Original article

Sero-epidemiology of Syphilis in a Tertiary Teaching Hospital in Kuala Lumpur

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Abstract

Background: Syphilis is common and resurgences predominantly occurs among men who have sex with men (MSM)**.** ***Objective:*** The aim of the study was to describe the epidemiology, clinical and serological aspects of patients with syphilis diagnosed at Universiti Kebangsaan Malaysia Medical Centre (UKMMC). ***Methods:*** A retrospective study was conducted whereby patients with serologically confirmed syphilis cases between January 2010 and December 2012 were included. The epidemiological and clinical data were gathered from the patient's progress note. ***Results:*** A total of 67 patients were selected in this research (41 males, 26 females). The mean age was 48.97 ± 17.45, where majority were from 20 to 39 years old (37.3%). Most patients were diagnosed at latent stage (65.7%). Identified risk factors for syphilis infection included sexual promiscuity either homosexual or heterosexual, intravenous drug user and partner diagnosed as syphilis. Penicillin is the antibiotic of choice for the treated cases. ***Conclusions:*** This study managed to provide an epidemiological and serological data of syphilis infection in our medical center where syphilis was diagnosed predominantly in male especially in young adults.

Keywords: Human Immunodeficiency Virus; rapid plasma regain; syphilis; syphilis IgG.

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Introduction

Syphilis is a systemic, chronic illness that affects the entire body and is caused by a spirochete *Treponema pallidum* subspecies *pallidum*[1].The causative agent is mainly transmitted via sexual contact although other modes of transmissions such as transplacental transmission, during delivery, from transfused blood and laboratory acquisition have been described[2]. Every year, the new cases of syphilis have been estimated to be around 12 million[1]. The clinical manifestations of syphilis are divided into several stages and progress from one stage to another if appropriate treatment is not provided to the patients. These clinical manifestations may be altered by HIV infection which include more than one chancre which are larger and deeper; concomitant primary and secondary syphilis at the time of presentation. Despite these minor differences, the progression is similar in those with or without HIV[3]. Serology test is currently the mainstay of laboratory diagnosis for syphilis as other diagnostic methods including molecular detection are not widely available.The serology test can be divided into two groups, which are the non-*Treponema pallidum* (non-TP) and the *Treponema pallidum* (TP) specific antibody tests[4]. First line of laboratory test is usually to perform non-

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TP tests that detect anti-cardiolipin antibodies such as rapid plasma reagin (RPR) and venereal diseases research laboratory (VDRL) tests. These tests are cheaper compared to treponemal antibody tests, but they detect a cardiolipin antigen that is also present in other conditions such as autoimmune diseases and malaria. Thus, they are a non-specific and might lead to a false positive result. Hence, confirmatory test by *Treponema pallidum* antibody detection is necessary. These tests are expensive, require a continuous supply of electricity, reagents and trained staff, and are rarely available outside of reference laboratories. The current communication is to describe the epidemiology and the serological profiles of patients diagnosed with syphilis in our hospital using the above tests.

Material and methods:

The study was conducted retrospectively where patients who were serologically confirmed to have syphilis by positive syphilis IgM or/and syphilis IgG from January 2010 until December 2012 were included in this study.

The epidemiology and clinical data were collected from the progress note of each patient. The information that were gathered consist of the basic epidemiological data (age, gender, race), underlying risk factor or risk behavior for syphilis acquisition, clinical symptoms and signs at the time of diagnosis, Human Immunodeficiency Virus (HIV) serology test result and treatment received by the patients. All these data were administered into the Statistical Package of Social Sciences (SPSS) for Windows Version 20 software for analysis.The epidemiological data were mainly described in frequency and percentages.

This study was approved by "The Research and Ethnic Committee of Universiti Kebangsaan Malaysia Medical Centre (FF- 2014-081)"

Results:

Baseline demographic data*:* A total of 67 serologically confirmed syphilis cases were included in this study. The mean age was 48.97 ± 17.45 years old, which ranged from 19 to 84 years. Majority of the patient were from the age group of 20 to 39 years (N=25 or 37.3%).The cases were more common in male contributing to more than half of the cases (N=41 or 61.2%).In addition, majority of patient were from ethnic group Malay (41.8%) followed by Chinese (31.3%), India (6.0%) and others (20.9%). The ethnics Malay, Chinese and Indian represent the three main ethnics in Malaysia. Other ethnic groups identified in this study comprises of Indonesian, Sikh, Pakistani and Burmese. The demographic data are shown in Table 1.

Table 1: Baseline characteristics of the study population

Number (N)=67		
Age (mean age ± SD)	48.97 ± 17.45	
	Frequency	**Percentage (%)**
1. Classification of age		
≤ 19 years	1	1.5
20-39 years	25	37.3
40-59 years	19	28.4
> 60 years	22	32.8
2. Gender		
Male	41	61.2
Female	26	38.8
3. Ethnicity		
Malay	28	41.8
Chinese	21	31.3
India	4	6
Others	14	20.9

Risk factors and clinical manifestations*:* Majority of the patients either were not aware of the information related to the mode of syphilis acquisition. As this is a retrospective study, the data regarding the mode of acquisition or the risk behavior were not stated in some of clinical notes. Among those that have the information, majority of them acquired syphilis sexually which included both homosexuality as well as heterosexual.In one case, syphilis was possibly acquired via parenteral transmission in which this patient was an intravenous drug user.

In terms of risk behavior twenty-five of the patients have identifiable risk behavior or risk factor and majority of them have sexual related risk-behavior either heterosexual or homosexual or both. Man who had sex with men (MSM) group contributed to 10.4% of the patients. Other risk factor included sexual partner who already diagnosed with syphilis and intravenous drug user.

Majority of the patients were asymptomatic at time of diagnosis (N=44), which represented as the latent stage of syphilis. Twenty-three patients (33.3%) were symptomatic. From those 23 symptomatic patients, 15 had more than one symptom at presentation. Three patients presented with chancre at time of diagnosis but were associated with other symptoms such as body rash, non-specific flu-like illness and therefore, they were classified as having overlapping primary and secondary syphilis. Four patients were diagnosed as having possible neurosyphilis thus were classified

as tertiary syphilis. The diagnosis of neurosyphilis was not confirmed by VDRL test on cerebrospinal fluid sample. The data regarding the risk factors and clinical manifestations are simplified Table 2.

Table 2: Risk factors and clinical manifestations

	Frequency	Percentage (%)
1. Mode of acquisition:		
Sexual	24	35.8
Parenteral	1	1.5
Unknown	42	62.7
2. Risk factors:		
Sexual promiscuity	15	
Homosexual (MSM)	7	
HIV infection	13	
Intravenous drug user (IVDU)	1	
Partner with syphilis	1	
3. Number of risk factors:		
No risk factor	42	62.7
1 risk factor	13	19.4
> 1 risk factors	12	17.9
4. Clinical manifestations:		
Asymptomatic	44	65.7
Symptomatic	23	33.3
Chancre	3	
Body rash	10	
Non-specific flu-like illness	10	
Lymphadenopathy	8	
Possible neurosyphilis/ uveitis	4	
5. Number of symptoms/ signs at diagnosis:		
1 symptom/sign	8	
>1 symptoms/signs	15	
6. Stage of syphilis at time of diagnosis:		
Primary	0	0
Secondary	16	23.9
Overlap primary & secondary	3	4.5
Latent	44	65.7
Tertiary	4	5.9

Laboratory data: At time of the diagnosis, 34 patients (50.7%) were detected to have low RPR titration (< 1:8), and 33 patients (49.3%) with high RPR titration (≥1:8). Of the 67 serologically confirmed syphilis cases, 53 (79.1%) were also screened for HIV infection in UKM Medical Centre. From this, 14 patients (26.4%) were HIV positive. Seven patients that engaged in MSM activity were all HIV positive. The laboratory data have been shown in Table 3.

Table 3: Laboratory data of the cases

	Frequency	Percentage
1. RPR titer detected at the time of diagnosis		
Low titer (<1:8)	34	50.7
High titer (≥1:8)	33	49.3
2. RPR titer distributions		
1:1	5	7.5
1:2	15	22.4
1:4	14	20.9
1:8	10	14.9
1:16	6	8.9
1:32	6	8.9
1:64	7	10.4
1:128	2	2.9
1:256	1	1.5
1:512	1	1.5
3. HIV serology test		
Done	53	79.1
Not done	14	20.9
4. HIV results (N=53)		
Positive	14	26.4
Negative	39	73.6

Treatment of syphilis: Data on syphilis treatment was available for only 37 patients (55.2%). The remaining 30 patients did not have documented treatment in UKMMC because the patients were already referred to the nearby health care facilities for treatment. All treated patients received penicillin except for one case, which received oral doxycycline 100mg. This patient was allergic to penicillin. Those who received penicillin, 34 of them were given via intramuscular route and the remaining two patients received penicillin via intravenous route.

Discussion

In this study, we found the cases of syphilis ranges from age 19 to 84 years with mean age of 48.97 and majority of the patients were male. We noticed that sexual transmission was the most important route of transmission. Most of the patients were asymptomatic thus corresponding to the latent syphilis being the predominant stage of syphilis in this study. Secondary syphilis was diagnosed as the main stage of syphilis among the symptomatic patients. RPR distribution ranges from 1:1 to 1:512 but in more than half of the patients, the titer was less than 1:8. HIV serology was positive in 26.4% of the patients tested for HIV,

and all homosexual patients were HIV positive. We noticed that the penicillin was the drug of choice for the treatment of syphilis either by intramuscular or intravenous routes.

In our study it was observed that syphilis predominantly diagnosed in male and young adults between ages 20 to 39 years with the mean age of 48.97. Various studies indicated the similar findings in which male and young adults population were the predominant group diagnosed with syphilis. The main age groups reported in the study were 17 to 46 years[5], 26 to 35 years[6], 30 to 39 years[7] and 20 to 39 years[8]. All these studies were also reported male as the predominant gender diagnosed with syphilis[5-8]. In one study, it was noted that among the female patients, the predominant age group was 25 to 29 years and 30 to 40 years while in male it was between 30 to 40 years[9]. However one study conducted in Kenya described that there was no different in term of syphilis prevalence in male and female[10].

With regard to the mode of acquisition, in majority of our patients, we could not identify them. Sexual route was perhaps the most common route of acquisition and it is generally known that syphilis is mainly transmitted by this route. Among the 41 male patients diagnosed with syphilis, 7 or 17.1% of them engaged with homosexual activity. Men who have sex with men population was reported to be the main factor contributing to recent increase in number of syphilis. The number of patients involved in homosexual activity has been reported with great diversity. The percentages were from as low as 12% to 86.8%[5,6,8,9]. A study in India reported those involved in homosexual activity were mainly between ages of 18 to 35 years[5]. In our study, we did not specifically analyse the age of the patients that engaged in this homosexuality.

Majority of our patients were asymptomatic at time of serological diagnosis thus corresponding to the latent stage as the predominant stage of syphilis diagnosed. Among those who were symptomatic, the predominant stage of syphilis was secondary syphilis. In Norway, it is believed that late latent syphilis probably contribute to the majority (> 50%) of the cases[8]. This finding was also supported by Muldoon et al., whereby 52.2% of their cases were asymptomatic[6]. However, there is another study that reported early syphilis as the predominant stage of syphilis whereby 83% of the patients presented with early syphilis, and 26.3% of them with genital chancre[9].Another study in India noted that the primary and secondary syphilis contributed to 68% of the cases where the primary syphilis represent majority of the cases[5].

Many studies have described syphilis and HIV co-infections. In this retrospective review, HIV serology was done for 53 patients (79.1%) where 14 patients (26.4%) were positive. Among these 14 patients, seven of them engaged in homosexual activity (50%). Data from Muldoon et al., described HIV positive in 28.7% of their syphilis patients and all except one of those HIV positive patients were MSM population[6].The review of the changing epidemiology of syphilis in United States also highlighted that the current syphilis epidemic has largely involved MSM population with the extreme male: female rate ratio is highly suggestive[11]. Similarly, the main feature of the re-emergence of syphilis in the United Kingdom has been the rapid increase in cases seen in MSM[12]. At the same time, there were high number of cases co-infected with syphilis suggested that epidemiology of syphilis has been influenced by HIV epidemics and behavioural change in MSM[12]. We previously described three cases of syphilis and HIV co-infections involving young male adults[13] and through this current communication perhaps syphilis and HIV co-infections should be described further in term of treatment and prognosis of the patients.

Conclusion:

In conclusion, this study provides an epidemiological review of syphilis in a tertiary centre in Kuala Lumpur. We noticed that our findings are similar to most of other studies whereby syphilis is commonly diagnosed in male and among young adult population.

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