Review Paper

Parasitological, Immunological, and Molecular Methods in Diagnosis of Human *Strongyloidiasis*

Zohreh Fakhrie-Kashan[1], *Meysam Sharifdini[2]

1. Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Medical Parasitology and Mycology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.

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ABSTRACT

Strongyloidiasis is caused by intestinal nematode called *Strongyloides stercoralis (S. stercoralis)* which can lead to hyperinfection syndrome and disseminated infections. If not diagnosed and properly treated, it can even lead to death. The sensitivity of parasitological methods is not high enough and multiple stool sampling over consecutive days is essential to improve the detection rate. The agar plate culture method is more sensitive to the detection of *S. stercoralis* in fecal samples than other parasitological techniques. Serological tests have demonstrated higher sensitivity, but they have low specificity because of cross-reactivity with other helminthes. Moreover, they are not helpful for follow-up of treatment, because they cannot distinguish between new and old infections. Recently, some Polymerase Chain Reaction (PCR)-based techniques have been developed for detection of *S. stercoralis* with high sensitivity and specificity. These methods are rapid but expensive and need well-equipped laboratories. In this paper, conventional and novel methods for laboratory diagnosis of *strongyloidiasis* are reviewed.

Extended Abstract

1. Introduction

Strongyloidiasis caused by intestinal nematode called *Strongyloides stercoralis* which is one of the most important neglected soil-transmitted helminth infections. This nematode is mostly found in tropical and temperate countries with poor sanitation standards; however, it has been increasing in non-endemic countries due to migration and travel [1]. The clinical presentation of *strongyloidiasis* is variable from asymptomatic infections to gastrointestinal, cutaneous, or pulmonary manifestations [1]. In immune-suppressed patients, chronic *strongyloidiasis* may lead to hyperinfection syndrome or disseminated infections [2]. With the increasing number of immunocompromised patients in the last decade, severe complicated *strongyloidiasis* has become a major health problem to such patients [2]. There is no definitive gold standard for the diagnosis of *strongyloidiasis* [3]. Therefore, reliable diagnostic techniques are needed for this purpose in at-risk people in order to decrease the mortality and morbidity rate. The aim of this study was to review the parasitological, immunological and molecular methods developed for the diagnosis of *strongyloidiasis*.

2. Materials and Methods

The search was conducted in a number of valid databases including PubMed, ScienceDirect, Scopus, Iran-

* *Corresponding Author:*
Meysam Sharifdini
Address: Department of Medical Parasitology and Mycology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.
Tel: +98 (13) 33690884
E-Mail: sharifdini@gums.ac.ir

Medex, and Google Scholar. A total of 63 relevant papers were selected for review.

3. Results

Many parasitological methods usually rely on the detection of larvae in stool samples, such as formalin ether concentration, Baermann apparatus, Harada-Mori culture, and nutrient agar plate culture [4]. Most of parasitological techniques are insensitive, because the release of larvae is usually low and irregular in fecal samples especially in chronic infections [1]. Several studies have shown that agar plate culture is more sensitive than other techniques in the detection of *S. stercoralis* larva in fecal samples [5-7]. However, this technique is labor-intensive and time-consuming and requires multiple fresh stool samples and skillful individuals [4, 5].

Several immunological methods such as indirect agglutination test, Enzyme-Linked Immunosorbent Assay (ELISA), Indirect Immunofluorescence Assay (IFA), and dipstick test have been developed with different sensitivity and specificity depending on the used antigen and immunoglobulin isotopes [8-10]. Overall, immunodiagnostic methods have higher sensitivity than conventional parasitological methods [11]. The gelatin particle indirect agglutination test is a simple, rapid, and sensitive method with no need for any specialized equipment. This method is useful for the mass-screening of *strongyloidiasis* [12]. The IFA test is useful for the diagnosis of *strongyloidiasis* by detecting antibody in the serum of patients; however, there are some difficulties in obtaining *S. stercoralis* antigens in addition to the risk of contamination, but using other species of Strongyloides can be helpful for immunological diagnosis [11]. This technique has high sensitivity and specificity with minimal cross-reactivity with other helminthic infections. It has the advantage of determining antibody titers that can help in following up on treatment process. Another use of this technique is in epidemiological studies among at-risk people in endemic areas [11].

The ELISA method is extremely useful and considered to be superior to other serological tests regarding its high level of sensitivity for the diagnosis of *strongyloidiasis*. This technique has been widely used for the diagnosis of *S. stercoralis* infection worldwide, but one of its important disadvantages is the possibility of immunological cross-reactivity with other helminthic infections [11, 13]. A major drawback to ELISA-based diagnosis is a reliance on crude extract antigen preparation which is time-consuming and needs larvae extraction from humans or experimental animals. IgG avidity ELISA can be useful in differentiating chronic infections from acute, past, and present infections. Another important advantage of this technique is its application in monitoring the reduction of antibody titers after treatment [11, 13]. Van Doorn et al. (2007) showed that dipstick assay has a high level of accuracy for the diagnosis of *strongyloidiasis*, and has important features such as practicality, simplicity and using a small number of antigens [14].

Molecular methods have shown different results in detection of *S. stercoralis* DNA in stool samples. The method of DNA extraction is an important key factor for increasing the sensitivity of DNA-based techniques [11]. In a study carried out by Repetto et al. (2013), an In-House DNA extraction method based on efficient lysis of larvae and removal of inhibitors in the stool samples was introduced [15]. Moghaddassani et al. (2011) developed single and nested Polymerase Chain Reaction (PCR) methods for specific detection of *S. stercoralis* DNA in stool samples but sensitivity of the single PCR was higher than that of nested PCR [16]. Among DNA-based techniques, real-time PCR targeting the 18S ribosomal RNA gene of *S. stercoralis* described by Verweij et al. (2009) has been shown to be a sensitive and specific method [17]. Sharifdini et al (2015) tested both nested and real-time PCR in comparison with parasitological methods (agar plate culture and formalin ether concentration) for the detection of *S. stercoralis* in fecal samples. In their study, molecular methods were superior to parasitological methods and nested PCR was more sensitive than real-time PCR [7]. Recently, Lodh et al. (2017) showed that DNA amplification from urine is significantly more sensitive than stool examination techniques [18].

4. Discussion

Human *strongyloidiasis* is a major neglected intestinal helminthiasis which is considered as an important cause of morbidity and mortality in immunocompromised patients. Therefore, early diagnosis and treatment of *S. stercoralis* infection, when it is still in the chronic phase, is necessary [1]. Parasitological methods are not sufficiently sensitive to detect *strongyloidiasis* due to the irregular release of larvae in feces [1]. The agar plate culture has been recognized as a more sensitive method than other parasitological techniques [5, 6]. Immunodiagnostic methods have demonstrated higher sensitivity and lower specificity, because of cross-reactivity with other helminthic infections. They are useful for screening the high-risk patients but not helpful for the follow-up of treatment [11]. Recently, molecular techniques have been developed for the detection of *S. stercoralis* with high sensitivity and specificity. These methods are rapid but expensive and need well-equipped laboratories [13].

Ethical Considerations

Compliance with ethical guidelines

This is a review study. No experiments were conducted on human or animal samples.

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Authors' contributions

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Conflicts of interest

The authors declared no conflicts of interest.

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