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Review Article

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Elimination of *Schistosoma japonica* in Central Sulawesi, Indonesia Intermediate Snail Control and Utilization Medicinal Plants

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ABSTRACT

Schistosomiasis is a zoonotic health problem caused by infection with the schistosoma class parasite, which lives in human blood vessels and around the intestines and bladder. Intermediate hosts in the form of snails and definitive hosts in animals and humans can be influenced by physical, chemical and biological environmental conditions. Schistosomiasis in Indonesia is caused by the trematode worm *Schistosoma japonica* (*S. japonicum*) with the intermediate host being the snail *Oncomelania hupensis lindoensis.* Schistosomiasis is still a public health problem in endemic areas. In Indonesia, schistosomiasis is only found in Central Sulawesi Province, namely the Napu Plateau and Bada Plateau, Poso Regency and Lindu Plateau, Sigi Regency. *S. japonica* is currently endemic in three very remote areas in Central Sulawesi Province, Indonesia. An integrated schistosomiasis control program has been implemented, however, the reported prevalence data shows a trend of increasing schistosomiasis prevalence in three endemic areas in Central Sulawesi. Eliminating schistosomiasis in Indonesia is not easy. This review will examine several challenges hindering the implementation and sustainability of schistosomiasis elimination programs, including the *S. japonica* intermediate snail control program and the use of medicinal plants for the treatment of schistosomiasis.

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INTRODUCTION

Schistosomiasis is a disease caused by parasites of the *S. japonica* , usually called *Bilharzia or* "snail fever" disease , which is mediated by aquatic snails if contaminated with schistosoma parasite (Kaunang *et al.*, 2022). Schistosomiasis is also a neglected tropical disease, and has been around for more than 80 years, namely since this disease was first discovered in the Lindu and Napu Valley areas in Indonesia. Several species of trematodes that cause schistosomiasis include *S. haematobium, S. mansoni,* and *S. japonicum*. Then the intermediate host for *Schistosoma* is the snail *Oncomelania hupensis lindoensis* which infects humans and several other mammal species including wild rodents (*Rattus exulans, Rattus hoffmani, Rattus chysocomus rallus, Rattus marmosurus*, and *Rattus celebensis*), wild boar (*Sus scrofa*), deer wild (*Cervus timorensis*), wild cedar (*Crocidura nigripes*), wild civet (*Viverra tangalunga*), cattle (*Bos* spp.), buffalo (*Bubalus bubalis*), horses (*Equus caballus*), and dogs (*Canis familiaris*) (Satrija, Ridwan and Rauf, 2015).

There are two main forms of schistosomiasis, namely intestinal and urogenital schistosomiasis. Intestinal schistosomiasis is common in Southeast Asia and the West Pacific, causing abdominal pain such as diarrhea and bloody stools. It is known that

the majority of chronic schistosomiasis patients show enlargement spleen and liver fluid buildup in the stomach (ascites) can be seen in the final stages of the disease which can cause death. Meanwhile, urogenital schistosomiasis is not often found in Indonesia, it can be characterized by indications of blood in the urine. Based on its epidemiology, this parasite spread through the migration of foreign tourists, and settled in three regions of Central Sulawesi in Indonesia, such as the Lindu, Napu and Bada highlands. If someone is infected with schistosomiasis, clinically it can cause itching and a rash on the skin area. Additional symptoms of schistosomiasis include fever, urticaria, eosinophilia, cough, lethargy, diarrhea, weight loss, hematuria, headache, joint and muscle pain, splenomegaly and hepatomegaly (Kaunang *et al.*, 2022). The effort to control the distribution chain *of schistosoma* is to use a "Geographic Information System" (GIS) strategy, namely by collecting a number of data to map distribution information with the level of occurrence in an area (Sakinah, 2022).

The integrated schistosomiasis control program is divided become 6 projects with responsibility for conducting fecal surveys and snail surveys every six months. This has resulted in snail habitat mapping, reservoir animal surveys, environmental modification through agricultural engineering, community participation, provision of clean water and sanitation facilities, and health education for affected community. This review covers various aspects of schistosomiasis control and elimination which are important steps to achieve the target of schistosomiasis elimination in Indonesia by year 2029. This review will examine several challenges hindering the implementation and sustainability of schistosomiasis elimination programs including the *S. japonicum* intermediate snail control program and the use of medicinal plants for the treatment of schistosomiasis. By overcoming challenges and implementing recommended control methods including the, Indonesia is moving closer to achieving the target.

MATERIALS AND METHODS

The research method used was a literature study referring to collecting data on *Schistosoma japonica* cases that occurred.

RESULTS AND DISCUSSION

Biology and Life Cycle *of S. japonicum*

Schistosomiasis in Indonesia is caused by the trematode worm type *S. japonicum* with the intermediate host being the snail are found throughout the plains in pockets, the area of which varies between a few square meters to several thousand square meters. There are two types of habitat, namely natural habitat (areas on the edge of the forest, in the forest or on the edge of a lake where these places are almost always protected from direct sunlight because of the presence of large and small trees and are always wet because of the water that comes out continuously continuous from the slopes above) and habitats that have been touched by humans (former rice fields that have long been abandoned and are no longer worked on, pastures from former farming areas, edges of irrigation canals, etc.) (Araujo Navas *et al.*, 2018). The presence of the snail *Oncomelania hupensis lindoensis*, and the like have an important role in the transmission of schistosomiasis. There are three different groups of *Oncomelania hupensis* which are separated geographically, namely *O. hupensis Robertsoni* (soft shell, without varix), *O. hupensis Tangi* (soft shell, strong varix), and *O. hupensis* (smooth or ribbed shell, strong varix) (Angelo *et al.*, 2018). The habitat of Oncomelania snails is also influenced by temperature conditions, soil type, vegetation type, and the adequacy of water to support the development of cercariae snails through distribution movements (Calata *et al.*, 2019).

Diagnosis

Stool examination is the key method used to diagnose suspected schistosomiasis infection. For examination purposes, several diagnostic techniques are available, Kato-Katz, miracidium hatching test (MHT), formol ether (FECT), circulating cathodic antigen (CCA), point of care test (POCT), and molecular test polymerase chain reaction (PCR) (Nelwan, 2019). The Kato- Katz technique is recommended by WHO for diagnosing and quantifying schistosoma infections and other helminth infections (e.g. food-borne trematodes) (Utzinger *et al.*, 2012).

Diagnosis of parasitic diseases is influenced by clinical epidemiology and the examination techniques used. Several qualitative fecal examination techniques consist of direct examination, sedimentation and flotation. The native method (slide direct*)* is the gold standard for qualitative stool examination because it is sensitive, cheap, easy and fast, but less sensitive for mild infections. Another method that is often used for qualitative examination of feces is the sedimentation method. Examination using the sedimentation method uses a solution with a lower specific gravity than parasitic organisms, so that parasites can settle at the bottom. This method consists of the ordinary sedimentation method which utilizes gravity, and the Formol-Ether sedimentation method which utilizes centrifugal force and a formalin-ether solution in its workings (Regina, Halleyantoro and Bakri, 2018).

Epidemiology

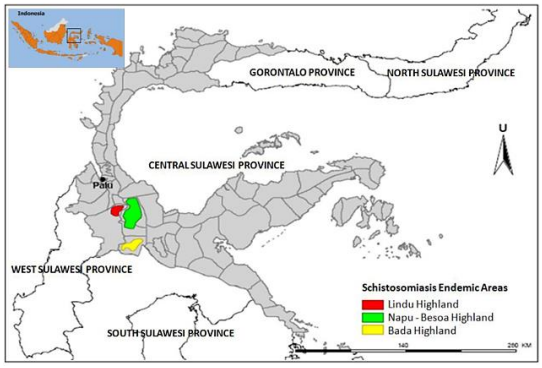

Figure 1. Schistosomiasis endemic areas in Central Sulawesi, Indonesia. (Satrija, Ridwan and Rauf, 2015)

Current Status of Schistosomiasis Control in Central Sulawesi

In the process of controlling the people of Central Sulawesi against schistosomiasis, it is necessary to enforce attitudes and behavior to overcome and prevent the disease from sources of infection, namely animals such as dogs, cats, ruminants, pigs and other mammals. This control is carried out through social activities such as giving questionnaires (pretest and posttest) and counseling. Before the counseling was carried out, a pretest was carried out and the results were that many people still got a good score of 12 (54.54%), because people did not really understand the importance of using in preventing schistosomiasis. People will be more susceptible to being infected with schistosomiasis due to the habits/behavior of the majority of people who still have the habit of bathing, washing and defecating in rivers. Likewise, the habit in the form of boots or rubber gloves is very effective in preventing contact with cercariae which are the infective form of the schistosoma. The results of the participants' counseling obtained a good average score, because many people already understand the importance of using PPE in preventing the community disease. Knowledge greatly influences people's attitude. Preventive care involves health-promoting activities including specialized health education programs, designed to help clients reduce the risk of illness, maintain optimal function and promote habits associated with good health. Theoretically, the conditions of formal and non-formal education influence people's actions. The knowledge that respondents gain through experience of events and environmental conditions of the community's natural resources (Jumain *et al*., 2024).

In the process of controlling the schistosomiasis vector, it is necessary to handle reservoir animals that are closely exposed to the disease, including cows, buffalo, horses, dogs and pigs. Treatment for cows, buffalo and horses is carried out for the entire animal population. This was done considering that the entire livestock population was grazed freely without supervision and selective treatment of populations that might still be infected as part of the surveillance system. Apart from that, there are control strategies for schistosomiasis intermediate snails, namely spraying molluscicides (snail poison) and environmental modification. However, the use of molluscicides must be limited to prevent the emergence of resistance and the death of other organisms which have the potential to disrupt environmental balance (Widjaja *et al*., 2022).

Prospects and Challenges of Schistosomiasis Control in Central Sulawesi

The risk of schistosomiasis occurring in the Bada, Napu and Lindu Highlands is that it must involve formal and informal figures such as traditional heads, regional heads and local health officers to provide education and form a schistosomiasis control team so that they can empower the community not to underestimate fever. snail. Apart from that, it can also be enforced through village regulations, community forums, PKK, RT meetings, recitation places, churches and posyandu to provide understanding regarding schistosomiasis. However, sometimes, the intervention level of community education is inadequate and health workers are also less skilled, resulting in schistosomiasis prevention being less effective. So, a variety of methods can be used, such as: the one health method and the socio-cultural method (Ningsih, 2022).

According to (Pitriani and Rau, 2017) stated that, it is known that PHBS (Clean and Healthy Living Behavior) behavior in the people of the Bada, Napu and Lindu Highlands is classified as less than optimal, this is supported by the lack of adequate sanitation, as well as a lack of clean water supply. Then the survey of the number of snail hosts is not very important, namely the administration of the drug praziquantel, is not optimal. Then, when compared with research, (Anastasia *et al.*, 2022) it shows that the low level of knowledge of schistosomiasis regarding the causes, symptoms, intermediate snails, and transmission methods caused the prevalence of infection to increase in 2018. Therefore, efforts such as GEMA-BERAKSI (Independent Community Movement to Eradicate Schistosomiasis Snails) have been promoted to suppress high prevalence of infection.

Vector Control

Control of schistosomiasis recommended by WHO focuses on reducing disease through regular and mass treatment with praziquantel and a comprehensive schistosomiasis control approach, including providing adequate clean water, good sanitation, and controlling snails which can reduce the transmission. Several community interventions carried out through community empowerment in several middle-income countries, for example India and Mongolia, have shown promising results in terms of sustainability. Health promotion strategy community empowerment requires high participation from the target so that it has a significant impact on behavior change (Erlan *et al*., 2020).

Mechanical control is carried out by management and/or environmental modification. Environmental management includes activities to repair water channels in focus areas, leveling grass on the edges of water channels with the aim of facilitating water flow. Smooth and strong water flow can reduce the potential of this place as a focus. Then environmental management too must be done by planting empty land using production crops, for example vegetables, chocolate and candlenuts. This processing activity focuses on reducing the potential for land to become a focus for intermediate snails. control activities with environmental modification are carried out by changing flooded areas into productive fish ponds. This is done based on the biological characteristics of snails which will die if they drown in water. By making a pond, the water that collects becomes large and deep, so that the schistosomiasis snails will die. Apart from that, people can also take advantage of other benefits, namely fish as a source of animal protein. Another

environmental modification activity is converting empty land into irrigated rice fields. By having a regular planting pattern in the rice fields, it will reduce the occurrence of empty land in the focus area. This environmental modification was implemented in the focus area of Mekarsari Village, namely the focus area was converted into rice fields and vegetable gardens such as cabbage and leeks. Control can also be done by changing the way rice fields are processed, for example by intensifying agriculture, using superior seeds, processing rice fields throughout the year, improving irrigation, agricultural mechanization Erlan, *et al*. (2020).

Treatment

1. Chemical drugs

Single-blind RCT *(*Randomized Controlled Trial) research where doses were randomly given to infected with *S. hematobium* as many as 186 PSAC and 195 SAC were randomly given a dose of 20, 40 or 60 mg/kg praziquantel or placebo. Demonstrated Praziquantel demonstrated high response rates in PSAC and SAC infected with *S. hematobium, with* high efficacy observed at 20 mg/kg (Coulibaly *et al.*, 2018). Treatment is basically to reduce and prevent pain and reduce sources of infection. The praziquantel treatment pattern is carried out by giving the drug to the patient according to a predetermined dose according to body weight (Tandi, 2018).

In general, schistosomiasis sufferers are those who always have habits that are inseparable from water. So frequent contact with waters infected with the schistosomiasis parasite has led to an increase in sufferers in surrounding communities. The government has made efforts to overcome schistosomiasis both preventively and curatively. Treatment issued by the Sub-Directorate of Filariasis and Schistosomiasis, Directorate of P2B2, Directorate General of PPM and PLP, Ministry of Health of the Republic of Indonesia uses praziquantel. Praziquantel works by treating all forms of schistosomiasis and schistosomiasis infections. Praziquantel itself is easily absorbed when administered orally and spreads. The drug is completely oxidatively metabolized, causing the half-life to be short and the metabolites to be inactive and excreted in the urine and bile (Syam, Bungawati and Faisal, 2018).

Praziquantel (PZQ) is a safe drug and has become the main strategy for controlling schistosomiasis. Mass treatment coverage using praziquantel in several endemic villages is still found to be very low. Praziquantel is very effective against all forms of schistosomiasis, both in the acute and chronic phases and those who have experienced splenomegaly or who have experienced other complications. This drug has safe effectiveness and has mild side effects so the required dose is 60 mg/Kg BW divided in half and taken within a period of 4-6 hours (Widjaja *et al.*, 2022).

2. Medicinal Plants (Herbs)

Areca seeds (*Areca catechu* L.) have an effect as a traditional medicine with properties that kill worms in the intestines, are antimutagenic, antioxidant, and accelerate healing. The components contained in areca seeds include arecain, arekoline, guvalokin, guvasine, arekolidine, and isoguvasine. Ethanol juice from areca nut seeds also contains flavans, phenolic compounds, tannins that undergo changes in form, tannins that undergo substance decomposition, oils that can evaporate and do not evaporate, glanic acid, lignin, and gum. The presence of this effect opens up the opportunity to develop areca nut (*Areca catechu* L.) as an anti-schistosomiasis agent. The areca nut ethanol extract nanoparticle preparation was made using a technique involving a cross-linking process between polyelectrolytes in the presence of multivalent ion pairs. In the formation process, 5 grams of areca seed ethanol extract was used, producing 0.5 g of areca nut ethanol extract nanoparticle preparation with a yield of 10%. The aim of forming this nanoparticle preparation is to avoid problems with the solubility of active substances that are difficult to dissolve, increase low bioavailability, and reorganize the drug distribution process so that the drug directly reaches specific areas. In addition, this dosage form is able to maximize the balance of active substances by protecting them from environmental degradation (such as enzymatic decomposition, chemical reactions, decomposition of substances in chemical reactions), increasing the absorption of macromolecular compounds, and minimizing the irritating effect of active substances on the digestive tract. The use of nanoparticles as a drug delivery method can accelerate the spread of drugs in the circulatory system and increase the speed of onset of drug effects. Nanoparticles are often a common choice as a drug delivery system. This study began by infecting mice via intraperitoneally induced cercariae. The mice were then incubated for 2 weeks, and fecal testing was carried out to count the number of *S. japonicum eggs*. As a result, the mice were diagnosed with schistosomiasis. Monitoring of the anti-schistosomiasis activity of the areca nut ethanol extract nanoparticle preparation was carried out after 3 days post-treatment. The results of the study using nanoparticle preparations of areca seed ethanol extract at doses of 30, 60 and 120 mg/kg BW had an anti-schistosomiasis effect on male white rats (*R. norvegicus*) infected with *S. japonicum* by reducing the number of eggs after the 3rd day of therapy (Handayani *et al.*, 2024).

African leaves (*Vernonia amygdalina* Delile) come from the Asteraceae family and grow widely on the western African continent, especially in Nigeria and Malaysia. African leaves (*V. amygdalina*) contain flavonoids, tannins, saponins and terpenoids which are able to kill parasites that cause malaria, anti-amoeba, anti-tumor, antimicrobial, antioxidant, HIV/AIDS, anti-diabetes. Essential oils have also been obtained from these leaves and are toxic (Nainggolan, Simaremare and Pratiwi, 2018).

One Health Approach

The approach is through the role of religious leaders and traditional leaders to provide an

understanding of schistosomiasis, both knowledge and healthy living behavior so as not to contract schistosomiasis. Another function is to mobilize the community during stool collection and treatment. Socialization is carried out during worship activities and traditional leaders have full authority to provide customary rules/sanctions for those who do not collect feces. Regarding customary sanctions, these are contained in village regulations, which are agreements between informal figures, namely traditional leaders, village heads, religious leaders.

Research (Majee *et al.*, 2023) , regarding the physical health and nutrition of the African-American (AA) community, shows that the influence of religious figures' intervention in health promotion can influence spiritual habits, improve congregational health and better social support to facilitate behavior change. Healthy. Faith-based health promotion can reduce health disparities and the church functions as a respected institution, entrusted with improving faith and community health. The role of the church as an intervention unit (Majee *et al.*, 2023). Research in Tetel village, Purbalingga Regency, developed a malaria control model in the form of village regulations (Perdes) regarding the discovery and supervision of community-based treatment of malaria cases. Involving village officials, religious leaders, PKK, health cadres, village midwives, the village regulations were socialized through health forums, study sites, posyandu and RT meetings. The result is that malaria cases in Tetel village tend to decrease even to zero after the implementation of the village regulation (Kesuma *et al.*, 2018).

The one health method is a multidisciplinary approach to respond, prevent or even reduce the rate of transmission of zoonotic diseases involving healthy human, animal and environmental sectors to break the chain of spread of schistosomiasis infection. However, in terms of implementation, it is said to be difficult because it has to start from small communities, the education sector, and the health workers on duty. This challenge must have a major impact, starting from knowledge related to schistosomiasis infection, clinical symptoms, epidemiology of the spread of schistosomiasis, treatment, control and appropriate treatment to form a one health-based society (Roostita, Hendarmawan and Supriatna, 2019). The preventive measures taken must be carried out continuously every year, so as to minimize the death rate due to schistosomiasis infection. Then, controlling schistosomiasis, with large-scale treatment of certain community groups, has a big impact on access to clean water, hygienic sanitation, changes in individual community behavior, control of wild snail pests and one health-based environmental management (Wartana *et al.*, 2023).

The 2018-2025 schistosomiasis elimination roadmap is used as a reference for planning, budgeting and evaluating annual achievements across sectors. Schistosomiasis elimination targets include schistosomiasis intermediate snails decreasing to 0%. China has succeeded in eradicating schistosomiasis by prioritizing community participation and involving cross-sectors in the management and development of snail habitats into tourism areas, theaters, restaurants and parking lots. This can be done because of the commitment of all parties together across sectors to eradicate schistosomiasis. The obstacle to controlling snails by related sectors is that controlling schistosomiasis is not yet a top priority so that budgeting for schistosomiasis control activities is very limited across sectors. Apart from that, the physical development targets carried out by cross-sectors have not been appropriate. The development of the Bada model in other endemic areas will integrate cross-sector activities to be more targeted. One strategy to change people's behavior is to use power or force through the implementation of village regulations regarding controlling snail fever. This strategy has proven to be quite effective in increasing community participation in the use of personal protective equipment (PPE), increasing the scope of feces collection, livestock must be kept in cages, utilize latrines, and play an active role in cleaning focus areas. This is a behavior that society must carry out to prevent the transmission of schistosomiasis to humans. Optimal prevention and control of schistosomiasis and regular receipt of Praziquantel (PZQ) treatment is very dependent on sustainable programs and knowledge, attitudes and practices (KAP) approaches in the community. Schistosomiasis control in Cameroon can only be successful and sustainable if people living in areas where snails are focused have the right knowledge, positive attitudes and correct prevention and control practices regarding schistosomiasis disease (Erlan *et al.*, 2020).

CONCLUSION

Schistosomiasis is a worldwide disease and requires the integration of several measures to promote its control. *S. japonica is* transmitted indirectly to humans and more than 40 and various wild animals are also infected with *S. japonica* in endemic areas. The existence of a new endemic area in the Bada valley indicates the possibility of expanding *S. japonica* endemicity to other areas in Central Sulawesi. Vector control through a cross-sector one health approach must be carried out to reduce environmental pollution, thereby reducing snail infection rates and limiting disease cycles over time. Clinical treatment with antiparasitic agents, as well as the use of molluscicides for biological control. The formulation of active compounds in medicinal plants has antiparasitic activity which can be used to break the *S. japonica* cycle. Further research is needed with active formulations and optimization of the best candidates for use in combating schistosomiasis in Indonesia.

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AUTHOR CONTRIBUTIONS

AMC. Contributed resources, supervision, AN. project and administration, AAP. writing original, RSA. software validation, FAS. data curation, HM. conceptualization, VLM. writing-review and editing, NH, KDA. project administration HA. software validation, SW. writing-review and editing. All authors provided critical feedback and helped shape the research, analysis and manuscript.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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