

# Male circumcision and Sexually transmitted Infections – An update

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## Abstract

Role of male circumcision (MC) as a tool to prevent sexually transmitted infections (STIs)/human immunodeficiency virus (HIV) was assessed. An attempt was made to search articles related to association between MC and STIs/HIV. A thorough search was carried out to find out quality articles published in indexed specialty journals. Centers for Disease Control and Prevention and World Health Organization (WHO) sites were also referred. Warm and moist environment of area under foreskin facilitates some pathogens to persist and replicate. Further, the thinness of foreskin predisposes it to minor trauma and abrasions that facilitate the entry of pathogens. MC reduces HIV infection risk by 50%–60% over time and reduces the risk of men acquiring herpes simplex virus-2 and human papillomavirus (HPV) that can cause penile and other anogenital cancers, by 30%. There is no significant reduction in risk of acquiring syphilis, but reduced risk of acquisition of *Haemophilus ducreyi* is reported. MC is reported to be beneficial in conditions such as traumatic injury, Balanitis Xerotica Obliterans, refractory balanoposthitis, and chronic, recurrent urinary tract infections. MC also reduces the chances of penile carcinoma by facilitating improved penile hygiene, lowering HPV/HIV transmission rates, and reducing chronic inflammatory conditions such as phimosis and balanitis. MC has been recommended by the WHO and UNAIDS in 2007 as an additional HIV prevention intervention in settings of high HIV prevalence. MC is an important adjunct to safe sex education, condom use, and vaccination (HPV) in reducing the global burden of HIV/STIs-related morbidity and mortality.

**Key words:** Centers for Disease Control, female genital mutilation, human immunodeficiency virus, male circumcision, sexually transmitted infections

## INTRODUCTION

### Foreskin and genital health

The foreskin is a part of our phylogenetic heritage. Chimpanzees, our closest living relatives, and other nonhuman primates have prepuces that partially or completely cover the glans penis.<sup>[1]</sup> The inner surface of foreskin contains modified sebaceous glands that secrete smegma. The area under the foreskin is warm, and moist environment may facilitate some

pathogens to persist and replicate, more so if penile hygiene is poor. The inner mucosal surface of the foreskin is only thinly keratinized, compared to the heavily keratinized penile shaft and the outer surface of the foreskin. The thinness of foreskin predisposes it to minor trauma and abrasions that facilitate the entry of pathogens.<sup>[2]</sup>

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**How to cite this article:** Mehta KS, Marfatia YS, Jain AP, Shah DJ, Baxi DS. Male circumcision and Sexually transmitted Infections – An update. Indian J Sex Transm Dis 2021;42:1-6.

**Submitted:** 11-Mar-2021

**Revised:** 13-Mar-2021

**Accepted:** 18-Mar-2021

**Published:** 03-May-2021

Access this article online	
Quick Response Code: 	<b>Website:</b> <a href="http://www.ijstd.org">www.ijstd.org</a>
	<b>DOI:</b> 10.4103/ijstd.ijstd_20_21

## Male circumcision

Male circumcision (MC) is the removal of some or the entire foreskin (prepuce) from the penis. The word “circumcision” comes from Latin *circum* (meaning “around”) and *caedere* (meaning “to cut”). In Jews, it is performed without anesthesia on the child’s 8<sup>th</sup> day of life, whereas in Muslims between 4 and 13 years of age. There are several advantages of circumcising males at a younger versus older age including a lower risk of complications, faster healing, and a lower cost.

Various studies support the claim of reduction of the risk of sexually transmitted infections (STIs) to justify neonatal circumcision even today.<sup>[3,4]</sup>

A study by Hutson claimed that the risk of urinary tract infection (UTI) had decreased from 7/1000 to 2/1000 after neonatal MC.<sup>[5]</sup> MC is reported to reduce risk of STIs including human immunodeficiency virus (HIV) infection and UTI in infants.

The aim of this article is to review systematically the evidence for an association between MC and ulcerative as well as nonulcerative STIs.

## HISTORY

Circumcision, a long-standing practice, is one of the most common procedures performed worldwide. It may be performed for religious (Jewish and Islamic faith), cultural (for example, Korean, Turkish, and African groups) or social reasons. Similar observations were reported at a meeting of traditional healers in South Africa in 1992 and in a study of circumcision practices in Mwanza.

## CENTERS FOR DISEASE CONTROL AND PREVENTION—MALE CIRCUMCISION RECOMMENDATIONS

The draft policy recommendations of Centers for Disease Control and Prevention<sup>[6]</sup> (CDC) (2014) affirmed MC as an important public health measure.

Clinical trials conducted between 2005 and 2010 have demonstrated safety and significant efficacy of voluntary adult MC performed by clinicians for reducing the risk of acquisition of HIV by a male during penile-vaginal sex. Three randomized clinical trials showed that adult MC reduced HIV infection risk by 50%–60% over time and reduced the risk of men acquiring two common STIs, herpes simplex virus type-2 (HSV-2) and types of human papilloma virus (HPV) that can cause penile and other anogenital cancers, by 30%.

CDC recommendations on MC include the following points:

1. Give parents of newborn boys comprehensive counseling about the benefits and risks of MC
2. Inform all uncircumcised adolescent and adult males who engage in heterosexual sex about the significant, but partial, efficacy of MC in reducing the risk of acquiring HIV, and some STIs through heterosexual sex, as well as about the potential harms of MC
3. Inform men who have sex with men (MSM) that while it is biologically plausible that MC could benefit MSM during insertive sex, MC has not been proven to reduce the risk of acquiring HIV or other STIs during anal sex.

## CIRCUMCISION AND HUMAN IMMUNODEFICIENCY VIRUS

Studies by Weiss *et al.* and Ed Susman show a clear evidence that circumcised men are at significantly lower risk of acquiring HIV infection,<sup>[7,8]</sup> probably because the inner surface of the foreskin contains numerous Langerhans cells and CD4+ T lymphocytes and also because of the warm, moist environment under the foreskin promoting infection persistence. The latter could also facilitate infection with other sexually transmitted pathogens. The protective effect of circumcision on HIV is especially strong among populations more highly exposed to STIs, suggesting that part of the effect on HIV may be mediated through protection against other STIs that facilitate HIV transmission. The CDC announced in 2007 that there is “sufficient evidence” to inform heterosexually active males about the significant, albeit partial, efficacy of MC in reducing the risk of HIV infection.

MC was recommended by the World Health Organization (WHO) and UNAIDS in 2007 as an additional HIV prevention intervention in settings of high HIV prevalence.

Studies conducted by Warner *et al.* in the USA and Chemtob *et al.* in Israel showed an inverse association between MC and HIV acquisition.<sup>[9,10]</sup> A systematic review of studies conducted in India included 13 observational studies and also similarly showed that circumcision may reduce HIV acquisition by approximately 40%.<sup>[11]</sup>

Based on the available evidence, two global HIV prevention targets for 2020 also focus on higher coverage of safe MC to achieve maximum impact on HIV incidence. The provision of safe MC services is one of the few HIV interventions that specifically target adolescent boys and men.<sup>[12]</sup>

## CIRCUMCISION AND SEXUALLY TRANSMITTED INFECTIONS

There are conflicting reports on the effect of circumcision on the incidence of STIs. Uncircumcised men may be at increased risk of STIs due to entry of pathogens through the inner surface of the foreskin and frenulum. The physical location of ulcers may also affect the role of circumcision on genital ulcerative diseases. Chancroid frequently occurs on the external and internal surfaces of the foreskin; hence, circumcision may be more protective against chancroid than against syphilis and herpes, where lesions tend to occur more on glans penis.

## CIRCUMCISION AND HERPES SIMPLEX VIRUS-2

In contrast to HIV, it has been found that HSV replicates largely in the epithelial cells and also infects Langerhans cells and other dendritic cells, while both stimulate and inhibit their immune function. Circumcision not only results in a smaller surface area for infection but also fewer immune cells to respond against HSV. HSV-2 is shed more widely from the female genital tract than HIV, and there are several portals of entry in female-male transmission besides the foreskin. The role of the foreskin on HSV-2 infection may thus be relatively minor. In a prospective trial on MC and risk of HIV and other STIs in India by Reynolds *et al.*,<sup>[13]</sup> it was found that MC had no significant protective effect on the incidence of HSV-2 in HIV seronegative men.

According to meta-analysis by Weiss *et al.* of ten cohort studies (eight from Africa, one from India, and one from the United States) on association of MC and HSV-2 seropositivity, in which six studies were among men at generally low risk for STIs (general populations and outpatients) and four were among men at higher risk of STIs (bar workers, truck drivers, and sexually transmitted disease clinic attenders); in six studies, circumcised men were at lower risk of HSV-2 seropositivity than uncircumcised men on universal analysis and the association was statistically significant ( $P = 0.05$ ) in three of these studies.<sup>[14,15]</sup>

In the Ugandan and South African, randomized control trials (RCTs) reviewed by Tobian *et al.*, the incidence of HSV-2 was approximately 30% lower among circumcised men.

However, MC did not affect HSV-2 acquisition among female partners.<sup>[16]</sup>

## CIRCUMCISION AND SYPHILIS

According to a meta-analysis by Weiss *et al.*,<sup>[15]</sup> 14 studies examined the association between MC

and serological evidence of syphilis infection from sub-Saharan Africa (9 studies), the United States (2 studies), Australia, India, and Peru, out of which 5 showed statistically significant reduced risk.

On the contrary, a randomized prospective trial including 5534 heterosexual men in Uganda by Tobian *et al.*<sup>[16]</sup> reported the impact of circumcision on serological syphilis and found no effect in circumcised men.

Another RCT, performed on 4761 males in Kenya and Uganda, showed that circumcision was associated with a 42% reduction in the incidence of syphilis. In a subgroup analysis among HIV-infected men, a 62% reduction in the incidence of syphilis was noted, whereas a nonsignificant reduction in the incidence of syphilis was observed among men without HIV.<sup>[17]</sup>

In a prospective trial on MC and risk of HIV and other STIs in India by Reynolds *et al.*, it was found that MC had no significant protective effect on incident syphilis in HIV seronegative men.<sup>[13]</sup>

In a systemic review study by Van Howe,<sup>[18]</sup> out of seven prevalence studies reviewed in heterosexual men, positive association of syphilis in uncircumcised men was seen primarily in populations at high risk for acquiring STIs, while in general populations, no statistically significant difference was found.

## CIRCUMCISION AND CHANCROID

According to meta-analysis by Weiss *et al.*,<sup>[15]</sup> seven studies examined the association between MC and chancroid. Of these, three were from Kenya and the remainder from the United States, the United Kingdom, and the US and Australian military. Six of seven studies found a reduced risk of chancroid among circumcised men, and this was statistically significant in four studies. According to Balachandra and Sathish Pai, uncircumcised men are more susceptible to infection with *Haemophilus ducreyi*.<sup>[19]</sup>

## CIRCUMCISION AND HUMAN PAPILLOMA VIRUS

In a large RCTs on immediate versus deferred circumcision by Tobian *et al.* and Gray *et al.*, it was demonstrated that circumcision decreases HPV infection rates among HIV-negative heterosexual men.<sup>[20,21]</sup>

In a systemic review study by Van Howe,<sup>[18]</sup> studies which reported infections with any strain of HPV showed a higher prevalence in uncircumcised men, but the association was not significant. Furthermore, studies on infections with selective

high-risk HPV showed no significant difference in the prevalence of HPV on the basis of circumcision status. No significant difference was found in either high-risk populations or general populations. This is in contrary to US CDC's draft circumcision recommendations.

## CIRCUMCISION AND GONORRHEA AND CHLAMYDIA

In a cohort study by Diseker *et al.*, uncircumcised men were significantly more likely to have gonorrhea than circumcised men. However, they also reported that there was no association between lack of circumcision and chlamydia infection.<sup>[22]</sup>

However, as per the study on MC and risk of HIV and other STIs in India by Reynolds *et al.*,<sup>[13]</sup> MC had no significant protective effect on the incidence of gonococcal urethritis in HIV seronegative men.

Furthermore, in a systemic review by Van Howe,<sup>[18]</sup> no significant association was found between the incidence or the prevalence of gonorrhoea and circumcision status of males. This was seen in both high-risk and general populations. There was no significant difference in the prevalence of genital chlamydia infections also, but a trend toward a lower prevalence in intact men was noticed.

According to the RCT conducted by Mehta *et al.*, adult MC had no protective effect against any of the nonulcerative STIs examined (*Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Trichomonas vaginalis* infection) in sexually active young men in Kisumu, Kenya.<sup>[23]</sup> *N. gonorrhoeae*, *C. trachomatis* and *T. vaginalis* infection may bind through multiple ligands and host receptors. Unlike the chlamydia organism, gonococci are not obligate intracellular organisms, and *T. vaginalis* has complex and multiple methods of adhering to and entering host cells. The preferred host cell site is cuboidal or columnar epithelium (internal to the urethra) for both *N. gonorrhoeae* and *C. trachomatis*; thus, it is very unlikely that intact foreskin would provide protection against these infections.

## CIRCUMCISION AND NONVENEREAL GENITAL CONDITIONS

The most common indication for MC is underlying physiologic phimosis or untreatable paraphimosis. It is also practiced in traumatic injury or Balanitis Xerotica Obliterans (BXO) (a risk factor for penile cancer), refractory balanoposthitis, chronic, recurrent UTIs, etc.<sup>[24]</sup>

## CIRCUMCISION AND PENILE CANCER<sup>[24]</sup>

Intact foreskin does not increase the risk of penile cancer. Phimosis is a common finding in men with penile carcinoma. Circumcision facilitates improved penile hygiene and lowers HPV and HIV transmission rates. There is reduction of chronic inflammatory conditions such as phimosis and balanitis. All these factors are likely to reduce the chances of penile carcinoma. Some authors have advocated for universal neonatal MC as a means to prevent penile cancer.

## IMPACT OF MC ON FEMALE PARTNERS

In a cohort study by Turner *et al.*, it was reported that women with circumcised partners had similar risk of chlamydial, gonococcal, and trichomonal infections as women with uncircumcised partners.<sup>[25]</sup>

Based on three RCTs conducted in Uganda by Tobian *et al.*, there is strong evidence that MC decreases HPV infection rates in female partners of circumcised HIV-negative males<sup>[26]</sup> but does not affect HPV transmission among couples when the men are HIV positive. Outside of Africa, a meta-analysis showed that MC is associated with a lower risk of cervical cancer among monogamous female partners of men with multiple sexual partners. However, the risk of HSV and genital mycoplasma infections is probably not reduced in females whose sexual partners have been circumcised.

## FEMALE CIRCUMCISION/FEMALE GENITAL MUTILATION

Female genital mutilation (FGM) involves the partial or total removal of external female genitalia or other injury to the female genital organs for nonmedical reasons. It is mostly carried out on young girls between infancy and age 15 and is practiced mainly in Africa, the Middle East, and Asia. FGM can cause severe bleeding and problems urinating, and later cysts, infections, as well as complications in childbirth and increased risk of newborn deaths.<sup>[27]</sup>

### Female genital mutilation: Cultural, religious, and social causes

The FGM is performed as a result of cultural, religious, and social factors within families and communities. FGM is considered a necessary part of raising a girl properly and to prepare her for adulthood and marriage. FGM is said to ensure proper sexual behavior, premarital virginity, and marital fidelity, and reduced woman's libido. A few recent reviews have suggested that female genital circumcision may increase the risk of HIV.<sup>[28]</sup> However, other studies have found no statistically significant associations.

The practice has no health benefits for girls and women and is a violation of the human rights of girls and women. The WHO is opposed to all forms of FGM and is opposed to health-care providers performing FGM (medicalization of FGM).

## TAKE HOME MESSAGES

- Practice of MC predates human history and it is performed for religious, cultural, or social reasons
- The area under the foreskin is warm and moist, and this environment may facilitate some pathogens to persist and replicate. The thinness of foreskin predisposes it to minor trauma and abrasions that facilitate the entry of pathogens
- MC reduces HIV infection risk by 50%–60% over time and reduces the risk of men acquiring HSV-2 and HPV that can cause penile and other anogenital cancers, by 30%
- Though adult MC confers protection against HIV infection, it is not protective against nonulcerative STIs. This can be explained on the basis of multiple differences in organism pathogenesis and host immunogenicity. Specific HIV-1 target cells may be protected through increased keratinization resulting from circumcision
- There was no significant reduction in risk of acquiring syphilis, but reduced risk of acquisition of *H. ducreyi* is reported
- MC is reported to be beneficial in conditions such as traumatic injury or BXO (a risk factor for penile cancer), refractory balanoposthitis and chronic, recurrent UTIs
- MC facilitates improved penile hygiene and lowers HPV and HIV transmission rates. There is reduction of chronic inflammatory conditions such as phimosis and balanitis. All these factors are likely to reduce the chances of penile carcinoma
- There is strong evidence that MC decreases HPV infection rates in female partners of circumcised HIV-negative males but does not affect HPV transmission among couples when the men are HIV positive. MC is associated with a lower risk of cervical cancer among monogamous female partners of men with multiple sexual partners
- MC was recommended by the WHO and UNAIDS in 2007 as an additional HIV prevention intervention in settings of high HIV prevalence.

MC is an important adjunct to safe sex education, condom use, and vaccination (HPV) in reducing the global burden of HIV/STIs-related morbidity and mortality.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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### Male Circumcision MCQs

1. Which of the following diseases doesn't have significant reduction in risk of sexual transmission after undergoing MC?
  - a) AIDS/HIV
  - b) HPV
  - c) Syphilis
  - d) Haemophilus ducreyi
2. Which of the following infections tend to have lesions on both external and internal surface of foreskin and are more likely to get benefited with MC?
  - a) Gonorrhoea
  - b) Chancroid
  - c) Haemophilus ducreyi
  - d) Herpes
3. Female genital mutilation (FGM) involves:
  - a) Partial or total removal of internal female genitalia
  - b) Partial or total removal of external female genitalia
  - c) Partial or total removal of both internal and external female genitalia
  - d) None
4. The immune cells involved in protection against acquiring HIV infections are
  - a) Langerhan's cells
  - b) NK cells
  - c) CD 4 cells
  - d) a) and c)
5. MC reduces the risk of men acquiring HSV-2 and HPV by:
  - a) 30%
  - b) 50%
  - c) 70%
  - d) None of the above

### ANSWER KEY

1. c)
2. b)
3. b)
4. d)
5. a)