SUMMARY

Purpose of the study: To investigate demographics, prevalence, risk factors and the different clinical forms and symptoms of syphilis in men who have sex with men (MSM).

Material/Methods: 50 MSM with syphilis were registered at the Clinic of Dermatology and Venereology in the city of Pleven, Bulgaria, for the period 2008-2022. The diagnosis was confirmed by serological tests. Patients were distributed by their socio-demographic status. Risk factors and sexual behavior were studied, as well as clinical symptoms and co-morbidities of syphilis.

Results: Of 50 MSM patients the most affected is the age between 20-29 years (54%). 34% of them are university graduates, 88% abused alcohol, nicotine and drugs in combination, 70% had sexual contacts with a casual partner, 26% of them had HIV co-infection. Secondary and early latent syphilis are the most common clinical forms of the disease (34%). The typical symptoms of primary and secondary syphilis were clinically manifested, 34% of them are localized in the genital. There is a significant correlation of the clinical form with the localization of the skin-mucosal lesions (p < 0.001). Antibiotic therapy is effective and leads to negative serological test results by the end of the second year of treatment.

Conclusions: For 15 years (2008-2022), the number of registered MSM with syphilis in the Clinic of Dermatology and Venereology in Pleven increased after 2016 especially in the time of the COVID-19 pandemic. Our results are close to the published data on the problem in the scientific literature for the last 10 years.

Keywords: sexually transmitted infections, risk factors, syphilides, MSM, HIV.

INTRODUCTION:

In the 1970s, published evidence showed that syphilis was a common disease among men who have sex with men (MSM). [1] Numerous local epidemics have been described in different countries of the world. [2] At the same time, the wide range of sexual practices, the public tolerance of same-sex sexual relationships and the high efficiency of transmission of the Treponema infection make it possible to increase the number of people infected with syphilis. [3, 4, 5]

Over the past twenty years, the percentage of MSM with syphilis/HIV co-infection has also increased. The most common reason for this is that the primary chancrre and/or syphilitic ulcers disrupt the integrity of the genital epithelium, thus becoming a gateway for HIV. A challenge of co-infection is the bidirectional synergistic effect that facilitates both contamination and transmission of both infections, altering the clinical progression of the diseases. At the same time, the effect achieved in recent years of antiretroviral therapy, which limited the spread of AIDS, predisposes to risky sexual behavior [6, 7]

It is known that Treponema pallidum is divided into 30–33 hours, and depot penicillin preparations (Benzathine penicillin) are effective enough and preferred in the treatment of patients with syphilis. However, outbreaks of the disease continue to occur worldwide, primarily in urban settings and among the MSM population. [8]
MSM population - harmful addictions, number of partners and frequency of sexual contacts, accompanying diseases;

3. With a thorough clinical examination, dermatological status and serological studies to determine the clinical stages of the disease, the frequency and localization of the clinical symptoms of the infection. After the diagnosis and prescribed antibiotic therapy, the effect of the treatment is to be traced over time;

4. The obtained results should be compared with published data on the problem in our available scientific literature.

MATERIAL AND METHODS:

Material

For the period 2008 - 2022, 323 patients with various forms of syphilis were diagnosed and treated at the University Clinic for Skin and Venereal Diseases in the city of Pleven. From them, 50 persons who had sexual contact with the same sex were selected. They were aged between 16 and 53 years (mean age 31.53 ± 9.026) self-identified as “male”. All signed informed consent for the use of clinical data without publication of personal information.

Methods

• Epidemiological analysis
  - Through a cross-sectional analysis, to determine the frequency and percentage of MSM
  - For the purposes of a retrospective epidemiological study, patients were divided by age, ethnicity, place of residence, family status, education, profession. An analysis of the risk factors for the spread of STIs among the MSM population was made.
  - The clinical method is carried out by taking a detailed history, thorough clinical examination and dermatological status with a description of clinical symptoms of the infection. The different clinical stages of the disease are registered - primary, secondary, latent. Antibiotic therapy was prescribed, the effect of which was monitored over time by negating the serological samples, and patients with syphilis/HIV co-infection were referred to an infectious diseases clinic for treatment.

  • Laboratory methods for diagnosis and control include the RPR serological tests (rapid plasma reagin), TPHA (Treponema Pallidum Hemagglutination Assay) and ELISA IgM-IgG for syphilis, and for HIV carrier ELISA HIV1+2 Ag-Ab were applied and HIV1/2 Rapid test.
  • The obtained results were processed with the statistical program SPSS v.26 and EXCEL. They are described through tables, graphs and numerical values (percentages, coefficients, average values, standard deviation, etc.). The statistical methods used to analyze the results are descriptive statistics, variation and correlation analysis. The level of significance was p < 0.05.

RESULTS:

For a 15-year period (2008-2022), 323 persons of both sexes with different forms of syphilis were diagnosed, registered and treated - 192 men and 131 women (1.5:1). The MSM population of 50 men represented 15.5% of the total treated patients with the same diagnosis and 26% of the affected men. They are aged between 16 and 53 years (mean age 31.53 ± 9.026). The high number of homosexual individuals registered after 2016 (41 patients, 82% of all) is striking, as 24, 48% of all are during the COVID-19 pandemic - 2020-2022. (Fig. 1.)

Fig. 1. Syphilis trends in the Pleven region between 2008 and 2022 among men, women and men who have sex with men.
58% actively sought medical help, 8% indicated as a source, and 6% indicated as a contact. In the course of preventive examinations, 28% of them were found - 8% during blood donation, 12% during examinations for other systemic diseases and only 4% by request. All patients were serologically verified with the screening RPR test and the syphilis-specific TPHA and ELISA IgM-IgG. All 50 were tested for HIV. 20% of RPR tests are negative, and tests with a titer of 1:16 (24%) and 1:32 (26%) are the most common. The diagnosis in negative screening tests, as in all others, was confirmed by TPHA. No correlative dependence of the titer in the screening RPR test with the clinical form of syphilis was found (p Å 0.05).

According to the age, the age group 20-29 (54%) is the most affected, followed by 30-39 (22%). 78% are of Bulgarian ethnic origin, 82% of them live in large and medium-sized cities, 92% of them have secondary and above secondary education (34% are university graduates), 84% are single, 56% are professionals in their work, 20% are unemployed.

When assessing the risk factors, it is striking that 28% abuse alcohol, cigarettes and narcotic substances at the same time, 32% with alcohol and only 12% do not report any harmful habits. Data related to sexual activities indicated that 88% of them had 2 or more sexual contacts, 30% had a permanent partner, 70% reported casual contacts. For 62%, the last sexual act was up to 3 months old, with 24% from 3 to 6 months. Risk calculations show that MSM who abuse alcohol or combine alcohol with drugs are more than 2 times more likely to be infected (OR 2.25; 95%CI: 1.0108-5.0083; p=0.0470), and those who had contact with a casual partner were at risk of Treponema infec-
tion 5.5 times compared to those with a permanent partner (OR 5.4; 95%CI: 2.3145-12.8072; p=0.0001).

More than half of the patients (52%) have no accompanying diseases, there are only a few cases of co-infection with chlamydia, candida and papilloma virus. The fact that out of 50 MSM, 13 have co-infection with HIV, which is 26% of them, is worrying. For comparison, out of a total of 323 individuals registered, 17 (5.3%) have the indicated co-infection.

The analysis of the clinical picture and serological diagnosis objectified 22% with primary syphilis, 34% each for secondary and early latent and 6% for late latent. Clinical symptoms were hard chancre in 28.6%, macular syphilides (roseolae and angina) in 49%, and papular syphilides (papules and flat condyloma) in 45% of the 50 MSM. (Fig. 2.)

![Fig. 2. Clinical symptoms in MSM with syphilis (sum of percentages is greater than 100% due to patients having more than one symptom)](image)

The localization of pathological skin-mucosal changes has the highest frequency in the genital area (34%), in the anorectal (10%), in the oropharyngeal (8%), with other extragenital localization in 8% and in 40% it cannot be established in the course of the latent forms of the disease. A significant correlation was found between the clinical form of the disease and the localization of the pathological skin-mucosal lesions (r=0.628; p=0.000; N=50), as well as the relationship between the clinical symptoms and the clinical form - ulcer durum with primary syphilis (r= 0.81; p=0.000; N=50), macular (r=0.912, p=0.000, N=50) and papular (r=0.68, p=0.000, N=50) eruptions with the secondary period.

Therapy included treatment with Benzathine benzylpenicillin 2,400,000 IU once weekly in 34% of patients, as well as a combination of antibiotics in 60% of them. The treatment effect was monitored periodically, with 58% having follow-up examinations and tests 1 to 3 times, 28% 4 to 7 times, 6% 8 to 10 times. As a result of adequate antibiotic therapy, 8% negative their positive serology by the 6th month, 12% by the 12th month, 28% by the 24th month. At the same time, there is no data for 34% of luetic
patients due to interrupted contact with the clinic (change of residence, departure abroad, of their own accord, etc.).

**DISCUSSION:**

The trend of increasing the number of syphilis cases in the 29 countries of the European Union was published in the latest report of the European Center for Disease Prevention and Control in 2022 - from 27,976 cases in 2015 to 35,039 in 2019. Among the registered persons, the incidence of syphilis in men is nine times higher than in women. The peak incidence is in the male age group 25–34 years. 74% of syphilis cases are reported in MSM. According to experts, the increase in the incidence of syphilis among men between 2010 and 2017 is due to an increase in the number of cases among MSM. [9] Our data indicate that during the study period in the clinic, the male-to-female ratio was 1.5:1, and MSM accounted for 26% of the male patients. This ratio corresponds to the one published in the report for Bulgaria [9], but the data on the frequency of syphilis among heterosexual men and MSM are quite different, bearing in mind that we indicate the results from only one center in the country.

The findings in our study shed light on the prevalent risk factors among MSM and the alarming rates of syphilis infection in this demographic. In the survey, the predominant age group among MSM falls in the 20 to 30 years range (54%). Similar data have been reported in other studies that indicate the susceptibility of the youth of this age to high-risk behaviors such as multiple sexual partners, unsafe sex, and substance abuse. [10, 11, 12] The fact is that with the advancement of technology, MSM are increasingly using social networks to search for sexual partners, which also increases the risk of STIs. [5, 13] In fact, 88% of the participants in our study showed a sufficiently high-risk behavior – 78% shared multiple sexual contacts, and 70% admitted to casual and partnered contacts, 84% of MSM patients were unmarried. Our results correspond to those published by Pereira Nogueira et al. in 2022. [14]

It is noteworthy that during the covid-19 pandemic (2020-2022), 24 MSM with syphilis were registered in our center (48%). For comparison, the remaining 26 patients were selected for a much longer period - 2008-2019. According to an analysis by Cusini et al., for the first year of the pandemic, in two centers in Lombardy, the number of STIs cases decreased, but the number of acute bacterial infections associated with MSM increased. It has to be concluded that despite the imposed social and physical distancing measures, the COVID-19 pandemic has not prevented risky behavior, especially by MSM. [15] The claim is also supported by Evangelou et al., who published a summary of results from epidemiological studies conducted in six different locations around the world. A general noticeable increase in syphilis cases has been observed everywhere, which supports the hypothesis that the restrictive measures against COVID-19 have not been able to effectively suppress the transmission of syphilis. [16]

In our study, a total of 26% of MSM with syphilis/HIV co-infection were recorded after 2013, compared to only 6% during the pandemic. The rate of syphilis/HIV co-infection among MSM has increased over the past decade. This phenomenon is particularly disturbing because of the biological and epidemiological associations between syphilis and HIV infection. The two infections interact synergistically to accelerate the progression of AIDS and increase the incidence of therapeutic resistance to the disease. [6, 17] Studies have shown that the immune response in syphilis stimulates and directs to the site of infection-activated macrophages, CD4 and CD8 T cells that can facilitate the acquisition of HIV infection, and that acute luteal infection can increase the risk of HIV seroconversion up to 2.5 times. [18, 19]

According to the clinical form of the disease in our study, 22% had primary, 34% secondary, 34% early latent syphilis, and 10% late latent and other unspecified – frequencies reported in large cohort studies over the years. [5,6,20] Jebbari et al. analyzed the epidemiology of syphilis in 11,838 patients in England and Wales between 1998 and 2008. They reported that 73% of cases occurred in MSM, a percentage much higher than in our patients. Primary syphilis was reported in 43% of cases, secondary in 33%, and early latent in 24%, which results are comparable to ours. [21]

Usually, genital involvement has the highest frequency, but involvement in extragenital areas is increasingly reported. Our data speak of 34% genital, 10% anorectal, 8% oropharyngeal involvement, and 48% asymptomatic, corresponding to latent forms. We found a high correlation of the clinical form with the localization of the pathological lesions (p<0.001), as well as of the hard chancre with primary syphilis (p<0.001), and of the macular (roseolae and specific angina) and papular (palmoplantar papules and condyloma) lesions with the secondary (also p<0.001) which corresponds to the theoretical knowledge of syphilis. [8, 9, 13, 22]

In connection with the different sexual patterns practiced by MSM, the frequency of the extragenital localization of the hard chancre is significantly increasing, but due to the fact that patients are not always inclined to share their sexual preferences, it is difficult to determine the exact anatomical area affected. [2, 8, 20]

Our treatment is in accordance with national and international guidelines and is tailored to the stage of the disease. [22,23] Benzathine benzylpenicillin 2,400,000 IU im weekly for a period of 3-5 weeks was administered to 47 patients. In 30 of them, the therapy was continued with the oral antibiotic Doxycyclin 2 x 100 mg daily for 20 days, and the patients were followed until the serological reactions became negative – 48% by the end of the sec-
ond year. It is a fact that 34% of patients have disturbed contact with the clinic, a phenomenon that occurs mainly in regions with a mixed population. [5, 11, 20]

CONCLUSION:
The results of our study indicate that the number of diagnosed and treated cases of syphilis at the Pleven Dermatology Clinic increased after 2016. The percentage of infected MSM also increased, as well as the number of homosexual individuals with syphilis/HIV co-infection. These facts reflect the experience of only one center in the country for the observation and treatment of syphilis patients and are not findings on the modern pathomorphosis of the disease on a nationwide scale but correspond to the data published in the scientific literature in the last 10 years. Assessment of sexual risk, recommendations for safe sex, restriction of sexual contacts and regular testing for sexually transmitted infections are only part of the activity for the prevention and control of syphilis among the MSM population.

REFERENCES:


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