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LETTER

Prevalence of COVID-19 infection in TB clinics in Kampala, Uganda

Dear Editor,

Global TB control has been hampered by the COVID-19 pandemic.[1–3] In 2020–2021, attendance at TB clinics dropped by over 50% during intense COVID-19 waves in Kampala, Uganda. Minimal data exist on SARS-CoV-2 prevalence among those who attended TB clinics at this time. Such information would improve our understanding of the vulnerability of TB clinic attendees to COVID-19, including transmission risks in this healthcare environment. Early differentiation between pulmonary TB and SARS-CoV-2 infection is difficult: they cause similar clinical syndromes[1,4] and have overlapping severity factors.[5,6] COVID-19 may increase susceptibility to TB and worsen disease progression. Reciprocally, TB is associated with an increased risk of mortality or delayed recovery among COVID-19 patients.[6,7] Numerous studies have described TB and SARS-CoV-2 coinfection.[8,9] Both diseases are transmitted by respiratory aerosols and droplets, increasing the cross-infection risk when patients with symptoms compatible with either diagnosis attend the same facility.

Here, we describe a cross-sectional study investigating the prevalence of current or prior SARS-CoV-2 infection among patients attending four high-volume TB treatment centres in Kampala from June to September 2021. The recruitment period coincided with the peak of the Delta variant wave (9,852 cases/week) of the COVID-19 pandemic in Uganda,[10] and a 42-day national lockdown starting on 7 June 2021 (when movement was restricted, including public and private transport). Sequential consenting patients aged ≥18 years attending TB clinics either for investigation of clinical TB symptoms (presumptive TB) or to continue existing TB treatment (established TB) were included. Sociodemographic and clinical characteristics were recorded using structured questionnaires. Nasopharyngeal swabs were collected to assess current SARS-CoV-2 infection using polymerase chain reaction (PCR) testing on the Abbott m2000 platform (Abbott, Chicago, IL, USA). Venous blood samples were collected for antibody tests to assess previous infection using Elecsys® Anti-SARS-CoV-2 spike (S) and nucleocapsid (N) assays (Roche Diagnostics, Basel, Switzerland), which had US Food & Drug Administration authorisation for emergency use. For all presumptive TB participants who could expectorate sputum, an Xpert® MTB/RIF Ultra (Cepheid, Sunnyvale, CA, USA) assay was performed. Participant characteristics were summarised using counts and percentages. Relationships between these characteristics and nasopharyngeal PCR results were examined through binary logistic regression analysis with results expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs). Modified Poisson regression analysis was preferred to investigate factors associated with positive SARS-CoV-2 antibodies due to the high prevalence (more than 10%) of COVID-19 antibodies among participants, with results expressed as prevalence ratios (PRs) and 95% CIs. Analyses were performed using Stata v14.0 (Stata, College Station, TX, USA). Ethical approvals were obtained from Mulago Hospital (Kampala, Uganda), the Uganda National Council of Science and Technology (UNCST; Kampala, Uganda), and the School of Medicine at the University of St Andrews (St Andrews, Scotland, UK).

We enrolled 342 participants across four facilities: 123 (36.0%) at the Infectious Disease Institute (Makerere University, Kampala, Uganda), 73 (21.3%) at Mulago National Referral Hospital (Makerere University, Kampala, Uganda), 70 (20.5%) at Kawaala Health Centre (Kampala, Uganda) and 76 (22%) at Kisenyi Health Centre (Kampala, Uganda); 220 (64.3%) were presumptive TB patients and 122 (35.7%) were established TB patients. Demographic and clinical characteristics are summarised in Supplementary Table S1. Of 342 participants, 180 (52.6%) participants were female; 177 (51.8%) were HIV-positive. Other comorbidities were uncommon: diabetes mellitus in 13 (3.8%) and hypertension in 29 (8.5%). Of 341 participants, 33 (9.7%) had positive nasopharyngeal swabs for SARS-CoV-2 PCR. HIV status was the only baseline covariate associated with a positive PCR result on multivariate logistic regression analysis (OR 2.65, 95% CI 1.08–6.51) (Table). The symptom profile of patients with positive PCR tests was similar to those with negative tests (Supplementary Table S2). Among the presumptive TB cases, 23/220 (10.5%) had positive nasopharyngeal SARS-CoV-2 PCR tests, 19/198 (9.6%) had positive sputum Xpert results, and one patient was positive for both. Of 122 confirmed TB patients, 10 (8.2%) had positive SARS-CoV-2 PCR results, giving a total of 11/342 (3.2%) with

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Table Factors associated with a positive SARS CoV-2 PCR or antibody test

Demographic and clinical factors	SARS CoV-2 PCR result*				SARS CoV-2 antibody test†			
	Positive ($n = 33$) *n* (%)	Negative ($n = 308$) *n* (%)	UOR (95%CI)	aOR (95% CI)	Positive ($n = 296$) *n* (%)	Negative ($n = 42$) *n* (%)	UPR (95%CI)	aPR (95% CI)
Sex								
Female	17 (51.5)	162 (52.6)	Reference		154 (52.0)	25 (59.5)		
Male	16 (48.5)	146 (47.4)	1.04 (0.51–2.14)		142 (48.0)	17 (40.5)		
Age, years								
18–29	5 (15.2)	94 (30.5)	Reference	Reference	89 (30.1)	10 (23.8)		
30–39	13 (39.4)	108 (35.1)	2.26 (0.78–6.58)	1.55 (0.51–4.75)	104 (35.1)	15 (35.7)		
≥40	15 (45.4)	106 (34.4)	2.66 (0.93–7.60)	1.59 (0.51–4.97)	103 (34.8)	17 (40.5)		
Smoking								
No	32 (97.0)	287 (93.2)	Reference		280 (94.6)	39 (92.9)		
Yes	1 (3.0)	21 (6.8)	0.43 (0.06–3.26)		16 (5.4)	3 (7.1)		
Drink/alcohol								
No	30 (90.9)	254 (82.5)	Reference		248 (83.8)	35 (83.3)		
Yes	3 (9.1)	54 (17.5)	0.47 (0.14–1.60)		48 (16.2)	7 (16.7)		
TB category								
Presumed‡	23 (69.7)	196 (63.6)	Reference		194 (65.5)	24 (57.1)	Reference	
Confirmed§	10 (30.3)	112 (36.4)	0.76 (0.35–1.66)		102 (34.5)	18 (42.9)	0.96 (0.87–10.4)	
HIV								
Negative	8 (25.0)	155 (50.5)	Reference		145 (49.3)	16 (38.1)	Reference	
Positive	24 (75.0)	152 (49.5)	3.06 (1.33–7.02)¶	2.65 (1.08–6.51)¶	149 (50.7)	26 (61.9)	0.85 (0.87–1.02)	
Diabetes mellitus								
No	30 (90.9)	298 (96.8)	Reference		286 (96.6)	39 (92.9)	Reference	
Yes	3 (9.1)	10 (3.2)	2.98 (0.78–11.42)		10 (3.4)	3 (7.1)	0.87 (0.65–1.18)	
Hypertension								
No	28 (84.8)	284 (92.2)	Reference		273 (92.2)	36 (85.7)	Reference	
Yes	5 (15.2)	24 (7.8)	2.11 (0.75–5.97)		23 (7.8)	6 (14.3)	0.90 (0.74–1.09)	
Possible COVID-19 contact								
No	19 (57.6)	207 (67.7)	Reference		189 (64.3)	35 (83.3)	Reference	Reference
Yes	14 (42.4)	99 (32.3)	1.54 (0.74–3.20)		105 (35.7)	7 (16.7)	1.11 (1.03–1.20)¶	1.12 (1.04–1.20)¶
Confirmed COVID-19 contact								
No	28 (84.8)	268 (87.0)	Reference		258 (87.2)	37 (88.1)	1	
Yes	5 (15.2)	40 (13.0)	1.20 (0.44–3.28)		38 (12.8)	5 (11.9)	1.01 (0.90–1.14)	

* 1 patient with missing SARS CoV-2 PCR result.
† 4 patients with missing SARS CoV-2 antibody result.
‡ Recent household contact with COVID-19 symptoms, but no PCR result for SARS-CoV-2.
§ Recent household contact with known positive SARS-CoV-2 PCR result test.
¶ Indicates significance at $P < 0.05$.
PCR = polymerase chain reaction; UOR = univariate odds ratio; CI = confidence interval; aOR = adjusted OR; UPR = univariate prevalence ratio; aPR = adjusted PR.

concurrent SARS-CoV-2 infection and active TB. Positive SARS-CoV-2 serology was detected in 296/338 (87.6%) participants; 226 (67.5%) were positive for both anti-S and anti-N antibodies, 68 (20.1%) were only anti-S-positive, and 2 (0.6%) were only anti-N-positive. At the time of sampling, 16 (4.7%) participants had received at least one dose of the COVID-19 (ChAdOx1-S) vaccine. The vaccinated participants were all positive for anti-S antibodies, with 14/16 (87.5%) also positive for anti-N antibodies. Exposure to a recent COVID-19 contact was associated with having a positive antibody test on multivariate analysis (adjusted PR 1.12, 95% CI 1.04–1.20; see the Table).

Overall, our reported prevalence of current SARS-CoV-2 infection (9.7%) among TB clinic attenders in Kampala is similar to the contemporaneous national prevalence of 8.8%.[10] Demographic and clinical characteristics were non-discriminatory between patients with positive SARS-CoV-2 or TB tests, but rapid SARS-CoV-2 diagnostics were not routinely available at TB clinics. More robust diagnostic infrastructure, preferably using point-of-care tests, is required at TB care facilities during respiratory infection outbreaks to facilitate appropriate patient triage for treatment and infection control. SARS-CoV-2 seroprevalence of 87.6% among our TB clinic attenders is strikingly higher than contemporaneous East African seroprevalence reports.[11–13] A national serosurvey conducted in Uganda 1 year earlier found 20.3% of the population to be positive.[14] Blood donor surveillance studies in Kenya in 2020 and 2021 described rising seroprevalence from 4.3% to 48.5%.[12,13] African pooled seroprevalence was estimated at 65% in late 2021.[11] Our seroprevalence considerably exceeds all of these reports. To the best of our knowledge, serological data, specifically among TB clinic attenders, have never previously been described and our findings underscore the likelihood of higher vulnerability in this group. High SARS-CoV-2 seroprevalence among TB clinic attenders may reflect overlapping host, viral and social risk

factors for respiratory infections. Although ChAdOx1-S vaccine can also cause anti-S positivity, less than 5% of this population was vaccinated. Seropositivity for both or anti-N only indicates previous SARS-CoV-2 infection. In other settings, anti-S positivity only may reflect COVID-19 vaccination. However, our study preceded widespread vaccine availability in Uganda. As anti-N titres in blood wane more quickly than anti-S,[15,16] the longer half-life of anti-S antibodies after viral exposure was the likeliest explanation for our patients who were anti-S-positive only.

This is the first report on the specific burden of COVID-19 among TB clinic attenders in an urban African setting during a period of high SARS-CoV-2 transmission. Study participants had respiratory symptoms, and the high seroprevalence depicts past or current infection. This emphasises that, with common clinical features and risk factors, simultaneous evaluation for both TB and COVID-19 is essential during pandemics. These findings highlight the need for prioritised interventions for this group, including accelerated access to rapid diagnostic tests and vaccinations for future SARS-CoV-2 variants and other respiratory pathogens.

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