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Full Length Research Paper

Schistosoma mansoni infection and hematological profile in an endemic foci in Western Burkina Faso

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Persistence of light infections of *Schistosoma mansoni* is common among individuals living in endemic settings despite the mass drug treatment with praziquantel. Therefore, it is of interest to understand the impact of *S. mansoni* on general health indicators such as hematological profile. In the present study, we investigated the impact of *S. mansoni* infection on complete blood counting an endemic foci in Western Burkina Faso. The results showed among schistosomiasis endemic population, in addition to anemia, participants having poor hematological profile had higher risk of being infected by *S. mansoni* (OR = 1.71; 95% CI 1.27 – 2.3; *P = 0.0003*). Conversely, *S. mansoni* positive subjects had a higher risk of harboring poor hematological profile (OR = 1.49; 95% CI 1.06 – 2.10; *P = 0.023*) when adjusted by age, gender and water contact. A longer follow-up would allow a better understanding of the long-term impact of schistosomiasis control program on important health indicators such as hematological profile.

Keywords: Schistosomiasis mansoni, hematological profile, ascending hierarchical clustering analysis.

INTRODUCTION

Because of its chronicity *Schistosoma mansoni* infection, is associated with various metabolic changes, and its impact on the hematological parameters was explored by several authors (WHO, 1987; Da Silva et al., 2005). Hence, it is reported that in hepatosplenic patients, anemia is common, but also a significant rise in monocytes, lymphocytes, and neutrophils and a mild eosinophilia occur (Da Silva et al., 2005; Mohammed et al., 2006). Recent studies have focused on the impact of schistosomiasis on anemia(King et al., 2005; Friedman et al., 2008, Stecher et al., 2017), but reports on the interaction between schistosomiasis and the complete hematological profile are still scarce. Because hematological parameters are intimately related, an analysis which mimics the in vivo status of patients will provide some important insights onto the impact of schistosomiasis on the general metabolic parameters.

Burkina Faso has undertaken a vast schistosomiasis control since 2005 which resulted in a significant reduction of schistosomiasis prevalence across the country among school age children (Ouedraogo et al., 2016), but no attempt has been made to assess the impact of schistosmiasis infection on the general or specific health related parameters. Therefore, the impact of *S. mansoni* infection on health status such as hematological profile is still of interest. In the present

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study we used a hierarchical ascendant classification model analysis to examine the relationship between *S. mansoni* infection and the complete hematological profile before and after praziquantel treatment among people living in an endemic focus in Western Burkina Faso.

MATERIAL AND METHODS

Study area and population

We carried out a field at the Kou valley, in the Houet province and at 20 Km from Bobo-Dioulasso, the second largest town in Burkina Faso. The presence of the Kou River provided water source for the creation of 1200 ha irrigated field for rice growing since 1968. The village has approximately 60,000 inhabitants and the presence of *S. mansoni* in Kou valley was already reported (Trotobas et al., 1977; Kpoda et al., 2013).
A cross sectional survey enabled the enrolment of 1185 subjects. The inclusion was made randomly within the whole population and on the basis of their willingness to participate. Children participation was submitted to the consent of their parents or guardians. Every enrolled subject was submitted to a questionnaire relative to his identity, activities and knowledge on schistosomiasis.

Parasitological and hematological surveys

The egg of *S. mansoni* in stool samples was detected by Kato-Katz thick smear while *S. haematobium* infection was detected by urine filtration. All subjects infected by *S. mansoni* were treated with a single oral dose of Praziquantel (40 $mg.kg^{-1}$ of body weight). All treated subjects were re-screened 45 days later to assess both the treatment efficacy and its impact on hematological profile. During the two cross-sectional surveys, a 5 ml of venous blood was obtained from each participant using a K2 EDTA tube for hematological analysis. Full blood counts of the collected blood samples were estimated using an hematology analyzer (Pentra ES 60, Horiba Medical, France).

Ethical considerations

Ethical approval was obtained from the institutional ethics committee of Centre Muraz and written informed consent was obtained from all participants. The participation of children was subjected to the consent from their parents or guardians.

Data analysis

The data were processed and analyzed using R software version 3.3.1 (R Development Core Team, R Foundation for Statistical Computing, Vienna, Austria), including the *FactoMineR* and *lme4* packages. Hematological profiles of the participants were established by proceeding as follow. Firstly, we performed a principal component analysis (PCA) including all the blood count parameters. The resulted components (from the PCA) were then used for a hierarchical ascendant classification. The end result grouped all the participants in two clusters or “hematological profiles”. Secondly, we used logistic regression to explore the effect of interactions between *S. mansoni* infection and hematological profile. Two sided Wald test was used for the statistical comparisons and $P< 0.05$ was considered as significant. For the post-treatment analysis, a linear mixt-effect model was used to explore the hematological parameters variation in relation to *S. mansoni* infection

RESULTS

Study participants and *Schistosoma mansoni* infection

A total of 1185 subjects were examined during the surveys and 901 succeeded to provide urine, stool and blood samples. Therefore, only these subjects will be considered for the further analysis. They were composed of 381 men and 520 women (sex ratio of 0.6). The age ranged from 6 to 80 years old with a mean of 26.8 ± 18.9 years. 57.6% (519/901) of the enrolled subjects were permanent worker in the rice fields and 74.4% (670/901) declared having regular contact with water in the irrigation schemes or ponds encountered in the village.
Urine samples filtration in two consecutive days revealed that only 11 subjects excreted *Schistosoma haematobium* eggs. This confirmed that urinary schistosomiasis is virtually absent from the study site. Contrary, the Kato-Katz slides examination showed that 244 subjects were actively infected by *S. mansoni* giving a global prevalence of 27.1%. This prevalence was 27.3% (104/381) and 26.9% (140/520) among male and female participants respectively. The results also showed that the highest infection rate was observed among participant aged between 6 to 10 years old (35.3%, 85/241). This prevalence were respectively 24.4% (58/234), 26.5% (53/200) and 21.2% (48/226) respectively for the age groups of 11 to 10, 20 to 40 and >40 years old. The majority of enrolled subjects 81.6 % (199/244) excreted less than 100 eggs of *S. mansoni* per gram of feces and only six participant harbored heavy infections (> 400 epg).

Hematological profiles of the study population

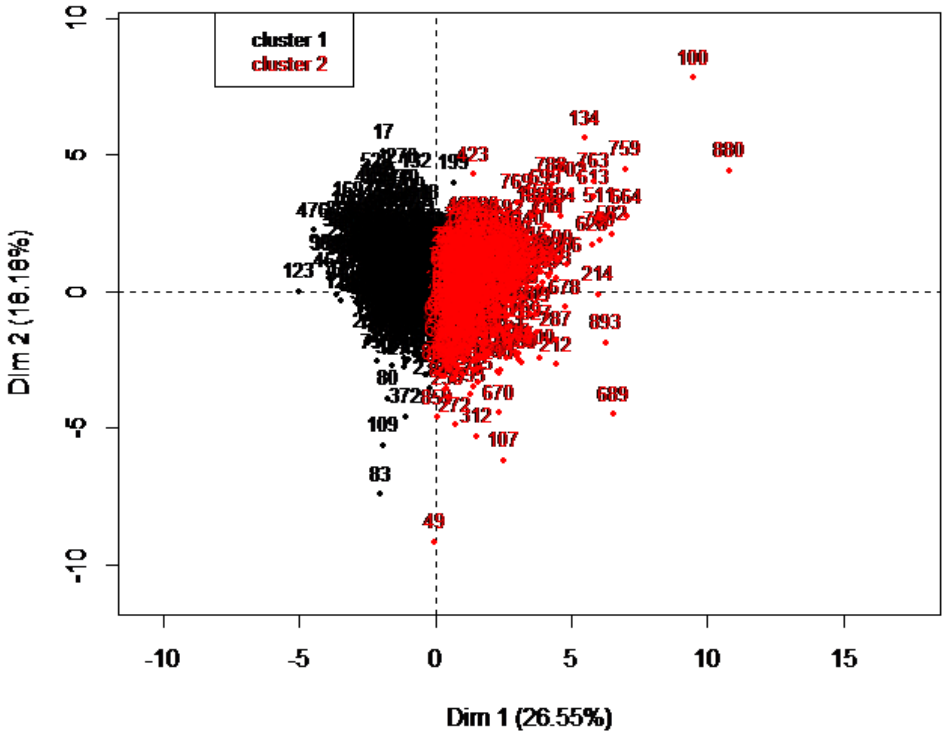
Details of the hematological parameters of study participants is shown in Table 1. The results showed that anemia (HGB < 12 g/dL) was very common among the study population and that *S. mansoni* infected subject had slightly lower hemoglobin level as compared to the non-infected subjects (P = 0.02).

Table 1. Hematological profile of the study participants.

Parameter	Whole population (*N = 901*)	*S. mansoni* positive subjects (*N = 244*)	*S. mansoni* negative subjects (*N = 657*)	*P value*
WBC (x 10^3/µL)	6.98 ± 2.22	6.92 ± 2.22	7.26 ± 2.57	*0.575*
RBC (x 10^6/µL)	4.47 ± 0.52	4.42 ± 0.28	4.40 ± 0.56	*0.684*
HGB (g/dL)	12.00 ± 1.41	11.57 ± 0.76	11.86 ± 1.51	***0.02****
HCT (%)	36.33 ± 4.09	35.08 ± 2.32	35.97 ± 4.46	***0.017****
MCV (µm^3)	81.41 ± 7.14	79.55 ± 4.91	82.20 ± 7.42	***0.023****
MCHC (pg)	26.92 ± 2.72	26.26 ± 1.83	27.12 ± 2.82	***0.039****
MCH(g/dL)	32.93 ± 1.92	33.02 ± 0.61	32.98 ± 0.72	*0.312*
PLT (x 10^3/µL)	229.60 ± 79.18	237.80 ± 104.68	225.93 ± 75.50	*0.993*
MPV (µm^3)	8.39 ± 0.77	8.69 ± 0.84	8.36 ± 0.71	***0.002****
LYM (x 10^3/µL)	3.07 ± 0.95	3.24 ± 1.09	3.17 ± 0.93	*0.434*
MON (x 10^3/µL)	0.64 ± 0.23	0.68 ± 0.25	0.67 ± 0.20	*0.567*
NEU (x 10^3/µL)	2.50 ± 1.16	2.59 ± 1.24	2.28 ± 1.08	*0.21*
EOS (x 10^3/µL)	0.54 ± 0.70	0.37 ± 0.17	0.66 ± 0.95	*0.992*
BAS (x 10^3/µL)	0.04 ± 0.03	0.04 ± 0.02	0.05 ± 0.03	*0.849*

Values are presented as mean ± standard deviation; *N*: number of samples,
* Statistically significant.

Figure 1. Representation of two clusters (or profiles) after ascending hierarchical clustering analysis.



Axes correspond to individual coordinates for the two main dimensions of the principal component analysis. Cluster 1: Normal hemoglobin rate. Cluster 2: Low hemoglobin rate.

The analysis of the hematological parameters clustering by PCA followed by hierarchical ascendant classification showed that the study participants could be grouped in two clusters or “profiles” representing the more possible hematological similarity harbored by individuals (Figure 1).

It is noticeable that participants in the profile 2 had lower levels of all analyzed parameters except for the

Table 2. Hematological profiles of study participants following cluster analysis.

Parameter	Profile 1		Profile 2	
	Mean	*Standard deviation*	*Mean*	*Standard deviation*
WBC (x 10^3/µL)	5.47	1.21	7.83	2.29
RBC (x 10^6/µL)	4.56	0.52	4.51	0.45
HGB (g/dL)	13.01	1.27	11.49	1.07
HCT (%)	39.07	3.85	34.94	3.10
MCV (µm^3)	28.65	1.98	25.55	2.32
MCHC (pg)	85.97	5.40	77.64	5.95
MCH(g/dL)	33.31	0.61	32.76	1.80
PLT (x 10^3/µL)	205.56	71.99	257.26	82.02
MPV (µm^3)	8.50	0.79	8.32	0.75
LYM (x 10^3/µL)	2.53	0.70	3.51	1.20
MON (x 10^3/µL)	0.48	0.15	0.72	0.28
NEU (x 10^3/µL)	2.16	0.78	2.98	1.32
EOS (x 10^3/µL)	0.25	0.23	0.55	0.66
BAS (x 10^3/µL)	0.03	0.02	0.07	0.21

Table 3. Multiple logistic regression of factors associated with *S. mansoni* infection adjusted by hematological profile, age group and sex, work and water contact.

Factor		Odd ratio (95% CI)	*P value*
Hematological profile:	Profile 1 (reference)		
	Profile 2	1.50 (1.06 - 2.11)	***0.021***
Age group (years):	> 40 (reference)		
	21 - 40	1.28 (0.81 - 2.01)	*0.286*
	11 - 20	1.02 (0.65 - 1.62)	*0.920*
	6 - 10	1.52 (0.94 - 2.44)	*0.086*
Sex:	Female (reference)		
	Male	1.03 (0.53 - 1.40)	*0.847*
Rice field worker:	Yes (reference)		
	No	0.84 (0.53 - 1.31)	*0.430*
Routine water contact:	Yes (reference)		
	No	0.99 9 (0.68 - 1.44)	*0.971*

platelet count, and lower level of hemoglobin (Table 2). The mean HGB level of profile 2 members was 11.49 ± 0.45 g/dL.

Factor associated with *Schistosoma mansoni* infection and hematological cluster

The bivariate logistic regression analysis using profile 1 as reference, showed that participants having profile 2 had higher risk of being infected by *S. mansoni* (OR = 1.71;95% CI 1.27 – 2.3;*P = 0.0003*). Similarly, the risk of *S. mansoni* infection decreased with increasing age and participants aged between 6 to 10 years old had significantly higher risk of being infected (OR = 2.02; 95% CI 1.34 – 3.06; P = 0.0007). However, when we adjusted *S. mansoni* risk factors by hematological profiles, age, gender, working in irrigated rice field and having routine water contact, only the hematological profile remained a significant risk factor (Table 3).

In order to confirm the tight link between hematological profile and *S. mansoni* infection, we performed the reverse analysis by testing the association between the poor hematological condition (here profile 2) and parasitic infection, gender, age and exposure of infective. The Multiple logistic regression showed that in addition to *Schistosoma mansoni* infection (P = 0.023),

Table 4. Multiple logistic regression of factors associated with hematological profile adjusted by *S. mansoni* infection, age group and sex, work and water contact.

Factor		Odd ratio (95% CI)	*P value*
S. mansoni infection:	No (reference)		
	Yes	1.49 (1.06 - 2.10)	***0.023***
Age group (years):	> 40 (reference)		
	21 - 40	1.60 (0.97 - 2.63)	0.068
	11 - 20	5.39 (3.42 - 8.50)	***< 0.001***
	6 - 10	16.82 (10.33 - 27.39)	***< 0.001***
Sex:	Female (reference)		
	Male	0.70 (0.51 - 0.96)	**0.025**
Rice field worker:	Yes (reference)		
	Non	0.86 (0.55 - 1.35)	*0.509*
Routine water contact:	Yes (reference)		
	No	0.99 9 (0.67 - 1.46)	*0.969*

Table 5. Linear mixed model analysis of the variation of hematological parameters post-treatment with praziquantel adjusted by age and sex.

Parameters		Coefficient value (95% CI)	P value
WBC (x 10^3/µL)	β_0	7.99 (7.16 - 8.82)	0.897
	β_1	0.05 (-0.74 - 0.847)	
RBC (x 10^6/µL)	β_0	4.41 (4.23 - 4.58)	0.918
	β_1	-0.01 (-0.21 - 0.19)	
HGB (g/dL)	β_0	11.32 (10.84 - 11.79)	0.316
	β_1	-0.267 (-0.80 - 0.26)	
HCT (%)	β_0	34.27 (32.98 - 35.58)	0.280
	β_1	-0.82 (-2.33 - 0.68)	
MCV(µm^3)	β_0	77.59 (75.731 - 79.45)	0.269
	β_1	-1.51 (-4.21 - 1.19)	
MCHC (pg)	β_0	25.62 (24.93 - 26.32)	0.360
	β_1	-0.49 (-1.55 - 0.578)	
MCH (g/dL)	β_0	33.02 (32.59 - 33.44)	0.684
	β_1	0.14 (-0.53 - 0.81)	
PLT (x 10^3/µL)	β_0	254.72 (232.91 - 276.53)	0.787
	β_1	-4.52 (-37.57 - 28.54)	
MPV(µm^3)	β_0	8.24 (8.03 - 8.45)	**0.003**
	β_1	0.48 (0.16 - 0.80)	
LYM (x 10^3/µL)	β_0	3.69 (3.40 - 3.98)	0.885
	β_1	0.02 (-0.31 - 0.36)	
MON (x 10^3/µL)	β_0	0.73 (0.66 - 0.80)	0.784
	β_1	0.01 (-0.08 ; 0.10)	
NEU (x 10^3/µL)	β_0	2.60 (2.22 - 2.99)	0.237
	β_1	0.25 (-0.17 - 0.69)	
EOS (x 10^3/µL)	β_0	0.65 (0.33 - 0.97)	0.877
	β_1	-0.02 (-0.24 - 0.21)	
BAS (x 10^3/µL)	β_0	0.06 (0.05 - 0.07)	0.804
	β_1	-0.00 (-0.01 - 001.)	

male subjects (P = 0.025) and mostly younger age were risk factor of having poor hematological profile. The details of the analysis are shown in Table 4.

Praziquantel treatment and hematological profile

Following the first parasitological examination, all infected subjects were treated with praziquantel and revisited 45

days later. This enabled us to effectively determine non-cured subjects and its impact on hematological parameters. For this purpose we used a Linear mixed model to compare the variation of the hematological parameters in relation with *S. mansoni* infection post-treatment. The results showed that there were no uniform variation of the measured parameters. Nevertheless, we observed a slight increase of the total WBC count and a decrease of all RBC related parameters (Table 5).

DISCUSSION

Mass drug administration programs has enabled tremendous advances toward schistosomiasis control throughout Africa this last decade (WHO, 2017). Despite this unprecedented achievement, the possibility of reinfection after cure and the lack of preventive vaccine make the elimination of this parasitic disease very challengingin one hand and in the other hand allow the persistence of light infections among endemic populations. Also, there still a need to understand the impact of non-severe infections on the general health indicators. To this purpose, we used robust statistical approach to assess the association between *S. mansoni* infection and various hematological profilesof people living in an endemic foci in western Burkina Faso. The basic results showed that although light *S. mansoni* infections are the most prevalent status, infected subjects had lower level of HGB, HCT, MCV, MCHC and MPV as compared to level recorded among Schistosoma negative subjects. Other parameters also varied with the presence of the parasite but this was not statistically significant (Table 1). This finding is similar to other recent report in Africa (Koukounari et al., 2006; Mohammed et al., 2006; Afrifa et al., 2017). If schistosomiasis related anemia and its impact on children health has been extensively studied (King et al., 2005; Stecher et al., 2017), the others pathological indicators such as leukopenia, thrombocytopenia, are less studied and are thought to be either associated with more immunological reactions (Souza et al., 2002; Stanley et al., 2003) or specific clinical features in schistosomiasis (Da Silva et al., 2005). Moreover, most studies have focused on hemoglobin level variation among school age children, therefore an analysis using complete blood count from patients of different ages should provide a more realistic view of the impact of *Schistosoma* infection on hematological profile.

Interestingly, the results of the hierarchical ascendant classification preceded by principal component analysis of the measured parameters showed that subjects living in a *S. mansoni* foci in Western Burkina Faso can be grouped in two clusters representing a relatively “normal” and “poor” hematological profile (Table 2). We later showed in a multiple regression analysis that subjects having the hematological profile 2 had a significantly higher risk of *S. mansoni* infection. Conversely, *S. mansoni* infection leads to poor general hematological profile even after adjusting for sex, age group of other exposure variables (Table3 and 4). These results confirm that in addition to anemia, light *S. mansoni* infection without severe clinical signs has deleterious impact on the hematological parameters of individuals regardless of age, gender and routine water contact. Experimental studies in mouse model and field studies in human populations have provided several indications on the mechanism leading to abnormal hematological parameters during the course of schistosomiasis. Hence anemia of inflammation, iron deficiency due to extra-corporeal loss and autoimmune hemolysis are generally accepted as possible cause of anemia (Friedman et al., 2005; Butler et al., 2012). Also, the existence of antibody responses induced by parasite antigens that cross-react with human platelet antigens has been suggested as the main reason leading to schistosomiasis related thrombocytopenia (Stanley et al., 2003). Finally, schistosomes like others helminths are well known to manipulate the host immune response toward their own survival (Maizels and Yazdanbakhsh, 2003; Jenkins et al., 2005). Therefore observed changes in circulating white blood cells numbers following *Schistosoma* infection is linked to basic immune response to the parasite but also to *Schistosoma* induced biased proliferation or decrease in specific immune cells according to the disease stage (Mohammed et al., 2006; Oliveira et al. 2007). Though the probable contribution of other parasitic infections such as malaria cannot be completely ruled out, the fact that *S. mansoni* negative individuals living in the same setting were part of the analysis is strengthening our findings.

In order to assess the effect of praziquantel treatment on the studied parameters, we repeated the same measurements 45 days post-chemotherapy among *S. mansoni* positive individuals using a linear mixed model. The results showed uneven and insignificant variation of the parameters. Koukounari et al. (2006) reported that the long-term effect of praziquantel treatment depends on the baseline intensity of infection as well as the time of control. Our results suggest that a much longer follow-up would enable a much clear differentiation of the trends of hematological profile.

CONCLUSION

Our results drawn from a relatively large number of subjects and a robust analytical approach have proven that light *S. mansoni* infection has a noticeable impact on the hematological profile. The presence of the parasite increased significantly the odd of harboring a poor hematological profile. Also it showed that in endemic setting in West Burkina Faso, a lower hematological parameter could be an indicator of intestinal schistosomiasis. Therefore schistosomiasis control programs should also take into account the

complete hematological disorder induced by infection in addition to anemia.

Competing interests

The authors declare that they have no competing interest.

Author's contribution

HS and JBO designed the study, HS, OD and BS collected the field data, HS, TR and HT performed the statistical analysis, HSc and HT drafted the manuscript and all authors read and approved the manuscript

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