Coinfection of Schistosomiasis and Hepatitis C in Egypt: Challenges and Possible Management Strategies

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1. Abstract

Schistosomiasis, also implied by Bilharzia is a parasitic infection, caused by worms. It has been reported that most human infectious worms are “Schistosoma mansoni, S. haematobium, and S. japonicum “, as they mainly depend on human blood for their nourishment. The parasites embark humans in their larval stages by puncturing the skin, and accordingly roaming via venous to the portal veins, wherein the worms lay eggs and finally cause Acute Schistosomiasis “ Katayama syndrome “, which is generally fever, and Chronic Schistosomiasis : abdominal ache, an Hepatomegaly, bleeding while urination and deflection, and complication ratifying urine are all symptoms. Chronic infection furtharly boost the threat of developing liver fibrosis or bladder cancer. A shift from Schistosomiasis to hepatitis C occurs in some cases as a result of egg sediment in the small portal venules , emerging liver cirrhosis and hepatocellular carcinoma, leading to a rise in death cases. Schistosomiasis and hepatitis C co-infection have been reported in most tropical countries, particularly Egypt. As Schistosomiasis with HCV is present in 50% of patients. The crucial problem arises from water contamination, specifically in Nile cities. We can survive against Schistosomiasis If we can reduce water contamination. The government is attempting to withstand the endemic in various strategies. Nevertheless, not all farmers and people serving in rural areas are conscious about the dilemma. The issue can be addressed through collaboration between the government, citizens, and health specialists, as well as WHO contribution and collaboration. In this write-up, we briefly reviewed how Schistosomiasis is entailing the Egyptian nation since the dawn of time, the challenges, and how the government handled possible surveillance strategies against it.

2. Introduction

Schistosomiasis is a parasitic affliction that is categorized second in preponderance and severity to malaria [1]. Infection was observed in mummies dating back to 5000 years ago. Scott was the prime to illustrate Schistosomiasis disorder patterns in the Egyptian Society. Schistosomiasis haematobium was popular (60%) in regularly irrigation sectors in both cases the Nile Delta and the Nile Valley at the southern part of Cairo, However, it was uncommon (6% in the basin irrigation district). Schistosoma mansoni infected 60% of the nation in the Northern and Eastern Nile Deltas, but merely 6% in the Southern Nile Delta. Its percentage in Egypt extends from 3% to 10% of the total infection rate around the world. Consequently, it has become an endemic problem in the country. [2]

Infection arises when skin touches the contaminated freshwater that contains the parasite-carrying snails. When infected people urinate or defecate in the water, Schistosome eggs pass into water. When the eggs hatch, the larval stage becomes the infective stage, evolving, and multiplying inside the snails if the relevant species of snails are existing in water. The parasite evacuates its intermediate stage, the snail and swims into water, where it can manage for 48 h. Cercaria (larval Stage of Schistosome) can pass into the skin of people who touch or swim in the contaminated water. Larval Schistosome migrates from tissues to blood vessels in weeks. On reaching the blood vessels of the rectum or urinary bladder they receive the needed nourishment in blood and develop into adult worms. When fully matured, males and females mate and produce
more eggs, some of them become resident in the liver and spleen causing their enlargement, and some pass through urine and feces to start new developmental stages on their direct contact with freshwater containing their suitable intermediate hosts. Diseases specific to the liver and spleen arise, emerging hepatosplenomegaly, portal hypertension, and eventually, gastrointestinal bleeding [3,4].

In endemic regions, Schistosomiasis and HCV infection coexist. Liver augmentation is broad in advanced cases, and it is frequently attributed to peritoneal fluid accumulation and abdominal blood vessel hypertension. The liver is deteriorated and becomes dysfunctional as a result of this co-infection [5].

There is still very limited published data concerning this infection. According to Atlas Schistosomiasis, 625 million people worldwide are in danger of Schistosomiasis infection, with Africans estimated to be 80% of this population at risk of infection [6].

Even though Egypt has conducted numerous programs of prevention and control to monitor and withstand the disease, the majority of the programs that have been executed are prosperous Modes of prevention according to Centers of Disease and Control Prevention are: When visiting countries where Schistosomiasis is existing, avoid paddling or bathing in freshwater. Wading in the sea and chlorinated pools are more protected. Infection can not prevail by drinking up the infectious stages, but if the contaminated water becomes in contact with the lips or face they may perforate the skin, so water to be boiled for 1 minute before drinking it, or filter to kill any dangerous parasites, that may be existing. Iodine handling will not guarantee that the water is protected and free of parasites. Towel rubbing after a random water disclosure may aid in the prevention of parasites penetrating the skin. While the aspects of control are: Getting rid of the snails that are compelled to maintain the parasite alive. Enhanced sanitation could lessen or eradicate the transmission of Schistosomiasis in all species. In addition, large-scale drug prescription as Praziquantel can be utilized in control programs, especially targeting youngsters. The government is yet in desperate need of modern means to bring up health awareness and work on more vaccination projects to be involved in the clinical trials. In this article, we will briefly explain the recent Schistosomiasis situation in Egypt and give some suggestions on how the government can cope with this endemic in possible alternative strategies [7] (Figure 1).

3. Dissociative Disorders

Schistosomiasis repeatedly coexists with supplementary serious diseases. Schistosomiasis can emerge a reduced physical barrier to HIV infection during sexual activity. Women genital Schistosomiasis is associated with a threefold or fourfold enhanced threat of HIV infection in population-based studies [8-10]. Increased CD4-positive cell concentrations in the sperm of men with serious S haematobium disorder inflicts this impact [11].

Furthermore, CD4-positive cells produce higher levels of HIV Co-receptors during functional Schistosomiasis, proposing more sites for HIV infection. Individuals with confirmed HIV Infection whom postpone Schistosomiasis medication had a promptly boost in HIV viral load and CD4 T lymphocytes depletion than whom received treatment earlier [12].

In a randomized trial, though, Schistosome or other helminth infection had no impact it took for HIV patients to become eligible for
antiretroviral medication. 64 Pediatric HIV viral load and Schistosomiasis co-infection, in which case prenatally HIV infection will ordinarily forego Schistosomiasis, has not yet been surveyed. Immunological defense against co-infecting infections, allergies, or even vaccinations may be altered by Schistosomiasis. During Schistosome infection, immuno-regulatory responses may down regulate IL-1 and T helper immune responses attributed with viral or protozoan infection control, or alter with vaccination. Schistosomiasis appears to modulate malaria in one of the most researched co-infections, however researches have shown varied results. [13, 14]. In children with Schistosomiasis, malaria prevalence, anemia, and pathological consequences are elevated in children with Schistosomiasis infection than in children without the disease, whereas immune responses of antimalarial infections are lowered. Additional research, on the other hand, has found that Schistosome infection has no effect on malaria, or even has a defensive effect, accompanied by enhanced immunological responses. Antigens related to Schistosomes and malaria might cross-react to some extent, complicating matters even more. The specific Schistosoma species involved could have a significant impact—for example, S haematobium may induce defensive responses while S mansoni enhances malaria susceptibility. This dissimilarity could be due to whether malaria sporozoites pass through an immune-compromised hepatic microenvironment caused by S mansoni egg granulomas [15].

4. How Egypt is trying to control the endemic

This neglected tropical disease, Schistosomiasis is found to be massive prevalent in Egypt with 60% distribution in Nile Delta and Nile valley cities, while down in established irrigation districts. The Lowest proportion perceived in middle and upper Egypt as Sohag, Qena, and Aswan [16] (Figure 2). Schistosomiasis was first observed in Egypt, as its eggs were discovered in the mummies of ancient Egyptians at 1600 B.C. The authorities battled to withstand and rectify the disease in a variety of ways. In Egypt, the introductory action to impede Schistosomiasis was initiated in 1920. The Egyptian Health ministry launched portable units to assess and care for all students at a substantial of those carried out in Egypt. They extended approximately Feddans with two million irrigated acres and a public of approximately 12 million population. Comprehensive land reclamation with drainage establishment has been finalized in several areas. The program was split into three groups: (1) Three-year intensive phase (2) Three-year consolidation phase 3) The upkeep

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phase. The intense phase included: (a) a three-times-per-year application of Niclosamide to a large area. (b) Meliorate (biracial) chemotherapy for infected people, three doses separated by 14 days. Praziquantel was first used as a therapy in 1988. A multinational investigating committee found out in 1985 that the prevailing in preponderance of Schistosomiasis haematobium had declined since the outset of management intervention. [22].

The project of Middle Egypt in 1977 estimation of almost 30% of the province has declined to around 8.5%. Furthermore, the Ministry of Health’s thorough statistics revealed a compatible declining tendency in prevalence rates. However, during the summer season, considerable Re-infections were realized among school-children, specifically among those of a younger age, showing that significant transmission was still occurring in the project area [26]. Despite the fact that an elevated status of control had been accomplished since the intervention’s inception, the findings revealed some increasing tendencies in infection majority during the upkeep phase. National Schistosomiasis Control Program in the Nile Delta (NSCP): This program started up in 1997 and was relied on the World Health Organization’s morbidity and mortality control protocol since 1984 [27].

The major activity was Praziquantel chemotherapy. All school children aged 6 to 18 years old, as well as all the village citizens where the preponderance of S. mansoni in outpatients from countrified health units was less than 20%, approved mass treatment without prior diagnosis. Treatment was only given to those who were infected. Furthermore, On water courses with an elevated snail consistency or harbouring sick snails, Niclosamide-based focused molluscicide was utilized. Moreover, Health education topics were carried out, as well as potential building through practicing of profession working in countrified health establishments or participating in snail management initiatives. The average of chemotherapy was high to 10% in 1999 as the programme proceeded and the plurality of S. mansoni decreased, in 2000 it declined to ,then 3.5% in 2002, and 3 percent in 2003. According to Ministry of Health records, 168 villages had a prevalence of more than 30%, 324 villages recorded a majority of 20–30%, and 654 villages had a prevalence of 10–20% in 1996, prior to the implementation of a major chemotherapy campaign. Foremost 20 villages in the region had a frequency of further than 3.5% by 2010 end, and none retained a preponderance of more than 10%.[27]

Currently, a multifaceted strategy is being wielded. This attempts to stop the spread of the disease and eliminate it by supplementing the recent strategy with other interventions such as chemotherapy campaigns for children and populations in high-risk areas, as well as increased condition awareness, public mobilization, snail influence as part of routine significant care actions, in addition to environmental sanity. The management approach used varies depending on the epidemiological situation. Surveillance and routine screening are carried out in freshly created areas where there is no transmission and no autochthonous cases. Effective society screening, post-treatment monitoring, snail control, in addition to water purification are all done in areas where Schistosomiasis prevalence is less than 3%. In the elevated prevalence regions, of more than 3%, however, chemotherapy treatment, snail discretion, and water sanitation are prioritized [21].

The use of Praziquantel on an annual basis significantly reduces the prevalence, severity, and reinfection of S. haematobium infection. Following medication, there was a decline in blocking IgG4 specific against schistosomal infections and a rise in IgG1, which is Schistosoma-specific defense [27] (Figure 3).

5. Praziquantel in the Treatment of Schistosomiasis

Eventually, the government utilizes Praziquantel as an anti-bilharzial mass drug. During its usage, a single dose verified considerable anti-schistosomal activity. Furthermore, it is affordable and non-toxic [28, 29].

Praziquantel proposes demonstrable benefits over previous Schistosomiasis therapy medications, and despite its 30-year use, no widespread resistance has developed. Surprisingly, Praziquantel’s extensive coup has reduced drug companies’ rationale to improve new Schistosomiasis medications. Nonetheless, Praziquantel possesses a variety of shortcomings. To begin with, it just acts on adult parasites, and a single dose is not adequate to eradicate all worms, especially in those with Severe intestinal outbreaks. Similarly, for people who have a lot of worms, treatment side effects can be extremely unpleasant, even if they are just provisional. [30].

For the foreseeable future, annual Praziquantel therapy will form the backbone of most control efforts, but extra therapies will almost certainly be compelled to control or eliminate Schistosomiasis in many districts. Annual MDA can not be enough to control morbidity in S. japonicum cases. [31].
Figure 2: Maximum point of prevalence of Schistosome spp. in Lower Egypt, while it gets lower prevalent in middle and upper Egypt

Figure 3: The authorities attempts to control and combat Schistosomiasis over other years

6. Egypt’s Government Protocols are Difficult to be Maintained

In the first instance, The government commenced to control the intermediate host of this worm. They are several species of snails that live in freshwater and play a crucial role in disease transmission. Firstly, the snails were manually collected from the water. The snails were accordingly dealt with chemicals such as Copper Sulphate or Niclosamide. Though, this strategy was troublesome to be pursued because gathering snails was tough for the staffers and the chemicals were diluted in water, therefore their desired action on the snails was not accomplished appropriately [32].
Treatment procedures had to be considered early on. Tartar emetic injections (Potassium antimony tartrate) were initially chosen as an antiparasitic injection against Schistosoma, but it has been broadcast that it has serious severe side effects [33].

The precautions while receiving injections were not suitably considered, as the poor sterilization and the poor hygiene, which in turn raises hepatitis B and hepatitis C infections [32].

Finally, the government compels Praziquantel, however it has lately been noted that some Schistosoma species have developed into multidrug-resistant organisms against Praziquantel. According to Ismaiel et al. in 1996, the three respectively doses of Praziquantel failed to treat 1.6% of the infected agriculturist in the Nile Delta district. As a result, these egg resistant eggs are subjected to more specific investigation, with their evolution being induced in mice to study their features more thoroughly. The developed worms from these eggs show disparities in the muscular tissues [34], the calcium influx [35], and finally the tegumental distribution in the worm, which in turn makes them less sensitive to Praziquantel [36].

In 1994 and 2005, a comparative study was conducted to examine the efficacy of Praziquantel. Praziquantel doses have lower activity, particularly against S mansoni, both in vivo and in vitro. In conclusion, S.mansoni revealed resistant action, which is inflicting health trouble in these villages. Last but not the least, the farmers’ manners were not manageable to be monitored by the government. Farmers urinate in the water. Step and swim in the water contaminated with cercaria or the snails. Living in conditions with poor sanitation and hygiene, that infection also could pass from person to another by fecal-oral contamination. [37]

7. What we can attain to withstand the endemic

The priority was to raise public health awareness about the misbehaviors of farmers. As a conclusion, TV health topics were executed by a TV public fan to the farmers Mohamed Reda, illustrating a statement to prevent urinating in the Nile and canals in order to exterminate this Egyptian endemic. These television campaigns were thriving in achieving their expectations, as urino-schistosomal infections dropped by 7% at that time [32].

Development and execution of novel procedure medications or protecting vaccines, more regular Praziquantel medication, or integrating treatment with policies that impede the function of cercaria-infested fresh water in propagation are all possibilities for improved interventions [38].

Observing novel chemicals and vaccines for Schistosomiasis has taken a lot of time and effort, and these endeavors should proceed. However, because no clinical trials are presently underway, these new technologies will take several years to be integrated into control or elimination programs. In the event of clinical resistance, Modified Praziquantel and Oxamnique derivatives and acceptable drug design could be significant, and approval may take less time because of closeness to the parent drugs. Although the antimalarial medicines Artesunate and Mefloquine show passive impact as against schistosomiasis, they do not appear to enhance effectiveness when used solely or in assortment with Praziquantel [39].

Medicinal plants can make a considerable contribution to resolving this problem. Garlic plants, in particular. Garlic has anti-schistosomal properties against S mansoni. It has been reported because of its anti-oxidant activity. An experiment was conducted on a group of infected mice, and garlic treatment resulted in a significant decrease in the eggs’ distribution and worms produced after infection [40, 41].

According to Shinaway et al. (2008) “aqueous Garlic extract hinders the growth and maturation of bilharzia eggs” [42].

Several tegumental changes were identified in male Schistosoma after garlic treatment. Worms that have been treated with garlic can recover and develop their tubercles, which are responsible for the worm’s attachment in the host’s blood tissues and veins. Pursuing treatment, the developed tubercles are found to be limited in number, and damaged. As a result, the worm’s attachment to blood vessels and veins is diminished [43]. Finally, ulcers were discovered to be present in the treated worms [44-46].

8. The active Schistosomiasis Diagnostic Criteria

Active Schistosomiasis is interpreted demonstrating viable eggs in the urine (S haematobium), feces (S japonicum, S mansoni), or generally in tissues. The presence of infectious Schistosomes cannot be ruled out conclusively at this time due to the restricted sensitivity of standard urinal and fecal investigations. Dipstick assays for hematuria, microscopic analysis of polycarbonate filters demonstrating eggs in urine [47, 48].

WHO approves the Kato-Katz fecal examination for Schistosome eggs Schistosomiasis mapping and field-based control. Despite the certainty that molecular techniques for observing Schistosome DNA in feces are more susceptible than microscopy, sampling limits persist due to the unequal distribution of eggs in the excrement. DNA detection in serum and urine is also being surveyed. Serological tests have been demonstrated to be useful in clinical settings [49].

Serology can be used to diagnose Schistosomiasis by identifying antibodies to schistosomal antigens, particularly in symptomatic travellers, but it cannot differentiate between ongoing infection and past exposure in those who live in Schistosomiasis-endemic areas. This challenge is handled by identifying circulating schistosomal antigen, and a point-of-contact circulating cathodic antigen assay is commercially available (Rapid Medical Diagnostics, Pretoria, South Africa). This lateral flow cassette technique uses urine to map S mansoni-endemic regions and appears to be more sensitive than the Kato-Katz assay. Its application enables on-the-spot S mansoni mapping without the requirement for stool collec-
Schistosome infection identification in snail hosts is an important public health element of monitoring, control, and elimination efforts. Snail xenodiagnosis, which uses so-called sentinel snails or wild collected snails, provides for the identification of environmental pollutants during control and eradication efforts [51]. Inducing cercarial shedding detects fully patent snail infections, whereas histological examination of snail tissues and molecular parasitological techniques such as PCR and loop-mediated isothermal amplification tests indicate pre-patent infections. According to comparisons of molecular and shedding assays, the majority of Schistosome-infected snails do not progress to patency [52].

9. Egypt Leverages Domestic Funding to Eliminate Schistosomiasis

The Ministry of Health and Population in Egypt (MoHP) has announced plans to speed up the elimination of Schistosomiasis (also known as bilharzia) by investing US$ 2 million per year over a five-year period. Funding for neglected tropical illnesses on a large scale is uncommon. According to Dr. John Jabbour, WHO Representative in Egypt, “the Egyptian government has made a significant commitment in response to the demand for domestic financing of NTDs, and WHO will push with global partners to help fill any remaining shortfall” [53].

A strong monitoring and evaluation component will allow areas to be reclassified from endemic to non-endemic, and will kick off post-intervention surveillance. Egypt wants to reduce Schistosomiasis transmission even more and eventually stop it [53].

10. The WHO Schistosomiasis Guideline for 2022 - New Schistosomiasis Control Strategies for HUGS

- To control schistosomiasis morbidity and eliminate the disease as a public health problem, WHO recommends annual preventive chemotherapy with Praziquantel in a single dose at 75 percent coverage in all age groups above 2 years old, including adults, pregnant women after the first trimester, and lactating women, in endemic communities with Schistosoma spp. prevalence of 10% or higher [54].
- Based on the program’s objectives and resources, WHO recommends one of two approaches in endemic communities with a Schistosoma spp. majority of less than 10%: (I) where there has been a regular preventive chemotherapy programme, continuation of preventive chemotherapy at the same or reduced frequency to interrupt transmission; (ii) where there has not been a regular preventive chemotherapy programme, a clinical approach of test-and-treat rather than preventive chemotherapy targeting a population [54].
- In endemic populations with a Schistosoma spp. incidence of 10% or more and a lack of an appropriate response to annual preventive chemotherapy despite adequate coverage, WHO suggests adopting biannual preventive chemotherapy instead of annual preventive chemotherapy (75 percent) [54].
- To control schistosomiasis morbidity, WHO recommends that all infected patients, regardless of age, have access to Praziquantel treatment, including pregnant and lactating women and children under the age of two [54].
- WHO advises water, sanitation, and hygiene programmes, environmental interventions (water engineering and targeted snail management with molluscicide), and behavioral modification treatments to help reduce Schistosoma spp. transmission in endemic areas. [54]
- WHO suggests a community verification process to seal the transmission halt, defined as no autochthonous human cases reported for five years. [54]

1- Using a diagnostic with a highly specific and sensitive test for infection in humans. This procedure may necessitate a two-step procedure involving available diagnostic procedures, beginning with a high test that is sensitive and followed by a high test that is specific [55].

2- Infection test in snails with a diagnostic with high sensitivity and specificity, if applicable. This procedure may necessitate a two-step procedure involving available diagnostic procedures, beginning with a high sensitive test and followed by a high specific test [55].

3- An infection test in animal hosts with a diagnostic with a highly sensitive and specific, if applicable. That procedure may necessitate a two-step procedure involving diagnostic procedures that is available, beginning with a test for the sensitivity and followed by a test for the highly specificity [55].

Egypt’s Ministry of Health and Population has announced the commencement of a campaign to certify the definitive elimination of schistosomiasis by 2020, after effectively reducing the prevalence of schistosomiasis to around 0.2 percent by the end of 2016. The campaign began in 2017 with the distribution of 14.5 million Praziquantel tablets, as well as an insecticide for the control of snails and cercaria-infested water, and the treatment of 6 million schoolchildren and citizens at a total cost of 40 million pounds, which included Praziquantel, pesticide, health teams, and water-course treatment in collaboration with the World Health Organization. The Central Administration of Endemic Diseases is organ-
ized around four major axes: mass therapy, snail control, health awareness and behavioral change, and environmental cleaning. The campaign will be conducted in two stages. The first phase began on July 30th and targeted one million and 35,900 citizens in 15 governorates: Alexandria, Gharbia, Ismailia, Menoufia, Damietta, Giza, Fayoum, Beni Suef, Qena, Sohag, Minya, Luxor, Aswan, and North Sinai, where the treatment was distributed to 573,269 citizens in the first week. Mass treatment of high prevalence areas is being done in 359 villages in these governorates, and 8,140 km of waterways in these governorates are being treated to eliminate the snail’s intermediate host of schistosomiasis. The second phase, which began in October 2017, targeted 5 million pupils and civilians while treating 10,120 kilometres of waterways in five governorates: Bohaira, Kafr El-Sheikh, Dakahlia, Sharqia, and Qalyubia. It have to be remembered that in 1983, the national prevalence of schistosomiasis was close to 40%, and that schistosomiasis is a health concern with social and economic consequences. There are around 300 localities in Egypt with a prevalence of more than 3%, mainly among kids. Reduce schistosomiasis prevalence to roughly 0.2 percent by the end of 2016, and conclude the campaign by 2020 to confirm the complete eradication of schistosomiasis in Egypt [55].

11. Conclusion

Schistosomiasis is a centuries-old human disease that affects people all throughout the world, especially in the poorest neighborhoods. Early intervention that works is available, reducing the negative consequences of Schistosoma infection on human health because of immune-mediated consequences Local implementation of contemporary diagnostic examinations and therapy implementation strategies is being prioritized.. The public health agenda will then shift from curative to truly preventive.

In the development of a schistosomiasis vaccine, various approaches are being examined. These comprise main Schistosome biology research, human epidemiological and immunogenetic studies, the improvement of several vaccines. Vaccination trials in experimental animals ranging from mice to water buffalo, as well as native proteins corresponding to its native source, or even recombinant proteins, multivalent peptide constructs, and RNA vaccines. When viewed as a whole, the scope of research on schistosomiasis vaccine development is significant. Hopefully, these efforts will pay off.

Schistosomiasis can now be treated with relative ease, because of the availability of a variety of effective medications, many of which are taken orally. The response to some prescriptions can vary greatly depending on where you live. The emergence of weakly susceptible (tolerant) strains is cause for concern, and it necessitates additional research to discover novel disease-control treatments.

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53. 2016 WHO, Egypt leverages domestic funding to eliminate schistosomiasis
