yes	0%	Wet mount of faeces	BAL direct examination and culture, PCR and sequencing	*Aspergillus niger, Aspergillus flavus*	Ivermectin (only for one day)	Death
Guo et al., 2014 [36]	China	74	M	Cough, expectoration, shortness of breath, fever, haemoptysis, poor appetite, weight loss	autoimmune pancreatitis	Yes	0.1%	Bronchoalveolar lavage fluid and stool examination	Sputum culture, BAL culture	Not stated	Voriconazole and albendazole	Favourable
Lertsburapa et al., 2021 [37]	USA	75	M	Tracheobronchomalacia, COPD, obstructive sleep apnea, atrial fibrillation, respiratory distress	Atrial fibrillation, acute kidney injury and respiratory failure	Yes	0.66 K/μL	BAL cytopathology, strongyloides IgG antibody	BAL cytopathology	Not stated	Voriconazole, Ivermectin aand albendazole	Favourable
[a]Upadhyay et al., 2001 [38]	USA	82	M	Cough, dyspnea, wheezing	Asthma	Yes	2%	Bronchoscopy	Bronchoscopy	Not stated	Amphotericin B, albendazole	Death
Chahin et al., 2019 [39]	USA	75	M	Dyspnea, expectoration of brownish sputum, wheezing	Asthma	Yes	13%	Positive strongyloides antibodies	High serum *Aspergillus* antigen	Not stated	Posaconazole and Ivermectin	Favourable
[b]Marchesi et al., 2011 [12]	Italy	66	F	Fever, diffused skin rash	T-cell acute lymphoblastic leukaemia	Yes	Not stated	-	Positive serum galactomannan	Not stated	Voriconazole	Death
Shrestha et al., 2019 [40]	USA	36	M	Dyspnea, malaise, fever, haemoptysis	Acute lymphoblastic leukemia	Yes	18%	Sputum cytology	Sputum and BAL cultures	*Aspergillus flavus*, *Aspergillus terreus*	Ivermectin	Favourable
Jacquemart et al., 2008 [41]	Not stated	58	F	Dyspnea, chest pain, cough, nausea, vomiting, anorexia	Asthma	Yes	17.2%	Bronchial aspirate cytology	High serum *Aspergillus* antibodies	*Aspergillus fumigatus*	Ivermectin	Favourable
[c]Tankanow et al., 1988[42]	USA	59	M	Hematuria, hemoptysis, hematemesis, respiratory failure	Chronic obstructive lung disease	Yes	Not stated	Stool and sputum microscopy	Sputum culture	*Aspergillus fumigatus*	Thiabendazole	Death

[a] Autopsy confirmed extensive lung infiltration with *S. stercoralis* and *Aspergillus* species

[b] A diagnosis of gastrointestinal strongyloidiasis with concomitant primary digestive aspergillosis was made at autopsy

[c] Postmortem examination demonstrated disseminated aspergillosis

Besides strongyloidiasis, *Mycobacterium tuberculosis* infection is also known to coexist with other intestinal parasites. A pooled prevalence of intestinal parasite coinfection of 33% was documented in a systematic review of studies conducted in Ethiopia with *Ascaris lumbricoides* (10.5%), Hookworm (9.5%), *Giardia lamblia* (5.7%) and *Strongyloides stercoralis* (5.6%) being the most common [43]. From Tanzania, the overall prevalence of helminth coinfections in adult TB patients was 22.9% and predominantly associated with *S. stercoralis* (42.4%) and *S. mansoni* (23.8%) [21]. Likewise, a systematic review of pulmonary TB patients from Africa and Asia documented a pooled prevalence of helminth coinfection of 29.69%; *Schistosoma mansoni* (9.98%) being the highest and followed by *S. stercoralis* (7.74%) and hookworm (6.91%) respectively [44]. An earlier global systematic review (1984–2012) on the same subject identified 24 cases from 22 studies and a total of 770 cases from five epidemiological surveys [45]. The findings from these review studies suggest a significant proportion of TB patients have intestinal helminth coinfections, thus the routine screening of TB patients for intestinal parasites should be encouraged especially in regions endemic for both clinical conditions as prompt diagnosis and initiation of treatment modalities are vital to attaining favourable outcomes.

Strongyloidiasis and aspergillosis coinfection

Generally, fungal infections are not commonly associated with the immunocompetent unless following activities that cause undue or severe exposure to the conidia of these fungal pathogens or due to prolonged contact with an infected person or via fomites as seen in dermatophytosis [15, 46]. On the other hand, the immunocompromised including individuals with underlying HIV infection, cancer patients, prolonged steroid therapy, patients undergoing organ transplantation, and diabetics, amongst others are frequently susceptible to fungal infections due to impaired immune functions [15]. The latter may account for the coexistence of *S. stercoralis* and opportunistic fungal pathogens as strongyloidiasis is also known to impair cellular immunity via the modulation of proinflammatory cytokines thereby dampening the basal immune response [7]. Moreover, strongyloidiasis as previously mentioned has an increased risk of lung cavitations which may predispose to aspergilloma formation [8, 47].

Risk factors

Reported cases of strongyloidiasis and TB or aspergillosis coinfections had notable underlying diseases and risk factors including malnutrition, cancers, chronic obstructive pulmonary diseases (COPDs), steroid use, rural residence and contaminated water sources. Malnutrition is an important risk factor for strongyloidiasis and TB as well as is often associated with reduced lymphocyte count and as such increases the risk for strongyloidiasis hyperinfection and TB reactivation [10, 31].

All cases of strongyloidiasis and aspergillosis coinfections highlighted in this review were on steroid therapy due to underlying illnesses including cancers, autoimmune conditions and COPDs. Prolonged use of steroids suppresses immune functions as it impairs T lymphocyte activation, enhances recruitment of T regulatory cells and promotion of M2 macrophage polarization [48], thus predisposing to opportunistic mycoses and or strongyloidiasis hyperinfection. Similarly, the use of steroids in the management of TB worsens strongyloidiasis and can lead to hyperinfection or disseminated disease [31, 32]. Although the underlying mechanisms of these are unclear, postulations by some authors hold that steroids may cause acute suppression of eosinophilia (important mediators of the immune response to *S. stercoralis*) or a direct effect on parasites by accelerating their transformation from filariform to rhabditiform larvae [32, 49].

The implication of rural residence in strongyloidiasis and TB coinfection may be linked with poor hygiene, overcrowding and the inability to adopt lifestyle changes that would reduce infection risk hence the likelihood of ingesting contaminated food or water which is a route of infection for most intestinal parasites [20]. Contrastingly, some studies reported a high prevalence of helminth and TB coinfection in urban areas but were however linked with poor urban planning and hygiene control [21].

Clinical implications

To begin with, the clinical presentation of strongyloidiasis is non-specific. It could mislead the attending clinician to consider other close mimics [11, 30]. Marchesi et al. reported systemic strongyloidiasis and primary aspergillosis of the gastrointestinal tract in a patient with T-cell acute lymphoblastic leukaemia which was unfortunately fatal due to a confounding clinical picture that suggested other differentials including chemotherapy side effects, neutropenic enterocolitis, drug-related hepatic failure and the concomitant presence of invasive aspergillosis. Diagnosis of strongyloidiasis was confirmed in this index patient at autopsy and invasive aspergillosis as well [12]. In the same vein, strongyloidiasis and TB coinfection may occur in an immunocompromised patient, or either of the two clinical conditions may predispose to an overt manifestation of the other [10, 31, 50]. As described in some case reports, some patients were seen to have developed TB infection after successful treatment for strongyloidiasis [31], and vice versa [27]. Thus, in either case, a diagnosis of TB should be considered or ruled out

in a patient with strongyloidiasis hyperinfection and likewise strongyloidiasis in a patient being managed for TB especially when steroid therapy is included as part of the treatment regimen and more so if the index TB patient is presenting with gastrointestinal symptoms [10, 26]. This is pertinent for the attending clinician as a delayed diagnosis of TB in the context of 'strongyloidiasis and TB coinfection', and a delayed diagnosis of strongyloidiasis in the setting of 'strongyloidiasis and aspergillosis coinfection' accounted for some of the fatalities documented in this review [10, 12].

Diagnosis

Besides mimicking other disease conditions, the diagnosis of strongyloidiasis is quite challenging for several reasons as the diagnostic tools have varied sensitivity and specificity, and as such false negatives or positives may be entertained which may be detrimental to patient care [51]. The common method used for diagnosis is stool microscopy, but this has a sensitivity of 50% attributed to the intermittent shedding of the rhaditiform larva even in a symptomatic patient [26]. Detection of antibodies against *Strongyloides* has improved sensitivities (74 to 98%) however not specific as cross-reactions can result in false positive results due to other parasitic infestations like filariasis or ascariasis [26]. Peripheral eosinophilia which is a laboratory feature consistent with parasitic diseases has been repeatedly shown in many case reports to be absent and as such not reliable [26, 31, 33]. On the other hand, in some case reports the only marker for strongyloidiasis was eosinophilia [28]. Baermann's technique has been shown to have the highest sensitivity and thus the most preferred method. In a study conducted in Iran comparing the sensitivity of five parasitological methods including direct smear of faeces in saline and Lugol iodine stain, Baermann technique, formalin-ethyl acetate concentration, Harada-Mori filter paper, agar plate culture and a molecular method, Baermann technique was the most sensitive with 90% positive outcomes while the least positive result was obtained with Harada-Mori method, 3.3% [52]. Howbeit, as the Baermann technique is not widely used and seemingly time-consuming, the deployment of multiple diagnostics would enhance prompt diagnosis and early initiation of antihelminth therapy.

Overview of immunology

The immunology of strongyloidiasis in TB patients is elaborately discussed in the literature with explanations as to why strongyloidiasis impairs the immunity of an individual with TB and vice versa. This is basically because the immune response pathway of both clinical entities counteracts each other; while the immune response to TB is mediated by proinflammatory T-helper type 1 (Th1) and Th17 cells cytokines which play a role in combating bacterial and viral infections, helminth infection contrastingly activates the release of anti-inflammatory Th2 cytokines, increased levels of circulating immunoglobulin E (IgE) antibodies, eosinophils, mast cells, regulatory T cells (Tregs) and transforming growth factor-β (TGF-β) [7]. One study investigating the effect of intestinal helminths on the immune response to PPD in naturally immunized or Bacille Calmette-Guerin (BCG) vaccinated individuals conducted in Ethiopia showed individuals with helminths infection had reduced T cell and PPD skin test responses while improved BCG efficacy following increased T cell proliferation and interferon were associated with antihelminthic therapy [53]. Likewise, some studies have also affirmed the above position stating the inhibitory effect of Th2 cell cytokines on Th1 immune response is reduced with the removal of the helminth following antihelminth therapy [54, 55].

Besides showing helminth infection to regulate cytokine responses in both pulmonary and latent tuberculosis infection, studies have also shown helminth-mediated modulation of the systemic and mycobacterial antigen-stimulated cytokine profiles to occur in individuals with extrapulmonary tuberculosis. A study investigating the association between *S. stercoralis* coinfection with tuberculous lymphadenitis showed plasma cytokines; specifically Type 2, regulatory and Type 17 cytokines were elevated while proinflammatory cytokines were reduced [56]. Modulation of monocyte responses in helminth-TB coinfection has also been described with a reduced capacity to phagocytose or exhibit respiratory burst activity and less expression of proinflammatory cytokines in *S. stercoralis* positive individuals compared with *S. stercoralis* negative individuals [57]. Regarding the immunological interactions between strongyloidiasis and aspergillosis, data was sparse in the literature, and this informs an area that needs to be urgently explored.

Limitations

Clinical outcomes were not documented in a significant number of cases which may have masked the burden of strongyloidiasis and TB coinfection in this review. In addition, we may have missed some studies or case reports relating to this review as the databases searched were limited to Google Scholar and PubMed. Howbeit, the data highlighted in this review was global and captured significant gaps in the management of strongyloidiasis coinfection with TB and aspergillosis with recommendations on how to mitigate these pitfalls.

Conclusion

Strongyloidiasis and TB coinfection are commonly encountered in sub-Saharan Africa and paradoxically less reported in other TB endemic regions probably due to paucity of studies investigating the co-occurrence of strongyloidiasis and TB. The predisposition of individuals with strongyloidiasis to develop TB is linked with the systemic immunomodulation associated with strongyloidiasis disease. On the other hand, besides the increased risk of cavitations, impaired immune status following prolonged steroid therapy was a major driver of strongyloidiasis coinfection in patients with aspergillosis. Further studies are required to decipher the molecular basis underlying the interrelation of aspergillosis and strongyloidiasis.

Abbreviations

TB	Tuberculosis
HTLV	Human T-lymphotropic virus
HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
WHO	World Health Organization
MeSH	Medical subject headings
COPDs	Chronic obstructive pulmonary diseases

Acknowledgements
None

Authors' contributions
Christian J. Ide: methodology, formal analysis, visualization, resources, writing—review and editing; David E. Elem: methodology, investigation, visualization, resources, writing—review and editing; Thelma E. Bassey: data curation, investigation, visualization, resources, writing—review and editing; Ofonime E. Benjamin: data curation, investigation, methodology, resources, writing—review and editing; Ikechukwu Okekemba: investigation, formal analysis, visualization, resources, writing—review and editing; Walter E. Odok: methodology, investigation, visualization, resources, writing—review and editing; Promise Owai: data curation, investigation, methodology, resources, writing—review and editing; Geraldine L. Edim: investigation, formal analysis, project administration, visualization, resources, writing—review and editing; Bassey E. Ekeng: conceptualization, writing—original draft, data curation, formal analysis, investigation, methodology, project administration, resources, validation, visualization, writing, review and editing, supervision and resources.

Funding
None.

Availability of data and material
All underlying data have been included in the manuscript.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 5 April 2024 Accepted: 12 August 2024
Published online: 22 August 2024

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