Seroprevalence of ancestral and Beta SARS-CoV-2 antibodies in Malagasy blood donors

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We recently described that, during the first wave of the COVID-19 epidemic in early 2020, the seroprevalence of anti-SARS-CoV-2 IgG antibodies among blood donors in Antananarivo, Madagascar, sharply increased from 0·0% to 43·5% (95% CI 43·3–43·8).[1] This sudden increase was associated with what seems to have been sufficient population immunisation to dramatically slow down virus circulation; a reproducible pattern found in all five investigated regions of the country and five major cities,[1] including the capital city of Antananarivo with 1 275 207 residents.[2]

High seroprevalence (in 255 [44·9%] of 568 people) was also described in Manaus, Brazil, in late 2020; however, it was not sufficient to avoid a second epidemic wave in January, 2021, due to circulation of the P.1 (Gamma) variant, which eludes the human immune response to the ancestral variant that was prevalent earlier in 2020.[3] Similar immune evasion of B.1.351 (also known as the Beta variant of concern) was also described in South Africa and has led to a major second wave.[4] Similar to these two countries, high seroprevalence was not sufficient to prevent Madagascar from having a second major peak in early 2021. Introductions of Beta in the country were first detected in early February, 2021 (GISAID accession IDs EPI_ISL_1660263, _1660266, _1660268, _1660270, _1660272-75, _1660278-79, _1660283-84 and _1660286-290), but the degree to which this variant contributed to the last epidemic wave remains unclear.

In 2020–21, we continuously monitored natural immunisation of the population of Antananarivo by sampling the city's blood donors from the Regional Blood Transfusion Centre in Antananarivo, as previously described[1] (from Oct 1, 2020, to May 26, 2021; mean of 421·9 samples per month, 3375 total samples; appendix p 3). The serum samples were analysed at the Infectious Diseases Immunology Unit of the Pasteur Institute of Madagascar, for antibodies against the SARS-CoV-2 nucleocapsid (N) protein, spike receptor binding domain (RBD),

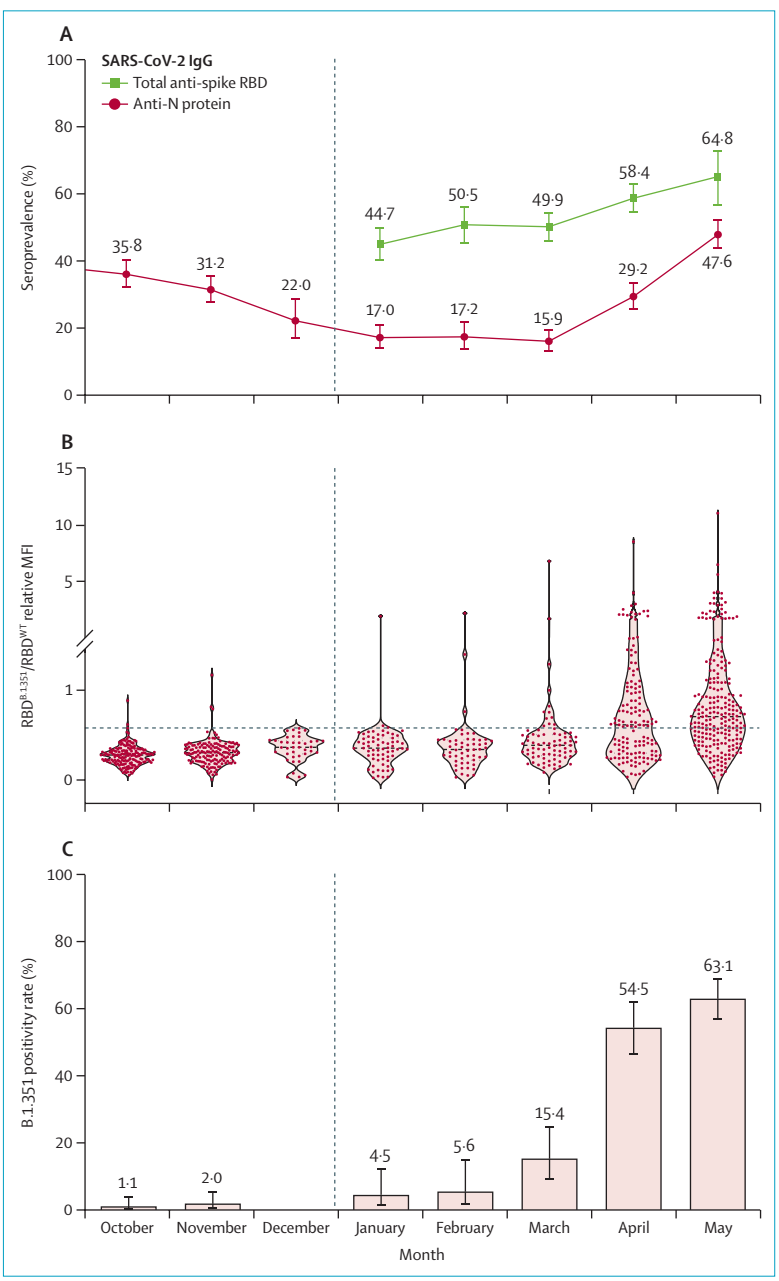

Figure: **Blood donor monthly anti-SARS-CoV-2 IgG seropositivity and Beta positivity rates in seropositive samples**

(A) Anti-N protein IgG and anti-spike RBD total Ig seroprevalences. (B) Anti-spike RBD^{Beta} to anti-spike RBD^{WT} MFI ratio among samples positive for anti-N protein IgG. (C) Beta positivity rate, as the rate of samples for which the RBD^{Beta} to RBD^{WT} MFI ratio was greater than a prespecified threshold that was based on samples from October, 2020 (when Beta variant was first identified; appendix pp 2–3). Error bars indicate 95% CIs. N=nucleocapsid. RBD=receptor binding domain. WT=wild-type. MFI=mean fluorescence intensity.

See Online for appendix

and Beta spike RBD (specific to RBDs containing mutations of Beta; appendix pp 1–2). Anti-N protein IgG seroprevalences reached their lowest point (since the summer of 2020) in March, 2021 (15·9% seropositive [95% CI 12·9–19·4], n=497), then sharply increased to a peak (47·6% [43·3–52·0], n=500) in May, 2021. Seroprevalence for total anti-spike RBD antibodies (IgA, IgG, and IgM), which are known to be more persistent,[5] increased from 49·9% (45·5–54·3) seropositivity to 64·8% (56·1–72·6) during the same period (figure A, appendix p 3).

To determine the proportion of infections caused by Beta among blood donors with seropositivity for anti-N protein IgG, we monitored the capacity of seropositive blood donor samples to bind either the ancestral RBD or the same subunit comprising three specific mutations found in Beta (appendix p 2), and used this information to define the proportion of individuals who had seroconverted due to infection with Beta. Increasing affinities for the Beta spike RBD were found in 2021 samples (figure B). The proportion of Beta-induced seropositivities increased throughout the last epidemic wave from 4·5% (1·2–12·5) in January to 5·6% (1·5–15·1) in February, 15·4% (9·0–25·0) in March, 54·5% (46·4–62·4) in April, and 63·1% (56·8–69·0) in May (figure C, appendix p 3). These results suggest an introduction of this variant soon after its first description in October, 2020, in South Africa,[4] and that the variant was responsible for two-thirds of the observed infections in May, 2021, at the peak of the early 2021 epidemic wave.

Our data describe both the dynamics of the early 2021 epidemic wave in Antananarivo, Madagascar, and how Beta contributed to it, partially escaping previous natural immunisation. Beta has been described in Madagascar, but the proportion of infections due to this variant have not been continuously monitored due to undertesting for COVID-19 in the general population and suboptimal variant identification in positive samples. Monitoring blood donors for both general SARS-CoV-2 and variant-specific antibody seroprevalences might be a useful tool when, as with Beta, serological responses seem to be affected.[6]

Vaccination of the general Malagasy population should be intensified, yet adapted to a population highly naturally immunised by exposure to ancestral SARS-CoV-2, variant Beta, or both. Early detection of new variants that might affect the course of the epidemic should be continuously monitored for immediate public health decision making.

We declare no competing interests.

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