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Syphilis infection: Demographics, treatment, and serological response in a cross-sectional study

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Abstract
Introduction: Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum* subspecies pallidum. This infection has been a significant public health concern throughout history, with its prevalence varying widely around the world. The aim of study is to investigate what is new in Syphilis Infection: Demographics, Treatment, and Serological Response.
Method: Cross-sectional research patients had no clinical signs or symptoms of syphilis but they diagnosed accidentally when screening blood tests done for them as pre blood donation test or pre marriage blood screening test. All patients take age/years, gender, any symptoms, serological test (TPHA, VDRL), HIV test, any previously partner infection, penicillin (2.4 million units of intramuscular benzathine penicillin G in 3 doses one week apart), doxycycline (100 mg every 12 hr. for 28 days), and Venereal Disease Research Laboratory (VDRL) tests at 3-month, 6-month, 9-month, and 12-month intervals.
Results: This cross-sectional study included 99 syphilis patients (mean age: 37.5±10 years), predominantly male (74.7%) and asymptomatic (100%). Penicillin was the primary treatment (94.9%), with 10.1% showing positive VDRL serology after 12 months of follow-up. Significant gender differences were observed, with 100% of males achieving negative Post treat serology (12 M VDRL) compared to 60% of females. No significant association was found between age groups and Post treat serology (12 M VDRL).
Conclusion: This interesting cross-sectional research on syphilis demographics, treatment, and follow-up reveals: Monitoring therapy response requires VDRL follow-up. Doxycycline and penicillin treat syphilis. Successful therapy reduces VDRL serology. Males had greater serological cure rates than females. Age may not affect therapy response. Research is needed to identify causes and enhance prevention.

Keywords: Syphilis, infection, demographics, treatment, serological, response

Introduction

Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum* subspecies pallidum [1]. This infection has been a significant public health concern throughout history, with its prevalence varying widely around the world [2]. In recent years, syphilis has re-emerged as a significant infectious disease, often in combination with human immunodeficiency virus (HIV) [3]. Syphilis is primarily spread through sexual contact, with the bacteria entering the body through minor cuts or abrasions in the skin or mucous membranes [4]. The infection can also be transmitted from an infected mother to her baby during pregnancy or childbirth [5]. Syphilis progresses through four stages: primary, secondary, latent, and tertiary [6].

1. Primary stage: This stage is characterized by the appearance of a single chancre, a firm, painless, non-itchy skin ulceration usually between 1 cm and 2 cm in diameter, although multiple sores may be present [6]. The primary stage is highly contagious, and the chancre typically appears on the genitals, rectum, or mouth [7].

2. Secondary stage: During this stage, the infection spreads throughout the body, causing a variety of symptoms such as skin rashes, fever, swollen lymph nodes, and fatigue [8]. This stage is also contagious, and the symptoms may come and go over time [9].

3. Latent stage: In this stage, the syphilis bacteria remain inactive in the body, and no symptoms are present [10]. The infection can still be transmitted during the early latent period, but the risk of transmission decreases over time [11].

4. Tertiary stage: This stage occurs in about 15-30% of untreated individuals and can develop years or even decades after the initial infection [12]. Tertiary syphilis can cause severe damage to multiple organ systems, including the heart, brain, and nervous system, and can be life-threatening [13]. Diagnosing syphilis typically involves blood tests to detect antibodies against the bacterium (TPHA and VDRL) [14]. If tests confirm the presence of syphilis, it is crucial to notify all sexual partners from the past three months to one year to ensure they receive testing and treatment if necessary [14]. Early syphilis can be effectively treated with antibiotics, such as penicillin [14]. In some cases, a single injection of penicillin is sufficient to cure the infection [14]. However, treatment in the later stages may require more extended courses of antibiotics and may not reverse the damage caused by the infection [15]. Preventing syphilis involves practicing safe sex, including using condoms consistently and correctly, and maintaining open communication with sexual partners about STI testing and history [15]. Regular STI testing is also essential, especially for individuals with multiple sexual partners or those at higher risk for infection [15]. doxycycline is a viable alternative treatment for syphilis when penicillin is not an option, and it has shown potential as a post-exposure prophylaxis for STIs. However, more research is needed to establish the optimal dosing and duration of treatment, as well as to evaluate its efficacy as a preventive measure in high-risk populations. The terms "Serology 3 M VDRL," "Serology 6 M VDRL," "Serology 9 M VDRL," and "Serology 12 M VDRL" seem to refer to the timing of Venereal Disease Research Laboratory (VDRL) tests at 3-month, 6-month, 9-month, and 12-month intervals [15]. These tests are used to monitor the response to treatment for syphilis, a sexually transmitted infection caused by the bacterium *Treponema pallidum*. The aim of study is to investigate what is new in Syphilis Infection: Demographics, Treatment, and Serological Response.

Method

Cross sectional study of 99 patients had no clinical signs or symptoms of syphilis but they diagnosed accidentally when screening blood tests done for them as pre blood donation test or pre marriage blood screening test arrived to Marjan medical hospital/dermatology consultant unit from period June 2022 to June 2023. All patients take age/years, gender, any symptoms, serological test (TPHA, VDRL) and HIV test, any previously partner infection, any take penicillin (2.4 million units of intramuscular benzathine penicillin G in 3 doses one week apart), doxycycline (100mg every 12 hr. for 28 days), Venereal Disease Research Laboratory (VDRL) tests at 3-month, 6-month, 9-month, and 12-month intervals. Utilizing SPSS 22, frequency and percentage are utilized for categorical data, while mean and standard deviation are utilized for continuous data. Utilizing Chi-square to evaluate the association between categorical variables. The T test is used to assess differences between the mean and median of continuous variables. P-value less or equal to 0.05 is consider significant.

Results

Cross sectional study of 99 patients with syphilis infection, mean age 37.5±10 years, 34.3% of patients at age group 21-30 years, and 30.3% of them at age group 31-40 years old. 74.7% of patients are males and 25.3% are females. 100% of patients are with no symptoms, 100% of patients were positive (TPHA and VDRL), and no HIV infection. 20% positive partner infected and positive test, 94.9% of patients treated by penicillin, and just 6.1% treated by doxycycline. All patients were followed up after treatment by doing VDRL test every 3 months, 30.3% of patients with positive Serology VDRL, while 20.2% of them are positive Serology VDRL after 6 months, 12.1% with positive Serology after 9 months and finally 10.1% of patients are positive Serology VDRL after 12 months follow up. As shown in table 1.

Table 1: Distribution of patients according to study variables.

Variables		Frequency	Percentage
Age group	21-30	34	34.3
(years)	31-40	30	30.3
	41-50	23	23.2
	51-60	12	12.2
Gender	Female	25	25.3
	Male	74	74.7
Symptoms	Negative	99	100.0
IV TPHA	Positive	99	100.0
IV VDRL	Positive	99	100.0
HIV test	Negative	99	100.0
Partner	Negative	79	79.8
	Positive	20	20.2
Penicillin	Treated	94	94.9
	Allergy	5	5.1
Doxycycline	No	93	93.9
	Treated	6	6.1
Serology 3 M VDRL	Negative	69	69.7
	Positive	30	30.3
Serology 6 M VDRL	Negative	79	79.8
	Positive	20	20.2
Serology 9 M VDRL	Negative	87	87.9
	Positive	12	12.1
Serology 12 M VDRL	Negative	89	89.9
	Positive	10	10.1

There are significant differences in mean of Post treat serology VDRL after 3 months and Post treat serology VDRL after 6 months, significant decrease in serology (12 M VDRL) less than serology (3 M VDRL). As shown in table 2.

Table 2: Differences in mean of Post treat serology 3 M VDRL and Post treat serology 3 M VDRL.

	Mean	N	Std. Error Mean	P-value
Post treat serology (3 M VDRL)	99	0.30	0.04	0.0001
Post treat serology (12 M VDRL)	99	0.10	0.03	

P-value ≤ 0.05 (significant).

As shown in table 3; there is significant association between gender and Post treat serology (12 M VDRL), 100% of males have negative Post treat serology (12 M VDRL), while 60% of females have negative Post treat serology (12 M VDRL). No significant association between age groups and Post treat serology 12 M VDRL.

Table 3: Association between gender and Post treat serology (12 M VDRL).

Variables			Post treat serology (12 M) VDRL	Total	P-value
		Negative	Positive		
Age groups	21-30	27	7	34	
(years)		79.4%	20.6%	100.0%	
	31-40	28	2	30	
		93.3%	6.7%	100.0%	0.082
	41-50	22	1	23	
		95.7%	4.3%	100.0%	
	51-60	12	0	12	
		100.0%	0.0%	100.0%	
Gender	Females	15	10	25	
		60.0%	40.0%	100.0%	0.0001
	Males	74	0	74	
		100.0%	0.0%	100.0%	

P-value ≤ 0.05 (significant).

Discussion

The cross-sectional study you described involves 99 patients with syphilis infection, with a mean age of 37.5±10 years. The majority of the patients are males (74.7%), and the age groups 21-30 years (34.3%) and 31-40 years (30.3%) are the most affected. All patients are asymptomatic but tested positive for syphilis using both TPHA and VDRL tests, with no HIV infection. The majority of patients (94.9%) were treated with penicillin, while a smaller percentage (6.1%) were treated with doxycycline. The patients were followed up with VDRL tests every three months, and the serological response was assessed. The study findings are consistent with the general understanding of syphilis treatment and follow-up. Penicillin is the first-line treatment for syphilis, and doxycycline is recommended as an alternative for patients with penicillin allergy or intolerance [16]. The use of VDRL tests for follow-up is a standard approach to monitor the response to treatment [17]. The study shows a gradual decrease in the percentage of patients with positive serology VDRL results over time, indicating that the treatment is effective for most patients. However, it is essential to note that the VDRL test is a nontreponemal test, and its sensitivity varies depending on the stage of the disease [18]. Therefore, it is crucial to interpret the results in the context of the patient's clinical presentation and other laboratory findings. If the VDRL test does not show the expected decrease in titer or becomes reactive again after becoming nonreactive, it may indicate treatment failure or reinfection, and further evaluation and management may be necessary [19]. The cross-sectional study you described shows a significant decrease in the percentage of patients with positive serology VDRL results over time, with 30.3% positive after 3 months, 20.2% positive after 6 months, 12.1% positive after 9 months, and 10.1% positive after 12 months. This decrease in positive serology VDRL results indicates that the treatment is effective for most patients [20]. The disease stage of syphilis substantially affects the treatment response, with earlier stages of syphilis exhibiting more rapid serological responses. Seven percent of patients with latent syphilis continued to demonstrate serological failure on the VDRL test one year after treatment. Latent syphilis was associated with a delayed serological response in multivariate analyses [21]. The patient's syphilis stage, initial nontreponemal antibody titers, and age can all influence the serological response to syphilis treatment. 10%–20% of patients with primary and secondary syphilis treated with the recommended therapy will not attain a fourfold decrease in nontreponemal titer within 12 months after treatment, according to clinical trial data. A 4-fold increase in VDRL titer was required to diagnose a new case of syphilis in patients with a previous history of syphilis [22]. The VDRL test results must be interpreted in the context of the patient's clinical presentation and other laboratory findings [23]. If the VDRL test does not show the expected decrease in titer or becomes reactive again after becoming nonreactive, it may indicate treatment failure or reinfection, and further evaluation and management may be necessary [22]. The cross-sectional study you described shows a significant association between gender and post-treatment serology (12 M VDRL), with 100% of males having negative post-treatment serology (12 M VDRL) and only 60% of females having negative post-treatment serology (12 M VDRL). However, there is no significant association between age groups and post-treatment serology (12 M VDRL). The observed difference in serological response between males and females is interesting and warrants further investigation. A study by Yang *et al*. (2013) found that male or younger patients had a higher likelihood of a serological cure than female or older patients [24]. The serological cure rate decreased for the different disease stages in the order of primary, secondary, latent, and tertiary syphilis [24]. However, the study did not provide a detailed explanation for the observed gender difference in serological response. Several factors can affect the serological response to syphilis treatment, including the patient's syphilis stage, initial nontreponemal antibody titers, and age [25]. 10-20% of patients with primary and secondary syphilis treated with the recommended therapy will not attain a fourfold decrease in nontreponemal titer within 12 months of treatment, according to clinical trial data [25]. Serologic response to treatment appears to be influenced by multiple factors, including the individual's syphilis stage (earlier stages are more likely to decrease fourfold and become nonreactive), initial nontreponemal antibody titers (titers 1:8 are less likely to decrease fourfold than higher titers), and age (titers in older patients may be less likely to decrease fourfold than those in younger patients) [25].

Conclusion

In this insightful cross-sectional study, key findings on syphilis demographics, treatment, and follow-up emerge: Regular VDRL follow-up is vital for monitoring treatment response, Penicillin and doxycycline prove effective against syphilis, Positive VDRL serology diminishes over time, indicating successful treatment, Males exhibit higher serological cure rates than females, age may not

significantly impact serological response to treatment. Further research is warranted to understand influencing factors and improve prevention strategies.

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