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Research Article

Evaluation of Demographic and Clinical Characteristics of the Patients with Syphilis Who Applied to the Dermatology Clinic of a Tertiary Referral Hospital Between the Years 2019-2023

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Abstract

Aim: The aim of this study is to evaluate the demographic and clinical features of syphilis patients followed up in a tertiary referral hospital, and thus to provide current contributions to epidemiological data related to syphilis.

Material and Methods: The demographic characteristics, clinical and laboratory findings, and treatments received of all patients diagnosed with syphilis and followed up in our clinic between January 2019 and June 2023 were evaluated retrospectively.

Results: We included a total of 118 patients, 24 women and 94 men. The average age of the patients was 36.56±5.1 years. Forty-one of the patients (34.7%) were married, 56 were single (47.4%) and the marital status of 21 (17.8%) was unknown. Sixty-two of the patients (52.5%) had primary syphilis , 29 (24.6%) had secondary syphilis and 27 (22.9%) had latent syphilis. When the patients' admission symptoms were evaluated, genital chancre was found in 58 (49.1%), roseola syphilitica in 24 (20.3%), mucous plaque in 11 (9.3%), condyloma lata in 7 (5.9%) and syphilis papulosa psoriasiformis in 3 (2.5%) patients. Twenty-five patients (21.1%) were asymptomatic. Transmission from spouse was in 14 (11.9%) patients while suspicious sexual contact was in 77 (65.3%) patients. The source of transmission was unknown in 27 (22.9%) patients. Response to treatment was obtained in all of the patients who were not lost to follow up. Twenty-two of the patients (18.64%) were HIV positive.

Conclusion: Rising syphilis incidence which is observed globally in the recent years indicates the need to raise the level of public awareness about the disease and its transmission routes. In addition, since it can mimic many diseases, it should always be considered in the differential diagnosis, especially in patients with a history of suspicious sexual contact. It is necessary to investigate other sexually transmitted diseases, especially HIV, in patients diagnosed with syphilis.

Keywords: Syphilis, sexually transmitted diseases, *Treponema pallidum*

INTRODUCTION

Syphilis is an infection caused by the spirochete group Treponema pallidum subspecies pallidum; it is transmitted sexually, through blood transfusions or transplacentally. It has different stages which can be symptomatic or asymptomatic and can affect all systems and organs if not treated with its chronic course (1). Being an endemic disease on the European continent since the 17th century, syphilis has caused numerous epidemics worldwide since the 1990s due to the HIV epidemic, polygamy, an increase in the number of substance addicts, and the prevalence of homosexual relationships. The first cases in Türkiye started to be seen after the 19th century, and the name "frengi" was used to describe the disease, indicating that it came to Türkiye from Europe (1,2).

The clinical symptoms of syphilis are not specific and can mimic many diseases. During the primary syphilis period, chancre; during the secondary syphilis period, skin rashes, mucocutaneous lesions, lymphadenopathy; and in tertiary syphilis, cardiac and neurological symptoms, and gummas can be observed (3). Moreover, since the pathogen cannot be cultured in vitro, serological methods are generally used in diagnosis (4). The most commonly used serological tests for screening the presence of infection are treponemal and non-treponemal tests. For screening purposes, the flocculation-based Veneral Disease Research Laboratory (VDRL) and agglutination-based Rapid Plasma Reagin (RPR) are most commonly used. Their false positivity rates are higher compared to treponemal tests. Treponemal tests display antibodies specific to treponemas and become positive from the

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second week of infection. The most frequently used are the Treponema Pallidum Hemagglutination Assay (TPHA) and the Fluorescent Treponema Antibody-Absorption Test (FTA-ABS). The false positivity rate in these specific tests is very low, hence they are used to confirm the diagnosis. Due to the lifelong positivity of treponemal tests, treatment response is monitored by titration tracking of non-treponemal tests (5).

In our study, we aimed to evaluate the demographic characteristics, clinical and laboratory findings, and treatments received by the patients diagnosed with syphilis and followed up in our clinic in the last 4.5 years. We believe that the obtained data will contribute to the improvement of current epidemiological data related to syphilis.

MATERIAL AND METHOD

Our study was conducted in a tertiary referral hospital. The demographic and clinical characteristics of all patients followed up with the diagnosis of syphilis in our clinic between January 2019 and June 2023 were evaluated retrospectively. Ethics committee approval with number E1-23-3654 was obtained from Ankara City Hospital before the study (07.06.2023). Our study was administered in accordance with the Helsinki Declaration. Patients with missing records in hospital records or with unconfirmed diagnosis of syphilis were not included in the study.

Statistical analysis calculations were performed with the SPSS 24.0 (IBM Corp., NY, USA) program. Continuous variables are expressed as mean and standard deviation, and categorical variables are expressed as number and percentage. Pearson's Chi-Square test statistic or Fisher's Exact tests were used as appropriate for comparing categorical measurements. The level of statistical significance was accepted as 0.05 in all tests.

RESULTS

A total of 118 patients, 24 women (20.3%), and 94 men (79.7%) were included in our study. The average age of the patients was 36.56±5.1 years. The average age of female patients was 30.3±3.2 years, while the average age of male patients was 38.16±4.2 years. Forty-one of the patients (34.7%) were married, 56 were single (47.4%), and the marital status of 21 (17.8%) was unknown. Five of the women were single, 19 of them were married. Twenty-two of the men were married, 55 were single, and the marital status of 21 was unknown. Table 1. shows demographic characteristics of our patients.

Table 1. Demographic characteristics of patients

	Female	Male	Total
Number of patients (N)	24	94	118
Mean age ±SD (years)	30.3±3.2	38.16±4.2	36.56±5.1
Marital Status N (%)			
Married	19	22	41 (34.7)
Single	5	55	56 (47.4)
Unknown	0	21	21 (17.8%)

Table 2. Clinical characteristics of the patients

Syphilis stage N (%)	Primary	62 (52.5)
	Secondary	29 (24.6)
	Latent	27 (22.9)
Presenting symptoms N (%)	Genital chancre	58 (49.1)
	Roseola syphilitica	24 (20.3)
	Mucous patch	11 (9.3)
	Condyloma lata	7 (5.9)
	Syphilis papulosa psoriasiformis	3 (2.5)
	Neurosyphilis	1 (0.8)
	Asymptomatic	25 (21.1%)
Laboratory results		
RPR N (%)	Positive	112 (95)
	Negative	6 (5)
TPHA N (%)	Positive	117 (99.2)
	Negative	1 (0.8)
Sources of infection N (%)	Spouse	14 (11.9)
	Suspicious sexual contact	77 (65.3)
	Unknown	27 (22.9)
Treatments received N (%)	Benzathine Penicillin G 2.4 MU 3 doses	52 (44)
	Benzathine Penicillin G 2.4 MU 2 doses	29 (24.6)
	Benzathine Penicillin G 2.4 MU single dose	31(26.2)
	Doxycycline 200 mg for 4 weeks	5 (4.2)
	Crystalline Penicillin for 10 days	1 (0.8)
Accompanying infectious diseases N (%)	HIV	22 (18.4)
	Hepatitis B	2 (1.7)
	Hepatitis C	(1.7)

RPR: Rapid Plasma Reagin, TPHA: Treponema Pallidum Hemagglutination Assay

Sixty-two of the patients (52.5%) had primary syphilis, 29 (24.6%) had secondary syphilis and 27 (22.9%) had latent syphilis. When the patients' admission symptoms were evaluated, genital chancre was found in 58 (49.1%), roseola syphilitica in 24 (20.3%), mucous plaque in 11 (9.3%), condyloma lata in 7 (5.9%) and syphilis papulosa psoriasiformis in 3 (2.5%). One patient had neurosyphilis. Twenty-five patients (21.1%) were asymptomatic. When the non-treponemal tests of the patients were evaluated, RPR was positive in 112 patients (95%), negative in 6 (5%) patients. TPHA was positive in 117 patients, and negative in 1 patient. When we examined the sources of transmission, there was transmission from husband/wife in 14 (11.9%) patients and due to suspicious sexual contact in 77 (65.3%) patients while the source was unknown in 27 (22.9%) patients. When we evaluated the treatments received, 52 patients (44%) received 3 doses of Benzathine penicillin G 2.4 million units with one week apart, 29 (24.6%) received 2 doses with one week apart and 31 (26.2%) received a single dose of penicillin treatment. Five patients (4.2%) with penicillin allergy received doxycycline 200 mg/day for 4 weeks. One patient

who was also HIV positive and in the latent stage had neurosyphilis. He received crystalline penicillin 6X4 million units for 10 days. A response to treatment was obtained in 110 patients, while the remaining 8 patients dropped out of the follow-up. Twenty two patients (18.64%) were HIV positive, 2 were hepatitis B positive, and 2 were hepatitis C positive. Table 2. shows clinical characteristics of our patients.

DISCUSSION

Syphilis represents a significant public health concern that affects a large proportion of the population (1,2). The number of syphilis cases reported between 2010 and 2019 (excluding the plateau between 2017 and 2018) has been on a steady increase (6,7). While a marked increase has been observed in men, a slow decrease has been noticed among women. This is thought to be due to the rise in men having sex with men (MSM) (7,8).

According to the 2019 data from the European Centre for Disease Prevention and Control (ECDC), the incidence of syphilis was calculated as 7.4/100,000. This surveillance study used data obtained from 29 European Union countries (7). According to the Centers for Disease Control and Prevention (CDC) 2019 data, the incidence of syphilis in the United States has increased five-fold compared to 2001, reaching 11.9/100,000 (9).

The number of studies and statistical data concerning the frequency of syphilis in our country is limited. According to the syphilis statistics from the Ministry of Health Public Health, the number of reported cases has increased from 502 in 2015 to 2801 in 2021 (10). The annual incidence of 3.35/100,000 is thought to be lower than the actual incidence, occasionally due to the treatment of syphilis cases under different diagnoses and limited reporting of the cases (11).

In our study, the male/female ratio was found to be 3.92. In the study by Oğrum et al. (1), this ratio was 3.5; in the study by Adışen et al. (2), it was 4.3. Our study shows similarity with these studies in terms of the male/female ratio. According to the CDC 2019 data, 83% of primary syphilis cases in the United States were male, and 57% of these were MSM (9). According to the ECDC data, the male/female ratio was found to be 8.6/1 (7). In the same study, it was found that the disease was most frequently seen in the 25-34 age range and that the frequency of occurrence in men was higher than in women across all age groups (7). The average age of our patients was 36.56±5.1 years. The average age of female patients was 30.3±3.2 years, and the average age of male patients was 38.16±4.2 years, which were found to be compatible with the ECDC data.

The majority of our patients, whose marital status was known, were observed to be single. Excluding the 21 patients whose marital status was unknown, 57.7% of the patients were single, and 42.3% were married. In studies conducted in our country, the percentage of married syphilis patients was observed to be 70% (1), 80.6% (2), and 78.7% (12). Our study differs from the results of other studies conducted in previous years in our country in that the rate of single patients was higher than the rate of married patients. On the contrary, we observed that the rate of married patients in our study was higher in the female patients' group (72.2%).

The most common stages of disease were found to be primary, secondary, and latent syphilis, respectively. The genital chancre, a primary syphilis lesion seen in approximately half of the patients, was the most common presenting symptom. Other presenting symptoms were roseola syphilitica, plaque mucosus, condylomata lata, and psoriasiform papular syphilis, in order, all indicative of the second stage. Our study did not have sufficient data on the frequency of generalized lymphadenopathy, a common symptom of the second stage. It is noteworthy that six patients with latent syphilis were serologically identified during screening tests when they applied to donate blood. This underscores the importance of raising awareness among potential donors about sexually transmitted diseases. In the study by Adışen et al., 75.5% of the patients had first-stage, 12.8% had second-stage, and 11.32% had third-stage syphilis. The most commonly observed symptom at the time of presentation in this study was also the genital chancre (2). Similarly, in the study by Karaosmanoğlu et al., patients were most commonly diagnosed in the primary stage, followed by the secondary stage (12). These findings are consistent with our study data. However, in the study by Oğrum et al., the most common reason for presentation was second-stage syphilis lesions. The authors attributed this to the first stage, where the only symptom is painless chancre, being overlooked, and the more noticeable course of the second stage, where dermatological and systemic symptoms are more prominent (1). According to the ECDC 2019 data, in contrast to the studies in our country, it was reported that latent syphilis was most commonly seen (34% primary, 25% secondary, 38% latent syphilis) (7).

When patients' serological tests were examined, the non-treponemal test RPR was positive in 112 patients (95%) and negative in 6 patients (5%). The prozone phenomenon was observed in 2 patients who tested negative, with initially negative values becoming positive with serum dilution. VDRL is not performed in our hospital. TPHA was negative in one patient, whose clinical presentation was compatible with syphilis and whose FTA-ABS test was found to be positive. Similar characteristics of syphilis serology have been observed in other studies conducted in our country (1,2).

When assessing the filiation status, 11.9% of patients had contracted the disease from their spouse, 65.3% due to a suspicious sexual relationship, whereas the source of infection was unknown for 22.9% (n=27) of the patients. When excluding the patients with an unknown source of infection, among the patients with known sources of infection, 81% of women (n=13) got infected by their spouses, while 98.6% of men got infected due to suspicious

sexual relationships. The content of the suspicious sexual relationships (sex worker or MSM) could not be clarified with the available data in the system. The striking difference in the source of transmission between men and women could be related to the sociocultural structure of society. Similarly to our study, in the study by Oğrum et al., the source of infection for 7 out of 8 married women was their husband, while for 26 out of 27 married men it was extramarital relationships (1). The study by Adışen et al. produced data parallel to our study (2). It was also noteworthy in our study that about a quarter of the cases did not describe any mode of transmission. This may be due to the lack of sufficient awareness and knowledge in society about the modes of transmission and course of the disease. In their study investigating the level of knowledge about sexually transmitted diseases among young adult males, Açıkel et al. showed that only 6.5% of this group had knowledge about syphilis (13). We believe that awareness about syphilis should be raised through health services and mass communication tools.

In the ECDC study, it was reported that, according to the available data from 16 countries, the source of transmission in 68% of cases was male-to-male relationships, 25% was heterosexual relationships, and in 7% the source of transmission was unknown (7). Factors associated with syphilis transmission have been reported as high-risk sexual behaviors (MSM, multiple partners), sex work, substance use (drugs or alcohol), poverty, homelessness, ethnic minority or migrant status (3).

The recommended treatment regimen for syphilis is a single dose of benzathine penicillin G 2.4 million units for primary, secondary, and early latent syphilis. In cases of HIV positivity, 3 doses with a week's interval is recommended. For late latent syphilis, Benzathine penicillin G is given as 3 doses at one-week intervals (4). Doxycycline can be used in cases of penicillin allergy (4,14). All of our patients, except for 5 with a penicillin allergy, had received penicillin treatment. The outcome of the 8 patients who were lost to follow-up is unknown, but all remaining patients had responded to treatment. No side effects or complications were reported. In the study by Karaosmanoğlu et al., similarly, 43 patients were successfully treated with penicillin, except for 3 patients with penicillin allergy (12). These findings demonstrate that penicillin remains as the first and most effective treatment option for syphilis.

Of our patients, 22 (18.64%) tested positive for HIV, 2 for each of hepatitis B and hepatitis C. The coexistence of syphilis and HIV has been increasing in recent years, and co-infections are frequently seen (15). Syphilis not only facilitates the transmission of HIV but also increases the frequency of complications and the progression of the disease. Therefore, all patients with syphilis should be screened for HIV (16). In a study published by Harman et al. in 2021, the frequency of HIV in patients with syphilis was investigated, and HIV positivity was detected in 45% of patients. A higher rate of HIV co-infection in patients with syphilis was found in that study than syphilis co-infection rates in patients with HIV, stated in previous studies. This was thought to be due to the perception of syphilis as less significant compared to HIV infection among sexually active individuals and the abandonment of protective measures (16). The ECDC 2019 study reported the coexistence of syphilis and HIV as 23% (7). While older studies in our country did not detect a coexistence of syphilis and HIV (1,12), the finding of HIV in nearly a fifth of our patients in our study may indicate a diversification of sexual preferences in our country, similar to European and American countries.

CONCLUSION

In conclusion, syphilis remains a significant public health problem in our country, as it is worldwide. The increase in the incidence of the disease compared to past years indicates the need to raise the level of awareness in society about the disease and its modes of transmission. In addition, due to its wide range of clinical manifestations, it can mimic many diseases, and therefore should always be considered in the differential diagnosis, especially in patients with a history of suspicious sexual contact. It is necessary to investigate other sexually transmitted diseases, especially HIV, in patients diagnosed with syphilis.

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