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Letter to the Editor

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Letter to the Editor

SARS-CoV-2 public health investigation in an aged care facility and challenges with serological screening in low pre-test probability settings

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Keywords: SARS-CoV-2, serosurvey, aged care facility

The prevalence of SARS-CoV-2, the virus responsible for coronavirus disease 2019 (COVID-19), is evolving across time and regions of the world as the COVID-19 pandemic spreads with varying voracity. A seroprevalence study in Sydney, Australia suggested that 0.15% of the Sydney population had been infected with SARS-CoV-2, while studies in the USA show considerable regional and temporal variation, with some regions showing seroprevalence above 25%.[1,2] It is in low-prevalence settings that positive or equivocal tests should undergo confirmatory testing, using gold standard tests such as a neutralisation test or reference laboratory assay to optimise the accuracy.[3]

On 14 May 2020, a staff member at a Central Queensland public residential aged care facility had SARS-CoV-2 detected by polymerase chain reaction (PCR) testing. Repeated interval testing of 105 residents using nasopharyngeal swabs was undertaken; none of the residents had SARS-CoV-2 detected by PCR. With no other active case of COVID-19 within Central Queensland and no apparent epidemiological link, the primary case was later considered to be non-infectious at the time of the outbreak and to have tested positive due to prolonged viral shedding, resulting in a low pre-test probability cohort in the residential aged care facility.

By mid May 2020, there were seven confirmed cases of COVID-19 in the region with no community transmission and no known evidence of previous SARS-CoV-2 infection in any residential aged care facilities in Central Queensland.[4] In this paper we report a SARS-CoV-2 public health investigation during this outbreak, with outcomes of serological screening in low pre-test probability settings. The Central Queensland Human Research Ethics Committee approved this research (LNR/2020/QCQ/68883).

In response to the COVID-19 pandemic, Queensland's public health reference laboratory developed an in-house multiplex microsphere immunoassay (MIA) utilising magnetic microspheres which were coupled to various commercially-available SARS-CoV-2 recombinant proteins (Sino Biological, Beijing, China) as well as whole inactivated SARS-CoV-2 antigen (produced in-house). Patient samples were reacted with the antigen-coupled microspheres followed by detection of bound antibody using specific immunoglobulin G (IgG) and IgM conjugates. Results were read on a Bio-Plex 200 instrument (Bio-Rad, USA) and were exported to Microsoft Excel® for interpretation based on the median fluorescence intensity (MFI) obtained for each component of the assay. Equivocal results were reported if the samples demonstrated low MFI values across several antigens or demonstrated reactivity to multiple antigens shown to have lower specificity. Where equivocal results were obtained, the plaque reduction neutralisation tests (PRNT) with SARS-CoV-2 virus was performed to assist with confirming or excluding the MIA result.

The MIA has been recently validated, using: sera from confirmed COVID-19 cases after 14

days (n = 73); negative sera collected pre-2020 (n = 90); and children who tested positive for a coronavirus (not SARS-CoV-2; n = 43). For IgG and a three-antigen-antibody reaction cut-off for a positive test, the metrics of the test (with 95% confidence intervals listed in parentheses) were as follows: sensitivity 95% (87, 98%); specificity 100% (97, 100%); positive predictive value 100% (95, 100%); negative predictive value 97% (93, 99%). Tests on 52 negative samples (PRNT, pre-2020 sera) all returned negative results.

The average age of residents was 81.3 years, with 49 (47%) of the residents being female. Paired sera were collected from the residents 13 days apart for SARS-CoV-2 serology. Thirty patients had at least one equivocal result either in the initial or follow-up testing. Six patients had negative follow-up serology following an equivocal initial sample and were reported as negative. A total of 21 patients remained equivocal after parallel testing. PRNT was performed on these 21 patients and COVID-19 infection was excluded based on negative results ($PRNT^{50}$ titres < 10) in all patients. These findings were subsequently used to adjust MFI interpretive criteria, and the MIA has been since updated with improved specificity.

These findings support the use of the SARS-CoV-2 MIA followed by neutralisation testing confirmation for screening in large-scale seroprevalence studies in low-pretest probability environments such as aged care facilities.

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