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Sexually Transmitted Infections and HIV Transmission: What Do We Know?

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Abstract

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Sexually transmitted infections have remained a public health problem mainly in the developing world, where the burden of HIV is also high. Effects of sexually transmitted infections can be devastating and have also been shown to enhance transmission of HIV. The risk of transmission depends on the type of infection, whether it presents with an ulcer or it is only inflammatory. Mixed infections further increase the probability of HIV transmission, making the overall risk even higher. Understanding the dynamics of transmission is important. It is also essential to know which groups of people are more at risk as this is fundamental in designing appropriate control interventions. This article gives an overview of sexually transmitted infections, and gives insight on their association with HIV infection, transmission risks and some control-based interventions. In addition we also aimed to increase the understanding of where preventive and management gaps may still exist and in what contexts.

Keywords: *Sexually transmitted, HIV, Transmission*

INTRODUCTION

Sexually transmitted infections (STIs) remain a major challenge globally, with a greater concentration in developing countries which also continue to face a devastating human immunodeficiency virus (HIV)/acquired immuno-deficiency syndrome (AIDS) epidemic. The spread of HIV infection in the developing countries is primarily sexual and overwhelming evidence has accumulated indicating that STIs enhance transmission of HIV [1,2]. Observational studies have shown the association between sexually transmitted infections and subsequent HIV acquisition and shedding [2]. This article is aimed at highlighting the association between STIs and HIV and the role that STIs play in HIV transmission. The initial part provides a general overview of STIs, including transmission patterns and the distribution and their consequences. The latter part of the article presents the association between STIs and HIV and the role that STIs play in HIV transmission. Lastly, the difficulties of estimating the effect of STIs on HIV transmission and the complexities of STI epidemics are discussed and finally STI control interventions in Zambia.

Overview and burden of STIs

STIs are a group of contagious conditions, whose principal route of transmission is through sexual intercourse [3,4]. Most of the microorganisms that are transmitted sexually rely on the sexual route of transmission due to their limited environmental survival and limited sites of primary infection which are mostly the mucosal surfaces [4]. Transmission can also occur vertically, during pregnancy, from mother to child, through blood products or tissue transfer and other non-sexual means [2]. Since most STIs can also be transmitted through other routes, the term “transmissible” may be preferred [4]. Over 30 pathogens can be transmitted sexually; these (among others) include bacteria, viruses, parasites, protozoa, and mycoplasma and hence can be classified as such [2, 4]. Broadly, STIs can also be classified into curable and non-curable infections. Among the non-curable are those due to viral infections such as those caused by HIV, herpes simplex virus type 2 (HSV-2) and the human papilloma virus. Curable STIs include infections caused by *Trichomonas vaginalis*, *Chlamydia trachomatis* which causes lymphogranuloma venereum, *Neisseria gonorrhoea* (gonorrhoea), *Mycoplasma genitalium* and *hominis*, *Ureaplasma urealyticum* (urethritis and cervicitis) and *Treponema pallidum* (syphilis) [2,5-9].

Others include *Haemophilus ducreyi* which causes chancroid and *Klebsiella granulomatis* (granuloma inguinale).

Some organisms not deemed to be sexually transmitted have occasionally been transmitted sexually, such as *Neisseria meningitidis*, *Haemophilus parainfluenzae* and the Epstein-Barr virus.

The annual estimate of new infections of curable STIs globally is approximately 500 million, with 75% or more of the total burden occurring in developing countries. Compared to other regions, sub-Saharan Africa has the highest incidence of over 100 per million cases [10]. In the history of STIs, industrialised countries too have borne the burden of STIs, mostly syphilis, gonorrhoea and chancroid which were at their peak during the Second World War and later began to decline in the mid-fifties. The sixties and early seventies were characterised by an increase. Since the late seventies western countries have had successful STI control programmes which led to the campaign for eradication of conditions like syphilis. However, an upswing has been documented in the recent past affecting mostly the urban populations in countries like the United States of America [11, 12]. The commonly encountered conditions in the developed countries are those due to *Chlamydia trachomatis*, genital herpes virus, human papilloma viruses and HIV, while in the developing world the above-mentioned conditions as well as the classical bacterial infections such as gonorrhoea and syphilis still remain major health problems [3, 11].

Importance of STIs

Although more than three quarters of the burden is in the developing countries, socio-economic factors, demography and migratory trends put all populations, including industrialised countries, at risk [2]. Attention needs to be drawn to sexually transmitted infections because of their potential consequences at macro and micro levels. According to the World Health Organization (WHO) STIs account for approximately 17% of economic loss due to ill-health and are one of the leading causes of loss of healthy life years [2]. At micro level there is loss of income due to absence from work and resources spent on medical and non-medical supplies [2]. The medical consequences range from asymptomatic infection to acute, life-threatening conditions, chronic infection and sequelae. Some of the conditions include pelvic inflammatory disease, infertility in both men and women, ectopic pregnancy, miscarriage, stillbirth, congenital infection and an

increased risk of HIV transmission [13]. Both men and women can be affected; however, the consequences are worse in women [2, 13, 14]. The WHO has indicated that the most important causes of illness and death in women from resource poor settings are STIs and reproductive tract infections (RTIs), and these account for up to a third of the 500 000 maternal deaths that occur annually in these regions [13]. Despite the risk posed by these infections, STIs are poorly addressed in many health care settings, especially in developing countries where the need is greater [15,16]. There has however been rekindled interest in the past decades because of the potential role of STIs in facilitating HIV transmission and acquisition [17-20]. The double burden of the HIV epidemic and high prevalence of STIs in Africa has led to the hypothesis that STIs could be responsible for the disproportional HIV situation [21-23], while limited access to diagnosis and treatment are documented as some of the contributing factors to curable STIs being concentrated in developing countries [15].

STIs and HIV infection

The presence of STIs has been shown to correlate with increased rates of sexual HIV transmission [24]. Some factors that make STIs and HIV interdependent are similar sexual behaviours such as frequent, unprotected sex with multiple partners, placing people at risk of both infections [25]. The interaction between STIs and HIV infection are described as bi-directional or as having epidemiological synergy where each may alter the transmission or manifestations of the other, resulting in mutually reinforcing infection [18, 19]. An STI increases the probability of HIV transmission by 2- up to 23-fold within a partnership [17-19, 26]. The presence of an ulcer additionally increases the risk 5- to 10-fold, thus the overall risk can range from 50 to 300 times higher [13, 21]. Concurrent STIs increase the probability of HIV transmission through an additive or multiplicative effect [24]. If co-factors have different interaction mechanisms, multiplication of their effects is biologically plausible. For example, an ulcer in an HIV-negative person is a port of entry for HIV, while a concurrent chlamydia infection increases the presence of HIV-susceptible inflammatory cells in the genital tract. The presence of 2 genital ulcers, on the other hand, may have multiplicative effects initially and reach a point of saturation at a certain stage [24].

STIs can enhance the infectivity of HIV positive individuals because of increased shedding of the HIV virus in their genital tract [18, 24, 26, 27]. When an STI is present, cellular

infiltration occurs at the site of infection leaving potential target cells for HIV infection exposed. In the case of genital ulcer disease, pathogens that because ulcers target the epithelial cells by causing necrosis to these surface cells, thereby exposing the sub-epithelial cells to infected genital secretions. Thus, due to the mucosal disruption, immune cells which are the main target cells for HIV are rendered accessible [22, 28]. Genital ulcers also bleed frequently during intercourse, and this may result in potential increase in HIV infectiousness [18]. Cohen and co-workers demonstrated an 8-fold increase of HIV-RNA in semen of HIV positive men with urethritis compared to the control group. A reduction in the seminal HIV-RNA was observed after antibiotic therapy [27]. Ghys and colleagues also demonstrated an increase in cervico-vaginal shedding of HIV among female sex workers co-infected with HIV and an STI compared to their counterparts with no STI, and treatment of the STI significantly reduced the viral shedding [26, 29]. In such a study, the level of immuno-suppression can be a potential confounding factor with regard to the relationship between STIs and genital HIV shedding. It would be expected that advanced immuno-suppression may promote HIV acquisition or persistence and/or recurrence of STIs, as well as HIV shedding in the genital fluids [29]. In their study, however, Ghys and colleagues did adjust for immuno-suppression and found no association between cervico-vaginal shedding and serum viral load. They concluded that local factors such as STIs were more important than circulating viral load in determining transmissibility [26, 29].

STI Control

The determinants for STIs include macro-environmental (i.e. socio-economic, cultural, epidemiological, demographic) and micro-environmental factors (i.e. biological, immunological and behavioural). Macro-environmental factors can influence an individual to engaging in risky sex leaving them at an increased risk of contracting an STI. Evidence based interventions therefore need to be tailored at different levels [2, 30]. Community or individual approaches can be applied as strategies for STI control. An individual approach targeted at high risk persons such as commercial sex workers or STI clinics attendees can include screening, case management and partner notification. Community strategies tailored at large populations include information, education and communication campaigns and mass treatment [31]. While latter can reach large populations but deliver a less intensive dose of the

intervention to individual members of the community [31, 32]. National control programmes need to identify who constitute high risk and who are the vulnerable populations for STIs, and what the drivers of the STI burden are, in order to design appropriate interventions, which could either be community or individual approaches or a mix of the two [2].

STIs in Zambia

STIs are recognised as a public health problem in Zambia, with over 200 000 cases being reported annually and about half of the new infections being in young people aged less than 29 years old [33, 34]. A study that analysed clinical diagnoses of STIs in the 1990s at the University Teaching Hospital in Zambia's capital, Lusaka, showed that chancroid and syphilis were the most common STIs in men and women (47% and 39% respectively) [35]. Maternal syphilis estimates based on serum antibody tests ranged from 8–18%. The high syphilis estimates contributed to the high number of mid-trimester abortions, still births, prematurity, morbidity and mortality of the child to the high estimates [36-38].

Current data has shown a reduction in syphilis prevalence both in pregnant women and in the general population [39], while a recent a study involving 200 patients with genital ulcers in Lusaka showed zero prevalence of chancroid and a high prevalence of HSV-2, similar to what has been found elsewhere [40-46]. The reasons for this were not clear from available information. However, these observations suggest that further monitoring is, required to ascertain the trends and provide information that can inform policy on treatment guidelines at country level. Creating functioning surveillance systems targeting the understanding of core determinants given country differential geographical and demographical contexts seems to be extremely critical in Zambia.

CONCLUSION

This article reviewed STIs and their role in the transmission of HIV, risk estimation and control interventions. In general, this overview has highlighted the need for setting context sensitive STI prevention programs. As demonstrated, the synergy between HIV and STIs calls for the need to re-examine the possible limitations and successes in past control efforts thereby helping to explore how to adjust and repackage preventative and health promotion messages with emphasis on joint programmes. STI control remains a primary strategy to control HIV and STI complications and sequelae. The complexities of the dynamics of STI epidemics

show that control should not only focus on treatment but have a multi-disciplinary approach too. This is with the recognition that different factors shape STI epidemics at different levels and therefore strategies need to be multi-dimensional.

In affected countries like Zambia, it seems reasonable to propose that programme managers and policy developers should thus seek to explore ways to increase the potential for integrated services, study associated cost differential dynamics and to measure the evolving effect such integration has on community and individual behaviors and inherent attitude bases. Such actions should nonetheless be embedded in country surveillance systems undertaken as both a moral and interventional responsibility. To do this political will is cardinal. This does not only have the potential to save millions of lives but has an additional benefit of re-directing savings made to many other areas to improve quality of life such as sanitation, nutrition and related child and maternal survival initiatives and thus improve human development.

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