RESEARCH ARTICLE

Deworming program for women of reproductive age implemented through national iron folate supplementation program reduces prevalence of anemia: evidence from a community trial in rural Bangladesh [version 1; peer review: 3 approved with reservations, 1 not approved]

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Abstract

Background: Anemia causes debilitating outcomes for women and children, and can be of multifactorial etiology, soil transmitted helminth (STH) infection being one of them. The Bangladeshi government does not have any regular deworming program for women of reproductive age (WRAs), who constitute an important portion of the population. Hence, we conducted this study to generate evidence on the effect of regular deworming on STH infection status and anemia status of WRAs in rural Bangladesh.

Methods: This was a quasi-experimental study conducted in rural Bangladesh using existing healthcare delivery platform (Community Clinics) for mass deworming of WRAs. Catchment areas of two community clinics constituted the intervention arm, where the WRAs received two cycles of deworming four months apart on top of government recommended iron-folate supplementation (IFA), and catchment areas of two different community clinics were considered as the control arm where the study population received IFA but no deworming medication. Baseline and endline surveys were conducted on randomly selected participants to measure prevalence of anemia and STH infection using HemoCue 201+ and Kato-Katz respectively.

Results: The study area contained 4791 women aged 15-49 years. Among them, 2441 lived in the intervention area and 2350 lived in the control area. Compliance to deworming medication and IFA was 82% (2001 out of 2441) and 79% (1938 out of 2441) for the two cycles, respectively. In the baseline survey there was no significant difference

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Any reports and responses or comments on the

in prevalence of anemia between the intervention and control arms (63.7% vs 65.7%; p=0.522). However, the endline survey yielded significant difference in anemia prevalence between the arms (47.5% vs 65.7%, p<0.001) rendering a 14% reduction in anemia due the intervention (p=0.004). Similarly, our intervention was shown to reduce STH infection by 16% (p<0.001)

Conclusions: Our study clearly showed that regular deworming of WRA benefits their anemia and STH infection status.

Keywords

Antihelmintics, helminths, anemia, women of reproductive age, iron folate supplementation, deworming, Community clinic, quasi-experimental design, Bangladesh

article can be found at the end of the article.

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Introduction

Anemia, defined as a hemoglobin concentration below average for the age and sex of the individual is one of the major public health problems in the world. Globally, 1.74 billion are suffering from anemia[1] and its consequences which include, decrease in cognitive and motor development[2–5], loss of economic productivity[6,7] and increased risk of low birth weight, still birth, pre term delivery and prolonged labor for pregnant women[8–10]. Children and women of reproductive age (WRA, 15–49 years) are most vulnerable to the consequences of anemia evident from the reported prevalence of 47.4% and 30% for children under 5 and WRAs respectively. Additionally, 42% pregnant women are suffering from anemia. Most of this anemia burden is from low and middle income countries (LMICs) in Africa and Asia[11]. In Bangladesh, the demographic and health survey 2011 reported that, 51% of 6–59 months old children and 42% of women aged 15–49 years are anemic[12]. The government of Bangladesh (GoB) has identified these age groups as high-risk groups and committed to take necessary steps to reduce the burden of anemia among them.

Anemia can be caused by different factors such as deficiency of nutrients including iron, folic acid, vitamin B 12 and vitamin A as well as different types of infections such as soil transmitted helminths, schistosomiasis and malaria[13]. Chronic infections like soil transmitted helminth (STH) infection are an important cause of anemia in tropical and sub-tropical countries, where ecological conditions of these regions allow larval development and poverty, poor water, sanitation and infrastructure to exacerbate this condition by facilitating the spread of the infection. Globally, species of intestinal nematodes that are most important for anemia are Round worm (*Ascarislumbricoides*), Whip worm (*Trichuris trichiuria*) and Hook worm (*Ankylostoma duodenale* and *Necator americanus*). These parasites infect humans through contact with parasite eggs or larvae, grow as adult worms and then, can live for years in the human gastrointestinal tract causing chronic infections. Hookworm, which can cause chronic blood loss are the major helminth species responsible for causing anemia. All the helminths cause injury to the mucosa of the small intestine, causing malabsorption and gastrointestinal losses of nutrients such as iron and folic acid resulting in anemia[14].

STHs, though causing anemia, can have serious impacts on health such as, impairment of growth and physical fitness. STH burden also have adverse effects on the future economy and productivity of a country. Studies show that, STH infection causes a reduction in income which can be reversed by deworming[15,16].

The government of Bangladesh (GoB) has taken steps to reduce the burden of helminth infection through the conduction of school-based deworming campaigns twice a year among school children aged 5–12 years since 2007. In this mass drug administration (MDA) campaign, a single dose of Albendazole 400mg tablet is administered to every primary school child irrespective of their infection status. This campaign has seen remarkable success considering the prevalence of decreasing from 80% to 16%[17]. However, there is no such campaign for women of reproductive age, who constitute a larger portion of the population and are also more at risk of anemia due to physiological reasons. Due to lack of any nation-wide data on the prevalence of STH infection, the high prevalence of anemia among WRAs in this country indicates that STH infection is also high among this age group.

In absence of any mass deworming program for the WRAs, we conducted a community trial to see the effect of regular deworming on WRAs conducted through an existing government health care delivery system in the rural setting of Bangladesh. We hypothesized that, regular deworming of WRAs would result in reduction of prevalence of anemia among them.

Methods

Study design, location and population

This was a quasi-experimental study, consisting of two arms: intervention and control. The study was conducted in rural area of Trishal upazila (sub-district) of Mymensingh district from December 2015 to July 2016. Trishal consists of 12 unions (smallest administrative unit of GoB) and has a population over 419,000 according to National Census data from 2011. The upazila has an area of 338.73 sq km. The community clinic (CC) setup was used to conduct our study. There were 39 fully functional community clinics during our project duration in the upazila to provide health services for the rural population.

The community clinic, which is the setup for our study, is the first-level one-strop service centre for primary health care and ideally there is one community clinic for about every 6000–8000 rural population. Community clinics, through the community health care providers (CHCPs) provide services on maternal and neonatal health care services, Integrated Management of Childhood Illness, reproductive health and family planning services; expanded program on immunization. They also distribute micronutrient supplementation among the risk groups and provide nutritional education, health education and counseling. These centers also provide treatment of minor ailments, common diseases, first aid and act as an effective referral linkage with higher facilities. We planned to integrate our deworming program with the existing community-based program of nutritional education and micronutrient supplementation (IFA supplementation of the WRAs).

We selected two CCs purposively out of 39 CCs and assigned WRAs living in the catchment area as our study population for the intervention arm. CCs were selected based on their previous performance, i.e., high performing CCs were given priority to ensure a better outcome of the project. The catchment area of those CCs was our intervention arm and of the remaining 37 CCs, those adjacent to the intervention arm were excluded from the sampling frame to prevent diffusion effect. Two CCs were selected as the control arm from the rest of

the CCs which also had a good performance record. Pregnant women were excluded from our deworming program.

Intervention

Our intervention package consisted of regular deworming of 2 rounds, 4 months apart for 8 months. The first round lasted from December 2015 to March 2016 and the second round lasted from April 2016 to July 2016 During this period, all WRAs except the pregnant women living in the catchment area of the CCs in the intervention arm were invited to receive deworming medication at an interval of four months. CC setup was used for this purpose. All WRAs visiting the CCs for any reason were provided with deworming medication by CHCPs, along with IFA tablets which are part of regular GoB program. Our trained field staff kept vigilance on compliance of community as well as CHCPs on project activities. Pregnant women visiting the clinic were not provided with deworming medication. To ensure this, a pregnancy register maintained by the government health care providers were followed. Also, thorough menstrual history was obtained from the WRAs to determine whether they could be pregnant before providing the deworming medication. Pregnant women were provided with IFA supplementation as per the government program.

After ensuring a WRA was not pregnant, a 400mg Albendazole tablet was administered on spot. Another two tablets were provided to them and our field staff asked them to take one tablet each day for the next two days. These additional tablets were given to eliminate Trichuris infection as per CDC guidelines[18]. At the same time the WRAs were advised to regularly consume IFA tablets provided as per GoB guidelines. WRAs were asked to come after four months to take the next round of deworming medication.

WRAs suffering from any severe disease that required referral were not provided with deworming medication. Rather they were asked to come back when they are cured from the disease and have their deworming drug. Women with minor illness like a fever, sore throat, cough, or diarrhea were provided with deworming medication as usual.

Evaluation of the project

This quasi-experimental design where change due to intervention was assessed through baseline and endline surveys on the sample population. The baseline survey started in June 2015, while the endline survey started in July 2016. The results were obtained through difference in difference calculation method of the intervention and control arms. The crude formula is:

The percent reduction (PR) of outcome of interest (anemia/STH infection) attributed by intervention was calculated as:

$$PR = (EI/A)*100$$

Where, EI (effect of intervention) = (B –A) – (D-C); and A=baseline value (# of women with anemia/STH) for the intervention group; B=post-intervention value for the intervention group; C=baseline value for the control group; D=post-intervention value for the control group. Effect is negative /positive if no. of anemia/STH or mean ova of STH is decreased /increased after intervention and effect should be zero if no. of anemia/STH or mean ova of STH are same as baseline.

Sample size calculation and Sampling

We calculated our study sample size based on the assumption, that our intervention would be able to reduce the prevalence of anemia by 35% from the baseline, which was 42% among the WRAs[13]. Considering a cluster of 200 and inter-cluster correlation coefficient (ICC) of 0.01, power of the study 80% a level of significance 5%, we calculated a total of 4 clusters would be required (2 in intervention and 2 in control). Considering a 15% attrition, the calculated sample size was 920 (460 in intervention and 460 in control arm). Before both the baseline and endline surveys were conducted, a household listing was done by enumeration of all the households in the study area to identify the number of WRAs in the region. In this process, our research workers went to every household and listed all the permanent members of the household. All the WRAs were assigned a unique participant ID. Then 460 WRAs from each arm (intervention and control) were randomly selected who comprised the sample for the surveys.

The selected WRAs were interviewed regarding their socio demographic condition, water, sanitation and hygiene practices and perception regarding helminth, and anemia. During the endline survey, additional data on different factors of compliance to the MDA deworming program was collected from WRAs in the intervention arm.

Additionally, stool samples were collected from the same WRAs which were tested for ova of common helminths (*A. lumbricoides, T. trichiura, A. duodenale,* and *N. americanus*) in Kato Katz method[19]. Moreover, the prevalence of anemia was determined by measuring hemoglobin concentration of the selected WRAs using HemoCue 201+ machine. Following strict aseptic precaution and explanation of the procedure to the WRA, a sterile lancet was used to make a needle prick. Blood drop was drawn into a HemoCue 201+ cuvette which was then placed in the HemoCue 201+ machine for detection of hemoglobin percentage.

To determine the direct effect of deworming on WRAs, during the selection of participants for endline survey, we intentionally selected half (115 from each CC catchment area) of the participants from those of the baseline survey.

Samples and testing

The stool samples were collected as the first stool in the morning. The WRAs were provided with a stool container labeled with their participant ID on the previous night. The field staff collected stool samples from the WRAs the next morning and stored them in a freezer overnight. The samples were transported to Parasitology laboratory of icddr,b where an expert dedicated laboratory worker counted the ova of

common helminths in the stool samples using the Kato Katz method. For this a small amount of fecal material was placed on newspaper or scrap paper and a piece of nylon screen was pressed on top so that some of the feces sieved through the screen and accumulated on top. A flat-sided spatula was scraped across the upper surface of the screen to collect the sieved feces. A template was placed on the slide and the sieved feces were added with the spatula so that the hole in the template was completely filled. The spatula was passed over the filled template to remove excess feces from the edge of the hole. The template was removed carefully so that a cylinder of feces was left on the slide. The fecal material was covered with a pre-soaked cellophane strip. The slide was inverted, and the fecal sample was pressed firmly against the hydrophilic cellophane strip to spread evenly. The slide was placed on the bench with cellophane upwards to enable the evaporation of water while glycerol cleared the feces. For all helminthes, except hookworm eggs, the slide was kept for one or more hours at room temperature to clear the fecal material, prior to microscopic examination.[19]. The results were reported as presence/absence of infection with different species of STH and severity of infection as per the World Health Organization (WHO) guidelines in case infection with a specific STH was present.

Statistical analysis

All data were entered into the computer after being carefully cross-checked and we used double data entry method to minimize error. Statistical analyses were done using STATA (Version 13.1; StataCorp, College Station, Texas, USA). Statistical significance was defined as $p< 0.05$. The distributions of data were checked for normality by using histogram, QQ plot and kurtosis and skewness. We compared baseline characteristics between two arms using Student's t tests, Pearson chi-square tests and Mann–Whitney U test wherever applicable. Both parametric and nonparametric approaches were used for analyses and reported as medians and interquartile ranges or mean and standard division. The effect of intervention was measured using difference in difference method as described above.

Ethics

The research protocol was approved by the Research Review Committee and the Ethical Review Committee of International Centre for Diarrhoeal Disease Research, Bangladesh (protocol number: PR-14-125). Complying with the deworming campaign was a voluntary process and hence consent was implied by WRA's attendance at CCs and voluntarily taking the deworming drug. However, during the baseline and endline surveys, our research workers obtained voluntary informed consent from the survey participants before commencing to data and sample collection. Consent was obtained from participants aged between 15 and 17 years along with consent from their legal guardians.

Results

The study area contained 4789 women aged 15–49 years. Among them, 2438 lived in the intervention arm and the rest (2351) lived in the control arm. Four hundred and fifty-nine WRAs in the intervention arm and 460 WRAs in the control arm comprised the sample for the baseline survey. After two rounds of deworming an end line survey was conducted where 412 and 411 WRAs were enrolled from intervention and control arms respectively (Figure 1). Mean (±SD) age of the participants was 28.93±9.04 and 30.94±9.68 for baseline and end line survey respectively. Socio demographic characteristics of the survey participants are provided in Table 1. The full dataset can be found under *Underlying data*[20].

Our intervention period lasted from December 2015 to July 2016, during which we conducted two rounds of deworming four months apart. During the first round, that lasted from December 2015 to March 2016, 82% (2001 out of 2441) women of reproductive age in the intervention arm voluntary attended the community clinics for the deworming drug. During the second round which lasted from April 2016 to July 2016, the compliance rate slightly reduced to 79% (1938 out of 2441).

For hemoglobin concentration, we were able to collect 459 and 460 capillary blood samples during the baseline survey. One participant enrolled in the baseline survey refused to provide capillary blood sample. The prevalence of anemia was 63.6% and 65.7% in the intervention and control arm respectively during the baseline survey. The mean hemoglobin level was 11.5±1.23 and 11.5±1.26 in the control and intervention arm respectively without any statistically significant difference. After two rounds of the deworming program the mean hemoglobin had significantly increased in the intervention arm (11.9±1.26) compared to the control arm (11.5±1.09). During the endline survey, we were able to collect 820 capillary blood samples from 823 enrolled participants, and 3 participants refused to provide blood samples. Prevalence of anemia during the endline survey was also significantly different between the intervention (47.6%) and control arm (63.7%). However, no significant difference in BMI was seen between the intervention and control arm, as a result of the intervention. Details are provided in Table 2.

For measuring the burden of STH infection, we were able to collect 918 stool samples during the baseline survey (out of 919 enrolled participant) and 822 stool samples (from 823 enrolled participants). The species of STH with highest prevalence was *Ascaris lumbricoides* with the baseline prevalence of 17.9% and 24.1% in the intervention and control arm respectively. After the intervention, the prevalence of A. lumbricoides as well as other species reduced significantly (Figure 2). The intensity of the infection which is expressed as mean eggs per gram also decreased in the intervention arm compared to the control arm (Table 3).

The crude difference in differences (DID) calculation was carried out to observe the effect of the intervention package on reduction of anemia and STH infection prevalence at both community and individual level. Table 4 and Table 5 show the level of protection against anemia and STH conferred by

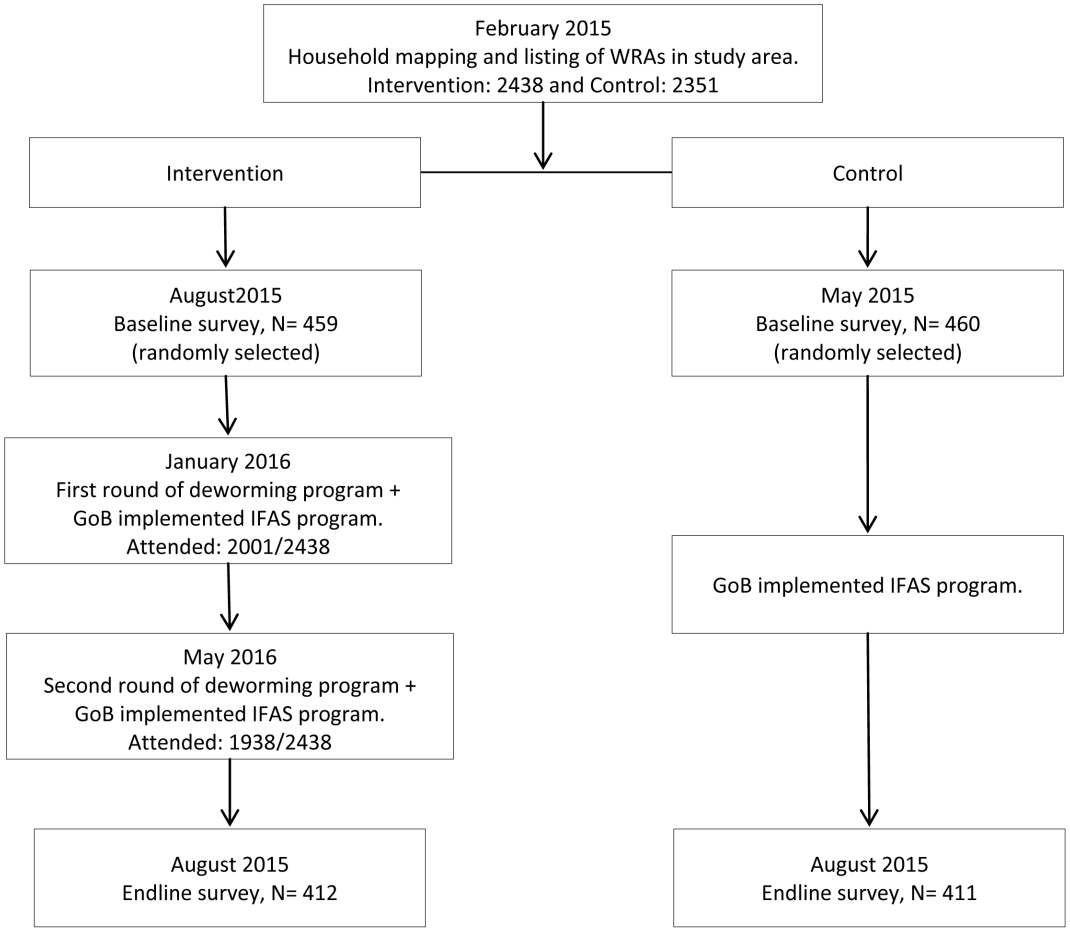

Figure 1. Study flow chart.

Table 1. Sociodemographic characteristics and WASH practice of the participants.

Characteristics	Baseline N=919 (%)	Endline N=823 (%)
Age (Mean±SD)	28.93±9.04	30.94±9.68
No education, n (%)	226 (24.59)	191 (23.21)
Use of safe water, n (%)	901 (99.23)	832 (99.76)
Use of sanitary latrine, n (%)	453 (49.89)	439 (52.64)
Wealth quintile		
Poorest, n (%)	221 (24.05)	128 (15.55)
Lower middle, n (%)	186 (20.24)	171 (20.78)
Middle, n (%)	206 (22.42)	196 (23.82)
Upper middle, n (%)	144 (15.67)	151 (18.35)
Wealthy, n (%)	162 (17.63)	177 (21.51)

Characteristics	Baseline N=919 (%)	Endline N=823 (%)
Households with no electricity, n (%)	208 (22.63)	105 (12.76)
Households with rudimentary floor, n (%)	783 (85.20)	675 (82.02)
Households with rudimentary wall, n (%)	137 (14.91)	103 (12.52)
Households with rudimentary roof, n (%)	10 (1.09)	6(0.73)
Hand washing knowledge		
Before eating, n (%)	598 (65.86)	559 (67.03)
Before feeding a child, n (%)	67 (7.38)	87 (10.43)
Before cooking food, n (%)	163 (17.95)	173 (20.74)
After defecation/urination, n (%)	859 (94.60)	785 (94.12)
After cleaning a child, n (%)	48 (5.29)	35 (4.20)
Use of soap for hand washing, n (%)	790 (87.00)	760 (91.12)
Use of slipper in latrine, n (%)	466 (51.32)	455 (54.55)

Table 2. Effect of intervention on hemoglobin level and nutrition status in the population.

Characteristics	Baseline (N=919)		p value	Endline (N=820)		p value
	Intervention n (%)	Control n (%)		Intervention n (%)	Control n (%)	
Anemia	N= 459	N= 460		N= 411	N= 409	
No anemia (>12 g/dL)	167 (36.3)	158 (34.3)	0.522	216 (52.5)	149 (36.4)	<0.001
Mild anemia (11.0-11.9 g/dL)	158 (34.4)	147 (32.0)		112 (27.3)	140 (34.2)	
Moderate anemia (8.0-10.9 g/dL)	130 (28.3)	151 (32.8)		80 (19.5)	119 (29.1)	
Severe anemia (<8.0 g/dL)	4 (0.9)	4 (0.9)		3 (0.7)	1 (0.2)	
Mean Hb level (SD) (g/dL)	11.5±0.1	11.4±0.1	0.589	11.8±0.1	11.5±0.1	<0.001
BMI	N= 459	N= 460		N= 412	N= 411	
Mean (SD) (kg/m2)	20.7±0.2	20.6±0.2	0.775	21.1±0.2	20.7±0.1	0.154
Low BMI (<18.5 kg/m2)	135 (29.4)	136 (29.6)	0.310	103 (25.0)	106 (25.8)	0.577
Normal BMI (18.5-24.9 kg/m2)	271 (59.0)	272 (59.1)		251 (61.0)	260 (63.3)	
Overweight (25.0-29.9 kg/m2)	42 (9.2)	48 (10.4)		47 (11.4)	38 (9.3)	
Obese (>=30.0 kg/m2)	11 (2.40)	4 (0.9)		11 (2.7)	7 (1.7)	

our intervention package at both individual and community level. The intervention package reduced anemia by 14% and 11% at community and individual level respectively. Similarly, STH infection were reduced by 16% and 17% respectively.

Discussion

In the absence of any GoB adopted regular deworming program for WRA, we conducted a community trial to test the efficacy of such programs implemented through an existing iron folic acid supplementation program. The successful implementation of our program yielded reduction in prevalence of anemia and STH infection by 14% and 16% respectively.

WHO recommends regular deworming of adolescent as well as WRAs where prevalence of STH is over 20%[21]. While the recommendation is a single dose of Albendazole, we opted for providing the medicine for three successive days, accounting

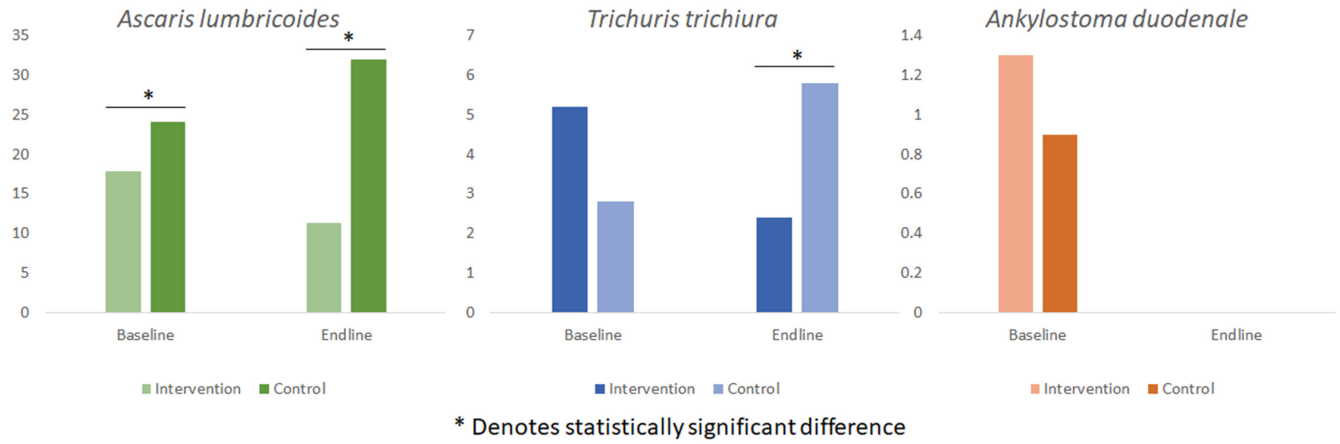

Figure 2. Change in prevalence of different helminths species at baseline and endline in two arms.

Table 3. Effect of intervention on STH infection by species among study population.

PREVALENCE						
	Baseline			Endline		
Species name	Intervention N= 458 n (%)	Control N= 460 n (%)	p value	Intervention N=411 n (%)	Control N=411 n (%)	p value
Ascaris lumbricoides	82 (17.9)	111 (24.1)	0.021	47 (11.4)	131 (31.9)	<0.001
Trichuris trichiura	24 (5.2)	13 (2.8)	0.063	10 (2.4)	24 (5.84)	0.014
Ankylostoma duodenale	6 (1.3)	4 (0.9)	0.520	0 (0)	0 (0)	-
Necator americanus	0 (0)	0 (0)	-	0 (0)	0 (0)	-
INTENSITY (Mean EPG)						
	Baseline			Endline		
Species name	Intervention N=458 Geometric mean	Control N=460 Geometric mean	p value	Intervention N=411 Geometric mean	Control N=411 Geometric mean	p value
Ascaris lumbricoides	2.871573	3.935747	0.218	1.189991	6.024528	<0.001
Trichuris trichiura	0.313686	0.150015	0.049	0.132239	0.336997	0.019
Ankylostoma duodenale	0.083933	0.044511	0.348	0	0	-
Necator americanus	0	0	-	0	0	-

for infection with *T. trichiura,* as per CDC guideline[18]. After the treatment of 2 rounds of deworming, 4 months apart, along with weekly iron folic acid supplementation, prevalence of anemia decreased from 63.6% during baseline to 47.6% during endline, indicating a 25% reduction from baseline. Similar results were observed in a large community trial in Vietnam that showed, from baseline anemia prevalence of 38%, regular deworming and weekly IFA supplementation reduced anemia prevalence to 26% in 3 months[22], 19% in 12 months[23], 18% in 54 months[24] and 14% in 72 months[25] indicating 28%, 50%, 52% and 63% reduction from baseline in 3, 12, 54 and 72 months respectively. Although, our intervention for 8 months yielded lower reduction than the program in Vietnam, it could be simply due to the sheer difference in population size (5,000 compared to 52, 000). Our program also increased mean Hb concentration by 3g/L in the intervention arm which was similar to the 3.5 g/L of the Vietnam study after 3 months[22]. Another randomized control trial in Peru failed to demonstrate any effect of single dose deworming administered in the post-partum period on maternal anemia after 6 months, although there was significant reduction in risk of STH infection in intervention arm[26]. This might be

Table 4. Community effect of intervention on prevalence of STH infection and anemia among study population.

Objective	Baseline			Endline			DID#	p value
	Intervention N=458 n (%)	Control N= 460 n (%)	p value	Intervention N=411 n (%)	Control N= 411 n (%)	p value		
STH prevalence*	101 (22.05)	121 (26.30)	0.133	50 (12.17)	134 (32.60)	<0.001	-16.19	<0.001
Anemia prevalence**	292 (63.62)	302 (65.65)	0.519	196 (47.57)	262 (63.75)	<0.001	-14.14	0.004

*STH positive = presence of single ova in stool

**Anemia= Hb <12 g/dL

#DID = Difference in differences

*** negative value indicates reduction from baseline

Table 5. Direct effect of intervention on prevalence of STH infection and anemia among study population.

Objective	Baseline			Endline			DID#	p value
	Intervention N=208 n (%)	Control N=208 n (%)	p value	Intervention N=209 n (%)	Control N=208 n (%)	p value		
STH prevalence*	47 (22.60)	55 (26.44)	0.362	25 (11.96)	68 (32.96)	<0.001	-16.83	0.001
Anemia prevalence**	127 (60.77)	141 (67.79)	0.135	104 (49.76)	140 (67.31)	<0.001	-10.52	0.052

*STH positive = presence of single ova in stool

**Anemia= Hb <12 g/dL

#DID = Difference in differences

*** negative value indicates reduction from baseline

due to the fact that, deworming alone has little to no impact on anemia[27]. However, coupled with IFA supplementation, this culminates in an effective reduction of anemia among WRAs.

Our intervention effective reduced the overall and species-specific prevalence of STH as well as the infection burden expressed as the mean of eggs per gram (EPG). A number of studies[22–25] of similar design in Vietnam looking at the reduction of STH infection reported similar results. Although, in contrast to these studies we did not observe a high prevalence of hookworm infection during the baseline survey in our study, probably due to decreased sensitivity of one sample test especially for hookworms[28], the overall decrease in STH infection shows resemblance to these studies. The Vietnamese studies reported a reduction of hookworm prevalence from 76% at baseline to 57%, 30%, 22% and 11% and 10% after 3, 12, 30, 54 and 72 months respectively. At the same time infection with *A. lumbricoides* and *T. trichiura* was also reduced from 19% and 29% at baseline respectively to 1.4% and 2.3% to endline respectively[22–25]. The Peruvian study also experienced a significant decrease in risk of infection from all STH species. The study showed single dose albendazole confers decreased risk of infection by 50% for Ascaris, 40% for Trichuris and 90% for hookworm infection[26]. The lowest risk reduction in Trichuris justifies the requirement of multiple doses for complete elimination.

It is well known that, in spite of their efficacy, the protection conferred by preventive chemotherapy is very short lived. A meta-analysis showed that within six months after treatment 68% become re-infected with Ascaris, 67% with Trichuris, and 55% with hookworm[29]. This requires arrangement of deworming campaigns at regular intervals. Bangladesh has seen a lot of success in deworming school children through school-based mass deworming programs. However, reaching adolescent girls and WRAs for such campaigns is a tangible challenge recognized by WHO[21]. Therefore, our utilization of the existing healthcare system of distributing IFA among such populations is undoubtedly a novel solution. The health setups we have used for this project serve 6000–8000 of the

population in the rural area and our project showed that, this setup can be effectively used to piggyback this important public health campaign that results in reduction in anemia and STH burden among WRAs. The fact that drug distribution was carried out by the existing government healthcare workforce indicates the sustainability of this approach. Our program enjoyed encouraging compliance in the first round which reduced a little during the second round. However, studies in similar context have shown increased compliance of 76% and 72% in 54 and 72 months respectively to weekly iron-folate supplementation (WIFS) as well as 95% and 85% to preceding deworming drug administrations in 54 and 72 months respectively[24,25]. This indicates that same level of compliance can be replicated in the context of Bangladesh. Such campaigns would also be cost effective to reduce helminth burden in the community as proved by cost effectiveness analysis of the Vietnamese program[30].

This study was conducted in a small community of a sub-district in Bangladesh where homogeneity of the population was very prominent. The timeline of the intervention was only 14 months. So the long term effect of the intervention could not be estimated through this project.

Our study clearly showed that existing health setups can be utilized effectively to incorporate a deworming campaign for WRAs and thus scale up of the national deworming program for successful elimination of STH. Future endeavors should focus on replicating the same efficacy in a large-scale trial, determining the cost effectiveness and exploring the barriers to compliance to the program. The efforts would yield valuable evidence and, together with the evidence from the present study, would encourage policy makers to incorporate the program of deworming WRAs into national policy that would lead to successful elimination of STH in Bangladesh and similar contexts.

Data availability

Underlying data

Figshare: Merged Deworming Dataset_Final.sav. https://doi.org/10.6084/m9.figshare.21400026.v1[20]

This project contains the following underlying data:

- Merged Deworming Dataset_Final.sav (deidentified data of 1742 reproductive-age women (WRA) from rural Bangladesh including information from baseline and endline surveys)
- Dataset_codebook.xlsx (codebook for the dataset containing the questions and options of each variable)

Author contributions

MS, PM, MGH, and DM conceptualized the research project and obtained funding for conducting the research. MDMH was involved in data curation, project administration and supervision. MS and PM analyzed the data with input from MAA, MMH, DM and TA. MS and PM wrote the manuscript with input from all other authors.

Acknowledgements

We acknowledge with gratitude the contribution from the Bill and Melinda Gates Foundation, who funded the project through Grand Challenges Explorations (Round 13). We are also grateful to Community Based Health Care (CBHC) of Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MoH&FW), Government of Bangladesh, and Office of Upazila Health and Family Planning Officer (UHFPO) of Trishal, Mymensingh for their continuous support in implementing the project.

References

1. Gardner W, Kassebaum N: **Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990-2019.** *Curr Dev Nutr.* 2020; **4**(Supplement_ 2): 830.
Publisher Full Text | Free Full Text
2. De Andraca I, Walter T, Castillo M, *et al.*: **Iron deficiency anemia and its effects upon psychological development at preschool age: a longitudinal study.** *Nestle Foundation annual report.* 1990; 53–62.
Reference Source
3. Ezzati M, Lopez AD, Rodgers A, *et al.*: **Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors.** OMS; 2004.
Reference Source
4. Hurtado EK, Claussen AH, Scott KG: **Early childhood anemia and mild or moderate mental retardation.** *Am J Clin Nutr.* 1999; **69**(1): 115–9.
PubMed Abstract | Publisher Full Text
5. Palti H, Meijer A, Adler B: **Learning achievement and behavior at school of anemic and non-anemic infants.** *Early Hum Dev.* 1985; **10**(3–4): 217–23.
PubMed Abstract | Publisher Full Text
6. Haas JD, Brownlie T 4th: **Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship.** *J Nutr.* 2001; **131**(2S–2): 676S–688S; discussion 688S–690S.
PubMed Abstract | Publisher Full Text
7. Horton S, Ross J: **The economics of iron deficiency.** *Food Policy.* 2003; **28**(1): 51–75.
Publisher Full Text
8. Abu-Saad K, Fraser D: **Maternal nutrition and birth outcomes.** *Epidemiol Rev.* 2010; **32**(1): 5–25.
PubMed Abstract | Publisher Full Text
9. Allen LH: **Anemia and iron deficiency: effects on pregnancy outcome.** *Am J Clin Nutr.* 2000; **71**(5 Suppl): 1280s–4s.
PubMed Abstract | Publisher Full Text
10. Zhang Q, Ananth CV, Rhoads GG, *et al.*: **The impact of maternal anemia on perinatal mortality: a population-based, prospective cohort study in China.** *Ann Epidemiol.* 2009; **19**(11): 793–9.
PubMed Abstract | Publisher Full Text
11. Benoist Bd, McLean E, Egll I, *et al.*: **Worldwide prevalence of anaemia**

1993-2005: WHO global database on anaemia. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. 2008.
Reference Source

12. NIPORT, ASSOCIATES MA, DHS M: **Bangladesh Demographic and Health Survey.** 2013.

13. Balarajan Y, Ramakrishnan U, Ozaltin E, *et al.*: **Anaemia in low-income and middle-income countries.** *Lancet.* 2011; **378**(9809): 2123–35.
PubMed Abstract | Publisher Full Text

14. Bethony J, Brooker S, Albonico M, *et al.*: **Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm.** *Lancet.* 2006; **367**(9521): 1521–32.
PubMed Abstract | Publisher Full Text

15. Gilgen DD, Mascie-Taylor CG, Rosetta LL: **Intestinal helminth infections, anaemia and labour productivity of female tea pluckers in Bangladesh.** *Trop Med Int Health.* 2001; **6**(6): 449–57.
PubMed Abstract | Publisher Full Text

16. Miguel E, Kremer M: **Worms: identifying impacts on education and health in the presence of treatment externalities.** *Econometrica.* 2004; **72**(1): 159–217.
Publisher Full Text

17. Ministry of Health & Family Welfare GoB: **A Situation Analysis: Neglected Tropical Diseases in Bangladesh.** 2010.
Reference Source

18. CfDCaP (CDC): **Trichuriasis- Treatment.** [Anthelminthic medications (drugs that rid the body of parasitic worms), such as albendazole and mebendazole, are the drugs of choice for treatment. Infections are generally treated for 3 days. The recommended medications are effective. Health care providers may decide to repeat a stool exam after treatment. Iron supplements may also be prescribed if the infected person suffers from anemia.]. 2013.
Reference Source

19. Montresor A, Crompton DW, Hall A, *et al.*: **Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level: a guide for managers of control programmes.** 1998.
Reference Source

20. Shomik M: **Merged Deworming Dataset_Final.sav.** *figshare.* Dataset. 2022.
http://www.doi.org/10.6084/m9.figshare.21400026.v1

21. World Health Organization: **Reaching girls and women of reproductive age with deworming: report of the Advisory Group on deworming in girls and women of reproductive age: Rockefeller Foundation Bellagio Center, Bellagio, Italy 28–30 June 2017.** 2018.
Reference Source

22. Pasricha SR, Casey GJ, Phuc TQ, *et al.*: **Baseline iron indices as predictors of hemoglobin improvement in anemic Vietnamese women receiving weekly iron-folic acid supplementation and deworming.** *Am J Trop Med Hyg.* 2009; **81**(6): 1114–9.
PubMed Abstract | Publisher Full Text | Free Full Text

23. Casey GJ, Phuc TQ, Macgregor L, *et al.*: **A free weekly iron-folic acid supplementation and regular deworming program is associated with improved hemoglobin and iron status indicators in Vietnamese women.** *BMC Public Health.* 2009; **9**: 261.
PubMed Abstract | Publisher Full Text | Free Full Text

24. Casey GJ, Montresor A, Cavalli-Sforza LT, *et al.*: **Elimination of iron deficiency anemia and soil transmitted helminth infection: evidence from a fifty-four month iron-folic acid and de-worming program.** *PLoS Negl Trop Dis.* 2013; **7**(4): e2146.
PubMed Abstract | Publisher Full Text | Free Full Text

25. Casey GJ, Tinh TT, Tien NT, *et al.*: **Sustained effectiveness of weekly iron-folic acid supplementation and regular deworming over 6 years in women in rural Vietnam.** *PLoS Negl Trop Dis.* 2017; **11**(4): e0005446.
PubMed Abstract | Publisher Full Text | Free Full Text

26. Mofid L: **Maternal postpartum deworming: a novel strategy to reduce infant and maternal morbidity in low-and-middle-income countries.** McGill University Libraries; 2016.
Reference Source

27. Smith JL, Brooker S: **Impact of hookworm infection and deworming on anaemia in non-pregnant populations: a systematic review.** *Trop Med Int Health.* 2010; **15**(7): 776–95.
PubMed Abstract | Publisher Full Text | Free Full Text

28. Tarafder M, Carabin H, Joseph L, *et al.*: **Estimating the sensitivity and specificity of Kato-Katz stool examination technique for detection of hookworms, *Ascaris lumbricoides* and *Trichuris trichiura* infections in humans in the absence of a 'gold standard'.** *Int J Parasitol.* 2010; **40**(4): 399–404.
PubMed Abstract | Publisher Full Text | Free Full Text

29. Jia TW, Melville S, Utzinger J, *et al.*: **Soil-transmitted helminth reinfection after drug treatment: a systematic review and meta-analysis.** *PLoS Negl Trop Dis.* 2012; **6**(5): e1621.
PubMed Abstract | Publisher Full Text | Free Full Text

30. Casey GJ, Sartori D, Horton SE, *et al.*: **Weekly iron-folic acid supplementation with regular deworming is cost-effective in preventing anaemia in women of reproductive age in Vietnam.** *PLoS One.* 2011; **6**(9): e23723.
PubMed Abstract | Publisher Full Text | Free Full Text

Open Peer Review

Current Peer Review Status: ? ? ✗ ?

Version 1

Reviewer Report 21 August 2023

https://doi.org/10.21956/gatesopenres.15128.r34432

?

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This is an important study, not only because of its focus on anemia, a highly preventable disease, but also because women of reproductive age are often neglected in government programs (that tend to focus mostly on pregnant women only).

There is some concern pertaining to the timeliness of the study findings and its publication. The intervention was run in 2015/16, but the results are only coming out now.

The primary threat to validity this study presents is the selection of the treatment and control clinics. Authors mention that the treatment clinics were deliberately chosen for their higher levels of performance; control clinics were chosen because they were not contiguous with the treatment clinics and which also had a good performance records. Authors need to define what is meant by this high/good level of performance, including the metrics they used. Given the selection process, the extent to which results can be attributed to the intervention remain largely unknown. After all, the well-performing clinics in one domain could also be well-performing in another domain. Hence, selectivity bias is a major threat in this study, which means that all results I(including those in the abstract) have to be couched in much more tentative terms than they currently are.

Selectivity bias also pertains to the fact that the study was confined to those who visited the clinic -- for any reason. Hence, women who were more proactive about their health (e.g., to receive contraception or to immunize their children) and those who were seeking medical attention were more likely to receive the intervention, as compared to the general population of the catchment areas.

Finally, selectivity bias is also likelihood to be high because the study drew only from the clinical catchment areas, meaning that women living at a distance from health facilities were less likely to be in the study.

The sample size calculations were based on an intraclass correlation, which was not taken into account in the data analysis. Authors need to conduct analyses that take the clustering into account by, for example, considering random and fixed effects and/or using a hierarchical linear model analysis.

It would be good to know why authors assumed such powerful effects (of 35% reduction in anemia) and why the ICC was assumed to be 0.01.

Pregnant women were excluded from the study. Authors should mention how they determined pregnancy status and why they adopted this exclusion. The same comments pertain to hemoglobin measurement.

Table 1 should also show the (t-test of Chi-square) statistic that compares the treatment and control groups.

It's not clear why only half the sample at endline were selected to assess the direct effect of deworming. It is also not known how the 50% group was selected.

A relatively minor point: When authors define anemia, they should provide the actual hemoglobin concentrations for the WRA (in g/dcl) that determine anemia status.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Social and behavioral interventions pertaining to adherence to nutritional supplement guidelines (including iron folic acid and multiple micro-nutrients).

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 21 August 2023

https://doi.org/10.21956/gatesopenres.15128.r34434

Pattanee Winichagoon
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This study is a report on a quasi-experimental study implemented the interventions through existing health delivery system in Bangladesh. The study could greatly contribute to the improvement of anemia in a setting where there could be multiple causes of anemia, and soil-transmitted helminths is one addressed in this study. Unfortunately, there are several questions about the conduct of the study and inconsistent information in several places which need author's careful attention. Lastly, a review by a statistician would help to ensure that the data analysis is properly performed.

Specific comments

1. Abstract: Results shown in the abstract is puzzling – which is a mix of results of the whole community and the randomly selected samples. Following the details in the MS, the abstract should report results on the samples taken from the whole communities where there was intervention vs control.

    1. Background – suggest to be less wordy, and clearly state the objective of the study (e.g., This study aims to determine the impact of deworming on STH infection and anemia among reproductive age women.' Please remove '... in rural Bangladesh, as this is stated again in the first sentence of the Method.

    2. Method – Please add brief statistical analysis methods.

    3. Results – it is puzzling why the compliance in the whole population is reported here, while it should have been that of the randomly selected samples, whereas the prevalence of anemia and STH (from the main text) were that from the randomly selected samples. All results need to be revised after proper analysis is performed as per several comments below.

2. Introduction:
    1. Some statements are not very logical. For example

        1. First paragraph: '*Children and women of reproductive age (WRA, 15–49 years) are most vulnerable to the consequences of anemia evident from the reported prevalence of 47.4% and 30% for children under 5 and WRAs respectively.*' Prevalence does not inform the consequences.

2. Middle of paragraph 4: The mention of 'mass deworming' as the intervention is unclear whether there is also specific educational messages related to deworming is also part of the intervention package.

3. Last sentence of paragraph 4: '*Due to lack of any nation-wide data on the prevalence of STH infection, the high prevalence of anemia among WRAs in this country indicates that STH infection is also high among this age group.*' This is not logical, as there are multiple causes of anemia. Thus, anemia is not a proxy for STH situation.

3. Methods:

1. The dates indicated for different activities in the text and that in Figure 1 are inconsistent. Study design & all information about the conduct of the study, including implementation of the intervention, and data collection for baseline and endline: Please recheck and align them.

2. Of note, the date for baseline survey in the two arms (May vs August) seem to be far apart and wonder if there could have been any seasonal difference in the general health status. For example, if August is during the rainy season, the chance for being infected with STH could be higher? Was this factor controlled for in the analysis (will come back to this issue again in data analysis).

3. Since this is a quasi-experimental design, please clarify to ensure the comparability of the two arms. It was mentioned that the 'high performance' CC were selected for the intervention arm, and the 'good performance' for control. Are the criteria for these terms comparable?

4. It is adequate to simply mention that 'pregnant women' were not included in the study. There is no need to give other information about how to manage WRA who were pregnant as if they are part of the study.

5. Intervention: Please clarify what was the IFA regimen, daily or weekly, and dose. Was the same IFA (GoB?) package implemented in all CCs in both study arms. There was a mention of IFA and nutrition education being part of the intervention package. Please clarify whether the messages in the nutrition education was the same for both intervention and control arms, except that about deworming, or if all messages were the same and including benefits of IFA and deworming?

6. Evaluation of the project: Can not understand why PR = EI/A, where EI is the difference between the differences in the intervention and control arms, but A is the prevalence of the intervention arm at baseline only? For example, would it be more correct to use average of or overall prevalence from both arms as a divider for calculating the % reduction. Need explanation for this algorithm. Last sentence of this paragraph does not seem necessary, as the results will be obvious whether there is an increase or decrease or null.

7. Sample size: from the sample size calculation consideration, it shows that WRA in each arm were randomly selected (n = 460 per arm) at baseline. Please clarify if it is

correct that the samples at baseline and endline are two cross-sectional randomly selected samples (but half of the same WRA in the baseline sample in each arm were included at endline).

8. Last paragraph under the section on Sample size and sampling: For endline, approximately half (but the figure is 115 from each CC, i.e. 230 for each arm. For clarity it would be easier to follow by indicating that (or including), '*a total of 230 women in each arm who were included in the baseline were included in the endline (and analysed as a cohort) while the rest (230 WRA) were randomly selected from the rest of WRA in the two CC for a total sample of 460 per arm.*' Please consider if this is correct. Note, it is recognized from the Table 5 that the final sample size which have data were only 208 or 209 per arm.

9. Statistical analysis: Suggest to consult statistician, the fact that this is a quasi-experimental design, and whether there is a need to consider analysis which takes into account possible confounding variables (e.g., some background characteristics of the samples within the two arms). Note a small error, 'standard deviation', not 'standard division'.

4. Results:

1. Is there any explanation for the sample size at the endline being much smaller than the baseline? Authors indicated, only 823 women (collective of two arms?) were enrolled. Is the missing number of WRA are those who were selected from the baseline (115/CC as indicated in the MS) or from the randomly selected WRA to make up supposedly 460/arm? Surprising, the final sample size of the WRA at endline as shown in Tables 3 and 4 were equal for both arms (411 each); whether the remaining pool of WRA at endline in each arm was about the same or more dropout in one group than the other. Clarification and reasons for dropouts are important to understand if it were related to the intervention or not.

2. Was there any information about the compliance to IFA in the control arm, as this was also implemented as part of GoB program? This is an important information since the intervention is a combined deworming + IFA (and compliance was monitored closely) vs IFA alone in the control arm. In case compliance to IFA is poor in the control arm, the observed difference between the two arms can not be interpreted as the effect of deworming alone. This point is critical for interpretation.

3. Of note, compliance to deworming and IFA was only reported for the whole population of WRA in the two CC (reported in the abstract). This information on compliance to intervention (dworming) and IFA among WRA who were sampled in the respective arms for the data analysis should be provided.

5. Results: All tables

1. Table 1: It is inappropriate to present the data combining WRA in both arms for baseline and endline. The two arms were planned for comparison, hence, data for each arm at each time point must be presented. Associated statistical tests should

also be presented to show if there is any difference in the background characteristics that may need to be controlled in the statistical analysis of the intervention effect.

2. Table 2, no need to indicate the total sample size for baseline and endline; it is more critical to see the sample size for each arm.

3. Figure 2 is not necessary, as the same results on prevalence of various helminths at baseline and endline were presented in Table 3.

4. Tables 4 and 5:

    1. Please clarify how the STH prevalence was calculated – counting the presence of any helminths combined into a total presence?

    2. Please clarify how the reduction of anemia or STH at community level was calculated and compared. Is it correct that n=2 communities for each arm and the # of WRA was nested within the community. So, what was the calculation of prevalence and statistical test used for this comparison.

    3. Use of the term 'community effect' (Table 4) and 'direct effect' (Table 5): Table 4 evaluates the effect of intervention at a group (community) level (see also comments in 5.4.2), whereas Table 5 evaluates the intervention effect at individual level (cohort). Suggest to consult statistician for appropriate terms and recheck the appropriateness of the statistical analysis.

5. While it was stated that the reduction of prevalence of anemia/STH is calculated using the algorithm provided (see 3.6), the reduction in anemia prevalence reported was 16 % (i.e., 67.6 at baseline vs 47.6% at endline of the intervention arm only). Were the indicated algorithm used to report any of the findings?

6. Discussion:

    1. Comparison of the size of anemia reduction to that in Vietnam and Peru is unlikely to be straightforward, as there could be many contextual factors e.g., severity of the infection, intervention package and possibly, other social-ecological factors. Would be useful to provide more critical comments or lessons.

    2. As pointed out in 4.2 and 4.3 above, it is critical to note that this study might have shown the combined effect of deworming + IFA, not deworming alone resulted in reduction of anemia. Please clarify since there is incomplete data on compliance in CCs of both arms; alternatively, provide data on compliance to IFA of each area to support the argument.

    3. Recommendation to provide deworming through the existing IFA delivery platform: There is no information on how good the coverage and compliance to IFA among non-pregnant WRA, at least from this study to justify this recommendation. The prevalence of anemia in the control arm did not change or was slightly worse off, which may indicate the ineffective GoB IFA program for non-pregnant WRA, despite

the selection of CCs which had 'good performance'. Therefore, the recommendation to piggy-back the deworming with the IFA distribution to non-pregnant WRA should be carefully addressed. Any lessons learned from the intervention arm regarding the implementation factors could be more useful.

4. Lastly, this study used a quasi-experimental design. It would be useful to give explanation why this design was chosen, instead of a RCT and its implication/limitation for the interpretation of results.

7. Editorial: To improve the clarity of the manuscript, a copy edit is needed.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Maternal and child nutrition; field efficacy and effectiveness trials in the community/population

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 21 August 2023

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Eliza Davidson
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This study is interesting and addresses a relevant Global Health issue: how to improve anaemia status in women of reproductive age? The approach taken in this Quasi-experimental study was to use Government-run clinics to deliver an anti-parasitic drug regimen, as soil-transmitted helminths are known to be associated with anaemia. The authors used the catchment area of 4 clinics (2x intervention and 2x control). This study is deserving of publication once some changes are effected.

Minor issues:

1. The manuscript would benefit from a copy edit to fix minor grammatical and orthographic errors.

2. Several statements in the introduction need citations.

3. We feel that 'Government of Bangladesh' should not be abbreviated to 'GoB'.

4. Page 3, the statement: *"Due to lack of any nation-wide data on the prevalence of STH infection, the high prevalence of anemia among WRAs in this country indicates that STH infection is also high among this age group"* is not necessarily a correct assertion. One thing does not directly imply the other since, as the authors clearly stated before, the etiology of anaemia is widely varied.

5. Page 3, the statement: *"This campaign has seen remarkable success considering the prevalence of decreasing from 80% to 16%"* does not specify the condition being referred to.

6. Methods, statistical analysis: The use of the term "*standard division*" should be corrected to "standard deviation".

7. Methods: citations for guidelines (e.g., GoB IFA guidelines, STH WHO guidelines) should be provided.

8. Discussion: The statement "*This might be due to the fact that deworming alone has little to no impact on anemia*" appears to contradict the introduction paragraph, which discusses the success of mass drug administration (MDA) in children.

Major issues:

1. Methods: These need more detail. In particular, we need more information regarding the definition of high-performing CC or CCs with good performance.

2. Methods: It reads from the methods that intervention CCs were chosen first, and after

eliminating adjacent CCs 2 control CCs were determined; however, the study flowchart shows that the control population were surveyed 3 months before the intervention population. Why?

3. The authors could provide more detail about the IFA.

4. The authors need to define the threshold for anaemia, and the method for anaemia measurement should state that hemoglobin was measured in capillary blood.

5. The PR formula shown in the "Evaluation of the Project" section is not the same formula used to calculate the values presented in Tables 4 and 5.

6. There is no clear definition of the study's primary outcome: anaemia or STH?

7. The selection criteria for of the participants chosen to be followed up for the direct effect of the deworming could be better explained.

8. A map with the location of the clinics would be beneficial.

9. Table 5: the DID value for STH prevalence seems to be incorrect.

10. Discussion: The discussion needs a more well-rounded approach and less direct citation of a single study.

11. Page 10: the sentence "*The timeline of the intervention was only 14 months*" is incorrect. The intervention started in January 2016, not in February 2015.

12. Methods: The authors could provide more detail about the control group

13. Methods: The process of randomly selecting 460 WRAs from each arm (intervention and control) needs further clarification.

14. Methods: how "*factors of compliance*" were measured should be clearly described

15. Results, Table 4 and 5: Clearly outline the difference between the community effect and the direct effect in both table footnotes and within the results text so that readers can interpret the results accurately.

16. Discussion: providing more context on the Bangladeshi health system and other available platforms would be beneficial. For example, discuss the utilization of Community Clinics compared to private clinics, Family Welfare Centres, and Upazila Health Complexes for primary healthcare.

17. Discussion: the analyses were not adjusted for confounders, this should be discussed as a limitation

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Global health trials in iron and anaemia, Infectious disease epidemiology and immunology, Maternal and Child Health outcomes

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Reviewer Report 14 July 2023

https://doi.org/10.21956/gatesopenres.15128.r33359

?

Binod Rayamajhee
University of New South Wales, Sydney, New South Wales, Australia

I found this manuscript to be an interesting and important read. However, I wonder why the authors only focused on anemia and did not examine the correlation between multi-micronutrient deficiencies and soil-transmitted helminthic infections among WRAs (women of reproductive age) right from the beginning. Considering the potential relationship between these factors, it would have been valuable to explore their interplay in this study. Additionally, I questioned why this study was hasn't published despite its completion in 2015. My specific comments are:

- Some parts of the introduction section are missing citations, so please insert relevant references in specific paragraphs.

- It is important to add a geospatial map of the study site showing details of the rural/district regions.
- The majority of the method section is without references. I advise adding citations.
- It is better to display the sociodemographic features of study participants graphically rather than in a tabular format.
- The discussion section of the manuscript appears to be quite lengthy and repetitive, which may detract from the overall impact of the study. To improve the clarity and focus of the discussion section, it may be helpful to condense the content and focus on the cardinal findings of the study, while avoiding the repetition of results that have already been presented in earlier sections of the manuscript. It is worth referencing other relevant studies from the region (https://doi.org/10.1038/s41598-022-24634-3) that have assessed the link between micronutrients and social status with the incidence of STH infections in WRAs.
- Grammatical errors and typos need to be fixed throughout the manuscript.

References

1. Mehata S, Parajuli KR, Rayamajhee B, Yadav UN, et al.: Micronutrients deficiencies and its correlation with the soil-transmitted helminthic infections among children and non-pregnant women in Nepal: findings from Nepal national micronutrient status survey.*Sci Rep*. 2022; **12** (1): 22313 PubMed Abstract | Publisher Full Text

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Molecular microbiology focusing infectious diseases, antimicrobial resistance,

genomics, and microbiome.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.