Evidence of increasing risk of schistosomiasis among school-age children in municipality of Calatrava, Province of Negros Occidental, Philippines

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OBJECTIVE: To explore risk of school-age children being infected with schistosomiasis in selected villages in the municipality of Calatrava, province of Negros Occidental, Philippines.

METHODS: As part of the monitoring and evaluation of the helminth control program in the province of Negros Occidental, parasitological monitoring, through the use microscopy of stool samples processed using Kato-Katz technique, was conducted to describe the baseline and follow-up parasitological status of school-age children in 2010 and 2012, respectively. Seven villages from the municipality of Calatrava were selected as study sites.

RESULTS: During baseline assessment, only one case of schistosomiasis was reported from the village of Marcelo. During follow-up assessment, 32 cases (6.9%) of schistosomiasis were reported and the prevalence of moderate-heavy intensity infection was 1.3% in six villages. Among the seven villages included in the follow-up, Minapasuk had the highest prevalence at 14.6%, while San Isidro reported no case of schistosomiasis.

CONCLUSIONS: Non-endemic villages, which have reported positive cases in school-age children, may need to be assessed for possible endemicity for schistosomiasis. Transmission of the disease may need to be determined in these villages through active parasitological and malacological surveillance. Other non-endemic villages adjacent to or share river networks with endemic villages in Calatrava may need to be explored for possible introduction of the disease, especially after typhoons and flooding. Establishing endemicity for schistosomiasis in these villages will help infected and at risk individuals to receive yearly treatment to reduce morbidities caused by this disease.

1. Introduction

Schistosomiasis is one the most neglected tropical diseases, estimated to affect 207 million people, with 779 million people at risk worldwide, many of whom develop severe and permanent disabilities[1–3]. In the Philippines, Schistosoma japonicum (S. japonicum) remains endemic in 28 provinces found in 12 regions in the country[4].

Schistosomiasis is transmitted through schistosome eggs excreted in human feces which contaminate water sources in areas that lack adequate sanitation[3]. Humans are infected through penetration in the skin by infective larvae. The distribution of S. japonicum is also affected by the presence of the intermediate snail host Oncomelania hupensis quadrasi. Since these parasites do not multiply in the human host, reinfection occurs only as a result of contact in contaminated freshwater[5,6].

Morbidity is directly related to worm burden. The greater the number of worms in the infected person, the greater will be the severity of disease. Schistosomiasis causes morbidity, and sometimes death, by adversely affecting nutritional status[7,8], impairing cognitive processes[9], and inducing reactions in tissues
More than 610 million school-age children are at risk of morbidity due to schistosomiasis[10]. School-age children are an important high-risk group for schistosomiasis because the infections occur during a period of intense physical growth and rapid metabolism resulting in increased nutritional needs, during a period of intense learning in a setting of continuous exposure to contaminated water, and children generally lack awareness of the need for good personal hygiene[5].

Recent studies have revealed two newly-described endemic foci in the Philippines[11–13], and one of them is the municipality of Calatrava in the province of Negros Occidental, Western Visayas region. The first schistosomiasis cases were reported in 2006 from the village of Marcelo by the Department of Health Regional Office (DOH RO) VI[12]. Currently, there are three endemic villages in Calatrava declared by the DOH RO VI namely, Marcelo, Hinabongan, and Mina-utok in which mass drug administration of praziquantel among 5 to 65 year-old residents started in 2007, 2009, and 2013, respectively. As part of the monitoring and evaluation for helminth control in the province of Negros Occidental, parasitological monitoring was conducted in selected villages in Calatrava to describe the baseline and follow-up parasitological status in 2010 and 2012, respectively, among school-age children.

2. Materials and methods

2.1. Study site and population

A total of seven barangays/villages from two school districts of the municipality of Calatrava (Figure 1), namely Hinab-ongan, Lo-ok, Marcelo, Minapasuk, Mina-utok, Patun-an, and San Isidro, were selected as part of parasitological monitoring of the Integrated Helminth Control Program of the DOH in the province of Negros Occidental. School-age children were the study participants.

![Figure 1. Map of the Philippines highlighting the municipality of Calatrava in the province of Negros Occidental.](image-url)

2.2. Study design and sampling

This study followed a descriptive cross-sectional study design. Third grade students, age eight to nine years old, enrolled in public elementary schools and residing in the selected villages were recruited. Baseline assessment was conducted in June 2010 and follow-up assessment was conducted in July 2012. A total of 250 students per assessment were targeted based on the WHO guidelines[5,14]. Excluded from the study were those who were: a) without assent and informed consent from their parents; b) not residing in the selected villages; and c) treated with praziquantel within the last six months prior to stool collection.

2.3. Parasitological assessment

Study participants were given specimen containers with stool collection instructions by the Department of Education nurses who were oriented by the project team. The same health workers collected stool samples from study participants prior to the conduct of mass drug administration of praziquantel in the selected villages. Stool samples were processed using the Kato-Katz technique[15] and two aliquots were examined by trained medical technologists in a field laboratory. Stool samples with insufficient amount were processed using Kato thick technique and examined only for the presence of helminth ova. Intensities of infection were categorized as light, moderate, or heavy based on the number of helminth ova present in the stool specimen following the WHO classification[14]. For the purpose of this study, moderate and heavy intensity infections were both classified as moderate-heavy intensity infections[16–18]. Ten percent (10%) of slides were re-examined blindly by a reference microscopist from the University of the Philippines Manila - National Institutes of Health as quality control measure.

2.4. Data analysis and processing

Data obtained was double encoded on pre-tested Microsoft Excel 2007 sheets, which were used to derive prevalence and intensity of S. japonicum infection, as well as geometric mean egg count (GMEC). To assess the statistical difference in prevalence between 2010 and 2012, Fisher’s exact tests and odds ratios were performed on case counts collected from both years per school. Odds ratios were calculated to compare the probability of schistosomiasis infection among school-age children in both 2010 and 2012. All tests were conducted in the statistical package R version 2.14.1.

2.5. Ethical considerations

The study protocol was approved by the Research Ethics Board, University of the Philippines Manila with code UPMREB-2012-041. Parents/guardians provided written consent and students provided assent. The study conformed to the national and international ethical guidelines to protect human subjects, upholding the confidentiality.
of all data collected. The results were shared with the study participants, and those infected with schistosomiasis and were referred accordingly to the rural health unit of Calatrava for proper treatment and management.

3. Results

A total of 365 school-age children submitted stool samples for the baseline assessment while 465 children submitted samples for the follow-up assessment. Village of Hinab-ongan was not part of the 2010 baseline assessment, but was included in the 2012 follow-up assessment. During baseline assessment, only one case of schistosomiasis was reported from the village of Marcelo. Thirty-two cases (6.9%) of schistosomiasis were reported during the follow-up assessment and the prevalence of moderate-heavy intensity infection was 1.3%. Among the seven villages during the follow-up, Minapasuk had the highest prevalence at 14.6%, while San Isidro reported no case of schistosomiasis (Table 1).

Significant increase in prevalence of schistosomiasis in Patun-an was notable from 0% to 11.8% (P=0.037). In Minapasuk, the prevalence significantly rose from 0% to 14.6% of examined participants (P=0.009). In Mina-utok, the proportion of examined participants positive for schistosomiasis reached 7.5% in 2012, compared with 0% in 2010 (P=0.040). On the other hand, a not significant increase in the prevalence of schistosomiasis from baseline to the first follow-up was observed in Lo-ok and Marcelo. In the three villages in the school district of Calatrava I, the prevalence significantly increased from 0% to 4.1% (P=0.016). In the three villages in the school district of Calatrava II, the prevalence also increased from 0.5% to 7.5% (P=0.0002). The odds ratio was estimated as 15.4 with a 95% confidence interval of 2.4 - 641.0, indicating that with 95% probability the odds of having schistosomiasis in Calatrava II in 2012 was at least 2.4 times higher than in the same area in 2010. Aggregated data from Calatrava I and II indicated that the prevalence increased from 0.3% to 6.5%, a highly significant difference (P=0.000). The odds ratio was estimated as 23.5 with a 95% confidence interval of 3.8-966.2, indicating that with 95% probability the odds of having schistosomiasis in the six villages of Calatrava in 2012 was at least 3.8 times higher than in the same villages in 2010.

Other infections observed during the two parasitological assessments include soil-transmitted helminthiasis (STH). During the baseline assessment, overall cumulative prevalence of STH was 49.8% and prevalence of heavy intensity STH of 12.4% were noted. In the follow-up, overall cumulative STH prevalence was 35.7% and prevalence of heavy intensity STH was 5.1%.

4. Discussion

Baseline parasitological assessment in 2010 noted a single schistosomiasis case from a school-age child in Marcelo, a known endemic village. After two years, follow-up assessment revealed a significant increase in the number of cases to 32 school-age children with a prevalence of 6.9%. Evidence of increasing risk for schistosomiasis among school-age children in selected villages in Calatrava was observed as supported by aggregate prevalence data. The positive cases of school-age children in Lo-ok, Patun-an, and Mina-utok were the first ever detected in these villages.

With these findings, the geographic distribution of schistosomiasis in the neighboring non-endemic villages from the endemic villages of Marcelo, Hinab-ongan, and Minapasuk may actually be more widespread. A number of factors may have led to the increased prevalence of schistosomiasis and the risk of infection in Calatrava. These include poor sensitivity of the diagnostic test, low coverage of mass drug administration, poor sanitation, river networks and flooding, migration of infected individuals to a non-endemic area, and exchange of animals for farming.

The current diagnostic test used for parasitological monitoring and

| School district/villages | Examined (KT’ + KK’) | Positive for Schistosoma | Schistosoma | Examined (KK’ only) | Moderate-heavy intensity infection |
|--------------------------|----------------------|--------------------------|-------------|---------------------|----------------------------------|
|                          | 2010 2012            | 2010 2012                | 2010 2012   | 2010 2012           | 2010 2012                        |
|                          | 2010 2012            | 2010 2012                | 2010 2012   | 2010 2012           | 2010 2012                        |
|                          | **-value**           | P-value                  | **-value**  | P-value             | P-value                          |
| Calatrava I              |                      |                          |             |                     |                                  |
| Lo-ok                    | 32 41 0 (0)          | 1 (2.4) 1.000 0         | 0 0.1       | 32 41 0 (0)         | 0 (0)                            |
| Patun-an                 | 47 34 0 (0)          | 4 (11.8) 0.036 5       | 0 0.7       | 47 34 0 (0)         | 1 (2.9) 0.426 8                  |
| San Isidro              | 79 46 0 (0)          | 0 (0) 1.000 0          | 0 0         | 79 46 0 (0)         | 0 (0) 1.000 0                    |
| Subtotal                 | 158 121 0 (0)        | 5 (4.1) 0.016 4       | 0 0.2       | 158 121 0 (0)       | 1 (0.8) 0.435 7                  |
| Calatrava II             |                      |                          |             |                     |                                  |
| Minapasuk               | 53 41 0 (0)          | 6 (14.6) 0.009 0       | 0 0.8       | 52 41 0 (0)         | 0 (0)                            |
| Hinab-ongan             | None 63 None 6 (9.5) | NA                      | None 0.5    | None 62 None        | 2 (3.2) NA                       |
| Marcelo                 | 73 200 1 (1.4)       | 12 (6.0) 0.194 9      | 0.05 0.3    | 72 191 0 (0)        | 1 (0.5) 1.000 0                  |
| Mina-utok               | 81 40 0 (0)          | 3 (7.5) 0.039 8       | 0 0.4       | 80 40 0 (0)         | 2 (5.0) 0.116 7                  |
| Subtotal                 | 207 344 1 (0.5)      | 27 (7.8) 0.000 2      | 0.02 0.4    | 204 334 0 (0)       | 5 (1.5) NA                       |
| Total                    | 365 465 1 (0.3)      | 32 (6.9) 0.000 0      | 0.01 0.3    | 362 455 0 (0)       | 6 (1.5) NA                       |

- Kato thick; b - Kato-Katz; c - geometric mean egg count; * - significant at 5% level; ** - significant at 1% level.
surveillance of schistosomiasis is microscopic examination of stool sample processed using Kato-Katz technique\cite{5}. A study by Olveda et al\cite{19} conducted in the Philippines revealed poor sensitivity of the Kato-Katz technique at 65\%\cite{19}. Other researches also mentioned the significant underestimation of Kato-Katz technique even with greater repetitions\cite{20,21}. While Kato-Katz technique is efficient for the early stages of a control program, this may be inappropriate and ineffective as the prevalence and intensity of infections are reduced, in turn, increases the risk of errors due to the inherently low sensitivity of the method\cite{22}. Diagnostic limitations and biases of this nature will persist until a more sensitive diagnostic tool with a higher predictive value for negative stool examinations is utilized, such as immunological techniques and polymerase chain reaction analysis.

Coverage rates of mass drug administration in Marcelo ranged from 23\% to 63\% in 2009 to 2013. In Hinab-ongan, coverage rates ranged from 48\% to 69\% in 2009 to 2013. In Minapasuk, coverage rate was 78\% in 2013 (Program Report from DOH RO VI, 2013). These coverage rates did not reach the DOH target of 85\%\cite{4}. Coverage of mass drug administration among individuals in the endemic villages may need to be increased as these individuals continue to be infected and suffer from morbidity. Without addressing and controlling the disease through efficient distribution of anthelmintics, schistosomiasis may be introduced in other nearby villages.

Poor sanitation was noted in Calatrava with the low percentage of households with sanitary toilets in the entire municipality at 36\% in 2012 (Municipal Health Office of Calatrava, 2013). Open defecation in freshwater contributes to the transmission of schistosomiasis in other areas. Snail-infested bodies of water in Marcelo and Hinab-ongan are far from human residences and frequented only by farmers. In Marcelo, indiscriminate defecation is deemed inevitable in the absence of nearby toilet facilities, while in Hinab-ongan, open defecation may be occurring in the wide marshy grasslands\cite{13}. Moreover, the relatively high prevalence of STH in Calatrava may reflect continuing open defecation in the locality.

Typhoons and heavy rains, brought about by climate change, may cause the river to rise and also cause the flooding in Calatrava, which may carry infected snails from higher elevations to lower elevations\cite{13,23,24}. Hydrological connectivity through river networks in villages in Calatrava coursing through various geographic locations, such as Minapasuk and Mina-utok, may transport snails into previously non-endemic villages. However, Mina-utok was found not suitable for habitat of \textit{O. h. quadrasi} with a low soil pH at 4.8\cite{13}. The most suitable soil pH for \textit{O. h. quadrasi} habitat is 5.6 - 7.9\cite{25}. On the other hand, a mathematical model showing the transmission of schistosomiasis may be sustained through a group of connected villages, even when the individual village conditions do not support endemicity. This suggests that the traditional targeting of villages with high infection without regard to village interconnection may not lead to optimum control of schistosomiasis\cite{26}.

Exchange of animals, such as carabaos and cattle, for farming may contribute to the transmission of the disease, and the snail intermediate hosts may possibly adhere to the skin and feet of the animals when they swallow in the water\cite{13,27}. In the animal survey conducted in selected villages in Calatrava in 2008 to 2009, no animals (\textit{ie}. carabaos, dogs, cattle, pigs, goats, and horses) were found positive for \textit{S. japonicum}\cite{13}. However, the number of animals included in the survey was not enough to confirm the presence of natural infection. Most of those sampled were tethered and penned preventing contact with water and reducing risk of infection. A bigger sample including both tethered and stray animals might give a different profile of animal infection\cite{13,28,29}. Lastly, infected individuals migrating to non-endemic villages may have also contributed to the transmission of schistosomes in previously known non-endemic villages in Calatrava\cite{30,31}.

With the results of this study, known non-endemic villages of Logok, Patun-an, and Mina-utok, which have reported positive cases in school-age children, may need to be further assessed for endemicity of schistosomiasis. Transmission of the disease may need to be determined in these villages through active parasitological and malacological surveillance. Furthermore, other non-endemic villages that are adjacent to or that share river networks with endemic villages in Calatrava may need to be explored for possible introduction of the disease, especially after heavy rains and flooding\cite{13}. Establishing endemicity for schistosomiasis will help infected and at risk individuals to receive free annual treatment helping reduce morbidities caused by the disease\cite{4}.

Similar to the threat of introducing schistosomiasis in non-endemic areas in Calatrava, other areas in the Philippines, which are nearby endemic areas for schistosomiasis, may need to be assessed for endemicity especially areas with reports of positive individuals. Climate change may have played a role in the introduction of schistosomiasis in other areas as stronger typhoons and heavy rains are causing flooding and displacement of families in many parts in the Philippines. Furthermore, existing geographical information system maps with flood-prone areas being developed by the national and local government may be utilized as guide to help determine the possible introduction of schistosomiasis to other non-endemic villages.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

[1] Gryseels B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. *Lancet* 2006; **368**: 1106-1118.

[2] Steinmann P, Keiser J, Bos R, Tanner M, Utzinger J. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. *Lancet Infect Dis* 2006; **6**(7): 411-425.

[3] Hotez PJ, Fenwick A, Savioli L, Molyneux DH. Rescuing the bottom billion through control of neglected tropical diseases. *Lancet* 2009; **373**: 1570-1575.

[4] Department of Health. *Administrative order 2007–0015: revised guidelines in the management and prevention of schistosomiasis*. Manila, Philippines: Department of Health; 2007.

[5] World Health Organization. *Helminth control in school-age children: a guide for managers and control programmes*. 2nd ed. Geneva, Switzerland: World Health Organization; 2011.

[6] World Health Organization. *Schistosomiasis progress report 2001–2011 and strategic plan 2012–2020*. Geneva, Switzerland: World Health Organization; 2013.

[7] Friedman JF, Kanzaria HK, McGarvey ST. Human schistosomiasis and anemia: the relationship and potential mechanisms. *Trends Parasitol* 2005; **21**: 386-392.

[8] Hall A, Hewitt G, Tuffrey V, de Silva N. A review and meta-analysis of the impact of intestinal worms on child growth and nutrition. *Matern Child Nutr* 2008; **4**(Suppl 1): 118-236.

[9] Jukes MC, Nokes CA, Alcock KJ, Lambo JK, Kihamia C, Ngorosho N, et al. Heavy schistosomiasis associated with poor short-term memory and slower reaction times in Tanzanian schoolchildren. *Trop Med Int Health* 2002; **7**: 104-117..

[10] World Health Organization. Soil-transmitted helminthiases: estimates of the number of children needing preventive chemotherapy and number treated. 2009. *Who Epidemic Rec* 2011; **86**: 257-266.

[11] Belizario VY, Martinez RM, de Leon WU, Esparaz DG, Navarro JR, Villar LC, et al. Cagayan Valley: A newly described endemic focus for *Schistosomiasis japonica* in the Philippines. *Phillip J Int Med* 2005; **43**: 117-122.

[12] Belizario VY, Martinez RM, de Leon WU. Negros Occidental: A newly described endemic focus for *Schistosomiasis japonica* in the Philippines. Unpublished. 2007.

[13] Leonardo L, Rivera P, Saniel O, Solon JA, Chigusa Y, Villacorte E, et al. New endemic foci of schistosomiasis infections in the Philippines. *Acta Trop* 2013. Epub ahead of print.

[14] Montresor A, Crompton DW, Hall A, Bundy DAP, Savioli L. *Guidelines for the evaluation of soil–transmitted helminthiasis and schistosomiasis at community level*. Geneva, Switzerland: World Health Organization; 1998.

[15] World Health Organization. *Bench aids for the diagnosis of intestinal parasites*. Geneva, Switzerland: WHO Press; 1994.

[16] Belizario VY Jr, de Leon WU, Lumampao YF, Anastacio MB, Tai CM. Sentinel surveillance of soil-transmitted helminthiasis in selected local government units in the Philippines. *Asia–Pac J Public Health* 2009; **21**(1): 26-42.

[17] Belizario VY Jr, Totanes FIG, de Leon WU, Lumampao YF, Ciro RNT, et al. Persistent foci of *Schistosoma japonicum* in civilians in the Philippines. *Acta Trop* 2011; **120S**: S12-S18.

[18] Belizario VY Jr, Martinez RM, de Leon WU, Lumampao YF, Anastacio MB, Tai CM. Sentinel surveillance of soil-transmitted helminthiasis in preschool-aged and school-aged children in selected local government units in the Philippines: follow-up assessment. *Asia–Pac J Public Health* 2013. Epub ahead of print.

[19] Olveda RM, Daniel BL, Aligui GD, Acosta LP, Fevidal P, Tiu E, et al. Sentinel surveillance of soil-transmitted helminthiasis in preschool-aged and school-aged children in selected local government units in the Philippines: follow-up assessment. *Asia–Pac J Public Health* 2013. Epub ahead of print.

[20] Lin DD, Liu JX, Liu YM, Hu F, Zhang YY, Xu JM, et al. Routine Kato technique underestimates the prevalence of *Schistosoma japonicum*: a case study in an endemic area of the People’s Republic of China. *Parasitol Int* 2008; **57**: 281-286.

[21] Yu JM, de Vlas SJ, Jiang QW, Gryseels B. Comparison of the Kato-Katz technique, hatching test and indirect hemagglutination assay (IHA) for the diagnosis of *Schistosoma japonicum* infection in China. *Parasitol Int* 2007; **56**: 45-49.

[22] Utzinger J, N’goran EK, Caffrey CR, Keiser J. From innovation to application: social-ecological context, diagnostics, drugs and integrated control of schistosomiasis. *Acta Trop* 2011; **120S**: S121-S137.

[23] Montaskersky R. *Health in hot zones: how would global warming affect humans?* Washington DC: Science News; 1996.

[24] Shope RE. Impacts of global climate change on human health: spread of infectious disease. In: Majumdar SJ, Kalkstein LS, Yarnal B, Miller EW, Rosenfield LM, editors. *Global climate change: implications, challenges, and mitigation measures*. Easton PA: The Pennsylvania Academy of Science; 1992; p 363-370.

[25] Nihei N, Kanazawa T, Blas BL, Saitoh Y, Itagaki H, Pangilinan R, et al. Soil factors influencing the distribution of Oncomelania quadrasi, the intermediate host of *Schistosoma japonicum*, on Bohol Island, the Philippines. *Ann Trop Med Parasitol* 1998; **92**: 699-710.

[26] Durrieu D, Seto EY. Connectivity sustains disease transmission in environments with low potential for endemicity: modelling schistosomiasis with hydrologic and social connectivities. *J R Soc Interface* 2009; **6**(35): 495-508.

[27] Grose S. *Schistosomiasis and water resource development: a re-evaluation of an important environment–health linkage*. Wisconsin, USA: University of Wisconsin-Madison; 1993. Technical working paper no. 2. p. 43.

[28] Dumag PU. Animal schistosomiasis: a review. *Phillip J Anim Ind* 1979; **34**: 50-64.

[29] Dumag PU, Gajudo CE, Sena CY, Cardenas EC, Fementira EB. Epidemiology of animal schistosomiasis in the Philippines. *Phillip J Vet Sci* 1980; **6**(2): 410-420.

[30] Southgate VR, Tchuem Tchuente LA, Sene M, De Clerq D, Theron A, Jourdan J, et al. Studies on the biology of schistosomiasis with emphasis on the Senegal River Basin. *Mem Inst Oswaldo Cruz* 2001; **96**: 75-78.

[31] He YX, Salafsny B, Ramsawamy K. Host-parasite relationships of *Schistosoma japonicum* in mammalian hosts. *Trends Parasitol* 2001; **17**(7): 320-324.