Sexually Transmitted Diseases in Malawi

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The prevalence of sexually transmitted diseases (STDs) in developing countries is high worldwide and the increasing resistance of several organisms to the penicillins and other low-cost readily available drugs has exacerbated the problem. While STDs have long been a cause of substantial morbidity and mortality in Africa and in other parts of the world, it is only now in the wake of the human immunodeficiency virus (HIV) epidemic that increased resources are being directed at their prevention and control.

The Importance of STDs

Morbidity and mortality

The bulk of the burden of STD complications and sequelae is borne by women and children. This is largely due to the high percentage of asymptomatic, and therefore untreated, cervical gonococcal and chlamydial infections in women. Studies from industrialized countries show that pelvic inflammatory disease (PID) occurs in 8-10% of women with untreated chlamydial cervicitis and in 10-20% of women with untreated gonococcal cervicitis. Complications of PID are the most serious sequelae of sexually transmitted diseases in women and include infertility, ectopic pregnancy and abscesses progressing to life-threatening infections[1]. In addition, several cervical infections (including those due to human papilloma virus, herpes simplex virus type 2 and *Chlamydia trachomatis)* are associated with increased incidence of cervical neoplasia, a problem of large dimensions in sub-Saharan Africa.[1]

STDs also affect the unborn child and are associated with foetal wastage, low birth weight, and congenital infections.[1] Data from Zambia[2] indicate that 57-72% of syphilitic pregnancies resulted in an adverse outcome (defined as abortion, stillbirth, preterm birth, low birth weight baby, or congenital syphilis in the newborn), compared to 10% of non-syphilitic pregnancies. From studies done in the pre-penicillin era, it is known that roughly one-third of cases of untreated syphilis during pregnancy result in spontaneous abortion or perinatal death, one third result in congenital infections, and one third result in healthy infants[3]. In Malawi, similar findings were seen in Mangochi where 3.6% of 3591 antenatal women screened had serological evidence of active syphilis (defined as VDRL titre ≥ 1:8 and positive MHA-TP). Syphilis was responsible for 22% of foetal loss, 26% of stillbirths, 21% of perinatal deaths, 11% of neonatal deaths and 8% of infant deaths in the study population.[3]

Vertical transmission from infected mother to the newborn also occurs in *Chlamydia trachomatis* infections. It is generally accepted that 25-30% of pregnancies in infected women result in neonatal respiratory and eye infections. Vertical transmission of *Neisseria gonorrhoeae* occurs in 30-50% of pregnancies where the mother is infected.[1] In a study done at Pumwani Maternity Hospital in Nairobi, 42% of babies exposed to maternal gonococcal infection and 31% of babies exposed to maternal chlamydial infections developed ophthalmia neonatorum.[4]

Increased Risk of HIV Transmission

In addition to the substantial morbidity and mortality associated with STDs, the risk of HIV transmission has been shown to be increased several-fold in the presence of both ulcerative and non-ulcerative sexually transmitted infections. Prospective studies have shown a 3- to 5- fold increased risk of HIV transmission even after controlling for sexual behaviour, demographics, and other possible confounding variables.[5,6,7] Dr. Merson, Director of the World Health Organization's Global Program on AIDS, is quoted as saying that STDs may increase the risk of HIV transmission "by as much as 10- to 100-fold for a single act of intercourse."[8] Syphilis, chancroid, herpes, chlamydial infection, trichomoniasis, gonorrhoea, and human papilloma virus have all been shown to increase risk of HIV transmission.[9,10]

There are several plausible biological mechanisms to account for the increased risk of HIV transmission in the setting of concurrent STD infection. HIV has been isolated from the exudates of genital ulcers in men and women and from the semen of HIV-infected men. Recent studies indicate that HIV-infected women with cervicitis have increased viral shedding. STDs may also increase HIV transmission by increasing the number of HIV-infected or HIV-susceptible cells in the genital area as part of the immune response. In addition, STDs disrupt the normal epithelial barrier, either by frank ulcers as in genital ulcer disease (GUD), or by micro-ulcerations in the genital mucosa as in gonorrhoea, chlamydial infections, or trichomoniasis.[9]

This association between HIV and other STDs has been observed in studies in Malawi. Cross-sectional data from Queen Elizabeth Central Hospital (QECH) in Blantyre shows significantly higher prevalences of all common STDs in HIV-infected antenatal women as compared to seronegative women.(Table 1.)[11] While the association between all of the studied STDs and HIV is strong is strong in this study, both the STDs and HIV serostatus were simultaneously determined. Therefore, it is not possible to know whether an individual acquired the HIV infection before or after contracting the STD.

The temporal relationship between STDs and HIV seroconversion is better observed in prospective studies. Several such studies in Africa have established the increased risk of HIV transmission in the presence of STDs.[5,6,7] In Malawi, the Johns Hopkins Study at QECH in Blantyre followed a cohort of HIV seronegative women in the antenatal clinic from November 1989 to February 1993. Development of trichomonas vaginitis infection during the study period was associated with an over three-fold increased risk for HIV seroconversion (OR 3.40, 95% CI: 1.13,10.3). Reported symptoms of STDs were associated with a similar increased risk (OR 3.00, 95% CI: 1.07, 8.42). Genital ulcers (OR 4.00, 95% CI: 0.36, 44.1) and genital warts (OR 3.00, 95% CI: 0.24, 37.5) were also positively associated with HIV seroconversion (although the association was not statistically significant in this study).[12]

STD patients

As expected from the results of studies relating STDs to HIV transmission, rates of HIV seroprevalence are higher in STD patients than that seen in the general population. In Lilongwe at Kamuzu Central Hospital in 1989,[13] 62% of all STD patients were HIV positive, (65% of ulcer patients and 57% of discharge patients). In Blantyre, where the 1992/93 rate of HIV among antenatal women was 27.1-31.6%,[14] the rate among 1272 male STD patients tested between November 1992 and March 1993 was 53 %.[15] The rate of HIV seropositivity among patients with genital ulcers was higher than that among patients with urethral discharge (5 8.9 % vs. 44.5 %, p<.001) in this study. This is consistent with the findings of studies in other countries showing a higher relative risk for HIV transmission in the presence of ulcer-

ative diseases when compared to non-ulcerative diseases. In addition, urethritis patients with positive syphilis serology had a 71.7% HIV seropositivity compared to 40.9% among those with negative syphilis serology (OR = 3.6, 95% CI 2.01-6.65, p<.001). In all groups, the risk of HIV seropositivity was higher among employed men and those who used alcohol.

Effect of HIV on STDs

Not only do STDs change the epidemiology of HIV transmission, but HIV infection may also influence the epidemiology of STDS.[9,10] Indeed, prospective data from the Johns Hopkins University - Ministry of Health (JHU-MOH) project at Queen Elizabeth Hospital (QECH) in Blantyre indicates that HIV seropositive women are more likely to develop gonorrhoea infection, trichomoniasis, genital ulcers and genital warts (Table 2).[14] This effect of HIV on the probability of contracting an STD may also partially account for the high rate of HIV seroprevalence seen in STD patients.

In addition to the increased incidence of STDs, other possible effects of HIV on STDs are the occurrence of atypical presentations, more frequent complications, change in laboratory results, and diminished response to standard therapy. Few data support these conclusions and while there have been case reports of these effects in HIV-positive individuals, there have been few studies with HIV-negative control groups.

The Extent of STDs in Malawi

STDs account for a significant burden on the health services in Malawi, as in other African countries. Taken together, STDs were the fourth most common reason for consultation in adult outpatient departments nationwide in 1991.[16] At Kamuzu Central Hospital in Lilongwe in 1989,[13] 4.4% of unselected outpatients presented with an STD (705 out of 16,218 patients over the age of 13 screened).

Even in populations thought to be at relatively low risk for STDs, the prevalences are high. See Table 3. At Queen Elizabeth Central Hospital in Blantyre in 1994, 22% of medical ward inpatients had visible evidence of an undisclosed STD.[17] In 1989, 42% of antenatal women at QECH were infected with gonorrhoea, trichomoniasis, syphilis, chancroid, and/or chlamydia at any one time.[11] Despite a national policy advocating routine antenatal syphilis screening and treatment, rural antenatal seroprevalence studies carried out by the National AIDS Control Programme show a wide range of prevalence of syphilis infections from 0% in several northern districts to an alarming 18% at Mulanje District Hospital.[18] As expected the geographical areas with the highest syphilis seroprevalence also have the highest HIV seroprevalence among antenatal women (OR 2.29, p=.001).[19]

STD Control in Malawi

The cornerstone of STD control is improved STD management. Comprehensive STD management includes proper diagnosis of STDs, effective antibiotic treatment, and preventive efforts beginning with patient education on risk reduction (including condom promotion) and partner notification.

Syndromic diagnosis

The syndromic approach to the diagnosis and management of STDs , recommended by the World Health Organization,[20] is a key aspect of the new national STD treatment guidelines. In syndromic management, health care providers diagnose and treat patients based on signs and symptoms, rather than identifying a specific STD by clinical or laboratory criteria. The guidelines for the clinical application of this approach are presented in flowchart format. A simplified example of two common flowcharts is provided in Figures 1&2 and a more extensive discussion of the flowcharts can be found in the Malawi Prescriber's Companion.[21]

There are several advantages to utilizing the syndromic approach, especially in a resource-poor health system. The greatest advantage is the lessened reliance on laboratory testing. This not only reduces the cost of STD management, but without the delay of waiting for the results of laboratory tests, diagnosis and treatment can be accomplished on the patient's first visit. Malawi's hospitals and health centres offer few laboratory tests that are helpful in the primary care diagnosis of STDs. Even when tests are available, they do not allow a definitive diagnosis. In the setting of urethral diarrhoea in men a positive gram stain for gram negative diplococci may confirm gonococcal infection but does not rule out a concomitant chlamydial infection.
Similarly, a positive VDRL in the setting of a genital ulcer does not definitely prove that the ulcer is due to syphilis since several asymptomatic patients in the latent phase of syphilis have a positive VDRL. At QECH, 12% of asymptomatic antenatal women (see Table 3) were syphilis seropositive. In addition, multiple infections are common. Nearly one in four (23.7 %) men at QECH with ulcers due to chancroid also had laboratory evidence of syphilis and similarly, 24.2% of GUD patients with laboratory evidence of syphilis also had laboratory confirmed chancroid.[22] A further complication in the laboratory diagnosis of syphilis stems from the fact that the VDRL test is often falsely negative in the early phases of syphilis when the ulcer is most commonly seen.

A common misconception is that an aetiologic diagnosis for genital ulcers can be made on clinical criteria alone. Several studies have refuted this. At QECH, the characteristics of the ulcer or inguinal lymphadenopathy, or the duration of symptoms did not allow accurate diagnosis.[15] While some signs are more often associated with either chancroid or syphilis, none are absolute predictors. In a South African study of the clinical diagnosis of genital ulcers, the overall accuracy was 68% for single infections. Another 15% of patients had more than one etiology for the ulcers.[23] A similar study comparing clinical diagnosis by venereologists in Kenya to laboratory diagnosis showed an overall diagnostic accuracy of 66%.[24] Using syndromic management, all patients with GUD are treated for both syphilis and chancroid. Similarly, all patients with urethral discharge, epididymitis, or cervicitis are treated simultaneously for gonorrhoea and chlamydial infections.

This concept of the simultaneous treatment of two etiologies for several of the STD syndrome has led some to question the overuse of antibiotics that are already in short supply. However, survey data on current STD case management" show that more than one drug is given in 55 % of cases of STD, even at this time when the majority of health care providers have not yet adopted syndromic management. In addition, the actual total cost of treatment of the STD cases observed during the survey was roughly the same as the calculated cost of treatment under the new syndromic management guidelines. WHO predicts that syndromic diagnosis will provide substantial cost saving due to the decreased use of laboratory diagnosis and fewer complications resulting from misdiagnosis and untreated or inadequately treated STDs.[26]

Effective antibiotic treatment

Due to increasing resistance of STD organisms to the commonly

used, widely available, and inexpensive drugs worldwide, several of the antibiotics commonly used in Malawi in the treatment of STDs have become ineffective. The AIDS Control and Prevention Project (AIDSCAP) study presented in this issue identifies affordable alternatives for the treatment of STDs in this country.[15] In determining the new antibiotic treatment guidelines for Malawi,[27] both the clinical efficacy (with a goal of 95%) and the cost of the drugs were considered.

The new national recommendation for the treatment of *Neisseria Gonorrhoeae* based on this study is gentamicin (240 mg IM in a single dose). While the cure rates for laboratory confirmed gonococcal urethritis were similarly high for gentamicin, ciprofloxacin, and a four-drug combination of amoxicillin, clavulanate, probenecid, and doxycycline,[15] the cost of the other two regimens is several fold higher.

The other substantial change in the treatment guidelines for STDs is in the case of *Haemophilus ducreyei* (chancroid). Ciprofloxacin and erythromycin were both effective in the treatment of chancroid (marked healing is 86% and 83%, respectively and some healing in 5% and 14%). However, since erythromycin is considerably less expensive than ciprofloxacin, erythromycin (250 mg TID for 5 days) was adopted in the national guidelines.

No changes in antibiotic recommendations were required for the treatment of *Treponema pallidum or Chlamydia trachomatis.* For chlamydial infections, doxycycline continues to be effective worldwide and for syphilis, benzathine penicillin is still the treatment of choice.

As mentioned in a previous section, HIV infection may alter the response to antibiotic therapy of STDS. However, the AIDSCAP clinical efficacy trial at QECH occurred in the setting of an overall HIV seropositivity rate of 53 %. Any regimen with a clinical cure rate of 95% in that setting can be expected to be efficacious in the presence of HIV infection. Currently, there is little conclusive evidence suggesting that the treatment of STDs should be changed in the setting of HIV infection except that singledose therapy should be avoided in chancroid.[9] Although there are several case reports of neurosyphilis due to failed therapy of a single dose of benzathine penicillin for primary syphilis in HIV-infected patients and higher rates of cerebral spinal fluid leukocytosis in primary syphilis have been reported in the presence of HIV infection, no controlled trials show a difference in response to 2.4 MU of benzathine penicillin in a single dose for early syphilis between HIV-infected and HIV-uninfected patients.[9]

Prevention

Prevention of STDs begins during the patient-provider encounter with patient education on compliance with medication, abstinence or condom use during the treatment period, partner notification and treatment, and behaviour change for HIV/STD risk reduction including condom promotion. Such education requires trained personnel and a setting of privacy and confidentiality. In an extensave focus group study, the most commonly identified of credible AIDS information was hospital/health personnel.[28]

Another aspect of prevention of STDs, and by extension HIV, is early treatment of high-risk groups. Complete elimination of STDs in population groups with large numbers of sexual contacts ("core transmitter groups") would dramatically change the epidemiology of STDs could theoretically cause STDs to disappear entirely.[29] It is of interest that 63% of male STD patients at QECH admitted to sexual contact with a "bargirl" (commercial sex worker) in the previous month.[15]

Outreach to bargirls, truck drivers, and other high prevalence groups must include messages on the recognition of STD symptoms and the importance of early care.

Since even low-risk groups have a high prevalence of asymptomatic STDs, casefinding through screening of these groups is required. As previously mentioned, the burden of the serious complications of STDs is borne predominately by women and children, and women have the highest proportion of asymptomatic STDs. Therefore, screening in family planning and antenatal clinics is essential. VDRL serology is a simple, low-cost test that can be done on large numbers of patients with relatively little manpower. The effect of screening and treatment of syphilis in antenatal clinics is dramatic. In Zambia, where the antenatal syphilis screening and treatment were suboptimal, a two-thirds reduction in adverse pregnancy outcomes was observed when compared to control centres without screening, at a cost of US $12 for each adverse outcome prevented[2].

Screening for other asymptomatic STDs in women is much more difficult due to the need for speculum examinations, laboratory equipment and personnel. The Program for Appropriate Technologies in Health (PATH) is attempting, along with others, to develop simple, low-cost, easily stored tests for the detection of STDs. One such technology that is being field-tested at QECH is dehydrated gonorrhoea culture plates that can be stored at room temperature for long periods.

Summary

In summary, STD control has been pushed to the forefront by the HIV epidemic. STDs are one of the most modifiable risk factors for HIV. Their control will not only substantially reduce HIV transmission — the benefits of diminished prevalence of STDs will also extend to the areas of maternal and child health.

There are several obstacles to the control of STDs, including multi-drug resistance, inadequate laboratory infrastructure, lack of partner treatment, and failure to heed behaviour change messages. These are currently being addressed in Malawi by the revision of national drug treatment guidelines, adoption of syndromic diagnosis, patient education, and outreach to high-risk core transmitter groups.

Table 1. Prevalence of STDs in antenatal women: HIV-1 seropositive and IIIV-1 seronegative women, JHU-MOH Project, QECH, Blantyre, 1989-90.[11]

STD	HIV-positive% (n= 1480)	HIV-negative% (n=5026)	Odds Ratio	p-value
Gonorrhoea cervicitis	11%	3%	3.69	<.001
Syphilis seropositivity	16%	10%	1.79	<.001
Trichomonas vaginitis	47%	28%	2.26	<.001
Genital ulcers	11%	6%	2.12	<.001
Genital warts	8%	2%	4.13	<.001
Any STD	61%	36%	2.73	<.001

Table 2. Incidence of STDs in antenatal women: HIV-1 seropositive and HIV-1 seronegative women, JHU-MOH Project, QECH, Blantyre, 1989-93[14]

	HIV-positive (%) (n = 644)	HIV-negative (%) (n = 677)	p-value
Gonorrhoea	19.8%	7.9%	<.001
GUD	26.9%	9.3%	<.001
Trichomonas	51.3%	35.6%	.009
Genital Warts	23.6%	13.6%	.030

Table 3: STD prevalence studies in Malawi in asymptomatic populations.

	Site	Population	Prevalence
Syphilis*			
Malaria Project, 1991-92[3]	Mangochi	antenatal women (n=3591)	3.6%
NACP surveillance, 1992[18]	Nationwide sample of rural sites	antenatal women (n=759)	4.7% (range: 0- 18 %)
JHU-MOH Project 1993[30]	Blantyre	antenatal women (n=2161)	12.2% (RPR only)
JHU-MOH Project 1990-91[31]	Blantyre	registered bargirls (n=273)	22% (RPR only)
Gonorrhoea			
JHU-MOH Project 1993[32]	Blantyre	antenatal women (n=2826)	2.4%
JHU-MOH Project 1990-91[31]	Blantyre	registered bargirls (n=273)	29%
Chlamydia			
JHU-MOH Project 1993[32]	Blantyre	antenatal women (n=2826)	1.0%
Trichomonas			
JHU-MOH Project 1993[32]	Blantyre	antenatal women (n=2826)	29.2%
JHU-MOH Project 1990-91[31]	Blantyre	registered bargirls (n=273)	27%
GUD			
JHU-MOH Project 1989-90[11]	Blantyre	antenatal women (n=6506)	7%
JHU-MOH Project 1990-91[31]	Blantyre	registered bargirls (n=273)	1%**

Syphilis seropositivity defined as positive RPR or VDRL with positive confirmatory test unless otherwise specified.

** Low value for GUD among CSWs probably due to self-exclusion since CSWs found with evidence of STD in food handler clinic are banned from work for 3 weeks.