Female genital schistosomiasis (FGS) is a neglected disease manifestation of schistosomiasis. A cross-sectional study was carried out to assess in a schistosomiasis-endemic area the proportion of women affected by FGS of the lower reproductive tract and to compare the frequency of symptoms and signs possibly associated with FGS between women with proven FGS (n = 134), endemic referents (n = 225, women living in an endemic site), and referents (n = 75, women living in a nonendemic site). Urinary schistosomiasis was diagnosed in 36% (239/657) and FGS in 37% (134/359) of the women. Cervical lesions occurred in 75% of the FGS cases, in 48% of endemic referents, and in 36% of nonendemic referents. The high prevalence of FGS in all age groups and the high levels of pathologic cervical alterations such as swollen and disrupted epithelium support the hypothesis that FGS might be a risk factor for the transmission of human immunodeficiency virus.

Female genital schistosomiasis (FGS) is a neglected disease manifestation of schistosomiasis. It is characterized by the presence of schistosome eggs and worms in the genital organs. According to postmortem and histopathologic studies, the frequency of FGS in the upper reproductive tract ranges from 2% to 83% [2]. In the lower reproductive tract (LRT), the prevalence is 33%–75% [3–5]. The manifestations of FGS depend on the localization of the eggs. Infertility, ectopic pregnancies, and vesicovaginal fistulae have been reported [2]. We previously suggested that, on the basis of the clinical and immunologic features of schistosomiasis of the LRT, FGS must be considered as a risk factor for the bidirectional transmission of sexually transmitted diseases (STDs) such as human immunodeficiency virus (HIV) and human papilloma virus [6, 7].

Subjects and Methods

**Endemic site.** Kileo and Kivulini are villages situated in Mwanga District, Kilimanjaro Region, Tanzania. According to a household census (September 1996), the populations were 2492 and 1280, respectively. A school survey carried out by the investigators showed a prevalence of 63% for *Schistosoma haematobium* and 34% for *S. mansoni*. No schistosomiasis control measures have been done in these villages.

**Nonendemic site.** Vuagha, Lomwe, and Kighare are neighboring villages in the highlands of the Northern Pare Mountains (Mwanga District, Kilimanjaro Region). The total population according the 1988 census was 3730 inhabitants [8]. Schistosomiasis is not endemic in this area.

**Study design.** The parasitologic and clinical findings of three groups of women were compared by cross-sectional study: women with proven FGS of the LRT (cases, n = 134), women living in the *S. haematobium*-endemic area without parasitologically proven...
FGS (endemic referents, \(n = 225\)), and women living in a schistosomiasis-free area (referents, \(n = 75\)).

Subjects at endemic site. All permanent female residents of the villages aged 15–45 years were eligible for enrollment in the study (\(n = 771\)). Pregnant women and virgins were not accepted for gynecologic examination. Of the eligible population, 657 (82%) agreed to urine examination; 622 women (81%) were interviewed and 359 women (47%) agreed to gynecologic examination. The median age (30 years) of the women did not differ among groups.

Subjects at nonendemic site. All women aged 15–45 years attending the health dispensary at Vuagha during 2 weeks in February 1998 were invited to participate in the study (pregnant women and virgins were excluded). Of 150 eligible women, 75 (50%) gave informed consent. The median age was 35 years. Women with diagnosed schistosomiasis were treated with praziquantel (40 mg/kg body weight). Diagnosed STDs and genital or bladder infections were treated appropriately.

Methods. The study participants were interviewed in Kiswahili about sociodemographic, behavioral, and health questions by use of a pretested questionnaire. Urine samples, obtained on 3 consecutive days, were examined for schistosome eggs by the trypsin-blue filtration technique [9]. Thirty minutes before micturition, the women were given 300 mL of beverage to minimize the day-to-day variation of egg excretion [10]. The mean egg excretion was calculated by use of the arithmetic mean of the three urine examinations.

The physical examination consisted of inspection and palpation of the lower abdominal area, gynecologic examination including colposcopy, preparation of a cervical smear, and a biopsy of cervical tissue, which was taken from lesions if present. The macroscopic lesions in the LRT were described as follows: tumor (papillomatous/polypous), sandy patches, edema, petechiae, erosion, and ulceration. Epithelial lesions detected by colposcopy were categorized as intact, disrupted or swollen epithelium, and intact and disrupted blood vessels.

One half of the cervical biopsies was stored in formaldehyde solution for the histopathologic investigation, and the other half was crushed between two slides and examined for schistosome eggs. The intensity of genital infection was determined in a semiquantitative manner by assessing the number of eggs per square millimeter of crushed material [3]. Study participants were considered to be an FGS case if at least 1 schistosome egg was detected in the crushed biopsy, cervical smear, or histologic section.

Serum, urine, and swab samples were stored in cooling boxes and deep frozen at \(-20^\circ\text{C}\) within 4–6 h after collection. A subsample of the study village (\(n = 282\)) and all nonendemic referents were screened for STDs. Screening for syphilis was done by the Treponema pallidum particle agglutination assay (Mast Diagnostica, Reinfeld, Germany). The urine-based ligase-chain reaction testing for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae was performed with 1-mL aliquots of specimen according to the LCX kit manufacturer’s instructions (Abbott Laboratories, Abbott Park, IL).

Statistical analysis. Comparisons were made by the Mann-Whitney \(U\) test and \(\chi^2\) tests (\(\alpha = 5\%\)). Odds ratios (ORs) are given with 95% confidence interval (CIs).

Results

Parasitologic Results

The prevalence of urinary schistosomiasis among the 657 women examined was 36% (CI, 31%–42%), with a median intensity of infection of 2.1 eggs/10 mL urine (CI, 1.7–3.5, positive cases only). The proportion of schistosomiasis of the LRT of the 359 women who underwent gynecologic examination was 37% (CI, 31%–45%); their proportion of urinary schistosomiasis was 42% (CI, 35%–49%). Among the 134 women with FGS, schistosome eggs were detected in the urine of 56% (CI, 47%–64%); however, after the first urine examination, urinary schistosomiasis was diagnosed in only 43% of these women.

The median egg load of the cervical tissue was 0.3 eggs/mm² (CI, 0.2–0.6). In 34 of 134 FGS cases, eggs were detected in macroscopically normal cervical tissue; however, cervical inflammation and intraepithelial neoplasia were detected by cytologic and histologic examination within this group (authors’ unpublished data). The occurrence of urinary schistosomiasis decreased with age, but the frequency of FGS remained stable for the whole age range examined (figure 1).

The median intensity of urinary schistosomiasis infection in FGS cases and endemic referents was 2.1 eggs/10 mL of urine (CI, 1.2–4.6) and 1.4 eggs/10 mL of urine (CI, 0.5–4.6), respectively. The intensity of urinary infection increased the risk of having FGS. Egg excretion of 1.1–10.0 eggs/10 mL (OR, 2.61; CI, 1.40–4.90) increased the OR by 64%, compared with 0.1 eggs/10 mL urine (OR, 1.59; CI, 0.65–3.91).

Symptoms and Signs

Self-reported symptoms. Symptoms linked to urinary schistosomiasis such as hematuria and dysuria were reported significantly more frequently at the endemic site. The frequencies of symptoms possibly related to STDs such as abdominal pain and discharge did not differ between sites. A history of postcoital bleeding (11% vs. 3%; \(P < .05\)) and genital ulceration (17% vs. 6%; \(P < .05\)) was more frequently given in the endemic site. Furthermore, in FGS cases with concomitant urinary schistosomiasis, irregular menstruation (46% vs. 22%; \(P < .01\)) and hypermenorrhea (44% vs. 25%; \(P < .05\)) were more frequently reported than in the endemic referents with only urinary schistosomiasis.

Gynecologic findings. Pathologic findings of the LRT were mainly present on the cervix in both groups. The frequencies of sandy patches (28% vs. 1%), edema (19% vs. 8%), and erosions (27% vs. 12%) were significantly higher in the endemic than in the nonendemic site. FGS cases had significantly more sandy patches on the cervix, compared with the endemic referents (49% vs. 15%; \(P < .001\), and were frequently associated with erosion (table 1). The median cervical egg load was significantly higher in women reporting dysuria (0.6 vs. 0.2 eggs/
Figure 1. Prevalence and intensity of infection of urinary and genital schistosomiasis in relation to age.

mm²; $P < .05$); furthermore, women reporting intermenstrual bleeding (0.6 vs. 0.3 eggs/mm²; $P = .34$) and irregular menstruation (0.3 vs. 0.2 eggs/mm²; $P = .26$) showed a higher egg load, although the results were not significant. The frequencies of cervical discharge did not differ between women at the endemic and nonendemic sites (35% vs. 33%; $P < .05$). Colposcopic alterations such as swollen epithelium (14% vs. 3%; $P < .01$) and disrupted epithelium (30% vs. 15%; $P < .01$) were more frequent at the endemic site and in women with FGS than in the endemic referents (59% vs. 35%; $P < .001$).

Laboratory examinations. Of the 282 women studied at the endemic site, 13 (5%) were infected with $C. trachomatis$, 3 (1%) with $N. gonorrhoeae$, and 28 (10%) with $T. pallidum$. In the 75 nonendemic referents, 1 (1%) had chlamydial infections and 2 (3%) had syphilis.

Discussion

Our data suggest that schistosomiasis of the LRT is common (37%) in all age groups. Although girls younger than 15 years were not enrolled in the study, it is unlikely that the frequency of FGS drops to zero in younger girls, given that 33% of women aged 15–19 years were afflicted.

FGS can occur in the absence of egg excretion in urine [11]. The intensity of urinary schistosomiasis, however, influences the risk of having FGS. There is a considerable increase of risk between cases with very light and cases with light infections, which can be missed when the diagnosis is based on a single examination of 10 mL of urine.

We investigated whether the presence of eggs in the lower genital tract translates into a schistosomiasis-related morbidity at the community level. The symptoms and signs we assessed are certainly not only caused by FGS. Reproductive-tract infections and STDs such as chlamydial and gonococcal infections must be taken into account as differential diagnosis. However, the frequencies of these infections did not seem to differ between cases and referents. Furthermore, we found similar frequencies of symptoms and signs that can be related to STDs (e.g., vaginal discharge, lower abdominal pain, and cervical discharge) in the endemic and the nonendemic site. The differences in the frequencies of symptoms such as menorrhagia and postcoital bleeding and in the frequencies of cervical lesions detected in FGS cases, compared with the endemic referents, and detected in the endemic site, compared with the nonendemic site, might be explained by FGS. The higher frequencies of symptoms and signs in the endemic referents, compared with the referents from the nonendemic site, might be due to the fact that women could be falsely categorized as FGS negative, since parasitologically FGS of the cervix could not be shown. Our findings are in accord with those of Leutscher et al. [5] who, in a community-based study in Madagascar, found that symptoms such as spontaneous abortion, irregular menstruation, and pelvic pain were more frequently reported by women from a village in which $S. haematobium$ was endemic than by women from a nonendemic village, although the frequencies of STDs did not differ between the sites. Therefore, one might conclude that FGS causes “extra morbidity” in the LRT.

The clinical and parasitologic findings—high prevalence of FGS, the presence of disease in young girls, and the high frequencies of pathologic cervical alterations—support the hypothesis that FGS might be a risk factor for the transmission of HIV. We do not have information about the HIV prevalence in the study sites; however, a study in a rural area in the same district found an HIV prevalence of 4.8% in women aged 15–44 years [12]. Since cervical epithelium is thought to be the likely virus entry point [13], the impairment of the physical barrier
of the cervical epithelium due to epithelial swelling and disrupted epithelium seen in the FGS cases might enable the entry or exit of HIV. Viable and dead schistosome eggs in cervical tissue induce a reaction, with a spectrum ranging from strong inflammatory to fibrous connective tissue reaction with diffuse infiltration of HIV-receptive cell types such as CD4 T cells and macrophages [14].

In conclusion, FGS must be considered to have considerable public health importance. Since FGS of the LRT frequently occurs in the absence of egg excretion in urine or in light infections and since FGS is associated with additional morbidity, a revision of schistosomiasis control strategies are needed.

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