Tropical Medicine and Health Vol. 36 No. 4, 2008, pp. 149-154

Original article

Female genital urinary schistosomiasis: Is there an association with infertility?

Innocent Takougang[1, 2*], Pierre Kamtchouing[3], Jean Meli[1], Ndedi Nkele[4], Jean-Joël Keuzeta[2], Siméon Fotso[5], Séraphin Fokoua[4] and Maurice Wamba Temgoua[4]

Received 9 January, 2008 Accepted 7 September, 2008 Published online 9 October, 2008

Abstract: Several authors have reported genital tract involvement in urinary schistosome infection, resulting in local lesions. Pathological changes in the lower and upper genital tract may affect couple sexuality and lead to infertility. Upon informed consent, 123 female subjects responded to a questionnaire related to infertility and history of urinary schistosome infection. A gynecological examination was carried out to assess lower and upper reproductive tract pathologies. Each participant submitted a urine sample for assessment of current urinary schistosome infection. Almost half of the women examined had signs of primary (21%) or secondary infertility (28%). Similarly, almost half of the urine samples collected (44.8%) were positive for microhematuria. The prevalence of infertility was significantly higher among women with microhematuria or a history of hematuria (χ^2=5.42, p=0.06). Women married more than once were 2.64 times more likely to report a history of hematuria than those married only once (p=0.06). Individuals who reported dyspareunia were 2.63 times more likely to report a history of hematuria (p= 0.004). There was an association between hematuria, history of hematuria, female genital schistosomiasis and infertility. An in depth assessment of the causal relationship between urinary schistosomiasis and infertility is warranted.

Keywords: Female Genital schistosomiasis, hematuria, dyspareunia, infertility.

INTRODUCTION

Schistosomiasis is a tropical parasitic disease affecting some 200 million people worldwide. In Cameroon, most of the transmission foci for *Schistosoma haematobium* are in the sahelian zone and in the forest zones of Kumba, Barombi Mbo and Barombi Kotto [1]. Pathological changes associated with urinary schistosomiasis are related to the inflammatory reaction to soluble egg antigens and to the accumulation of eggs in tissues of the genito-urinary tract, leading to injurious granuloma and a wide array of symptoms [2] including petechiae or sandy patches, which are painful on contact [3]. Indicators of urinary schistosome infection include hematuria, dysuria or a combination of such signs [4]. Vaginal schistosomiasis was described for the first time in Egypt. Since then, the involvement of female organs from the vulva to the ovaries has been reported in most endemic countries [5-6]. Female genital schistosomiasis (FGS) thus appears as a neglected disease that affects up to 75% of women living in urinary schistosomiasis endemic areas [7-8]. Amenorrhea, delayed or heavy menses, hormonal imbalances, atrophy of the corpus luteum or developmental discontinuance thereof [9] have been reported in murine schistosomiasis and may explain infertility and subfecundity in humans [10]. Urinary schistosome egg antigens and egg-induced lesions in the vulva, vagina and cervix increase the risk of infection with sexually transmitted diseases agents, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and HIV [11-12], and have been associated with tubal obstruction [13]. The pathological changes

[1]Department of Public Health, Faculty of Medicine and Biomedical Sciences - University of Yaoundé 1; P O Box 1364 Yaoundé, Cameroon
[2]Foundation for Health Research & Development (FOHRED) P O Box 8526 Yaoundé, Cameroon.
[3]Department of Animal Biology and Physiology, Faculty of Science-University of Yaounde 1; P O Box 812 Yaoundé, Cameroon
[4]Department of Gynecology, Faculty of Medicine and Biomedical Sciences - University of Yaoundé 1; P O Box 1364 Yaoundé, Cameroon
[5]Department of Mathematics, Higher Teachers Training College - University of Yaoundé 1; P O Box 47 Yaoundé, Cameroon
Financial support: UNDP/WORLDBANK/WHO: Special Programme for Research Development and Research Training In Tropical Diseases.
*Corresponding author:
Department of Public Health, Faculty of Medicine and Biomedical Sciences - University of Yaoundé 1; P O Box 1364 Yaoundé, Cameroon.
Tel: (237) 22.31.87.53
Fax: (237) 22.22.69.10
E-mail: itakougang@yahoo.com

in the upper and lower genital tract may be associated with a variety of symptoms including intermenstrual and post-coïtal bleeding, vaginal discharge, lower abdominal pain and pain during sexual intercourse [14]. These symptoms may reduce interest in sexual intercourse, as the infected female partner regards it as a painful exercise. The inadequacy of sexual intercourse may lead to couple infertility. Infertility is a common cause of anxiety, resignation, polygamy, divorce, prostitution, frustrations and depression [15]. The present study was a cross sectional community-based study designed to assess the level of association between FGS and infertility.

STUDY DESIGN AND METHODS

The present investigation was a cross-sectional study designed to assess the level of association between urinary schistosomiasis and infertility. Ethical clearance for the investigation was obtained from the Ministry of Public Health and the ethical review committee of the Faculty of Medicine & Biomedical Sciences (FMBS) at the University of Yaoundé 1.

The study was carried out in the village of Barombi Kotto in the Meme Division of Cameroon (South-West Province) in February 1997. Women aged 17 to 35 years were invited to participate after providing informed consent. The infection status was determined based on the history of hematuria outside the menstrual period, hematuria and oviuria [16]. Study participants were submitted to a gynecological examination and a questionnaire related to infertility, couple sexuality and history of sexually transmissible diseases. Infertility was defined as the inability of a couple to achieve pregnancy after one year of regular, unprotected sexual intercourse. Secondary infertility was where the woman had previously been pregnant but not necessarily with the same partner [17]. Women were chosen as the entry point because they are the best indicator of couple infertility. Lesions of the upper genital tract were assessed during a gynaecological examination including guided palpation of the pelvic region. Mucosal erosion, sandy patches, petechiae, papillomatous and granulomatous lesions in the lower reproductive tract were assessed by visual inspection, using a speculum. Each participant provided a urine sample in a 50 ml conical tube. The degree of hematuria was determined to be negative «-», traces « TR», light «+», moderate «++» or large «+++» using Meditest Combi7 reagent strips. Samples were preserved by adding 0.1 g of sodium azide and transported to a central laboratory where they were examined microscopically using the sedimentation technique [4]. *Schistosoma haematobium* eggs where identified and counted. The intensity of infection was determined as the number of *S. haematobium* eggs per 10 ml of urine and classified as light (1-99 eggs), moderate (100-399 eggs) or heavy (more than 400 eggs). All hematuria positive women were treated with Praziquantel 40 mg per kg body weight. The proportion of women that were positive for indicators of infertility and urinary schistosomiasis were compared by computing the Chi-square with Yates correction [18]. Significance of statistical tests was determined at 10% level.

RESULTS

Almost half (49.5%) of the 123 participants showed signs of primary or secondary infertility. Similarly, almost half of the urine samples (44.8%) were positive for microhematuria (Table I). Among these, 24.4% were light «+», 4.2% were moderate «++» and 14.9% were large «+++». A few of the urine samples supplied (13%) were positive for oviuria, among which the intensity of infection was light (11.1%), moderate (2%) or heavy (0.3%).

The rate of primary infertility was higher in subjects positive for oviuria (16.7%) than those unaffected (13.8%). The prevalence of infertility was significantly higher among participants with a history of hematuria than among negative cases (χ^2=5.42, p=0.06). Infertility was associated with microhematuria (χ^2=4.76, p=0.09) but not oviuria (χ^2=1.65, p=0.43). (Table I).

Women who reported matrimonial mobility were 2.64 times more likely to report a history of hematuria than those who had been married only once (p=0.06). Individuals who reported dyspareunia were 2.63 times more likely to report a history of hematuria (p=0.004). Women who reported genital ulcerations were 2 times more likely to report a history of hematuria (p=0.06). The rate of polygamy (p=0.47),

Table I: Comparison of the rate of infertility by various indicators of urinary schistosomiasis in the village of Barombi Kotto (N=123)

Indicator of urinary schistosomiasis	Fertile	Primary infertile	Secondary infertile	Total (%)	χ^2	P value
Oviuria	18 (60.0)	5 (16.7)	7 (23.3)	30 (24.4)	1.65	0.43
Microhematuria	39 (61.9)	6 (9.5)	18 (28.6)	63 (52.2)	4.76	0.09
History of hematuria	13 (43.3)	8 (26.7)	9 (30.0)	30 (24.4)	5.42	0.06

last pregnancy resulting in abortion (p=0.88), history of congenital disease (p=0.75), frequency of sexual intercourse (p=0.24) were independent of the history of hematuria (Table II).

There was an association between history of hematuria and several gynaecological pathologies. Women with abnormal vaginal discharge (OR=2.2) and/or the presence of a pelvic mass were 3.5 times more likely to report a history of hematuria than those without (p=0.01). Women with inguinal adenopathy were 2 times more likely to report a history of hematuria (p=0.09). There was no correlation between history of hematuria and odor (OR=1.25), presence of lesions on the vulva (OR=1.31), uterus (OR=1.13) or cervix (OR=1.35), ovary mobility (OR=1.63) or inguinal adenopathies (OR=1.82) (Table III). Women who had abnormal vaginal discharge were 2 times more likely to have schistosome eggs in the urine (p=0.02). The presence of cervical lesions was independent of oviuria (OR=1.35, p=0.49) (Ta-

Table II: Odds ratios of socio-demographic variables by history of hematuria

Predictor	ni/Ni	%	OR (95%CI)	χ^2	P value
Monogamous marriage	19/123	14%	1.5 (0.49-4.51)	0.54	0.47
More than 1 marriage	6/27	22.2%	2.64 (0.93-7.5)	2.99	0.06
History of congenital diseases	17/123	11.9%	1.19 (0.39-3.57)	0.10	0.75
History of tuberculosis	18/123	13%	0.0	2.44	0.11
History of syphilis	2/5	40%	4.72 (0.52-36.77)	2.36	0.12
Last pregnancy resulting in abortion	9/60	15%	1.13 (0.44-2.86)	0.02	0.88
Genital ulcerations	12/59	20.3%	1.97 (0.93-4.11)	3.30	0.06
History of dysuria	25/78	32.1%	5.71 (2.77-11.82)	30.42	0.000
History of pelvic inflammatory disease	10/51	19.6%	1.98 (0.81-4.76)	2.84	0.09
1-2 sexual intercourses per week	13/114	11.4%	2.32 (0.28-51.16)	1.33	0.24
Desire to change frequency of intercourse	11/69	15.9%	1.35 (0.33-1.69)	0.63	0.42
Experience of dyspareunia	18/86	20.9%	2.63 (1.25-5.55)	7.97	0.004

ni/Ni indicates the proportion of individuals showing the condition in infected and uninfected group
N indicates the total number of observations.

Table III: Odds ratios of gynecologolical pathologies and history of haematuria

Predictor	ni/Ni	%	OR (95%CI)	χ^2	p value
Abnormal vaginal discharge	17/120	14.2%	2.22 (1.18-5.88)	5.15	0.02
Vaginal discharge with full smell	6/42	14.3%	1.25 (0.43-3.49)	0.22	0.64
Abnormal quantity of discharge	7/48	14.6%	1.31 (0.29-2.08)	0.37	0.54
Genital tract pathology					
Vulva with lesions	3/20	15%	1.31 (0.29-3.48)	0.18	0.66
Vaginitis	1/3	33.30%	1.66 (0.2-7.97)	1.25	0.26
Uterus with lesions	6/44	13.6%	1.13 (0.32-2.56)	0.07	0.78
Ovaries abnormal	9/55	16.4%	1.63 (0.25-1.54)	1.36	0.24
Cervicitis	29/138	13.2%	1.35 (0.53-361)	0.46	0.49
Pelvic mass	5/16	31.3%	3.59 (1.16-11.04)	5.58	0.01
Presence of inguinal adenopathy	20/125	16%	1.82 (0.85-3.92)	2.85	0.09

ni/Ni indicates the proportion of individuals showing the condition in infected and uninfected group.
N indicates the total number of observation

ble III).

DISCUSSION

Infertility was independent of oviuria, but its prevalence was significantly higher among women with microhematuria and a history of hematuria. The fact that an association was found between infertility and hematuria, with a history of hematuria, but not oviuria may be attributable to the fact that infertility is a present status related to past influences [19-20]. In further investigations, chronic changes should be assessed through ultrasonographic examination of the urinary bladder, liver and urethers for calcified eggs as an indicator of past urinary schistosomiasis. Other signs such as dysuria should be assessed, as they may precede hematuria. The relevance of history of hematuria as an indicator has not been sufficiently explored. Microhematuria and macrohematuria have been used widely in the diagnosis of urinary, but not genital schistosomiasis [4, 21]. The fact that infertility is a chronic process justifies the use of hematuria and history of hematuria as indicators of past urinary schistosome infection. Several authors have linked hematuria to *S. haematobium* egg antigens that are released through the pores in the walls of eggs that become lodged in genital tissues [2].

The higher rate of genital ulcerations, dyspareunia, and matrimonial mobility among women with history of hematuria corroborates previous findings [22-23]. Dyspareunia may be related to lesions in the lower genital tract but also to granuloma in the upper genital tract, provided there are adhesions or lesions [24]. Dyspareunia has an inhibitory effect on sexual intercourse as the patient sees it as a painful exercise. The pain experienced during sexual intercourse limits its frequency and exerts a deleterious impact on fertility [25]. These conditions cause disharmony in family life and negatively affects emotional well-being, social equilibrium and fertility. The stress generated by this disharmony may deregulate the function of the hypotalamo-hypophysal axis [26]. Genital ulcerations, pelvic inflammatory disease and dyspareunia are a continuum of the conditions caused or exacerbated by urinary schistosomiasis. The fact that these conditions bear an association with history of hematuria reveals the relationship most likely to exist between past urinary schistosomiasis and infertility. Dyspareunia, post-coïtal hemorrhage and infertility were also reported in case series studies in Niger and Egypt [27-28]. Inability to have intercourse may be a source of marital violence, dysharmony and even divorce [29-30].

Women with abnormal vaginal discharge and/or a pelvic mass were more likely to report a history of hematuria. This corroborates findings from Egypt, where FGS was associated with abnormal vaginal discharge and vaginal or cervical polyps [28].

The results of the present study indicate that urinary schistosomiasis is more closely associated with secondary than primary infertility. In the rural communities studied, marriages occur just after the first menses, between 14 and 17 years. At this time, urinary schistosome lesions are not yet calcified within the tissues. Calcification occurs later in life, probably after the subject has already had a few pregnancies. This is consistent with the apparent relationship between the topographic localization of schistosomiasis lesions and age. The vulva is often more affected in very young girls, whereas lesions in the vagina, cervix and upper genital organs occur at a later age [31-33]. Further indications that chronic urinary schistosomiasis leads to infertility can be found in reports of primary infertility coinciding with bilateral hydrosalpinx and inflammatory peritoneal reaction in one case, an ectopic pregnancy, and chronic salpingitis in *S. haematobium* infected females [34]. The fact that the highest rate of infertility was found among older women indicates that other causes of infertility coexist in our study community. Other determinants of infertility which may confound with urinary schistosomiasis are STDs, which are more likely to occur in older women. Ulcerations resulting from *S. haematobium* egg extrusion expose the urogenital tract to secondary bacterial infections and sexually transmitted infections, including STDs which are the leading cause of infertility in Africa [35]. In further assessment of infertility, hysterography and/or hysterosalpingography promise to yield valuable results in confirming potential associations.

CONCLUSION

The present study was designed to assess the association between urinary schistosomiasis of the genital tract and infertility. Infertility was independent of the oviuria and hematuria but associated with a history of hematuria. Women who were married more than once, had dyspareunia, genital ulcerations, or a history of dysuria were more likely to be infertile. In further investigations, ultrasonographic examination of the urinary bladder, liver and urethers for calcified eggs should be included as indicators of past urinary schistosomiasis.

ACKNOWLEDGEMENT

The authors thank Drs. Heli Bathija Human Reproduction Programme (WHO/HRP) and Robert I. Leke, WHO collaborative Centre for Research in Human Reproduction – Faculty of Medicine and Biomedical Sciences- University

of Yaoundé 1 (HRP/FMBS/UY 1).

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