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Schistosomiasis: Epistemology and Systematic Review of Its Diagnosis

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Abstract

Schistosomiasis is one of the neglected diseases caused by parasites and endemic in forest, coastal and wilderness areas. The diagnosis of this disease becomes an important step that must be constantly improving, since they help in the contribution of a correct therapeutic intervention. The objective of this study was to collect data on the evolution of the diagnosis of Schistosoma mansoni diseases through a systematic review and epistemological analysis according to Fleck [1] and to understand the modifications and / or modernizations obtained up to the present moment search. The data for analysis were obtained through scientific and registered research sources from 2007 to 2017. We found 101 articles and analyzed. Based on the analyzes, it was evidenced that the diagnosis has evolved over the years. It is concluded that the facts found in this research show that the systematic analysis with the help of the Iramuteq software facilitated the observation of the information described in the literature on the subject in question and the epistemological analysis shows that the knowledge evolution added new information which had, over the period studied, absorption from 2007 to 2017.

Keywords: Parasitoses; Schistosomiasis; Diagnosis

Introduction

Neglected diseases (DN) are characterized by a set of different pathologies that have as common aspect the prevalence in regions of poverty, being an obstacle to the social and economic development of a nation. (OF PRIORITIES, 2010). In Brazil, DN has called the attention of the Federal Government, which instituted the Research and Development Program on Neglected Diseases MS, Santos et al. [2,3]. An important characteristic that must be considered in the study of such diseases is that human behavior interferes in several ways in the transmission nd propagation of diseases Araújo &Telles [4]. DN, has a significant impact since it triggers debilitating factors that compromise the physical and intellectual development of the affected population Silva & Santos [5,6]. Schistosomiasis, according to the program SANAR (Specific Program to address neglected diseases of the Executive Secretariat of Health Surveillance), is one of the DN caused by parasites in Pernambuco Pernambuco [7]. Schistosomiasis is a parasitic disease caused by the parasite Schistosoma mansoni, being considered an important disease for the Brazilian public health Souza & Vitorino et al. [8,9]. In Pernambuco, schistosomiasis is endemic in areas of forest, coastal and wild Abath, Araújo & Farias et al. [3,4]. Therefore, considering the vast area of circulation of the disease, knowledge about diagnosis, epidemiology and measures of prophylaxis and control of this disease must be conditioned with extreme seriousness for the population of the state of Pernambuco Vitorino et al. 2012 [9]. Parasite diseases are important areas for scientific studies and diagnostic methods must be improved to contribute to the correct therapeutic intervention Uecker et al. [10].

One of the ways to aid in this scientific knowledge is through literature reviews that aim to update information about a particular topic. In the same way, epistemology can be used as a tool to update knowledge about a particular subject. Epistemology is a set of knowledge that aims at scientific knowledge Ferreira [11]. In the area of science, epistemology studies the construction of scientific knowledge and its concepts Silva-Arioli et al. [12]. Based on the above, the diagnosis of diseases caused by Schistosoma mansoni can be object of epistemological study as demonstrated in the studies of Marques et al. [13], where the evolution of knowledge about Toxocara sp. was analyzed and the epistemology evidenced that there were gaps in knowledge about Toxocara sp. which need to be consistently fulfilled by the researchers. The objective of this study was to obtain data on the evolution of the diagnosis of Schistosoma mansoni diseases through a systematic review and epistemological analysis

according to Fleck [1] and to understand how the changes and / or up to the present moment of the research.

Methodological Procedure

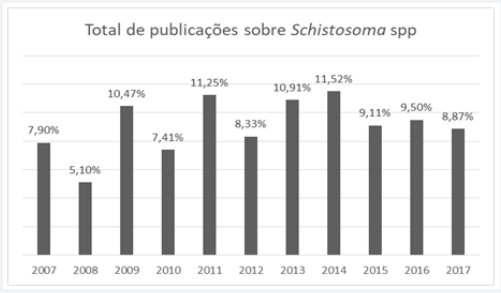
A data collection was performed through a bibliographic survey. The scientific texts were obtained from the Pubmed, Medline, SciELO, databases from 2007 to 2017. The following descriptors were used to search the scientific texts: diagnosis; parasitic, schistosomiasis in English and Portuguese, including only studies with the focus for the diagnosis of the parasite Schistosoma mansoni. Those that did not belong to the chronological time established and those that did not involve the species Schistosoma mansoni were excluded.

The analysis of content according to Bardin [14] and the use of the free software IRAMUTEQ, for statistical analyzes of texts Camargo & Justo [15], were carried out. IRAMUTEQ identifies the most frequent words, organizing them and grouping them into graphs according to their frequency, co-occurrences, statistical representativity and word connectivity, allowing visual observation of lexical analysis. The Reinert method, the similitude and cloud of words analysis, were the analyzes selected to be carried out in this research.

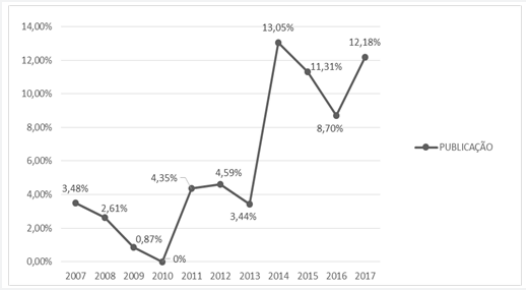
The Reiner method is an analysis of the Iramuteq made from a statistical logic and applied lexically. It uses the correlation logic through the segmentations of the textual corpus to present a hierarchical scheme of classes. These vocabulary classes show which ideas the textual corpus wishes to convey. The frequency of words is exemplified in the cloud in relation to the size of the word; the greater the word, the greater its frequency in the texts. The analysis of similarity, which is anchored in the graph theory, forming the interface tree, identifying the co-occurrences between the words contained in the scientific articles and indicating the connectivity between them. This analysis allowed the categorization of ideas, highlighting the common ideas to be analyzed by the epistemology Ludwik Fleck Fleck [1] and thus evidence the styles of thought.

Results and Discussion

Through the descriptors, 14,468 scientific texts related to Schistosoma spp. between 2017 and 1990, of these 2,941 reported on Schistosoma spp. in the years selected for this research. Of the 2,941 were pre-selected 543 referring to the species Schistosoma mansoni. In this last stage, all the scientific texts that did not deal with the diagnosis of Schistosoma mansoni were excluded, leaving 101 papers for the analysis. As for the type of scientific text, 95% were original articles, 2% were case reports and 3% were framed as literary review. All selected articles were analyzed and the information necessary to visualize the evolution of the diagnosis was taken. In this way, the information that underpinned the research target was highlighted and some were mentioned that contemplated these ideas or information that deserved the due prominence. Therefore, not all 101 articles analyzed were cited.



Graph 1: Scientific texts found on the subject and separated by year of publication).



Graph 2: Scientific texts found and analyzed on the subject and separated by year of publication.

Regarding the number of publications found with Schistosoma mansoni in relation to the total number of publications of Schistosoma spp. per year researched and scientific texts analyzed in this study, the following graphs were obtained. In Graph 1, the year with the lowest number of publications was in 2008, with 5.10% published articles, differently from the year 2014, which obtained the highest publications among the period studied on Schistosoma mansoni (11.52%). Regarding the publications related to the subject of this study, it was found that in 2010 no scientific texts were found that reported the diagnosis, 2009 was the year that least published articles in this field with 0.87% and 2014 was the most published year on the subject (13.05%) (Graph 2).

Figure 1: Dendogram representative of class distributions and percentage of analytical forms of articles on schistosomiasis diagnosis.

The analysis of textual content of the scientific articles included in the research highlighted groups of words which

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discriminated groups of thoughts, that is, from this analysis we can infer that the texts present similar discursive essences - the diagnosis, but the objectives have different ends. These results were presented through the method of Reinert, of the analysis of similitude and cloud of words. The separation of classes has shown that there are two Styles of thought discussed later. This method of Reinert applies the modeling of Descending Hierarchical Classification, from which two classes composed of different text segments were obtained. Through (Figure 1) it is possible to observe that the scientific texts were divided into two categories. In each of the classes was presented the title of the class and the percentage value in relation to the total of the corpus analyzed. As can be seen in Figure 1, class 1 covered most of the studies (58.1%) and its content was directed towards the use and improvement of the Kato Katz technique or comparison with other techniques such as ELISA, POC-CCA, Mini- flotac, Helmintex, TF-Test. The PCR technique was also compared, although it was not disseminated in laboratories as a diagnostic technique for schistosomiasis. It was observed that this class grouped the words Kato Katz, Comparison, Smear, Feces, Urine, Sensitivity, Egg, Helmintex, Microscopy, Routine, Kappa, among others.

The second class grouped 41.9% of the articles that investigated the development of new techniques for the diagnosis of schistosomiasis. Among the most cited are the PCR and ELISA techniques that were compared with studies to improve the tests to be routinely used to diagnose and introduce other techniques known to be used as future diagnostic tests such as Western blot, Mini -Flotac, Immunoinformatics, Indirect Immunofluorescence Reaction (RIFI-IgM), paramagnetic granules in a magnetic field, salt gradient and scanning microscopy. This class grouped words like: PCR, Schistosomiasis, detection, assay, diagnostic, approach, tool, antibody, new, RIFI-IgM, Polymerase, Chair, DNA, magnetic field, Western, Blot, Mini-Flotac, Immunoinformatics, paramagnetic field, magnético, gradiente, salino, microscopia, varredura, fluxo, Imunofluorescência entre outras.

The articles belonging to class 1, highlight studies for the improvement of Kato Katz by means of substitutions in components used in the staining and fixation of the samples was observed in 2007 in the researches of Odongo-aginya et al. [16]. After this study of improvement of Kato Katz technique, only in 2013 was observed in the article by Mello-Silva et al. [17] that presented a significant improvement in the Kato-Katz method making it faster and more efficient for the visualization of fertile eggs in faecal samples. The modification was with the use of sodium acetate as a fixative and revealing the intensity of the infection in less than 1h, thus reducing the time of diagnosis without increasing the cost.

Articles published in 2007 report the use of Kato Katz for efficient diagnosis in the detection of Schistosoma mansoni in human faeces from endemic areas. However, this parameter has been modified over the years by comparative studies with other techniques. A proven statement in observing the results of the studies by Ibrahim and Elbasheir [18] report the Kato Katz technique as limited, even though quantitative stool examination is generally recommended by specialists in schistosomiasis as the standard method. However, they state that it is less sensitive in the evaluation of Schistosoma mansoni infection and indicates the study of more sensitive tests.

The articles belonging to class 1 showed the comparison of the Kato Katz technique with other techniques, exemplifying this fact with the works of Gentile et al. [19] with ELISA and PCR and Siqueira et al. [20] with TF-Test. In 2012, these comparisons were continued, however, the Kato Katz comparison with the PCR technique was initiated by means of a study by Enk et al. [21]. Barda et al. [22] carried out comparative studies of the Kato Katz technique with the Mini-Flotac Technique in 2013. Also, this year Caldeira et al. [23] compared Kato Katz with the Helmintex commercial test. Coulibaly et al. [24] also compared Kato-Katz and circulating cathodic antigen (POC-CCA) techniques. His studies have concluded that the POC-CCA test appears to be more sensitive than the multiple Kato-Katz thick smears for the diagnosis of S. mansoni. Wichmann et al. [25] investigated real-time PCR in blood samples for the diagnosis of acute schistosomiasis and compared them with the serological tests (ELISA and Immunofluorescence) and parasitic microscopy. The authors state that a costly and time-consuming diagnosis should be avoided and the search for an early and rapid diagnosis encouraged. It also proposes that the classical diagnosis does not have considerable sensitivity in the initial stage of infection. And they conclude that real-time PCR is more sensitive than classical diagnostic tools.

The studies of Carneiro et al. [26,27] compared other techniques with the performance of PCR for the diagnosis of schistosomiasis in faecal samples of individuals living in an area of low endemicity in Brazil. Samples were assayed with the ELISA technique, Kato-Katz and Helmintex. The researchers concluded that while none of these methods produced 100% sensitivity, a combination of techniques should be effective in improving the detection of Schistosoma mansoni infection in areas of low endemicity. Espirito-Santo et al. [28] also performed comparisons of Kato Katz with the ELISA technique and Hoffman technique with the objective of evaluating the sensitivity of ELISA-IgM and ELISA-IgG in an environment of low endemicity. As results obtained that the highest positivity was the ELISA-IgM test corroborates the previous results described in the scientific literature.

Lodh et al. [29] compared three diagnostic tests to detect Schistosomiasis mansoni infection in urine. They emphasize in their analysis that the diagnosis for Schistosoma mansoni lacks sensitivity and is difficult to conduct. Kato-Katz, circulating cathodic antigen (POC-CCA) and polymerase chain reaction (PCR) techniques were compared. The conclusion was that PCR is an effective means to detect low-intensity infection and increase the

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efficacy of schistosomiasis surveillance and control programs. Degarege et al. [30] performed a similar study to that of Lodh et al. [29], evaluated the day-to-day variation in the CCA-urine test scores and the fecal egg count by Kato Katz. The mean egg count as well as the intensity of urine-CCA results varied over the three days of examination. More than 85% of the samples showed day-to-day variations in the status of S. mansoni infection from negative to positive or vice versa by Kato-Katz and CCA methods. These results indicated the need for more than one urine sample or feces collected on different days for a more reliable diagnosis in low endemic areas. After this year, Kato Katz's comparative studies and the rapid test using cathode-circulating antigen (POC-CCA) were observed in 2016 with Siqueira et al [31].

Carvalho do Espírito-Santo et al. [32] investigated the detection of Schistosoma mansoni antibodies in an area of low endemicity using indirect immunofluorescence and circumoval precipitation (COPT) compared to the Kato Katz technique. According to the researches, the immunodiagnostic techniques presented better results in comparison to Kato Katz. They suggest the combined use of diagnostic tools for indirect immunofluorescence and circumoval precipitation (COPT) for the diagnosis of schistosomiasis in epidemiological studies in areas of low endemicity. Among the three tests, the positivity rates were higher using IFA-IgM compared to parasitological technique and COPT. However, further studies are needed to identify the most accurate and representative method for detection in these areas. All the comparative studies performed between 2007 and 2016 pointed out that the Kato Katz technique compared to the others is less effective, however, because it is an inexpensive technique compared to others, it continues to be used as the main test for the diagnosis of Schistosoma mansoni in humans. Corroborating with the findings of Massenet, et al. [33], they affirm the Kato-Katz technique as the gold standard for all schistosomiasis studies, although sensitivity is low, but easy to handle, cheap and fast. Suitably suited for epidemiological surveys or to monitor environmental impact. Comparative studies with ELISA techniques, PCR, were observed until the year 2017.

Class 2 of the articles published in 2007 only by Teixeira et al. [34] referred to the study of new diagnostic techniques. They report a technique with the detection of eggs in the feces of Schistosoma Mansoni by means of paramagnetic granules in a magnetic field. According to the authors, at the time of the study the diagnosis of schistosomiasis in low-endemic areas was a problem, since classical coproparasitological methods could not accurately identify such cases. The authors concluded that molecular methods are a not very effective option due to the absence of an established standard with sensitivity and specificity for this situation. And present a new diagnostic method for the isolation of Schistosoma mansoni eggs in feces, paramagnetic granules. Over the years up to 2017, no studies similar to this have been found.

The article by Gargioni et al. [35] investigated the indirect immunofluorescence reaction (RIFI-IgM) as a novelty for the diagnosis of the parasite studied. They state that parasitic stool techniques vary considerably in sensitivity. They point to the proven advantages of serological techniques on parasitological techniques in the diagnosis of schistosomiasis. However, they express in their research that even with this advantage they are not part of the diagnostic routine of public and private health laboratories. However, the objective of the investigators of the aforementioned work is to present the indirect immunofluorescence reaction and to incorporate it in the program of control of schistosomiasis in municipalities with a low. It is worth noting that until the end of this research, 2008 was the only year that proposed the indirect immunofluorescence reaction as a new and potential method for the diagnosis of schistosomiasis.

In 2009, only the article by Coelho et al. [36] was classified as class 2 by the Iramuteq software analysis. It presents the use of a salt gradient for the diagnosis of schistosomiasis. They direct their research for the development of a new method of parasitological diagnosis highly sensitive and low cost. The proposal is based on differential egg sedimentation when subjected to a slow continuous flow of saline from a porous plate. As results emphasize the good performance of the new saline gradient technique for the diagnosis of schistosomiasis, suggesting that the same in field conditions is more sensitive than the Kato Katz, being read by the light microscope faster and easier. The study states that this new test corresponds to the recommendations of the 2006 WHO report on new diagnostic tools for schistosomiasis WHO [37] however there are ongoing field surveys to validate their use in large populations. About this report after 2009 was not found in this research nor another similar investigation. The Western Blot technique was described as a possible diagnosis for schistosomiasis for the first time in 2011 by the article by Carvalho et al. [12] and was observed in other studies in the years 2017. It proposes the development of a more sensitive diagnostic serological test for areas of low endemia. He says testing is a promising strategy. They corroborate with the scientific literature that the Kato-Katz method in patients with low parasitemia is not very sensitive. They conclude that the analyzed Western Blot has good results regarding sensitivity.

The study by Elhag et al. [38] reported the ELISA technique for diagnosis of schistosomiasis with urine instead of serum. The results showed that there was no significant difference between the IgG levels in the serum and urine samples, which confirms by their results that the detection of antibodies in the urine can replace the serum for the diagnosis of schistosomiasis. The year 2012 was continued researches with tests to improve the technique of ELISA, but this year also there was an article that put as a new proposal in the diagnosis the microscopy of confocal laser scanning.

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In 2013, the Grenfell et al. [39] study indicates the use of a new ELISA technique for the diagnosis of acute schistosomiasis. It is cheaper, sensitive and specific for the routine diagnosis of schistosomiasis, the SmTeg ELISA. The results of this research demonstrated that the new methodology compared with unmodified ELISA, parasitological examination, nuclear magnetic resonance and clinical findings was able to detect 80% of positivity. Coming to the conclusion that SmTeg ELISA could serve as the initial diagnostic tool for acute stages of infection in non-endemic areas.

In 2013 the researches by Coulibaly et al. [40] presented a new rapid diagnostic test for the detection of anti-Schistosoma mansoni and anti-Schistosoma haematobium antibodies. Parasitological methods are widely used for the diagnosis of schistosomiasis, however, they are insensitive, particularly in areas of low endemicity. The authors advocate a rapid diagnostic method called SmCTF-RDT for Schistosoma mansoni and S. haematobium infections by comparing it with the Kato-Katz and cathodic circulating antigen methods. SmCTF-RDT is as sensitive as Kato-Katz and the cathodic circulating antigen. But it needs more studies. Van Dam et al. [41] used the lateral flow of dry reagent for the diagnosis of active schistosomiasis by detecting Schistosoma circulating anode antigen as a possible method of improved diagnosis of cCA circulating antigen. The assay format was based on lateral flow (LF) using ultra-sensitive phosphorus conversion (UCP) fluorescent reporter particles to be read by a portable reader. The results obtained from the UCP-LF dry format assay showed to provide a robust and easy-to-use format for rapid serum CAA antigen tests, less as good as ELISA for sensitivity and specificity.

Corstjens et al. [42] studied as a tool for diagnosis lateral flow-based assays and ascending-conversion phosphorus (UCP-LF) tags. The authors compared UCP-LF with the circulating canodic antigen method (CAA) in serum or urine. They concluded that the different UCP-LF-based assays for the diagnosis of schistosomiasis provide tests with low complexity and high sensitivity. Fernández-Soto et al. [43] carried out a study on the isothermal amplification test with loop measurement (LAMP) in feces and serum samples from already infected murine models. This research aimed to overcome the disadvantages of classical parasitological and serological methods in the detection of S. mansoni infections mainly in the acute phase of the disease. Compared with the PCR-based assays, LAMP has the advantages of the simplicity of the reaction, the speed, the specificity and the higher amplification efficiency. It concludes with the research that there is potential for use in low-income countries. And it may be a readily adaptable potential for field diagnosis and disease surveillance in areas endemic for schistosomiasis. Ferrer et al. [43] studied the polymerase chain reaction as a future diagnostic tool for areas of low endemicity. The aim of the study was to develop an alternative molecular technique that requires prior standardization. According to the authors the standardized PCR technique is highly sensitive and specific for the detection of S. mansoni DNA and can be an important tool for the diagnosis in areas of low endemicity.

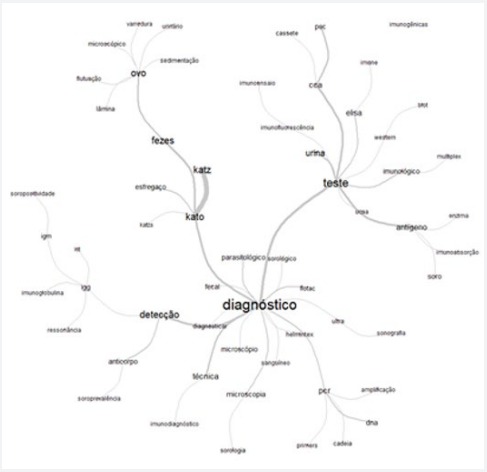

Figure 2: The tree of similarities that identifies the occurrences between words and the connection between them.

From 2015 to 2017 for the two classes found, all the techniques cited here for diagnostic use, whether routine or in scientific research, except those indicated in the course of the texts were flagged as the only report, obtained articles that conducted research on its functionality as a diagnosis, no new methodology or results were obtained from the last articles described in the classes. Another analysis performed by Iramuteq was the similarity analysis that allowed the identification of the occurrences between the words and indicated the connection between them. From the graphic representation of (Figure 2), it can be observed that a semantic range of more frequent words occurred, the main being the word diagnosis. The tree of similitude can be considered through the connections that, diagnosis and the different types of methods used to obtain it are important in its evolution and improvement, be they in the scope of scientific research or routine use.

It is observed that the thicker the line between the words the more connection they have. It is emphasized from the connections that the routine serological and parasitological techniques are those that have the greatest connection with the word diagnosis, mentioning that this type of techniques are the most used for the diagnosis of Schistosomiasis. This confirms what was seen in the classes described earlier by the other Iramuteq analysis. These two techniques have undergone, over the years, technological advances, but are reported with more efficient techniques. What perpetuates these two methods are cost issues.

The method of the cloud of words, also occurs the grouping and graphic organization of the words according to their frequency. By the word cloud method, it was verified that the words that obtained relative frequency were practically the same as those found in the similarity analysis, which confirms the connection of these words (Figure 3). Epistemological checks based on the reflections of Fleck [1] introduce parameters of

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analysis on the procedure of production and dissemination of knowledge, because they are based on the idea that knowledge is the result of socio-historical actions carried out by a community of individuals with interactions sociocultural Pfuetzenreiter [44,45], Fleck &Marques et al.[1,13]. This community is observed in the articles analyzed as the group of several researchers. In this group one can identify two Thinking Styles according to Fleck. Fleckiana epistemology considers that the construction of knowledge in the health area is based on historical facts and on the practices and experiences of the professionals that integrate the area Matos, et al. [46], Fleck [1]. From the epistemological point of view, the scientific knowledge about Schistosomiasis diagnosis evolved from initial ideas, represented by the articles found in the articles of 2007, but it was observed that although they did not enter the analysis of this research, there was a report of a parasitological and serological method before this date which indicates that they also served as a basis for the 2007 research. Reflecting on the results obtained, it is noted that the knowledge contained on the subject was reinterpreted and gradually modified and according to the researchers' thinking, however, the initial knowledge continued existing basis for future modifications and / or innovations. This fact is defended by Fleck [1] that indicates that knowledge always comes from an old base that is suffering reinterpretation and as a result provides advances in this knowledge [47-50].

Figure 3: Method of cloud of words.

With the help of Iramuteq software analysis two classes of articles were found. What demonstrates the formation of two groups of ideas and two styles of thought according to Fleck's epistemology were evidenced. They are: Comparison of the Kato Katz technique with other diagnostic methods for use and improvement of diagnosis and the second style of thinking was: New techniques for the diagnosis of schistosomiasis. These two styles of thinking were necessary for comparisons and improvements for the diagnosis of schistosomiasis. These two thoughts provide the vision of two groups of scientists, those who seek to perfect existing techniques and those who seek to improve the diagnosis through technological innovations [51-55].

Conclusion

The issues raised historically about the diagnosis of the parasite Schistosoma mansoni made it possible to understand how the evolution of diagnosis (modifications and modernizations) occurred, as well as the ideas that motivated the groups of scientists to have two experiments trajectories, ideas that established two Styles of thought. Even with these additions of knowledge to the diagnosis the Kato Katz technique is reported as the most used in routine identification of fecal biological samples with the parasite, since it is among the most financially viable, but it is not the most sensitive, which leaves as challenge studies that can unite an effective technique, cheap and more sensitive.

Systematic analysis with the help of Iramuteq software facilitated the observation of the information described in the literature on the evolution of the subject in question and the epistemological analysis applied to the subject shows that the evolution of knowledge added new information which, during the studied period, assimilated from 2007 to 2017, being used to improve and innovate the diagnosis of schistosomiasis and thus improve research for human health.

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