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REVIEW ARTICLE

A review on the Immunological Techniques Use for Detection of *Schistosoma* spp Infection

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ABSTRACT

Over 200 million people are suffering from the debilitating *Schistosomiasis*, which has the greatest morbidity and mortality rates in African nations. *Schistosomiasis* continues to be a tropical disease that receives little attention from governments and healthcare Institutions while having a wide range of negative impacts on society's health and socioeconomic hardship. The establishment of precise investigation for both gut and urinary Schistosomiasis is one of the crucial areas that are severely undeveloped. A review was conducted to highlight immunological methods used to detect *Schistosomiasis*. Databases from Science Direct, World Health Organization, and PubMed were used. Articles for which at least the abstract was available in English were selected for the present study. Relevant articles were screened, duplicates were eliminated, eligibility standards were followed, and qualified studies were reviewed. Techniques including Skin Reaction Test/Biopsy, Indirect Immuno-Fluorescence Test (IFT), Indirect Hemagglutination Test (IHAT), Circumoval Precipitin Test (Copt), Monoclonal Antibodies Test (Mabt), ELISA, and others were discussed. The challenges faced by these techniques were also highlighted. Among the techniques discussed, ELISA was found to be the most widely used as it is the most effective, easy to use, and could detect both chronic and acute *Schistosomiasis*

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INTRODUCTION

The physiological and socioeconomic well-being of individuals in vulnerable communities is severely harmed by schistosomiasis, with school-aged children and adults being the most infected groups with the highest morbidity and mortality rate (Infurnari *et al.,* 2017). Six species, namely *Schistosoma mansoni, S. haematobium, S. japonicum, S. mekongi, S. guineensis,* and *S. intercalatum*, are known to cause *schistosomiasis* globally (Chernet *et al.,* 2017). In Sub-Saharan Africa, *S. mansoni* (agent of intestinal schistosomiasis) and *S. haematobium* (agent of urogenital schistosomiasis) are the two main schistosome pathogens (Cioli and Pica-Mattoccia, 2013). Host reactions to schistosome eggs cause the chronic disease's clinical symptoms (Gryseels *et al.,* 2016). Eggs from *S. mansoni* and *S. japonicum* most frequently become lodged in the liver or intestine's blood vessels, resulting in diarrhea, constipation, and blood in the urine (John, 2014). In cases of severe infections, liver fibrosis and portal hypertension may also occur as a result of systemic inflammation, which can also cause gut wall ulceration, hyperplasia, and peptic ulcer disease (Lindholz *et al.,* 2018).

Infections with *Schistosoma* species are mostly identified through microscopic analysis of the parasites' eggs in urine or stool samples taken from infected individuals (Akinwale *et al.,* 2011). However, the immunological method develops are more quickly, and technically cheaper, than microscopic examinations (Cioli and Pica-Mattoccia, 2013). Aside from providing tests with high sensitivity and specificity, the immunological approach in epidemiologic studies also evaluates the efficacy of various control methods in regions where parasitic infections are prevalent (Barakat, 2013). These tests can be employed even when parasites are reproducing (Hamburger *et al.,* 2017).

Since some schistosome-infected individuals may exhibit clinical symptoms in endemic areas, a review of the immunological diagnosis is crucial for the present situation. The methods also lead to the development of

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tools that allow treatment monitoring and also assessing the effectiveness of chemotherapy as well as other curative interventions (Hervé *et al.,* 2013; Devaney *et al.,* 2010). Rates of Immunoglobulin E (IgE) to the Schistosomes peptides have been associated in some regions of the world with susceptibility to superinfection after treatment (Pearson *et al.,* 2012). The effectiveness of vaccine programs can be anticipated in the future when anti-parasitic vaccination is available (Pennington *et al.,* 2017). The Discovery of this effective vaccine could be greatly influenced by a study of the methods for detecting these antigens since it will aid in identifying those people who develop immunity to parasite infection (Fitzsimmons *et al.,* 2005).

Immunological Diagnosis

The identification of *Schistosomiasis* is mostly based on conventional methods (mostly microscopic examination) (Gray *et al.,* 2021). However, the identification of adult worms and antigens in serum or urine has a lot of diagnostic capabilities and it may eventually replace the conventional techniques (Hervé *et al.,* 2013). The antigens found in serum or urine are either cathodic (circulating cathodic antigen) or anodic (circulating anodic antigen) (Pennington *et al.,* 2017). The most common methods include the skin reaction test/biopsy, indirect immunofluorescence test (IFT), indirect hemagglutination test (IHAT), circumoval precipitin test (COPT), various monoclonal antibody tests (MAbT), and various e-PCR formats (Deelder, 2013; Meurs *et al.,* 2018; Knopp *et al.,* 2019). For the diagnosis of *Schistosomiasis*, some immunological techniques have been put forth, but only a select handful have been able to advance to the large field and confirmation steps (Luciana *et al.,* 2013).

Skin Reaction Test/Biopsy

Skin Reaction Test also known as "Biopsy" comes from the Greek words "bio-life" and "opsia," to see," (Patton *et al.,* 2018). Technically, Biopsy is the removal of tissue from living things for microscopic analysis and diagnosis (Sanjay *et al.,* 2014). Ernest Besnier first used the term "biopsy" in medical terminology in 1879 (Karkera *et al.,* 2011). The primary goal of a biopsy is to confirm a clinical and radiographic diagnosis, guide surgical treatment, and verify whether a lesion has been completely removed (Kumaraswamy *et al.,* 2012). It is also helpful in choosing the type of treatment to implement for specific disorders (Catherine *et al.,* 2008). If necessary, biopsy reports can also serve as medical records (Karkera *et al.,* 2011). In China during the middle of the 1950s, *Schistosoma* adult worm skin test antigen was employed regularly, and various epidemiological studies on skin reaction tests were also carried out during the years 1963, 1969, and 1976 (Smithers and Terry, 2015). However, it was discovered that test results remained low also when given a good prediction (Lalonde *et al.,* 2015).

The method primarily usually used for skin biopsies in the detection of Schistosoma infection is a punch biopsy (McManus *et al.,* 2010). This method can be applied to both therapeutic and diagnostic objectives (viz, punch excision of small pyogenic granuloma, verruca, tattoo) (Guegan *et al.,* 2019). Any hard lesion and microscopic vesicles that fit inside the perforation can be treated using this technique (Thomson *et al.,* 2017).

With a disposable or sterilizable punch of various sizes, the lesion or region to be biopsied is removed. A 4-mm punch is acceptable for non-facial lesions (Gray *et al.,* 2011). However, biopsies of 5 mm or greater are preferred in granulomatous disorders or conditions with unusual features (Friedman, 2004). It is advised against taking biopsies that are less than 3 mm since important features could be overlooked (Krunic *et al.,* 2014).

Just after the region has been put under anesthesia, the skin is pulled in a perpendicular direction to the lines of the skin that is at rest. With this technique, the round skin defect is transformed into an ellipse, reducing the possibility of dogear development after suturing (Rabello *et al.,* 2012). The thumb, middle finger, and index finger are used to support, rotate, and apply pressure to the punch, whereas the index finger stabilizes and applies pressure to the punch (Wilhelmi *et al.,* 2011). Pressing the punch into the skin with rotating motions causes a sensation to be felt (Zhu, 2015). This is due to punching penetration into the gelatinous mass subcutaneous tissue plane (Gray *et al.,* 2011). The wound that results from this can either be sutured or left untreated to allow for further healing (Krunic *et al.,* 2014). The face, genitals, and mucosa, have excellent flow, heal fast, and leave little scars (Perez *et al.,* 2013).

It's crucial to avoid hitting the periosteum when doing a biopsy on the forehead, shin, dorsum of the nose, or scalp because doing so produces excruciating pain and agony (Mutalik, 2018). Punch biopsy has the benefits of being simple to do and collecting evenly shaped tissues, but the drawbacks include the possibility of insufficient material being retrieved and the tendency for the biopsy to exclude deeper tissue (Zhu, 2015).

Indirect Immuno-Fluorescence Test (IFT)

Indirect Immuno-Fluorescence Test is a common method for detecting antibodies, the indirect immunofluorescence antigens (IFA), detects antibodies by their unique ability to bind to parasitic antigens produced in infected cells (Vendrame *et al.,* 2021). IFT is also called the Secondary immunofluorescence test used as the laboratory technique for identifying circulating autoantibodies in patient serum also a method is employed to identify autoimmune disorders that rupture (Grenfell *et al.,* 2013). In this form of test bound antibodies are visible after being incubated with fluorescently labeled antihuman antibodies (Zhu, 2015). IFT is one of the cell imaging methods which rely on the use of antibodies to mark a particular target antigen with a fluorescent dye called fluorescein isothiocyanate (FITC) (Smith *et al.,* 2012).

In IFT, primary conjugated antibodies with chemically labeled fluorophores are frequently utilized (Grenfell *et al.,* 2013). Two antibodies are used in indirect IF; the primary antibody is unconjugated, while the secondary antibody is directed against the primary antibody and conjugated to a fluorophore for detection (Deelder *et al.,* 2020). Studies have shown that an indirect immunofluorescence reaction, using paraffin-embedded sections of adult worms, allows for the detection of immunoglobulin M (IgM) antibodies against antigens of the parasites' digestive tract, making it a highly sensitive method for the diagnosis of acute and chronic schistosomal infections (Vendrame *et al.,* 2021). The specificity of this reaction has also proved to be adequate (Smith *et al.,* 2012).

In 1998, in a low-endemic region of Brazil, immune-epidemiologic studies of *Schistosoma mansoni* infection used IFT as a diagnostic tool (Zhu, 2015). It was discovered that stomach fluorescence, which can appear forty-four (44) days after infection and is always connected to acute *Schistosoma mansoni* infection, can be detected by IFT using adult worm segments (Kanamura *et al.,* 2019). Once fluorescence is found in the parenchyma and/or stomach of the worms, frozen sections of a sample are classified as positive for the igg Antibodies immunofluorescence test (IgG-IFT), and as positive for the IgM-indirect immunofluorescence test (IgM-IFT) (paraffin sections) when fluorescence is found in only the gut of the worms (Burlandy-Soares *et al.,* 2013).

Indirect immunofluorescence has the benefits of high sensitivity and easy signal color change dependent on different second antibodies that may be purchased commercially; it is simple to obtain the second antibodies that have been tagged (Alem *et al.,* 2017). The advantages of indirect immunofluorescence include high sensitivity and simple signal color change depending on various second antibodies that may be bought commercially; the second antibodies that have been labeled are easy to obtain, High sensitivity and a quicker processing time are two advantages indirect immunofluorescence over direct immunofluorescence; direct immunofluorescence must be performed when there are several antibodies from the same species (Eriksson *et al.,* 2011). The use of direct immunofluorescence has some drawbacks; compared to indirect immunofluorescence, the first has a lesser signal; the second is that direct immunofluorescence is more expensive than indirect immunofluorescence because the labeling process is more complicated and less flexible when there are no commercially available direct conjugates (Hargraves, 2019).

The primary drawback of the indirect immunofluorescence method is the inability of the anti-immunoglobulin sandwich reagent to differentiate between exogenous and endogenous immunoglobulin (Lodh *et al.,* 2013). For instance, independent of the presence or absence of additional antibodies, a sandwich reagent of rabbit anti-mouse immunoglobulin would detect membrane immunoglobulin in mouse B cells. Since rabbit or rat antimouse immunoglobulin will only weakly or completely cross-react with human immunoglobulin, the issue is not as serious when mouse monoclonal antibodies are employed to stain human cells (Aryeetey *et al.,* 2013). By passing over human immunoglobulin-coupled beads, antihuman antibodies from several commercial antisera to mouse immunoglobulins have been removed (Carvalho *et al.,* 2012). Nevertheless, there is a chance for the cross-reactions, hence it is necessary to do controls in which the first antibody is not used (Enk *et al.,* 2012).

Indirect Hemagglutination Test (IHAT)

An indirect hemagglutination test is a form of immunological test in which an antigen is entrapped onto erythrocytes of a specimen and agglutination of the antigen-sensitized erythrocytes is induced by the action of an antibody specific to the adsorbed antigens, said method being characterized by the removal of heterologous agglutinins from the serum to be tested that may react with the homologous red blood cells used (Ahmed, 2019).

The surface proteins that agglutinate red blood cells (RBC) of diverse species are encoded by the nucleic acids of different Schistosomes (Whitty *et al.,* 2018). Hemagglutination is the process by which Schistosoma hemagglutinins interact with red blood cells to produce a lattice of agglutinated cells that settle unevenly in a tube or microtiter well and unagglutinated cells condense into a button-like structure (Erkol *et al.,* 2009).

The procedure for the hemagglutination test involved; obtaining a parasites preparation with a known HA titer, of the particular parasite, or determining the HA titer of the parasites, then preparing two-fold dilutions of the patient/test serum, say from 1:4 to 1:1024 for the test, except for the serum control wells, add a constant quantity of parasites to each well on a 96-well plate that is equal to 4 HA units, 60 minutes should be given for the plate to stand at room temperature (time varies according to specific requirements); Red blood cells (RBC) are added, and 30 minutes are spent incubating at 4 °C then check out the wells (Ortu *et al.,* 2017).

The IHAT kit's reagents and samples must be allowed to reach room temperature before the test is conducted (serum will be separated from a blood sample by centrifugation) (Azab and El Zayat, 2016). A disposable tube containing 0.05 ml of test serum and 1.95 ml of buffer solution must be used to deliver the 1/40 stock dilution of test serum (El Ganayni *et al.,* 2012). Using a micro pipettor, deliver 50µL of buffer solution into the wells. After setting up the microplate widthwise, add 50µL of serum stock dilution in the first well that was mixed with buffer. Next, transfer the 2µL from the first well into the second well, preferably using a microdilution. Finally, discard 50µL into the wells before adding 50 µL of the

serum stock-dilution (from step 1) and mixing it with buffer, the 1:80 dilutions is used as "serum control," which helps to prevent the occurrence of natural anti-sheep agglutinins in some sera (Feldmeier *et al.,* 2013).

Suspensions of red blood cells gently jiggle One drop of non-sensitized red blood cells was added to the seventh well (serum control), one drop of sensitized red blood cells was added to the eighth well (reagent control), and one drop of sensitized red blood cells was added to the ninth well. One "reagent control" was set up per microplate, and the content of the well was very carefully homogenized by lateral thrumming on the edge (do not use orbital vibration). Read the response after two hours (El Ridi *et al.,* 2016).

The Indirect Haemagglutination (IHA) strategy utilizes different extracts of red blood cells encapsulated with an enzyme, typically straightforward solubilized egg antigen (SEA), for the identification of positive patient sera via agglutination (Gui *et al.,* 2019). Although this method is not currently used, it was used in Chinese population studies as a substitute test to identify human infection with *S. haematobium* Its social acceptability is also limited, and because of its poor or variable precision, which renders it inappropriate for personal management and therapy, it can only be advised as an additional technique for or before usages (Yu *et al.,* 2017).

Few researchers have previously studied indirect haemagglutination (IHA) tests employing adult worm antigens for *Schistosomiasis* diagnosis; Most of the previously utilized IHA test kits were not commercially accessible for use during Epidemiological application, with a few exceptions, Sensitivity and specificity were reported in these earlier research to range from 71 to 100% and 80 to 100%, respectively (Van Gool *et al.* 2002).

The identical commercial kit IHAT developed by Fumouze Laboratories was evaluated by (Tom-Van *et al.,* 2002) for the identification of *Schistosoma haematobium*; the study's sensitivity was 80% and its specificity was 98.9%. The study used a cutoff of 1/160 and included only 25 *S. haematobium*-infected cases (Van Gool *et al.,* 2002); Kinkel *et al.* (2012) discovered that the IHA's sensitivity for *S. haematobium* was 71.4% and specificity was 99.0%.

Some researchers used a commercial IHA kit (Cellognost *Schistosomiasis* H) manufactured by Dade Behring Marburg GmbH, Germany, and the test was carried out according to the manufacturer's instructions, it was reported that the sensitivity of the IHA test for the diagnosis of *Schistosomiasis mansoni* was found to be 83%, while the specificity was lower (53%) (Berhanu Erko *et al.,* 2009).

Circum Oval Precipitin Test (COPT)

One of the primary techniques for use in the immunodiagnosis of *Schistosomiasis* is the Circumoval Precipitin (COP) test, which was first described by Oliver Gonzalez (1954). (Kagan and Pellegrino, 2016). Although the method is very straightforward, it was further simplified by the use of lyophilized eggs (Revera de Sala *et al.,* 2012; Yogore *et al.,* 2018). These updates were thought to be quite useful and appropriate for surveys in rural areas (Nosenas *et al.,* 2015; Tanaka *et al.,* 2015; Matsuda *et al.,* 2017).

The paddock COP test has also become more useful as a result of the recent research on the availability of air-dried *S. japonicum* eggs (Kamiya, 2013). Additionally, a noteworthy article on the use of microscope slides with perforated Dubl-style tape describes how lyophilized eggs were exposed to test blood and how the reaction was viewed via the microscope coverslips (Lewert and Yogrore, 2019).

For the COP test, a roll of PVC electrical insulating tape is drilled with heated 11 mm and 5 mm tubular-cork borers, the two holes are positioned so that they have a common edge that opens to each other (Tanaka *et al.,* 2015). The slide is normally left in a room for at least 2 days to ensure tight adhesion of the tape; otherwise, leakage would occur through minute gaps. Then, about 10 l of S. japonicum egg suspension containing roughly 100 eggs obtained from an 8-week infected rabbit is placed in the large hole using a micropipette, spread evenly, and allowed to dry (Yokogawa *et al.,* 2016); this procedure is described by Kamiya (2013), A drop of serum will be placed in the large hole at the edge enclosing the small hole, and a piece of cellulose tape (24 mm wide, 35 m long, 0.02 mm thick, Sekisui Co. Ltd., Japan) is applied to the insulating tape starting from the side of the large hole toward the small hole with continuous gentle pressing with the index and middle fingers, this procedure caused the serum to enter the space between the tape and the slide (Tanaka *et al.,* 2015).

According to preliminary investigations, just a single hole would not be sufficient because the adhesiveness of the tape is diminished when too much serum is applied (Nosenas *et al.,* 2015). Therefore, a smaller hole is required as a reservoir for any overflow (Lewert and Yogrore, 2019). After the final slide has been incubated for 48 hours at room temperature, the COP response is microscopic and examined using cellulose tape (Nosenas *et al.,* 2015).

The circumoval precipitin test (COPT) is an immunological test based on the precipitation of patient serum with lyophilized eggs or purified live eggs identified under a microscope, is helpful for the prognosis of *S. mansoni* and *S. japonicum* due to its high sensitivity (92-100%) and specificity (96-100%) (Zhou *et al.,* 2017); this method was used in China and Venezuela to identify low transmission zones, together with other coproscopic and serologic testing, in a modified form as a component of a commercial product (Dunne *et al.,* 2014). The disadvantages of this test include that it takes a very long time (48 hours), is difficult to perform, and has a variable period of seroconversion after treatment, according to the

experiences reported for Venezuela (negative rate of 64% of patients after 12 months of praziquantel treatment) and China (negative rate of 0% after 12 months) (Alarcón *et al.,* 218).

Serologic assays have shown clinical value for diagnosis by the identification of antibodies against schistosomal antigens due to the exceptionally broad spectrum of the reported immunodiagnostic assays (Doenhoff *et al.,* 2013); this approach is particularly useful for symptomatic travelers or serological surveys (Webster *et al.,* 2019). Current serologic tests cannot differentiate between active infection and prior exposure in people residing in *Schistosomiasis*-endemic locales, although several isotypic assays can frequently group active or inactive illnesses (Dunne *et al.,* 2014).

Since many years ago, monoclonal antibodies have been employed to identify circulating schistosomal antigens, which has the advantage of semi-quantitatively identifying active infections (Hagan *et al.,* 2011). A point of contact circulating cathodic antigen (POC-CCA) assay is now available from Rapid Medical Diagnostics, Pretoria, and RSA to map Schistosoma infections (Colley *et al.,* 2017). This parallel flow cassette test allows for on-site tracking of S. mansoni without stool samples, and it looks to be more sensitive than the Kato-Katz assay for mapping Schistosoma endemic areas (Rihet *et al.,* 2017). This assay will be an essential tool for conducting control programs in new sites (Towbin *et al.,* 2019).

Monoclonal Antibodies Test (MAbT)

Using specific monoclonal antibodies (MAbs) to identify circulating schistosome antigens secreted by living schistosomes in bodily fluids has while back been shown to be a hopeful technique for detecting active infection, assessing the effectiveness of treatment, and determining the efficacy of upcoming vaccines (Van Etten *et al.,* 2014). The antigen detection assays' typically high levels of sensitivity have been confirmed by contrasting their findings with those of quantitative parasitological techniques (Deelder *et al.,* 2014).

Subjects demonstrated a sensitivity of 80 to 90% when excreting at least 100 eggs per gram (EPG) of feces, and 100% when excreting at least 400 EPG. Techniques for detecting antigens, all of which rely on the use of MAbs, have nearly 100% specificity (Polman *et al.,* 2015). Numerous antigen error-checking assays have both high specificities and high sensitivities; however, because they need costly, special tools and bureaucratic procedures, it is challenging to adapt them for use in the field (Nash, 2018).

Enzyme-Linked Immunosorbent Assays (ELISA)

It is mentioned that one form of immunodiagnostic test that can be used to find *Schistosomiasis* is the dot enzyme-linked immunosorbent assay (ELISA). To establish a more field-applicable test format, many changes have been recorded (Ambroise *et al.,* 2018). The most used test for *Schistosomiasis* diagnosis is the ELISA, which allows for detecting many antibody classes and uses several antigens (Stete *et al.,* 2019).

Low specificity was discovered in early investigations on the detection of Schistosoma antigens, which prompted researchers to look for pure antigen preparations such as cationic fraction 6 (CEF6), adult microsomal antigens for *S. mansoni* (MAMA), *S. japonicum* (JAMA), and *S. haematobium*. Hemocyanin from keyhole limpets, gut-associated antigen (KLH), crude soluble egg antigens (SEA), and soluble adult (HAMA) were initially used for the detection of *Schistosoma* antigens (Olliaro *et al.,* 2020).

CEF6 is an isolated antigen from Schistosoma eggs that, compared to other antigens, has the highest association with egg production and an ELISA platform that demonstrated 91.7% sensitivity and 90% specificity (Dunne *et al.,* 2017). Three field investigations conducted in *S. mansoni* endemic regions of Kenya (Doenhoff *et al.,* 2016), Burkina Faso (Sorgho *et al.,* 2015), and Saudi Arabia since the publication of that article have continually assessed this antigen (Ghandour *et al.,*2017).

The accuracy was still low, though (59%, 55%, and 17.2%, respectively). All of these investigations raised concerns about the usefulness of the reference tests, and the low specificity was attributed to the Kato-Katz method's poor sensitivity, which served as the gold standard. All three assessments' sensitivity levels were confirmed to be high (97%, 90%, and 97%, respectively), but their specificity was still low (59%, 55%, and 17.2%) (Luciana *et al.,* 2013).

According to a study conducted in Egypt employing MAMA and HAMA as screening tests in a region where *S. haematobium* has been endemic in which MAMA FAST-ELISA had a responsiveness of 83.6% and HAMA FAST-ELISA had an attentiveness of 98.5%. All egg-passing subjects passed the test using the HAMA FAST-ELISA together with the Western blot method for additional examination. Combining adult worm mitochondrial antigens with both the Falcon assay screening test enzyme was explored (Al-Sherbiny *et al.,* 2019).

A systematic serosurvey involving nearly all Peurto Rican Towns investigated 2,955 normal healthy blood samples using MAMA FAST ELISA and the results showed that 15.4% of samples were positive and 10.6% had EITB confirmation, the highest seroprevalence rates (21.1-38.5%) were concentrated in 17 municipalities which together showed 48.8% of all seropositive samples and 18.8% of all samples with EITB confirmation (Tsang *et al.,* 2021).

The FAST-HAMA test demonstrated a positive rate of 95% in recent research, showing that it can be used as an application required for *S. haematobium* contamination. This test uses a purified HAMA antigen that is highly

specific for S. haematobium and a unique standard curve. Additional research is required to confirm the assay's specificity and usefulness in real-world settings (Abdel-Fattah *et al.,* 2018).

Epidemiological data on *S. mansoni* in Sudan and *S. japonicum* in China found high sensitivity but low specificity for kilodalton adult *Schistosoma* antigens; this low specificity was justified by some factors, including cross-reaction, infection with non-human Schistosoma species, and lack of sensitivity of the parasitological reference test; regrettably, additional assessments of the accuracy of this methodology are not available, and this issue continues (Wen *et al.,* 2019).

Other Immunological Methods

Quick tests for the detection of antibodies for S. japonicum include the dot immunogold filtration assay, the silver-enhanced colloidal gold metalloimmuno assay, and the colloidal dye immune filtration assay, similarly, an immunoblot test of the *S. mansoni, S. intercalatum*, and *S. haematobium* membrane antigen has also been examined for the detection of antibodies against *S. mansoni* (Cesari *et al.,* 2018).

Advantages and Drawbacks of Immunological diagnosis

Numerous different immunological methods have some common shortcomings, including sensitivity (depending on the standard used), intrinsic test characteristics (such as antigen and erythrocyte type), the prevalence of infection in the investigated community, the potential for positive reactions to persist after treatment, and cross-reactions with other helminths (Sorgho *et al.,* 2015).

Although immunological detection methods are quite effective, they are not frequently utilized for epidemiological research and do not form part of the diagnostic process for *Schistosomiasis* (Cesari *et al.,* 2018). Immunological methods are frequently criticized for their lack of specificity and inability to discriminate between an infection that is present today and one that was present in the past (Utzinger *et al.,* 2015; Worrell *et al.,* 2015). Alternative hypotheses for the lack of specificity, however, include the possibility that egg-negative, antibody-positive patients may have infections that are missed by imprecise parasitological techniques that failed to detect eggs in subjects with mild infections (Coulibaly *et al.,* 2013; Hawkins *et al.,* 2014;), or who received sub-curative drug doses (King, and Bertsch, 2014; Hinz *et al.,* 2017). Of course, there is also a chance that false-positive antibody tests are brought on by antigens from other schistosomes (Abdel-Fattah *et al.,* 2018). Another drawback is the gradual drop in particular antibody levels following therapy (Corstjens *et al.,* 2014). Additionally, in endemic locations, blood collection is difficult to implement under field conditions (Van Lieshout *et al.,* 2017). Despite these drawbacks, antibody detection is still likely to be the best diagnostic tool for schistosome infection in low-infected areas for some time to come. Antibody tests may also be useful for monitoring *Schistosomiasis* exposure in places that are moving toward elimination (Barda *et al.,* 2013).

Moving Forward

Most developing nations still rely mainly on microscopy for the diagnosis of intestinal and urogenital *Schistosomiasis*. Although this is the WHO-approved method for treating urogenital *Schistosomiasis*, many cases of intestinal *Schistosomiasis* as well as urogenital schistosomiasis go unreported in nations with low rates of schistosome transmission. For stakeholders and partners, finding affordable diagnostics for highly sensitive conditions is a difficult obstacle to overcome. Africa's endemic nations will not be able to afford monitoring kits without assistance from the international community. As we move closer to the suggested eradication of Schistosomes, this poses a barrier to tracking the effectiveness of control measures being implemented. It is important to put more effort into creating RDTs that are less expensive, more sensitive, and more targeted, especially for *S. haematobium*. Last but not least, a lower price review is required for the ELISA test kit, to make it more widely applicable and useful in endemic areas.

CONCLUSION

Immunological detection is the form of diagnosis that involved the use of reagents experimental approach as diagnostic tools and approach to research the immune system, the most popular techniques used for the detection of *Schistosomiasis* infection are Biopsy, IFT, IHAT, COPT, MAbT, and ELSA; Although immunological methods are more specific and sensitive than conventional methods ELISA was more often used while conducting immune epidemiological studies of *Schistosomiasis.*

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