Status of Schistosomiasis in the Philippines: Prevalence, Control and Innovative Methods for Detection and Elimination

Jan Michael P. Chan[1], Helenar G. Chan[1], and Mary Jane C. Flores[1,2]*

1 Biology Department, De La Salle University, 2401 Taft Ave., Manila 0922, Philippines

2 Biological Control Research Unit (BCRU), Center for Natural Sciences and Environmental Research (CENSER), College of Science, De La Salle University, 2401 Taft Ave., Manila 0922, Philippines

**Corresponding Author: mary.jane.flores@dlsu.edu.ph*

Abstract: Schistosomiasis is globally recognized by the World Health Organization as one of the neglected tropical diseases (NTDs) caused by parasitic blood flukes. *Schistosoma japonicum* is reported to be the most pathogenic species wherein approximately 280 million people are infected worldwide. In the Philippines, *Schistosoma japonicum* is endemic in 28 provinces and still poses a great threat in the healthcare and welfare of the Filipino communities particularly those who are situated in impoverished areas. This review paper aimed to assess an updated data on the surveillance and transmission of schistosomiasis that will set targets and direct significant innovative approaches to the areas of highest need. The current national prevalence of schistosomiasis in the country is 4.68% and >5% prevalence rates were recorded in 435 out of 1,599 endemic barangays. The high prevalence rates may be associated to the country's topography and rapid transmission of the disease from exposure of humans and animals to cercarial infested waters during domestic and agricultural activities. Mammals including water buffaloes (carabaos), cats, dogs and rats contribute to the transmission of schistosomiasis. Other high-risk factors such as the play habits of children, lack of proper sanitation facilities and poor hygiene have increased the vulnerability of individuals in acquiring the infection. In addition, various cases of anemia, malnutrition, growth retardation, poor cognitive function and mortality associated with *S. japonicum* infection were also recorded. To date, detection of schistosomiasis by utilizing techniques with higher sensitivity and specificity such as by ultrasound, Polymerase Chain Reaction, Circum-oval Precipitin Test and Enzyme-Linked Immunosorbent Assay have been applied. Moreover, detection of eDNA contribute to the surveillance leading to formulation of integrated multidisciplinary one health approach strategy towards control and eventually elimination of the disease.

Key Words: Schistosomiasis; *S. japonicum*; prevalence; control; elimination

1. INTRODUCTION

Schistosomiasis (SCH) is recognized by the World Health Organization (WHO) as the third most devastating neglected tropical disease (NTD) after malaria and intestinal helminthiasis worldwide (WHO, 2020). It is a disease of poverty caused by parasitic oriental blood flukes which lead to chronic illness and a major source of morbidity and mortality. *Schistosoma* infections are widely reported from 78 developing countries in Africa, Asia, Caribbean,

Middle East and South America that affect approximately 280 million people (Colley & Secor, 2014). Among the five main *Schistosoma* species, *Schistosoma japonicum, Schistosoma mansoni*, and *Schistosoma haematobium* are considered to be highly pathogenic and have attributed to the burden of disease (Francisco *et al.,* 2019).

Schistosomiasis in the Philippines is driven by the zoonotic and most virulent *Schistosoma japonicum* which has a very wide host range that can infect about 40 different mammalian species including humans (Costain *et al.,* 2018). It was first discovered in 1906 by Wooley in a Filipino man who had never went out of the country but died with clinical manifestations of schistosomiasis. The growing cases of this parasitic disease were reported yearly after its introduction which have given rise to several studies and attempts to determine its mode of transmission. The identification of *Oncomelania hupensis quadrasi* as the intermediate host by Dr. Tubangui in 1932, has opened numerous studies in relation to clinical manifestations and pathological characteristics of schistosomiasis (Blas, 2004). However, due to inconsistent implementation of research programs as well as limited funding, schistosomiasis in the Philippines is not well documented and is still very far from the goal of eradication.

The aim of this review paper is to assess an updated data on the surveillance and transmission of schistosomiasis that will set targets and present the innovative approaches which can be significant to the areas of highest need. Innovative tools are needed to quickly become available to identify communities at risk and to provide preventive and curative treatment for the control and eradication of neglected tropical diseases.

2. PREVALENCE STATUS AND PUBLIC HEALTH IMPACT OF SCHISTOSOMIASIS IN THE PHILIPPINES

At present, schistosomiasis remains as a public health concern in the Philippines and is widely prevalent in 28 endemic provinces, 190 municipalities and 2,230 barangays across the 12 different geographical zones in the three major island groups of Luzon, Visayas and Mindanao. The major foci are found in Eastern Visayas particularly in islands of Leyte and Samar (Olveda & Gray, 2019). There are also two new endemic foci reported in Gonzaga, Cagayan (North) and Calatrava and Negros Occidental (Central) parts of the country in 2004 and 2006, respectively (Leonardo *et al.,* 2015). These endemic regions have mostly no distinct dry season and are composed of mostly rice growing zones which exploit contact between humans and freshwater snails (Blas *et al.,* 2004).

The Philippines' current national prevalence for schistosomiasis is recorded at 4.68% wherein an estimate of 12 million Filipino people are at risk and over 800,000 people were diagnosed with active *Schistosoma* infection (Nicdao, 2018). According to studies, the annual mortality rate due to schistosomiasis is 1.78% of the estimated positive cases (Blas *et al.,* 2004). The prevalence of schistosomiasis in the country with respect to age, sex, occupation, and environment, follows a pattern that can be explained on the basis of contact with infested water sources (Gordon *et al.,* 2019). Age has been identified as an important factor in *S. japonicum* infections as revealed in the study of Belizario *et al.* (2015) that the infection during childhood and adolescence of school-aged children is associated to their lack of proper hygiene and play habits which exposed them in infested waters. There are also studies that showed significant sex differences between age groups and distinction of higher prevalence for males than in females (Soares-Magalhães *et al.,* 2014). Based on the different occupational classes, farmers have the highest rate of infection with 74.1% followed by fishermen, tuber gatherers with 60% prevalence rate. Their livelihood of agricultural and domestic daily activities exposes them in contact with contaminated waters during farming and inland fishing in rivers, swamps, and streams (Gordon *et al.,* 2019).

The involvement of reservoir host animals in the transmission of the disease is now given attention. Being zoonotic as one of the characteristics of *S. japonicum*, the disease is not limited to man. It can also affect domestic animals including dogs, pigs, cats, goats, cows, water buffaloes and even wildlife such as monkeys and field rats which can all serve as reservoirs of infection (McGarvey *et al.,* 2006). However, despite of having initial data, the role of animals as reservoir hosts in the transmission of schistosomiasis remains undefined (Soares-Magalhães, 2014).

3. INNOVATIVE METHODS IN DETECTION OF *S. JAPONICUM*

Schistosomiasis control in the Philippines lies in the available diagnostic procedures which include coproparasitological examination (CopE), immunological methods and molecular methods (Gordon *et al.,* 2019). CopE approaches depend on direct detection and visualization of parasitic eggs in fecal samples which include formal-ethyl acetate sedimentation-digestion (FEA-SD) and miracidial hatching technique (MHT) and Kato-Katz thick smear procedure (KK) which is the backbone of control programs (Jurberg *et al.,* 2008). These traditional CopE methods are widely used due to its comparative low cost and ease of performing the tests but the main disadvantage among these methods is the lack of sensitivity in low-intensity infections (Habtamu *et al.,* 2011).

Immunological methods are also being applied which rely on detection of circulating parasite antigens or antibodies generated against parasite antigens. The key immunological approaches are enzyme-linked immunosorbent assay (ELISA) and circumoval precipitation test (COPT) (Zhou *et al.,* 2011). Moendeg *et al.* (2015) focused on the development and optimization of cocktail-ELISA for a unified surveillance of zoonotic schistosomiasis in multiple host species with the aid of combining the antigens used in previous studies. The thioredoxin peroxidase-1 (SjTPx-1) and Sj1TR, Sj7TR tandem repeat proteins are combined together in a cocktail-ELISA to not just improve their diagnostic capacities but may also produce a multi-host species detection for zoonotic schistosomiasis. The combination of these three antigens has displayed better specificity with positive predictive and kappa values from the samples collected from several endemic areas in the Philippines. SjTPx-1/Sj7TR/Sj1TR recorded the highest sensitivity in humans and water buffaloes with 84.1 % and 80 %, respectively. Both have obtained a specificity of 100 % in all host species. Therefore, their study suggests that the use of cocktail-ELISA is significant and efficient in improving the zoonotic surveillance in schistosomiasis endemic areas.

In addition to these advances, molecular methods are being utilized based on parasite DNA in experimental samples for detection such as conventional polymerase chain reaction (cPCR), real-time PCR (qPCR), digital droplet PCR (ddPCR) and the loop-mediated isothermal amplification method (LAMP) (Kumagai *et al.,* 2010). In a diagnostic study of *S. japonicum* by Gordon *et al.* (2019), 560 stool samples were collected and examined by Kato-Katz method and real-time PCR (qPCR) assay. Based on the results, a higher human prevalence rate of 90.2% was recorded by qPCR than the Kato-Katz method with a prevalence of 22.9%. The authors have concluded that the use of molecular diagnostic approach using qPCR to assess the prevalence of *S. japonicum* was considerably a better diagnostic procedure than the Kato-Katz and therefore could be an important tool in the future for surveillance of the intensity of infection in endemic areas as well as in low endemic areas.

Another molecular method recently practiced in the country is the use of environmental DNA (eDNA) for the detection of schistosomiasis. A recent study focused on the detection of *Schistosoma japonicum* and *Oncomelania hupensis quadrasi* environmental DNA and its potential utility to schistosomiasis japonica surveillance in the Philippines was conducted by Fornillos *et al.* (2019). A species-specific real-time PCR (qPCR) assay was applied to determine the presence of *S. japonicum* and *O. hupensis quadrasi* in freshwater samples using environmental DNA. Results revealed *S. japonicum* is positive in 9 sites, *O. hupensis quadrasi* positive in 9 sites, and 5 sampling sites positive for both *S. japonicum* and *O. hupensis quadrasi.*

4. CONTROL PLANS AND IMPLEMENTATION PRACTICES

Community-based mass drug administration (MDA) campaign using praziquantel (PZQ), an anti-schistosome drug, campaign has proven to decrease the prevalence rates and reduced the morbidities among endemic areas in the Philippines (Inobaya *et al.,* 2015). Although, after more than 30 years of implementation of mass drug administration, challenges with this program have been raised wherein MDA was not able to interrupt parasite transmission thereby failed to eliminate schistosomiasis in the country (Olveda *et al.,* 2016; Olveda & Gray, 2019). Specific and sensitive diagnostic procedures are essential to monitor the success or failure of schistosomiasis control programs. The Integrated Helminth Control Program (IHCP) and WHO have both adopted several helminth control approaches including health promotion and education, preventive chemotherapy, Community-Led Total Sanitation (CLTS) and developments in water, sanitation and hygiene (WASH) (Belizario *et al.,*

2016). However, despite the established control programs implemented for years, the prevalence rate of these parasitic diseases still increases and remains to be a public health concern in the country (Waite *et al.,* 2016). This is mainly because the strategies were not sustained due to limited funding allotted to programs to eliminate schistosomiasis (Olveda & Gray, 2019).

5. ELIMINATION OF SCHISTOSOMIASIS IN THE PHILIPPINES

Due to the complex epidemiology of schistosomiasis in the Philippines, the existing national control program of mass drug administration alone seems not to effectively eliminate or even control the spread of the disease. Several factors that have contributed to failure to eliminate these diseases but remains to be under investigated include poverty in endemic areas, poor hygiene and sanitation practices, complex life cycle of schistosomes, low sensitivity of diagnostic tests, and the potential role of animals such as dogs, water buffaloes, cats, rats and other mammals as reservoir hosts in the transmission of the disease to humans.

Hence, an integrated multidisciplinary one health approach strategy involving surveillance, more specific and sensitive diagnostic tests, preventive methods and an understanding of the role of reservoir hosts in the transmission of diseases must be developed to impact and improve the control of schistosomiasis in endemic areas and move towards the elimination in the country.

6. CONCLUSION

Over the years of exposure to this neglected tropical disease, *Schistosoma japonicum* infection still poses a great threat in the healthcare and welfare of the community particularly those that are situated in poor rural areas. Regardless of the limitations of the current control strategies, it is firm that community-wide mass drug administration of PZQ will be continuous for an indefinite period to control this parasitic disease in the country. Continuous and more extensive researches on innovative strategies that provide precise and updated data about the transmission, prevalence and the integration of control strategies are necessary to expand, design and improve the national control strategies against NTDs particularly schistosomiasis to move beyond just morbidity control and advancement in the direction of elimination.

7. REFERENCES

Blas B.L., Rosales M.I, Lipayon I.L., Yasuraoka K., Matsuda H. & Hayashi M. (2004) The schistosomiasis problem in the Philippines: a review. *Parasitol Int.* 2004;53(2):127–34. Epub April 9, 2004.

Belizario V.Y., Delos Trinos J., Silawan B., De Veyra C., Hornido A., Amoguis H., Basalo D. & Dema-Ala C. (2018). Evaluation of Fecal and Serological Tests for the Diagnosis of Schistosomiasis in Selected Near Elimination and Endemic Areas in the Philippines. *Thaiscience.info.*

Belizario, V.Y., Ng, J., & Amarillo, M. L., delos Trinos, J.P. C., Reyes, M. & Fudalan, O. (2016). High Burden of Soil-Transmitted Helminthiases in Preschool-Age Children in Masbate: A Decade of Implementation of the Integrated Helminth Control Program in the Philippines. *The Southeast Asian journal of tropical medicine and public health*. 47.

Belizario V.Y., Erfe J.M., Naig J.R. & Chua P.L. (2015). Evidence of increasing risk of schistosomiasis among school—age children in municipality of Calatrava, Province of Negros Occidental, Philippines. *Asian Pacific Journal of Tropical Medicine* Volume 8, Issue 5, May 2015, Pages 373-377. https://doi.org/10.1016/S19957645(14)60346-1

Colley D.G. & Secor, W.E. (2014). Immunology of human schistosomiasis. *Parasite immunology*, 36(8), 347–357. https://doi.org/10.1111/pim.12087

Costain A.H., MacDonald A.S., Smits H.H. (2018). Schistosome Egg Migration: Mechanisms, Pathogenesis and Host Immune Responses. *Frontiers in immunology*, 9, 3042. https://doi.org/10.3389/fimmu.2018.03042

Francisco I., Jiz M., Rosenbaum M., Baltazar P., Steele J.A. (2019) Knowledge, attitudes and practices related to schistosomiasis transmission and control in Leyte, Philippines. *PLoS Negl Trop Dis* 13(5): e0007358.https://doi.org/10.1371/journal.pntd.0007358

Fornillos R., Sato M.O., Tabios I., Sato M., Leonardo L.R., Chigusa Y., Minamoto T., Kikuchi M., Legaspi E.R. & Fontanilla I. (2019). Detection of *Schistosoma japonicum* and *Oncomelania hupensis quadrasi* environmental DNA and its potential utility to schistosomiasis japonica surveillance in the Philippines. *PloSone*, https://doi.org/10.1371/journal.pone.0224617

Gordon C.A., Kurscheid J., Williams G.M., Archie C., Li. Y., Zhou X., Utzinger J., McManus D. & Gray D. (2019). Asian Schistosomiasis: Current Status and Prospects for Control Leading Elimination; *Tropical Medicine and Infectious Disease Review* Published: 26 February 2019

Habtamu K., Degarege A., Ye-Ebiyo Y., Erko B. (2011). Comparison of the Kato-Katz and FLOTAC techniques for the diagnosis of soil-transmitted helminth infections. *Parasitol. Int.* 2011, 60, 398–402.

Inobaya M.T., Olveda R.M., Tallo V, McManus DP, Williams GM, Harn DA, *et al.* (2015). Schistosomiasis mass drug administration in the Philippines: lessons learnt and the global implications. *Microbes Infect.* 2015;17(1):6–15. pmid:25448635.

Jurberg AD, de Oliveira AA, Lenzi HL, Coelho PMZ (2008). A new miracidium hatching device for diagnosing schistosomiasis. *Mem. Inst.* Oswaldo Cruz 2008, 103, 112–114

Kumagai T, Furushima-Shimogawara R, Ohmae H, Wang T, Lu S, Chen R, Wen L, Ohta N. (2010). Detection of early and single infections of *Schistosoma japonicum* in the intermediate host snail, *Oncomelania hupensis,* by PCR and loop-mediated isothermal amplification (LAMP) assay. *Am. J. Trop. Med. Hyg.* 2010, 83, 542–548.

Leonardo L, Rivera P, Saniel O, Antonio Solon J, Chigusa Y, Villacorte E. *et al.* (2015). New endemic foci of schistosomiasis infections in the Philippines *Acta Trop*, 141 (Pt B), pp. 354-360

McGarvey S.T., Carabin H., Balolong E. Jr., Bélisle P., Fernandez T., Joseph L., Tallo V., Gonzales R., Tarafder M.R., Alday P., Willingham A.L. & Olveda R (2006). Cross-sectional associations between intensity of animal and human infection with *Schistosoma japonicum* in Western Samar province, Philippines. *Bull World Health Organ. 2006 Jun; 84(6):446-52.*

Moendeg, K., Angeles, J.M., Goto, Y., Leonardo, L., Kirinoki, M., Villacorte, E., Rivera, P., & Inoue, N., Chigusa, Y. & Kawazu, S. (2015). Development and optimization of cocktail-ELISA for a unified surveillance of zoonotic schistosomiasis in multiple host species. *Parasitology research*. 114. 10.1007/s00436-015-4312-7.

Nicdao J. (2018). Infographic: Schistosomiasis in the Philippines: By the numbers. MIMS Today. Online resource: https://today.mims.com/schistosomiasis-in-the-philippines--by-the-numbers

Olveda R. & Gray D. (2019). Schistosomiasis in the Philippines: Innovative Control Approach is Needed if Elimination is the Goal. Tropical Medicine and Infectious Disease Opinion Schistosomiasis in the Philippines: Innovative Control Approach is Needed if Elimination is the Goal 13 April 2019

Olveda R., Tallo V., Olveda D., Inobaya M., Chau T. & Ross A. (2016). National survey data for zoonotic schistosomiasis in the Philippines grossly underestimates the true burden of disease within endemic zones: implications for future control. *International Journal of Infectious Disease.* https://doi.org/10.1016/j.ijid.2016.01.011

Soares-Magalhães R.J., Salamat M.S., Leonardo L., Gray D.J., Carabin H., Halton K., McManus D.P., Williams G.M., Rivera P., Saniel O., Hernandez L., Yakob L., McGarvey S. & Clements, A. (2014). Geographical distribution of human *Schistosoma japonicum* infection in The Philippines: tools to support disease control and further elimination. *International journal for parasitology*, *44*(13),977–984. https://doi.org/10.1016/j.ijpara.2014.06.010

Waite R.C., Velleman Y., Woods G., Chitty A., & Freeman MC (2016). Integration of water, sanitation and hygiene for the control of neglected tropical diseases: a review of progress and the way forward. Int Health. 2016 Mar; 8 Suppl 1(): i22-7.

World Health Organization (WHO) (2020). Facts about Schistosomiasis. Online resource: https://www.who.int/news-room/fact-sheets/detail/schistosomiasis

Zhou Y.B., Zheng H.M. & Jiang Q.W. (2011). A diagnostic challenge for Schistosomiasis japonica in China: Consequences on praziquantel-based morbidity control. *Parasit. Vectors* 2011, 4, 194