Review Article

An Overview of Schistosomiasis in Africa: Evolutional Origin and Diagnostic Challenges

Abstract

Schistosomiasis is an overlooked tropical illness that is caused by the blood fluke that dwells human blood vessels. It manifest as an acute yet chronic sickness and is normally found at all developing nations with poor health services frameworks. Strong phylogenies dependent on molecular data of species inside the family Schistosoma have been produced lately. The impressive advancement made in understanding the connections between considerable perceived types of Schistosoma is explored with specific consideration being given to the discovery and investigation of parasite variety as appeared by studies on ribosomal RNA qualities, mitochondrial DNA and Random Amplified Polymorphic DNA. Generally, molecular phylogenies concur with perceptions dependent on morphological or life-history attributes. Plainly the parasites of man don't shape a monophyletic group and that cozy connections exist between parasites inside species groups, particularly in the *S. haematobium* group of species. The *S. japonicum* group has all the earmarks of being the most dissimilar of the species groups but then little DNA succession variety has been seen between different isolates of *S. japonicum*. Diagnosis is key to all parts of schistosomiasis and decision on individual and community treatment, estimations on prognosis and appraisal of dismalness, assessment of chemotherapy and control estimates all require the outcomes from diagnostic tests. Lamentably, present techniques are characterized by indicative flaws.

Keywords: Tropical diseases; Neglected diseases; Phylogeny; Schistosoma

1. INTRODUCTION

Schistosomiasis is infectious parasitic disease caused by *trematode* (flukes) of the genus schistosome. The parasite can be classified on the basis of their egg/ova morphology; they are characterized as the most second devastating parasite commonly found in the tropical region of the world. They cause mortality and morbidity in developing countries especially in Sub-Saharan Africa, although places like the Caribbean, the South America, Middle East and Asia has reported a significant prevalence [1]. Human become infected through skin penetration when comes in contact with an infective stage of the parasite/cercariae often during various water contact activities in an infested water [2]. Five major species are known to infect humans (the first three are of most significant public health problem) *S. haematobium*, *S. mansoni*, S. *japonicum S. mekongi* and *S. intercalatum* [3]. Other schistosome that occasionally infects human causing dermatitis or insignificant infection includes *S. bovis* and *S. mattheei* together with some avian schistosome. These species differ biologically from one another and to their geographic distribution and the type of disease they cause [3].

S. haematobium a causative agent of urinary schistosomiasis causes complication like fibrosis, stricture and urinary tract calcification similarly advanced intestinal schistosomiasis may result in hepatosplenomegaly, liver fibrosis and portal hypertension [2]. However, at the time of infection most of the eggs become trapped in some tissues. Organ in the body like liver become infected with S. *mansoni* and S. *japonicum* worm, on the other hand bladder and urethras are the major organs affected by the species of *S. haematobium* worms [1]. The pathology is not due to the number of worms in the body but instead due to immunologic response to schistosome egg that is being trapped in the host tissues. Antigen which is secreted by the egg stimulates a granulomatous reaction involving T- lymphocyte, macrophages and eosinophils, which initiate the clinical sign [1].

Urinary schistosomiasis is endemic in Sub-Saharan Africa including Nigeria with substantial transmission in most of the state of the federation and high prevalence among school age children. Inadequate basic social amenities, weak primary health-care and poor infrastructure, facilitate transmission of schistosomiasis in the country and up till now control program is not available due to the absence of detail distribution of the disease. Intestinal schistosomiasis represents another form of Schistosoma affection. Among spectrum of intestinal lesions, polyps are the commonest. Intestinal schistosomiasis is essentially due to *basically Schistosoma mansoni, S, japonicum and S. mekongi* infection. Theyb are distributed primarily across sub-Saharan Africa and South America. Intestinal schistosomiasis are responsible the major public health burden and health problem, concentrated in sub-Saharan. Africa.

2. LITERATURES ACQUISITION

Peer-reviewed journal articles search were conducted via Medline, SCOPUS and Google Scholar search engine. All searches were limited to, publication from 1999 to 2019 except where necessary an older publication was used. All publications were in English, and duplicates, conference abstract, comments and short communications were removed. The initial search result gave us 2584 articles which were screened based on the title relevance, retaining 196 full text review articles out of which we cited 71 articles in this review.

3. EPIDEMIOLOGY

Schistosomiasis is one of the most common in the world found in approximately 76 countries more located in Africa, Middle East, South America and the Southern Asian continent [4]. An estimation of 779 million people are at risk of infection by schistosome with 207 million reported to have been infected, most of which are in Africa (97%) [5]. It was estimated that at least 20,000 deaths were reported as a result of schistosomiasis infection yearly [6].

Many African countries provide epidemiological data regularly regarding the prevalence and extents of infection cause to humans, and associated with malacological surveys and schistosome prevalence in intermediate host snails. West African epidemiological data related to schistosomiasis prevalence are available from Burkina Faso [7], Ivory Coast [8], and Niger [9]. Most of the schistosome found in Africa are *S. haematobium* and *S. mansoni* as shown in Figure 1. Previous evolutionary history, climate and environmental changes shows a significant selection and pattern of schistosome with increase in fluctuation and pattern of the population size, definitive mammalian hosts, including human and the snail distribution has tremendous impact on the infection change in human social development, in addition has immensely favoured the distribution and survival of the parasite and help in changing the prevalence of the infection in recent years [10].However, some researchers highlighted that establishing freshwater sites from dam irrigation system on constructed dams, site of human settlements close to freshwater sites has relationship with potential host, with high increase in size and number of human [5, 11, 12].

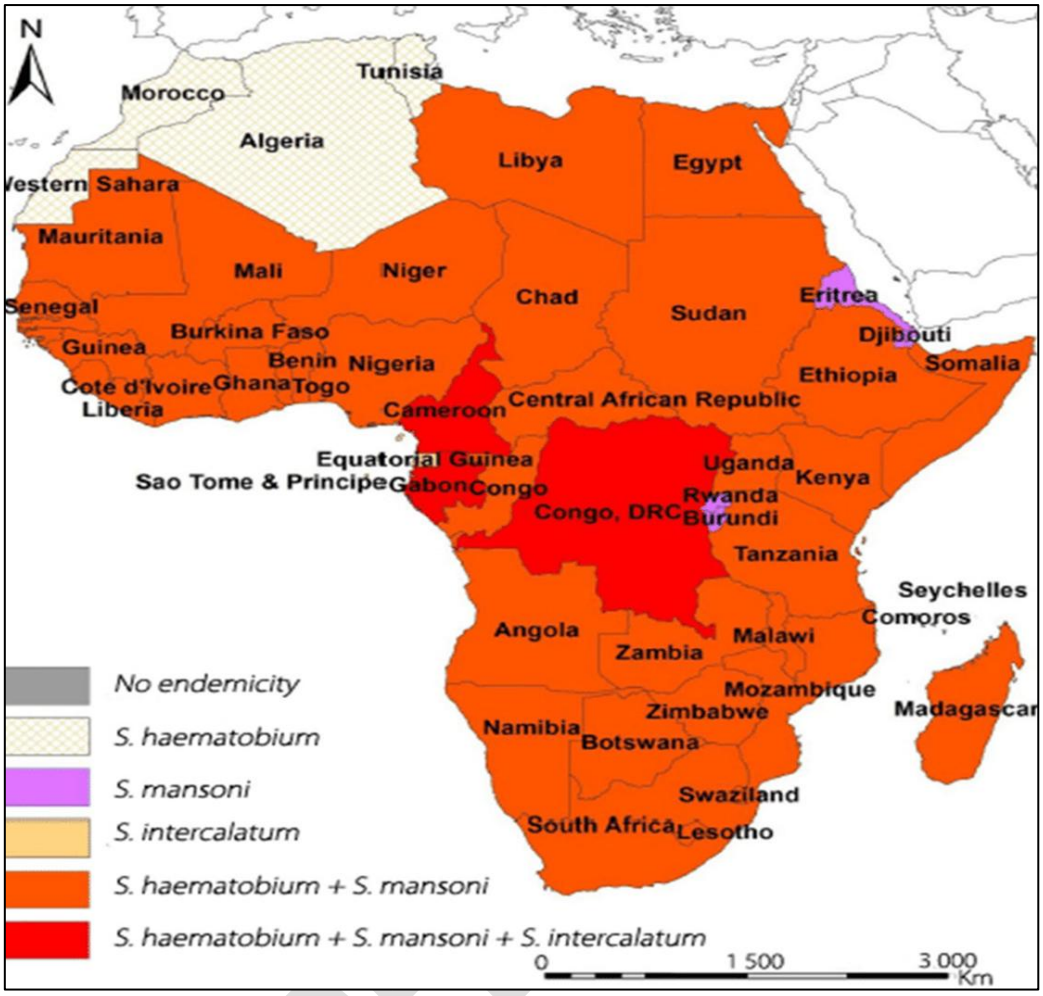

Figure 1: Distribution of Schistosoma species in Africa

It was equally pointed out that, large rivers may not be the main source of schistosomiasis, but waters retained by them through seasonal flooding, and extraction for irrigation schemes and impoundment are likely to be the major transmission sites [13]. The disease is distributed over rural and agricultural where the life style of people increases contamination of inland water with human excreta. In Nigeria more than 200 (62%) of the constructed dams were built in ten most endemic states, the remaining ones in twenty six less endemic states [14]. An example of such dams located in South-West Nigeria is that of Oyam dam found in Ogun State which were constructed in was 1984. However, there was an outbreak of urinary schistosomiasis in some couples of years after its construction in two resettlement communities around the dam [15].

The study of the prevalence and severity of *Schistosoma* infection based on age and water contact activities has revealed that adolescents and children are most infected. The severity of the infection is gender and age specific with globally, rate of infections peak at age 10 to 19 years. In some areas, the prevalence in this group may approach up to 100% [16, 17]. In relation to gender, more males than females were often been reported to had higher infection in most of the studies reviewed. In the study conducted by [18] lower prevalence

rate of 37.2% was observed among the females when compared to their counterpart males having prevalence of 45.5%. This attributed to the fact that males are more in contact with the breeding site through swimming, fishing and related activities than their female counterparts who may just visit the stream to fetch water for primary domestic activities [16]. However, other studies revealed that gender distribution of urinary schistosomiasis could change due to some variation in behaviour and cultural practices regarding water activities [19]. Therefore, infection pattern may be attributed to differences in geographic and environmental setting, their cultural and religious beliefs.

4. EVOLUTIONARY ORIGIN OF *SCHISTOSOMA*

Schistosoma species are found throughout the tropical and developing region of the world, namely Africa, Asia and South America (Figure 2). The distribution of schistosome parasite is related with the distribution of Schistosoma parasite is related with water contact and geography of the intermediate hosts that each species has adapted to exploit within given regions [20, 21]. *S. japonicum* in Asia has an egg with minute spine and develop in operculate snails of the family Pomatiopsidae. On the other hand, species of the *S. mansoni* and *S. haematobium* groups in Africa (and adjacent regions) and South America (*S. mansoni* only) utilize pulmunate snails. Members of the former group have eggs with a lateral spine, while the *S. haematobium* group has eggs with a terminal spine, with species from both groups often sharing overlapping geographical ranges [22, 23]. Therefore, the size and shape of the egg, intermediate host specificity and the geographical origin of isolates are sufficient to identify species infecting man.

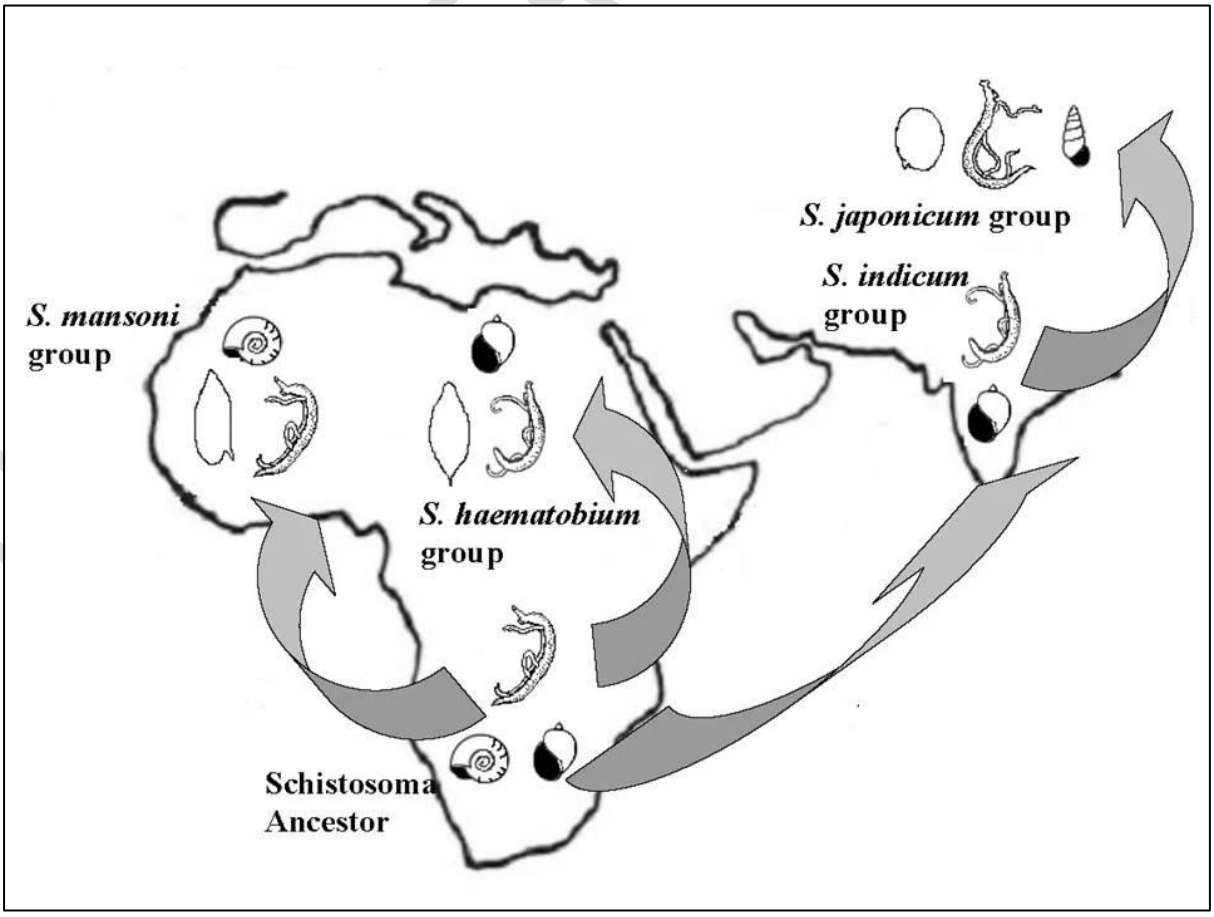

Figure 2: Map showing the African origin Schistosoma moving over to Asia on the Indian giving rise to the *S. indicum* group and diversifying into the S. japonicum suggest the Schistosoma ancestor remaining in Africa diverged giving rise to the *S. mansoni* and *S. haematobium groups.*

A considerable amount of literature has been published on the origin of schistosome which had earlier developed and reviewed, following argument for both an African and Asian origin [23, 24]. However, it was suggested that the genus *Schistosoma* originated before the separation of the super continent Gondwana land (that was made from today's Africa, Antarctica, South America, and Australia) for the past 150 million years [24, 25]. Moreover, are said to begun in order to exploit pomatiopsid and pulmonate snails, to which extensive fossils records suggested that, is from Gondwanan origin. This shows that spread of parasite were due to continental drift. Similarly suggested that ancestors of the Asian schistosomes were translated to Asian when India separated from Africa and merge to Asia, this gives rise to the *S. japonicum* and *S. indicum* [24]. This theory also suggest that the remaining other African stock began to radiate over, given rise to the ancestral linage of the *S. haematobium* and *S. mansoni* groups [23].

5. SCHISTOSOMA PHYLOGENY AND SPECIATION

Recent years, progress in advances in DNA sequencing, molecular tools also have promoted greater records and exploration of genetic diversity of schistosome species and their hosts [23]. A range of genetic markers have been used to construct phylogenetic trees, the nuclear marker ribosomal RNA gene unit (18S, 5.8S, 28S, internal transcribed spacer region (*ITS)*. Variations in the sequences of mitochondrial cytochrome oxidase sub-unit 1 (cox1) gene were compared among some samples specimens in order to identify the evolutionary differences, and possible similarities. Those studies show a benefit on the knowledge of the complete mitochondrial genome of *S. haematobium*, and other species [26, 27], thereby enhancing population focus - studies [27]. Previous study reported that, the genus schistosome was categorized in to 6 clades that correlate to different geographical distributions of the parasites [20, 23, 28]. In addition, species forming S. *japonicum* complex (*S. ovuncatium, S. sinensium, S. japonicum, S. mekongi, and S. malayensis*) are seeing basal on the tree, the position of the clade gives an evidence for the Asiatic origins of this parasite, it suggest an oriental origin and its colonization for both south eastern and the eastern provinces of Asia [20, 29, 30] as shown in Figure 3.

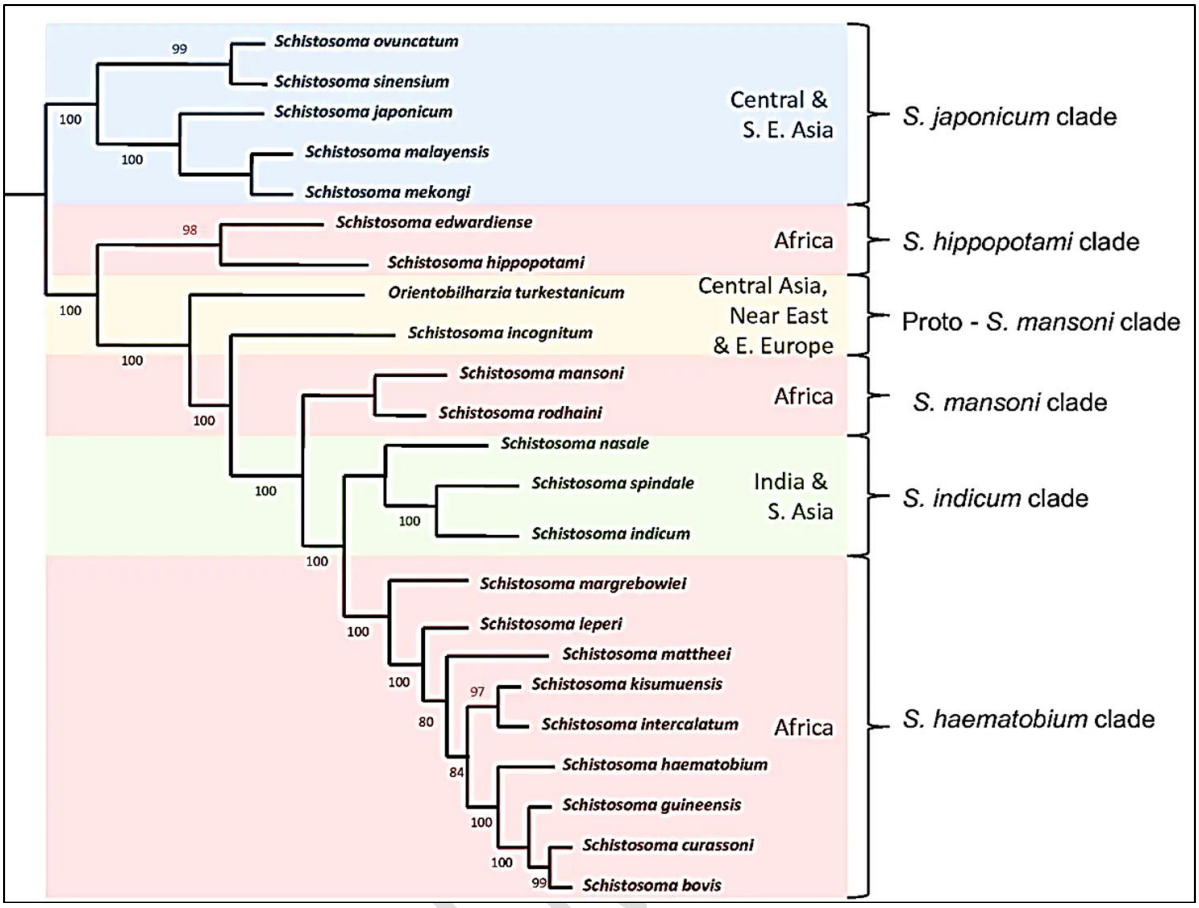

Figure 3: Schematic phylogeny of the interrelationships of members of the species within the Schistosoma genus estimated with a Bayesian analysis of combined partial *lsrDNA* , complete *ssrDNA* and partial cox1. The tree also illustrates the basal nature of Asian schistosomes, being ancestral to the African stock due to the relative positions of *S. hippopotami, S. edwardiense* (Inferred from partial cox1), Oriento-bilharzia and *S. incognitum* (adopted with modification [26])

On the other hand, the second major split in the phylogeny encompasses the species that are parasites found throughout Africa. However, there appears to be several distinct clades within this major split, most basal lineage is *S. hippopotami* clade, containing both *S. hippopotami* and *S. edwardiense*, which were both described from the western Uganda [21]. The third category within the phylogeny was described as proto-*S. mansoni* clade, proven to be basal to the true African species which is represented by two species, *Orientobilhazia turkestanicum,* now known to belong to the genus *Schistosoma* and *S. incognitum* [23]. Two species are known to be found in Southern and Western Asia, throughout the Middle East, adding more emphasis on the argument of an Asian origin for the African schistosome and may even give an insight into different species that occurred before the colonization of the African continent [20, 29, 31]. Moreover, African schistosomes form two distinct clades, the *S. mansoni* clade (*S. mansoni* and *S. rodhaini*) and the *S. haematobium* clade (*S.margrebowiei, S. guineesis, S. leipri, S. mattheei, S. intercalatum, S. haematobium, S. curassoni, S. bovis* and *S. kisumuensis)*. However, between the two major African clades is the *S. indicum* group (*S. indicum, S. spindale* and *S. nasale*) which are found throughout Southern and Western Asia suggesting a reinvasion of the Asiatic subcontinent [20, 32, 33].

6. LABORATORY DIAGNOSIS OF SCHISTOSOMIASIS

Despite the fact that recent information is available among places of genitourinary schistosomiasis like that of global burden of the disease, control and prevention, and other associated morbidity, some practical issues are yet to be clarified as regard to basic diagnostic tools associated with this public health important parasitic disease [34, 35]. The direct microscopic sedimentation technique of urine, and examination of urine using filtration method for the detection of schistosome ova including the indirect methods i.e. detection of haematuria, circulating egg antigens, schistosome specific antibodies and ultrasound scans are among others of the genitourinary system of *Schistosoma* infection. Therefore, many reasons are related to the inability in the detection of genitourinary schistosomiasis, citing example with differences in egg deposition levels and/or duration of infection which may influence the potentiality and sensitivity in achieving the most exact and recent infection status [36]. Conventional and new tools to diagnosis, determination of response to therapy, and morbidity assessment are indicated under community and institutional settings in hierarchic order (Figure 4)

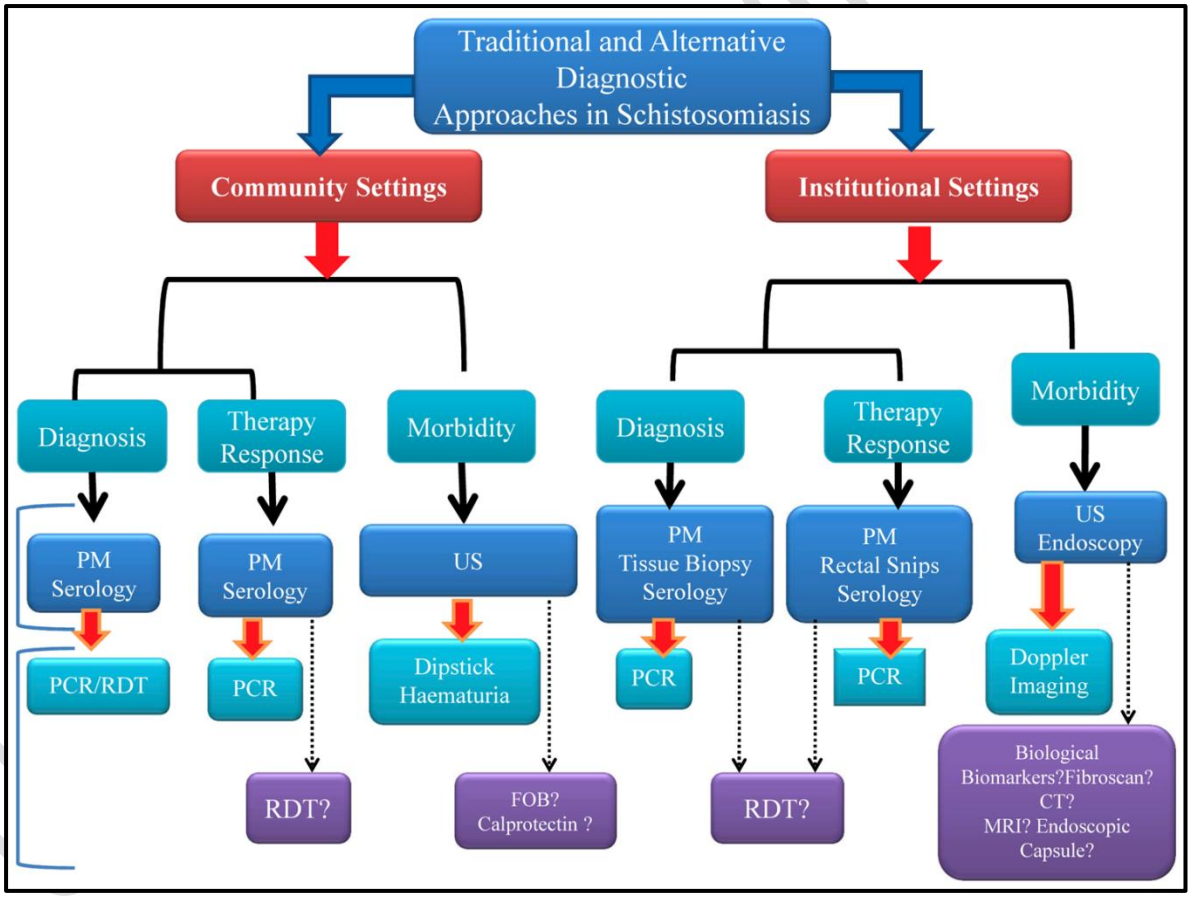

Figure 4: Schistosomiasis flowchart for clinical management in community and institutional settings. The above conventional tests, new tools were depicted according to the strength of literature evidence (red boxes). Approaches still under investigation and/or diagnostic platforms that show debatable results are inside the gray boxes. **PM:** parasitological method; **US:** ultrasonography; **PCR:** polymerase chain reaction; **RDT:** rapid test **FOB:** fecal occult blood; **CT:** computed tomography; **MRI:** magnetic resonance imaging.

6.1 Filtration Technique

Membrane used in urine filtration remain a common egg concentration technique, although the actual cases of schistosomiasis are high than what is documented after first screening [37, 38]. This is especially among individuals who excrete few numbers of eggs [39]. Although the sensitivity of the method can be improved by either increasing the number of samples tested and/or sampling of a larger volume of urine, but such methods are not easily performed. In a testing of monoclonal antibody assay [40] evidence proved that more than eight samples are needed for the examinations of urine through centrifugation and filtration and which are necessary before an infected individual can be identified. However, several studies that assess the accuracy with regards to its sensitivity and specificity of urine filtration method were not seen established. During recent time as mass praziquantel were distributed and well informed mass education, a significant light infection were reported, therefore, it is important that sensitivity of this diagnostic methods should perfectly be characterized [41, 42].

6.2 Sedimentation Method

Sedimentation is an important substitute to other techniques especially filtration methods. The sensitivity and specificity of sedimentation method was compared to filtration of 10mls in low intensity infection, must probably because the intrinsic loss rate is lower and the sample size larger. The presence of epithelial cells for example might likely disguise egg of *S. haematobium* in the sediment. In addition menstrual blood also contaminates urine and lysis of the red blood cells discloses ova in sediment or on filter membrane. This can record success as few drops of 10% hydrochloric acid are added to the urine sample.

6.3 Haematuria (dipstick) Method

Haematuria is a common symptoms of urogenital schistosomiasis, usually appears when *S. haematobium* eggs induced inflammation and blood vessels ruptures [43]. Reagent dipsticks are readily available for testing presence of blood in urine (haematuria), though it often indicates infection; however it is a non-specific marker since haematuria is not specifically caused by *S. haematobium* infection [44]. Several studies carried out were able to estimate the sensitivity, specificity, and false positive rates of the dipstick test [45, 46]. Further studies has shown that number of screening tests are possible and could be considered in other to facilitate and improved detection rate, accurately diagnose as well as proper estimates of incidence and prevalence of urinary schistosomiasis within sub-samples of many populations [47, 48]. The sensitivity and specificity of two screening methods; reagent dipstick for haematuria and urine filtration were evaluated among Ghanaian children with light *S.haematobium* infection. It was highlighted that strips reagent for urine analysis yielded a significant positive result for *S. haematobium* after diagnosis, with sensitivities of 70% and 97% and specificities of 59 – 80% [48, 49], showing concerns as to the possibility of this as the overall technique for screening populations in an endemic setting.

6.4 Immunological techniques for diagnosis of schistosomiasis

To date various methods have been developed and introduced to measure immunological response using crude or purified egg and adult worm antigens in other to detect anti- *S. haematobium* antibodies [50, 51]. Immunodiagnostic technique for detection of light infections is developed by aiming to detect the presence of schistosome circulating Antigens (SCA) in the urine, serum or antibodies specific to schistosome antigens [52]. The commonly reported assays are Enzyme Linked. Immunosorbent Assay (ELISA) [53, 54],

Immunofluorescence or Western Blotting (WB) [55].However, ELISA is a laboratory based test that is useful for larger-scale operations but its importance in the field is limited [56]. The detection of Soluble Egg Antigen (SEA) in serum and urine could be more valuable in diagnosis; hence early treatment would be applied before irreparable damage occurs [1]. However, an antibody detection method often has its own limitations as it cannot distinguish between current and past infection. Furthermore, it may also present a high level of cross reactivity, molecular methods should be considered for sensitive and specific assay [57]. Kato Katz technique is used for qualitative and semi-quantitative diagnosis of intestinal helminthic infestations; caused by Schistosoma spp. World health organization has recommended Kato Katz technique in areas with moderate to high transmission rates of soil transmitted helminths. People infected with intestinal schistosome pass the eggs of the worms through their faeces. In the Kato-Katz technique faeces are pressed through a mesh screen to remove large particles. A portion of sieved sample is then transferred to the hole of a template on a slide. After filling the hole, the template is removed and the remaining sample is covered with a piece of cellophane soaked in glycerol. The glycerol clears the faecal material from around the eggs. The eggs are then counted and the number calculated per gram of faeces. The Kato-Katz technique is the diagnostic method recommended for a known species of parasite that is associated with intestinal schistosomiasis and part of the plan for 2020 that focuses on "elimination of disease as a public important. Similarly, direct stool smear, formol-ether concentration technique can detect upto 65.26% of positive intestinal Schistosoma specimens.

6.5 *Molecular Based Technique*

Recently, many investigators launched molecular approaches for detecting schistosomiasis: Detection of parasite (schistosome) DNA in clinical human samples such as faeces [58], sera [59] and urine [60], confirmed the existence of parasite DNA in the host and provide evidence of the infection. Parasite DNA may be a helpful guideline for selecting the appropriate treatment for schistosomiasis. In another study conducted by [61] reported that data generated obtained from genetic techniques do not only give an insight of the history of these organisms, also into the biology of these parasites that has direct impact on species identification and disease epidemiology. In addition [62] demonstrated new polymerase chain reaction (PCR) primers for the identification and differentiation of major human *Schistosome: S. haematobium, S. mansoni, S. mekongi* and *S. japonicum.* A considerable amount of literature has been published on PCR methods and is proven to have improved the direct detection of *Schistosoma*. DNA seems to be prepared from egg prior to PCR amplification from urine, stool, or organ biopsy as samples [58, 60]. However, DNA is extracted from a small volume of sample success is dependent whether sample processed contains eggs or not [63]. Several studies have revealed that the random amplified polymorphic DNA markers (RAPD) technique can be applied successfully to study helminths [64]. Several DNA-based methods have been developed to investigate genetic diversity, differentiate strains and species and an analyse phylogenies of schistosome [62]. Demonstrated that RAPD can be employed to differentiate between strains of *S. mansoni* and species of *Schistosoma.*

In order to improve understanding of the epidemiology of the *S. haematobium*, genetic variation within this species has to be studied extensively [65]. Genetic studies are often carried out on DNA extracted from miracidia, from hatched egg, cercariae released from the snail or adult worms, most often collected from the laboratory animals. In addition, facilities were so limited making the practice so difficult for the isolation and storage of this parasite. Although several attempts has been made to simplify isolation of eggs on the filter paper since it does not require laboratory facilities, DNA can still be successfully extracted at

latter stage [66]. Mitochondrial genes have been used in molecular analysis to demonstrate the relationship between different species, because they showed high mutation rates compared to nuclear markers and exist in high number. Moreover, this led to their exploitation for studying phylogenetic variation in these parasites [67, 68]. Similarly *Schistosoma* phylogeny has primarily been based on alignment of multiple gene sequences. From a handful of genes such as cox1, cox2, ITS1, ITS2, nad4, rrnl, and rrnS [21, 23]. This might be very vital because it allows the exploration of genetic heterogeneity of parasites among a sample and also between children coming from the same area, the methods could also provide an insight into the knowledge of hybridization among different species after a long period of time as it has been observed that in west Africa, *S. haematobium* can hybridize *S. bovis* [69]. However, many children could be infected with one or more schistosome haplotype or even species at a time [70].

Previous studies have reported that presently there were complete mitochondrial genomes available for 6 species of schistosome including *S. japonicum, S. malayensis, S. mekongi, S. mansoni, S. spindale* and *S. haematobium* [68, 71]. Moreover, in 2001, Le *et al*. demonstrated that the mitochondrial genomes of *S. japonicum* and *S. mekongi* displayed the same gene order as each other and that of other digenea and Cestodes [68]. However, *S. mansoni* shows several differences in gene order when compared to the species from the *S. japonicum* clade. The *S. mansoni* type rearrangement was also seen in *S. haematobium* and *S. spindale* [68]. The rearrangement of the gene order among African schistosome and their descendants is of particular interest putting in to consideration the phylogenetic position of *S. incognitum* and *O. turkestanicum* and their geographical differences. These species might provide a clue into the exact time on when these genomic changes happened during the inversion of Africa and the radiation of the schistosome.

CONCLUSION

The greatness of molecular methodologies for the examination of schistosomes at the individual and community level is presently obvious, particularly for *S. mansoni*. Significant inquiries remain concerning the upkeep of parasite diversity and how schistosomes react to selection pressures either during characteristic movement through the life-push or through medication treatment or immunization. Gene revelation and gene mapping activities are prompting a superior comprehension of the schistosome genome and can be relied upon to contribute fundamentally to future relative transformative examinations. Choice and utilization of strategies ought to subsequently compare to the sort of data looked for by the general wellbeing of the epidemiologist or the medical officer and test result interpretation must mull over the downsides and limitations characteristic to every one of the different diagnostic procedures.

CONFLICT OF INTEREST

None to declare

AUTHORS' CONTRIBUTIONS

SAH designed the study, wrote the protocol, and wrote the first draft of the manuscript. SU managed the literature searches. All authors read and approved the final manuscript.

REFERENCES

1. Mahfouz A, Mahana N, Rabee I: Evaluation of Different Immunological Techniques for Diagnosis of Schistosomiasis haematobium in Egypt. *Life Science Journal* 2011, 8(4).

2. Gray DJ, Ross AG, Li Y-S: Diagnosis and management of schistosomiasis. *BMJ: British Medical Journal* 2011, 342.

3. Ukoroije B, Abowei J: Some Occupational Diseases in Culture Fisheries Management and Practices Part Two: Schistosomiasis and Filariasis. *Int J Fish Aquat Sci* 2012, 1(1):64-71.

4. Engels D, Chitsulo L, Montresor A, Savioli L: The global epidemiological situation of schistosomiasis and new approaches to control and research. *Acta Tropica* 2002, 82(2):139-146.

5. Steinmann P, Keiser J, Bos R: Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. *The Lancet infectious diseases* 2006, 6(7):411-425.

6. Strickland GT: Liver disease in Egypt: hepatitis C superseded schistosomiasis as a result of iatrogenic and biological factors. *Hepatology* 2006, 43(5):915-922.

7. Koukounari A, Gabrielli AF, Touré S, Bosqué-Oliva E, Zhang Y, Sellin B, Donnelly CA, Fenwick A, Webster JP: Schistosoma haematobium infection and morbidity before and after large-scale administration of praziquantel in Burkina Faso. *Journal of Infectious Diseases* 2007, 196(5):659-669.

8. Matthys B, Tschannen AB, Tian- Bi NT, Comoé H, Diabaté S, Traoré M, Vounatsou P, Raso G, Gosoniu L, Tanner M: Risk factors for Schistosoma mansoni and hookworm in urban farming communities in western Côte d'Ivoire. *Tropical Medicine & International Health* 2007, 12(6):709-723.

9. Labbo R, Djibrilla A, Zamanka H: Bulinus forskalii: a new potential intermediate host for Schistosoma haematobium in Niger. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2007, 101(8):847-848.

10. Rollinson, Knopp S, Levitz S, Stothard JR, Tchuem Tchuenté L-A, Garba A, Mohammed KA, Schur N, Person B, Colley DG: Time to set the agenda for schistosomiasis elimination. *Acta tropica* 2013, 128(2):423-440.

11. Southgate V: Schistosomiasis in the Senegal River Basin: before and after the construction of the dams at Diama, Senegal and Manantali, Mali and future prospects. *Journal of helminthology* 1997, 71(02):125-132.

12. Jobin W: Dams and disease: ecological design and health impacts of large dams, canals and irrigation systems: CRC Press; 1999.

13. Mafe M, Stamm Tv, Utzinger J: Control of urinary schistosomiasis: an investigation into the effective use of questionnaires to identify high- risk communities and individuals in Niger State, Nigeria. *Tropical Medicine & International Health* 2000, 5(1):53-63.

14. Ofoezie IE: Human health and sustainable water resources development in Nigeria: Schistosomiasis inartificial lakes. In: *Natural Resources Forum: 2002*: Wiley Online Library; 2002: 150-160.

15. Akinwale, Ajayi M, Akande D, Adeleke M, Gyang P, Adeneye A, Dike A: Prevalence of Schistosoma haematobium infection in a neglected community, south western Nigeria. *International Journal of Health Research* 2009, 2(2).

16. Sam-Wobo S, Ekpo U, Ameh I: Continued high endemicity of urinary schistosomiasis in Ogun State, Nigeria. *Nigerian Journal of Parasitology* 2009, 30(1).

17. Akinwale, Ajayi M, Akande D, Gyang P, Adeleke M, Adeneye A, Adebayo M, Dike A: Urinary Schistosomiasis around Oyan Reservoir, Nigeria: Twenty Years after the First Outbreak. *Iranian journal of public health* 2010, 39(1):92.

18. Houmsou R, Amuta E, Sar T: Profile of an epidemiological study of urinary schistosomiasis in two local government areas of Benue state, Nigeria. *International Journal of Medicine and Biomedical Research* 2013, 1(1):39-48.

19. Aboagye I, Edoh D: Investigation of the risk of infection of urinary schistosomiasis at Mahem and Galilea communities in the Greater Accra Region of Ghana. *West African Journal of Applied Ecology* 2009, 15(1).

20. Agatsuma: Origin and evolution of Schistosoma japonicum. *Parasitology international* 2003, 52(4):335-340.

21. Morgan, DeJong RJ, Kazibwe F: A newly-identified lineage of Schistosoma. *International journal for parasitology* 2003, 33(9):977-985.

22. Rollinson, Kaukas A, Johnston DA: Some molecular insights into schistosome evolution. *International journal for parasitology* 1997, 27(1):11-28.

23. Webster BL, Southgate VR, Littlewood DTJ: A revision of the interrelationships of Schistosoma including the recently described Schistosoma guineensis</i>. *International journal for parasitology* 2006, 36(8):947-955.

24. Davis, M G: Evolution of prosobranch snails transmitting Asian Schistosoma; coevolution with Schistosoma: a review. In: *Progress in Clinical Parasitology.* edn.: Springer; 1993: 145-204.

25. Davis, Bruce J, Sornmani S: Snail hosts of Asian Schistosoma infecting man: Evolution and coevolution. *The Mekong schistosome(Malacological Review, Supplement 2)* 1980:195-238.

26. Kane R, Southgate V, Rollinson D, Littlewood DTJ, Lockyer A, Pagès J, Tchuem Tchuentè L, Jourdane J: A phylogeny based on three mitochondrial genes supports the division of Schistosoma intercalatum into two separate species. *Parasitology* 2003, 127(02):131-137.

27. Johnston D, Kane R, Rollinson D: Small subunit (18S) ribosomal RNA gene divergence in the genus Schistosoma. *Parasitology* 1993, 107(02):147-156.

28. Majoros G, Dán Á, Erdélyi K: A natural focus of the blood fluke Orientobilharzia turkestanica (Skrjabin, 1913)(Trematoda: Schistosomatidae) in red deer (Cervus elaphus) in Hungary. *Veterinary parasitology* 2010, 170(3):218-223.

29. Attwood S, Fatih F, Mondal M, Alim M, Fadjar S, Rajapakse R, Rollinson D: A DNA sequence-based study of the Schistosoma indicum (Trematoda: Digenea) group: population phylogeny, taxonomy and historical biogeography. *Parasitology* 2007, 134(14):2009-2020.

30. Agatsuma, Iwagami M, Liu C, Rajapakse R, Mondal M, Kitikoon V, Ambu S, Agatsuma Y, Blair D, Higuchi T: Affinities between Asian non-human Schistosoma species, the S. indicum group, and the African human schistosomes. *Journal of helminthology* 2002, 76(01):7-19.

31. Agatsuma T, Iwagami M, Liu C, Saitoh Y, Kawanaka M, Upatham S, Qui D, Higuchi T: Molecular phylogenetic position of Schistosoma sinensium in the genus Schistosoma. *Journal of helminthology* 2001, 75(03):215-221.

32. Morgan, Dejong R, Snyder S: Schistosoma mansoni and Biomphalaria: past history and future trends. *Parasitology* 2001, 123(07):211-228.

33. Agatsuma, Iwagami M, Liu C, Saitoh Y, Kawanaka M, Upatham S, Qui D, Higuchi T: Molecular phylogenetic position of Schistosoma sinensium in the genus Schistosoma. *Journal of helminthology* 2001, 75(03):215-221.

34. King CH, Dickman K, Tisch DJ: Reassessment of the cost of chronic helmintic infection: a meta-analysis of disability-related outcomes in endemic schistosomiasis. *The Lancet* 2005, 365(9470):1561-1569.

35. Rudge JW, Stothard JR, Basáñez M-G, Mgeni AF, Khamis I, Khamis AN, Rollinson D: Micro-epidemiology of urinary schistosomiasis in Zanzibar: Local risk factors associated with distribution of infections among schoolchildren and relevance for control. *Acta Tropica* 2008, 105(1):45-54.

36. Hatz C, Savioli L, Mayombana C, Dhunputh J, Kisumku U, Tanner M: Measurement of schistosomiasis-related morbidity at community level in areas of different endemicity. *Bulletin of the World Health Organization* 1990, 68(6):777.

37. Bosompem, Bentum IA, Otchere J, Anyan W, Brown C, Osada Y, Takeo S, Kojima S, Ohta N: Infant schistosomiasis in Ghana: a survey in an irrigation community. *Tropical Medicine & International Health* 2004, 9(8):917-922.

38. Opara K, Udoidung N, Ukpong I: Genitourinary schistosomiasis among pre-primary schoolchildren in a rural community within the Cross River Basin, Nigeria. *Journal of helminthology* 2007, 81(4):393-398.

39. Gryseels B, Polman K, Clerinx J, Kestens L: Human schistosomiasis. *The Lancet* 2006, 368(9541):1106-1118.

40. Bosompem, Asigbee J, Otchere J, Haruna A, Kpo KH, Kojima S: Accuracy of diagnosis of urinary schistosomiasis: comparison of parasitological and a monoclonal antibody-based dipstick method. *Parasitology international* 1998, 47(3):211-217.

41. King CH: Parasites and poverty: the case of schistosomiasis. *Acta tropica* 2010, 113(2):95-104.

42. WHO: Prevention and control of schistosomiasis and soil-transmitted helminthiasis. *World Health Organization technical report series* 2002, 912:i.

43. Algahtani HA, Aldarmahi AA, Al-Rabia MW: Acute paraplegia caused by Schistosoma mansoni. *Neurosciences (Riyadh, Saudi Arabia)* 2014, 19(1):47-51.

44. Doehring E, Vester U, Ehrich JHH: Circadian variation of ova excretion, proteinuria, hematuria, and leukocyturia in urinary schistosomiasis. *Kidney Int* 1985, 27(4):667-671.

45. Eltoum IA, Sulaiman S, Ismail BM, Ali MM, Elfatih M, Homeida M: Evaluation of haematuria as an indirect screening test for schistosomiasis haematobium: a population-based study in the White Nile province, Sudan. *Acta Tropica* 1992, 51(2):151-157.

46. French MD, Rollinson D, Basáñez M-G, Mgeni AF, Khamis I, Stothard JR: School-based control of urinary schistosomiasis on Zanzibar, Tanzania: monitoring micro-haematuria with reagent strips as a rapid urological assessment. *Journal of pediatric urology* 2007, 3(5):364-368.

47. Klempner MS, Hu LT, Evans J, Schmid CH, Johnson GM, Trevino RP, Norton D, Levy L, Wall D, McCall J: Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. *New England Journal of Medicine* 2001, 345(2):85-92.

48. Kosinski KC, Bosompem KM, Stadecker MJ, Wagner AD, Plummer J, Durant JL, Gute DM: Diagnostic accuracy of urine filtration and dipstick tests for Schistosoma haematobium infection in a lightly infected population of Ghanaian schoolchildren. *Acta tropica* 2011, 118(2):123-127.

49. Mott K, Dixon H, Osei-Tutu E: Relation between intensity of Schistosoma haematobium infection and clinical haematuria and proteinuria. *The Lancet* 1983, 321(8332):1005-1008.

50. Chen M, Mott K: Progress in assessment of morbidity due to Schistosoma intercalatum infection: a review of recent literature. *Tropical Diseases Bulletin* 1989, 86(8).

51. Feldmeier H, Bienzle U, Dietrich M: Combination of a viability test and a quantification method for Schistosoma haematobium eggs (filtration--trypan blue-staining-technique). *Tropenmedizin und Parasitologie* 1979, 30(4):417-422.

52. Salah F, El Bassiouny A, Rabia I, Demerdash Z, Roshdy M, Shaker Z: Human schistosomiasis haematobium: effective diagnosis of active infection using a pair of monoclonal antibodies against soluble egg antigen. *Parasitology research* 2006, 99(5):528-533.

53. Whitty CJ, Mabey DC, Armstrong M: Presentation and outcome of 1107 cases of schistosomiasis from Africa diagnosed in a non-endemic country. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2000, 94(5):531-534.

54. Amorosa V, Kremens D, Wolfe MS, Flanigan T, Calill K, Judy K, Kasner S, Blumberg E: Schistosoma mansoni in family 5 years after safari. *Emerg Infect Dis* 2005, 11(2):339-341.

55. Thors C, Holmblad P, Maleki M: Schistosomiasis in Swedish travellers to sub-Saharan Africa: can we rely on serology? *Scandinavian journal of infectious diseases* 2006, 38(9):794-799.

56. Xue C, Taylor M, Bickle Q: Diagnosis of Schistosoma haematobium infection: evaluation of ELISA using keyhole limpet haemocyanin or soluble egg antigen in comparison with detection of eggs or haematuria. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1993, 87(6):654-658.

57. Bergquist R, Johansen MV, Utzinger J: Diagnostic dilemmas in helminthology: what tools to use and when? *Trends in parasitology* 2009, 25(4):151-156.

58. Pontes LA, Oliveira MC: Comparison of a polymerase chain reaction and the Kato-Katz technique for diagnosing infection with Schistosoma mansoni. *American Journal of Tropical Medicine and Hygiene* 2003, 68(6):652-656.

59. Pontes LA, Dias-Neto E, Rabello A: Detection by polymerase chain reaction of Schistosoma mansoni DNA in human serum and feces. *American Journal of Tropical Medicine and Hygiene* 2002, 66(2):157-162.

60. Sandoval N, Siles-Lucas M, Perez-Arellano J, Carranza C, Puente S, Lopez-Aban J, Muro A: A new PCR-based approach for the specific amplification of DNA from different Schistosoma species applicable to human urine samples. *Parasitology* 2006, 133(05):581-587.

61. Lawton SP, Hirai H, Ironside JE: Genomes and geography: genomic insights into the evolution and phylogeography of the genus Schistosoma. *Parasit Vectors* 2011, 4:131.

62. Kato-Hayashi N, Kirinoki M, Iwamura Y, Kanazawa T, Kitikoon V, Matsuda H, Chigusa Y: Identification and differentiation of human schistosomes by polymerase chain reaction. *Experimental parasitology* 2010, 124(3):325-329.

63. Ibironke OA, Phillips AE, Garba A: Diagnosis of Schistosoma haematobium by detection of specific DNA fragments from filtered urine samples. *The American journal of tropical medicine and hygiene* 2011, 84(6):998-1001.

64. Barral V, This P, Imbert-Establet D: Genetic variability and evolution of the Schistosoma genome analysed by using random amplified polymorphic DNA markers. *Molecular and Biochemical Parasitology* 1993, 59(2):211-221.

65. Rollinson: A wake up call for urinary schistosomiasis: reconciling research effort with public health importance. *Parasitology* 2009, 136(12):1593-1610.

66. Reinstrup L, Jørgensen A, Vennervald BJ: DNA extraction from dried Schistosoma haematobium eggs isolated on nylon filters. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2012, 106(4):270-272.

67. Johnston D, Dias Neto E, Simpson A: Opening the can of worms: molecular analysis of schistosome populations. *Parasitology Today* 1993, 9(8):286-291.

68. Littlewood DTJ, Lockyer AE, Webster BL: The complete mitochondrial genomes of Schistosoma haematobium and Schistosoma spindale and the evolutionary history of mitochondrial genome changes among parasitic flatworms. *Molecular phylogenetics and evolution* 2006, 39(2):452-467.

69. Huyse T, Webster BL, Geldof S, Stothard JR, Diaw OT, Polman K, Rollinson D: Bidirectional introgressive hybridization between a cattle and human schistosome species. *PLoS Pathogens* 2009, 5(9):e1000571.

70. Brouwer KC, Ndhlovu P, Munatsi A: Genetic diversity of a population of Schistosoma haematobium derived from schoolchildren in east central Zimbabwe. *Journal of Parasitology* 2001, 87(4):762-769.

71. Zarowiecki M, Huyse T, Littlewood D: Making the most of mitochondrial genomes–Markers for phylogeny, molecular ecology and barcodes in Schistosoma (Platyhelminthes: Digenea). *International journal for parasitology* 2007, 37(12):1401-1418.