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Introductory Chapter: The Latest Knowledge

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1. Introduction

Sexually transmitted infections (STIs) are caused by the transmission of more than 30 various bacteria, viruses, and parasites from one individual to another [1, 2]. Transmission can occur in different ways such as vaginal, anal, and oral sexual contact. Besides, they can also be transmitted from pregnant women to their fetus during pregnancy, during birth, through breast-feeding, and by parenteral routes [1, 3].

STIs are still a serious public health problem despite efforts and precautions worldwide. According to the World Health Organization (WHO), it is estimated that more than 1 million new STIs occur everyday globally. In the United States (US), the total number of STIs is around 110 million per annum and 20 million of these cases are newly acquired [4]. In England, the rates of most of the STIs had rapidly increased from the late 1990s to 2012 and approximately 500,000 STI diagnoses are now made annually [5]. In 2012, more than 40,000 new cases of HIV/AIDS and more than 1.5 million cases of syphilis, gonorrhoea, and hepatitis B were reported in China [6]. Approximately 250 million women are affected by gonorrhoea, chlamydia, syphilis, or trichomoniasis per year [7].

1.1. Sexually transmitted bacterial infections

Chlamydia trachomatis infections are the most reported bacterial STI in the US [8]. In the United Kingdom (UK), although it is the most commonly diagnosed bacterial STI, it is thought that there are many chlamydial infections that cannot be diagnosed and treated. Therefore, its frequency is not clearly known, but there were approximately 240,000 diagnosis in 2012 [5]. A study reported that the overall prevalence of *C. trachomatis* infection was 11% with the highest prevalence observed in women between 16 and 20 years of age in Brazil [9]. Because most cases are asymptomatic, the detection of the infection depends on the screening [10].

Gonorrhoea caused by *Neisseria gonorrhoeae* is usually characterized by urethritis in men and cervicitis in women [11]. *N. gonorrhoea* is the second most common reported bacterial STI in the US [12]. More than 350,000 cases of gonorrhoea were reported in the US in 2014.

Syphilis caused by *Treponema pallidum* is one of the bacterial STIs that has been known for centuries [13]. Globally, 12 million new cases are estimated annually. Most of the new cases are probably in Southern Asia and Sub-Saharan Africa according to WHO [14]. The number of syphilis cases reported was about 46,000 in the US in 2010 [15].

Chancroid caused by *Haemophilus ducreyi* is more common in Africa, Asia, and Latin America. But recently, this infection is less common both in developed and in less-developed countries. Due to diagnostic challenges, the exact frequency is not clearly known [16]. It is more common in men than in women and male circumcision is thought to reduce the risk of transmission of infection [17].

Donovanosis (also known as granuloma inguinale) caused by *Klebsiella granulomatis* (formerly known as *Calymmatobacterium granulomatis*) is less common disease that occurs with genital ulceration.

Lymphogranuloma venereum (LGV) is caused by *C. trachomatis* serotype L1, L2, and L3. Although the disease is endemic in East and West Africa, India, Southeast Asia, and the Caribbean, it is less common in Europe [18]. Also, LGV is traditionally described as “a sporadic disease” in North America, Europe, and Oceania, but highly prevalent in parts of Africa, Asia, and South America [19, 20].

1.2. Sexually transmitted viral infections

Human papilloma virus (HPV) is the most common STI in the US [21]. It is estimated that 14 million people are infected with HPV annually [22]. Although there are over 100 strains of HPV, only about 40 HPV strains that cause benign or malign lesions are detected on the surface of anogenital skin. HPV strains are divided into two categories: high-risk strains and low-risk strains. High-risk strains, especially, HPV types 16 and 18, are responsible for malignant lesions such as cervical, penile, vulvar, vaginal, anal and oropharyngeal cancers, and premalignant lesions such as cervical dysplasia. Low-risk strains are responsible for benign lesions such as anogenital warts, benign or low-grade cellular changes, and recurrent respiratory papillomatosis (RRP) [21].

Genital herpes caused by the *Herpes simplex virus* (HSV) is the most common disease with genital ulceration worldwide. To date, it is estimated that about 50 million people are infected with HSV-2 in the US and it is thought that there are over 750,000 new cases each year [23]. HSV is divided into two subtypes: HSV-1 and HSV-2. The main cause of genital herpes is HSV-2; but in recent years, the frequency of genital diseases caused by HSV-1 has increased due to increasingly common oral sex among adolescents and adults [24].

Human immunodeficiency virus (HIV)-1 may transmit vertically and through blood in addition to sexual intercourse. About 78 million people have suffered from HIV and 39 million deaths have occurred since the beginning of this epidemic. While the global prevalence of HIV was 31 million in 2002, at the end of the next 10 years, this number exceeded 35 million [25].

While *Hepatitis C virus* (HCV) is transmitted primarily through blood exposure, it has globally emerged as a STD among HIV-infected men that have sex with men for the last 20 years [26]. Moreover, illicit drug use, unprotected anal intercourse, potentially traumatic sexual practices such as first sexual experience and inappropriate and common use of sex toys are the other factors facilitating transmission [19].

1.3. Sexually transmitted parasitic infections

Trichomoniasis caused by *Trichomonas vaginalis* that is highly prevalent in the US affects 11 million people per year. Approximately 62% of this figure is women. Trichomoniasis is commonly asymptomatic (70–100% of male population and 35–85% of female population) and transmission between partners easily occurs [27, 28].

2. Management of STIs

While STIs continue to be a general public health problem worldwide, unfortunately, there is no globally established STI surveillance system. While passive STI surveillance is performed using reports from STI control programs and public health laboratories in some countries such as the US, Canada, and Australia, there are limited published STI surveillance reports from Middle East and Northern Africa and Sub-Saharan Africa [29].

2.1. STI preventive counseling

In preventive counseling, interactive individual communication between health-care provider and patient is very important. Providers should also inform to their patients about risk-reduction strategies such as abstinence, condom use, limiting the number of sex partners, modifying sexual practices, and vaccination. High-risk behaviors are defined by the US Preventive Services Task Force (USPSTF) as having multiple current partners, having a new partner, using condom inconsistently, having sex while under the influence of alcohol or drugs, or exchanging sex for money or drugs [30, 31].

2.2. Sexual abstinence

One of the most reliable ways to prevent STIs is to abstain from oral, vaginal, and anal sexual intercourse or to have a long-term relationship with an uninfected partner. If any of the partners are being treated, couples should be informed that they should avoid sexual intercourse until the treatment is completed [30].

2.3. Vaccination

To prevent infectious diseases, vaccination seems to be the best strategy for long-term protection [32]. Although preexposure vaccination is a very effective method for preventing transmission of STIs, vaccines have not yet been developed except for three viral diseases including HPV, hepatitis A, and hepatitis B [30, 31].

There are three different prophylactic HPV vaccines approved by the Food and Drug Administration (FDA): Cervarix (GlaxoSmithKline, NY), Gardasil (Merck&Co, Kenilworth, NJ), and Gardasil-9 (Merck&Co) [25, 33]. The first generation HPV vaccines (bivalent Cervarix and quadrivalent Gardasil) are licensed in more than 100 countries since 2006. The second generation HPV vaccine (9vHPV vaccine) was licensed in the US in December 2014 [34]. Both males and females can be vaccinated with HPV vaccines according to Advisory Committee on Immunization Practices (ACIP). Vaccine can be applied from 9 years old. Furthermore, vaccination is recommended for females aged 13–21 years and for males 13–21 years who have not been vaccinated previously or who have not completed the three-dose series. Any of the three different vaccines is recommended for females, although either Gardasil or Gardasil-9 is recommended for males [22]. Quadrivalent HPV vaccine prevents both anal intraepithelial neoplasia (AIN) and anogenital warts in men [35].

Hepatitis B vaccine is recommended for everyone who has a risk of transmission of STIs [30, 36].

Hepatitis A vaccine, the same as hepatitis B vaccine, is recommended for men who have sex with men (MSM), injection drug users, and HIV-infected persons who have not yet been infected with hepatitis A virus [30].

2.4. Using condom and other barrier methods

Male and female condoms play an important role both in preventing pregnancy and in reducing the risk of transmission of infections including HPV, HIV, HSV, gonorrhea, chlamydia, syphilis, hepatitis B, hepatitis C, and Trichomonas. For these purposes, condoms can be used alone or in combination with other contraceptive methods [7, 30]. Using male latex condoms recommended by Centers for Disease Control and Prevention (CDC) is quite important to protect HCV transmission, because there is no vaccine for hepatitis C infection [26]. Only one vaginally inserted condom is approved in the US. But, research on new vaginal female condom models like Origami female condom is still ongoing [7].

2.5. Male circumcision

Male circumcision may reduce the risk of transmission of HIV and some STIs in heterosexual men and is recommended for preventing heterosexually acquired HIV infection by the WHO and the Joint United Nations Program on HIV/AIDS (UNAIDS) [30]. Male circumcision also increases the tendency to genital discharge syndrome. With contradictory results, the efficacy of male circumcision in preventing STIs in the general population has not been clearly demonstrated [37].

2.6. Postexposure and preexposure prophylaxis

Postexposure prophylaxis (PEP) and preexposure prophylaxis (PrEP) of the uninfected partner are the other preventive strategies [7]. Genital hygiene methods (e.g., vaginal washing) after sexual exposure should not be recommended as preventive methods [30]. In addition,

the reasons such as a clinician visit and medication initiation within 72 h after exposure limit the use of PEP. But on the contrary, oral PrEP approved by the FDA is an effective HIV prevention tool [7]. With the implementation of PrEP and other preventive strategies, it has been observed that there is a significant reduction in the number of newly diagnosed HIV cases that occur among MSM in the US each year [38, 39].

2.7. Partner management

The first step of partner management should be partner notification. Knowing the sex- and needle-sharing partners of infected persons allow to communicate with them directly or through state and local health departments. Thus, health counseling can be provided to the partners at risk and may be encouraged for medical evaluation and treatment in health care services [30].

3. Risk factors for STIs

The distribution of STIs in the population varies depending on different factors including individuals, social, and structural factors [6]. All sexually active people including heterosexual persons, MSM, and women who have sex with women are at risk. Most of the STIs are transmitted more easily from a man to a woman than from a woman to a man. Adolescents and young adults are the age groups at greatest risk of acquiring of STIs due to some reasons such as having multiple sex partners, unprotected sexual intercourse, and substance use [3].

Younger age is a significant risk factor for STIs [6]. Young people, especially aged 15–24 years, have a large number of sexual partners than older adults and these young individuals do not have the habits of using regular condom during sexual intercourse. In women, STIs, mostly for chlamydia, genital warts, and gonorrhea, are usually seen from the age of 15, peak at 19 years, and begin to decline from the first year of the third decade [5].

Concurrent of HIV/STIs is significant risk factor for acquiring other STIs [5]. Some studies have shown that the transmission rates of HCV as a STI is very low among heterosexual couples. Similarly, the rate of sexually transmitted HCV infection in HIV-negative MSM is low [40].

Socioeconomic status such as level of education, occupation, and number of sexual partners of the individual is the other risk factor for STIs. Individuals with low level of education, especially drug users, are at high risk for HIV. The frequency of HIV/STIs has increased in some occupations such as long-distance truck drivers and sex workers. Due to possibility of multiple sex partners, STIs are frequently seen in people and regions with high-income levels [5]. While more than half of four curable STIs including chlamydia, gonorrhea, trichomoniasis, and syphilis occurred in upper-middle income countries, other remaining infections occurred in lower-middle income countries with 23%, low-income countries with 12%, and high-income countries with 9%, respectively [2].

Some behaviors including having multiple sex partners, sexual intercourse without condom use, illicit drug use, sharing of injected equipment's, and alcohol use are generally associated with a higher prevalence of HIV/STIs [5]. High-risk behaviors such as serosorting and chem-sex may increase the rate of sexually transmitted HCV [40].

3.1. Complications and morbidities of STIs

Most of the STIs are asymptomatic. For this reason, there may be unnoticed, undetected, and untreated cases and serious complications can be seen in these cases [1, 36]. Possible complications are shown in **Table 1**.

3.2. Screening of STIs

As noted below, the screening of certain groups is urgently recommended:

1. Everyone between the ages of 13 and 64 years should be tested at least once for HIV.
2. Sexually active females up to 24 years should routinely be screened for chlamydia every year.
3. Nonpregnant women at higher risk of infection should be screened for gonorrhea and syphilis.
4. Pregnant women, regardless of risk, should be screened for chlamydia, hepatitis B, HIV, and syphilis; pregnant women at higher risk of infection should also be screened for gonorrhea and hepatitis C.
5. Men should be screened for HIV, and men at higher risk should also be screened for syphilis.

-
- Female infertility
 - Genital neoplasia
 - Pelvic inflammatory disease (PID)
 - Epididymitis
 - Urethritis
 - Prostatitis
 - Ectopic pregnancy
 - Cervical cancer
 - Cardiovascular and neurological damage
 - Fetal and neonatal morbidity and mortality (stillbirths, neonatal death, preterm or low-birth-weight baby, blindness)
 - Aseptic meningitis
 - Preterm rupture of membranes during pregnancy
-

Table 1. Possible complications caused by STIs [1, 5, 28, 41–43].

6. MSM should be screened at least annually for HIV and syphilis and undergo a test for urethral chlamydia and gonorrhea infection. Men who participate in receptive anal intercourse should be tested for rectal chlamydia and gonorrhea and, in those who participate in oral intercourse, for pharyngeal gonorrhea [31].

4. STIs in children

STIs can also be seen in children. As transmission may be in utero, it may occur during delivery or after contact with contaminated devices and infected persons. But it should always be kept in mind that there may be sexual abuse [44]. Victims of sexual abuse were reported as 1.8 per 1000 children in 2006 [45].

In asymptomatic prepubertal children, STIs screening for all organisms from all sites is not recommended by American Academy of Pediatrics (AAP) guidelines. However, the clinician should consider the following situations when deciding whether to screen or not:

1. History of penetration or evidence of recent or healed penetrative injury to the genitals, anus, or oropharynx.
2. Abuse by a stranger.
3. Abuse by a perpetrator known to be infected with an STI or at high risk of STIs (intravenous drug users, MSM, or people with multiple sexual partners).
4. Sibling or other relative in the household with an STI.
5. Residence in an area with a high rate of STI in the community.
6. Signs or symptoms of STIs.
7. Already diagnosed with one STI (and therefore should be screened for other STIs) [45].

Child sexual assault (CSA) survivors may have a risky sexual life in their future. Therefore, HPV vaccination for CSA survivors aged 9–26 years for females and aged 9–21 years for males is recommended in accordance with ACIP [45].

5. Conclusion

At present, STIs are not fully under control with current strategies and continue to cause serious public health problems. From early ages, individuals, especially those at high risk, should be informed about STIs and the methods of prevention from these infections. Health care providers should communicate individually with infected individuals and their partners. Proper

screening of high-risk individuals is crucial for early detection and treatment. Considered the data in recent years, it seems likely that the addition of vaccines that are proven efficacious to national vaccination programs of all countries would be beneficial.

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