A CASE-CONTROL STUDY OF OCULAR SYPHILIS IN BRITISH COLUMBIA, CANADA, 2010-2018

BC Centre for Disease Control
An agency of the Provincial Health Services Authority

THE UNIVERSITY OF BRITISH COLUMBIA

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Background

- The incidence of syphilis has been increasing worldwide in the last 20 years, and has disproportionately impacted those living with HIV. Alongside this increase, several jurisdictions have reported increasing incidence of ocular syphilis (OS).
- If untreated or treatment is delayed, OS can lead to permanent blindness
- We sought to characterize OS cases in British Columbia (BC), Canada, and identify associated factors.

Methods

- We compared OS cases to syphilis controls (1:4 ratio) diagnosed in BC between 01/2010 – 03/2018.
- 'Ocular syphilis' was defined according to the definition utilized by the US Centers for Disease Control (CDC): clinical signs or symptoms consistent with ocular disease in a person with laboratory-confirmed syphilis of any stage.
- Cases and controls were matched on age, sex, and date of syphilis diagnosis. Data were extracted via chart review of the provincial STI surveillance database.
- Potential risk factors were entered into the logistic regression model, where the dependent variable was OS. Variables were included in the final multivariable logistic regression model if significant at the 0.05 level.

Results

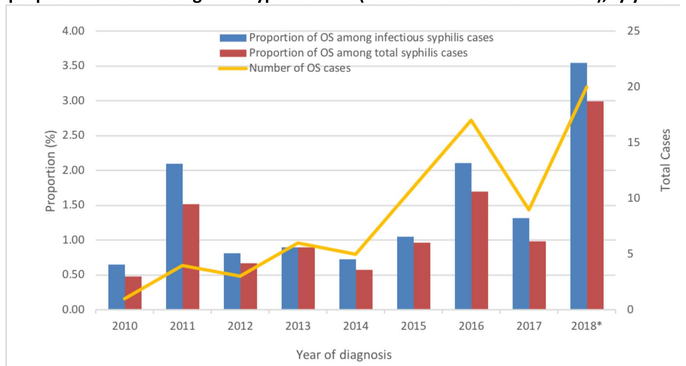
- 5681 syphilis cases were diagnosed in BC during the study period, where 61 (1.1%) had OS. **Figure 1** outlines the number of primary, secondary, and early late staged OS cases (n=55) as proportion among all infectious syphilis cases (n=4165) by year, and the total number of OS cases (n=61) among total syphilis cases (n=5681), by year. The proportion of syphilis cases with ocular involvement increased significantly from 0.48% in 2010 to 2.99% in 2018 (P=0.04). **Table 1** outlines demographic and clinical characteristics of the study population. Median age of OS cases was 47 years and 88.5% of cases were male, among whom 55.7% identified as men who have sex with men. The most common ophthalmologic diagnoses in cases were panuveitis (44.3%), optic neuritis (19.1%), and retinitis (18.3%). More than half of cases (50.8%) were HIV-positive at the time of syphilis diagnosis, compared to 25.8% of controls (P<0.001). Among HIV-positive individuals, 42.9% of cases had a suppressed viral load, compared to 79.7% of controls (P=<0.001). Cases also had higher HIV viral loads (P=0.011) and lower CD4 counts (P=0.014) than HIV-positive controls. Unadjusted and multivariable logistic modeling analysis findings are shown in **Table 2**. Infectious syphilis stages and HIV co-infection were statistically significantly associated with OS.

Table 1: Demographic and Clinical Characteristics of Population

Characteristic	N (%)		
	Cases N=61 (%)	Controls N=244 (%)	P value
Age, years (median (IQR))	47 (37-59)	47.5 (36-57)	0.753
Gender			
• Male	54 (88.52)	216 (88.52)	1.000
• Female	7 (11.48)	28 (11.48)	
Sexual Orientation			
• MSM	34 (55.74)	133 (54.51)	0.953
• Heterosexual (Male)	14 (22.95)	51 (20.90)	
• Heterosexual (Female)	6 (9.84)	27 (11.07)	
• Bisexual	1 (1.64)	7 (2.87)	
• Unknown	6 (9.84)	26 (10.66)	
Stage of Syphilis Infection			<0.001*
• Primary/Secondary	24 (39.34)	63 (25.82)	<0.001*
• Early latent	31 (50.82)	96 (39.34)	0.001*
• Late latent	6 (10.17)	83 (34.02)	Ref
Previous Syphilis Infection			0.4235
• Yes	5 (8.47)	28 (11.52)	
• No	54 (91.53)	215 (88.48)	
• Unknown	2 (3.28)	1 (0.40)	
HIV Serostatus			<0.001*
• HIV-positive	31 (50.82)	62 (25.83)	
• HIV-negative	30 (49.18)	178 (74.17)	
• Test not done	0 (0.00)	4 (0.16)	
HIV Viral Load (copies/mL)			<0.001*
• <50	12 (42.86)	47 (79.66)	
• 50-999	1 (3.57)	4 (6.78)	
• 1000-100000	11 (39.29)	6 (10.17)	
• >100000	4 (14.29)	2 (3.38)	
CD4 Count (cells/mm^3)			0.014*
• median (IQR)	470 (320-630)	615 (430-815)	
RPR Titre			<0.001*
• <1:8	5 (8.20)	118 (48.36)	Ref
• 1:8-1:32	2 (3.28)	62 (25.41)	0.682
• >1:32	54 (88.52)	64 (26.23)	<0.001*

*statistical significance

Figure 1: Number of OS cases, proportion of OS among infectious syphilis cases, and proportion of OS among total syphilis cases (infectious and non-infectious),by year



*2018 number of cases represents a projection, as data collection was only until March 2018. .

Table 2: Multivariable modeling of factors associated with ocular syphilis

Variable	Unadjusted analysis			Multivariable analysis		
	Odds ratio (OR)	95% CI	p-value	Adjusted odds ratio (aOR)	95% CI	p-value
Stage of Syphilis Infection			<0.001*			
• Primary/Secondary	5.67	2.16- 14.9	<0.001*	4.06	1.52-10.8	0.005
• Early latent	5.13	1.95-13.5	0.001*	3.71	1.39-9.95	0.009
• Late latent	Ref	-	Ref	Ref	-	Ref
HIV Serostatus						
• HIV-positive	3.35	1.79-6.30	<0.001*	2.49	1.27- 4.88	0.008
• HIV-negative	Ref	-	Ref	Ref	-	Ref
HIV Viral Load (copies/ml)**						
• Suppressed (<50)	7.51	1.59-35.51	0.011*	--	--	--
• Not Suppressed (50+)	Ref	-	Ref			
Syphilis reinfection						
• Yes	0.67	0.24-1.85	0.424	--	--	--
• No	Ref	-	Ref			
RPR Titre**			<0.001*			
• <1:8	Ref	-	Ref	--	--	--
• 1:8-1:32	0.70	0.02-2.30	0.682			
• >1:32	24.3	7.92- 74.63	<0.001*			

*Statistical significance. **Variables were not included in multivariable analysis due to interaction and multicollinearity.

Conclusion

- OS incidence increased over the study period, both in absolute numbers and as a proportion of all syphilis cases, a finding consistent with other jurisdictions.
- In this study, OS was associated with positive HIV status and infectious syphilis stage.
- These findings help predict those at risk, and highlight the importance of vigilance for OS, particularly those in the early stages of syphilis and those living with HIV, to avoid diagnostic and treatment delays.

Conflicts of interest: None declared.

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