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REVIEW

The Impact of Targeted Treatment and Mass Drug Administration Delivery Strategies on the Prevalence and Intensity of Schistosomiasis in School Aged Children in Africa: A Systematic Review

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Abstract: Schistosomiasis is a public health problem in more than 78 countries in the world. The disease is most prevalent among children than adults due to their high exposure to infectious water sources. Various interventions such as mass drug administration (MDA), snail control, safe water provision and health education have been implemented independently or jointly to control, reduce and ultimately eliminate Schistosomiasis. This scoping review focused on studies reporting the impact of different delivery strategies of targeted treatment and MDA on the prevalence and intensity of schistosomiasis infection in school aged children in Africa. The review focused on *Schistosoma haematobium* and *Schistosoma mansoni* species. A systematic search for eligible literature from peer-reviewed articles was done from Google Scholar, Medline, PubMed and EBSCO host databases. The search yielded twenty-seven peer-reviewed articles. All articles found reported a decrease in the prevalence of schistosomiasis infection. Five studies (18.5%) reported a prevalence change below 40%, eighteen studies (66.7%) reported a change between 40% and 80%, and four studies (14.8%) reported a change above 80%. The infection intensity post-treatment was varied: twenty-four studies reported a decrease, while two studies reported an increase. The review showed that the impact of targeted treatment on the prevalence and intensity of schistosomiasis depended on the frequency at which it was offered, complementary interventions, and its uptake by the target population. Targeted treatment can significantly control the infection burden, but cannot eliminate the disease. Constant MDA programs coupled with preventative and health promotional programs are required to reach the elimination stage.

Keywords: schistosomiasis, mass drug administration, prevalence, intensity, targeted treatment, impact, school aged children

Introduction

Schistosomiasis is a neglected tropical disease that causes a considerable public health problem in 78 countries.[1] *Schistosoma haematobium* causes urogenital Schistosomiasis and intestinal Schistosomiasis is caused by either *Schistosoma guineensis, Schistosoma intercalatum, Schistosoma mansoni, Schistosoma japonicum*, or *Schistosoma mekongi*.[2] Globally, approximately 700 million people are at risk of being infected with *Schistosoma*. More than 240 million people are estimated to be infected with schistosomiasis, and 90% of the cases are in Sub-Saharan Africa, where it is estimated to cause about 200 000 deaths per annum. Since the mid-1980s, the World Health Organization (WHO) emphasised the use of praziquantel as the central pillar for a global strategy to control schistosomiasis morbidity.[3] In 2001, World Health Assembly (WHA) resolution 54.4, formally recognised the global burden of schistosomiasis infection and emphasised the reduction of schistosomiasis- associated morbidity and mortality through treatment of school children.

WHO recommends the mass drug administration (MDA) program, a diagnosis-free annual/biannual distribution of single-dose, oral preventive chemotherapy (praziquantel) to reduce schistosomiasis morbidity and mortality in endemic

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areas. MDA, involves the mass treatment of a whole population of people in a given community who want it, regardless of their age, sex, socioeconomic status, or degree of infection. The level of endemicity in a given area determines the frequency of mass drug administration. According to WHO, for areas of high schistosomiasis endemicity (prevalence ≥ 50%) all school-aged children and adult people at risk of contracting the infection should be treated annually. This is also known as the community wide treatment (CWT) strategy. In areas of moderate endemicity (prevalence 10–50%) treatment should be targeted, ie given to school children once in two years[3] or in areas of low endemicity (prevalence ≤ 10%) treatment is done at least twice in the primary education: first at school entry and second, when they are in their final year of primary education.[4] The latter implies that children are generally treated for the first time at age of 6 years and will receive another treatment after seven years of primary education at age of thirteen. Targeted treatment is different from MDA because unlike MDA which targets the whole population group, targeted treatment may specify a certain group membership to be treated based on age, sex, religion, occupation, or other factors.

School-aged children between six and 15 years are often targeted for regular treatment with praziquantel in large-scale drug delivery programs, mainly because they suffer a disproportionate burden of schistosomiasis morbidity. On the other hand, a mass drug delivery strategy that treats all members of the community has been suggested in a move towards elimination of schistosomiasis as a public health problem. The impact and success of both targeted treatment and mass drug administration are evaluated through measuring the change in prevalence and intensity of the infection and also the treatment coverage.[5] A number of trials have been implemented to assess the effectiveness of different control strategies in reducing the burden of schistosomiasis infections. For instance, MDA programs have been implemented differently in different countries with regard to duration, frequency and mode of delivery. Some are run for only a year,[6] while others run for upto five years.[7] The frequency of MDA ranges from annual to biennial[8] while the delivery mode is either school-based or community-based.

Studies have revealed that praziquantel significantly lowers morbidity and schistosomiasis transmission in sub-Saharan Africa. Cases of failure or resistance have however been documented following the administration of a single standard dose of praziquantel at a dosage of 40 mg/kg body weight.[9] Other limitations of PZQ include its inability to control immature worms, which leads to less desired results during MDA programs.[10] More efforts are being done to try and fight schistosomiasis through the use of vaccines. There are four main recombinant antigens which are being developed and trialed on human subjects, these include Schistosoma mansoni tetraspanin, a 9-kDa surface antigen (Sm-TSP-2), Schistosoma haematobium 14-kDa fatty acid-binding protein (Sm14), Schistosoma haematobium 28-kD glutathione S-transferase (rSh28GST), and Schistosoma mansoni (Sm-p80).[10]

This review aims at identifying the impact of differential delivery strategies associated with targeted and mass drug administration on the prevalence and intensity of schistosomiasis in school aged children in Africa. More specific aims of this study are: (a) to summarize existing findings on the effects of mass and targeted praziquantel distribution on schistosomiasis prevalence and intensity in school-aged children, and (b) to examine different delivery strategies of mass and targeted praziquantel delivery on schistosomiasis prevalence and intensity in school-aged children in Africa. The focus on Africa was based on this region having the greatest burden of schistosomiasis globally and the greatest need for information about optimal implementations strategies at national and subnational levels.

This review provides a clearer understanding of the impact of targeted and mass drug administration on the prevalence and intensity in context of the delivery strategies such as treatment duration, frequency, mode of delivery and other complementary interventions. This will contribute to efforts to reduce the burden of schistosomiasis infection in African school-aged children in line with the WHO millennium goals of eliminating schistosomiasis and interrupting its transmission by 2025.[4]

Materials and Methods

This scoping review was conducted in adherence to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.[11] Literature search was done between June 2019 and June 2022 by two investigators (NC and TM) in the following databases: PubMed, Medline, Google Scholar and EBSCO

host, for articles published from 2010 to 2022. Studies that reported the impact of targeted treatment or Mass Drug Administration (MDA) with praziquantel on the prevalence and intensity of schistosomiasis infection in African primary school children aged 5 to 19 years were targeted. The eligibility criteria were: inclusive of only primary research studies published in peer-reviewed journals; The studies explicitly reported on the changes to the prevalence and intensity of schistosomiasis infection after MDA; The infection type was restricted to *S. haematobium* and *S. mansoni*; other species like *S. japonicum* were excluded since their burden of infection in Sub-Saharan Africa is not too significant. Only studies published in English language were included. Studies that did not have baseline results on prevalence of intensity of schistosomiasis or out of Africa were excluded. The search keywords and Boolean operators used were; Schistosomiasis OR Bilharzia AND Targeted treatment OR Mass Drug Administration AND Prevalence, Intensity AND African Children OR Primary School. The search algorithm for Google Scholar is shown in Table 1.

Any conflict/discrepancies between reviewers were resolved through meetings between the two reviewers, any articles that were questionable where also reviewed together by the reviewers. Eligible articles based on assessment of titles were exported to bibliography software, Zotero, for storage, management and organization of references. Duplicates were removed and the selected titles were further screened through reading the abstracts and then full texts to finalise the article selection. In addition, references and bibliographies of selected articles were screened for potential leads to other relevant studies for inclusion in the review. The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) flow diagram (Figure 1) illustrates the stages taken in the screening and selection process.

A data charting form was used to guide the extraction of relevant information from each article included in the study, and it had the following four main domains; (i)Study Identification: Country, Author and Journal full reference; (ii) Methodology: study population, study design, sample size, infection type, intervention and duration; (iii) Outcomes: Impact on prevalence or intensity of schistosomiasis infection and treatment/intervention coverage; (iv) Conclusions. Two independent researchers (NC and TM) summarized the data from the selected articles using the Microsoft Excel spreadsheets guided by the data charting tool. The two spreadsheets were merged into one report shown in Table 1.

For quality assessment of chosen articles, a Mixed Method Appraisal Tool (MMAT) was adopted and used to scrutinize the relevance of selected papers, adequacy, methodology, study design, data collection, data analysis, presentation of findings, discussion and conclusions. The MMAT was used because it clarifies the essential aspects of quantitative descriptive studies[12] and randomized control studies which make up this scoping review. The risk of bias for each outcome across individual studies was summarized as a descriptive statement, whether it was low or not.

Results

The systematic literature search yielded 846 articles, including abstracts, books and duplicates. Sixty-five duplicates were removed. Six hundred and eighty-two articles were excluded because the titles and abstracts were not addressing the impact of targeted treatment on schistosomiasis, and some were studies out of Africa. Ninety-nine full text articles were assessed for eligibility, and 72 were excluded because they did not provide baseline prevalence or intensity and some did not address the impact of targeted MDA on the prevalence or intensity of schistosomiasis. Thus, the total number of articles that were accepted for this scoping review were 27.

Quality Assessment of Articles Included

All the studies included had research questions on the impact of mass drug administration on the prevalence and intensity of schistosomiasis in primary school children ranging from 5 years to 15 years. Some articles included other questions such as the impact of treatment on schistosomiasis infection complications such as anemia and immune system development.[15,25] Other studies had research questions on comparison of the effects of different intervention methods ranging from variance frequency of MDA[19,32] to method of administering treatment (school-based against community-based.[31] All the articles selected answered the research question by providing the changes in the prevalence and intensity of schistosomiasis infection post mass drug administration. They all gave data on the baseline prevalence and intensity; and after treatment which allowed us to calculate the percentage change in infection burden post treatment as shown in Table 1. The post-treatment data showed that even after treatment, the infection burden remained high with the prevalence of schistosomiasis way above 50% two years post one round of MDA.[30]

Table 1 Data Collected from Selected Studies

	Author	Country	Study Population	Study Type	Sample Size	Infection Type	Intervention Duration (Years)	Intervention	Change in Prevalence	Change in Mean Intensity	Treatment Coverage	Comments/ Impact
1	Abudho et al[5]	Kenya	Primary and high school	Repeated cross-sectional	1440	*S.mansoni*	1	1 year School based MDA	↓44,7–17%= 62%	↓ Mean intensity 90.1–8 epg Prevalence of high intensity ↓6,8–0,3%	N/A	Huge drop in infection prevalence and intensity
2	Assare et al[3]	Cote' D'Ivoire	Primary schools (9–12 years)	Cluster-randomized trial	4 966	*S.mansoni*	1	1 Year of School based MDA	↓19,7–12,8%=35%	↑ 92,2–109,3 epg	75%	Slight change in prevalence but intensity increased. 1 year not enough
3	Bar et al[13]	Siera Leone	Primary (9–14years)	Cross-sectional	3632	*S.mansoni* *S.haematobium*	6	6 years of school-based MDA	↓42,2–20,4%=52% ↓18,3–2.2%=85%	↓100,5–52,8epg ↓1.12–0,4 e/ 10ml	↓78,5–96,3%	Huge drop in infection prevalence and intensity
4	Bronzan et al[14]	Togo	Primary Children (6–9yrs)	Cross-sectional survey	1 129	*S.haematobium* *S. mansoni*	4	4-year Community-based MDA	↓23,5–5,0%=79% ↓3,6–0,8%=76%	Microhematuria ↓ 21,0–4,2%	94%	Huge drop in infection prevalence and intensity
5	Yomba/yumbe Tanzania	Uganda,	Primary school children (8–9yrs) Primary schools	Cohort study Cross-sectional survey	695	*S.mansoni* *S.haematobium*	2	2years of school-based MDA	↓26–15%=42% Prev:3.1 vs 28	No baseline results	39,5% and 43,6%	moderate drop in infection prevalence
6	Chisango et al[15]	Zimbabwe	Primary schools (7–13years)	Longitudinal study	212	S.haematobium	2	2 years of school-based MDA	↓23,1–0,47%=98%	Mean egg count ↓15,9–2eggs/ 10mls	N/A	Increase in the immune defense system after MDA
7	Hodges et al[16]	Siera Leone	Primary (9–14 years)	Cross-sectional survey	448	S.mansoni	0,5	6 months	↓ 69.0–38,3%=44%	170,8 epg–47.3 epg	N/A	Moderate drop in both infection prevalence and intensity
8	Kabaterein et al[17]	Uganda	Primary schools	Longitudinal study	1871	S.mansoni	2	2 years	↓42,4%–26,8%–17,9%=15–58%	309;4 epg–76,8epg–21.9epg	N/A	Moderate drop in infection prevalence and intensity
9	Karanja et al[18]	Westen Kenya	School children 9–12 years	Cluster randomised trial/ 3 clusters of 25 schools each	4701	S.*mansoni*	2	Arm 1- annual MDA, Arm 2- first two years. Arm 3 MDA biannual.	Arm 1: 17,65–7,12=59% Arm 2: 17,82–10,46=43% Arm 3: 17,57–8,57= 51%	Arm 1–16,08–7,89 Arm 2–14,08–10.41 Arm 3–17,3–7,89	90% in all arms	Moderate drop in infection prevalence and intensity throughout the 3 arms of the study
10	Knopp et al[19]	Zanzibar	School children 9–12	Repeated cross-sectional cluster-randomised trial	9024	S.haematobium	5	5-year biannual MDA Arm 1 – Only Arm 2- snail control. Arm 3- behaviour change	Arm 1: ↓ 4,2–1,45=65.4% Arm 2: 7,8–1,7%= 78% Arm 3: 6,4–1,9%= 70%	Heavy intensity↓ 1,6–0,3	90%	Huge drop in infection prevalence and intensity. There is more impact with added interventions
11	Landoure[20]	Mali	School children from 6 schools in 3 districts (640)	Cross-sectional survey.	640	S.*haematobium* S.*mansoni*	5	5 years of school-based MDA	↓88,0–61,7%=30% ↓17,3–12,7=26%	↓180,4–33egg/ 10ml ↓88,2–43,2epg	93%	Huge drop in infection intensity but a very low decrease in prevalence
12	Lee et al[21]	Sudan	School children	Cross-sectional survey	78 615	S.*haematobium* S.mansoni	1	9months MDA & health education. Clean water provision to half of the sample	↓28,5–13,5=53% ↑0,4–0,9=125%	Not done	60–70%	More impact with the introduction of clean water source

13	Massa et al[22]	Tanzania	School children	Cross-sectional	1140	S.*haematobium* S.*mansoni*		CBT & School based MDA	No baseline	N/A	N/A	ComDT is as effective as SBT
14	Mwandawiro et al[23]	Kenya	School children	Cross-sectional	6174	S.*haematobium* S.*mansoni*	5	SBMDA for 5 years	↓14,8–2,4=84% ↓2,1–1.7=19%	↓16,0–2,0 ↓12_-2,0	N/A	Huge drop in prevalence and intensity for S.heam but a very low drop is S.mansoni burden.
15	Njenga et al[6]	Kenya	School children	Repeated cross-sectional	1022	S.*haematobium*	1	One round of MDA then monthly screen	↓49,4–17,7=64%	↑161,6–167,8	N/A	Moderate drop in infection prevalence but an increase in intensity due to massive re-infections
16	Wiegand et al[24]	Kenya	School based and village wide adults. Arm 1(5–8yrs) Arm 2 (9–12yrs) Arm 3 adults	Repeated cross-sectional	150	S.*mansoni*	5	5 rounds of MDA to the target groups	Arm 1: ↓ (20,34–8,89) =56% Arm 2↓ (59,47–19,0) =68% Arm 3↓ :44,68–12,0 =72%	Arm 1↓ (19,72–6,68) Arm 2↓ (50,40–10,31) Arm3↓ (50,0–7,93)	N/A	Moderate drop in prevalence and intensity but persistent hot spots were identified where there was no significant drop in infection burden
17	Zilahatou et al[25]	Nigeria	School children 8–11 yrs	Cross-sectional survey	1 642	S. haematobium	1	One round of MDA	↓75.4–38,0%=50%	Anemia ↓ 61,6–50,4%	68%	Moderate decrease in infection burden and a partial decrease in anemia due to the treatment of schistosomiasis and STH
18	Toure et al[26]	Burkina Faso	School aged children 6–14yrs	1.Longitudical cohort survey 2.Cross-sectional survey 3. ComBT	1 727	S.haematobium	1	One round of MDA over 2 years	Arm 1: ↓59.6–7.7%=87% Arm 2: ↓25-2 to 3%= 88% Arm 3: ↓41.6 14.2% = 66%	1.↓94.2–6,8eggs/10ml 3.↓63.5–13.7 eggs/10mls	90%	Significant and sustainable reduction of S.haematobium was achieved by biennial treatment in SAC
19	Adewale et al[27]	Nigeria	School children 5 to 18 years	Cross-section survey	434	S.haematobium	1	Single dose of praziquantel	↓ 24.4 to 2,1 at 6months then ↑ to 7,7% at 12 months = 68%	↓9,87 to 1.98 then 1,27 at 12 months	N/A	There was moderate overall decrease in intensity and prevalence after treatment, but there was an increase prevalence from the 6th month to 12 months evidencing re-infections.
20	Chaula and Tarimo[28]	Tanzania	School children 10 to 16 years	Cross-sectional survey	488	S. haematobium	2	1.Two annual rounds of MDA 2.MDA campaigns on knowledge on urinary schistosomiasis, safe water uses and contact with unsafe water bodies	↓26–15%= 42% Prevalence: Low 3,2% in the up taking community and high 28,5% in non-uptake	There was a significant impact on knowledge of disease borderline impact on the safe water use and no impact on conduct on unsafe water	39% uptake first year and 43,6% uptake second year	MDA reduced prevalence, but due to low uptake below the WHA resolution, 54.19 target of 75% the non-participating was the source as snails kept on shedding. More educating needed.

(*Continued*)

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Table 1 (Continued).

	Author	Country	Study Population	Study Type	Sample Size	Infection Type	Intervention Duration (Years)	Intervention	Change in Prevalence	Change in Mean Intensity	Treatment Coverage	Comments/ Impact
21	Lelo et al[29]	Kenya	School children	Longitudinal study	67	S.mansoni	4	4 annual MDA and screening	↓ 97–68% = 30%	No change in intensity		Low decrease in prevalence and reduction in intensity and infection transmission
22	Masaku et al[30]	Kenya	School Children	Cross-sectional study	387	S.mansoni	1	One round of MDA and 2 years follow-up.	53.7% after 2 years	n/a	n/a	There was persistent high prevalence after 2 years post MDA
23	Olsen et al[8]	Tanzania	School children	Cross-sectional study	14 620	S.mansoni	4	6 arms were created and given variable modes of regiments	↓60.6–49, 3% = 49%	151,0–40,8epg	N/A	Moderate drop in prevalence and intensity and no difference between arms
24	Onkanga et al[31]	Kenya	Community and Schoolchildren 9 to 12 years	Cross-sectional study	150 villages and the schools in the district	S.mansoni	3	Community-wide treatment to 3 arms and SBT to other three arms	Decreased in both arms	Decreased in both arms but more in SBT	62.4% in CWT and 84.6% in SBT	SBT has better coverage and has more impact on infection intensity but similar effect on prevalence as CWT
25	Phillips et al[32]	Mozambique	Schoolchildren 9 to 12 years	Cluster- randomised trial	81 167	S.haematobium	4	6 arms were created with varying frequency of deworming and using either SBT or CWT	↓60.5% to 38,8% across the groups. =36%	Heavy infection ↓ 17.6–11.9%		Higher prevalence in arm which had 2year MDA break and greater infection reduction in arms which had no breaks.
26	Sesay et al	Sierra Leon	School children 10–14 years	Cross-sectional survey	1300	S. mansoni	3	3 years of MDA	↓49.7–16,3%= 67%	↓134.53–18.98epg	81,6%	Significant drop in prevalence and intensity
27	Shumbej et al[33]	Ethiopia	597 school children 5–15 yrs	Repeated prospective cross-sectional study	597	S. mansoni	1	Biannual MDA	↓12.9–1.2%= 13%	↓25,9–4,5% of heavy intensity	N/A	Very low reduction in infection prevalence and intensity
28	Abudho et al[34]	Kenya	School children 6–18 yrs	Cross-sectional	295	S. mansoni	4	4 years of Annual MDA	↓100–18,8% = 81,8%		90%	
29	Ouattara et al[35]	Cote d'Ivoire	School children 13–14 yrs	Cluster randomized trial	6092	S. haematobium	5	4 arms of MDA, 4 Annual, 1 Biannual (5yrs)	Arm 1 24,8–7,5% = 17,3% Arm 2 10,1–3,5% = 6,6% Arm 3 13,9–0,6% = 13,3% Arm 4 15,9–3,4% = 12,5%		79,4%	
30	Ouattara et al[36]	Cote d'Ivoire	School children 13–14 yrs	Cluster randomized trial	7410	S. mansoni		3 arms MDA	Arm 1 17,4–10,1% = 7,3% Arm 2 20,2–18,2% = 1,8% Arm 3 25,2–17,5% = 7,7%	Arm 1 12,4–7,9% Arm 2 17,4–11,5% Arm 3 20,1–15,4%	Arm 1 64,2% Arm 2 64,4% Arm 3 47,9%	

31	Trippler[37]	Zanzibar	School children 9–12	Cluster randomized trial	20000	S. haematobium	5	Biannual MDA (5yrs)	6,6–1,2% = 5,4%	1,8–0,3%		
32	Gebreyesus[38]	Southern Ethiopia	School children 10–12	Cros sectional study	3162	S. mansoni	5	Annual MDA (5yrs)				
33	Philips[39]	Niger	School children 9–12	Cluster randomized trial	108231	S. haematobium	5	Annual and Biannual MDA (5yrs)	15,8–9,58% = 6,22%	3,05–1,45%	75–100%	
34	Mduluza[40]	Zimbabwe	School children 8–15	longitudinal study	15818	S. haematobium	6	6 annual rounds of MDA (6yrs)	31,7–0% = 100%	28.75 eggs/10ml - 0	90,3%	
						S. mansoni			4,7–0% = 100%	0.28 eggs/25mg - 0	90,3%	
35	Okoyo[41]	Kenya	School children 1–20	Cross sectional	9801	S.mansoni	6	5 annual rounds of MDA (6yrs)	2,4–2,2 = 0,2%	20-0		
						S. haematobium			18,0–0,3 = 17,7%	14–12		

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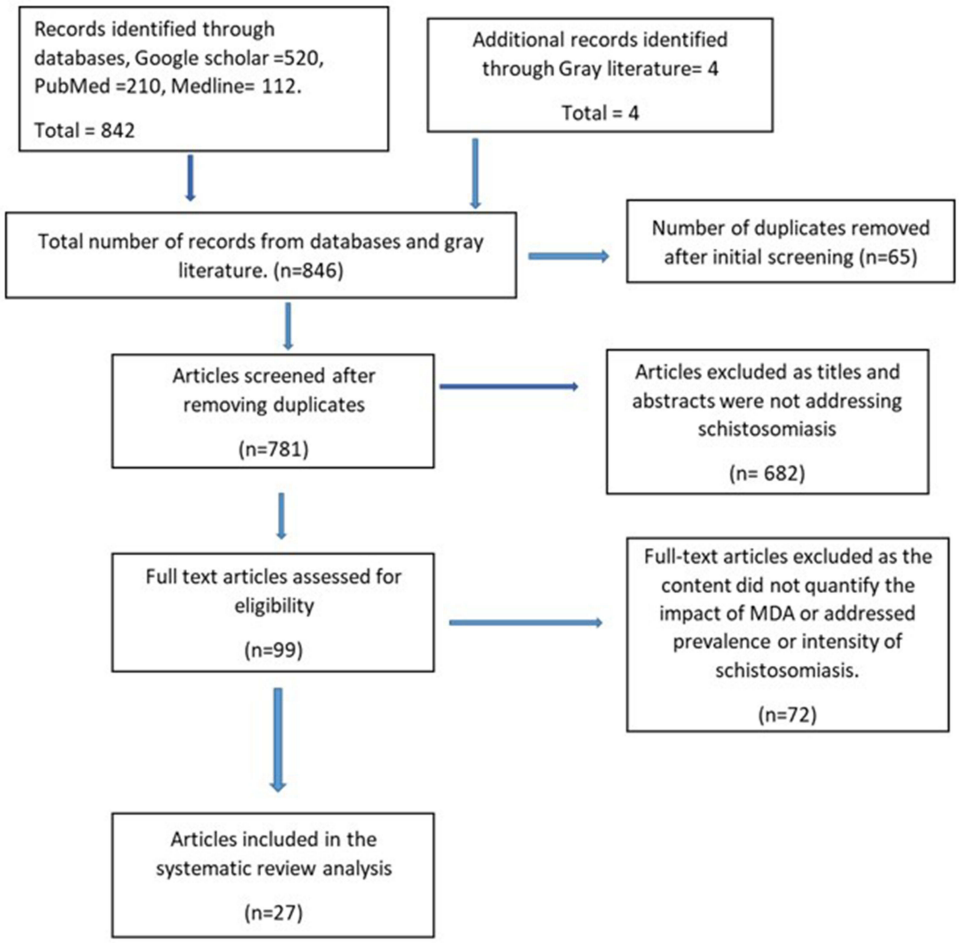

Figure 1 Prisma flow diagram.

All articles used a random sampling method that was suitable for answering the research and they all included the school children. However, some articles had additional secondary school children and adults in high schistosomiasis endemic areas.[21,24] All the studies took appropriate measurements and statistical methods to calculate prevalence and intensity before and after interventions. Chi-square tests were appropriately used to compare groups in randomised cluster studies. In the randomised cluster trials, the assessors and the participants in all the reviews were not blinded. All the study groups adhered to the intervention method they offered. Refer to Supplementary files 1 and 2 to see the quality assessment scores for all the articles included in the review. Each table in the quality assessment files provides a list of questions which the researcher used to assess the quality of the paper. During the assessment, we allocated 1 if the answer was yes and 0 if the answer was no. The questions were 7 in total, hence if the paper had a total score of 6–7 we rated it as good, if the paper scored below 4 it was rated as bad and if between 4 and 5 it was average.

Study Population

Out of 35 articles reviewed 13 had participants aged nine years to 12 years, and three articles had younger participants under 5 years old. The rest of the studies had an age range from 6 years to 19 years. Most of the participants were primary school children from grade 3 to 7.

Intervention

Methods Used to Disseminate Treatment

Various treatment modes for control of schistosomiasis morbidity were used. These methods included community delivered treatment and School Based Treatment coupled with health education.[19,21] With the help of the teaching

staff, MDA was mainly done in schools and seventy five percent (75%) of the studies had school-based treatment compared to community-based treatment. In all the reviewed studies, praziquantel was offered for treating schistosomiasis. To enrol children into school-based treatment or MDA, extensive publicity efforts were used through provincial administrators, church leaders, parents and community members.[7,42] Directly observed treatment was the method offered to all participants by trained staff members of the MDA programs.[5] In community delivered treatment, community health care workers were involved in distributing and administering the drugs.[31] Both community-based treatment and school-based mass drug administration were common. School based treatment is the most used method in the preventative chemotherapy as morestudies[20] from the 27 used it to access their target population.

Five articles used MDA in combination with health education,[19,21–23,28] and one study included snail control,[19] another study reported on the provision of clean source of water in addition to the MDA.[21] The rest of the studies only offered preventive chemotherapy without any other interventions.[15]

Duration of Intervention

The intervention period varied in most of the articles, ranging from 1 round of MDA in one year to 6 rounds over six years.[13,27,43] Three studies used the annual intervention strategy.[3,5,6] In such cases a once-off intervention in a year and screening was done. Other studies ran biannual MDA while other studies only did once off treatment[18,19,33] and followed up participants over a variable time ranging from 6 months to 2 years (Table 1).

Outcomes

Treatment Coverage

In 14 of the studies reviewed, treatment coverage was way above 75%, which is the recommended target for MDA according to World Health Assembly 2001[2,3,14,18–20,26,31] and six studies did not meet the expected target.[21,28,31,44,45] The remaining 13 articles did not provide data on the percentage coverage. Treatment coverage gave a measure of how the general population accepted the interventional programs and also displayed the extent to which the intervention providers had gone to educate the general population about schistosomiasis infection. The measure of treatment coverage also provided some key information as it showed a positive relationship with a positive impact on the reduction in schistosomiasis infection prevalence and intensity. In studies where there was high treatment coverage of above 90% there was an 80% drop in the schistosomiasis infection prevalence and intensity.[13,14,26] The study done in Yombe Uganda, an area where treatment coverage was below 43% showed minimal to no significant change in the prevalence and intensity of the schistosomiasis. There were many cases of reinfection in areas where treatment uptake was low. This was due to religious beliefs, low socio-economic status, low education levels, and other factors.[28] We also observed a slight difference in the uptake and effectiveness of school-based interventions and community-based interventions. The studies done by Onkanga and Toure[26,31] that measured the difference between Community based treatment (CBT) and school based treatment (SBT) observed that the overall effects on prevalence and intensity were similar but school-based treatment had a slightly higher coverage as it was easier to access the target population.[22]

Impact of Targeted Treatment on the Prevalence of Schistosomiasis

Several studies displayed a wide range of effects on schistosomiasis' burden in different communities. The results varied depending on the various modalities used to deliver the mass drug administration. In all the 35 studies, there was a significant reduction in schistosomiasis prevalence after the initial rollout of the MDA program (Figure 2). The most significant decrease in prevalence was observed in 4 studies (3; 6; 14 and 18) where the change in prevalence was greater than 80%.[13,15,23,26] Some of the studies also showed a high uptake by the community with an MDA coverage above 90% (15).[26] The least change in prevalence was observed in 5 studies (14; 27; 2; 11; 25) which had a percentage change less than 40%.[3,20,23,32,33] The studies reported that the low prevalence shift was associated with a low uptake of the MDA program, which was evident from the low treatment coverage ranging from 43% to 60%. Ten of the reviewed studies (3; 5; 7; 8; 9; 12; 16;17; 20; 22) observed a decrease in prevalence of between 40% and 60%,[13,16–18,21,24,28,30] and the remaining eight were between 60–80% (1;5;,6;,10;,18;,23;,29;,37).

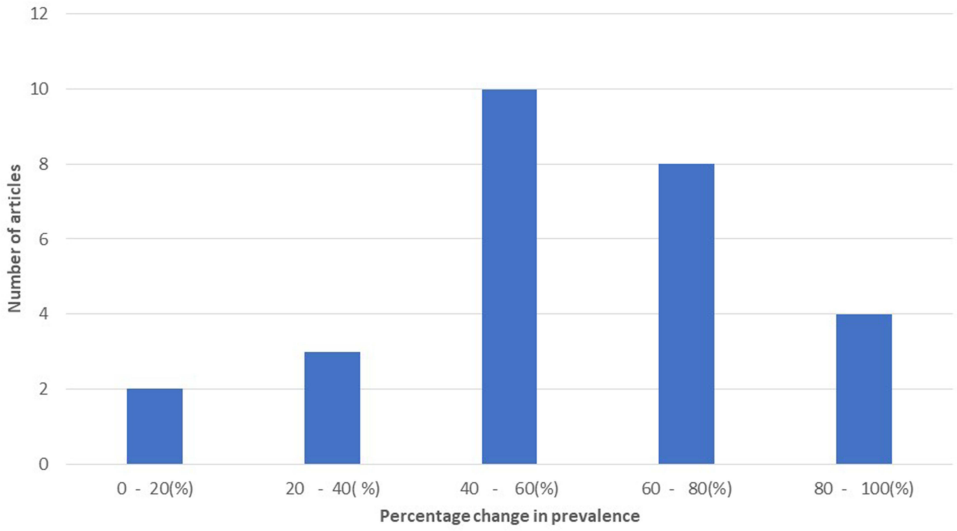

Figure 2 Impact of targeted treatment on the prevalence of schistosomiasis.

The frequency of treatment also played a significant role in determining the magnitude of prevalence change. In studies with a low change, the treatment was offered once only or once a year over five years. The studies conducted in Kenya[18], Sudan[21] and Tanzania[28] showed a moderate decrease of around 40 to 60%. That could have been due to a low baseline prevalence and the community's poor treatment uptake as was the case for Uganda[17] and Sudan.[21] The slight decrease in prevalence could also have been due to the absence of additional interventional strategies such as provision of a clean source of water to the public as was the case in the Sudanese study[21] or provision of health education to the participants and communities. Prevalence of Schistosomiasis continued to decrease at a steady rate in communities that received annual MDA like Mali,[20] Kenya[24] and Zanzibar.[19] In studies that skipped some years or had only one round of MDA as witnessed in the research done in Kenya Mwatunga district, high cases of reinfections and continued transmission were evident.[23] Some studies demonstrated that, if MDA frequency is less than twice a year in high endemic areas, there would not be any significant drop in Schistosomiasis infection prevalence. These areas were reported as persistent hot spots. Such persistent hot spots were observed in villages around Lake Victoria, Kenya.[24]

Schistosomiasis Intensity

Schistosomiasis infection intensity after mass treatment with praziquantel varied across the studies. Some studies[17,21,23] showed a decrease, others[3,6] an increase and in one article there was no significant change.[29] More than 70% of the reviewed articles showed decrease in schistosomiasis infection intensity after the MDA. Reduction in infection intensity was demonstrated by a reduction in the number of eggs in urine and stool and reduction in hematuria in a study by Bronzan in Togo[14] and anaemia in the research done by Zilahatou in Nigeria.[44] The shift in infection intensity was significantly associated with the frequency of mass drug administration. Studies which had more than two rounds of MDA showed a significant drop in infection intensity such as the massive drop of mean egg count of 134.53 to 18.98 eggs per gram of stool.[46] The two studies[3,6] which reported an increase in infection intensity post-MDA had only done one round of treatment and where coupled with massive re-infections and increased intensity,[3,6] proving that more rounds of MDA are needed to control the disease. The annual MDA was not enough to reduce the prevalence and intensity of two studies.[3] Only one study showed no change in infection intensity[29] and four others[8,21,22,30] did not give sufficient data on it to determine the overall change in intensity.

Discussion

After reviewing the 35 articles on the impact of targeted treatment on the prevalence and intensity of schistosomiasis in school-aged children, various outcomes were noted. The change in infection burden varied from one study to another and the most determining factors were firstly, the frequency of chemotherapy, secondly, additional interventions to

complement the chemotherapy, eg snail control, provision of safe water and sanitation or education on the disease. The third determining factor was uptake of the MDA by the community or school, and lastly, the mode of treatment delivery which was either school-based or community based.[22]

Assare and Njenga who did one round of MDA, concluded that one round of MDA to primary school children was insufficient to control the disease[3,6] as that approach only reduced the burden of active infection in individuals but the overall infection intensity remained high due to high reinfection rates.[6] Adewale's study[27] in Nigeria showed an initial decrease in prevalence from 24.2% to 2.1% six months post-treatment and then a rise to 7.7% 12 months post-treatment.[27] Other studies which had just one round of MDA showed a similar trend. These are the studies that made up the group with the lowest change in prevalence post-treatment. Communities that received multiple rounds of chemotherapy showed a significant reduction in both schistosomiasis infection prevalence and intensity. Multiple rounds of mass drug administration proved to be an effective method seen in Phillips's random cluster studies in Mozambique.[32] These studies showed that more rounds of MDA were more effective in controlling the diseases than those that had some breaks in-between the 5-year program.[24] The importance of doing more rounds of chemotherapy was further elaborated by a study done by Wiegand in Kenya.[24] The study showed that in areas of a high prevalence of schistosomiasis, one round of MDA was insufficient to reduce the infection prevalence and intensity. Post-treatment data showed an insignificant drop in the two. The author concluded that at list two rounds were needed per year to reduce the infection burden.[24,29] Assare also proved one round of MDA was not sufficient to control schistosomiasis in Cote D'Ivoire study, which showed a slight decrease in prevalence after one round of MDA but an increased intensity one year post-treatment.[3]

Targeted treatment on its own without other complementary interventions such as snail control, provision of safe water and proper sanitation and education on schistosomiasis prevention has failed to eliminate the disease.[14,21,27] A randomised cluster study by Knopp in Zanzibar which compared groups with addition of snail control and education on schistosomiasis prevention confirmed the importance of complementary interventions. The group that received snail control and education on schistosomiasis prevention in addition to MDA had a more significant decrease in the infection prevalence and intensity.[19] Moreover, a study in Sudan, where education on schistosomiasis was given to both groups in addition to MDA showed similar results. The results showed a remarkable decrease in infection burden in the group which had an additional supply of clean water source and better sanitation.[21] Although there were other interventions offered, there was no elimination of the disease.[21]

Failure to eliminate schistosomiasis after rounds of mass treatment signifies that reinfection rates are high[6] as seen in the Kenyan study.[6] Masaku[30] showed an infection prevalence of 57%[30] after two years following one round of MDA. This suggests that more interventions and strict control of both the vectors and humans are necessary for a better outcome.[30] Of the studies reviewed 75% had an MDA coverage above the 75% recommended by the World Health Assembly.[2] In areas where treatment uptake was below 75%, the decrease in infection prevalence and intensity was below as seen in the Chaula, and Tarimo study in Tanzania where MDA uptake was as low as 36% in one group and 43% in another group.[28] Infection prevalence, post mass treatment was low (3.2%) in the higher MDA up-taking community and (28,5%) in the low treatment-uptake group.[28] The MDA offered to the two communities in Chaula study,[29] reduced prevalence, but there were reinfections due to low treatment uptake. The non-participating community members were the sources of infection as snails in rivers kept on shedding. The persistence of reinfections showed the need for educating the community on the schistosomiasis infection prevention. The overall percentage drop in prevalence was 42%, which was far too low compared to other studies such as Toure in Tanzania, which had a high percentage change in infection prevalence of over 88% and MDA coverage over 90%.[26] Prevalence and reinfection rates reduced in areas where there was water provision, and there was also improvement in the livelihoods of the people. Health education increases knowledge about transmission and encourages people to exercise caution and avoid risky behaviour, as evidenced by a study conducted in Sudan by Lee.[14]

Over 90% of the reviewed articles used the school-based mode of treatment and fewer studies used both SBT and CBT involving village health workers.[22,32] From Massa's[22] comparisons, no significant difference between the models in terms of reducing the infection prevalence and intensity was noted. It was easier to implement the SBT than the CBT because of easier access of the target population through the SBT. The CBT was more effective where the target

population was the whole community, including adults at risk.[22,32] The treatment coverage was slightly higher with SBT than the CBT. The use of both models was more effective than using one as they complement each other.[22]

We found that the impact of targeted treatment on the prevalence and intensity of schistosomiasis depends on several factors that include the frequency at which it is offered, complementary interventions, and its uptake by the target population.[24] In most cases, we have noted that targeted treatment reduces the prevalence and intensity of active infections with moderate to high percentages but, the once a year program does not do enough to bring significant control of the disease in endemic areas. In areas of high endemicity or persistent hot spots, targeted treatment has minimal effect on the infection prevalence and intensity; and more robust methods are needed to reduce the reinfection rates.[19] Additional interventions such as snail control,[19] provision of clean water and sanitation, and educating the primary school children are essential to mitigate high reinfection rates and eliminate schistosomiasis.[21] Other complementary methods for schistosomiasis elimination include the ongoing trials for human schistosomiasis vaccines. The vaccines hold a promise that elimination is possible given the effectiveness of vaccines for other diseases which have proven to be effective in bringing infections to elimination stage. The four vaccines which are currently undergoing trial (Sm-TSP-2, Sm14, rSh28GST, and Sm-p80)[10] can be better alternatives to MDA which is often riddled with drug resistance cases and the more common challenge of PZQ being ineffective against juvenile worms. Another recommendation is that targeted treatment should be timed according to the weather and transmission cycle of schistosomiasis within an area. It is common that transmission begins during the hot season when learners swim. Also in some areas infection usually begins after the rains, when water bodies have settled and snail colonies have grown. Aligning MDA programs to these seasons helps to prevent chances of reinfection.[9]

Limitations

The limitations that we faced in this study included failure to access certain articles during the article search. Some articles that had been selected for review needed to be purchased in order to be accessed. Institutional access was not available with a majority of the papers, reviewers were also working from home during the pandemic which meant that access to the University librarian was limited.

Conclusion

This study is relevant to the readers who want to determine the impact of MDAs on the control of schistosomiasis. It shows the impact that MDA targeted treatment can significantly control infection burden, but it cannot eliminate the diseases. To reach the sustainable schistosomiasis control, there should be ongoing MDA programs in endemic areas. There should be a constant MDA program coupled with massive preventative and health promotional programs targeted at fighting the transmission of schistosomiasis to get to the elimination stage. The current WHO guidelines on control and elimination of schistosomiasis should invest more in prevention than treatment as high rates of re-infections post treatment evidence it. The scoping review also supports the WHO recommendation which states that, treatment uptake should be greater than 75% in a community for it to significantly reduce infection burden. Schistosomiasis elimination relies heavily on the improvement of socioeconomic conditions of people affected. It is not enough to just provide medicine, we need to address other major areas of human life that lead to the transmission cycle. Issues such as poverty and lack of infrastructural improvement are needed, governments need to invest more on improving the care to children and the environment. Other aspects of the child's life like nutrition also need to be improved. Control of schistosomiasis has relied on PZQ administration, however this may not be sustainable, other methods of schistosomiasis control need to be developed further. There is need for more studies which are investigating other prophylactic supplements such as arachidonic acid, curcumin, and garlic. Another development that needs to be implemented is the use of safe and effective vaccines, these may help to get out of the danger of continuous PZQ administration.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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