original article

Seropositivity of syphilis among individuals screened in a tertiary hospital in the Eastern Province of Saudi Arabia

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BACKGROUND: Sexually transmitted infections are a serious public health problem. Syphilis, a multistage, curable chronic disease caused by the spirochete *Treponema pallidum*, remains a major health problem worldwide. The disease re-emerged in the era of HIV in many countries despite the accessibility of curative therapy and continuing public health efforts to eliminate it.

OBJECTIVE: Analyse the seropositivity for syphilis.

DESIGN: Retrospective cross-sectional.

SETTING: Tertiary hospital.

PATIENTS AND METHODS: We retrospectively studied individuals who underwent screening tests for syphilis between January 2014 and December 2018. The samples that were positive by both screening and confirmatory tests were considered as confirmed positive for syphilis.

MAIN OUTCOME MEASURES: Syphilis positivity identified by chemiluminescence immunoassay, the rapid plasma reagin test, and specific antibodies against *Treponema pallidum*.

SAMPLE SIZE: 11 832.

RESULTS: Of the 11 832, 54 (0.45%) were confirmed as seropositive for syphilis. Thirty-three (61.1%) were non-Saudi; 21 (38.9%) were Saudis. Thirty (55.6%) cases were males. Twenty-two (40.74%) were married and 29 (53.70%) were unmarried. Of the 54 diagnosed as syphilis positive, 28 (51.9%) were expatriate workers screened for pre-employment. The percentage of syphilis among Saudis was 0.36%. In an overall chi-square analysis, a $P<.0001$ indicated a difference among nationalities in the frequency of syphilis. A post-hoc analysis showed that Somalians ($P=.004$) and Sudanese ($P=.005$) differed significantly from other nationalities.

CONCLUSION: The study showed that syphilis was low among the screened population. More than half of the syphilis positive cases in this study were household employees. Screening for syphilis assists in planning complementary services for target populations and improves syphilis control.

LIMITATIONS: Retrospective design. Hospital-based findings may not be representative of the seroprevalence of syphilis in the general population.

CONFLICT OF INTEREST: None.

Syphilis is a multistage, curable chronic disease caused by the spirochete *Treponema pallidum*, subspecies pallidum. This disease is usually acquired by sexual contact with infectious lesions, and from an infected mother to her fetus. Transmission via blood products and organ donation has also been reported.[1] Syphilis presents with distinct successive clinical stages from primary stage to the tertiary stage, with different signs and symptoms associated with each stage including a small painless ulcer that typically appears in the genitalia, generalized maculopapular rash and long-term neurological and cardiac diseases. If left untreated, syphilis may cause substantial morbidity and mortality in adults as well as in young children and infants through congenital syphilis.[2] Diagnostic testing for syphilis is performed on patients with signs or symptoms of infection. Screening for syphilis is required for patients at high risk of having acquired syphilis or at risk of transmitting the disease to others. Screening for syphilis is also part of the prenatal and donor screening routine. Screening is also conducted for HIV seropositive patients, sexually transmitted diseases (STDs) clinic attendees, expatriate workers during pre-employment screening, and for medical screening among new medical staff. Prompt diagnosis of syphilis cases and proper management can successfully decrease the transmission of ongoing syphilis and mitigate its morbidity.[3]

Syphilis continues to be a major public health concern globally.[4-6] Prevalence has varied significantly during the last century with an estimated 12 million new infections annually, and with more than 90% occurring in developing nations. The global impact target of the World Health Organization's (WHO) Global Health Sector Strategy on STIs 2016–2021 is to reduce incidence of syphilis by nearly 90% by the year 2030. Numerous countries have made a commitment to reduce the incidence of adult syphilis and to eliminate congenital syphilis,[7,8] but the progress toward these targets is hampered by limited comprehensive data on the prevalence of syphilis in many developing countries.[9] Data on syphilis in Saudi Arabia and other countries are scarce. The aim of this study was to analyse syphilis seropositivity among individuals screened for syphilis in a tertiary hospital in the Eastern Province of Saudi Arabia.

PATIENTS AND METHODS

This retrospective study was conducted at a tertiary hospital in Al Khobar city, in the Eastern Province of Saudi Arabia. The King Fahd Hospital of the University (KFHU) is a university teaching hospital that comprises more than 600 beds. The hospital serves the whole province, which has a population of about 5 million. The study included individuals who underwent screening for syphilis from January 2014 through December 2018. Data was obtained from the archived medical records at the hospital. Diagnostic testing for syphilis in our study was performed for clinically suspected patients, HIV seropositive patients, patients with STD, and as part of routine health screening for all newly arrived foreign residents, pregnant women and newborns, employment candidates, preoperative patients, and blood donors. Serum samples were screened for syphilis using the reverse syphilis screening algorithm (**Figure 1**). The specimens were screened by chemiluminescence immunoassay (CIA) ARCHITECT Syphilis TP (Abbott, Illinois, United States). The CIA non-reactive specimens were considered syphilis negative. The CIA-reactive specimens were tested by the rapid plasma reagin (RPR) test from IMMUTREP RPR (Omega Diagnostics, Alva, United Kingdom). When the RPR test result was "reactive", the sample was considered as syphilis positive, while in case of non-reactive RPR results, a confirmatory test was performed such as the treponemal-specific antibody test using INNO-LIA line immunoassay (Fujirebio Europe N.V., Ghent, Belgium).[10,11] The samples that were positive by both CIA assay and the confirmatory tests were considered as confirmed positive for syphilis.[12] The sensitivity and specificity of these assays vary with the disease stage and are described elsewere.[13,14] Compared to the traditional algorithm, the reverse testing algorithm for syphilis showed improved specificity and sensitivity and therefore was recommended by the Centers for Disease Control and Prevention (Atlanta, Georgia, United States) and the Association of Public Health Laboratories (Silver Spring, Maryland, United States) to be used in areas with low disease prevalence.

Results were tabulated, frequencies and proportions were calculated for qualitative data presentation. Statistical calculations were performed using the OpenEPI software version 3.01 (Emory University, Atlanta, Georgia, United States). The difference in syphilis seropositivity between nationalities was assessed by an overall chi-square test with the *P* value set at .05 and then by post-hoc analysis with a Bonferroni correction of the *P* value. The ethical approval for the study was obtained from the Institutional Review Board at Imam Abdulrahman Bin Faisal University (IRB number 2018-01-156).

RESULTS

Of 11832 individuals tested for syphilis, 6940 (58.6%) were females and about one third (31.4%) were married. Half of the study population was Saudis (49.4%) followed by Egyptians (11.3%), Filipinos (10.4%), then

Indians, Jordanians, Sudanese, Pakistani, Somalian, and others. The frequency of syphilis increased with increasing age (*P*=.0002) (**Table 1**).

Fifty-four individuals (0.45%) were syphilis positive by both screening and confirmatory tests. Out of these 54 diagnosed syphilis seropositive cases, 33 (33/5983, 0.55%) were expatriate workers screened for syphilis as part of a residency permit checkup, which is mandatory for all expatriates to obtain a residence permit. The remainder were screened for various other reasons, including blood donation and newborn screening. Among these 54 syphilis positive patients, 24 were females and 30 were males (**Table 1**). The males were significantly more likely to be syphilis positive (*P*=.037) (**Table 1**). Twenty-one individuals from the 54 (38.9%) were Saudis; single cases were from Palestine, Yemen, Pakistan, Tunisia, Chad and South Africa (others in **Table 1**).

Twenty-two individuals were married while 29 were unmarried with no statistically significant difference among them (**Table 1**). The median (IQR) age of the 54 seropositive patients was 29.3 (18.2) years, with a range from newborn to 65 years. Twenty-one Saudis (0.36%) were seropositive for syphilis (**Table 1**). The overall chi-square for the differences in seropositivity for all nationalities was 55.7 (df=7, P<.0001). After Bonferroni correction of the P value to .00625 (.05/8), the seropositive cases were significantly higher among Somalians (P=.004) and Sudanese (P=.005) than other nationalities combined (**Table 1**).

The agreement between treponemal (CIA and FTA) and non-treponemal (RPR) tests was almost perfect (% of agreement: 99.9% and Cohen's k: 0.89). The agreement between treponemal tests (CIA and RPR) was perfect (% of agreement: 100% and Cohen's k: 1).

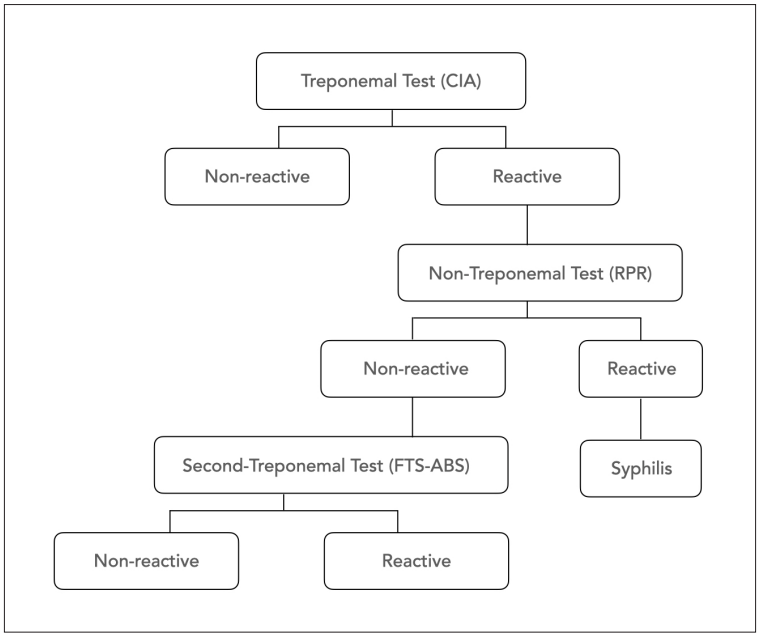

Figure 1. Reverse testing algorithm for syphilis screening. CIA: chemiluminescence immunoassay; RPR: rapid plasma reagin; FTA-ABS: fluorescent treponemal antibody absorption.

DISCUSSION

Syphilis continues to present challenges for global public health and is an additional challenge for diagnostic laboratories. Data on syphilis in Saudi Arabia is limited. This study revealed the seropositivity of syphilis among individuals screened for syphilis in KFHU over a five-year period using the reverse testing algorithm. The study also assessed the seropositivity pattern with age, sex, marital status and nationality.

The main finding of our study was the low seropositivity for syphilis (0.45%) among individuals screened at a tertiary hospital in the Eastern Province of Saudi Arabia. A slightly higher prevalence was reported in a national seroprevalence survey in 2015 in Saudi Arabia, which showed a prevalence of 0.55%.[15] Similarly a low prevalence was observed among blood donors and prenatal obstetric population in several other pulbications.[16-21] A high prevalence was reported in the first broad-based investigation in Saudi Arabia in 1986 and on a five-year surveillance study (1995 -1999) for STIs, in which the reported findings were 2.7% and 8.7%, respectively.[22-24] This indicates that the prevalence of syphilis in Saudi Arabia is declining over time. The explanation for the decline might be related to increased awareness, improvements in testing, and better management of cases. The WHO global estimates of syphilis prevalence in (2016) showed differences in prevalence among regions, where Eastern Mediterranean, European and African regions showed prevalence of 0.5%, 0.1%, and 1.7%, respectively.[25]

The seropositivity among Saudis in this study was 0.36% while among expatriates it was 0.55% with the highest rate among Somalians followed by Sudanese and Indians. This high rate of detection among Somalians might be inflated by the low number of individuals tested compared to other nationalities. A higher rate of seropositivity among certain nationalities was also observed in other studies. Hamdi and Ibrahim analyzed the prevalence of STDs in expatriate workers screened for pre-employment in Jeddah.[26] The syphilis seroprevalence in their study group showed that the highest rates among expatriates were from India 1.7%, Indonesia 0.78%, and the Philippines 0.44%. Aziz et al found that the prevalence of syphilis among 20 670 ex-

Table 1. Demographic data for all syphilis positive and negative individuals (n=11 833) over five years (January 2014-December 2018) in a tertiary hospital in the Eastern Province of Saudi Arabia.

Variable	N	Positive	(%)	Negative	(%)	*P* value	Odds ratio (95% CI)
Gender							
Female	6940	24	0.4	6916	99.6	.037	0.5 (0.32-0.96)
Male	4891	30	0.6	4861	99.4		
Age group (years)							
0-15	1602	6	0.4	1596	99.6		
16-30	6407	23	0.4	6384	99.6		
31-45	2968	14	0.5	2954	99.5	<.001[a]	12.8
46-60	664	4	0.6	660	99.4		
>60	153	7	4.6	146	95.4		
Nationality							
Saudi	5849	21	0.4	5828	99.6	.123	0.6 (0.37-1.12)
Sudan	575	8	1.4	567	98.6	.005	3.4 (1.51-7.10)
Philippines	1230	5	0.4	1225	99.6	.830	0.9 (0.31-2.10)
India	686	5	0.7	681	99.3	.293	1.7 (0.60-3.92)
Egypt	1342	3	0.2	1339	99.8	.171	0.5 (0.11-1.31)
Jordan	643	2	0.3	641	99.7	.631	0.7 (0.11-2.31)
Somalia	20	2	10.0	18	90.0	.004	25 (3.85-96.8)
Others	1487	8	0.5	1479	99.5		
Marital status							
Married	3595	22	0.6	3573	99.4		
Single	7839	29	0.4	7810	99.6	.080	1.6 (0.94-2.90)
Unknown	398	3	0.8	395	99.3		

[a]Chi-square for linear trend. Information about gender, age and marital status are missing in a few syphilis negative cases.

patriates in Sharjah (one of the United Arab Emirates) was 0.51% with the highest prevalence among expatriates from India (0.38%), Pakistan (0.88%), and Bangladesh (0.66%).[27] In our study, syphilis seropositivity was high among expatriates with variation among certain nationalities. A possible reason for the greater seropositivity of syphilis among the non-Saudi population could be the requirement of routine screening of non-Saudi workers for different infections as a pre-employment requirement. Differences in the demographics of the screened expatriate workers may explain the discrepancy in the seropositivity among certain nationalities.

Since our study population was from a tertiary hospital, our findings may not be representative of the seroprevalence of syphilis in the general population; nevertheless, it is a useful data on the assessment of syphilis in Saudi Arabia. Whether this study reflects a decline in the prevalence of syphilis in the general Saudi population compared to previous studies needs further investigation. Furthermore and despite the high specificity of the employed assays, the prevalence of syphilis in our study could be influenced by the standard error, which is increased when the disease prevalence is low.[28]

The findings of this study provide new information on the seropositivity of syphilis in the Eastern Province of Saudi Arabia. It provides an initial baseline for monitoring progress towards prevention and control of syphilis in Saudi Arabia. The low seropositivity of syphilis observed in this study could be interpreted as an indicator of improved programs for the prevention and management of syphilis. However, the observation that more than half of the syphilis positive cases were non-Saudi

emphasizes the importance of pre-employment screening for household expatriate employees, especially expatriates that come from countries where STDs are highly endemic. Finally, assessing syphilis prevalence assists in planning complementary services for target populations, and improves syphilis control.

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Author contribution

NHOW, KRK, and RA designed the study and obtained the ethical approval for the study. OEO, NA, and ZIS participated in clinical and laboratory data acquisition. AAE, NHOW, and KRA analysed and interpreted the data. ZIS and OEO wrote the introduction. NHOW, RA, and KRA wrote the materials and methods and the results. NA and AAE wrote the discussion. All authors critically revised the manuscript and agreed on the final version for publication.

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