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Schistosomiasis

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ABSTRACT

Schistosomiasis, also known as bilharzia, is a zoonosis disease caused by blood flukes (trematodes) of the genus Schistosoma sp. There are a few species that can infect humans and animals, including *Schistosoma japonicum*, *Schistosoma mansonia, Schistosoma hematobium, Schistosoma intercalatum Schistosoma guineensis* and *Schistosoma mekongi*.[1] This disease is endemic in 78 countries, in which 52 of them are countries with moderate-high level of endemicity. Schistosoma sp are very difficult to eliminate, because the transmission is highly influenced by evironmental, habitual, parasitic, vector, and host factors.[1,2]

Schistosomiasis atau bilharzia adalah penyakit zoonosis yang disebabkan oleh trematoda darah spesies Schistosoma sp. Terdapat beberapa spesies yang dapat menginfeksimanusia dan hewan, yaitu: Schistosoma japonicum, Schistosoma mansonia, Schistosomahematobium, Schistosoma intercalatum Schistosoma guineensis dan Schistosoma mekongi.[1] Penyakit ini endemik di 78 negara dan 52 diantaranya merupakan negara dengan tingkat endemisitas sedang-tinggi. Schistosoma sp. sangat sulit dieliminasi karena transmisinya sangat dipengaruhi oleh faktor lingkungan, kebiasaan, parasitik, vektor dan host.[1,2]

Where are schistosomiasis endemic areas in Indonesia?

Schistosomiasis is endemic in tropical and sub-tropical countries, especially those with high-altitude geographical nature, and contain a lot of freshwater lakes or streams. Data from WHO informs that, in 2014, 258 million people in the world had received preventive treatment against schistosomiasis and 61,6 million people who suffered from this disease had received treatment.[1] The prevalence of schistosomiasis in Indonesia is 5,68 %, while the WHO expects that these cases should be under 1%. In Indonesia, schistosomiasis can only be found in the province of Central Sulawesi, especially in the district of Poso and Sigi.[3,4,5]

In Indonesia, schistosomiasis was first reported in 1937, and its intermediary host was then discovered after a few years. The species of Schistosoma found in Indonesia is Schistosoma japonicum, and its intermediate host is Oncomelania hupensis lindoensis. The intermediate host of Schistosoma sp. are amphibians that cannot live in an environment which contain a lot of water (submerged) or an environment that is too dry. This nature of Oncomelania sp. is then used by the Indonesian government in an effort to eliminate and break its chain of transmission.[4,5]

The geographical location and the prescence of streams as the natural habitat of its host (especially around forest, ranches, and agricultural irrigation) make schistosomiasis very difficult to eradicate. Multi-sectors

collaboration, including health, agriculture, animal husbandry, and forestrty, is needed to eradicate this disease.[3] This multi-sectors collaboration is indispensable, because streams and river flow in endemic area is a good breeding place for the intermediary host of Schistosoma sp.

The number of schistosomiasis patients has fluctuated from year to year, and a lot of studies has been done to evaluate this condition. The interesting thing about these studies is that people in endemic areas actually have a good perception toward this disease, but lack of public hygiene and the opening of new agricultural lands led to a still high schistosomiasis prevalence in endemic area.[3]

How is the morphology and life cycle of Schistosoma sp.?

Schistosoma is included in the class of trematodes, sub-class digenea, order strigeidida, schistosomatidae family, and genus schistosoma. Adult worms are large leaf-shaped, and are dioecious. They also have two suckers, the oral and ventral suckers. The oral suckers serves as attachment and suction, while ventral suckers serves as attachment and to hold its mate. Adult worms reside in the mesentric veins of their hosts. Adult female worms are longer than males, but adult male worms are thicker. One of Schistosoma sp.unique feature is their cercariae bifurcated tails.[4,5,6]

The life cycle of Schistosoma sp. occurs in two hosts, humans and snails.The infective stage of Schistosoma sp. is the free-swimming cercariae upon release from the snails into water. It will then infect humans if the cercariae manages to penetrate the skin into the circulation and become schistosomulae in the veins. The schistosomulae will migrate to the heart and lungs, and reside in the liver where they maturate into adult worms and mate.[4,5,6]

Paired adult worms will migrate to its habitat in the mesentric veins to lay their eggs. The mesentric venules where they lay their eggs will vary among species. For instance, in Schistosoma japonicum and Schistosoma mansoni, adult worms will occupy the mesentric veins in the intestinal tract, resulting in lessions of the intestinal and hepatosplenic tract. Adult worms of Schistosoma hematobium will lay their eggs in the venous plexus of bladder, renal, and ureter, resulting in lessions in those area.[7]

The development from eggs to adult worms requires around 40 days. In one day, adult female worms can produce hundreds or thousands of eggs. Most of these eggs will remain inside human body, and might even infiltrate the billiary tract.[4,5]

Some eggs that are laid near the intestinal and urinary tract will remain in their place. These eggs will then be excreted with feces or urine. The eggs will hatch and continue their life cycle on contact with water. People or society who have a habit of defecating near water flow will cause the eggs to have easier contact with water.

Under optimal condition, the eggs will hatch and release miracidia. These miracidia are covered with cilia, hence they are able to be motile, swim, and penetrate their spesific snail intermediate host. Miracidia can survive for 2 days in the water. Inside the snail tissue, mirasidia will develop into primary sporocyst, and then into daughter sporocyst, and lastly become cercariae. The cercariae is enveloped with long cilia, it has bifurcated tail, and swim backwards. The development of cercariae requires 24 hours, while its sporocyst can survive for 3 months inside their host.[4,5]

Why are Schistosomiasis very hard to eradicate?

Schistosomiasis is an infectious endemic disease. Comunities with a lot of outdoor activities and easier contact with cercariae-contaminated water are at a major risk factor. Until now, schistosomiasis has not been able to be eradicated. Eventhough people who live in endemic area actually has a good perception towards this disease, the prevalence of schistosomiasis is still more than 1 %.[2] This illustrates that there are other factors that influence the transmission of schistosomiasis. One of the factors that influence its transmission is behavioral factor. People in endemic areas have a behavior that does not support the prevention of this disease. For instance, they neglect using boots when in contact with water, and a lot of them still defecate in the river.[3]

The transmission of schistosomiasis is also very closely related to the prescence of its reservoir and intermediary hospes. The reservoir hospes of this disease include dogs, cats, rodents, pigs, anoa deers, and cows.[6] While, its intermediary host in Indonesia is snail *Oncomelania hupensis lindoensis.* There are a few other intermediary hosts of *Schistosoma sp*. For instance, Snail *Biompalaria sp*. are the intermediary host of *Schistosoma mansonia*, snail *Bulinus sp.* are the intermediary host of S*chistosoma intercalatum* and *Schistosoma hematobium*, snail *Tricula sp.* are the intermediary host of *Schistosoma mekongi*. The habitat of this intermediary host in Lindu Lake is around unused agricultural and plantation area, near or at the edge of watercourse between rice fields, and in a wooded area on the border of the hill.[4] These snails are mostly found in muddy area, watery, and all-year wetland; and in areas that are covered from direct sunlight due to the prescence of trees, shrubs, and thick grass.[4,5]

How are the clinical manifestations of schistosomiasis?

The clinical manifestations of schistosomiasis is very dependent on the types of species that cause the infection. This disease is caused by an infection of blood flukes in the veins of gastrointestinal and urinary tracts. Therefore, local symptoms could occur around the area where the parasites reside.[4]

The pathogenesis of this disease is divided into acute and chronic phase. Early symptoms of schistosomiasis infection are redness and itchiness after contact with cercariae-contaminated water. The skin lession nomenclature of schistosomiasis is micropapular rash, also known as "swimer itch", which will subside within 48 hours after contact with water.[9] Three to eight weeks after cercariae penetrates the skin, patients will complain of symptoms such as fever, dry cough, fatigue, and headache, accompanied with an increase of eosinophil counts, also called Katayama fever or Katayama syndrome.[9]

In some acute cases of infection, fever could reach up to more than 39°C, accompanied with cough and fatigue. The marker of acute immune response can be seen by the increase of blood sedimentation, C reactive protein (CRP), and amyloid serum. Eosinophil count would increase up to 33-42% and persist until 32 weeks. CT scan would also show opacity in the liver and lungs.[9,10] These conditions are caused by patients immune response against parasite antigen (cercariae, schistosomulae, adult worms, and eggs).[9,11-13] These symptoms would mainly appear in people who do not come from endemic areas.[12]

In chronic condition, symptoms would include blood in feces or urine, and can sometimes occur in the form of bladder cancer, liver cirrhosis, and esophageal varices.[11,14]

Common signs and symptoms of *S. Hematobium* infection include : hematuria, dysuria, nocturia, proteinuria, leukocyturia, hydroureter, and hydronephrosis. In a more rare occurence, hematospermia could also be found.[15] During bladder biopsy, bladder calcification, bladder neck fibrosis, and bladder cancer could also be found.[11,14]

Hepatic schistosomiasis or schistosomal hepatopathy is a chronic sign of *S. Mansonia* and *S. Japonicum* infection, which can cause liver fibrosis in the future.[2] Hepatic schistosomiasis is different with liver cirrhosis, eventhough portal hypertension and spleen enlargement is most commonly found, but failure of hepatocellular function is not present.[2] Adult worms of S. mansonia and *S. Japonicum* will lay their eggs in the plexus of inferior mesentric veins. This eggs deposition will cause changes in the mucosal, sub-mucosal, sub-serous, and musculary mucosa layer, thus showing various types of presentation including polyps, granulomas, or even necrotics. [2]

How to diagnose Schistosomiasis?

Schistosomiasis can be diagnosed by various examinations, like microscopic, serologic, and biopsy examination. These examinations have their own benefits. Microscopic examination can easily be done using feces and urine sample.

Determining the choosen types of examinations is based on the stage of parasite life cycle, especially where the parasite eggs are laid. The gold standard for diagnosing S. hematobium infection, is to use microscopic examination of urine. The urine samples can

be centrifuged or filtrated prior to examination, so that the eggs would be more concentrated.[14] In a mild infection, less than 50 eggs/10ml of urine would be found, while in a more severe infection more than 50 eggs/10ml of urine would be found.[16] This diagnostic gold standars requires equipments, skilled personels, and time. Hence, this microscopic examination would not be suitable to be done if it aims for screening in remote areas with a large number of samples. Therefore, a new, faster, cheaper, and easier diagnostic method is needed. One of these new method is the Rapid Diagnostic Test S. hematobium (RDT-Sh). The main principle of this method is to detect the IgG against *S. hematobium* in urine samples, with a sensitivity of 97% and specificity of 78%. This method is able to detect the parasite eggs if the concentration is more than 1 eggs/10ml of urine.[17] Another method is by using the RDT SmCTF (Schistosoma mansonicercarial transformation fluid) which detect the antibody anti-schistosoma against *S. mansonia* and *S. hematobium*. This method is not only able to diagnose schistosomiasis, but also able to map and measure the prevalence of schistosomiasis patients.[17-19]

Feces examination using the Kato katz method is frequently used to detect the infection of *S.mansonia* and *S. japonicum*. This microscopic methods is still becoming the gold standard, compare to other similar microscopic examinations using smartphone microscope aplications.[20]

In areas with low endemicity of Schistosoma infection, diagnosis is difficult to establish using microscopic examination. This is because the intensity of infection was low, so the eggs in the stool is harder to find. One of the methods that can be used in this kind of Schitosomal infection is PCR. This method is able to detect many parasites protein, such as internal transcriber-spacer-2 sequence (ITS2), Dra1.[21,22] This method is very good to use as a detection method in areas with low endemicity of Schistosoma infection; as well as in program control, epidemiology research, microscopic examination control, and post-therapy evaluation. [21]

Biopsy is done by collecting tissue samples from patient. This tissue samples might be originated from gastrointestinal or urinary tract. Biopsy is done especially in patients with positive clinical presentations, but without eggs finding in examinations. [11]

The diagnosis of Schistosomiasis in acute phase is very difficult, therefore a diagnosis model that can detect the prescence of parasite in any stage of its life cycle is needed. A study showed that Cell-free parasite DNA (CFPD) method was able to detect the prescence of schistosoma DNA in blood plasma on every stage of its life cycle. Even patients in the acute phase of Schictosomiasis or Katayama syndrome were able to be diagnosed, where as serology and microscopic examination usually showed false negative result in this phase of the disease. This examination used Polimerase chain reaction (PCR) method.[11] CFPD is not only effective to detect acute phase of Schistosomiasis, but also suitable to evaluate its treatment course. It has been known that post-therapy Schistosomiasis patients has lower parasite DNA concentration and would turn negative after 1-2 years.[11]

How is the management of Schistosomiasis?

Management of Schistosomiasis includes the administration of medicine either in community or individually, sanitation management, environental modifications, and health education.[2] Schistosomiasis patients can be treated using Praziquantel. This medicine is effective to eliminate adult worms in the initial phase (5-6 weeks) in *S. mansoni* and *S. japonicum*, as well as 10-12 weeks in S. haematobium, but not for its schistosomulae.[9] The reccomended dose for Praziquantel is 40 mg/kgBW single dose, or 50 mg/kgBW in *S. japonicum infections*.[9]

A newer study showed that anti-malarial medicine like artemisinin, mefloquine, and trioxolane derivate, can also be used as anti-schistosoma. Thesse medicine will be more effective in combination with Praziquantel.[23,24] Anti-Schistocoma vaccine is currently under development. There are 10 main antigens that originated from eggs and schistosomulae membrane.[25] With the advancement of studies and research on Schistosoma, the number of Schistosomiasis patients is expected to decrease.

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