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Epidemiology of *Schistosoma japonicum* in Sulawesi, Indonesia: A review for eliminating the parasite

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Abstract

Purpose: In this review, I report a study of schistosomiasis japonica that focused on some important issues, such as life cycles, clinical manifestations, diagnosis, and schistosomiasis japonica control. **Main results**: Schistosomiasis japonica occurs in China, Indonesia, and the Philippines. The life cycle of Sulawesi schistosomiasis japonica requires two intermediate hosts: *O. lorelindoensis* snails (formerly *Oncomelania hupensis lindoensis*) and definite hosts. Definite hosts include mammals and nonmammals. The disease occurs in the Bada Valley, the Lindu Valley, and the Napu Valley. It may have also prevailed in other areas, such as the Lariang River, the Palu River, and the Salo Karangan River (formerly the Lariang River in the Bada Valley). Clinical manifestations include Katayama syndrome and chronic manifestations. Many methods are available for detecting schistosomiasis. These may include the Kato-Katz, dot-blot enzyme-linked immunosorbent assay (dot-blot ELISA), soluble egg antigen and indirect hemagglutination assay (SjSEA-IHA). (Ar)praziquantel are drugs that can be helpful for the treatment of Sulawesi schistosomiasis japonica. Several drug candidates have been studied such as garlic extracts. In addition, in the future, genetic manipulation techniques on the intermediate host can be useful for eliminating the parasite. Vaccine candidates include *Schistosoma japonicum* acetylcholinesterace (SjAChE) and *Schistosoma japonicum* insulin receptor 1 (rSjLD1). Vaccines can be potential approaches for eliminating the disease. **Conclusion**: The Kato-Katz technique, dot-blot ELISA, and SjSEA-IHA are methods for detecting schistosomiasis japonica. Sulawesi schistosomiasis japonica may have prevailed in new areas such as the Lariang River and the Salo Karangan River. Treatment, diagnosis, and, in the future, vaccines may be helpful approaches for eliminating Sulawesi schistosomiasis japonica.

Key words: *Oncomelania lorelindoensis, Elimination, Epidemiology of schistosomiasis, Praziquantel, Schistosoma japonicum, Schistosomiasis japonica, Transmission of schistosoma japonicum*

1. Introduction

The epidemiology of schistosomiasis includes clinical manifestations, distribution, endemic areas, intermediate hosts, life cycle, and *Schistosoma* parasites (Gordon *et al.*, 2019; Mazigo *et al.*, 2012; World Health Organization, 2023). Schistosomiasis is second only after malaria, which causes human suffering in endemic countries

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(Olveda *et al*., 2014) and public health problems. It needs to be controlled or eliminated to resolve public health problems due to schistosomiasis, especially Sulawesi schistosomiasis japonica. Sulawesi schistosomiasis japonica elimination can be achieved through control, such as diagnosis and treatment. In the future, it could be through vaccination of animals and humans and genetic manipulation techniques.

Schistosomiasis japonica derives from infection with blood fluke of the *Schistosoma japonicum*. The parasite occurs in China, Indonesia, and the Philippines (Nelwan, 2019). In Indonesia, it occurs in Central Sulawesi Province. In this province, this parasite occurs in two districts: Poso and Sigi. These comprise the Bada Valley, the Lindu Valley, and the Napu Valley. The Bada Valley and the Napu Valley are in Poso District, while the Lindu Valley is in Sigi District. Budiono *et al.* (2019) stated that the Bada Valley is a new habitat of *S. japonicum* (Budiono *et al*., 2019). Schistosomiasis, including schistosomiasis japonica, can also occur in nonendemic areas. It can spread through water-based development projects and movements of populations with this disease, i.e., from rural areas to urban areas, immigration (Nelwan, 2019), and travel and tourism (World Health Organization, 2023).

Brug and Tech reported the presence of *S. japonicum* eggs in human bodies in Palu Hospital, Central Sulawesi, in 1937 (Budiono *et al*., 2019). In 1948, Faust and Bonne reported the finding of adult worms of Sulawesi *S. japonicum* in humans, mice, and other wild-type animals in the Lindu Valley (Kurniasih *et al*., 2002). Carney *et al*. found the intermediate host of the parasite in the Lindu Valley in 1971 in *Oncomelania lorelindoensis* (formerly *Oncomelania hupensis lindoensis*) within the *O. hupensis* group (Sudomo, 1983). Nelwan named this intermediate host *O. lorelindoensis* and beyond the *O. hupensis* group (Nelwan, 2022; ZooBank, 2022).

Two hosts are involved in the life cycle of Sulawesi schistosomiasis japonia: *O. lorelindoensis* (Nelwan, 2022) and definite hosts that include mammals, nonmammals (Budiono *et al*., 2019), or animals (Budiono *et al*., 2020). Definite hosts of schistosomes may also comprise birds (Walker, 2011). This means that it is likely that *S. japonicum* likely infect birds due to the genus schistosomes have adaptability to new hosts (Diaz *et al*., 2023). Nelwan suggested that asexual reproduction occurs in *O. lorelindoensis* and sexual reproduction occurs in definite hosts. Clinical manifestations of the disease comprises acute or Katayama syndrome and chronic manifestations. Katayama syndrome can comprise fever and headache. Chronic manifestations can comprise blood in the stool, constipation, and diarrhea (Nelwan, 2019).

To diagnose Sulawesi schistosomiasis japonica, several approaches are available. These can comprise the Kato-Katz, miracidium hatching test (MHT), dot-blot enzyme-linked immunosorbent assay (dot-blot ELISA), *Schistosoma japonicum* soluble egg antigen and indirect hemagglutination assay (SjSEA-IHA), recombinase polymerase amplification in combination with lateral flow dipstick (LFD-RPA), and ultrasonography (US). Vaccines are currently unavailable. Nevertheless, studies are ongoing. Candidate vaccines can comprise *Schistosoma japonicum* acetylcholinesterace (SjAChE) and *Schistosoma japonicum* insulin receptor 1 (rSjDL1). For treatment, (ar) praziquantel could be an effective drug for treating Sulawesi schistosomiasis japonica. Additionally, in the future, vaccination can be useful to eliminate the disease (Nelwan, 2019), especially in Sulawesi.

In this review, I report a study of schistosomiasis japonica that focused on some important issues, including Sulawesi *S. japonicum*, *O. lorelindoensis* as an intermediate host, the habitat expansion of the parasite, its life cycle, clinical manifestations, diagnosis, and schistosomiasis japonica control as purposes of the review.

2. Methods

I used Google, ScienceDirect, and the PubMed Database at NCBI to search articles on schistosomiasis japonica published between 2009 and 2024. However, other relevant publications published before 2009 were also included if the articles were suitable for review. In addition, Keywords for searching articles comprised diagnostic tools for the detection of schistosomiasis japonica, drugs for schistosomiasis japonica, Sulawesi *Schistosoma japonicum,* schistosomiasis japonica, and Sulawesi schistosomiasis japonica.

3. *Schistosoma japonicum*

The hypothesis "out of Asia" suggests a migration followed by the spread of the *Schistosoma* parasites from Asia to Africa. This parasite had at least two descendants that invaded the African continent independently and parasitized exclusively planorbid snails. Back in Asia, the parasites diversified into a group of species, marked by the absence of the spike in the eggs (Nahum *et al*., 2012). In Asia, the genus *Schistosoma* forms an *S.*

japonicum complex that comprises *S. japonicum, S. malayensis, S. mekongi, S. ovuncatum,* and *S. sinensium* (Lawton *et al.,* 2011).

The data suggest that the development of rice cultivation might play an important role in the expansion of *S. japonicum* in Asia. The data show that it originated in the lake area of China and radiated to Japan approximately seven thousand years ago and to the mountainous region of China approximately five thousand years ago. Then, it radiated to the Philippines and Sulawesi approximately four thousand years ago (Yin *et al.,* 2015). In Sulawesi, *S. japonicum* occurs in Central Sulawesi (Budiono *et al.,* 2019; 2020), the National Park of Lore Lindu and its surroundings.

4. Expansion of *Schistosoma japonicum* in Sulawesi

In 1940, Sandground and Bonne found that 53% of the Lindu Valley population was positive for Sulawesi schistosomiasis japonica (Rosmini *et al.,* 2010). In 1973, Carney *et al*. found it in the Napu Valley. The authors also reported that a few cases of the disease occurred in the Kulawi Valley and the Palu Valley. Individuals in these cases spending considerable time visiting or working in the Lindu Valley (Sudomo and Carney, 1974), suggesting that the Kulawi Valley and the Palu Valley are potentially endemic areas for Sulawesi schistosomiasis japonica. The Bada Valley is a schistosomiasis endemic area found in 2008 (Budiono *et al.,* 2019). The opening of land transportation to the Bada Valley caused the spread of the disease in this area (Rosmini *et al.,* 2014).

The genus *Schistosoma* has adaptability to new habitats (Diaz *et al.* 2023). In the case of schistosomiasis in Corsica, France, this disease occurs in a river, the Cavu River. Utzinger *et al*. (2015) stated that blood fluke worms with schistosomiasis infected a healthy people after bathing in that river in southern Corsica River. In Corsica, *S. hematobium x S. bovis* hybrid infections have occurred in the Cavu and Solenzara Rivers in people bathing in those two rivers (Rothe *et al.,* 2021). The presence of a new endemic area in the Bada Valley and habitats of *O. lorelindoensis* could be in rivers (Hariyanto, 2007), indicating that Sulawesi *S. japonicum* may have also prevailed in rivers around the Bada Valley, the Lindu Valley, and the Napu Valley. The endemic area of Sulawesi schistosomiasis japonica in the Bada Valley is near the Salo Karangan River (formerly the Lariang River in the Bada Valley) (Nurwidayati *et al.,* 2018). The Salo Karangan River flows through the Bada Valley and in South Sulawesi Province. Birds (Brant and Loker, 2005; Walker, 2011; Head *et al.,* 2016), cattle, dogs (Adenowo *et al.,* 2015), humans (Budiono *et al.,* 2019), mice, swine (Adenowo *et al.,* 2015), and wild pigs can excrete infected feces into the Salo Karangan River. An infected animal could excrete feces contaminated with *S. japonicum* and reach the snail *O. lorelindoensis* in the river. Snails could occur in the Salo Karangan River by floods from the headwaters of the river. People or animals could accidentally bring snails to the river. Therefore, it is possible that Sulawesi schistosomiasis japonica should have occurred in the Salo Karangan River.

Local snail dispersal mainly occurs along waterways (Hauswald *et al.,* 2011). The Salo Karangan River flows through Central Sulawesi and South Sulawesi. In addition, this river merges with the Lariang River and flows toward West Sulawesi. The headwaters of these two rivers are near or in Lore Lindu National Park. It is an endemic area of Sulawesi schistosomiasis japonica. This means that these two rivers are suitable habitats for *O. lorelindoensis*. The Palu River flows in the Palu Valley. Sulawesi schistosomiasis japonica was found 82 years ago in Palu. In addition, the river originates from the Gumbasa River (the Lindu Valley) and has irrigation system (Gumbasa Irrigation) finished in the 1970s. The Gumbasa River originates from the Lindu Valley, which is an endemic area of Sulawesi schistosomiasis japonica. The headwaters of the Lariang River also originate from the Kulawi Valley and the Napu Valley. Therefore, it strengthens that Sulawesi *S. japonicum* and *O. lorelindoensis* could occur in the Lariang River (the Kulawi Valley and the Napu Valley), the Palu River (the Palu Valley), and the Salo Karangan River (the Bada Valley).

The Bada Valley, the Lindu Valley, and the Napu Valley are not far from Palu, the capital of Central Sulawesi Province. For example, the Lindu Valley is only approximately 60 kilometers or less from Palu. Movements of populations between these two areas are very high. Palu residents can easily travel to the Lindu Valley and vice versa. It only takes approximately three hours from Palu to Lake Lindu by car. In addition, transportation from Palu to the Bada Valley and the Napu Valley is relatively easy. For example, people from Palu can reach the Napu Valley by car within appuroximately one and a half hour. It seems that movements of populations with Sulawesi schistosomiasis japonica from the Bada Valley, the Lindu Valley, and the Napu Valley to Palu can cause the spread of the disease in the Palu Valley. These findings supported the movement of populations can cause schistosomiasis in new areas (Alemu *et al.,* 2018; Rosmini *et al.,* 2014), especially in an urban areas (de Souza Gomes *et al.,* 2021).

The temperatures of the Palu Valley and the Bada Valley are not much different. The temperature of Lore Lindu National Park is 20 °C to 30 °C. In the Palu Valley, the temperature is 22 °C to 32 °C. Unsuitable mating for *O. hupensis* is 30 °C or more and 10 °C or less (Niu *et al.*, 2019). Again, it supports that the Lariang River, the Palu River, and the Salo Karangan River are suitable for habitats of Sulawesi *S. japonicum* and *O. lorelindoensis* as intermediate hosts of the parasite.

5. Life cycle of *Schistosoma japonicum*

The life cycle of Sulawesi schistosomiasis japonica involves *O. lorelidoensis* (Nelwan, 2022), mammals (Nelwan, 2019), and nonmammals (Budiono *et al.*, 2019). Either asexual or sexual reproduction occurs (Figure 1). Asexual reproduction occurs in *O. lorelindoensis* snails. In this snail, this begins with the development of miracidia into a sporocyst. Sporocysts multiply and grow into cercariae. In mammal or nonmammal hosts, parasites grow to become mature, mate, and produce eggs (Nelwan, 2019).

Outside mammal or nonmammal hosts, the eggs hatch in freshwater to release the free-swimming miracidia. In snails, miracidia become the mother sporocyst and then form several daughter sporocysts (Nelwan, 2019). Daughter sporocyst maturation is complete ten to fifteen days after the miracida penetrates the snail (World Health Organization, 1974). Sporocysts produce free-swimming infective cercarias (We and Halim, 2000; Nelwan, 2019). The cycle within *O. lorelindoensis* between the penetration of the miracidia larvae and the production of mature cercariae lasts approximately seven or more weeks for *S. japonicum* (World Health Organization, 1974). A cercaria is approximately 0.5 millimeters long, comprises a head end, and has oral and ventral suckers, and a fork-shaped tail (World Health Organization, 1974; We and Halim, 2000). *Oncomelania lorelindoensis* snails release free-swimming infective cercariae into the water. Nelwan (2019) suggested that the genus *Oncomelania* can shed 15 to 160 cercariae of *S. japonicum* daily (Nelwan, 2019).

Cercariae penetrate into the definite host skin and form the schistosomula stage. Schistosomulae stay in the skin for several days. After skin penetration, schistosomulae enter the blood circulation through the lymphatic system and venules and arrive at the lung within five to seven days (World Health Organization, 1974). After more than two weeks, schistosomulae arrive at the hepatoportal circulation and develop into adult worms. Adult worm pairs migrate to the mesenteric veins, mate, and produce eggs after approximately four weeks in the circulation (Schwartz and Fallon, 2018). Adult worms of Sulawesi *S. japonicum* live mostly in the *vena porta*, not in the *vena mesenterica* (Kurniasih *et al.*, 2002). In humans, adult males and females live more frequently in the mesenterica (Oey *et al.*, 2018), small intestine (Center for Disease Control and Prevention, 2023), and portal. Females release eggs that become embedded in the intestinal wall and other tissues or are excreted through feces (Oey *et al.*, 2018).

Adenowo *et al.* suggested that a single schistosome pair can theoretically produce up to 600 billion schistosomes. Freshwater snails inhabit calm or slow-moving lakes, rivers, ponds, or freshwater streams. The

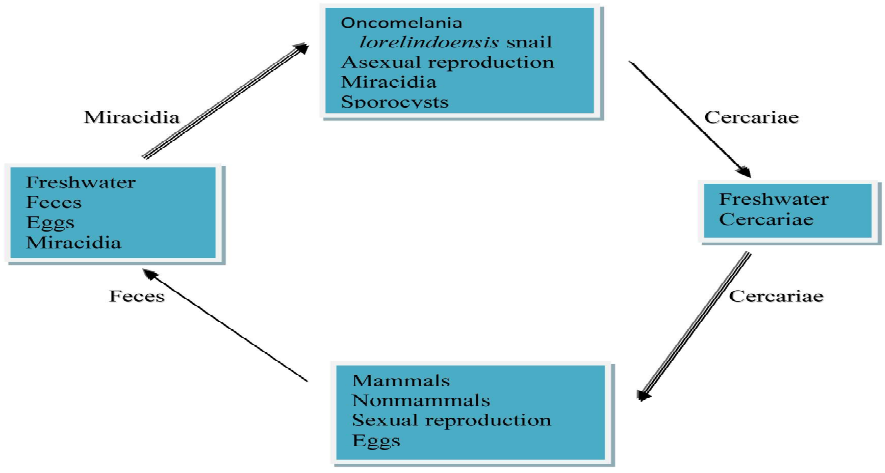

Figure 1: ***Schistosoma japonicum*** **life cycle**

Note: Asexual reproduction in *Oncomelania lorelindoensis* snails and sexual reproduction in mammals or nonmammals. Mammals can include cattle, humans and mice. Nonmammals likely include birds.

rate of infection increases with the duration of time spent in water with infected snails (Adenowo *et al.*, 2015). Exposure to cercariae of *S. japonicum* can occur in contact with wet vegetation, walking through rice fields, or other watery areas inhabited by infective snails (Attwood *et al.*, 2015).

6. Clinical manifestation

Two clinical manifestations exist in schistosomiasis: acute schistosomiasis (Katayama syndrome) and chronic manifestations. The incubation period of KS is approximately two weeks to 12 weeks (Nelwan, 2019). Nocturnal fever is typical of acute schistosomiasis. It occurs in 60% of people with schistosomiasis. Patients may also complain of sputum-free cough and significant malaise. Diarrhea, urticaria, and vomiting are commonly present. Physical examination can show abdominal tenderness and liver enlargement. In general, symptoms and signs relating to the respiratory tract tend to arise from the early phase of acute schistosomiasis. In addition, signs and symptoms of the abdomen tend to arise much more slowly during the syndrome route. During the early phases of acute schistosomiasis, neurological manifestations typically appear. The most common neurological syndrome is transverse myelitis (Kapoor, 2014). Clinical manifestations of chronic disease in schistosomiasis japonica are blood in the stool, constipation, and diarrhea. Chronic inflammation in *S. japonicum* can cause fibrosis, hyperplasia, polyposis, portal hypertension, ulceration of the intestinal wall (Nelwan, 2019), eosinophilia, and iron deficiency (Olveda *et al.*, 2014).

Clinical manifestations of Sulawesi schistosomiasis japonica could comprise diarrhea, fibrosis, and hepatosplenic. The symptoms of the disease are diarrhea, weight loss, decreased appetite, and slow growth of children. In chronic patients, it can cause swelling to the liver, which generally results in death (Samarang *et al.*, 2018).

Hepatosplenic is the pathology of chronic infection with *S. japonicum*. Clinical symptoms comprise granulomatous inflammation, periportal fibrosis, portal hypertension, hepatosplenomegaly, ascites, and vascular shunt formation (Cai *et al.*, 2013).

7. Diagnosis of *Schistsosoma japonicum*

Diagnostic tools are very important for eliminating schistosomiasis (Hinz *et al.*, 2017). These tools can help to determine whether schistosomiasis in an area has been eliminated. Several diagnostic are available to investigate schistosomiasis japonica: microscopic, serological, molecular and imaging methods. However, the microscopic methods are the sole essential examinations for diagnosing this disease. In Indonesia, diagnostic tools for detecting Sulawesi schistosomiasis japonica include the Kato-Katz method, MHT, dot-blot ELISA, and SjSEA-IHA. Serological methods that can beneficial for detecting schistosomiasis japonica can include KLH-dot-ELISA and rSj23-LHD-ELISA (Table 1).

Table 1: Serological diagnosis methods of *Schistosoma japonicum*

Methods	Sensitivity (%)	Specificity (%)
KLH-dot-ELISA	100	100
Sj16FA-ECISA	100	100
rSjSP-216-ELISA	100	100
JAMA-EITB	98	97
SjSEA-MELISA	95	94
SjSEA-DLIA	95	95
SjSEA-DIGFA	92-100	91-100
SmCTF-ELISA	100	63
SmSEA-ELISA	81-100	63-92
SjSEA-dot-ELISA	90	86

Table 1 (Cont.)

Methods	Sensitivity (%)	Specificity (%)
SjSEA-DDIA	91-100	53-97
SjSEA-ELISA	79-100	38-100
rSj26GST-rSj14-3-3	81-94	95
r*Sj*Gep-Sj23-ELISA	91*	98*
rSjGep-Sj23-Sj28-ELISA	90*	93*
rSjTPx1-ELISA	86-98*	89*-97
rSj23-LHD-ELISA	90*	91*

Note: AWA: adult worm antigen; CTF: cercarial transformation fluid; ELISA: enzyme-linked immunosorbent assay; FA: fraction antigen; JAMA: mitochondrial SjAWA; KLH: keyhole limpet haemocyanin; MELISA: magnetic particle-based ELISA; r: recombinant; SEA: soluble egg antigen; Sj: *Schistosoma japonicum*; Sm: *Schistosoma mansoni*; * animal model (modified from Hinz et al., 2017).

Kato-Katz and MHT are standard methods for detecting *S. japonicum* infections in Sulawesi (Budiono *et al.*, 2019; Budiono *et al.*, 2020; Sutrisnawati *et al.*, 2022). Kato-Katz stool sample examinations need three slides and use light microscope. The investigator takes approximately 42-milligram of stool sample and places it in a 200-micrometer Kato-Katz screen mesh. The stool is transferred into a six-millimeter hole in the template on the microscopic slide. A glycerol-soaked cellophane strip covers the stool. The investigator then checked the stool for schistosomal eggs. After that, eggs per gram of stool can be calculated (Nelwan, 2019). The miracidium hatching test involves egg concentration in stool samples through a nylon tissue bag and suspension in distilled water in a flask. The presence of miracidia that hatched from ova could be a sign of schistosomiasis. Flask investigation should be at 4, 6, 8, and 24 hours (He *et al.*, 2018; Budiono *et al.*, 2020).

Samarang *et al.* (2017) used dot-blot ELISA for detecting Sulawesi schistosomes in humans in the Napu Valley. Dot-blot ELISA has 74% sensitivity and 78% specificity (Budiono *et al.*, 2020; Samarang *et al.*, 2017). However, further investigations are still needed regarding the strengths and limitations of dot-blot ELISA compared with other diagnostic techniques (Samarang *et al.*, 2017). In addition, the authors did not state possibility of false positives/negatives of the method.

Budiono et al. used SjSEA-IHA for detecting schistosomiasis in domestic animals. The authors concluded that SjSEA-IHA is better than the MHT technique. The sensitivity and specificity of SjSEA-IHA were 88.24% and 41.37%, respectively. However, this tool, a serology-based diagnosis, cannot differentiate past and current infections. It can only be useful at the community level (Budiono *et al.*, 2020). This means that other more sensitive tools are needed.

Alternative tools that are needed include LFD-RPA and ultrasonography (US). The sensitivity and specificity of LFD-RPA reached 97.22% and 100% in mice and 93.75% and 100% in goats, respectively. The tool has no cross-reactivity from other parasites, such as *Fasciola gigantica* and *Spirometra*, and is effective in low-endemic areas. The test can be completed at 39 °C within 15 minutes. However, the tool is expensive (Guo *et al.*, 2021). Ultrasonography can detect schistosomiasis in mice. It can detect an adult *S. japonicum* worm in the portal vein. The worm moved spontaneously and slowly; in addition, the worm length was comparable to the size of adult parasites. Ultrasonography is inexpensive, noninvasive, portable, and radiation-free (Sah *et al.*, 2015). This suggests that US can be useful for detecting *S. japonicum* both in mice and humans (Maezawa *et al.*, 2018), especially in Indonesia. It can also be beneficial to detect the diseases of other species, such as *S. malayensis* and *S. mekongi*.

8. Control of schistosomiasis

Indonesia has made a large step in decreasing the prevalence of Sulawesi schistosomiasis japonica. However, the lack of coordination and collaboration between the Ministry of Health and other ministries has hampered efforts to control and prevent this disease. In addition, insufficient financial and human resources inhibited

these efforts. The lack of funds for supervision and control from the Ministry of Health may be due to the limited area. It may also be due to the Indonesia government system: decentralization and autonomy (Gordon *et al.*, 2019).

8.1. Control efforts and elimination of Sulawesi schistosomiasis japonica

In Indonesia, the National Objectives for Health (NOH) set schistosomiasis control strategies. These strategies vary by endemic levels: high, moderate, and low. Mass drug administration (MDA) is used for 85% of the population in high endemic areas. Active treatment of choice is in moderate endemic areas, and passive treatment of choice is in low endemic areas. The Indonesian Ministry of Health has used preventive chemotherapy with strategies focused on the treatment of domestic animals, health education, and snail control. It also focused on providing schistosomiasis-free water and sanitation, monitoring, evaluation, and capacity building in an effort to meet the elimination target (Gordon *et al.*, 2019).

In Indonesia, a Roadmap for the elimination of Sulawesi schistosomiasis japonica was established in 2017. It is a cross-sector and community joint action to eliminate the disease. The Roadmap lists three phases toward eradication: the accelerated phase during 2018-2019, the phase of maintaining 0 percent prevalence during 2020-2024, and the phase of verification and declaration of eradication in 2025. The project duration is five years. This is in accordance with the WHO recommendation, which recommends 0 percent infection in intermediate hosts and definitive hosts for five consecutive years (Widayati *et al.*, 2022). Cross-sector intervention in the pilot project decreased snail density by approximately 0 to 6.53% in 2018 (Anastasia *et al.*, 2022), 0.1% among humans in 2019, and 1.45% in 2022 (World Health Organization, 2023). This means it is impossible to declare the eradication status of schistosomiasis in Indonesia in 2025. Thus, the following five-year roadmap should be established to meet the WHO requirements. The government hopes that eradication of this disease will be achieved in 2029.

Indonesia carried out surveillance of Sulawesi schistosomiasis japonica in endemic areas twice a year to measure the prevalence of the disease in humans, rodents, and snails. Unfortunately, schistosomiasis surveillance in mammals such as buffalo, cattle, and horses is not continuous. Schistosomiasis japonica is of particular concern because it is zoonotic, meaning that Sulawesi *S. japonicum* can infect nonmammal hosts (Budiono *et al.*, 2019). However, the authors did not state nonmammal animals that Sulawesi *S. japonicum* can infect. Nonmammal animals in Lore Lindu National Park can comprise birds (e.g., *Aceros cassidix, Cacatua sulphurea,* and *Macrocephalon maleo*) and fish (e.g., *Cyprinus carpio* and *Oreochromismossambicus*). Brant and Locker (2005) stated that schistosomes infect mammals (Brant and Loker, 2005) or birds (Brant and Loker, 2005; Walker, 2011), indicating that Sulawesi *S. japonicum* also likely infect birds/nonmammals. Additionally, the genus *Schistosoma* shows the ability to deviate and adapt to new hosts and habitats beyond its evolutionary origins (Diaz *et al.*, 2023). For example, *S. hematobium x S. bovis* hybrids occur in Corsica, France (Rothe *et al.* 2021) and *S. bovis* can infect humans (Diaz *et al.*, 2023). Moreover, *Schistosoma japonicum* clade originated from avian parasites (Diaz *et al.*, 2023; Lawton *et al.*, 2011).

Budiono *et al.* (2019) reported that *S. japonicum* infections in Sulawesi occur in mammals such as buffalo and cattle in areas where schistosomiasis japonica is endemic. The authors also reported that there is no specific intervention to treat Sulawesi schitosomiasis japonica in animals (Budiono *et al.*, 2019).

Indonesia has been trying to control *O. lorelindoensis* since 1974. Control measures include the construction of waterways, the clearing of forest in focus areas, and the clearing and burning of focus areas. However, thus far, it has not worked. The geographical factor of the Bada, Lindu, and Napu valleys is one of the factors causing the disease control to not successful (Samarang *et al.*, 2018).

To control schistosomiasis japonica, ending the transmission cycle of *S. japonicum* is an important strategy. Botanical molluscicides may be useful for this purpose. This technique does not damage the environment. Multiple botanical sources are available for this molluscicide technique. These include *Allium sativum* (Wan *et al.*, 2017) and *Buddleja lindleyana* (Han *et al.*, 2012). Both are safe botanical molluscicides. Wan *et al.* (2017) suggested that schistosomiasis japonica may occur after contact with free-swimming *S. japonicum* cercariae. It seems that prevention of schistosomiasis japonica may be by avoiding fresh water containing cercariae. For eliminating cercariae, several methods are available: use of praziquantel, control of snails, and use of plant extracts. Garlic, for example, is active against *Schistosoma* and intermediate hosts such as *O. lorelindoensis*. Garlic is the bulb of the plant *Allium sativum* Linnaeus (Wan *et al.*, 2017).

To prevent and eliminate schistosomiasis in Central Sulawesi, there must be earnest effort. Garlic extracts may be useful against *O. lorelindoensis*. For the use of praziquantel in humans, 60 mg/kg per day can be given orally in three divided doses for one day. It could be 3 x 20 mg/kg a day every 4 hours, or 2 x 30 mg/kg a day every 4 to 6 hours. These doses are suitable for treating schistosomiasis japonica. For preventive measures, a single dose of 40 mg/kg is effective (Gordon *et al.*, 2019). For preschool- and school-aged children, the dosage is 40 mg/kg (Zwang and Olliaro, 2017). To increase effectiveness, retreatment is needed after two to four weeks. Examination at one to two months posttreatment helps confirm successful cure, as suggested by the Centers for Disease Control and Prevention (Abdel-Haq and Asmar, 2021). Administration of praziquantel for treating animals in Indonesia can help eliminate schistosomiasis japonica in this country. Therefore, treatment of schistosomiasis japonica should also include animals infected with *S. japonicum* (Budiono *et al.* 2019). World Health Organization stated that arpraziquantel is a useful drug for treating schistosomiasis in children under five years (World Health Organization, 2024). It seems that this drug can also be useful for treating schistosomiasis japonica.

Praziquantel is efficacies and safe drug for treating human schistosomiasis in preschool-aged children, school-aged children, adolescents, and adults (Oliaro *et al.*, 2022). However, it is unsuitable for preschool-aged children due to its bitter taste. Arpraziquantel is a tablet for treating human schistosomiasis in preschool-aged children (World Health Organization, 2024).

8.2. Vaccination

Clinical trials for vaccine candidates are underway. More than ten vaccine candidates have been tried; most of them failed to move forward. For schistosomiasis japonica, for instance, Sj23 is a vaccine for water buffaloes (Elbaz and Esmat, 2013).

Vaccines play an important role in preventing reinfection of schistosomiasis japonica. Nelwan suggested that SjAChE blocked parasite growth and progression. *Schistosoma japonicum* acetylcholinesterase could decrease male worm numbers by 33% and the density of liver granulomas by 41%, and decrease numbers of intestine eggs by 73% (You *et al.*, 2018; Nelwan, 2019). In addition, a vaccination with rSjDL1 would be safe for protecting bovines and humans against schistosomiasis. For example, rSjDL1 reduced the number of fecal eggs by 61 to 68% and mature intestinal eggs by 58 to 63%. It seems that SjAChE and rSjDL1 may be potential vaccines for eliminating schistosomiasis japonica (Abdel-Haq and Asmar, 2021), especially Sulawesi schistosomiasis japonica.

9. Conclusion

Schistosomiasis japonica in Indonesia occurs in Central Sulawesi in two districts: Poso and Sigi. In Sigi District, this parasite occurs in the Lindu Valley. In Poso District, *S. japonicum* occurs in the Bada Valley and the Napu Valley. In Indonesia, it infects the snails of *O. lorelindoensis*, both mammal and nonmammal hosts. *Oncomelania lorelindoensis* is a full species beyond the *O. hupensis* group. Mammal hosts can comprise cattle, dogs, humans, mice, pigs, and wild pigs. Nonmammal hosts of schistosomes likely comprise birds. It still requires further investigations. *Oncomelania lorelindoensis* and Sulawesi *S. japonicum* worms may have prevailed in the Lariang River, the Palu River, and the Salo Karangan River. The Palu River flows in the Palu Valley and in the middle of Palu city, Central Sulawesi. The Salo Karangan River flows in Central Sulawesi and South Sulawesi. The Lariang River flows in Central Sulawesi and West Sulawesi. The diagnosis plays an important role in controlling the disease. The diagnostic techniques can comprise the Kato-Katz, MHT, SjSEA-IHA, and dot-blot ELISA. Currently, praziquantel is the only effective drug for treating Sulawesi schistosomiasis japonica. The PZQ dose is 60 mg/kg per day orally in three divided doses for one day. Treatment needs repetition after two to four weeks. In addition, one to two months posttreatment, there must be an examination. Arpraziquantel can be useful for the treatment of Sulawesi schistosomes in preschool-aged children. Studies for several drug candidates are underway, including *Alium sativum* and *Buddleja lindleyana*. Both are safe drugs for molluskcicides. Currently, vaccines are unavailable for schistosomiasis japonica. Vaccine candidates such as SjAChE and rSjLD1 have been studied. Vaccination is a potential approach for controlling schistosomiasis in Sulawesi.

Conflicts of interest

I declare that no competing interest exists.

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