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SOCIO-DEMOGRAPHIC RISK FACTORS OF SCHISTOSOMIASIS *MANSONI* IN PATIENTS WITH GASTROINTESTINAL SYMPTOMS: A SEROPREVALANCE STUDY IN EGYPT

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Abstract

Limited data is available on the epidemiologic status of schistosomiasis *mansoni* in Egypt. The present work aimed to explore the seroepidemiological status of *Schistosoma mansoni* infection in Egypt by screening inhabitants of different Egyptian governorates and its correlation with morbid symptoms and risk factors. Health questionnaires and indirect haemagglutination test (IHAT) were performed upon a cross-sectional study of 1788 individuals from 22 governorates. Socio-demographic variables included sex, age, residence and canal water contact. A multivariate regression model was used to assess associations between *S.mansoni* infection and socio-demographic variables. *S.mansoni* significant titre ≥ 1:160 was detected in 43% of samples. *S. mansoni* showed the highest prevalence in Al-Fayoum (15.2%), Kafr El-Sheikh (11.2%) then Assiut (10.9%) while the least positive results were from Matrouh (0.2%). This may be the first indication to emerging foci in Cairo, Luxor, Aswan, Suez, Port Said and the Red Sea Governorates. Anti-*S.mansoni* antibodies were least detected at 11-20ys while they were the highest at 41-50ys, the highest titres (1/1280) were achieved by the age group 31-40ys.Male gender was a risk factor as 48.2% of males were IHAT +ve. Contacting canal water tends to be advantageous for schistosomiasis *mansoni* as 72.6% had a history of canal contact and 96.7% of them achieved the highest titre. The alteration in the actual prevalence of schistosomiasis *mansoni* in Egypt with emergence of new foci including Cairo, Luxor, Aswan, Mersa-Matrouh and the north-eastern province alongside Suez Canal that may be explained by the associated socioepidemiologic risk factors.
Keywords: Egypt, *Schistosoma mansoni*, Seroepidemiology, IHAT.

Introduction

Schistosomiasis is a crucial public health problem that impedes social and economic progress in endemic areas (Xie *et al*, 2014). It has been recognized as one of the chief parasitic problems worldwide with considerable socio economic consequences (WHO, 2008). In tropical and subtropical countries, schistosomiasis is prevalent in more than 200 million people in 76 countries (Zhou, 2005). On a universal scale, one of thirty are affected with schistosomiasis and approximately 779 million people are in endemic areas in the Middle East, South America, Caribbean, Southeast Asia and predominantly the sub-Saharan Africa (Chitsulo *et al*, 2004). Intense poverty, ignorance of risks, shortage of health conveniences in addition to the contaminated environment are all contributing to the possibility of the infection (Fenwick *et al*., 2003). The WHO (2007) considered the previous factors as responsible for resurrection of the disease. Significantly, low schistosomiasis endemicity was distinguished in the Eastern Mediterranean Region (EMR) in particular; Egypt, Iraq, Syria, Libya, Oman (Allam, 2012) and Saudi Arabia (Al-Quraishy *et al*, 2014).This is apart from hepatic schistosomiasis is consi-dered to be one of the most prevalent forms of chronic liver disease worldwide, resulting in the morbidity and mortality due to complications of the liver fibrosis (El Moghazy *et al*, 2015) as well as co-infection of *Schistosoma* species with hepatitis B or hepatitis C viruses (Abruzzi *et al*, 2016)

In Egypt, in 1967, the overall prevalence of schistosomiasis was about 40% before the national control program started by WHO/ EMRO. In 2006, due to the organizational measures, it improved to less than 3%. However, spreading foci with prevalence rate about 10% are still there (Liu *et al,* 2011).

Parasitological and immunological assays for schistosomiasis are crucial diagnostic approaches (Cheesbrough, 2004). Yet, diagnosis of schistosomiasis by detection of specific antibodies is expected to be more sensitive than the conventional detection of eggs in stool or urine (Hamilton *et al*, 1998). Moreover, in low intensity infections, with only few or no eggs being excreted, parasitological testing is inadequate and antibody detection may be the only means to diagnose schistosomiasis (Liu *et al*, 2011).

In order to incorporate serodiagnostics in large scale screening practice, an easy to use, sensitive and specific serological tests as ELISA and IHAT were recommended. Nevertheless, difficulties in soluble egg antigen (SEA) preparation in large amounts for ELISA tend to restrict its use making IHAT, using the adult worm antigen (AWA) proved easier and more commercially available (van Gool *et al*, 2002)

Thus, owing to its high sensitivity and simplicity, IHAT was and still widely used in schistosomiasis diagnosis as considered the quick screening assay for schistosomiasis in target populations (Kinkel *et al*, 2012).

Consequently, the present work aimed to explore the seroepidemiological status of *Schistosoma mansoni* infection in Egypt by screening patients inhabit different Egyptian governorates and its correlation with the presenting morbid symptoms and some risk factors.

Subjects, Material and Methods

This cross-sectional study included 1788 individuals over the period from September 2011 till June 2014. The main target populations in the present study were cases suspected clinically as having schistosomiasis *mansoni*. Including inpatients admitted to the Tropical Medicine Department at Kasr Al-Ainy Teaching Hospital and patients attending the Internal Medicine outpatient clinics, Faculty of Medicine, Cairo University. All subjects subjected to history taking, full clinical examination and IHAT for serum samples. Data were collected and recorded (demographic data; age, sex, residence, history of contact with canal water**)**. All information was documented in a data collection sheet.

Sample processing: Fresh blood samples were taken, left to stand, centrifuged and sera were kept in a deep freezing (-20°C) till needed. Schistosomiasis Fumouze adult worm antigen indirect haemagglutination test (AWA/IHAT) was used for quantitative detection of antibodies in sera of patients with symptoms suggestive of *S. mansoni* (Bilharziose Fumouze previously A.D.M. manufactured by SERFIB 2, rue de la Bourse 75002 Paris/France, Distributed by Fumouze Diagnostics, France No: 1300132-09/04). Since cross-reactive antibodies (parasitic or autoimmune) were frequently seen with other serological tests for schistosomiasis (Tsang, *et al,* 1984; Aronstein, *et al*, 1986, Correa-Oliveira, *et al*, 1988), the included large sequences of controls in the present study. Titres <1:160 were considered non-significant reactions. It may correspond with a past or an already treated infection. These tests were repeated 2 to 3 weeks later. A corresponding Titre ≥1:160 were considered as a significant reaction (Presumption of acute infection). Subjects who received any antibilharzial treatments were excluded

Statistical analysis: Data were analyzed using Statistical Package for Social Sciences (SPSS) version 17 (Chicago, IL, USA). Positive rates were expressed as percentages. The differences in prevalence rates among groups of the studied variables were compared by the Chi-square test. Data were considered significant for a p-value<0.05.

Conflict of Interest: The present authors declare that they have neither competing interests nor got any financial support.

Ethical approval: All procedures performed though out the study involving human participants were in accordance with the ethical standards of ethical committee of Faculty of Medicine, Cairo University and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participation in the present study was optional and participants or their guardians signed an informed consent for sample collection and subsequent analysis according to national guidelines.

Results

Of 1788 studied individuals, *S. mansoni* significant titre (≥1:160) was detected in 769 (43%) sera (Tab.1). *S. mansoni* was significantly higher in rural than urban governorates among IHAT+ve cases significant titres were detected at Al-Fayoum governorate (15.2%), followed by Kafr El-Sheikh (11.2%) and then Assiut (10.9%) while the least positive results were those from Mersa-Matrouh (0.2%). Infection rates were reported in Great Cairo (9.8%), Luxor (0.3%), Aswan (0.4%), Suez (1.3), Port Said (1.6) and the Red Sea Governorates (0.8%)(Tab. 3). The mean age of the studied individuals was 38.75±12.31 yrs old. Anti-*S. mansoni* antibodies were least detected at age group from11-20ys (15.1%) while they were the highest at age group from 41-50ys (52.7%) while highest titres (1/1280)(17.8%) were achieved by age group 31-40ys.1417 males were included, of them, 48.2% were IHAT +ve while out of the participated 371 females, 23.2% were IHAT +ve. 15.8% of males achieved the highest titre (1/1280) while detected only in 5.1% of females (Tabs. 2, 4 &5). The prevalence of Anti-*S. mansoni* antibodies were the highest in patients presenting with vague abdominal symptoms (58.6%), in whom the highest titre (1/1280) was detected (48%) (Tabs. 6 & 7).

A total of 72.6% population had a history of canal water contact, of them, 93.7% were anti-*S. mansoni* +ve by IHAT. 96.7% of them achieved the highest titre; 1/1280 (Tabs. 2&8). Taking in consideration the size and diversity of the control groups, the specificity observed with the WA/IHAT was 98.6 % for the cutoff titers of 1:160.

Table 1: Distribution of *S. mansoni* IHAT *+ve* titres among individuals

Titer	Frequency	%
1/1280	243	13.6
1/640	162	9.1
1/320	180	10.1
1/160	184	10.3
Negative	1019	57
Total	1788	100

Table 2: Univariate and multivariate logistic regression analysis of potential risk factors associated with anti-*S. mansoni* antibodies seropositivity among individuals

items	Total No. (%)	Infected No. (%)	Univariate analysis OR(CI)	*P*	Multivariate analysis [a] OR(CI)	*P*
Age 1-10(y)	18(1)	4(22.2)	1 (Ref.)	-		
11-20	86(4.8)	13(15.1)	2.121(0.666-7.235)	-		
21-30	377(21.1)	106(28.1)	2.134(0.687-8.463)	0.191		
31-40	522(29.2)	266(51.0)	3.465(0.853-10.473)	0.006		
41-50	455(25.4)	240(52.7)	3.021(0.652-6.235)	0.024	1.36(0.521-6.234)	0.041
51-60	274(15.3)	119(43.4)	2.012(0.432-9.216)	0.287	1.12(0.325-6.884)	0.062
Male	1417 (79.2)	683 (48.2)	1.6(0.832-5.266)	0.012	1.42(0.365-7.125)	0.004
Female	371 (20.7)	86 (23.2)	1(Ref.)	-		
Exposure to contaminated water						
Exposed	1298 (72.6)	721(93.7%)	3.256(0.565-7.223)		0.003 1.698(0.987-8.565)	
Non exposed	490 (27.4)	48 (6.2%)	1(Ref.)		0.011	

[a] Only variable with $p < 0.2$ included in multivariate model analysis. Confidence intervals and p values derived from univariate and multivariate logistic regression models, CI = confidence interval; OR = adjusted odds ratio.

Table 3: Residence distribution of *S.mansoni* IHAT +*ve* individuals from different Egyptian governorates

Governorate	Frequency among IHAT +ve cases	% among IHAT+ve cases	P value
Al- Menofia	6	0.3	0.125
Al-Bahr Al-Ahmar	15	0.8	
Al-Behira	85	4.7	
Dakahlia	161	9.0	
Gharbia	53	3.0	
Al-Minia	104	5.8	
Qualyobia	132	7.3	
Sharkia	21	1.2	
Alexandria	69	3.8	
Assiut	194	10.9	
Aswan	8	0.4	
Bani-Suef	86	4.8	
Suez	24	1.3	
Al-Fayoum	272	15.2	
Damietta	19	1.1	
El-Sadat	7	0.4	
Kafr El-Sheikh	202	11.2	
Giza	105	5.9	
Ismailia	12	0.7	
Cairo	176	9.8	
Luxor	5	0.3	
Mersa-Matrouh	3	0.2	
Port Said	29	1.6	
Total	1788	100.0	

Table 4: Anti-*S.mansoni* antibodies titres distribution among different age groups

Ages / Titre	1-10y (n=18)	11-20y (n=86)	21-30y (n=377)	31-40y (n=522)	41-50y (n=455)	51-60y (n=274)	Pearson Chi-Square	*P*
1/1280	0(0)	5(5.8)	33(8.8)	93(17.8)	69(15.2)	43(15.6)	111.646	0.0000
1/640	1(5.6)	0(0)	25(6.6)	61(11.7)	47(10.3)	28(10.2)		
1/320	0(0)	2(2.3)	21(5.6)	56(10.7)	68(14.9)	33(12.04)		
1/160	3(16.7)	6(7.0)	27(7.2)	56(10.7)	56(12.3)	36(13.1)		
Negative	14(77.8)	73(84.9%)	271(71.9%)	256(49.0)	215(47.3)	190(69.3)		

Table 5: Anti-*S.mansoni* antibodies titres distribution according to sex

sex / Titre	Male (n=1417)	Female (n=371)	Pearson Chi-Square test	*P* value
1/1280	224(15.8%)	19(5.1%)	77.951	0.000
1/640	144 (10.2%)	18(4.9%)		
1/320	155 (10.9%)	25 (6.7%)		
1/160	160 (11.3%)	24 (6.5%)		
Negative	734 (51.8%)	285(76.8%)		

Table 6: Seroprevalence of anti-*S.mansoni* antibodies according to gastrointestinal symptoms

Main Symptom	Frequency (n=1788) No. (%)	Infected (n=769) No. (%)	Pearson Chi-Square test	*P*
Abdominal distension	543(30.4%)	254(33%)	146.089	0.000
Abdominal pain	267(14.9%)	121(15.7%)		
Haematemesis	94(5.2%)	29(3.7%)		
Jaundice	73(4.1%)	32(4.2%)		
RT hypochondrial pain	280(15.7%)	126(16.4%)		
Vague abdominal symptoms	1376(76.9%)	451(58.6%)		

Table 7: Anti-*S.mansoni* antibodies titres distribution according to gastrointestinal symptoms

Symptom / Titre	Abdominal distension (n=543)	Abdominal Pain (n=267)	Haema-temesis (n=94)	Jaundice (n=73)	RT.hypochondrial pain (n=280)	Vague abdo-0minal symp-toms (n=1376)	Pearson Chi-Su-are test	*P*
1/1280 (n=243)	77(31.7%)	45(18.5%)	15(6.2%)	17(7%)	28(11.5%)	117(48%)	219.898	0.0000
1/640 (n=162)	54(33.3%)	33(20.4%)	7(4.3%)	5(3.1%)	34(21%)	110(68%)		
1/320 (n=180)	39 (21.7%)	26(14.4%)	6(3.3%)	6(3.3%)	26(14.4%)	68(37.8%)		
1/160 (n=184)	84(45.7%)	17(9.2%)	1(0.5%)	4(2.2%)	38(20.7%)	156(84.8%)		
Negative (n=1019)	289 (28.3%)	146 (14.3%)	65(6.4%)	41(4%)	154(15.1%)	925(90.7%)		

Table 8: Anti-*S.mansoni* antibodies titres distribution according to contaminated water exposure

Exposure to canals water / Titre	Exposed (n=1298)	Non Exposed (n=490)	Pearson Chi-Square test	P value
1/1280 (n=243)	235 (96.7%)	8(3.3%)	306.347	0.0000
1/640 (n=162)	152(93.8%)	10(6.2%)		
1/320 (n=180)	169(93.9%)	11(6.1%)		
1/160 (n=184)	165(89.7%)	19(10.3%)		
Negative (n=1019)	577(56.6%)	442(43.4%)		

Discussion

Although it is well documented that schistosomiasis *mansoni* is endemic in Egypt, yet detailed studies describing its pattern of prevalence are still in need. The WHO reports suggested that substantial reductions in *S. mansoni* have been achieved on a countrywide level and the entire obtainable records pointed to a generally decrease of *S. mansoni* rather than increase (El Alamy and Cline, 1977). These records ascertain that by the end of 2010, only 20 villages in the whole Egypt had prevalence more than 3.5% and none had prevalence more than 10% (WHO, 2011). These reports were based on Egyptian Ministry of Health (MOH) data described incessant descending prevalence rates (Webbe and El Hak, 1990). Noteworthy, the MOH evaluations are, in the main, considered reasonably strict. Though, they may show some incongruity depending on the impact of the technician, the intensity of the infection besides the constancy of recording systems.

Consequently, in this study screened the seroepidemiological status of *S. mansoni* infection in Egypt correlating the infection with other sociodemographic and morbidity factors. The first country-wide survey was published by Scott in 1937(Hussein *et al*, 2000). Later on, MOH records ascertained and extended Scott's data (Weir *et al*, 1952; Wright, 1973).

Miller *et al*. (1976) used a stratified random sample of 11,337 participants from Kafr El Sheikh in Lower Egypt, Beni-Suef in the Middle of Egypt, and Aswan in Upper Egypt. They revealed infection rates of *S. mansoni* from 20% in Kafr El Sheikh to less than1% in Middle and Upper Egypt.

Several studies were performed later on included six governorates in Lower Egypt; Kafr El-Sheikh, Gharbia, Menofia, Qalyobia, Sharkia and Ismailia, where *S. mansoni* was thought to be endemic with prevalence rates ranged from 17.5% to 42.9% with an average of 36.45% (El Khoby *et al*,1991; El-Enien *et al*,1993; Medhat *et al*,1993; Barakat *et al*,1995; Nooman *et al*, 2000; Abdel-Wahab *et al*, 2000; El Khoby *et al*, 2000; Abo-Madyan *et al*, 2004; Othman, 2013; Kamel *et al*, 2014).

In continuity with these studies, herein an indication of lower infection rates than those prior reports (Menofia, Gharbia, Qualyobia and Kafr El-Sheikh Governorates: 0.3%, 3.0%, 7.3% and 11.2% respectively).

However, the present study spotlights some alteration in *S. mansoni* distribution to include additional areas in Southern Delta (Al-Behira, Dakahlia, Sharkia, Alexandria, Damietta and El-Sadat Governorates 4.7%, 9.0%, 1.2%, 3.8%, 1.1%, & 0.4% respectively).

Samples of the present study obtained from patients inhabit the Nile Valley including Great Cairo, Giza, Al-Fayoum, Beni-Suef, Al-Minia, Assuit, Luxor and Aswan showed 9.8%, 5.9%, 15.2%, 4.8%, 5.8%, 10.9%, 0.3% and 0.4% infection rates respectively.

The present results reported higher records of infection in Al-Fayoum, Beni-Suef, Al-Minia, and Assuit than previous research surveys (Miller *et al*, 1981).

On the other hand, in Giza, higher infection rates (33.7%) were previously reported by Talaat *et al*. (1999) which could be alleviated by proper application of control and mass treatment programs

The present study reported for the first time infection rates in some localities including Great Cairo (9.8%), Luxor (0.3%) and Aswan (0.4%) especially that no available current records on foci of *S. mansoni* in great Cairo and reports analyzing infection in the fishing communities located on Lake Nasser found no cases were reported among fishermen examined (Miller *et al*, 1981, Hammam *et al*, 2000). This agreed with El Khoby *et al*. (2000) who found that *S. mansoni* was almost spread into Upper Egypt, where sporadic areas of transmission were expected.

During this search through literature, no available data were found on infection rates in Suez and Port Said governorates that we report infection rates to be1.3% and 1.6% respectively. Our study reported that Ismailia governorate show decreased infection rates to 0.7% from 42.9% (Nooman *et al*, 2000).

In addition, little is known about the actual prevalence in some newly emerging foci as Mersa-Matrouh and The Red Sea governorates that was found to be 0.2% and 0.8% respectively. Some of these localities were described as completely free of *S. mansoni*. These changes may be due to changing the pattern of irrigation used.

The current study reported that the strongest risks for *S. mansoni* were male gender, middle ages and males bathing in canal water. The present study reported a higher prevalence of infection in males than females as males have 1.6 times higher risk for *S. mansoni* infection.

The significant differences ($p<0.0005$) between sexes in *S. mansoni* prevalence in all age groups could also be explained by their larger contact to canal water during agricultural activities. This factor promotes 3.256 higher risk of contracting schistosomiasis *mansoni* and is strongly correlated to living in rural areas including the majority of inhabitants of these governorates.

The present study also confirmed that age was a risk factor as the middle ages (21-40ys) prevalence's were respectively double and triple that in adolescents (11-20ys). Higher risk was at 31-40y who have 3.465 times more than other age groups. What is more was that reported a statistically significant correlation between seroprevalence of anti-*S.mansoni* antibodies and various gastrointestinal symptoms ($P<0.0005$). Thus, the prevalence of GIT morbidity is strongly correlated to *S. mansoni* infection. Jaundice, haematemesis and right hypochondrial pain are significantly correlated to *S.mansoni* infection ($p<0.000$) which may indicate the concomitant hepatic morbidity. This probably results from the long-standing schistosomiasis *mansoni* which increased intensity of infection, leading to augmented morbidity. Despite that our study confirmed the significant correlation of abdominal pain and distension with *S. mansoni* ($P<0.0005$) however, one is unaware of comparable studies correlating them to *S. mansoni* morbidity.

It is noteworthy that, the contribution of some other risk factors (occupations, seasonal variations& concomitant parasitic infections) could not be consistently projected as they perplex each other. Thus, requiring more complicated statistical methods indulging multivariant analysis.

Conclusion

The outcome results conjecture that there is an incessant alteration of *S. mansoni* infection patterns in Egypt including newly reported foci as Great Cairo, Luxor, Aswan, Mersa-Matrouh and the north-eastern province of Egypt including some areas alongside Suez Canal. More prominently, extended surveys are needed to indicate the real shift of schistosomiasis *mansoni* infection.

This progress may guarantee the involvement of exploration factors that may give approaching into why *S. mansoni* is still being established thus, considerably diminish the prevalence of schistosomiasis in numerous areas.

Recommendations

Schistosomiasis is one of the major communicable diseases of public health and socioeconomic importance. The mass treatment, provision of adequate clean-water supply and controlling the intermediate snail host are a must.

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