Journal of Microbiology, Immunology and Infection 56 (2023) 172—181

Available online at www.sciencedirect.com

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Original Article

# Epidemiology, clinical features, and outcomes of strongyloidiasis in Taiwan from 1988 to 2020: A case series and literature review

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Received 26 January 2022; received in revised form 14 May 2022; accepted 29 June 2022
Available online 14 July 2022

**KEYWORDS**
*Strongyloides stercoralis*;
Autoinfection;
Hyperinfection;
Disseminated infection;
Immunocompromised host

**Abstract** *Objectives:* We described a case of *Strongyloides* hyperinfection syndrome, reported a case series, and reviewed published cases of strongyloidiasis in Taiwan.
*Methods:* Confirmed cases of strongyloidiasis at the National Taiwan University Hospital (NTUH) and NTUH Hsin-Chu Branch from 1988 to 2020 were identified in the medical record database. Literature search was carried out through Pubmed, Google Scholar, and Index to Taiwan Periodical Literature System to identify published cases of strongyloidiasis in Taiwan from 1979 to 2020. Data pertaining to the demographics, underlying medical conditions, clinical manifestations, laboratory findings, and outcomes were extracted.
*Results:* A total of 117 cases of strongyloidiasis were identified, including 20 previously unpublished cases from the two hospitals and 97 published cases in the literature. Overall, 85 (73%) were male and the mean age was 64 years (range, 6—95 years). Classical symptoms such as diarrhea, cough, and skin rash were only observed in 43%, 37%, and 18% of the patients, respectively, whereas eosinophilia at presentation was only found in 48%. *Strongyloides* hyperinfection syndrome and disseminated strongyloidiasis were identified in 41 (35%) and 4 (3%) patients, respectively. Four (3%) patients had concurrent meningitis. In univariable analysis,

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https://doi.org/10.1016/j.jmii.2022.06.007

being older and having pre-existing chronic obstructive pulmonary disease or asthma were associated with hyperinfection or dissemination ($p = 0.024$ and 0.003, respectively). The mortality rate was 43% among those with hyperinfection or disseminated infection.
*Conclusions:* Strongyloidiasis can cause serious complications and mortality. Efforts to diagnose strongyloidiasis early are urgently needed to improve the outcome of patients with strongyloidiasis in Taiwan.


## Introduction

Strongyloidiasis is a human infection caused by the soil-transmitted helminth, *Strongyloides stercoralis*, with an estimated prevalence of up to 600 million globally.[1] Most people with strongyloidiasis present with mild or no symptoms.[2,3] However, because of its characteristic autoinfection life cycle, *S. stercoralis* is capable of persisting lifelong in infected individuals.[4] When such an individual becomes immunocompromised, such as following the use of corticosteroids, malnutrition, or human T-lymphotropic virus type 1 (HTLV-1) infection, intensified autoinfection cycles can occur, which may lead to life-threatening complications from *Strongyloides* hyperinfection syndrome or disseminated strongyloidiasis.[5]

Although the prevalence of strongyloidiasis remains unknown in Taiwan, it was estimated that Southeast Asian Region has the highest burden of strongyloidiasis worldwide.[1] Improved water safety and sanitation infrastructures in recent years could have reduced the risk of new infections in Taiwan, but would not have eliminated chronic infections. In an aging community, increased co-morbid medical conditions, such as malignancies, and increased use of immunosuppressants may put individuals with chronic, subclinical strongyloidiasis at risk for hyperinfection and/or dissemination.[6]

In this study, we reported a case of chronic strongyloidiasis who presented with acute meningoencephalitis and *Streptococcus gallolyticus* bacteremia, as a result of hyperinfection. To explore the epidemiology, the clinical features, and the outcomes of strongyloidiasis in Taiwan, we reviewed cases collected at two hospitals, and published cases of autochthonous strongyloidiasis in Taiwan.

## Methods

### Case presentation

A 56-year-old man, an indigenous Taiwanese, was evaluated at a hospital in northern Taiwan because of acute change of consciousness in February 2020. He had been in his usual state of health until a few days before the admission, when headaches developed. On the day of admission, he was found confused and agitated at work.

When he arrived at the emergency department of the hospital, his Glasgow coma scale was E2M4V2. The temperature was 36.7 °C, the heart rate 120 beats per minute, the blood pressure 124/70 mm Hg, and the oxygen saturation 98% while he was breathing supplemental oxygen from a nasal cannula at a rate of 3 L per minute. Physical examination revealed pale conjunctivae, neck stiffness, and symmetrical weakness of the extremities. Laboratory examinations disclosed leukocytosis without eosinophilia and elevated levels of serum creatinine (2.1 mg/dL; baseline 1.2 mg/dL), procalcitonin (109.4 ng/dL), and C-reactive protein (5.5 mg/dL) (**S1 Table**). Plain computed tomography of the chest, abdomen, and pelvis revealed diffuse ground-glass opacities in both lungs. A lumbar puncture yielded turbid cerebrospinal fluid (CSF) with a high opening pressure (>40 cm $H_2O$), pleocytosis, an elevated total protein level, and a low glucose level. A diagnosis of bacterial meningitis was made and combination broad-spectrum antibiotic therapy was begun. Shortly afterwards, tracheal intubation for respiratory failure was performed and he was admitted to the intensive care unit. On the second hospital day, blood culture yielded *S. gallolyticus*. The hospital course was complicated with recurrent seizures that required the administration of combination antiepileptics. Magnetic resonance imaging after the administration of contrast material revealed findings suggestive of meningitis, ventriculitis, and focal infarction. On the 6th hospital day, a diagnosis of critical illness-related adrenal insufficiency was made, for which intravenous hydrocortisone was administered at a dose of 50 mg every 6 h. On the 12th day of hospitalization, he was successfully extubated and was transferred to general ward 4 days later. To investigate the source of *S. gallolyticus* bacteremia, colonoscopy was performed on the 19th hospital day and revealed a 0.5-cm tubular adenoma in the ascending colon.

His past medical history included alcoholic liver disease, gout, diabetes mellitus, and several episodes of deep-seated abscesses in different body cavities. He had been diagnosed with left empyema twice in 12 years, retroperitoneal abscess 7 years and intra-abdominal abscess 6 years before this admission. He had undergone multiple surgeries for the drainage and debridement of these abscesses; and eventually, left hemicolectomy and colostomy of the transverse colon were performed. During the previous hospital courses, hypereosinophilia (absolute eosinophil count [AEC] up to 10,833 cells/μL) and skin rash were documented, which were attributed to allergic reactions to piperacillin-tazobactam and cefepime, respectively.

On the 31st day of this admission, hypereosinophilia (AEC 3828 cells/μL) and intermittent wheezing developed when the dose of hydrocortisone was tapered to 50 mg daily. The recurrent eosinophilia, the isolation of *S.*

*gallolyticus* in the blood, and the history of skin rash and repeated deep-seated abscess formation prompted etiological survey for strongyloidiasis. On the next day, direct microscopic examination of a stool specimen showed numerous motile rhabditiform larvae of *S. stercoralis* (Fig. 1A). A revised diagnosis of *Strongyloides* hyperinfection syndrome complicated with acute meningoencephalitis and *S. gallolyticus* bacteremia was made. Ivermectin was prescribed. The patient was discharged on the 46th hospital day. Two months after discharge, levels of hemoglobin and AEC normalized (**S1 Table**). Follow-up stool examinations showed no larvae of *S. stercoralis* up to 458 days after treatment. A pathologist reviewed the tissue section obtained from his previous appendectomy in 2014, and a nematode surrounded by an eosinophilic abscess was identified (Fig. 1B). Chronic strongyloidiasis was confirmed, which provided explanations for the hypereosinophilia and skin rashes observed during previous hospital courses and the annotations of allergy to piperacillin-tazobactam and cefepime were cancelled. In retrospect, he reported moving from the mountainous area to a city in northern Taiwan in his teens and did not recall walking barefoot or being engaged in any soil-contact activities after adulthood.

## Case identification

Medical records of all patients who had received a diagnosis of strongyloidiasis at the National Taiwan University Hospital (NTUH) and at NTUH Hsin-Chu Branch (NTUH-HC) from 1988 to 2020 were extracted from the hospital medical record system. Because of a system transition, the medical records were only available after 2013 at NTUH-HC. After thorough review, we included confirmed cases of strongyloidiasis, which was defined by documentation of characteristic larvae in the clinical samples or in the tissues from biopsy or autopsy. Serological, antigenic, or molecular tests for diagnosis of *S. stercoralis* infection were unavailable during the study period. Unconfirmed cases and cases who were born outside of Taiwan were excluded. The study was approved by the Research Ethics Committees of the NTUH and NTUH-HC (registration numbers, 202110030RIND and 110-145-E, respectively) and was conducted in accordance with the approved ethical guidelines and regulations. The patient whose medical history was presented in detail in this study provided written informed consent.

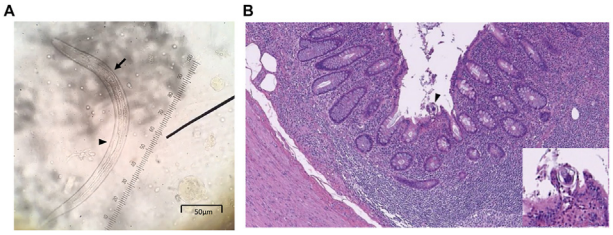


**Figure 1.** (A) A wet preparation of stool contained rhabditiform larvae of *Strongyloides stercoralis* with the characteristic short buccal canal, bulbous esophagus (arrow), and a prominent genital primordium (arrowhead). **(B)** Hematoxylin and eosin staining of an appendectomy specimen (x 400) shows dense inflammatory infiltrates involving the mucosa and submucosa, with prominent eosinophils. The crypt epithelium contains a cross-section of an adult *S. stercoralis* (arrowhead).

## Literature search

Literature search was carried out in Pubmed (https://pubmed.ncbi.nlm.nih.gov/), Google Scholar (https://scholar.google.com.tw/), and Index to Taiwan Periodical Literature System (https://tpl.ncl.edu.tw/NclService/) to identify cases of strongyloidiasis in Taiwan published from 1979 to 2020. The electronic literature search was updated until February 2021. Articles in English and Chinese languages were included. The following search terms were used: (strongyloides) OR (strongyloidiasis) AND (Taiwan). Articles were reviewed in two stages. In the first stage, articles were screened for eligibility by titles and abstracts. In the second stage, the full text of the eligible articles was reviewed and analyzed. Duplicate cases and imported cases were excluded, as the study was focused on autochthonous strongyloidiasis.

## Definitions

We defined *Strongyloides* hyperinfection syndrome as (1) the development or worsening of symptoms and signs attributable to increased larval migration, along with detection of increased numbers of larvae in stool and/or sputum specimens, or (2) the presence of concurrent bacteremia of enteric origin.[5,7,8] Disseminated strongyloidiasis was defined by the identification of larvae in the tissues other than the skin, lungs, and digestive tract.[5,7,8] Concurrent meningitis was defined if there was evidence of pleocytosis or elevated total protein in the CSF specimens examined.

We defined eosinophilia as an AEC of $\geq$500 cells/$\mu$L in the peripheral blood and used the AEC at the time closest to the time of initial presentation. If the patient had multiple hospitalizations, we used the data in the hospital stay during which the diagnosis of strongyloidiasis was made.

## Data collection and analysis

A standardized case report form was used to collect information on demographics, underlying medical conditions, symptomatology, laboratory findings, and outcome from each published case reports and from the medical records of NTUH and NTUH-HC. In the 2 case series, which included 27 and 41 cases, respectively, data in the individual patient level were not available, and cohort-level data were used instead. These data were pooled with categorical variables expressed as total counts and frequencies and continuous variables as means and standard deviations.

Differences in the clinical characteristics and outcomes between the patients with intestinal infection and those with hyperinfection or disseminated infection were compared using Fisher's exact test for categorical variables and two-sample t-test for continuous variables. Variables with a significant amount of missing data were excluded in this analysis. A $p$-value of $< 0.05$ was deemed statistically significant in this study.

## Results

### Data synthesis

From 1988 to 2020, 20 cases with confirmed strongyloidiasis were identified from the hospital databases, 18 at NTUH and 2 at NTUH-HC (Fig. 2). Through the literature search strategy, 2196 articles were identified and 2158 were excluded based on the evaluation of their titles and abstracts, resulting in 38 articles for review (Fig. 2). After excluding studies of foreign workers and duplicated cases, 30 articles were selected, including 28 case reports[9—29] and 2 case series,[30,31] yielding a total of 97 cases of autochthonous strongyloidiasis from the literature. These reports were published between 1988 and 2018. Combining the cases reported by us and those published in the literature, a total of 117 cases were included in this analysis.

### Clinical features

The mean age of the included cases was 64.2 years (range, 6—95 years) and 85 (73%) of them were male (Table 1). The cases were reported in different regions of Taiwan, with more cases being reported in eastern and southern Taiwan than northern and central Taiwan. Twenty-seven patients were indigenous Taiwanese, while only 4 patients had reported a travel history to either China or Thailand.

Steroid use (41%), alcoholism (36%), chronic liver disease (29%), and chronic obstructive pulmonary disease (COPD) or asthma (28%) were the most common underlying medical conditions. Important risk factors for severe strongyloidiasis, including transplantation and HTLV-1 infection, were uncommon in this report (bowel transplantation preceding the diagnosis of strongyloidiasis in 1 patient and HTLV-1 coinfection in the other). There were 2 patients with confirmed HIV infection. Only 45% of the included patients reported having engaged in soil-contact activities or walking barefoot.

Fever and dyspnea were the most common presentations of strongyloidiasis, which occurred in almost half of the included patients (Table 2). Classical symptoms associated with strongyloidiasis, including diarrhea, cough, and skin rashes, were seen in only 43%, 37%, and 18% of the patients, respectively. Leg edema and altered mental status were repeatedly reported in 20% and 17% of the patients, respectively. While anemia occurred in 70% of the patients, eosinophilia was present in only 48% at the time of presentation. Among patients with concurrent bacteremia, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus* spp., *Enterobacter cloacae*, and *Aeromonas* spp. were most commonly isolated (**S2 Table**). Most of the patients had the diagnosis of strongyloidiasis confirmed through stool examinations; and 14% and 6% had larvae identified in the sputum and bronchoalveolar lavage specimens, respectively.

### Disease spectrum and outcomes

*Strongyloides* hyperinfection syndrome or disseminated strongyloidiasis were diagnosed in 42 patients (36%). Among them, 4 patients (3%) had laboratory or pathologic evidence of disseminated strongyloidiasis. The foci of dissemination included heart and pericardial space, kidney, lymph nodes, thyroid gland, and parotid gland. In univariable analysis, being older and pre-existing COPD or asthma were associated with hyperinfection or dissemination ($p = 0.024$ and 0.003, respectively) (Table 3).

Concurrent meningitis was observed in 4 patients, all of whom presented with neurologic symptoms and CSF

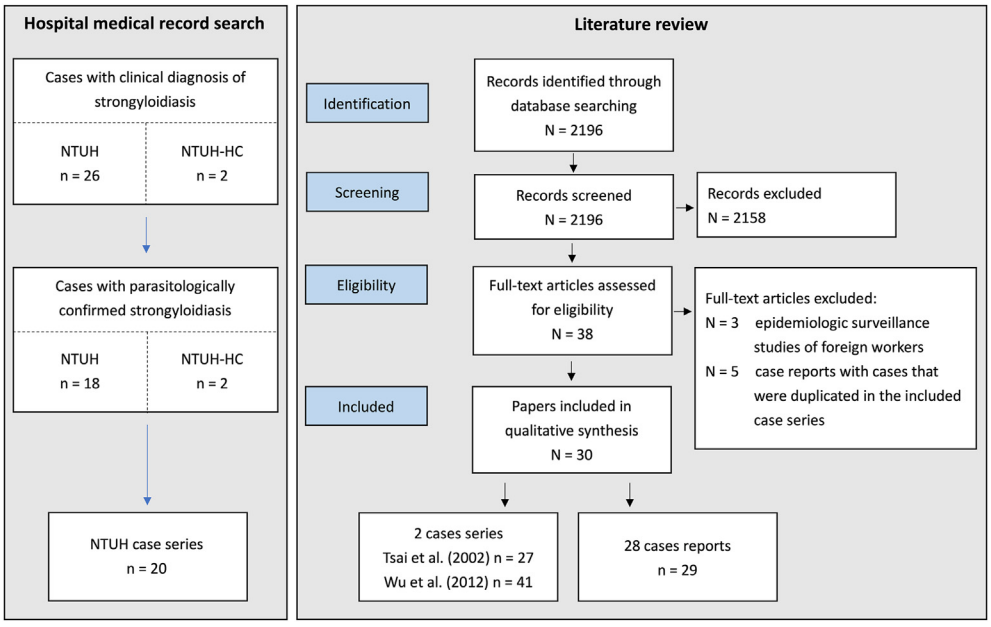


**Figure 2.** Case identification flow and PRISMA flow chart of data collection and selection of studies (capital N indicates the number of studies and lower case n indicates the number of cases) Abbreviations: NTUH, National Taiwan University Hospital; NTUH-HC, National Taiwan University Hospital, Hsin-Chu Branch.

**Table 1** Demographics and clinical characteristics of the 117 Taiwanese patients with strongyloidiasis.

| | Cases from NTUH and NTUH-HC[c] (N = 20) | Tsai et al. (N = 27) | Wu et al. (N = 41) | Individual case reports (N = 29) | Total (N = 117) |
|---|---|---|---|---|---|
| **Study period** | 1990–2020 | 1990–2001 | 1989–2009 | 1988–2018 | 1988–2020 |
| **Patient source** | Hospital case series | Hospital case series | Hospital case series | Case reports | |
| **Age, mean (± SD), years** | 64.7 (±14.6) | 66.3 (±17.6) | 62.3 (±13.7) | 64.6 (±16.8) | 64.2 (±15.6) |
| **Male sex, n (%)** | 14 (70) | 22 (81) | 27 (66) | 22 (76) | 85 (73) |
| **Geographic distribution[a], n (%)** | | | | | |
| Northern Taiwan | 15 | 0 | 0 | 11 | 26 (22) |
| Central Taiwan | 1 | 0 | 0 | 7 | 8 (7) |
| Southern Taiwan | 1 | 27 | 0 | 9 | 37 (32) |
| Eastern Taiwan | 3 | 0 | 41 | 2 | 46 (39) |
| **Ethnic group, n (%)** | | | | | |
| Indigenous Taiwanese[b] | 5 (25) | NA | 22 (54) | 1 (3) | 28/90 (31) |
| **Underlying medical conditions, n (%)** | | | | | |
| Steroid exposure | 7 (35) | 15 (56) | 13 (32) | 13 (45) | 48 (41) |
| Alcoholism | 9 (45) | NA | 22 (54) | 1 (3) | 32/90 (36) |
| Chronic liver disease | 7 (35) | 8 (30) | 13 (32) | 6 (21) | 34 (29) |
| COPD or asthma | 8 (40) | 9 (33) | 8 (20) | 8 (28) | 33 (28) |
| Diabetes mellitus | 5 (25) | 3 (11) | 8 (20) | 3 (10) | 19 (16) |
| Tuberculosis | 3 (15) | 4 (15) | 6 (15) | 0 (0) | 13 (11) |
| Malignancies | 4 (20) | 3 (11) | 2 (5) | 3 (10) | 12 (10) |
| **History of walking barefoot or engagement in soil-contact activities** | 8 (40) | NA | NA | 14 (48) | 22/49 (45) |

[a] The 4 regions of Taiwan were defined by: northern Taiwan (Taipei City, New Taipei City, Taoyuan City, Hsinchu City and County, Miaoli County, and Keelung City), central Taiwan (Taichung City, Changhua County, Yunlin County, Chiayi City and County, and Nantou County), southern Taiwan (Tainan City, Kaohsiung City, and Pingtung County), and eastern Taiwan (Yilan County, Hualien County, and Taitung County).

[b] Indigenous Taiwanese groups included Amis, Atayal, Truku, Bunon, Saisiyat, and others in this study.

[c] Cases from National Taiwan University Hospital (NTUH) and NTUH Hsin-Chu Branch (NTUH-HC) were included.

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; NA, not available.

**Table 2** Clinical and laboratory features of the 117 Taiwanese patients with strongyloidiasis.

| | Cases from NTUH and NTUH-HC[a] (N = 20) | Tsai et al. (N = 27) | Wu et al. (N = 41) | Individual case reports (N = 29) | Total (N = 117) |
|---|---|---|---|---|---|
| Clinical presentations, n (%) | | | | | |
| Gastrointestinal symptoms | | | | | |
| Diarrhea | 11 (55) | 20 (74) | 10 (24) | 9 (31) | 50 (43) |
| Abdominal pain | 5 (25) | 16 (59) | 18 (44) | 6 (21) | 45 (38) |
| Anorexia | 6 (30) | 5 (19) | 25 (61) | 8 (28) | 44 (38) |
| Abdominal distension | 5 (25) | 11 (41) | NA | 8 (28) | 24/76 (32) |
| Nausea/Vomiting | 7 (35) | 11 (41) | 16 (39) | 3 (10) | 37 (32) |
| Constipation | 1 (5) | 7 (26) | NA | 1 (3) | 9/76 (12) |
| Airway symptoms | | | | | |
| Dyspnea | 10 (50) | 11 (41) | NA | 15 (52) | 36/76 (47) |
| Cough | 10 (50) | 10 (37) | 11 (27) | 12 (41) | 43 (37) |
| Hemoptysis | 0 (0) | 1 (4) | NA | 2 (7) | 3/76 (4) |
| Dermatologic symptoms | | | | | |
| Skin rash or pruritus | 6 (30) | 4 (15) | NA | 4 (14) | 14/76 (18) |
| Other symptoms | | | | | |
| Fever | 8 (40) | 19 (70) | 14 (34) | 13 (45) | 54 (46) |
| Leg edema | 3 (15) | NA | NA | 7 (24) | 10/49 (20) |
| Altered mental status | 2 (10) | 3 (11) | NA | 8 (28) | 13/76 (17) |
| Interval from symptom onset to diagnosis, days, mean (±SD) | 46 (±40)[b] | 20 (±13)[c] | NA | 46 (±43)[d] | 36 (±33) |
| Hyperinfection or disseminated infection, n (%) | 7 (35) | 10 (37) | 4 (10) | 21 (72) | 42 (36) |
| Laboratory findings, n (%) | | | | | |
| Anemia or hemoglobin level <12 g/dL at presentation | 12 (60) | 18 (67) | 31 (76) | 13/18 (72) | 74/106 (70) |
| Eosinophilia or absolute eosinophil count >500 cells/μL at presentation | 9 (45) | 12 (44) | 24 (59) | 11 (38) | 56 (48) |
| Diagnostic methods, n (%) | | | | | |
| Stool microscopy | 20 (100) | 24 (89) | 37 (90) | 19 (66) | 100 (85) |
| Airway sample microscopy | | | | | |
| Sputum | 0 (0) | 5 (19) | 2 (5) | 9 (31) | 16 (14) |
| Bronchoscopic lavage | 0 (0) | NA | 1 (2) | 4 (14) | 5/88 (6) |
| Biopsy of the gastrointestinal tract | 1 (5) | 1 (4) | NA | 11 (38) | 13/76 (17) |
| Others | 0 (0) | 2 (7)[e] | 1 (2)[f] | 5 (17)[g] | 8 (7) |

[a] Cases from National Taiwan University Hospital (NTUH) and NTUH Hsin-Chu Branch (NTUH-HC) were included.
[b] Interval from symptom onset to diagnosis was obtained in 18 patients.
[c] Interval from symptom onset to diagnosis was obtained in 23 patients.
[d] Interval from symptom onset to diagnosis was obtained in 16 patients.
[e] Autopsies were performed in two patients: larvae were found in the lungs, the heart, the small and large intestine, the mesentery, the kidney, the thyroid, and the subcarinal lymph node in one patient, and in the intestinal tract and the lungs in the other patient.
[f] One patient had larvae in the pericardial effusion specimen.
[g] One had larvae in the parotid gland confirmed with biopsy; one had larvae in the urine specimen; two had larvae in the pleural effusion; one had larvae in ascites.
Abbreviations: NA, not available; SD, standard deviation.

**Table 3** Comparisons of characteristics between patients with intestinal strongyloidiasis and those with Strongyloides hyperinfection syndrome or disseminated strongyloidiasis.

| | Intestinal infection (N = 75) | Hyperinfection/disseminated infection (N = 42) | *p*-value |
|---|---|---|---|
| **Age, mean (± SD), years** | 62.0 (±16.8) | 68.1 (±11.9) | 0.024 |
| **Male sex, n (%)** [N = 90][a] | 38/58 (66) | 25/32 (78) | 0.239 |
| **Patient characteristics, n (%)** | | | |
| Steroid exposure | 26 (35) | 22 (52) | 0.078 |
| Chronic liver disease | 25 (33) | 9 (21) | 0.207 |
| COPD/Asthma | 14 (19) | 19 (45) | 0.003 |
| Diabetes Mellitus | 13 (17) | 6 (14) | 0.796 |
| Tuberculosis | 7 (9) | 6 (14) | 0.541 |
| Malignancy | 7 (9) | 5 (12) | 0.754 |
| **Treatment, n (%)** [N = 114][b] | | | |
| Ivermectin-containing | 22/74 (30) | 12/40 (30) | >0.999 |
| Non-ivermectin-containing[c] | 52/74 (70) | 28/40 (70) | |
| **Outcome, n (%)** | | | |
| ICU admission [N = 49][d] | 2/21 (10) | 12/28 (43) | 0.013 |
| Mortality | 6 (8) | 18 (43) | <0.001 |

[a] Details on sex of patients with or without hyperinfection/disseminated infection were not provided in one case series.
[b] Two patients died before treatment and 1 patient had no treatment documented in the medical record.
[c] Non-ivermectin-containing antiparasitic agents Including mebendazole, albendazole, thiabendazole, and pyrantel embonate.
[d] Data unavailable from the 2 case series.
AbbreviationsCOPDChronic obstructive pulmonary diseaseSDStandard deviation.

findings compatible with acute meningitis, while no pathogens were isolated from the cultures of CSF specimens (Table 4). All 4 patients experienced respiratory failure and prolonged hospital course. Of note, two of them developed symptoms of meningitis during the hospital stay, after exposure to increased doses of steroids.

ICU admission was not uncommon (14/49, 29%) and the overall mortality rate was 21%. Hyperinfection or disseminated infection carried a significantly higher mortality, with the rate as high as 43% ($p$ <0.001).

## Discussion

In this study, we described a 56-year-old man with chronic strongyloidiasis, previously undiagnosed despite multiple hospitalizations over the course of more than 10 years and eventually led to meningoencephalitis, bacteremia, respiratory failure, prolonged hospitalization, and permanent disabilities. Including our case series and other published cases, a total of 117 cases from different regions in Taiwan were identified during the 33-year study period. Clinical presentations were non-specific but complicated, diagnosis was commonly delayed, and the mortality rate was high. Our findings provide the most comprehensive update on strongyloidiasis in Taiwan.

The diagnosis of strongyloidiasis has been challenging for several reasons. Most patients with strongyloidiasis are asymptomatic,[3] and, when the symptoms do appear, they are generally non-specific.[32,33] In this study that consisted of more than one-third of patients with hyperinfection, the classic gastrointestinal, respiratory, and dermatologic symptoms occurred in only a minority of the cases. Moreover, soil-contact history as an important clinical information is usually remote and difficult to recall in chronic strongyloidiasis. As shown in our study, less than 50% of the patients were able to provide such information. Although peripheral eosinophilia may provide a helpful clue in the diagnosis of parasitic infection, it is not a universal feature in strongyloidiasis.[2,3] In those with hyperinfection, the sensitivity of peripheral eosinophilia is especially low.[34] Only 48% of the patients in our study had eosinophilia at the time of presentation. The case presented in this study also highlights that peripheral eosinophil count could be affected by the state of hyperinfection, superimposed bacterial infections, and the administration of corticosteroids.

The presence of *S. gallolyticus* bacteremia raised the suspicion of strongyloidiasis in our case. In a Dutch cohort, *S. gallolyticus* was an uncommon cause of bacterial meningitis, and, among 34 patients with *S. gallolyticus* meningitis in the literature, 14 (41%) were found to have co-infection with *S. stercoralis*.[35] Translocation of enteric bacteria, either carried by migrating larvae or through damaged mucosal barrier, into the blood stream and to other body parts can develop in patients with *Strongyloides* hyperinfection syndrome.[7] In another review, among 133 patients with *Strongyloides* hyperinfection syndrome, concomitant bacterial infections were common, including 25.6% with bacteremia, 17.3% with pneumonia, and 10.5% with meningitis.[34] Similar to our findings, most of the bacteria implicated in these co-infections were *Enterobactericeae*, while enterococci, streptococci, and *P. aeruginosa* were also commonly found. These findings suggest that, in patients with bacteremia due to enteric pathogens, screening for strongyloidiasis should be considered.

In our cohort, the proportion of hyperinfection or disseminated infection was 36% and almost half of the

**Table 4** Summary of 4 patients with strongyloidiasis and concurrent meningitis.

| | Chiu et al. 2005 | Liu et al. 2009 | Hu et al. 2011 | Our case |
|---|---|---|---|---|
| Age, years | 60 | 76 | 73 | 56 |
| Sex | Male | Male | Male | Male |
| Characteristics | Indigenous Taiwanese, alcoholism, gastrectomy | Soldier, COPD | Farmer, COPD, DM | Indigenous Taiwanese, alcoholism, DM |
| Timing of diagnosis of meningitis | At initial presentation | During hospital stay | During hospital stay | At initial presentation |
| History of steroid exposure | − | + | + | + |
| Leukocytosis at initial evaluation | + | + | + | − |
| Eosinophilia at initial evaluation | − | − | − | − |
| Respiratory failure | + | + | + | + |
| From admission to diagnosis of strongyloidiasis | 16 days | 7 days | NA | 32 days |
| Samples with documented larvae of *Strongyloides stercoralis* | Stool | Stool and sputum | Stool and sputum | Stool and biopsy of the appendix |
| CSF findings | | | | |
| Glucose (mg/dL) | 38 | 45 | 139.4 | 96 (blood glucose 238) |
| Protein (mg/dL) | 519 | 220 | 26.96 | 664 |
| WBC (cells/μL) | 2490 | 360 | 20 | 10,065 |
| Neutrophil (%) | 64 | 66 | 0 | 89 |
| Lymphocyte (%) | 20 | 34 | 98 | 11 |
| Monocyte (%) | 16 | NA | NA | NA |
| Bacteria isolated from the CSF | No | No | No | No |
| Concurrent bacteremia or fungemia | No | No | *Trichosporon asahii* | *Streptococcus gallolyticus* |
| Anthelmintics | Albendazole | Albendazole | Ivermectin | Ivermectin |
| Outcome | Expired | Expired | Cured | Cured |

AbbreviationsCOPDchronic obstructive pulmonary diseaseCSFcerebrospinal fluidDMdiabetes mellitusNAnot availableWBCwhite blood cell count.

included patients presented with fever, and almost 20% had altered mental status at the time of presentation. On the contrary, in a large retrospective Spanish cohort of immigrants and returning travelers, the proportions of patients with hyperinfection and fever were only 0.4% and 2.7%, respectively.[3] These discrepancies could partly be explained by the fact that patients included in our review in Taiwan were older (mean age 64 years vs. 38 years) and had more immunocompromising conditions. Reporting bias and significant under-diagnosis of strongyloidiasis in Taiwan were also likely contributory. While serologic tests are employed as part of routine screening and diagnosis of strongyloidiasis in some parts of the world,[3,32,36] the diagnosis of strongyloidiasis in Taiwan relies mostly on microscopic examination, which has notoriously low sensitivity, especially in patients with a low parasitic burden.[32] In order to diagnose strongyloidiasis early and to reduce the risk of its complications, higher clinical vigilance and better diagnostic tools are apparently needed.

Screening for *S. stercoralis* infection has been recommended in transplant recipient candidates to prevent severe complications of hyperinfection after transplantation.[37] In the era of COVID-19 pandemic, cases of hyperinfection and disseminated infection after corticosteroid exposure have been reported.[38] Screening algorithms before the use of corticosteroids are proposed to prevent complications from strongyloidiasis.[39,40] For example, in non-endemic countries such as Italy, it was recommended that serologic screening for strongyloidiasis be performed on intermediate-risk subjects before starting immunosuppressive agents, such as patients 65 years or older.[39] Similar approaches could be adopted in Taiwan after taking local prevalence and risk factors into consideration. Other than the classic immunocompromising conditions known to be associated with severe strongyloidiasis, the findings of previous case series in Taiwan suggest that aboriginal ethnic group and those with alcoholism may also be at risk of severe strongyloidiasis.[30] In the present study, it was estimated that 80% of the patients with strongyloidiasis were 50 years or older and a history of COPD or asthma was associated with hyperinfection or disseminated infection. Further studies focusing on local epidemiology are critical for informing appropriate risk factors of strongyloidiasis in Taiwan and for cost-effective screening.

This study summarized the current understandings of the epidemiologic and clinical features of strongyloidiasis in Taiwan. Because of the limitations of the study, including small case number, frequent missing data, the publication bias, and the heterogeneity of the data source, the findings should be interpreted with cautions. A larger, prospectively designed study is needed to verify these findings.

In conclusion, strongyloidiasis is still seen in different parts of Taiwan and *Strongyloides* hyperinfection syndrome and disseminated strongyloidiasis can cause serious

complications and mortality, probably due to delayed recognition and diagnosis. Efforts to detect and diagnose strongyloidiasis early are urgently needed to improve the outcome of strongyloidiasis in Taiwan.

## Funding

This study was supported by grants from National Taiwan University Hospital, Hsin-Chu Branch (grant number 110HCH-004 and 111HCH-002 to S.-H. H.). The funding source had no role in study design and conduct; data collection, analysis, or interpretation; or in the writing of the manuscript or the decision to submit it for publication.

## Declaration of competing interest

The authors had no competing interest that could be construed to have influenced the work.

## Acknowledgements

The authors would like to thank Prof. Aristine Cheng for her assistance in English editing of the manuscript and Prof. Min-Tsun Liao and Dr. Chieh Chiang for their advice on the statistical analysis. We also want to thank the Medical Records Departments at the National Taiwan University Hospital and National Taiwan University Hospital Hsin-Chu Branch for supporting the data collection, and Miss Chi-Wei Tseng and Miss Wen-Chun Liu for assisting the administrative work.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2022.06.007.