REVIEW ARTICLE   **OPEN ACCESS**

MALE CIRCUMCISION: ITS ROLE IN HIV PREVENTION

Roohi Rasool, A. Syed Sameer, and Mushtaq A. Siddiqi*

Department of Immunology and Molecular Medicine; Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir, INDIA

ABSTRACT

BACKGROUND: The findings from observational studies, reviews and meta-analyses, supported by biological theories, that circumcised men appear less likely to acquire human immunodeficiency virus (HIV) has contributed to support for considering MC as a strategy for preventing sexually acquired infection. We sought to elucidate and appraise the global evidence from published studies that circumcision can be used as an intervention to prevent HIV infection. **OBJECTIVES:** This review summarizes the evidences for the potential of MC to prevent HIV. **SELECTION CRITERIA:** We searched for reviews and observational studies and compare acquisition rates of HIV-1 in circumcised and uncircumcised heterosexual men. **CONCLUSIONS:** We found insufficient evidence to support an interventional effect of MC on HIV acquisition in heterosexual men. The results from existing observational studies show a strong epidemiological association between MC and prevention of HIV, especially among high-risk groups. However, observational studies are inherently limited by confounding which is unlikely to be fully adjusted for. In the light of forthcoming results from RCTs, the value of IPD analysis of the included studies is doubtful. The results of these trials will need to be carefully considered before circumcision is implemented as a public health intervention for prevention of sexually transmitted HIV.

*Corresponding author: Email: mousvi786@gmail.com, vc.tmuk@gmail.com; Tel: PABX +91-194-2401013, Ext: 2262, Fax: +91-194-2403470

[I] INTRODUCTION

Male Circumcision (MC) is practiced in different societies all over the world, for religious, cultural/secular, and medical reasons. MC as a religious tradition is practiced by Jews and Muslims, usually during the neonatal period [1]. Within sub-Saharan Africa, MC is most often performed for cultural reasons and is largely determined by ethnicity [2]. In all situations, cultural differences between circumcised and uncircumcised men may affect their sexual and hygienic behavior, including their exposure to various STD and HIV-1 infection. About 30% of men are estimated to be circumcised worldwide, although this rate is still less than 20% in Europe. The procedure is often done shortly before or at puberty and is considered a rite of passage to adulthood.

In United States, MC is largely a secular decision, and its frequency has changed over time. The American Academy of Pediatrics Task Force on Circumcision stated in its 1999 revision on circumcision policy that circumcision conferred potential medical benefits, which could be considered by parents but that the scientific evidence, was insufficient to warrant recommending routine neonatal circumcision [3]. Currently, 80% of men in the United States are circumcised,

with higher rates for Caucasians than for African Americans and Hispanics [2]. In contrast, circumcision is less often practiced in Canada and in Europe [4] and within Asia there is considerable country-to-country variation in circumcision prevalence [5]. Circumcision has many health benefits which include: easier hygiene, decreased risk of urinary tract infections, prevention of penile problems like phimosis, decreased risk of penile cancer, decreased risk of sexually transmitted diseases including HIV-1.

In the 150 years since Moses [6] published his findings, a number of studies have evaluated the effect of circumcision on the acquisition of HIV-1 and STDs. The majority has found a protective effect of MC on acquisition of genital ulcers and HIV-1. Despite the consensus that emerges from the literature, the implementation of circumcision promotion as a population-based intervention to reduce HIV-1 and STD incidence has not been seriously entertained. We acknowledge that attitudes toward MC may be difficult to change in some settings, but we encourage behavioral scientists to conduct acceptability studies, particularly in high HIV -1 prevalence communities, to begin assessing feasibility of circumcision promotion.

[II] EPIDEMIOLOGICAL EVIDENCES

Male Circumcision markedly decreases the acquisition of HIV-1 infection, the major epidemic of our time. This is the first biological intervention shown to prevent HIV-1 infection and will not depend upon continuing behaviour change to give protection. In 1986, five years after the description of AIDS, the first article suggesting that MC is associated with lower risk of human immunodeficiency virus (HIV-1) infection was published. During the following years, different studies almost exclusively from sub-Saharan Africa, which quickly became the centre of HIV-1 epidemic increasingly supported this hypothesis [7]. The tribes and other defined populations with low prevalence of MC had high prevalence of HIV-1 infection, suggesting a correlation between MC and HIV-1 prevention [8, 9, 10].

Several physiologic mechanism MC might explain the association between an intact foreskin and increased risk of HIV-1 and genital ulcers. In uncircumcised men, the epithelium lining the glans and preputial sac is thinner and less cornified than that of circumcised men and therefore may be more susceptible to traumatic lesions during sexual intercourse and to the transfer of microorganism between partners [11]. The environment of the preputial sac may be favorable for the survival and replication of bacteria and viruses, allowing for a longer exposure time for infections to occur. This effect may be accentuated by poor hygienic practices. Finally, the stratified squamous epithelium of the foreskin contains target cells for HIV-1 (Langerhans cells and macrophages that are coated with CD4 receptors) [12]. It has been suggested that following circumcision, the surface epithelium of the glans develops a protective keratin layer, a form of natural condom [13]. Thus, circumcision could reduce the HIV-1 incidence by directly decreasing the susceptibility of uninfected men to HIV-1. Circumcision could also reduce the incidence of HIV-1 by directly decreasing the infectivity of men with HIV-1, as suggested by the studies of tissue samples collected from macaques infected with the simian immunodeficiency virus (SIV), which showed infected mononuclear cells in the dermis and epidermis of the penile foreskin [14].

Despite that, there is still uncertainty among many scientists and public health scientific societies, mainly due to the fear that circumcised men have different (safer) sexual practices than men who are not, and that this and not MC led to lower rates of HIV-1 infection in circumcised men and in populations where circumcision is common. Furthermore, some or all sexually transmitted diseases (STD) may increase men's susceptibility to HIV-1 [15, 16]. If circumcision reduces the transmission of genital infections, either by improving local hygiene or by accelerating the healing of otherwise subpreputial lesion circumcision may also delay HIV-1

transmission [17]. Therefore, potential associations between the lack of circumcision and STD other than HIV-1 are also of interest.

Surprising to some, multiple studies have consistently shown that populations which do not traditionally circumcise their children or young adults will readily accept MC. In 13 studies carried out in sub-Saharan Africa, 65% of men were willing to be circumcised and 69% of women favoured MC for their male partners. Improved hygiene, sexual satisfaction, and partial protection from HIV-1 are cited as principal reasons. The widespread implementation of MC in Southern sub-Saharan Africa, where prevalence of MC is generally low and HIV-1 is very common, could prevent 2,000,000 infections over a 10-year period. While it is unclear if a circumcised man who is HIV-positive is less likely to transmit HIV-1 to a woman than if he is not circumcised, women in general would benefit from increasing rates of MC because fewer men would become infected with HIV-1. WHO recommends that countries where the incidence of heterosexually acquired HIV-1 infection is high and the diffusion of MC is low urgently consider implementing the access to MC services as a priority. WHO examined all the available data about the effectiveness of MC in preventing HIV-1 infection, and recognized MC as an additional important intervention to reduce the risk of heterosexually acquired HIV-1 infection in men. Adequate resources should be rapidly mobilized to support the expansion of safe MC services within the context of moving towards universal access to comprehensive HIV prevention, treatment and care [18, 19].

Over the past decade, numerous epidemiological studies have reported a significant association between lack of MC and risk for HIV -1 infection, leading to recommendations for MC to be added to the armamentarium of effective HIV-1 prevention strategies. We review the epidemiological data from studies that have investigated this association, including ecological, cross-sectional/case-control, and prospective and retrospective studies. An individual's choice to undergo MC or a community's decision to promote the practice should be made in the light of the best available scientific evidence.

According to a recent meta-analysis conducted by Vermund *et al*., MC has been shown to protect men from acquiring HIV-1 infection during sex with women. It has reduced female-to-male transmission rates by 48% to 60% in sub-Saharan Africa but that protective effect appears less reliable among men who have sex with men. It encompasses data from 15 studies conducted in seven countries, involving more than 53,000 men, most of whom were Caucasian and approximately half of whom were circumcised. The authors concluded that being circumcised reduced a man's risk of acquiring HIV-1 by 14%. Though the finding was statistically non significant, but the authors advocated that it should be regarded as a launching point for future trials. Millett's analysis found that in studies

©IIOAB-India

Rasool et al. IIOABJ; Vol. 2; Issue 5; 2011:19–24   **20**

INFECTIOUS DISEASE

www.iioab.org

THE IIOAB JOURNAL

www.iioab.webs.com

conducted before 1996 before the advent of highly active antiretroviral therapy circumcision was associated with a statistically significant 53% reduction in HIV-1 transmission risk, which is on par with the 48% to 60% reduction in infection rates reported by the 2007 trials in Kenya, South Africa and Uganda that studied heterosexual men. After 1996, however, when antiretroviral (ARV) drugs turned HIV-1 into a condition that people lived with rather than died from, the protective effect of circumcision became non significant [19, 20, 21].

Bailey *et al*., in 2007 conducted the two studies and found a protective effect of 53% and 60% respectively in men who were circumcised, compared to those who were not The trial enrolled 2,784 men and was carried out on the behalf of the U.S. National Institutes of Health and the Canadian Institute for Health Research, while the other study, also sponsored by the National Institutes of Health, randomized 4,996 men. Each of these trials was also stopped prematurely in December 2006, due to an extremely high efficacy rate. The findings of the studies are similar, and remarkably consistent with the protective effect (58% on average) found in a systematic review of observational studies available in medical literature. This is the first published prospective study with this finding in an occupationally based cohort, which may be more representative of the general population than cohorts recruited from STD clinics. In this prospective cohort study, uncircumcised men were at 4-fold increased risk for acquiring HIV-1 infection. In addition to HIV-1 risk, uncircumcised status was associated with a 2.5-fold increased risk of genital ulcer disease [22].

Auvert *et al*., in 2005 showed a 60% protective effect against HIV-1 infection among the men who were circumcised. The study was conducted on the behalf of the South African National Institute for Communicable Diseases (Johannesburg) and the Institute National de la Santé et de la Recherche Médicale (ANRS Paris, France), involving 3,274 men who were randomized to receive circumcision or not. The subjects were followed over a mean period of 18.1 months, and the trial was stopped prematurely because of the high efficacy observed among circumcised patients [23].

Reynolds *et al*., in 2003, in a prospective study of 2298 HIV-1uninfected men attending sexually transmitted infection clinics in India, noted that circumcision was strongly protective against HIV-1 infection (adjusted relative risk 0•15; 95% CI 0•04–0•62; p=0•0089); however, they noted no protective effect against herpes simplex virus type 2, syphilis, or gonorrhoea. The specificity of this relation suggests a biological rather than behavioural explanation for the protective effect of MC against HIV-1[24].

Szabo and Short, in their excellent review made compelling epidemiological evidence from over 40 studies which showed that MC provided significant protection against HIV-1 infection; circumcised males were two to eight times less likely to become infected with HIV [25]. Furthermore, circumcision also protected against other sexually transmitted infections, such as syphilis and gonorrhoea [26] and since people who had a sexually transmitted infection were two to five times more likely to become infected with HIV-1[27] circumcision may be even more protective. The most dramatic evidence of the protective effect of circumcision came from study of couples in Uganda who had discordant HIV-1 status; in the study the woman was HIV-1 positive and her male partner was not [28] No new infections occurred among any of the 50 circumcised men over 30 months, whereas 40 of 137 uncircumcised men became infected during this time. Both groups had been given free access to HIV testing, intensive instruction about preventing infection, and free condoms (which were continuously available), but 89% of the men never used condoms, and condom use did not seem to influence the rate of transmission of HIV-1. These findings focused the spotlight of scientific attention onto the foreskin. That is its removal reduces a man's susceptibility to HIV-1 infection [29].

Grey *et al*., determined HIV-1 acquisition in a cohort of 5507 HIV-negative Ugandan men, and in 187 HIV-negative men in discordant relationships. Transmission was determined in 223 HIV-positive men with HIV-negative partners. HIV-1 incidence per 100 person years (py) and adjusted rate ratios (RR) and 95% confidence intervals (CI) were estimated by Poisson regression. HIV-1 serum viral load was determined for the seropositive partners in HIV-1discordant couples. The prevalence of circumcision were 16.5% for all men; 99.1% in Muslims and 3.7% in non-Muslims. Circumcision was significantly associated with reduced HIV-1 acquisition in the cohort as a whole (RR 0.53, CI 0.33-0.87), but not among non-Muslim men [30].

Prepubertal circumcision significantly reduced HIV-1 acquisition (RR 0.49, CI 0.26-0.82), but post pubertal circumcision did not. In discordant couples with HIV-negative men, no seroconversions occurred in 50 circumcised men, whereas HIV-1 acquisition was 16.7 per 100 py in uncircumcised men (P = 0.004). In couples with HIV-positive men, HIV transmission was significantly reduced in circumcised men with HIV-1 viral loads less than 50 000 copies/ml (P = 0.02).Prepubertal circumcision may reduce male HIV-1 acquisition in a general population, but the protective effects are confounded by cultural and behavioral factors in Muslims. In discordant couples, circumcision reduces HIV acquisition and transmission. This analysis confined to circumcised men, suggests that Muslims may generally be at lower risk of HIV-1 acquisition than non-Muslims, particularly in the age group 20-29 years. Although Muslims have a generally lower risk profile than circumcised non-Muslims, it is unclear what specific behaviors, other than

abstinence from alcohol, might reduce the risk among Muslim men. However, key informant interviews suggest that the Islamic practice of post-coital cleansing before prayer may be an important factor explaining the lower incidence of HIV-1 in circumcised Muslim men [31, 32].

Moses *et al*., identified 26 cross-sectional studies regarding circumcision and HIV-1 prevention. Eleven studies found a significant difference in HIV-1 prevalence between circumcised and uncircumcised men after adjusting for potential confounders, including indices of sexual behavior, with odds ratios of 1.5–5.6. Six other studies found a significant difference, but no adjustment for possible confounders was reported [33, 34].

Lavrey *et al*., in 1999, conducted another prospective cohort study involving 746 HIV-1 seronegative trucking company employees, in Mombasa, Kenya; during the course of follow-up, 43 men acquired HIV-1 antibodies, yielding an annual incidence of 3.0%. The annual incidences of genital ulcers and urethritis were 4.2% and 15.5%, respectively. In this analysis, after controlling for demographic and behavioral variables, uncircumcised status was an independent risk factor for HIV-1 infection (hazard rate ratio [HRR= 4.0; 95% confidence interval [CI], 1.9–8.3) and genital ulcer disease (HRR= 2.5; 95% CI, 1.1–5.3). Circumcision status had no effect on the acquisition of urethral infections and genital warts. Uncircumcised status was associated with increased risk of HIV-1 infection and genital ulcer disease, and these effects remained after controlling for potential confounders [35].

Another meta analysis of 27 studies, conducted by Weiss *et al*. in 1999, that included circumcision as a risk factor for HIV-1 infection among men in sub-Saharan Africa, 21 studies showed a reduced risk of HIV-1 among circumcised men, being approximately half that in uncircumcised men (crude RR = 0.52, CI 0.40-0.68). In 15 studies that adjusted for potential confounding factors, the association was even stronger (adjusted RR = 0.42, CI 0.34-0.54). The association was stronger among men at high risk of HIV-1 (crude RR = 0.27; adjusted RR = 0.29, CI 0.20-0.41) than among men in general populations (crude RR = 0.93; adjusted RR = 0.56, CI 0.44-0.70). The meta analysis showed MC is associated with a significantly reduced risk of HIV infection among men in sub-Saharan Africa, particularly those at high risk of HIV-1. These results suggest that consideration should be given to the acceptability and feasibility of providing safe services for MC as an additional HIV-1 prevention strategy in areas of Africa where men are not traditionally circumcised [36].

Cameron *et al*. Studied the effect of circumcision on the risk of HIV-1 sero conversion in a group of male STD patients in Nairobi and found a risk ratio of 8.2 for uncircumcised men after adjusting for potential confounders. In studies of STD clinic patients in New York City and in Pune, India, there were

trends for uncircumcised men to be at increased risk of HIV-1 acquisition, but these associations were not statistically significant [37, 38, 39].

Various retrospective studies including partner studies were done by researchers like Guimeraes in 1991 in Brazil, (sample size 109, O.R 0.4),Moss Kenya, 1991(sample size 70, O.R 0.4), Allen Rwanda,1991(sample size 1458 O.R 1.1) showed no statistical significance of association between HIV-1 serostatus and lack of circumcision, while as studies by Fischl,USA,1988, (sample size 92 OR 9.6) Hunter Kenya 1990,(sample size 623 , OR 3.7)and Hellman Uganda 1991 (sample size 42 OR 5.4) showed statistically significant association between HIV-1 sero status and lack of circumcision. In several other retrospective studies [40-49] male populations were recruited to look for risk factors for HIV infection, four (12, 38, 40, 42) reported significant associations between the lack of circumcision and an increased susceptibility to HIV-1 infection in men.

Furthermore, in a recent study by Baeten *et al*., 2010 MC modestly reduces the risk of an HIV-positive man transmitting HIV to a female sex partner. This prospective study was carried on a total of 1096 African HIV-1-serodiscordant couples which were analyzed for the relationship between circumcision status of HIV-1-seropositive men and risk of HIV-1 acquisition among their female partners. Analysis showed that HIV incidence was approximately 40% lower in these genetically linked transmissions amongst women whose partner was circumcised (hazard ratio 0.57; 95% CI, 0.29-1.11, p = 0.10). However, this could have been down to chance as this reduction in risk was not statistically significant [50].

[III] CONCLUSION

The About 70% of men infected with HIV-1 have acquired the virus through vaginal sex, and a smaller number have acquired it from insertive anal intercourse [49]. Thus, on a global scale most men who are HIV-1 positive have acquired the virus via the penis. Of the estimated 50 million people infected with HIV worldwide, about half are men, who become infected through their penises. The inner surface of the foreskin, which is rich in HIV receptors, and the frenulum, a common site for trauma and other sexually transmitted infections, must be regarded as the most probable sites for viral entry in primary HIV-1 infection in men [50, 51]. Although condoms must remain the first choice for preventing the sexual transmission of HIV-1, they are often not used consistently or correctly, they may break during use, and there may be strong cultural and aesthetic objections to using them. Cultural and religious attitudes towards MC are even more deeply held, but in the light of the evidence presented here circumcising males seems highly desirable, especially in countries with a high prevalence of HIV-1 infection. Circumcision at puberty, as practiced by many Muslim communities, would be the most immediately

©IIOAB-India

Rasool et al. IIOABJ; Vol. 2; Issue 5; 2011:19–24

22

effective intervention for reducing HIV-1 transmission since it would be done before young men are likely to become sexually active. MC may protect HIV-1 negative men from acquiring HIV -1 infection to varying degrees. The effects are more modest in the general population, in which HIV-1 exposure and incidence are relatively low. Also, the apparent protective effects of circumcision are not consistently observed in all subgroups and are largely associated with Muslim religious affiliation, which could be a marker for unmeasured differences in cultural practices or sexual behaviors. [51] However, circumcision appears to be highly protective among HIV-1 negative men in a discordant relationship with an HIV-1 positive female partner, and circumcision may reduce HIV-1 transmission from HIV-1 positive men with viral loads of less than 50, 000 copies/ml. We believe that these observational data are not sufficient to justify the promotion of voluntary circumcision for HIV-1 prevention in the general population or in high-risk groups and those clinical trials are needed before policies on circumcision for HIV-1 prevention can be established.

It is also to be noted that nobody should frame MC as some sort of panacea. But it may prove to be one more tool in the toolbox. If we can add it to behavioral risk reduction, prompt diagnosis and access to care, it may be the combination needed to really knock the socks off the HIV-1 epidemic.

REFERENCES

[1] Piot P, Laga M. [1989] Genital ulcers and other sexually transmitted diseases, and the sexual transmission of HIV. *BMJ* 298:623–624.

[2] Hudson CP, Hennis AJM, Kataaha P, *et al*. [1988] Risk factors for the spread of AIDS in rural Africa: Evidence for a comparative seroepidemiological survey of AIDS, hepatitis B and syphilis in southwestern Uganda. *AIDS* 2:255–260.

[3] Carael M, van de Perre PH, Lepage PH, *et al*. [1988] Human immunodeficiency virus transmission among heterosexual couples in Central Africa. *AIDS* 2:201–205.

[4] Surick I, McLaughlin M, Chaisson M. [1989] HIV infection and circumcision status. *International Conference AIDS, Montreal* 5:113.

[5] Chiasson MA, Stoneburner RL, Hildebrandt DS, Ewing WE, Telzak EE, Jaffe HW. [1991] Heterosexual transmission of HIV-1 associated with the use of smokable freebase cocaine. *AIDS* 5:1121–1126.

[6] Moses S, Bradley JE, Nagelkerke NJD, Ronald AR, Ndinya Achola JO, Plummer FA. [1990]Geographical patterns of Male Circumcision practices in Africa association with HIV seroprevalence. *Int J Epidemiol* 19:693–697.

[7] Mertens TE, Hayes RJ, Smith PG. [1990] Epidemiological methods to study the interaction between HIV infection and other sexually transmitted diseases. *AIDS* 4:57–65.

[8] Marx JL. [1989] Circumcision may protect against the AIDS virus. *Science* 245:470–471.

[9] Greenough FB. [1881]Herpes progenitalis. *Arch Dermatol* 7:1–29.

[10] D'Costa LJ, Bowmer I, Nsanze H, *et al*. [1986] Advances in the diagnosis and management of chancroid. *Sex Trans Dis* 62:44-46.

[11] Hart G. [1974] Factors influencing venereal infection in a war environment. *Br J Ven Dis* 50:68–72.

[12] Hellmann NS, Desmond-Helmann SD, Nsubuga P, Mbidde EK. [1991] Risk factors for HIV infection among Ugandan couples. *VII Intl Conf on AIDS*. Florence.

[13] Fischl M, Fayne T, Flanagan S, *et al*. [1988] Seroprevalence and risks of HIV infections in spouses of persons infected with HIV. IV *International Conference on AIDS* Stockholm.

[14] Fink AJ. [1987] Circumcision and heterosexual transmission of HIV infection to men [Letter]. *N Engl J Med* 316: 1546–1547.

[15] Miller CJ, Vogel P, Alexander NJ, Sutjipto S, Hendrickx AG, Marx PA. [1992] Localization of SIV in the genital tract of chronically infected female rhesus macaques. *Am journal path* 141(3): 655–660.

[16] Rachel A, Royce Arlene Seña, Willard Cates J, Myron S. [1997] Cohen, Sexual Transmission of HIV. *N Engl J Med* 336:1072–1078.

[17] Hunter D, Maggwa A, Mati J, *et al*. [1992] Risk factors for HIV infection among women in a low-risk population in Nairobi, Kenya. *The Journal of Infectious Diseases* 166:1.

[18] Guimaraes M, Castilho E, Ramos-Filho C, *et al*. [1991] Heterosexual transmission of HIV-1: a multicenter study in Rio de Janeiro, Brazil. *VII International Conference on AIDS* Florence.

[19] WHO. [2007] Male circumcision and HIV prevention: operations research implications. *International consultation report* Nairobi, Kenya, 21- 22 June.

[20] Vermund SH and Qian HZ. Circumcision and HIV Prevention Among Men Who Have Sex With Men: No Final Word *JAMA* 300:1698–1700.

[21] Dotinga R. [2008] Role of Circumcision in Reducing HIV Risk Still Unclear, Review doesn't find a protective effect in post-HAART era. *Health Day Reporter* Oct 7.

[22] Bailey RC, *et al*. [2008] The protective effect of Male circumcision is sustained for at least 42 months: results from the Kisumu, Kenya trial. *Lancet* 369:643–656.

[23] Auvert B, *et al*. [2008] Effect of Male circumcision on human papilloma virus, Neisseria gonorrhoeae and Trichomonas vaginalis infections in men: results from a randomized controlled trial. *PLoS Med* 2:209.

[24] Reynolds S, Shepherd M, Risbud A, Gangakhedkar R, Brookmeyer R, Divekar A, Mehendale S, Bollinger R. [2003] Male circumcision and risk of HIV-1 and other sexually transmitted infections in India. *The Lancet* 9414: 1039–1040.

[25] Szabo R, Short RV. [2000] How does Male circumcision protect against HIV infection? *British Medical Journal* 320:1592–1594

[26] Halperin DT, Bailey RC. [1999] Male circumcision and HIV infection: 10 years and counting. *Lancet* 354: 1813–1815.

[27] Cook LS, Koutsky LA, Holmes KK. [1994] Circumcision and sexually transmitted diseases. *Am J Public Health* 84: 197–201.

[28] Fleming DT, Wasserheit JN. [1999] From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect* 75: 3–17.

[29] Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire Mangen F, *et al*. [2000] Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 342: 921–929

[30] Gray RH, Kiwanuka NQ, Thomas C and its Project Team. [2000] MC and HIV acquisition and transmission: cohort studies in Rakai, Uganda. *AIDS* Volume 14: 2371–2381.

[31] Wawer MJ, Sewankambo NK, Berkley S, *et al*. [1994] Incidence of HIV-1 infection in a rural region of Uganda. *BMJ* 308: 171 –173.

[32] Kangeya Kayondo JF, Kamali A, Nunn AJ, *et al*. [2000] Incidence of HIV-1 infection in adults and sociodemographic characteristics of seroconverters in a rural population in Uganda. *Int J Epidemiol* 25: 1077–1082.

[33] Moss GB, Clemetson D, D'Costa L, *et al*. [1991] Association of cervical ectopy with heterosexual transmission of HIV: results of a study of couples in Nairobi, Kenya. *Infect Dis* 164:588–591.

[34] Moses S, Bailey RC, Ronald AR. [1998] MC: assessment of health benefits and risks. *Sex Transm Infect* 74: 368–373.

[35] Lavreys L, Rakwar JP, Thompson ML, *et al*. [1999] Effect of circumcison on incidence of human immunodeficiency virus type 1 and other sexually transmitted diseases: a prospective cohort study of trucking company employees in Kenya. *J Infect Dis* 180: 330–333.

[36] Weiss HA, Quigley MA, Hayes RJ. [2000] MC and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis *AIDS* 14:2361–2370.

[37] Cameron DW, Simonsen JN, D'Costa LJ, *et al*. [1989] Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 2: 403–407.

[38] Allen S, Lindan C, Serufilira A, *et al*. [1991] HIV infection in urban Rwanda. *JAMA* 266:1657–1663.

[39] Whittington WL, Jacobs B, Lewis J, Lee F, Edwards T, Nahmias A. [1989] International Conference on AIDS. HIV-1 in patients with genital lesions attending a North American STD clinic: assessment of risk factors. *Int Conf AIDS* 5: 118.

[40] Simonsen JN, Cameron DW, Gakinya MN, *et al*. [1988] HIV infection among men with STD. *NEJM* 319:274–278.

[41] Mehendale MM, Rodriguez JJ, Brookmyer RS, *et al*. [1995] Incidence and predictors of human immunodeficiency virus type-1 seroconversion in patients attending sexually transmitted disease clinics in India. *J Infect Dis* 172: 1486–1491.

[42] Tyndall M, Odhiambo P, Ronald AR, *et al*. [1991] The increasing seroprevalence of HIV-1 in males with other STD in Nairobi, Kenya. *VII International Conference on AIDS* 7:325.

[43] Hira SK, Kamanga J, Macuacua R *et al*.[1990] Genital ulcers and MC as risk factors for acquiring HIV-1 in Zambia. *J Infect Dis* 161:584–585.

[44] Greenblatt RM, Lukehart SA, Plummer FA, *et al*. [1988] Genital ulceration as a risk factor for HIV infection. *AIDS* 2:47–50.

[45] Van de Perre P, Carael M, Nzaramba D, Zissis G, Kayihigi J, Butzler JP.[1987] Risk factors for HIV seropositivity in selected urban-based Rwandese adults. *AIDS* 1: 207–211.

[46] Konde-Lule JK, Berkley SF, Downing R. [1989] Knowledge, attitudes and practices concerning AIDS in Ugandans. *AIDS* 3:513–518.

[47] Gershy-Damet G-M, Koffi K, Soro B, *et al*.[1991] Seroepidemiological survey of HIV-1 and HIV-2 infections in the five regions of Ivory Coast. *AIDS* 5:462–463.

[48] Roddy RE, Feldblum PJ. [1991] Analytical methodology in a cohort study of cofactors for sexual transmission of HIV. *J Infect Dis* 164: 1236–1237.

[49] Joint United Nations Programme on HIV/AIDS. The HIV/AIDS situation in mid 1996: global and regional highlights. Geneva: United Nations, 1996.

[50] Baeten JM, Donnell D, Kapiga SH, Ronald A, John-Stewart G, *et al*. [2010] Partners in Prevention HSV/HIV Transmission Study Team. MC and risk of male-to-female HIV-1 transmission: a multinational prospective study in African HIV-1-serodiscordant couples. *AIDS* 24:737–44.

[51] Morris B. [1999] In favour of circumcision. Sydney, *University of New South Wales Press*.

INFECTIOUS DISEASE

©IIOAB-India

Rasool et al. IIOABJ; Vol. 2; Issue 5; 2011:19–24

24