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SARS-CoV-2 Seropositivity among Pre-Pandemic Specimens from Pregnant Women using Four Serologic Assays – Zambia, 2017-2018

Mpanji Siwingwa[1], **Jonas Z. Hines[2]**, Sombo Fwoloshi[1,3], Samuel Yingst[2], Peter A. Minchella[2], Adam Wolkon[2], Gershom Chongwe[4], Simon Agolory[2], Lloyd B. Mulenga[3]

[1]University Teaching Hospital, Lusaka, Zambia; [2]U.S. Centers for Disease Control and Prevention, Lusaka, Zambia; [3]Ministry of Health, Lusaka, Zambia; [4]Tropical Diseases Research Centre, Ndola, Zambia

BACKGROUND

Serologic assays that provide reliable indication of prior SARS-CoV-2 infection are needed to accurately measure prior exposure. However, several countries in Africa have reported lower-than-expected specificity, potentially related to assay cross-reactivity with other non-coronavirus pathogens such as *Plasmodium spp*. We used four SARS-CoV-2 serologic assays to assess positivity in archived serum specimens collected in Zambia prior to the Covid-19 pandemic and explored seropositivity associations with participant characteristics and HIV and syphilis infection.

METHODS

- SARS-CoV-2 antibody seropositivity was measured using serum specimens collected from pregnant women aged 15-49 years enrolled in an HIV and syphilis sentinel surveillance study in 26 sites across Zambia during 2017-2018
- Of 9,508 participants with archived specimens, 1,500 (16%) were selected using stratified random sampling by study site
- SARS-CoV-2 antibody seroprevalence was measured using the Euroimmun spike IgG enzyme-linked immunosorbent assay (ELISA), Wantai pan-Ig ELISA, Panbio IgM/IgG lateral flow assay (LFA), and Lyher IgM/IgG LFA
- HIV infection was measured with Alere Determine and Uni-Gold HIV tests and syphilis was measured with Alere Determine and Rapid Plasma Reagin syphilis tests
- We reported concordance between serologic tests (i.e., when both tests were negative or both tests were positive)
- We compared age group and HIV and syphilis status with SARS-CoV-2 antibody seropositivity using chi-square test.

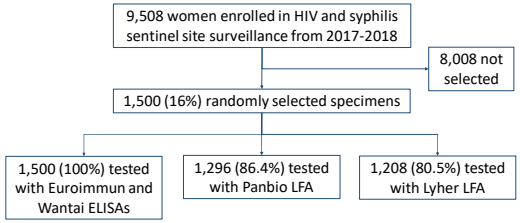


Figure 1. Study flow diagram of women attending antenatal clinic in 2017-2018 tested with four SARS-CoV-2 serologic assays — Zambia

SARS-CoV-2 antibody seropositivity on four assays ranged from 1.5% to 14.2% among women attending antenatal clinic in 2017-2018

RESULTS

- Among the 1,500 female participants, all (100%) were tested with Euroimmun and Wantai ELISAs, 1,296 (86.4%) were tested with Panbio LFA, and 1,208 (80.5%) were tested with Lyher LFA (Figure 1)
- Median participant age was 25 years (interquartile range: 21-30 years)
- HIV and syphilis prevalence were 14.9% and 5.6%, respectively
- Overall, 25.5% of participants were positive on at least one SARS-CoV-2 antibody assay
- SARS-CoV-2 antibody seropositivity was 5.5% on the Euroimmun ELISA, 1.5% on the Wantai ELISA, 13.7% on the Panbio LFA, and 14.2% on the Lyher LFA (Table)
- Concordance of positive results between the four assays was low (Figure 2)
- Associations with geographic location (i.e., province) were noted with all assays except Wantai ELISA (Table); Lusaka and Southern Provinces had low seropositivity with all assays
- With the Lyher LFA, younger persons had higher seropositivity and persons living with HIV had lower seropositivity

Table . Associations of demographic characteristics and HIV/syphilis status with seropositivity on four SARS-CoV-2 serologic assays among women attending antenatal clinic in 2017-2018 — Zambia

	Euroimmun, n (%) (N = 1,500)	Wantai, n (%) (N = 1,500)	Panbio, n (%) (N = 1,296)	Lyher, n (%) (N = 1,208)	Any assay, n (%) (N = 1,500)
Age group					
15-24 years	40 (5.7)	9 (1.3)	91 (15.1)	**98 (17.1)**	195 (27.9)
25-34 years	30 (4.9)	9 (1.5)	69 (12.9)	**58 (12.0)**	143 (23.2)
≥35 years	13 (7.0)	4 (2.2)	18 (11.2)	**16 (10.7)**	45 (24.3)
Province					
Central	**47 (27.3)**	2 (1.2)	**27 (15.7)**	**12 (21.1)**	**74 (43.0)**
Copperbelt	**2 (1.5)**	2 (1.5)	**29 (21.6)**	**36 (26.5)**	**53 (39.0)**
Eastern	**0 (0.0)**	1 (0.8)	**6 (10.2)**	**11 (18.3)**	**18 (15.1)**
Luapula	**4 (2.4)**	4 (2.4)	**37 (21.9)**	**53 (31.2)**	**73 (42.9)**
Lusaka	**3 (1.2)**	3 (1.2)	**7 (3.9)**	**8 (4.1)**	**20 (7.8)**
Muchinga	**3 (2.4)**	2 (1.6)	**26 (21.7)**	**26 (21.1)**	**47 (38.2)**
North Western	**4 (2.3)**	6 (3.4)	**33 (18.8)**	**14 (8.0)**	**52 (29.5)**
Northern	**5 (4.4)**	0 (0.0)	**7 (6.2)**	**8 (7.1)**	**19 (16.8)**
Southern	**0 (0.0)**	2 (1.7)	**5 (8.6)**	**4 (6.6)**	**11 (9.2)**
Western	**15 (12.8)**	0 (0.0)	**1 (0.9)**	**0 (0.0)**	**16 (13.7)**
Urban					
Urban	**55 (7.1)**	11 (1.4)	**74 (10.3)**	**63 (11.5)**	**177 (22.7)**
Rural	**28 (3.9)**	11 (1.5)	**104 (18.1)**	**109 (16.5)**	**206 (28.6)**
Parity					
1	24 (6.1)	**0 (0.0)**	46 (13.2)	41 (13.1)	93 (23.6)
2	21 (5.8)	**9 (2.5)**	41 (12.6)	52 (18.8)	103 (28.3)
3	14 (5.2)	**6 (2.2)**	36 (16.1)	27 (12.3)	70 (25.9)
≥4	23 (4.9)	**7 (1.5)**	55 (14.0)	52 (13.2)	116 (24.9)
Missing	1 (14.3)	**0 (0.0)**	0 (0.0)	0 (0.0)	0 (0.0)
HIV status					
Positive	15 (6.7)	3 (1.3)	19 (9.5)	**14 (8.4)**	48 (21.5)
Negative	68 (5.4)	19 (1.5)	159 (14.5)	**158 (15.3)**	335 (26.4)
Syphilis status					
Positive	4 (4.8)	2 (2.4)	12 (15.4)	13 (18.6)	23 (27.4)
Negative	79 (5.6)	20 (1.4)	166 (13.6)	159 (14.1)	360 (25.6)
Total	83 (5.5)	22 (1.5)	178 (13.7)	172 (14.2)	383 (25.5)

Bolded cells are p<0.05

a)

Euroimmun	100%			
Wantai	0.1%	100%		
Panbio	0.4%	0.2%	100%	
Lyher	0.3%	0.1%	6.1%	100%
	Euroimmun	Wantai	Panbio	Lyher

b)

Euroimmun	100%			
Wantai	92.7%	100%		
Panbio	79.4%	85.0%	100%	
Lyher	82.8%	84.3%	75.4%	100%
	Euroimmun	Wantai	Panbio	Lyher

Positive concordance calculated as the proportion of specimens positive for SARS-CoV-2 antibodies on both assays. Negative concordance calculated as the proportion of specimens negative for SARS-CoV-2 antibodies on both assays. Discordant results not shown

Figure 2. Positive (a) and negative (b) concordance of four SARS-CoV-2 serologic assays among women attending antenatal clinic in 2017-2018 — Zambia*

CONCLUSIONS

- Four SARS-CoV-2 serologic assays showed antibody positivity in pre-pandemic specimens, possibly indicating cross-reactivity with antibodies to other antigens in Zambia
- Lyher, Panbio, and Euroimmun assays yielded more false positives than would be expected based on manufacturer-reported specificities
- Although there was no clear pattern of association between SARS-CoV-2 antibody seropositivity with HIV or syphilis status, testing for other pathogens might provide information about the identities of cross-reacting antibodies with these assays
- The low seropositivity on all assays in Lusaka and Southern Province is notable since these are the low malaria burden provinces in Zambia
- Assessing for virus neutralizing capability of cross-reacting antibodies in SARS-Cov-2 antibody positive specimens could provide information about possible pre-existing SARS-CoV-2 immunity

ADDITIONAL INFORMATION

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Author Contact: Jonas Z. Hines (jhines1@cdc.gov)