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Estimating the true prevalence and incidence of human immunodeficiency virus (HIV) infection in the general population and high-risk sub-populations in India continues to be a challenge reflected by the wide interval estimated by UNAIDS: 3.4-9.4 million, now amended by the more recent UNAIDS re-estimation of approximately 2.5 million adults living with HIV. Several groups have addressed this challenge through population-based studies; however, sub-group analyses of high-risk populations are limited by sample size and migrant populations such as truck drivers may not be represented accurately, especially those away from their primary residence the most. Although final analyses are pending, preliminary evidence from the most recent National Family Health Survey (NFHS-3) demonstrates that with an HIV prevalence of 0.97 (0.7-1.25) in Andhra Pradesh (AP) and 1.13 (0.82-1.44) in Manipur, these two states continue to have the highest prevalence of HIV infection among the six high-burden states in India (Andhra Pradesh, Manipur, Uttar Pradesh, Karnataka, Maharashtra and Tamil Nadu).[1] The heterogeneity of the epidemic and geographical variation is further evidenced by up to threefold higher rates of HIV infection 0.97 (0.7-1.25) in AP when compared with the neighbouring and also industrialized southern state of Tamil Nadu 0.34 (0.18-0.50).[1] Sentinel surveillance conducted by the state has included all sub-populations thought to be at high-risk for HIV and STIs and men who have sex with men (MSM) from only one site, but has not included truck drivers. Both groups are consistently thought to be at high-risk for HIV and STIs and men who have sex with men (MSM) from only one site, but has not included truck drivers. Both groups are consistently thought to be at high-risk for HIV and other STIs, some of whom are targeted by state and private programmes. In AP, MSM prevalence rates of HIV infection have risen from 6.5% in 2005 to 10.25% in 2006 at the one sentinel surveillance site in the state (personal communication APSACS/PHMI Askhay Mishra September 30, 2007). Overall the lower estimates of HIV infection rates in India warrant a shift in resources and emphasis to focus on prevention efforts as evidenced by the recent National AIDS Control Program-3 (NACP-3) implementation plan for 2007-2012, which allocates 67.2% of the entire budget to HIV prevention efforts. Typically, in India, the burden of sexual and reproductive health has been borne by women, with male participation being very low. Current condom use is 5% and vasectomy rates are 1%. Improving the behaviour and HIV prevention activities among high-risk men can benefit the women they are in contact with.

Men continue to drive the HIV epidemic in India. As the menu of potential prevention measures grows, careful attention and analysis of the specific scenarios related to geography, behaviour, acceptability and sexual networks is needed, which will allow for effective utilization of novel techniques both inside and outside of the clinical trial. Such prevention interventions will need to be tailored to individual clients and may often depend upon rates of HIV and associated STIs in this population, level of covert use required by the individual, the sexual partner type, location of sexual exchange and behaviour. These and other safety variables must be better understood in order to inform current HIV/STI prevention programmes in high-risk men such as those run by the Andhra Pradesh State AIDS Control Society (APSACS), Hindustan Latex, CDC GAP, Clinton Foundation and Avahan. For example, understanding the beliefs and attitudes of high-risk men towards microbicides - typically thought as a female centric prevention intervention - could improve future development, clinical trials and eventual rollout of such agents. Moreover, there is an ethical imperative to potentially include men in the development process of topical microbicides to assess safety and tolerability of a substance that partners of women who use the substance covertly may be unknowingly exposed to. Understanding the acceptability of microbicides in men becomes important in countries where women are disempowered. Additional examination into the acceptability of such products in high-risk MSM or women who participate in receptive anal intercourse is also a priority. Additionally, in order to have the greatest generalisability, large cohorts of study subjects who are distinct from clinical care are required. This becomes increasingly important in India where access to allopathic health care is limited by geographical distance and health beliefs often based upon infectious disease models rather than the chronic disease model that often requires long and repeated follow-up periods. The importance of examining potential for non-condom prevention interventions outside of the wife and female sex worker (FSW) paradigm becomes increasingly important. Condom use and behavioural change as the sole prevention measure continues to be met with challenges within the Indian cultural and historical context compounded by complicated sexual networks. Examples of networks affecting perceptions of risk include...
HIV serosorting among MSM and risk reduction strategies among those who perceive themselves to be at risk - reducing number of partners, careful selection of partners and increased condom use. Lay risk assessment may be powerfully shaped by embeddedness in social networks, past experiences with helping professionals or social location. Acceptability of specific HIV prevention techniques may be dependent upon the network of involvement such as husband only or wife and girlfriend and/or FSW. Cohorts at high risk of HIV infection are commonly used to understand perceptions of risk, sexual networks and prevention preferences. Given the amount of resources and number of prevention programmes in the state of AP, there has been a surprising paucity of dedicated prevention studies in AP on high-risk men and any topic related to HIV/STIs.

Exploring HIV Incidence - The First Step

Studies of incidence testing through longitudinal follow-up or qualitative PCR testing for acute infection are rare in India with no such studies of high-risk male populations and no published reports on the use of detuned antibody assays such as the BED assay for estimation of recent HIV infection. Despite a UNAIDS statement in 2005, there is increasing data to support the use of BED assay in subtype-C-infected patients.\[2\] Absolute value of BED-derived incidence may or may not be close to expected incidence, depending on the population tested and other confounding factors. In South Africa, with subtype C infections, adjusted incidence fits in well with expected incidence from a recent population-based study.\[2\] However, the use of the BED assay in populations infected with subtype C needs further investigation and validation by longitudinal studies accounting for viral load, use of HAART and CD-4 count. Recent HIV infection detected through the BED assay or HIV-DNA testing may help us identify specific and recent high-risk characteristics and behaviours that can be potentially modified among sub-populations of men.

Exploring HSV-2 Infection as an HIV Transmission Modifier

Little is known about the HSV-2 infection in high-risk men, such as MSM, those who have concurrent sexual partners or truck drivers or their cleaners in India. Surveys conducted by the Bill and Melinda Gates Foundation Avahan Program of STIs in this population were meant to inform their future syndromic management programmes. However, these initial studies did not include important testing for HSV-2 serostatus or active infection.\[3,4\] A baseline understanding of the rates of infection and potential nodes for intervention are needed. Both asymptomatic shedding of HSV-2 and lack of history of genital lesions in men could compromise syndromic management programmes already in existence for clients of FSW or truck drivers in India. There is rapidly growing evidence of the importance of HSV-2 infection and subsequent treatment on HIV transmission dynamics as well as its potential association with circumcision status. These findings make studies of HSV-2 infection dynamics crucial to the development of prevention interventions in this high-risk male population. A better understanding of this could inform current HIV prevention programmes in the state and country, which rely on syndromic management of genital lesions and expand the options beyond condom promotion and HIV education.

Men positive for HSV-2 and without symptoms should be counselled according to international guidelines on the signs, symptoms, natural history and mechanisms of transmission and methods of prevention of infection in HSV uninfected partners. For example, men who have genital herpes would be advised to avoid intercourse with women who are in the third trimester of pregnancy. The psychological effect of a serologic diagnosis of HSV-2 infection in a person with asymptomatic or unrecognized genital herpes appears small and transient. Informing policy on circumcision and potential future acyclovir prophylaxis in preventing HIV heterosexual (and potentially homosexual) infection might first be incorporated in high-risk male populations such as the following.

High-Risk Heterosexual Men

Multiple epidemiological and behavioural studies in India demonstrate the increased rates of HIV and STIs in men who have concurrent sexual relationships and who visit commercial sex workers.\[5,6\] This group often encompasses or overlaps with other categories designated by investigators such as truck drivers (see below), wine-shop patrons, attendees of STD clinics and MSM (see below). The heterogeneity of such a group is remarkable, however, the homogeneity of the risk factors, number and frequency of sexual partners is not and is well characterized.\[7,8\]

Truck Drivers

There are about three million trucks, often with both a driver and younger male helper or cleaner, on the roads in India. All published research studies examining HIV or STI prevalence of truck drivers in India have been cross-sectional in nature. These have taken place at generally high-risk roadside stop or border checkpoint areas where commercial sex work is easily available. There is one examination of truck driver behaviour over time, however, the sample was small and not tested for HIV or other sexually transmitted infections.\[9\] Information on rates of HIV and HSV infection when combined with sexual/social network information will improve our understanding of what prevention packages might be effective and where they might be implemented in this surprisingly understudied yet high-risk mobile population.

Men Who have Sex with Men

In India, MSM may represent a group of largely invisible individuals who may be at high risk for HIV infection.
and, therefore, formative research is important with this population. There are, however, two recent studies, one through India’s National AIDS Control Organization[40] and the other in a sample of individuals living in slums in South India,[41] which suggest high prevalence rates among MSM compared with the general population. There are a number of sociocultural issues regarding the sexual behaviour of MSM in India, which also call for formative research to develop HIV prevention interventions for this population. In India, MSM may be at sexual risk for HIV transmission and because of strong societal pressure to marry, they may also be a bridge population in terms of potentially transmitting the virus to their wives. Despite this, there are very few published data on issues related to HIV prevention among MSM in India, which may in part be because of societal stigma. With MSM in India being a hidden population for the most part, it is difficult to identify them and, therefore, also difficult to lay the groundwork for HIV prevention efforts.

**Novel HIV Prevention Science in India**

**Microbicides**

There is little information on the knowledge attitudes and beliefs among women towards HIV preventive microbicides in India and only a few small studies on these factors among male partners.[12-14] Additional information on the potential use of microbicides in MSM or women participating in anal intercourse in India is also unknown at this time. In India, microbicides are generally well accepted by female study participants; however, both studies highlighted the need to better understand the potential for covert use of the products in a setting where there are great challenges in improving the status of women. Additional male preference such as sexual satisfaction may play a role in women’s eventual uptake of the microbicide in question and has been documented as the main factor in on acceptability study in a population of Indian male partners.[14] Male approval for partner participation in clinical trials evaluating efficacy is not ethically appropriate; however, actual effectiveness of the microbicide will be dependent upon the safety profile in men who may be exposed to the investigational products over the long term, which may deserve ethical consideration. Attitudes, safety and acceptability among Indian men will have to be evaluated while preparing to introduce vaginal and potentially rectal microbicides in India.

**Circumcision**

The role of circumcision in India is unclear and considerations of local culture and sensitivities are warranted when examining the evidence supporting circumcision among high-prevalence male populations. Fears of communal strife with a 13% Muslim population should be taken seriously by policy makers who warn of increased rates among certain religious ethnicities. However, the particular population that will be targeted is of great importance and protection can be dramatic. In the Indian scenario, circumcision was strongly protective against HIV infection among attendees of an STD clinic.[15] In preliminary analyses from a population-based study in Guntur district, circumcision had the highest population impact on reducing HIV number among urban men. Baseline information on rates of circumcision and the availability of the technique is needed. It is important to note that 34% of circumcised men in one STD clinic in Pune self-identified as Hindu.[16] Qualitative data on barriers to acceptance would guide development of communication messages and help in sensitizing communities. Authorities suggest learning lessons from India’s failed vasectomy programme, which could prove valuable in guiding us with providing safe and affordable circumcision services to at-risk segments of the population.

*Pre-exposure prophylaxis/non-occupational post-exposure prophylaxis and STI suppression*

There are no studies on the use of pre-exposure prophylaxis (PREP)/non-occupational post-exposure prophylaxis (nPEP) or STI suppression strategies to prevent HIV acquisition or transmission in India. Studies underway examining PREP and the use of acyclovir for treatment of herpes simplex infection could prove to be viable prevention interventions for high-risk male populations. However, effectiveness studies will need to be carried out in the Indian context. Challenges in recommending therapies that may not be 100% effective in a setting where pills are generally taken when symptoms are present will need to be addressed.

**Future Direction**

The state of AP can be described as a country. AP has its own distinct language and, with a population of 80 million, is larger than Vietnam or Germany, and has the distinction of having the highest rates of HIV infection in the country according to preliminary estimates from the National HIV Estimates Consensus Workshop this past summer.[1] Located in the centre of the country, the capital of AP - Hyderabad, is directly connected to four other major cities in India through the national highway system and to other high-risk highway networks in the state, including the high HIV prevalence districts in coastal AP such as East Godavari. Therefore, it is imperative that we better understand HIV infection dynamics in high-risk male populations such as the estimated six million truck drivers in the country. Decreasing the rates of infection of this group could have potential impact on the infection rates in other parts of the country. The potential for transmission of resistant viruses throughout the country as the HIV epidemic continues to evolve could also be a devastating outcome of unchecked HIV/STI co-infection. Despite high rates of HIV infection and a large population, there remains a lack of Indian Council of Medical Research (ICMR) or National Institutes of Health (NIH) funded Indo-American collaborations in AP. There are no collaborative Fogarty
International Centres in AP and no collaborative HIV-related R01 or R03 grants in the state. Well-conducted research on HIV infection dynamics and evidence-based prevention strategies for understudied high-risk populations could inform programmes that are currently in transition in the state and country. For example, the APSACS truck driver interventions are in the process of being downsized. The Avahan truck driver interventions use syndromic management for the treatment of potential STIs, did not test for HSV-2 during their impact assessment[3,4] and do not offer onsite HIV testing, even after a new STI has been diagnosed. Additionally, using cohorts in India, which are susceptible to subtype C virus will be important for prevention interventions that take place in the future worldwide and that are desperately needed in regions hardest hit by the epidemic, such as sub-Saharan Africa.

References

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