Human Immunodeficiency Virus-infected men who have sex with men with syphilis: A 5-year multicentre study in Malaysia

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ABSTRACT

Objectives: High rates of syphilis have been reported worldwide among men who have sex with men (MSM). This study aims to describe the clinical pattern and treatment response of syphilis among human immunodeficiency virus (HIV)-infected MSM in Malaysia.

Methods: This is a retrospective study on all HIV-infected MSM with syphilis between 2011 and 2015. Data was collected from case notes in five centres namely Hospital Kuala Lumpur, Hospital Sultanah Bahiyah, Hospital Umum Sarawak, University of Malaya Medical Centre and Hospital Sungai Buloh.

Results: A total of 294 HIV seropositive MSM with the median age of 29 years (range 16-66) were confirmed to have syphilis. Nearly half (47.6%) were in the age group of 20-29 years. About a quarter (24.1%) was previously infected with syphilis. Eighty-three patients (28.2%) had other concomitant sexually transmitted infection with genital warts being the most frequently reported (17%). The number of patients with early and late syphilis in our cohort were almost equal. The median pre-treatment non-treponemal antibody titre (VDRL or RPR) for early syphilis (1:64) was significantly higher than for late syphilis (1:8) (p<0.0001). The median CD4 count and the number of patients with CD4 <200/µl in early syphilis were comparable to late syphilis. Nearly four-fifth (78.9%) received benzathine-penicillin only, 5.8% doxycycline, 1.4% C-penicillin, 1% procaine penicillin, and 12.4% a combination of the above medications. About 44% received treatment and were lost to follow-up. Among those who completed 1 -year follow-up after treatment, 72.3% responded to treatment (serological non-reactive – 18.2%, four-fold drop in titre – 10.9%; serofast – 43.6%), 8.5% failed treatment and 17% had re-infection. Excluding those who were re-infected, lost to follow-up and died, the rates of treatment failure were 12.1% and 8.8% for early and late syphilis respectively (p=0.582).

Conclusion: The most common stage of syphilis among MSM with HIV was latent syphilis. Overall, about 8.5% failed treatment at 1-year follow-up.

KEY WORDS:

Sexually transmitted infections, syphilis, men having sex with men (MSM), human immunodeficiency virus (HIV)

INTRODUCTION

According to the latest data of Joint United Nations Programme on HIV/AIDS (UNAIDS) from 160 countries, about 34.0 to 39.8 million people were living with HIV in 2016.[1] The main mode of transmission of human immunodeficiency virus (HIV) is through sexual contact. Key populations at increased risk of HIV infection include sex workers, people who inject drugs, transgenders, prisoners, gay men and other men who have sex with men (MSM).

In 2014, more than 90% of new HIV infections in central Asia, Europe, North America, the Middle East and North Africa were among people from key populations and their sexual partners.[1] Gay men and other MSM accounted for 49% of new HIV infections in western and central Europe and North America, 30% of new infections in Latin America, 18% of new infections in Asia and the Pacific.[1]

In many studies in developing countries in Asia, HIV is increasingly identified to be more prevalent among MSM. Acquisition of HIV infection through homosexual and bisexual routes now accounts for the majority of cases.[2-4] In Singapore, there has been an increasing trend for homosexuals and bisexuals accounting for newly diagnosed individuals with HIV, from 31.8% in 2005 to 51% in 2011.[2] In China, India, Taiwan and Thailand, the number of HIV among MSM is increasing steadily in recent years.[3,4]

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There are no published information on the MSM men in Malaysia. Most of them tend to hide their sexual identities due to social stigma and homophobia. Furthermore, same sex marriage is illegal in Malaysia. As a notifiable disease in Malaysia, the data on syphilis among HIV-infected MSM is regrettably lacking. Hence, we aim to describe the clinical pattern and the treatment response of syphilis in newly acquired HIV-infected MSM in Malaysia.

METHODS

Study design

This was a multicentre, retrospective study conducted between January 2011 and December 2015. The study population included male patients from Genitourinary Medicine (GUM) Clinic of Hospital Kuala Lumpur, Department of Dermatology and Infectious Disease Unit of Hospital Sultanah Bahiyah, Alor Setar Kedah, Department of Dermatology and Infectious Disease Unit of Hospital Sungai Buloh, Infectious Disease Unit and Division of Dermatology of University of Malaya Medical Centre, and Dermatology and Infectious Disease Unit of Hospital Umum Sarawak. These five centres have established GUM services. Data was retrieved from case notes of patients of the respective centres.

HIV-infected MSM patients with syphilis were included in this study if they were 12 years or older, reported to have penetrative oral or anal sex with another man, had reactive rapid plasma reagent (RPR) and a reactive result of *Treponema pallidum* haemagglutination assay (TPHA) or *T.pallidum* particle agglutination (TPPA) test. The study was registered with the Malaysian National Medical Research Register (NMRR) with the number of NMRR-17-459-34278 and was approved by the Malaysian Research Ethics Committee (MREC).

Definitions

According to the UNAIDS Action Framework, the term 'men who have sex with men' is used to describe those males who have sex with other males, regardless of whether or not they have sex with women or have a personal or social identity associated with that behaviour, such as being 'gay' or 'bisexual'.[5] Consistent use of condoms in the past six months is defined by the wearing of condoms at all times during all modes of sexual intercourse by all participants involved during the period mentioned.

Criteria for Diagnosis of syphilis

Serological diagnosis of syphilis included a positive non-specific serology with non-treponemal test rapid plasma reagin (RPR) test or venereal disease research laboratory (VDRL) test, together with a positive specific treponemal test TPHA/TPPA.[6]

The terms early syphilis include primary syphilis, secondary syphilis and early latent syphilis.[6] Late syphilis includes late latent syphilis, latent syphilis of unknown duration and tertiary syphilis.[6] Primary syphilis is a stage of infection with *T.pallidum* characterised by one or more ulcerative lesions (e.g., chancre), which might differ considerably in clinical appearance.[7] Secondary syphilis is a stage of infection caused by *T.pallidum* characterised by localised or diffuse mucocutaneous lesions (e.g., rash – such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalised lymphadenopathy.[7] Other symptoms can include mucous patches, condyloma lata, and alopecia.[7] The primary ulcerative lesion may still be present.[7]

Latent syphilis is asymptomatic, characterised by positive syphilis serology with no clinical manifestations. Early latent syphilis is a stage of infection caused by *T.pallidum* in which organisms persist in the body of the infected person without causing symptoms or signs when initial infection has occurred for less than two years.[8] Late latent will be considered when there is the presence of the disease for two years or more.[8] Latent syphilis of unknown duration is considered late syphilis.[8]

Tertiary syphilis clinically manifests after a period of 15–30 years of untreated infection.[7] Manifestations of neurosyphilis include syphilitic meningitis, meningovascular syphilis, optical involvement including interstitial keratitis and uveitis, general paresis, including dementia and tabes dorsalis.[7] Laboratory criteria for a diagnosis of neurosyphilis include a reactive VDRL in cerebrospinal fluid (CSF) via a lumbar puncture, and either a reactive treponemal serologic test for syphilis or a reactive nontreponemal serologic test for syphilis, and elevated CSF protein or leukocyte count (CSF protein >50mg/dL, >5 white blood cells/cubic millimetre CSF) in the absence of other known causes of these abnormalities.[7]

Inflammatory lesions of the cardiovascular system, e.g. aortitis, coronary vessel disease, aortic aneurysm, coronary stenosis, aortic insufficiency, rarely myocarditis may occur in tertiary syphilis. Tertiary syphilis with gummatous lesions of the skin may present as solitary or multiple benign, soft, rubbery tumorous lesions of varying sizes, which subsequently ulcerate and healed with pigmented scars and pits on the surface. Osteitis may be a manifestation of tertiary syphilis in the bone.

Diagnosis of Human Immunodeficiency Virus (HIV)

HIV serology was determined by using enzyme-linked immunosorbent assay (ELISA) and confirmed by HIV-1/2 using western blot assay.

Treatment of syphilis

In this study patients were treated with benzathine penicillin G, oral doxycycline, crystalline penicillin, procaine penicillin G and ceftriaxone based on different treatment guidelines adopted by the managing clinicians with modifications according to clinical situations.

Syphilis treatment response

A diagnosis of syphilis reinfection can be established if a patient had either (a) a ≥ four-fold increase in RPR titre or (b) a positive RPR test, following successful antibiotic treatment that was confirmed by a four-fold decline in RPR titre or loss of RPR seroreactivity.[9] Syphilis *serological zcure* is defined as a four-fold decrease in RPR titre by one-year post-treatment, or seroreversion to non-reactive result after treatment.[10,11] Syphilis *serofast* is defined as a persistently positive low titre of RPR 1:8 or less by one year post-treatment, after initial four-fold decline.[10,11] Serological non-response is defined by less than four-fold decline in non-treponemal antibody titres at ≥ six months after treatment for early

Table I: Demography of 294 HIV seropositive MSM with syphilis

Characteristics		n=294
Age in years, Median (range)		29 (16–66, IQR 11)
Age group in years, n (%)	<20	10 (3.4%)
	20-29	140 (47.6%)
	30-39	95 (32.3%)
	40-49	37 (12.6%)
	50-59	10 (3.4%)
	60-69	2 (0.7%)
Ethnicity, n (%)	Malay	165 (56.7%)
	Chinese	100 (34.0%)
	Indian	9 (3.1%)
	Bumiputra (Iban, Bidayuh, Bajau, Melanau)	18 (6.1%)
	Foreigner (Philippines & Indonesian)	2 (0.7%)
Number with documented substance abuse, n (%)		25 (8.5%)
Number of bisexual, n (%)		75 (25.5%)
Type of partners, n (%)	Casual	164 (55.8%)
	Steady	96 (32.7%)
	Commercial	16 (5.4%)
Number of patients with 2 or more partners in the past 6 months, n (%)		164 (55.8%)
Number with documented consistent use of condom in the past 6 months, n (%)		39 (13.3%)
Number with previous history of sexually transmitted infections, n (%)		111 (37.8%)
Type of previous sexually transmitted infection (STI), n (%)	Syphilis	71 (24.1%)
	Gonorrhoea	26 (8.8%)
	Genital warts	19 (6.5%)
	Herpes genitalis	18 (6.1%)
	Hepatitis B	8 (2.7%)
	Non-gonococcal urethritis	4 (1.4%)
	Chlamydia	0 (0%)
Number with other concomitant STI, n (%)		83 (28.2%)
Concomitant STI apart from syphilis, n (%)	Genital warts	50 (17.0%)
	Herpes genitalis	24 (8.2%)
	Gonorrhoea	12 (4.1%)
	Hepatitis B	10 (3.4%)
	Chlamydia	3 (1.0%)
	Non-gonococcal urethritis	4 (1.4%)
CD4 count, Median (range)		334 (2–998)

Table II: Characteristics of Syphilis in 294 HIV-infected MSM

Characteristics			n=294	p
Type of syphilis	Early syphilis (n=149)	Primary	8 (2.7%)	0.861*
		Secondary	83 (28.2%)	
		Early Latent	58 (19.7%)	
	Late syphilis (n=145)	Late latent	65 (22.1%)	
		Latent of unknown duration	72 (24.5%)	
		Tertiary	8 (2.7%)	
Median Pre-treatment VDRL/RPR titer (range)	Early syphilis		1:64 (0-1:2048)	<0.0001
	Late syphilis		1:8 (1:1-1:1024)	
Median CD4 count (range), cell/µl	Early syphilis		341 (2-998)	0.315
	Late syphilis		312 (3-978)	
Number of patients with CD4 < 200/µl (%)	Early syphilis		30 (20.1%)	0.402
	Late syphilis		36 (24.3%)	
Type of treatment, n (%)	Early syphilis	Benzathine penicillin	131 (87.9%)	-
		Doxycycline	41 (27.5%)	
		Crystalline penicillin	2 (1.3%)	
		Procaine penicillin G	3 (2.0%)	
	Late syphilis	Benzathine penicillin	135 (95.7%)	
		Doxycycline	11 (7.8%)	
		Crystalline penicillin	3 (2.1%)	
		Procaine penicillin G	1 (0.7%)	
		Ceftriaxone	1 (0.7%)	

*early syphilis vs late syphilis

Table III: The treatment outcomes with serological responses at one year after treatment

Treatment outcome with serological response		Early syphilis n=149	Late syphilis n=145	Total n=294	p
Responded to treatment	4-fold drop at 1 year	8	10	18 (6.1%)	0.80
	Serology non-reactive	15	15	30 (10.2%)	0.84
	Serofast (1:8 or less)	35	37	72 (24.5%)	1.00
Fail treatment		8	6	14 (4.8%)	0.78
Four-fold drop at 6 months but re-infected		17	11	28 (9.5%)	0.32
Treated and Defaulted	Defaulted right after treatment	36	46	82 (27.9%)	0.04
	Treated with 4-fold drop at 6 months & defaulted	23	14	37 (12.5%)	0.12
	Treated with NO 4-fold drop at 6 months & defaulted	7	3	10 (3.4%)	0.33
Died before completed treatment		0	3	3 (1.0%)	0.12

Table IV: The characteristics and treatment outcome of syphilis among HIV-infected MSM reported in other countries

Author, year	Country	n	% MSM	Early syphilis (%)			Late syphilis (%)			% responded to treatment at 1 year
				Primary	Secondary	Early latent	Late latent	Latent of unknown duration	Tertiary	
Manavi et al, 2007 [15]	UK	129	82	31	21	-	-	-	-	70
				48 undetermined stage						
Jinno et al, 2013 [14]	US	560	96.7	14	26	60	-	-	-	90.9
Tsai et al, 2014 [13]	Taiwan	349	94.9	8.9	55.3	35.8	-	-	-	67.8
Yang et al, 2014 [34]	Taiwan	573	94.1	8.9	57.8	33.3	-	-	-	70.9
Nishijima et al, 2016 [44]	Japan	112	100	62	unspecified	4	18	-	-	-
Current study 2017	Malaysia	294	100	2.7	28.2	19.7	22.1	24.5	8	Early syphilis - 87.9 Overall - 89.6

UK – United Kingdom; US – United State of America; MSM – Men having sex with men

months following treatment of late latent syphilis.[11] Treatment failure is defined as clinical symptoms or signs that persist or recur as a result of inadequate treatment, or an initially high VDRL/RPR titre (1:16 or more) which failed to decrease four-fold by one-year, or a sustained four-fold rise in VDRL/RPR titre in the absence of reinfection.[6,10,11]

Statistical analysis

Descriptive statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS 19.0, IBM, USA). The normally distributed continuous variables are summarised in mean while the non-normally distributed are expressed as median. For categorical variables, frequencies and percentages (%) were tabulated. The significance level was set at $p<0.05$.

RESULTS

A total of 294 HIV-seropositive MSM with syphilis were included in this study. The median age was 29 years (range 16-66, IQR 11). Nearly half (47.6%) were in the age group of 20-29 years. Majority (62.6%) had previous history of sexually transmitted infections (STI), and about a quarter was previously infected with syphilis (24.1%). More than half (55.8%) had multiple sexual partners. Three-quarters of the patients were homosexual (74.5%) while the others were bisexual (25.5%). Only a minority of patients had documented substance abuse (8.5%). There was only 13.3% of patients reported consistent use of condoms in the past six months. Eighty-three patients (28.2%) had other concomitant sexually transmitted infection with genital warts being the most frequently reported (17%). The median CD4 count was 334/μL (range 2-998). The demography results are as shown in Table I.

Sixty-six (22.4%) had CD4 less than 200/μL. Two-third of the patients (66.3%) had latent syphilis; 28.2% secondary syphilis, 2.7% each for primary syphilis and tertiary syphilis. We further analysed the data based on early syphilis and late syphilis. The numbers of early and late syphilis in our cohort were almost equal (149 vs 145 respectively). As shown in Table II, the median pre-treatment non-treponemal antibody titre (VDRL or RPR) for early syphilis (1:64) was significantly higher than the late syphilis (1:8), $p<0.001$. The median CD4 counts and the number of patients with CD4 <200/μl in early syphilis were comparable to late syphilis (341/μl vs. 312/μl, $p=0.315$).

Nearly four-fifth (78.9%) received benzathine penicillin G as the only treatment regime, 5.8% had doxycycline, 1.4% C-penicillin, 1% procaine penicillin, and in 12.4% a combination of the above medications. Among the patients with early syphilis, 80 (53.7%) had 3 doses while 20 (13.4%) had 1 dose of benzathine penicillin G 2.4MU. Late latent syphilis was the most frequent (68 out of 145; 46.9%) type of late syphilis encountered in this cohort and benzathine penicillin G remained the preferred treatment option in late syphilis (n=135; 93.1%). For those with late syphilis, 119 (82.1%) had 3 doses while only 3 (2.1%) had 1 dose of benzathine

penicillin G 2.4MU. Among the 3 patients with late syphilis who received only a dose of benzathine penicillin G 2.4MU, one was lost to follow-up after a dose of benzathine penicillin, one was changed to doxycycline for 28 days, and another one was changed to intravenous crystalline penicillin for 2 weeks. Among those who received re-treatment with benzathine penicillin G (25 in early syphilis and 20 in late syphilis), most were retreated with 3 doses (12 in early syphilis [48.0%]; 12 in late syphilis [60.0%]) compared to 1 dose (7 in early syphilis [28.0%]; 4 in late syphilis [20.0%]). Intravenous penicillin was used only in 4 patients (2.8%) with late syphilis.

About 43.9% lost to the scheduled follow-up despite receiving treatment as shown in Table III. Among those who completed 1-year follow-up after treatment, 72.3% responded to treatment (serological non-reactive – 18.2%, four-fold drop in titre – 10.9%; serofast – 43.6%), 8.5% failed treatment and 17% had re-infection.

DISCUSSION

High rates of syphilis have been reported worldwide among MSM. In a cross-sectional survey targeting MSM in 61 cities in China, the prevalence of HIV-syphilis co-infection was 12.5%.[12] In Taiwan, a multicentre, retrospective study among HIV-infected patients with early syphilis in 9 hospitals showed 94.9% were MSM.[13] In the United States of America (USA), a retrospective review of all early syphilis in HIV-infected patients in two large urban clinics demonstrated that 96% were MSM.[14] Another study in three genitourinary medicine clinics in the United Kingdom (UK) showed that 35% of patients with syphilis were HIV-infected and of these 63.5% were MSM.[15] A study in Germany reported that HIV-syphilis co-infection was 27.1% among HIV-positive MSM.[16]

Syphilis and HIV co-infection has been labelled as a dangerous duo.[17,18] Syphilis enhances the risk of contracting HIV infection and HIV may alter the natural course of syphilis.[19] The incidence of syphilis among HIV-infected persons was 77 times greater than that of the general populations.[20] Co-infections between HIV and other sexually transmitted infections (STI) are common due to shared routes of sexual transmission. Syphilis presents with ulcers and is associated with HIV acquisition.[21] *T.pallidum* co-infection increases viral load of HIV and decreases CD4 count in HIV-infected person.[22,23] HIV infection may also increase clinical lesions and accelerate progression of syphilitic infection.[24] HIV was also described to be associated with a higher rate of asymptomatic primary syphilis or more aggressive disease manifestations in early syphilis.[25] Neurosyphilis may occur more frequently, at a much earlier stage and progress more rapidly in the presence of HIV infection.[26,27] Treatment failure is noted to be higher and serological cure has been shown to be slower in HIV-infected patients with syphilis.[28-30]

The burden of syphilis among MSM is known to be high worldwide. Data from the National Notifiable Diseases Surveillance System (NNDSS) of USA showed that the proportion of male primary and secondary syphilis cases attributed to MSM increased from 77.0% in 2009 to 83.9% in 2012.[31] Increasing incidences of syphilis were observed among MSM of all ages and ethnicities from all regions.[31] According to surveillance report of STI in Europe by the European Centre for Disease Prevention and Control (ECDC), about 42% of all syphilis cases were reported among MSM in 2011.[32]

To date there is no registry to tabulate the prevalence of STIs among MSM with HIV in Malaysia. Our study is probably one of the early studies in Malaysia which focused on syphilis in this group of patients. The clinical characteristics and treatment outcome of syphilis among HIV-infected MSM have been described in a few studies as shown in Table IV. Most papers reported only early syphilis and data on the treatment outcome of late syphilis is limited. The treatment and the response rates of early syphilis in our cohort were comparable to other studies. A significant proportion of patients in our study failed to follow up after treatment. This is a common problem reported from other centres. In a study in the UK, failure to attend post-treatment follow-up appointments was documented in 22% of HIV-infected patients.[15] Another audit of 40 consecutive patients with early syphilis in Newcastle, Australia showed that 42.5% failed to attend any post-treatment serological tests, 42.5% attended the first appointment and only 32.5% attended 12-month follow-up.[33] A 5-year study of HIV-infected patients with syphilis in Los Angeles, USA showed that 6.18% patients were lost to follow-up.[14] In Taiwan, a 5-year study among HIV-infected patients with syphilis revealed as many as 57 out of 1128 patients were lost to follow-up the second day after treatment.[34]

The greatest challenge is to convince the patients to stay in contact with our medical services. Otherwise, these STI will not be treated adequately and they put others at risk. An effective lost to follow-up strategy needs to be established to ensure patients adhere to the treatment plan. This strategy has been described well by Rayment et al., which include confirmation of complete contact details of patients and those of their primary care provider at each clinic visit, reminders before appointments, and active recall by phone calls, text messages, e-mails and letters to the registered home address after a non-attendance at a scheduled appointment.[35] The involved healthcare professionals may pay home visits to the patients who defaulted follow-up if possible.[35] Good communication with other health care providers like inclusion of primary care physicians into all recall correspondence, and regular monitoring details of non-attendance are important too.[35]

In our study, management differences were observed among the clinicians for early syphilis in HIV-infected patients. According to the 2006 US CDC treatment guidelines for syphilis, three doses of weekly 2.4MU benzathine penicillin G were recommended for HIV-infected patients with early syphilis.[36] However, a randomised control trial conducted before the introduction of combination antiretroviral therapy (cART) demonstrated no difference in treatment response between HIV-infected and HIV-uninfected patients treated with a single dose of 2.4MU benzathine penicillin G.[37] Therefore, a single dose of 2.4MU benzathine penicillin G for early syphilis has been recommended in the most recent

guidelines in the UK, USA and Europe.[9,37,38] The latest guideline by 2010 Centers for Disease Control and Prevention (CDC) STD Treatment Guidelines recommended treatment of early syphilis with a single dose of 2.4MU benzathine penicillin G.[38] However, differences in the management continue to exist among infectious diseases specialists as to the appropriate dose of benzathine penicillin G to be administered in the management of early syphilis in HIV-infected patients.[39] Several studies have shown that HIV-infected patients with syphilis demonstrated higher failure rates after 1-dose of benzathine penicillin G,[28,34] while other studies have not.[14,15] These inconsistencies can be attributed to various limitations of the studies. We were unable to analyse the serologic failure rates in patients who received 1 dose versus 3 doses of benzathine penicillin G due to the high defaulter rate post treatment. In Malaysia, the decision to treat early syphilis with 1 or 3 doses of benzathine penicillin G is the choice of the managing clinicians, with the latter being favoured. This preference could be due to their fear of treatment failure in this special group of patients with just a dose of benzathine penicillin.

In our study, 5.8% of patients received doxycycline. Doxycycline is recommended as an alternative treatment of syphilis in patients with allergy or intolerance to penicillin. Due to a high number of patients who were lost to follow-up, we were unable to assess the success rate of using doxycycline as compared to penicillin in treating syphilis in HIV-infected MSM. Not many studies were done to compare the serological response of doxycycline versus benzathine penicillin G in treatment of syphilis among HIV-infected patients. A multicentred study among HIV-infected patients with early syphilis in Taiwan showed that the serological response of patients treated with benzathine penicillin G appeared to be higher when compared to doxycycline at 6 months (72.3% vs 63.4%, p=0.075) and at 12 months of treatment (68.3% vs 65.9%, p=0.681). Nevertheless, the differences were not statistically significant.[13]

A systematic review of 20 studies had revealed that the median proportion of serological non-response patients was 20.5% at 6 months, which decreased to 11.1% at 12 months or later.[11] Interestingly, the effect of HIV status on the rate of serological cure was inconsistent in this systemic review. A slower rate of decline in VDRL/RPR titre after treatment was nevertheless observed among HIV infected patients in two studies.[14,15] Manavi et al., observed that 70% of HIV-infected patients with syphilis were successfully treated after 12 months, and the rate reached 82% at 24 months after treatment.[15] Data from another study in the USA suggested that a proportion of HIV-infected patients may need longer than a 12-month period to show a four-fold decrease in their VDRL titre following treatment.[14] Treated patients who were followed up for more than 24 months had higher probability for successful treatment.[15] Perhaps a different set of definition for the serological responses in this group of patients is needed to guide the managing clinicians.

Future prospective studies are vital to describe the effect of highly active antiretroviral therapy (HAART) on the clinical course and treatment outcome of syphilis in HIV-infected MSM. Ghanem et al., observed that the use of HAART may reduce syphilis serologic failure in HIV-infected patients with syphilis.[40] On the contrary Farhi et al. concluded that the serologic response to syphilis treatment was minimal or absent in patients who received HAART.[41] A study by Rekart et al. has hypothesised that substantial increase in syphilis incidence primarily affecting HIV-positive MSM may be linked to HAART.[42] There was a 235% increase in syphilis and a much smaller increase in chlamydia (56.9%) and gonorrhoea (42.1%). Their research suggested that the depletion of CD4+ memory T-cells in HIV-infected patients have enhanced their susceptibility to syphilis reinfection. In addition, an upregulation of CCR5 receptors by treponemal lipoproteins may boost the susceptibility of monocytes to HIV infection, further weakening immune responses to *T.pallidum*. As a result, it was advocated that HAART must be combined with frequent monitoring for syphilis infection. However, Tuddenham et al., noted that the increase in syphilis rates compared with other STIs may reflect inadequate screening, with over 90% of extra-genital infections are asymptomatic.[43]

CONCLUSIONS

The most common stage of syphilis among MSM with HIV in our study was latent syphilis. We found that 8.5% failed treatment at 1-year follow-up. Treatments centres should step up measures taken to reduce the number of patients lost to follow-up. Future research efforts should concentrate on determining the most effective treatment regime for syphilis among MSM with HIV and to increase clinical and serological follow-up among this group of patients.

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