SHORT REPORT

Clinical factors associated with syphilis concordance in men in sexual partnerships: a cross-sectional couples study

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ABSTRACT

Background Syphilis infections continue to increase among men who have sex with men (MSM) in many countries, with rates often higher among HIV-positive MSM. There is limited understanding of the risk and determinants of syphilis transmission between men. We aimed to examine the concordance of early syphilis infection between male sexual partners and clinical factors associated with transmission.

Methods Men attending Melbourne Sexual Health Centre with their male partners, where at least one was diagnosed with early syphilis, were identified from linkage of partner records between March 2011 and April 2016. Early latent syphilis was defined as a new asymptomatic syphilis presentation of less than 2 years' duration. Associations between concordance and potential risk factors were examined using Fisher's exact test.

Results Among 43 couples (86 men) identified, there were 13 couples (26 men) where both were diagnosed with early syphilis, representing a concordance rate of 30.2% (95% CI 17.2% to 46.1%). Among the 13 concordant couples, 5 men had primary syphilis (4 penile, 1 anal), 11 secondary syphilis (8 generalised rash, 3 penile, 2 anal, 1 oral lesion) and 10 early latent infections. Concordance was higher among couples where at least one partner had secondary syphilis compared with couples where neither partner had secondary syphilis (53% (9/17) vs 15% (4/26), P=0.016). Furthermore, concordance was higher among couples where one was HIV positive compared with couples where both were HIV negative (62% (5/8) vs 23% (8/35), P=0.042).

Conclusions There was an overall concordance rate of 30%. Higher concordance rates for early syphilis infection between male sexual partners were associated with HIV and secondary syphilis.

BACKGROUND

Syphilis remains a major public health problem among men who have sex with men (MSM). Syphilis rates in MSM are in many cases higher among HIV-positive men, who have disproportionately accounted for repeat syphilis infections.[1] Untreated syphilis infection can lead to serious morbidity and increased HIV risk.

There are limited data on the risk of syphilis transmission between men or factors that influence transmission. Most studies on syphilis transmission are more than three decades old.[2–5] Only one study, from 1983, specifically examined syphilis among male partners of men.[6] In this study, 76 index men with primary or secondary syphilis had 98 male sexual contacts, with 48 (49%) of contacts diagnosed with early syphilis. No data on factors associated with transmission were presented.[6]

The aim of this study was to determine the concordance of early infectious syphilis between men within sexual partnerships and clinical factors associated with this.

METHODS

Study setting

This was a retrospective study of routinely collected clinical data from the Melbourne Sexual Health Centre between March 2011 and April 2016. The centre consists of a walk-in STI clinic and an outpatient HIV clinic. All asymptomatic MSM were routinely screened for syphilis. MSM who presented with symptoms suggestive of syphilis were serologically tested for syphilis and those with mucocutaneous lesions routinely had a swab for *Treponema pallidum* PCR (Tp PCR) collected. In the outpatient HIV service, syphilis serology was performed as part of routine HIV monitoring. Patients attending the clinic completed a computer-assisted self-interview (CASI) asking whether their partner had attended on the same day, enabling partners to be identified.

Case definition

Men within sexual partnerships were identified using CASI. Male partners were those who attended the clinic together either on their day of syphilis testing, or on the day of syphilis treatment. Couples were included in the study if one or both partners were diagnosed with early infectious syphilis.

A review of medical records was performed to identify the clinical characteristics and pathology results. All syphilis infections were confirmed serologically as early syphilis: either *T. pallidum* seroconversion within 24 months or, in the case of a syphilis reinfection, a fourfold increase in rapid

plasma reagin (RPR) titre. Some men with lesions had concurrent positive Tp PCR; however, all were also serologically confirmed cases. Two sexual health physicians (JMT and ID) independently reviewed each record to confirm the stage of syphilis infection. Men were classified as having primary, secondary or early latent syphilis. Staging was according to the Australian Public Health Laboratory Networks syphilis case classifications.[7] In Australia, early latent syphilis is defined as a new asymptomatic syphilis presentation of less than 2 years' duration. The duration of early latent syphilis infections was determined from the medical records. Couples were classified as having either concordant or discordant syphilis infection.

Laboratory methods

Serological and Tp PCR testing was performed by the Victorian Infectious Diseases Reference Laboratory. Prior to January 2016, all sera were tested with RPR (Becton Dickinson), *T. pallidum* particle agglutination (TPPA) assay (Fujirebio) and a recombinant total antibody ELISA immunoassay (EIA) (Trepanostika EIA, BioMerieux). Sera were also tested for *T. pallidum* IgM with whole-cell lysate IgM EIA (Mercia) until December 2011 when the assay was discontinued, and replaced with the Bio-Rad Syphilis IgM EIA. From January 2016, the BioMerieux EIA was replaced with a LIASON Treponema screen (DiaSorin), an automated chemiluminescence immunoassay (CLIA). Due to improved sensitivity of the laboratory syphilis testing algorithm with the CLIA assay, the RPR, TPPA and IgM assays were then only performed if sera were screened positive on the CLIA assay or there was a contemporaneously positive Tp PCR result. The Tp PCR assay used was one targeting the *pol*A gene.[8]

Statistical analysis

Clinical characteristics and laboratory results for each couple were compared between the concordant and discordant couples to identify factors associated with transmission. These included: anatomical site and type of lesions (oral or anogenital lesions or generalised rash), HIV status, RPR titre, PCR result, stage of infection and whether infection was a first or reinfection. As data on sexual behaviour were not systematically collected, no behavioural associations were investigated. Associations between concordance and potential factors were examined using Fisher's exact test. Due to the small sample size, multivariate regression analysis was not undertaken. SPSS V.22 was used for statistical analyses. This paper was checked against the Reporting of Studies Conducted Using Observational Routinely Collected Health Data guidelines.

RESULTS

During the study period, 43 couples (86 men) were identified where at least one partner was diagnosed with early syphilis. This included 30 couples (60 men) with discordant results and 13 couples (26 men) where both were infected with syphilis, representing a concordance rate of 30% (95% CI 17% to 46%).

Of the 56 cases of syphilis, there were 10 (18%) men with primary syphilis, 19 (34%) men with secondary syphilis and 27 (48%) men with early latent syphilis. Of the men diagnosed with early latent syphilis, 18 (67%) were of less than 1 year's duration based on previous negative syphilis serology. The clinical characteristics and laboratory results of all men with syphilis are shown in online supplementary table 1.

There were 13 men with a history of previous syphilis infection, 11 of whom had serological evidence of syphilis reinfection: all had a fourfold rise in RPR titre on parallel testing.

Table 1 Characteristics and laboratory results for male sexual couples concordantly infected with early syphilis

Couple number	Partner number	HIV status	RPR	EIA IgM	Tp PCR	Stage	Symptoms
1	1	–	32	Reactive		EL	
1	2	+	32	Not done		EL	
2	1	–	16	Non-reactive	+	P	Penile ulcers
2	2	–	64	Non-reactive		S	Palmar rash
3	1	–	64	Reactive	+	P	Penile ulcers
3	2	–	4	Non-reactive		EL	
4	1	–	4	Reactive	–	P	Penile ulcers
4	2	–	4	Reactive	+	P	Anal lesion
5	1	–	0	Not done	+	P	Penile ulcers
5	2	–	64	Reactive		S	Generalised rash, penile lesions
6	1	–	16	Reactive		S	Generalised rash
6	2	–	0	Not done		EL	
7	1	–	16	Non-reactive		EL	
7	2	+	128	Reactive		EL	
8	1	–	64	Non-reactive	+	EL	
8	2	+	128	Non-reactive		EL	
9	1	–	32	Reactive		S	Generalised rash
9	2	–	8	Equivocal		EL	
10	1	+	32	Reactive		S	Generalised rash
10	2	–	0	Not done		EL	
11	1	–	128	Reactive		S	Generalised rash
11	2	–	128	Reactive		S	Alopecia
12	1	–	64	Reactive	–	S	Generalised rash
12	2	–	16	Reactive		EL	
13	1	–	32	Reactive	+	S	Anal condyloma, generalised rash
13	2	+	16	Reactive	+	S	Anal condyloma, penile ulcers

EIA IgM, ELISA immunoassay IgM; EL, early latent syphilis; P, primary syphilis; RPR, rapid plasma reagin; S, secondary syphilis; Tp PCR, *Treponema pallidum* PCR.

Eight of the 86 men (9%) were HIV positive. A contemporaneous CD4 count was known for seven men. The median CD4 count was 525 and 6 men had an HIV viral load of <100 copies/mL on antiretroviral therapy. Seven of the eight HIV-positive men were diagnosed with syphilis, including three with secondary syphilis and four with early latent syphilis. There were no couples where both partners were HIV positive.

Among the 13 concordant couples (26 men), 5 men had primary syphilis, 11 secondary syphilis and 10 early latent infection. The characteristics and laboratory results for couples concordantly infected are shown in table 1.

Concordance was higher among couples where at least one partner had secondary syphilis compared with couples where neither had secondary syphilis (53% (9/17) vs 15% (4/26), P=0.016). Five of the eight HIV-positive men were in syphilis concordant relationships, and three in discordant relationships. Concordance was higher among couples where one was HIV

positive compared with couples where both were HIV negative (62% (5/8) vs 23% (8/35), P=0.042).

DISCUSSION

In this study of male sexual partners, the concordance rate for syphilis infection within partnerships where at least one man had early syphilis was 30%. Concordance between male sexual partners was more likely when at least one partner had secondary syphilis, or when one partner was HIV positive. To our knowledge, this is the only study to identify factors associated with a greater likelihood of concordance between men. There is only one other study published that estimates infection rates between men within sexual partnerships.[6] This previous study also did not include index cases with early latent syphilis as we have.

There are a number of limitations to this retrospective study. Sample size was limited to 43 couples. We were unable to determine the number or types of specific sexual acts that took place between sexual partners or duration of sexual relationships. The direction of transmission could not be determined. Furthermore, we could not determine when transmission occurred or exclude infection of either man from a third person. Concordance may be biased upwards if men were more likely to attend the clinic because of symptoms.

The precise mechanism of syphilis transmission between MSM is not fully understood. *T. pallidum* can be identified in primary and secondary lesions but transmission is also believed to occur during early, asymptomatic infection. In one study, 40% of HIV-positive MSM with syphilis had oral *T. pallidum* detected without lesions, which supports the potential oral transmission of syphilis.[9] That secondary syphilis was associated with a greater likelihood of syphilis concordance in our study supports the hypothesis that secondary syphilis is a relatively contagious stage, notwithstanding the limitations discussed above.

The association of syphilis concordance with HIV positivity in our study could have resulted from bias associated with HIV-positive MSM being over-represented among syphilis infections. But hypothetically, immune suppression associated with HIV could predispose to greater forward syphilis transmission and/or risk for acquisition. Impaired immune responses and clearance of *T. pallidum* have been shown in HIV-positive individuals.[10] While HIV positivity was associated with a higher syphilis concordance, because of limited numbers, we could not determine which factors explained this observation. Further research is required to clarify the precise routes of transmission of syphilis between men and the role of asymptomatic treponemal shedding. Such information would help inform biomedical and other interventions aimed at curtailing the syphilis epidemic among MSM.

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