JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1030661
J Contemp Med 2022;12(4):532-536

Original Article / Orijinal Araştırma

# Frequency of Asymptomatic Human Immunodeficiency Virus, Syphilis, Hepatitis B and Hepatitis C in Circumcised Male Patients Diagnosed with Urethritis

## Korunmasız Cinsel İlişki Sonucu Üretrit Tanısı Alan Sünnetli Hastalarda Asemptomatik HIV, Hepatit B, Hepatit C ve Sifiliz Görülme Sıklığı

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## Abstract

**Aim**: In this study, it was aimed to determine the frequency of asymptomatic Human Immunodeficiency Virus (HIV), Hepatitis B, Hepatitis C, and syphilis in circumcised patients diagnosed with urethritis transmitted by sexual intercourse because of unprotected sexual contact.

**Material and Method**: We retrospectively investigated the serological results of HIV, Hepatitis B, Hepatitis C, and Syphilis diseases in 364 male patients diagnosed with urethritis, all of them were circumcised during childhood. The study included patients who applied to the urology outpatient clinic of secondary state hospital between January 2017 and December 2019 with symptoms or signs of urethritis. In the examination, only urethral discharge could be seen without symptoms. After the patients were examined, first void urine samples were taken. Also at the first examination, peripheral blood samples were tested for HIV, Hepatitis B, Hepatitis C, and syphilis antibodies.

**Results**: As a result of retrospective screening of the serological results of 364 male patients diagnosed with urethritis, Hepatitis B positivity was 1.09% with 4 cases, Hepatitis C positivity was found as 0.27% in 1 case and the Syphilis positivity rate was 1.92% with 7 cases in 364 patients. None of the patients had HIV positivity.

**Conclusions**: The fact that HIV-positive patients were not encountered in patients diagnosed with urethritis due to unprotected sexual contact has led to the thought that circumcision might have a protective contribution in these patients with urethritis who were all circumcised. Also, screening tests, especially syphilis, should be performed on all patients diagnosed with STI infection.

**Keywords:** Sexually transmitted disease, circumcision, HIV, syphilis, hepatitis B and hepatitis C

## Öz

**Amaç**: Bu çalışmanın amacı korunmasız cinsel ilişki sonucu üretrit tanısı alan sünnetli hastalarda asemptomatik HIV, Hepatit B, Hepatit C ve sifiliz görülme sıklığının incelenmesidir.

**Gereç ve Yöntem**: Çocukluk döneminde sünnet olan ve üretrit tanısı almış olan 364 hastada HIV, Hepatit B, Hepatit C ve sifiliz için seroloji sonuçları retrospektif olarak incelenmiştir. Çalışma grubu Ocak 2017-Aralık 2019 yılları arasında ikinci basamak devlet hastanesine üretrit semptomları ile başvuran hastalardan oluşmaktadır. Hastaların bir kısmında sadece muayene bulgusu olarak üretral akıntıları vardı. Muayene sonrasında idrar örnekleri ve bunu takiben de HIV, Hepatit B, Hepatit C ve sifiliz için periferik kan örnekleri alındı.

**Bulgular**: Üretrit tanısı alan 364 hastanın seroloji sonuçları retrospektif olarak incelendiğinde 4 hastada (%1,09) Hepatit B pozitif, 1 hastada (%0,27) Hepatit C pozitif ve 7 hastada (%1,92) Sifiliz pozitif olarak bulundu. Hiçbir hastada HIV pozitifliği bulunmadı.

**Sonuç**: Korunmasız cinsel ilişki sonrası üretrit tanısı alan hiçbir hastada HIV-pozitif olmamasında sünnetin koruyucu etkisinin olabileceği düşünülmektedir. Bununla birlikte cinsel temasla bulaşan enfeksiyon tanısı alan hastalarda başta sifiliz olmak üzere diğer cinsel temasla geçen hastalıkların da taraması yapılması önerilmektedir.

**Anahtar kelimeler:** Cinsel yolla bulaşan hastalıklar, sünnet, HIV, sifiliz, hepatit B ve hepatit C

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**Received *(Geliş Tarihi)*:** 30.11.2021 **Accepted *(Kabul Tarihi)*:** 19.05.2022

## INTRODUCTION

A sexually transmitted infection (STI) is defined as an infection that results from the transmission of a pathogenic organism by sexual contact with any genital or anal contact with another person's genitals, anus, or mouth.[1] STI are a major public health problem and the key marker of unprotected sexual contact. STIs can be seen at all ages, while often affecting adolescents and young people. STIs cause pelvic inflammatory disease, infertility, genital malignancies and increase the risk of Human Immunodeficiency Virus (HIV) acquisition and transmission while having negative effects on sexual life and maternal-child health. Asymptomatic or symptomatic STIs enhance HIV shedding at genital mucosal sites and increase infectiousness from HIV-positive individuals. Therefore, timely recognition of STIs, their treatment, and prevention are of great importance in preventing HIV transmission. According to Joint United Nations Programme on HIV/AIDS (UNAIDS) 2020 data, while 38 million HIV-positive people lived in the world, 1.7 million new HIV-positive cases were detected in 2019, while 690 thousand people died from AIDS-related illnesses.[2]

In many countries, the most common STI syndrome seen in men is urethritis.[3] Since STIs can be asymptomatic, their screening is important for early detection of infection and prevention of its spread. Testing is the only way to screen and diagnose these infections. The epidemiological data on syphilis, Hepatitis B (HBV), Hepatitis C (HCV), and HIV in our country consist of blood bank data, since the largest series of blood donors belong to the selected, healthy population that does not give a history of risky sexual contact. According to Izmir Ataturk Training and Research Hospital Blood Center data, 80454 Blood donors applied to the center between 2004 - 2010, were investigated by VDRL, HBsAg, anti-HVC, anti-HIV. There were 39 VDRL positive donors (0.04%), 1,054 HBsAg positive donors (1.31%), 312 anti-HCV positive donors (0.38%), and 2 anti-HIV positive donors (0.002%).[4]

Male circumcision is one of the oldest surgical procedures, and almost all Muslim and Jewish men are circumcised. [5] 99% of the male population of almost all ages in our country is circumcised for religious and social reasons.[6] The relationship between STI and male circumcision was first reported by Hutchinson in 1855 in the study that 61% of non-Jews and 19% of Jewish patients had syphilis.[7] Subsequent studies support this finding by reporting higher than expected cases of uncircumcised men compared to be circumcised in case series of genital herpes, syphilis, chancroid, and gonorrhea.[8-10] Three randomized controlled trials demonstrating the effectiveness of circumcision in HIV prevention in young men in Africa have been very promising. [11-13]

In this study, we aimed to investigate the frequency of asymptomatic HIV, HBV, HCV, and Syphilis in patients who developed urethritis after unprotected sexual intercourse in a country where almost all the population is circumcised.

## MATERIAL AND METHOD

Between 2017 January to December 2019, 1100 patients diagnosed with urethritis applied to the secondary state hospital urology outpatient clinic. 8 urologists work in our outpatient clinic. During this period, it was seen that only 364 patients were screened for HIV, HBV, HCV and syphilis disease, depending on doctors' preferences. All these 364 patients are primary and circumcised during childhood were retrospectively investigated. Since female patients with the same complaints and symptoms apply to the gynecology department, female patients are not seen in the urology outpatient clinic. Patients had complaints of dysuria, urethral discharge, and urethral pruritus. In the examination, only urethral discharge could be seen without symptoms. An anogenital examination includes inspection of the penis, scrotum, perianal area, and palpation of the penoscrotal contents. Clinicians also asked each patient if they used condoms for sexual contact. After the examination, the first void urine was examined. For the diagnosis of urethritis positive leukocyte esterase test on first-void urine or greater than or equal to 10 leukocytes per high-power microscopic field of the first-void urine sediment were used. Differential diagnosis of Neisseria gonorrhoeae and Chlamydia trachomatis could not have been made. Also at the first examination, peripheral blood samples were tested for HIV, HCV, HBV, and syphilis antibodies.

For syphilis screening, firstly the nontreponemal test was applied, Venereal Disease Research Laboratory (VDRL) test method (MedNet Gmbh Germany, Acro Biotech Inc USA). If VDRL was reactive, a treponemal test was applied, Treponema pallidum hemagglutination assay (TPHA) (MonlabTest Barcelona, Spain). HBsAg, anti-HCV, and anti-HIV screening tests were performed by enzyme-linked immunosorbent assay (ELISA) (Architect System, Model i 2000sr Abbott Diagnostics, USA). Anti-HIV positive cases were studied again and in cases of repetitive anti-HIV positivity, serum samples were sent to Refik Saydam Hygiene Center for Western Blot confirmation. Samples with positive HBV and HCV results were re-tested and when they were positive again, the patients were referred to the infectious diseases department for confirmation tests and follow-up.

Syndromic urethritis treatment was applied after the laboratory results of the patients were obtained. For partner treatment, all patients were informed that those with whom the patients had sexual contact should also use medication. All patients with urethritis were informed for serologic analysis again in the 6$^{th}$ and 12$^{th}$ months after serological analysis was performed at the time of admission.

The study protocol was approved by Izmir Demokrasi University Buca Seyfi Demirsoy Training and Research Hospital Non-interventional Clinical Researches Ethics Committee (Date: 31.03.2021, Decision No: 2021/3-24).

### Statistical Analysis

Patients' age was defined as mean ± SD. All statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS) Version 24.0.

## RESULTS

The electronic medical records were analyzed. There were 364 men enrolled in the study, all circumcised during childhood. The age of the patients varied between 16 and 59 and the average age was 27,65 (M=27.65, sd=8.7). When the age distribution of the patients is observed, the majority is between the ages of 20-29 with 63.2%, and especially between 20-24, it comes first with 37.3%. We learned from the anamnesis of all the patients that they had heterosexual intercourse and they did not use condoms regularly. 275 of 364 patients were single (75.54%) 89 were married (24.45%). Anogenital examinations of all patients were evaluated as normal.

When the serological test results were evaluated, there were not any anti-HIV positive patients. We identified 7 (1.92%) people after screening them with VDRL and TPHA for syphilis. When the patients with syphilis are examined by age groups, it is the most intense group with 3 patients (42%) over the age of 35. The treatment of these 7 patients was initiated and their follow-up continued. While anti-HCV positivity was detected in only one patient (0.27%) in the HBC screening, HbsAg positivity was found in 4 patients (1.09%) for HBV. No HIV was found in patients with urethritis, and the distribution of Hepatitis B, Hepatitis C and Syphilis cases according to age groups is given in **Table 1**.

Table 1: Age distribution of the study population (n= 364)

| | n (%) | Hepatitis B HBsAg | | Hepatitis C Anti-HCV | | Syphilis VDRL | | Total | |
|---|---|---|---|---|---|---|---|---|---|
| | | f | % | f | % | f | % | f | % |
| Age < 19 | 29 (8.0) | - | - | - | - | - | - | - | - |
| Age 20-24 | 136 (37.3) | 1 | 25.0 | - | - | 1 | 14.3 | 2 | 16.7 |
| Age 25-29 | 94 (25.9) | - | - | - | - | 2 | 28.6 | 2 | 16.7 |
| Age 30-34 | 46 (12.6) | 1 | 25.0 | 1 | 100 | 1 | 14.3 | 4 | 33.3 |
| Age 35 | 59 (16.2) | 2 | 50.0 | - | - | 3 | 42.8 | 4 | 33.3 |
| Total | 364 (100) | 4 | 100 | 1 | 100 | 7 | 100 | 12 | 100 |

HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C, VDRL: Veneral Disease Research Laboratory test method.

## DISCUSSION

Urethritis is the most common STI and we encounter it frequently in our daily practice. Circumcision not has effect on preventing urethritis.[14] Again, no mention has been made of the relation between hepatitis transmission and circumcision. The HbsAg and anti-HCV rates that were found as a result of the study are close to the blood bank results in our country. In the study group, HbsAg positivity was 1.09% in 364 patients with 4 cases. In our country, according to Izmir Ataturk Training and Research Hospital Blood Center data, 80454 Blood donors HBsAg was positive in 1.054 donors (1.31%). Since we live in the same geography, if European Centre for Disease Prevention and Control (ECDC) data is looked at, in Europe HBV prevalence is estimated to be 0.9% corresponding to almost 4.7 million HBsAg-positive cases.[15] In the study group, anti-HCV positivity was found as 0.27% in 1 case in 364 cases. While anti HCV positivity was 0.38% according to the data of our country's blood bank when we looked at the patients in our study group, it was found 0.27%. Studies have shown that adults in a stable heterosexual relationship with HCV-infected partners were not associated with an increase in virus transmission risk.[16] In recent years, however, outbreaks of HCV have been reported in men who have sex with men, probably due to the sexual practices involving anorectal mucosal trauma and presence of genital ulcerative disease, especially those co-infected with HIV. It is important to investigate the prevalence of sexual transmission of HCV in risky sexual behavior.[17] According to ECDC, prevalence for HCV is 1.1%, corresponding to around 5.6 million anti-HCV-positive cases.[18]

In the study group, syphilis was the highest in asymptomatic patients with urethritis due to unprotected sexual contact, and the rate was 1.92% with 7 cases in 364. Syphilis is closely related to public health because of its sexual transmission, latent course, and can be transmitted through transfused blood. Our country's blood bank syphilis screening results are 40/100000 and ECDC data syphilis prevalence result is 7/100000.[18] It was mentioned that previous studies that circumcision reduces the transmission of syphilis disease. The rate of asymptomatic syphilis in patients diagnosed with urethritis as a result of risky sexual behaviors, whether circumcised or not, is 1.92%, which is a high rate. This high rate indicates the need for public health interventions, and the implementation of risk reduction strategies that focus on those with unprotected sexual contact. It has been reported that this rate reaches up to 15% in people who engage in risky sexual behavior around the world.[19-21]

As it is mentioned before, circumcision reduces the transmission of ulcerative diseases such as HIV and syphilis in many studies. There was not anti-HIV positivity in any of 364 patients who had unprotected sexual contact and were diagnosed with urethritis accordingly. The first AIDS case in Türkiye was diagnosed in 1985, and the total official number was reported as 6188 at the end of December 2012.[22] Türkiye is one of the lowest countries in Europe with HIV-1/AIDS prevalence. Our country's blood bank HIV screening results are 2/100000. HIV positivity continues to be at a lower level compared to the European countries in which Türkiye is in the same geography. According to ECDC HIV prevalence was 6.3/100,000 population.[23]

While 80% of HIV-positive cases are through sexual contact, 70% of them are through vaginal intercourse, the rest are through anal sex. As it turns out, the penis plays an important role in contamination. After three RCTs showed that circumcision reduces the spread of HIV infection in young men in Africa, there have been many studies on how circumcision prevents this. However, the mechanism of how circumcision reduces the transmission is still not fully understood. The uncircumcised penis is more susceptible to minor trauma and ulcerative disease, and the

preputial sac acts as a reservoir for pathogenic organisms that accumulate under the prepuce.[24] Depending on the infection, immune system cells consisting of CD4 + T cells, Langerhans cells, and macrophages are collected in the mucosal epithelium. While these immune system cells protect from infectious microorganisms, when they encounter HIV, CD4 receptors form portals for HIV uptake and are transported to Langerhans cells. Langerhans cells bind with HIV and migrate rapidly, forming conjugates with T cells and transferring HIV to T cells. Thus, T cells can initiate the spread of the infection. The removal of the preputium during circumcision results in the removal of portal cells for HIV entry, which is densely located in the inner part of the foreskin.[25-27] During intercourse in the uncircumcised penis, the foreskin retracts and exposes a large surface area of high-density superficial Langerhans and other HIV target cells to HIV-infected secretions. After circumcision, a significant reduction in anaerobic bacteria was observed due to the removal of subpreputial anoxic microenvironments. The reduction in anaerobic bacteria reduces the number of Langerhans cells activated, thus eliminating the gate to HIV.[28,29]

When the age distribution of the patients with urethritis is looked at, it is seen that they are in the adolescent group with a rate of 8.5%. It is thought that this figure is high and remarkable. Despite the contribution of circumcision in reducing the rates of some sexually transmitted diseases, it is necessary to see that it is not enough by itself and is ineffective at preventing every STI. Sexual health education at schools and counseling people with risky sexual behaviors on ways to avoid STIs are being done. When used correctly and consistently, male latex condoms are the most effective method to reduce the risk of STI.[30] Pre-exposure vaccination of people at risk could be effective for vaccine-preventable STIs. Identification of asymptomatically infected people and people with symptoms associated with STIs; effective diagnosis, treatment, counseling, and follow-up them. Postexposure prophylaxis should be kept in mind in appropriate cases. It is necessary to also evaluate the partners of the people infected with STI, to treat them if they are ill, and inform them about the STIs.

This study was subject to several limitations. Firstly, the cases included in our study consisted of male patients with a history of risky sexual behavior and, according to them, suffering from urethritis. However, due to the conditions of our country, the urology outpatient clinics of the hospitals mainly serve male patients in the young and adult age groups. The fact that female patients prefer gynecology outpatient clinics prevents a healthy interpretation in terms of gender distribution, which can be considered as a limitation of our study. Another limitation is that the study was retrospective, a nonrandomized small number of patients, and single centered. Large multicenter studies are necessary for more detailed results.

## CONCLUSION

We examined men who were circumcised due to social and cultural reasons of 99% of the men in the society and who were diagnosed with urethritis because of sexual intercourse without using a condom. Although HIV positive rates in terms of our geographical location are still low, there has not been any encounter of HIV positivity in patients with STI because of risky behaviors. It is thought that circumcision may contribute to this. In addition, as a result of the study, the rate of asymptomatic syphilis to be 1.92% is considered as a high rate. This result indicates the need for public health interventions, and the implementation of risk reduction strategies that focus on those with unprotected sexual contact. It was found that only 364 out of 1100 patients who applied to the urology outpatient clinic with urethritis were screened. Due to the 1.92% detection rate of syphilis, it is thought that more willingness and determination should be made in screening for asymptomatic STI diseases in STI cases.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study protocol was approved by Izmir Demokrasi University Buca Seyfi Demirsoy Training and Research Hospital Non-interventional Clinical Researches Ethics Committee (Date: 31.03.2021, Decision No: 2021/3-24).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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