

**Review article****Bacterial and Viral Sexually Transmitted Infections**

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**Abstract**

There are two terms often used interchangeably, Sexually Transmitted Infection (STI) and Sexually Transmitted Disease (STD), but in fact, they are different. STI is infection that can lead to STDs, so every STD is preceded by an STI but not every STI leads to STD severe reproductive complications can result from STDs, including congenital infection, infertility, and ectopic pregnancy. In addition, STDs can increase the chance of acquiring and transmitting Human Immunodeficiency Virus (HIV) infection. STIs or STDs typically result from sexual contact, and the causative agents can be bacteria, parasites, or viruses. The most prevalent STDs are viral infections, as they are treatable but not curable. Symptoms vary according to the viral type and range from skin lesions and warts to immune deficiency and cancer. The treatment of infections that are transmitted sexually relies on the infection type. It is important for sexually active members at higher risk to undergo regular screenings. Neglecting the use of condoms represents a significant risk of infection.

**Keywords:** Sexually transmitted diseases, sexually transmitted infections, Vaccination, Human immunodeficiency virus.

**Introduction**

There are two terms often used interchangeably, sexually transmitted infection (STI) and sexually transmitted disease (STD), but in fact, they are different. STI is infection that can lead to STDs, so every STD is preceded by an STI, but not every STI leads to an STD. Individuals who suffer from STIs

may exhibit no symptoms or signs of the disease, but can be contagious [1].

In 1997, the Institute of Medicine [IOM] reported that 50% of STDs in the age of 15 to 24 can have constant health implications, for example, infertility, making STDs a "hidden epidemic" with economic and health consequences [2]. In Europe,

there has been an increase in sexually transmitted diseases, especially Chlamydia, Gonorrhea, and Syphilis during the past century [3]. Globally, STIs are a significant public health problem, where more than 1 million people acquire the infection daily, according to the World Health Organization [4]. Severe reproductive complications can result from STDs, congenital infection, infertility, and ectopic pregnancy. In addition, STDs can increase the chance of obtaining and transmitting HIV infection [5].

In high-income countries, precise STIs diagnostic tests are widely used, which are important for the diagnosis of asymptomatic cases. However, in countries of low and middle-income countries, the diagnostic tests are largely unavailable. As a result, the development of some rapid tests for STIs has begun and have the possibility to enhance the treatment and diagnosis of STIs. Sexual (oral, vaginal, or anal) contact is the main route for transmitting viruses, parasites, and bacteria involved [6]

The global statistics of STI still uncertain because of different factors including, many STIs may be asymptomatic, making it difficult to estimate their prevalence, also some of affected countries lacking the reliable diagnostic methods, as well as the surveillance systems are absent or inadequate in many areas worldwide, STI or STD are typically resulted from sexual contact and the causative agents can be bacteria, parasites or viruses. Young individuals are affected due to a collection of biological and behavioral factors. Adolescents (15 - 24) years old represent 50% of the annual reported cases in developing nations [1].

## Bacterial STIs

### 1- *Chlamydia trachomatis*

*C. trachomatis* is STD STD-causing bacterium. The transmission of infection usually occurs through unprotected sexual contact. It can infect both women and men and affect various body parts, such as the rectum, cervix, and throat. Additionally, transmission can pass to the baby during birth, resulting in various complications, for example, *C. trachomatis* may cause pelvic inflammatory diseases (PIDs), ectopic pregnancy, and infertility [7].

Chlamydia is one of the main causes of bacterial infections that is transmitted sexually, distributed in both underdeveloped and developed nations. Non-lymphogranuloma venereum (LGV) serovars often produce asymptomatic infection but can lead to offensive manifestations such as anus, perianal, or rectal ulceration with discharge and pain [8].

*C. trachomatis* establishes infections in the upper and lower parts of the genital tracts of both genders. Many females infected by Chlamydia may not show any symptoms or signs of infection, while over 70% of males may exhibit symptoms like penile discomfort, urethral discharge, and painful urination, which can result in serious complications, such as irreversible damage and infertility if untreated [9,10]

### 2- *Neisseria gonorrhoeae*

*N. gonorrhoeae* is a fastidious bacterium with distinctive features that separate it from other members of this genus. It is diplococci, stained Gram-negative with a unique spherical shape, commonly occurring in pairs. One of the interesting features of *N. gonorrhoeae* is its metabolic tendency, as it oxidizes glucose only. As well as this bacterium has different antigens from other *Neisseria* species. *N. gonorrhoeae* prefer to

colonize the mucosal surfaces of both animals and humans [11,12].

*Neisseria gonorrhoeae* is a pathogenic bacterium transmitted by sexual interaction. This bacterium was discovered by Neisser in 1879 from urethral and cervical discharges. The only reservoir is human, and the period of incubation ranges from one day to two weeks. *N. gonorrhoeae* may produce asymptomatic rectal, urethral, or endocervical infection. Additionally, it is the 2<sup>nd</sup> most common bacterium causative agent of STDs [13,14].

Gonorrhea is one of the oldest reported sexually transmitted illnesses caused by *N.gonorrhoeae* (gonococcus). Over time, infections with gonococcus represent a global health issue, with more than eighty-eight million reported cases annually around the world. the site of infection with *N. gonorrhoeae* determines the symptoms [15,16]. The conventional identification method for *Gonococcus* depends on cultivation, but the challenge lies in that the bacterium is fastidious to cultivate [17].

### 3- Ureaplasma

Both *Ureaplasma parvum* and *Ureaplasma urealyticum* are isolated from the urethra of infected males and can pass with semen during ejaculation. *U. urealyticum* was isolated from 5 to 42% of infertile men where they were positive for ureaplasmas [18,19].

Some reports didn't find a direct relation between *U. urealyticum* and sperm quality; others have documented decreased sperm motility, abnormal morphology, and reduced concentration [20].

Ureaplasmas are one of the smallest cell-wall-lacking, self-replicating cells. They produce ATP through the hydrolysis of urea and attach to the

mucosal surfaces of the respiratory tract in newborns and the genitourinary tract of adults [21]

### 4- Mycoplasma

Mycoplasmas are sexually transmitted microorganisms commonly isolated from the urogenital tract of males. *M. genitalium* and *M. hominis* are the most frequently isolated species from the urogenital tract, it usually associated with UTI in males, infertility, and non-gonococcal urethritis (NGU). However, studies have explored their potential role in the development of cancer of prostate cancer [22].

### 5- Haemophilus ducreyi

Gram-negative bacteria that produce ulceration of cutaneous skin in children and chancroid in adults that considered sexually transmitted diseases [23]. Infection with *H. ducreyi* typically starts as a papule associated with erythema. A few days later, the papule becomes a pimple and ruptures, forming an aching ulcer with festering discharge. By avoiding antibiotic treatment, these ulcers will remain for several weeks or months before incomplete recovery. In males, the lesions are commonly observed on the frenulum and prepuce, while in females, the lesions are noticed on the perianal, cervix, and vulva [24,25].

### 6- Treponema pallidum

Syphilis is a sexually transmitted illness that remains a significant challenge despite being curable. It is caused by *Treponema pallidum*, which is transmitted by sexual contact which infecting about 12 million individuals around the world yearly and attracting attention due to its relationship with HIV [26].

Despite of the role of this bacterium in men infertility is not documented, the fertility can be

negatively affected by the complications of syphilis [27].

#### 7- *Enterococcus faecalis*,

This bacterium is found naturally in feces; it is normally present in the gastrointestinal part of the digestive system, and commonly isolated from meat, soil, sewage, dairy products, water, and plants [28].

It is gram-positive, spherical, singly or in pairs or as short chains. *E. faecalis* is immotile, non-spore-forming, and produces hemolysis on blood agar medium [29,30].

*Enterococcus faecalis* can resist antibiotics and possesses a number of virulence factors, including the formation of biofilm, so it plays an important role in nosocomial infections. It has been involved in different infections, for example, endocarditis, urinary tract infections, wound infections, infections of the dental root canal, and post-operative contamination [30,31].

*E. faecalis* produces enterocin (bacteriocins) [32]. It colonizes the digestive system and passes to various sites by various means. Some strains are relatively stable and can be utilized as probiotics, as they can produce elements and essential vitamins during digestion [33]

#### Viral STDs

The most prevalent STDs are viral sexually transmitted diseases, as they are treatable but not curable. Symptoms vary according to the viral type and range from lesions, warts, to deficiency in the immune system and cancer [34].

Viral sexually transmitted infections are diverse, widespread, and mostly incurable. Hepatitis B causes damage to the liver, Zika virus causes symptoms resembling mild flu as well as congenital birth defects, Herpes simplex virus

(HSV) infects the nerves and produces skin lesions, Cytomegalovirus usually produces no symptoms in healthy adults, but may result in congenital birth defects., Human Papillomavirus (HPV) produces warts in the genital parts and some kinds of cancer, HIV infects WBC and disrupts the immunity [34].

#### Diagnosis

It is important for sexually active members at higher risk to undergo regular screenings. Neglecting the use of condoms represents a significant risk of infection [13,14].

For bacterial STDs, the conventional methods for detecting and identifying bacteria in urine and swab samples, like using the selective culture media along with microscopic and macroscopic characteristics, can be used, as well as the modern techniques like Vitek 2 compact system, Polymerase Chain Reaction (PCR), and STD Direct Flow Chip technique [35].

For viral STDs, cervical cancer is screened during a female exam yearly. On a Pap smear, cell dysplasia is considered an abnormal result that may indicate a cancerous or pre-cancerous condition, so follow-up testing is required [36].

HIV testing involves two main parts: screening and confirmation. Screening includes ELISA or Western blot to detect antibodies against HIV, which perhaps require about 6 weeks to be produced in enough quantity to be detected, within 7-28 days after exposure. NAT detects the viral load. It is utilized as a confirming test and a test for the acute phase in patients exposed [34].

For HSV-1 and HSV-2, direct immunofluorescence tests have been used; nucleic acid testing is the recommended technique, which can identify the type and determine whether the

virus is actively eliminated by the patient. [37] Serologic tests for the identification of the production of specific antibodies against HSV-1 and/or HSV-2 can be used. [34]

### Treatment

The treatment of STIs relies on the infection type. Bacterial sources, such as chlamydia and gonorrhea, are treated with antibacterial medications and are curable in spite of the development of antibiotic resistance [38], while viral infections are managed with antivirals. Most STIs caused by viruses are treated with antiviral or antiretroviral orally; viral STIs are manageable, but are incurable [27].

The treatment of non-cancerous HPV includes erasing the infected sites. Since, FDA approval of HPV vaccines, the focus has changed for avoiding. Recent recommendations of the CDC are two doses of vaccine for children before their 15<sup>th</sup> birthday. The vaccine is recommended to start at age 11-12, to ensure immunity before sexual maturity and exposure can occur. [34], while HIV can evolve quickly, with about 10 mutations per replication cycle, leading to antiretroviral therapy (ART) failures [39]

At early stages of infection, treatment with ART may shorten the number of HIV mutants in an infected person on a long-term treatment regimen because viral proliferation occurs due to the proliferation of the original, infected, immune cells despite viral replication stopping [40].

ART use and when to start the treatment have been recommended as a modern medicines that target different viral functions [39]. During the 1990s, antiretroviral products were changed, with the now-standard mixture of antiretroviral medicines, which can suppress viral load to, undetectable

range [41]. Nowadays, a number of different kinds of medicines can be used in combination in ART, such as inhibitors of each non-nucleoside reverse transcriptase, nucleoside/nucleotide reverse transcriptase, protease, integrase, small-molecule-C chemokine, receptor (CCR5), antagonists, and entry [39].

For the herpes virus, the level of infection determines what treatment is specified; larger doses of antivirals, valacyclovir, acyclovir, or famciclovir are used for the initial infections [34]. To prevent future outbreaks, suppressive therapy can be described after initial treatment, which includes lower doses of initial antiviral treatment medications [42]. Intravenous acyclovir or cidofovir is used to treat encephalitis in neonates [43].

### Prevention

#### 1/ Pre-exposure prevention

##### 1- Vaccination

One of the most functional ways to prevent transmission of HAV, HBV, and HPV Pre-is exposure vaccination, all of which may be transmitted sexually. Vaccine is recommended for HPV routinely for males and females (11 or 12 years). The HPV vaccine is recommended at age 26 years for unvaccinated individuals [44]. A vaccine for HBV is recommended for unvaccinated, uninfected sexually active people with multiple sexual partners or who are being treated for an STI. HAV and HBV vaccines are also required for MSM, chronic liver disease patients, and persons with HIV or HCV infections who have not acquired hepatitis A or B [45].

##### 2- Condoms

###### A- External Condoms

During a relationship, including one infected and one uninfected individual where condoms were used, HIV-negative individuals were 71%–80% less likely to acquire HIV infection in comparison to individuals in the same relationships but without using condoms [46,47]. Studies showed that using condoms constantly decreases the risk of infection with other STIs, such as trichomoniasis, gonorrhea, hepatitis B, and chlamydia [48-51]. Condoms may also decrease the risk of pelvic, PID among females by avoiding infections of the lower genital tract [52]. External condoms made up of polyurethane give protection against STIs and pregnancy when compared with latex condoms [50,53]. So latex condoms can be replaced by people with latex sensitivity [53].

#### **B- Internal Condoms**

Female condoms (condoms used internally for the vagina) are widely available (e.g., Reddy condom, the FC2 Female Condom, and Cupid female condom) [53,54]. Internal condom usage can protect against transmission and acquisition of STIs. Female condoms are cost-effective in comparison with male condoms, but they can be controlled by the receptive individual as an STI and HIV prevention method [55].

#### **3- Topical, Microbicides, and Spermicides**

Topical microbicides are inactive against HIV [56-61]. Tenofovir gel has been evaluated for protection against HSV-2 and HIV [62,63]. HIV prevention, particularly in females, has not been explained [63,65]. Vaginal rings with dapivirine have supply some HIV reduction [66,67]. For male and transgender women who have anus intercourse, tenofovir gel seems safe when used before and after intercourse [68]. Spermicides with nonoxynol-9 (N-9), may disrupt the epithelia of genital organs or

rectum, and this may increase the risk for infection with HIV. N-9 may also play a role in increased risk for infection of the urinary tract by bacteria among females [69,70].

#### **4- Pre-exposure, Prophylaxis**

##### **A- HIV**

antiretroviral PrEP of oral daily use with a constant-dose, combination of tenofovir alafenamide (TAF), or tenofovir,disoproxil fumarate (TDF), and emtricitabine (FTC) has proven safety [71] and a fundamental reduction in HIV infection rate for MSM [72]. TDF/FTC has proven safety and activity for mixed-status, heterosexual partners [73]. However, no proof is available yet about TAF/ FTC among heterosexually active females [74]. A study including heterosexual mixed-status partners explained essential activity and safety of daily, oral PrEP with TDF. High commitment to oral PrEP was firmly associated with protection against HIV infection [73].

STIs of bacterial origin are the main danger indicators of HIV acquisition among sexually active, HIV-free males and females. Sexually active people must be examined for STIs (gonorrhea, chlamydia and syphilis), infected people must be treated with PrEP, and also USPSTF advises that individuals at risk of infection with HIV can be given PrEP, People at risk of HIV infection include HIV-free individuals whose partners are infected with HIV, persons who have infected with syphilis or gonorrhea during last 6 months, and drug injectors who share injection tools [75].

##### **B- For STIs**



No evidence supplying HSV treatment to people who are HSV and HIV positive can play a role in reducing HIV transmission among uninfected partners [76].

Testing of doxycycline prophylaxis against bacterial STIs has been done where 30 MSM living with HIV with previous syphilis, were randomly assigned to doxycycline 100 mg for 48 weeks, where a 73% reduction in bacterial STI occurred, without changes in sexual behaviour [77].

## 2/ Post-exposure

Include prophylaxis for HIV and STIs where guidelines for PEP use directed to prevent HIV and other STIs as a result of sexual exposure, sexually active people depending HIV PEP must be evaluated for PrEP after finishing PEP course and testing negative for HIV hygiene of genital parts (e.g., vaginal washing and douching) after sexual intercourse have no effectiveness against HIV and STIs and may increase the risk for certain STIs, bacterial vaginosis and HIV [78].

Doxycycline 200 mg when taken after unprotected anal sex as PEP has been evaluated among MSM and transgender women; results showed a reduction in syphilis and chlamydia infection by 73% and 70% respectively, but had no activity against gonorrhea [79]. No enough data are available about the effects of STIs PEP on the microbiome and antibiotic resistance. Extensive studies are required to determine the effectiveness of STIs PEP, and its advantages as a strategy for STI prevention.

## Conclusions:

1- There are several ways to prevent STDs.

2-The possibility of treating sexually transmitted diseases.

3-There is a relationship between STDs and HIV.

4-Some contraceptive methods can decrease the risk of acquiring STDs.

## Recommendations

1. Avoid illicit and promiscuous relationships.
2. Decrease the number of sexual partners.
3. Follow preventive and protective measures.
4. Strengthening and developing of Immune system.
5. Conduct regular checkups

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