

# Unexplained Iron-Deficiency Anemia Attributable To Hookworm Infection: A Decade of Case Reports In Asia

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## ABSTRACT

Iron-deficiency anemia (IDA) remains a major public health concern, with hookworm infection a significant yet often overlooked contributor, particularly in Asia. Hookworms (*Ancylostoma duodenale*, *Necator americanus*, and *Ancylostoma ceylanicum*) cause chronic intestinal blood loss, leading to progressive microcytic anemia, fatigue, and pallor. Susceptible populations include children, the elderly, and individuals with comorbidities or nutritional deficiencies. Diagnosis is challenging due to nonspecific symptoms and low sensitivity of routine stool microscopy, often resulting in misdiagnosis as nutritional anemia or other chronic conditions. Case reports highlight the utility of endoscopy and molecular assays in detecting low-burden or occult infections. Treatment with anthelmintics, iron supplementation, transfusion, and nutritional support results in favorable hematological recovery. This scoping review maps published case reports in Asia (2015–2025), summarizing patient characteristics, diagnostic approaches, species identified, and treatment outcomes. Findings emphasize the need for heightened clinical awareness, comprehensive diagnostic strategies, and preventive measures to reduce the burden of hookworm-associated anemia.

**KEYWORDS:** Hookworm, Iron-Deficiency Anemia, *Ancylostoma*, *Necator*, Asia.

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## INTRODUCTION

Iron-deficiency anemia (IDA) remains one of the most common hematologic disorders worldwide and is a major public health concern in many low- and middle-income countries. While nutritional deficiency and chronic blood loss are widely recognized causes, parasitic infections, particularly hookworm, continue to contribute significantly to the burden of anemia in endemic regions. Hookworms, primarily *Ancylostoma duodenale* and *Necator americanus*, infect approximately 400 to 500 million people globally, with the highest prevalence in tropical and subtropical regions of Asia, Africa, and Latin America.

Hookworm infection causes chronic intestinal blood loss due to the parasite's attachment to the mucosa of the small intestine, resulting in iron depletion and progressive anemia. In endemic areas, the condition may remain asymptomatic for long periods or manifest with non-specific symptoms such as fatigue, weakness, and pallor. Consequently, hookworm infection is frequently overlooked as a potential etiology of unexplained iron-deficiency anemia, particularly in clinical settings where routine stool examination is not consistently performed or when patients present with atypical symptoms.

Several case reports in recent years have documented instances where hookworm infection was initially misdiagnosed as nutritional anemia, gastrointestinal disease, or other chronic conditions. In some cases, the diagnosis was only established after endoscopic visualization of worms in the duodenum or repeated parasitological examinations. These reports highlight persistent diagnostic challenges and emphasize the need for greater clinical awareness of parasitic etiologies in cases of unexplained anemia.

Given the increasing recognition of such diagnostic pitfalls, a synthesis of published case reports is warranted. This scoping review aims to map the available evidence on hookworm infections presenting as unexplained iron-deficiency anemia in Asia between 2015 and 2025. Specifically, the review seeks to summarize patient characteristics, diagnostic approaches, misdiagnosis patterns, and treatment outcomes reported in the literature.

## METHODS

### 2.1. Research Design

This study was conducted as a scoping review following the methodological framework proposed by Arksey and O'Malley (2005) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. The review aimed to map the available literature on hookworm infection presenting as unexplained iron-deficiency anemia in Asia.

### 2.2. Search strategy

A comprehensive literature search was performed across multiple electronic databases, including PubMed/MEDLINE, Scopus, Google Scholar, and Web of Science. The search included studies published between January 2015 and March 2025. To identify relevant articles, a combination of keywords and Boolean operators was used. The search terms included "hookworm," "*Ancylostoma duodenale*," "*Necator americanus*," "iron deficiency anemia," "microcytic anemia," "case report," and "Asia." These terms were combined using Boolean operators to refine the search strategy as follows: ("*hookworm*" OR "*Ancylostoma*

*duodenale*” OR “*Necator americanus*”) AND (“iron deficiency anemia”) AND (“case report”) AND (“Asia”). Reference lists of relevant articles were also manually screened to identify additional eligible studies.

### 2.3. Inclusion criteria

Studies were included if they met the following criteria: (1) published between 2015 and 2025, (2) conducted in Asian countries, (3) reported case reports or case series describing hookworm infection, (4) involved patients presenting with iron-deficiency anemia or unexplained anemia, and (5) had full texts available in English. Studies were excluded if they were epidemiological prevalence studies without detailed clinical case descriptions, animal studies, review articles, editorials, or conference abstracts without primary patient data, or if anemia was not described as a clinical presentation.

### 2.3. Data extraction

Data from the included studies were extracted and organized using a standardized data collection form. The extracted information included author(s) and year of publication, country of origin, patient demographics (age and sex), initial clinical presentation or misdiagnosis, diagnostic methods used, hookworm species identified, treatment administered, and reported clinical outcomes. The extracted data were subsequently synthesized narratively to summarize patterns in clinical presentation, diagnostic approaches, and treatment outcomes among the reported cases.

## RESULTS AND DISCUSSION

### 3.1. Overview of Included Studies

The included studies highlight the burden of hookworm infection as a significant cause of severe anemia across a broad age spectrum, from infants to elderly individuals, in regions including China, Japan, India, and Indonesia (Bao et al., 2025; Singh et al., 2023; Purwanto & Tuda, 2025; Yoshikawa et al., 2018). Susceptible populations, such as young children, elderly patients, and those with comorbidities or nutritional deficiencies, are particularly prone to severe manifestations due to increased vulnerability to chronic intestinal blood loss and impaired hematopoietic recovery (Hotez et al., 2004). Travel and occupational exposure, particularly in endemic rural or agricultural settings, further increase risk, as infective larvae penetrate the skin during barefoot contact with contaminated soil (Jourdan et al., 2018). Epidemiologically, hookworm prevalence is influenced by poor sanitation, soil type, climatic conditions favoring larval survival, and socioeconomic factors, which collectively facilitate transmission and sustained infection cycles (Bethony et al., 2006). Notably, travelers and migrants from endemic areas may present with severe anemia due to delayed recognition, highlighting the importance of epidemiological history in clinical assessment (Yoshikawa et al., 2018).

### 3.2. Clinical Presentation and Misdiagnosis

Hookworm infections predominantly present with chronic microcytic hypochromic anemia, fatigue, pallor, and gastrointestinal disturbances such as abdominal pain, diarrhea, vomiting, and occasional hematemesis (Bao et al., 2025; Singh et al., 2023). Severe iron-deficiency anemia is often observed, with hemoglobin levels as low as 2.1 g/dL in infants and 3.3–4.3 g/dL in adults, resulting from chronic intestinal blood loss caused by adult hookworms feeding on mucosal capillaries (Hotez et al., 2004; Wu et al., 2016). Persistent anemia can lead to growth retardation in children, cardiac strain in elderly patients, and long-term neurocognitive deficits if untreated (Bethony et al., 2006). Misdiagnoses are common and include chronic anemia of unknown origin (Purwanto & Tuda, 2025; Bao et al., 2025), chronic kidney disease–related anemia (Wu et al., 2016; Shou et al., 2016), travel-related gastrointestinal infections (Yoshikawa et al., 2018), and nutritional anemia in children (Singh et al., 2023). These misclassifications underscore the nonspecific nature of hookworm infection, particularly in low-intensity or chronic cases, and illustrate the limitations of relying solely on clinical presentation and routine stool microscopy (Jourdan et al., 2018).

### 3.3. Diagnostic Approaches

Effective diagnosis of hookworm infection requires a combination of conventional parasitological methods, endoscopic visualization, and molecular techniques. Stool microscopy remains the standard for detecting eggs, employing wet mount, formalin-ethyl ether sedimentation, Harada-Mori culture, and flotation methods; however, sensitivity is often reduced in low-burden or chronic infections (Jourdan et al., 2018; Yoshikawa et al., 2018). Endoscopic procedures, including gastroscopy, capsule endoscopy, and double-balloon enteroscopy, allow direct visualization and removal of adult worms, especially when stool examinations yield negative results (Bao et al., 2025; Zhao et al., 2021). Molecular techniques, such as PCR targeting mitochondrial *cox1* or ribosomal ITS genes, provide species-level confirmation and can detect occult infections that may otherwise go unrecognized (Yoshikawa et al., 2018). Combining parasitological, endoscopic, and molecular approaches improves diagnostic accuracy, particularly in regions with low endemicity or among travelers and immunocompromised hosts.

### 3.4. Species Identified

The studies reviewed demonstrate diversity in hookworm species infecting humans. *Ancylostoma ceylanicum* was reported among Japanese travelers returning from Southeast Asia, reflecting its zoonotic potential (Yoshikawa et al., 2018). *Ancylostoma duodenale* was predominantly identified in adults with chronic anemia in China and India (Bao et al., 2025; Zhao et al., 2021), whereas unspecified hookworm species were found in pediatric and rural adult populations in Indonesia and India (Singh et al., 2023; Purwanto & Tuda, 2025; Kateshiya et al., 2024). Clinical severity correlates with worm burden, host age, nutritional status, and species-specific blood-feeding behavior. Zoonotic species may present asymptotically or with milder disease in adults but can cause significant anemia in children due to limited iron stores (Hotez et al., 2004; Bethony et al., 2006).

### 3.5. Treatment and Outcomes

Treatment of hookworm infection in the reviewed cases involved a combination of anthelmintic therapy and supportive care. Albendazole, administered as a single 400 mg dose or over multiple days, was the most frequently used agent, whereas pyrantel pamoate was applied in *A. ceylanicum* infections (Yoshikawa et al., 2018). Supportive management included packed red blood cell transfusions, oral or intravenous iron supplementation, albumin for hypoalbuminemia, and nutritional rehabilitation for children with severe acute malnutrition (Singh et al., 2023; Wu et al., 2016). Hematological outcomes were favorable, with rapid improvement in hemoglobin and hematocrit, resolution of fatigue and pallor, and recovery of growth parameters in pediatric patients. These findings reinforce the efficacy of integrated anthelmintic and supportive therapy for reversing hookworm-induced anemia. Persistent anemia with negative stool microscopy, eosinophilia, or positive fecal occult blood should prompt endoscopic evaluation to detect adult worms (Hotez et al., 2004; Jourdan et al., 2018).

## CONCLUSION

Hookworm infection remains a critical, yet often underrecognized, cause of severe iron-deficiency anemia worldwide, particularly among children, elderly, and nutritionally vulnerable populations. Nonspecific clinical presentation and low diagnostic sensitivity of stool microscopy frequently lead to misdiagnosis. Comprehensive diagnostic strategies, including endoscopy and molecular assays, are essential for accurate detection, especially in chronic or low-burden infections. Prompt administration of anthelmintics, coupled with iron supplementation, transfusion support, and nutritional rehabilitation, leads to substantial hematological recovery and symptom resolution. These findings underscore the need for heightened clinical awareness, targeted screening in endemic regions, and preventive strategies including improved sanitation and public health education to reduce the burden of hookworm-associated anemia.

### Conflict of Interest

The authors hereby confirm that they have no financial, personal, or professional conflicts of interest that could have influenced the work reported in the manuscript.

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Year	Authors	Country / Setting	Patient Details	Clinical Presentation / Initial Misdiagnosis	Diagnostic Method	Hookworm Species Identified	Treatment	Outcome
2025	Bao et al.	China	60-year-old female who has been living in rural Sichuan, where she had received multiple red blood cell transfusions at a local hospital for persistent anemia	iron deficiency anemia for 6 months, fatigue, malaise, loss of appetite; multiple RBC transfusions prior; stool microscopy negative; positive fecal occult blood	Gastroscopy and colonoscopy; worms visualized in pyloric ring, antrum, and duodenum; morphological examination	<i>Ancylostoma duodenale</i>	Biopsy forceps removal of worms; single 400 mg albendazole dose; supportive care	Hemoglobin improved to 85 g/L at discharge and normalized to 126 g/L after 3 months

Year	Authors	Country / Setting	Patient Details	Clinical Presentation / Initial Misdiagnosis	Diagnostic Method	Hookworm Species Identified	Treatment	Outcome
2023	Singh <i>et al.</i>	India	3-year-old female	progressive pallor for 3 months, generalized body swelling, watery diarrhea with blood/mucus; severe microcytic hypochromic anemia, hypoalbuminemia, and severe acute malnutrition	Upper GI endoscopy showing adult worms in duodenum; duodenal aspirate and stool microscopy showing hookworm eggs	Adult female Hookworm spp. (not specified)	PRBC transfusion (2 units), albendazole 400 mg single dose, albumin injections, nutritional rehabilitation (F75 → F100 diet)	Hemoglobin improved to 8.5 g/dL post-transfusion; edema reduced; nutritional status improved; patient stabilized
2025	Purwanto and Tuda	Indonesia	Case 1: 72-year-old female living in a coastal rural area of North Sulawesi	severe iron-deficiency anemia, fatigue, shortness of breath; initially considered chronic anemia of unknown origin	Stool microscopy (direct wet mount with eosin stain); parasitological confirmation of hookworm eggs	Hookworm spp. (not specified)	Albendazole 400 mg daily × 3 days + oral ferrous sulfate 325 mg TID + 2 units packed RBC transfusion	Hemoglobin improved from 4.3 g/dL to 7.0 g/dL at 2 weeks; symptoms resolved; patient recovered
			Case 2: 1-year-old male infant with progressively worsening condition over the past two weeks	severe pallor, lethargy, poor feeding, and critical microcytic hypochromic anemia; initially considered nutritional anemia	Stool microscopy showing hookworm eggs in 6-cell cleavage stage	Hookworm spp. (not specified)	Urgent packed RBC transfusion + oral ferrous sulfate 6 mg/kg/day + albendazole 200 mg single dose	Hemoglobin improved from 2.1 g/dL to 10.2 g/dL in 3 days; clinical symptoms improved; infant recovered
2025	Si <i>et al.</i>	China	60-year-old female who had received multiple red blood cell transfusions at a local hospital for persistent anemia	severe iron-deficiency anemia, fatigue, malaise, and loss of appetite; initially treated with multiple RBC transfusions for unknown cause	<i>Gastroscopy and colonoscopy; worms removed via biopsy forceps; morphological identification</i>	<i>Ancylostoma duodenale</i>	Single dose Albendazole 400 mg + hematinics	Hemoglobin improved from 38 g/L to 126 g/L over 3 months; patient recovered
2016	Shou <i>et al.</i>	China	70-year-old farmer undergoing peritoneal dialysis	chronic renal anemia, fatigue, hematemesis; initially managed as CKD-related anemia unresponsive to iron and erythropoietin	Upper endoscopy showing numerous actively feeding hookworms in duodenum	Hookworm spp. (not specified)	Albendazole 200 mg orally 3×/day for 1 month + iron and erythropoietin supplementation	Hemoglobin rose to 98 g/L; stool negative for eggs; patient recovered
2018	Yoshikawa <i>et al.</i>	Japan	Case 1: 25-year-old male who stayed in a rainforest in Malaysia for 4 weeks	abdominal pain, watery diarrhea, eosinophilia; initially considered general travel-related GI infection	Stool microscopy (formalin-ethyl ether sedimentation), Harada-Mori larval culture, adult worm	<i>Ancylostoma ceylanicum</i>	Single dose Pyrantel pamoate 10 mg/kg	Eleven adult worms expelled; symptoms resolved; eosinophilia improved

Year	Authors	Country / Setting	Patient Details	Clinical Presentation / Initial Misdiagnosis	Diagnostic Method	Hookworm Species Identified	Treatment	Outcome
					morphology, PCR of cox1 gene			
			Case 2: 26-year-old male who spent 2 years as an overseas cooperation volunteer for agriculture in Papua New Guinea.	asymptomatic but with mild eosinophilia during medical check-up; initially no clinical suspicion	Stool microscopy, floatation method, PCR of ITS-1, ITS-2, and cox1 genes	<i>Ancylostoma ceylanicum</i>	Pyrantel pamoate	Eggs cleared from feces; eosinophil count normalized; patient remained asymptomatic
			Case 3: 47-year-old male who spent 1 month in a rural village in Lao People's Democratic Republic	abdominal pain, watery diarrhea, eosinophilia; initially considered general travel-related GI infection	Stool microscopy (formalin-ethyl ether sedimentation), Harada-Mori larval culture, capsule and double-balloon enteroscopy, PCR of cox1 gene	<i>Ancylostoma ceylanicum</i>	Pyrantel pamoate; adult worms removed via enteroscopy	Symptoms resolved; additional worms expelled in feces; eosinophilia normalized
			Case 4: 27-year-old male who participated in group travel to India for 5 days	abdominal pain, watery diarrhea; initially considered general travel-related GI infection	Stool microscopy, Harada-Mori larval culture, PCR of cox1 gene	<i>Ancylostoma ceylanicum</i>	Albendazole 400 mg/day for 7 days	Eggs cleared from feces; eosinophil count normalized; symptoms resolved
2024	Kateshiya <i>et al.</i>	India	36-years-old male with no history of travel	Severe anemia (Hb 3.3 g/dL), generalized weakness, pallor, eosinophilia; initially treated empirically for abdominal pain and suspected bacterial infection	Stool microscopy showing characteristic hookworm eggs (8-blastomere, thin shell)	Hookworm spp. (not specified)	Albendazole 400 mg every 12 hrs × 2 days + 4 units blood transfusion + IV ferric carboxymaltose and multivitamins	Hemoglobin improved; patient stabilized; symptoms resolved
2016	Wu <i>et al.</i>	China	70-year-old male CKD patient	chest tightness, shortness of breath, both lower extremities edema, chronic renal anemia, fatigue, hematemesis; initially managed for CKD-related anemia unresponsive to iron and erythropoietin	Upper endoscopy showing numerous actively feeding hookworms in duodenum	Hookworm spp. (not specified)	Albendazole 200 mg orally 3×/day for 1 month + iron and erythropoietin	Hemoglobin increased to 98 g/L; stool tests negative; patient recovered
2021	Zhao <i>et al.</i>	China	35-year-old female with no history of travel	Fatigue, weight loss, chronic anemia	Gastroscopy; biopsy of gastric parasite	<i>Ancylostoma duodenale</i>	Albendazole 400 mg single	Clinical improvement

Year	Authors	Country / Setting	Patient Details	Clinical Presentation / Initial Misdiagnosis	Diagnostic Method	Hookworm Species Identified	Treatment	Outcome
				unresponsive to iron; initially suspected gastric tumor or digestive disease			dose + parasite removal	following therapy