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Invited Review

Female genital schistosomiasis (FGS): from case reports to a call for concerted action against this neglected gynaecological disease

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ABSTRACT

In recent years, control of neglected tropical diseases has been increasingly gaining momentum and interventions against schistosomiasis are being progressively scaled-up through expansion of donated praziquantel and preventive chemotherapy campaigns. However, the public health importance of female genital schistosomiasis is not fully recognised nor its control is adequately addressed. Taking a clinical and anatomopathological perspective, we evaluated the available literature to highlight the importance of female genital schistosomiasis and its connections with two sexually transmitted infections of global importance, Human Immunodeficiency Virus (HIV) and Human Papilloma Virus. Outside the long list of clinical descriptive reports beginning in 1899, there is presently a shocking gap in epidemiological assessment and a significant underestimation of the burden of FGS remains. The scarcity of integrated approaches to address female genital schistosomiasis calls for more concerted action in its detection, treatment and prevention alongside other concomitant women's health issues, otherwise female genital schistosomiasis will remain a neglected gynaecological disease.

1. Introduction

Schistosomiasis is a water-borne parasitic disease caused by infection with trematode worms of the genus *Schistosoma*. The disease was originally described in Egypt by Theodor Bilharz in 1851 and today can be found throughout Africa, South America and Asia (Colley et al., 2014). Infection may affect humans of all ages and genders, and globally it has the highest burden of disease among the 17 recognised neglected tropical diseases (World Health Organization (WHO), 2016b). Owing to a variety of factors underlying an individual's exposure and infection, there can be substantial differences in prevalence and intensity of infection across communities, as well as an associated spectrum in the severity of disease. These manifestations are determined by a number of causal factors such as the species of schistosome, the duration of infection, host-specific factors that influence immuno-pathological lesions to the worm eggs and access to praziquantel treatment (Hirayama, 2006). Furthermore, as individuals rarely harbour schistosomiasis alone, prior infection with *Schistosoma* can increase the severity of other bacterial, protozoal or helminth infections acquired later (Abruzzi and Fried, 2011).

Schistosomiasis can be broadly classified as either acute or chronic presentations (Colley et al., 2014). Upon initial percutaneous infection by cercariae, acute symptoms may include dermatitis, then later non-specific symptoms of fever, headache and cough. Acute symptoms normally resolve in a few weeks but in exceptional cases, death by hyper-infection may occur. As adult schistosomes mature within the body and commence egg deposition, chronic manifestations ensue, typically related to immunopathological lesions and the formation of granulomata in various organs around eggs (Colley et al., 2014). The involvement of the intestinal tract with hepato-splenic disease and the urinary tract with its associated organs is well-known (Centers for Disease Control and Prevention (CDC), 2012 http://www.cdc.gov/parasites/schistosomiasis/disease.html; WHO, 2016, http://www.who.int/mediacentre/factsheets/fs115/en/). Since eggs can be found throughout the body in variable amounts, other clinical and pathological diseases can be found in the heart, lungs, brain and spinal cord as well as in the genital organs of both genders (Barsoum et al., 2013).

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The pathological alterations due to the presence of schistosome eggs in the genitalia of women have been defined as a particular entity called female genital schistosomiasis (FGS). In 1997, the Gender Task Force of the Tropical Disease Research Programme (TDR) of the WHO included FGS in a list of scientific areas that deserve higher research priority (Poggensee et al., 1999). Since then, however, the extent of morbidity ascribed to FGS, which can be found in both the lower and upper genital tract, has continued to be insufficiently addressed. Moreover, FGS has failed to be reported at national levels which has hampered an international appraisal. As an unfortunate outcome, prevention and control of FGS is largely disconnected from global efforts to improve the reproductive and sexual health of women. To address this, we attempted to draw together the available literature to give a continental perspective and highlight how FGS should be integrated into a broader vision of improving women's health.

2. Methodology

PubMed was used as the search tool. The key words used to gather information on FGS in general were 'female', 'genital' and ' schistosomiasis'. Only publications treating the clinical and anatomopathological aspects of FGS were selected and mapped or displayed in the table. Articles published between 1899 and September 2015 were included. Articles in English, French, German and Spanish were considered. Articles in Portuguese, Japanese or Chinese were included only as cited in Table 1 or Fig. 1. A specific review was performed on FGS attributed to *Schistosoma haematobium* and its association with HIV infection. The following keywords were used: 'HIV' OR 'acquired immunodeficiency syndrome' AND 'schistosomiasis' OR 'bilharzia' or 'haematobium'. Owing to their wider implications, publications that addressed schistosomiasis during pregnancy and HPV/cervical cancer, when encountered during the initial literature review, were also inspected but the topic was formalised in the initial search algorithm.

3. An overview of the FGS literature

A total of 193 publications featuring reports on the clinical and pathological presentation of FGS were identified while preparing this review. A considerable proportion describe African cases published during the colonial era (Fig. 1). Some 44 publications were from Europe, USA and Oceania, describing FGS in migrants or travellers coming from schistosomiasis-endemic countries (Table 1). The large majority of the reviewed publications were case reports or case series; the oldest published FGS case was reported in the Lancet in 1899 (Madden, 1899). The analysis of case reports and case series shows that every female genital organ (vulva, vagina, uterine cervix, uterine body, Fallopian tubes and ovaries) can be affected by schistosomiasis. We note that uterine body involvement is greatly under-reported in such reports, being clearly revealed upon comparison with findings from post-mortem studies. These latter studies demonstrate that the most frequently affected gynaecological organs are the uterine cervix and the uterine body, followed by the adnexa and the vulvo-vagina (Charlewood et al., 1949; Gelfand and Ross, 1953; Youssef et al., 1970; Gelfand et al., 1971; Edington et al., 1975). Of the three schistosomes of most medical significance, the majority of FGS is caused by *S. haematobium* but in Brazil, for example, FGS has been shown to be caused by *Schistosoma mansoni* (Chaves and Palitot, 1964; Coelho et al., 1979; Poggensee et al., 2001; Downs et al., 2011; Goncalves Amorim et al., 2014). In Asia, cases of FGS have also been described as resultant from *Schistosoma japonicum*. Less important schistosome species such as *Schistosoma intercalatum* have also been shown to cause FGS (Koller, 1975; Berry, 1976; Yang, 1984; Picaud et al., 1990; Qunhua et al., 2000; WHO, 2016, http://www.who.int/schistosomiasis/genital_schistosomiasis/en/).

Most of the FGS cases reported before 1990 probably underrepresented the real burden of FGS for, in our opinion, they were based on reports from African urban centres or in northern countries where more advanced screening tools were available. Several more recent studies attempted to address this systemic bias by

Table 1
Forty-six publications out of the 193 reviewed papers are from Europe, USA and Oceania describing Female Genital Schistosomiasis in migrants or travellers coming from schistosomiasis endemic countries. The table provides an overview of countries of diagnosis, countries of infection, patient number and age, clinical condition and *Schistosoma* spp.

Country of diagnosis	Schistosomiasis infestation origin	Age (years)	Schistosomiasis-associated clinical condition	*Schistosoma* spp.	Publication reference number
UK	Malawi Lake, Zimbabwe (t), Zambia, Nigeria, Zimbabwe (m)	34, 43, 51, 26, 39, 37, 27, 31, 28, 29, 28, 29	Vulvar granuloma (3 cases), adnexal mass, infertility, tubal carcinoma, ectopic pregnancy, teratoma, HPV/HIV infection, cervicitis, cervical carcinoma in situ	*S. haematobium*	14, 17, 37, 107, 147, 148, 156, 168, 183
USA	Senegal, East Africa, Liberia, Guinea, South Africa (m)	27, 20, 28, 41, 22, 20, 63, 32, 37	Cervical dysplasia with HPV, cervical dysplasia with HPV/HIV, sandy patches, ectopic pregnancy, salpingitis, infertility, perianal fistula, cervical cancer without HPV	*S. haematobium*, *S. mansoni* (1 case)	2, 13, 45, 54, 93, 131, 154
France	DRC (m), Mauritania (m), Senegal (ms), Tunisia (m), Mali (m), Mali (t), Senegal (m)	28, 34, 22, 29, 32, 35, 29, 21, 33, 27	Infertility, cervical dysplasia, tubal obstruction, hydrosalpinx, adnexal mass, secondary amenorrhea, endometritis, ectopic pregnancy	*S. haematobium*, *S. mansoni* (DRC, 1 case from Senegal)	51, 58, 60, 108, 123, 124, 165
Germany	Angola, Sierra Leone, Togo (m)	24, 30, 21	Ectopic pregnancy, leiomyoma, infertility, adnexal tumour	*S. haematobium*	86, 118, 161
Netherlands	Malawi Lake, Mali (t)	37, 33	Leiomyoma, infertility	*S. mansoni*, *S. haematobium*	29, 79
Spain	Nigeria (m) Mali (t)	26	Infertility, vulvitis	*S. haematobium*	15, 50
Switzerland	Egypt, Malawi Lake (t)	54, 26	Vulvar granuloma, asymptomatic ovarian and tubal schistosomiasis, vulvar lesion and cervical lesions	*S. haematobium*	28, 76, 105
Portugal			Ovarian schistosomiasis, external genital mass		104, 179
Australia					91
Belgium	Mali, Senegal (t)	20	Vulvar mass	*S. haematobium*	39
Czech Rep.	Brazil		Hydrosalpynx, tubal schistosomiasis	*S. mansoni*	136
Israel	Ethiopia (m)	19	Recto-vaginal fistula		102
Ireland	Nigeria (m)	31	Ectopic pregnancy, tubal schistosomiasis		67
Italy	South Tunisia (t)		Vaginal mass	*S. haematobium*	23
New Zealand	Malawi Lake	30, 28	Adnexal mass, vulvar lesion	*S. haematobium*	52, 111

m, migrants; t, travellers; HPV, human papilloma virus; HIV, human immunodeficiency virus.

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