Perspective

National survey data for zoonotic schistosomiasis in the Philippines grossly underestimates the true burden of disease within endemic zones: implications for future control

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SUMMARY

Zoonotic schistosomiasis has a long endemic history in the Philippines. Human mass drug administration has been the cornerstone of schistosomiasis control in the country for the past three decades. Recent publications utilizing retrospective national survey data have indicated that the national human prevalence of the disease is <1%, hence the disease is now close to elimination. However, the evidence for such a claim is weak, given that less than a third of the human population is currently being treated annually within endemic zones and only a third of those treated actually swallow the tablets. For those who consume the drug at the single oral dose of 40 mg/kg, the estimated cure rate is 52% based on a recent meta-analysis. Thus, approximately 5% of the endemic human population is in reality receiving the appropriate treatment. To compound this public health problem, most of the bovines in the endemic communities are concurrently infected but are not treated under the current national control programme. Given this evidence, it is believed that the human prevalence of schistosomiasis within endemic regions has been grossly underestimated. Inherent flaws in the reporting of national schistosomiasis prevalence data are reported here, and the problems of utilizing national retrospective data in making geographic information system (GIS) risk maps and advising policy makers of the outcomes are highlighted.

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1. Introduction

Schistosomiasis, or Bilharzia, is a neglected tropical parasitic disease caused by blood flukes of the genus Schistosoma. Globally, it ranks third among the most devastating tropical diseases, and is a major cause of morbidity in the tropics. Schistosomiasis was first reported in the Philippines in 1906. Approximately 12 million people, residing in 28 endemic provinces located in 12 different geographical zones, are at risk of infection in the country. Overall, a total of 190 municipalities and 1212 barangays (villages) are currently endemic for the disease based on surveys conducted over the past decade. Two new endemic foci reported in the northern (Gonzaga, Cagayan) and central (Calatrava, Negros Occidental) parts of the country were confirmed in 2004 and 2006, respectively.

Considerable optimism surrounds mass drug administration (MDA) for the control of schistosomiasis globally, for which praziquantel has served as the cornerstone since its development in 1979. Numerous studies have claimed that preventive chemotherapy (i.e., 40 mg/kg of praziquantel), given annually or biannually, can significantly reduce the prevalence and intensity of infection, and control morbidity in the long term. In the last decade, close to one billion US dollars has been raised for MDA campaigns against neglected tropical diseases, largely from international donors, and delivered vertically to local endemic communities through national health care services.

There is now strong evidence that large mammals (e.g., water buffaloes, cattle, and dogs) are contributing significantly to disease transmission and complicating control. Given the zoonotic nature of the disease in the Philippines it is evident that the incidence,
prevalence, and morbidity of this disease will not be controlled by MDA alone. There is the need for innovative cost-effective strategies to control schistosomiasis japonica in the long term. The inherent flaws in the reporting of the national schistosomiasis prevalence data are described herein, and the problems of utilizing national retrospective data in making geographic information system (GIS) risk maps and advising policy-makers of the outcomes is highlighted.

2. National schistosomiasis surveillance

The control programme for schistosomiasis in the Philippines has been under the supervision of the Schistosomiasis Control Service (SCS). The human prevalence of *Schistosoma japonicum* infection was defined as the proportion of individuals who showed at least one parasite egg on two Kato–Katz (KK) thick smears versus the number of people examined in the endemic population. The estimated exposed population for schistosomiasis in the Philippines is approximately 1.8 million. The annual results of case finding are shown in Table 1. From 1985 to 1990, approximately 30% (range 26–37%) of the target population was examined. In 1990, the SCS received additional funds from the World Bank through the Philippine Health Development Programme (PHDP), and from 1991 to 1993 it managed to examine approximately 75% of the target population (range 75–79%) with the increased funding. However, funds through the PHDP were subsequently reduced in 1994 and funding was eventually terminated in 1995. As a direct result, the proportion of individuals examined annually from 1994 to 1999 decreased to approximately 25% (range 22–44%). The percentage of individuals examined plummeted further from 2000 to the present. In sum, due to limited financial resources, active surveillance for schistosomiasis in the Philippines now comprises approximately 10% of the known endemic population in the country. This has resulted in a gross underreporting of the disease given its highly focal nature and clumped distribution.

With support from World Health Organization (WHO), a stratified two-step systematic cluster sampling survey was conducted from 2005 to 2008 in order to determine the national prevalence of schistosomiasis. Provinces in both endemic and non-endemic regions were identified for inclusion in the survey. Five municipalities were selected randomly from the selected provinces, and one village per municipality was selected for follow-up. Two hundred and seventy-four eligible subjects were chosen randomly from the selected households in each village, and eligible subjects were requested to submit two stool samples. From each stool sample, two KK thick smears were examined for the presence of *S. japonicum* eggs. This sampling strategy selected 115 villages out of a total 1212 known endemic villages. Compliance for the first stool submission of eligible subjects was 45% in Mindanao, 60% in the Visayas, and 76% in Luzon. It is noteworthy that this national survey strategy examined less than 10% of the known endemic population and many individuals refused to provide stool for examination. Thus the generalizability of these findings for ‘endemic zones’ is questionable and should be viewed with considerable caution. It is well known that the distribution of the disease is highly focal (clumped) in nature, thus the random selection of a small segment of the endemic population (<10%) could lead to a gross underestimation of the true burden. This combined with the fact that only one or two slides were read for each individual raises concerns in the reporting of national prevalence in the Philippines.

3. Problems with the national control programme

Population-based chemotherapy as the sole control strategy for zoonotic schistosomiasis in the Philippines was initiated in 1980. The initial approach was the treatment of positive cases with the drug praziquantel, administered at an oral dose of 60 mg/kg, divided into two equal doses taken 4 h apart. The compliance rate from 1985 to 1999 for annual free treatment was reportedly high at approximately 85% in those who were found positive by case finding. However, it is important to note that only 30% of the endemic population was covered by yearly case finding and treatment. This suggests that 70% of the endemic population was left untreated.

In 2000, the SCS implemented a policy of annual MDA for residents 5–65 years of age residing in endemic villages with a human prevalence of infection greater than 15%. Case finding and treatment was continued in villages with a prevalence of <15%. In 2009 the MDA policy was changed to provide treatment to all individuals aged 5–65 years residing in endemic villages regardless of the prevalence. In 2011, following the recommendation of the WHO, the SCS reduced the dosage of praziquantel in the MDA programme to a single oral dose of 40 mg/kg.

Despite the fact that only a third of the infected population was treated annually (except from 1991 to 1993) through the case finding and treatment scheme, and that less than a third complied with the free treatment, the yearly national prevalence of *S. japonicum* in the country was reported to have declined dramatically from a high of 10% in 1985 to a low of 0.49% in 2008. Table 1 illustrates the continuous drop in national human prevalence of schistosomiasis from more than 10% in 1985 to less than 4% in 1999. The prevalence was reportedly maintained at less than 5% until 2005. Subsequent prevalence surveys (2005–2008) using the above-mentioned stratified two-step systematic cluster sampling approach, recorded a very low national level of infection of less than 1%. The remarkably low national prevalence reported for *S. japonicum* infection in the last 10 years has now created the impression that the disease is no longer a serious public health problem by the government and that the continuous implementation of the existing national MDA programme for humans could lead to disease elimination. However, given the poor drug coverage (less than one third of the endemic population covered) and poor compliance with the free annual treatment (only one third of the population actually take the drug), it is difficult to believe that the current national human prevalence has dropped to <1%. Moreover, given the zoonotic nature of the disease, where over 80% of bovines are infected, the likelihood of a

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of individuals examined</th>
<th>Percentage of target population of 1.8 million individuals</th>
<th>Number positive</th>
<th>Prevalence (%)</th>
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</thead>
<tbody>
<tr>
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<td>505,851</td>
<td>26.8</td>
<td>39,046</td>
<td>10.4</td>
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<tr>
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<td>459,291</td>
<td>26</td>
<td>34,150</td>
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<td>683,918</td>
<td>37</td>
<td>44,925</td>
<td>6.6</td>
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<tr>
<td>1988</td>
<td>423,708</td>
<td>24</td>
<td>26,953</td>
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<tr>
<td>1989</td>
<td>468,355</td>
<td>27</td>
<td>35,197</td>
<td>7.5</td>
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<tr>
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<td>1995</td>
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<tr>
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<td>392,133</td>
<td>22</td>
<td>12,871</td>
<td>3.3</td>
</tr>
</tbody>
</table>

*Note: From 1985 to 1999, case finding was done by examining two Kato–Katz thick smears from a single stool sample. Source of data: Department of Health Schistosomiasis Control Service annual reports, 1997 and 1999.*
reduction in the national prevalence is highly unlikely.13–15 So, what is the true burden of this disease within endemic zones?

4. National burden of disease

Figure 1 summarizes the national schistosomiasis prevalence for humans reported by Leonardo et al. in 2012, Magalhães et al. in 2014, and by various other authors during 2002–2014 in known endemic zones.8,16 The national survey conducted in 2008, which used the stratified two-step systematic cluster sampling scheme, recorded very low prevalence rates in the known highly endemic provinces of Western Samar, Northern Samar, and Leyte, with reported prevalence rates of 0.8%, 2.4%, and 0.9%, respectively.8 In the newly identified areas of transmission in Cagayan Province, the recorded prevalence was 0.4%.9 The prevalence rates generated by Magalhães et al. in 2014 for the same endemic provinces were 0–3%, 0–3%, 0–5%, and 0.4%.10 In contrast, other research teams performing studies from 2002 to 2014 reported prevalence rates ranging from 0.7% to 47% for Western Samar, 5% to 46% for Northern Samar, and 25% to 60% for Leyte (Table 2). In Cagayan, two endemic villages were surveyed and the prevalence rates were found to be 10% and 31%, respectively.

Table 2 illustrates the key outcomes of various studies that have investigated the prevalence of schistosomiasis in various endemic regions throughout the country from 2002 to 2014. In 2002, a longitudinal study completed in Leyte, investigating immune correlates of resistance to infection, showed that the human prevalence in those aged 15–30 years was 60% (1262/1699).17 Another study, which examined S. japonicum infection among pregnant women, conducted in Leyte between 2008 and 2012, showed that 25.4% (373/1468) of the subjects were positive for schistosomiasis.18 A cross-sectional survey of 50 endemic villages in Western Samar Province in 2006, as part of the Schistosomiasis Transmission Ecology Project (STEP), reported prevalence rates ranging from 0.7% to 47% (mean 15%).19 Another cross-sectional survey of schistosomiasis was conducted in 2012 on 18,221 individuals residing in 22 schistosomiasis endemic villages in the province of Northern Samar.20 Despite an active schistosomiasis control programme in Northern Samar for over 30 years, which included an MDA campaign in the last 5 years, the mean prevalence of schistosomiasis among 10,435 subjects evaluated was 27.1% (95% confidence interval 26.3–28.0%).20 Moreover, a cross-sectional ultrasound study in the same study location showed high levels of schistosomiasis–induced morbidity in the schistosomiasis endemic communities. Left lobe liver enlargement (>70 mm) was evident in 89.3% of subjects. Twenty-five percent of the study population had grade II/III liver parenchyma fibrosis and 13.3% had splenomegaly (>100 mm).20,21 In 2012, two communities in the province of Cagayan (Magrafil and Santa Maria) were screened for the prevalence of schistosome infection and this was found to be 10% and 31%, respectively (personal correspondence).22

5. Discussion

The recently reported national human prevalence (and GIS risk maps) of schistosomiasis in the Philippines has been estimated to be less than 3% in the endemic regions of the country.18,19 As a result, the disease is no longer considered to be a major public health problem by the government. Moreover, it is now recommended that the limited national control funds be spent on more targeted MDA, leading to disease elimination.16 However, when one examines more closely how the national surveys were conducted and how the current national programme is being deployed, it is difficult to ascertain by what means that national prevalence could have dropped to such a low rate over the past decade. Moreover, other studies over the past decade (2002–2014) have shown evidence that the disease remains highly endemic throughout the country in both human and bovine populations, with reported human prevalence rates as high as 50% in some

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**Figure 1.** Comparison of the human schistosomiasis prevalence rates in highly endemic zones of the Philippines: Leonardo et al.8 (left panel), Magalhães et al.16 (centre panel), and of various other authors for the period 2002–2014 (right panel).
localities, and over 80% in bovine populations.\textsuperscript{13–15,20} Given the zoonotic nature of the disease, it is difficult to ignore such evidence. Clearly, this discrepancy in reported findings warrants closer scrutiny given the implications for national control and future policy.

It is noteworthy that the recent national surveys were based on only one or two KK thick smear stool slides for those who provided stool, thus this will lead to a gross underestimation of the true prevalence. It has been estimated that a single KK misses approximately 55% of light infections and that five KK smears would be needed to detect 95% of such infections.\textsuperscript{23} ‘Intra-individual’ variation has been observed in repeated egg counts.\textsuperscript{23} Additionally, it has been shown that a small number of individuals in endemic communities excrete a large proportion of eggs. This ‘inter-individual’ variation in egg counts is thought to reflect the variation in worm loads.\textsuperscript{3} Quality control in reading such slides is paramount if one wants to truly determine the underlying prevalence in an endemic population. In the Philippines, based on the personal research experience of the present investigators, the ability of microscopists to correctly identify schistosomiasis eggs varies considerably (0–60%) among trained personnel; thus, if quality measures are not in place, this again will lead to a gross underestimation of the human prevalence.

The national schistosomiasis control programme, using MDA of humans as the sole strategy, has stated that the human prevalence has dropped dramatically over the past decade. However, the evidence for such a claim is weak given that less than a third of the human population residing within endemic zones are currently being treated annually and only a third of those treated actually take the drug. For those who take the drug at the single oral dose of 40 mg/kg, the estimated cure rate is 52% based on a recent meta-analysis.\textsuperscript{1} In sum, approximately 5% of the endemic human population is in reality receiving the appropriate treatment. Moreover, in these same endemic communities, most of the bovines are currently infected (>75%) but are not being treated under the current control programme. Given this evidence, it is believed that the prevalence of schistosomiasis has been grossly underestimated within endemic areas. Through the present authors’ own research, it has been found that the disease is moderately endemic (5–25%) in most endemic regions.\textsuperscript{14,15,17–20}

### 6. Conclusions

Schistosomiasis remains a major public health problem in the Philippines despite recent published reports. Given the zoonotic nature of the disease, mass drug administration in humans as a sole national control strategy will not lead to disease elimination. An integrated national control programme that carefully considers the role of bovines in human transmission, along with irrigation, focal mollusciciding, annual mass drug administration of both humans (60 mg/kg) and bovines (25 mg/kg), and health education is advocated. Although this intersectoral approach will require a substantial effort, it is the only strategy that will lead to sustainability.

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