Risk Factors for Slow Viral Decline in COVID-19 Patients

during the 2022 Omicron Wave

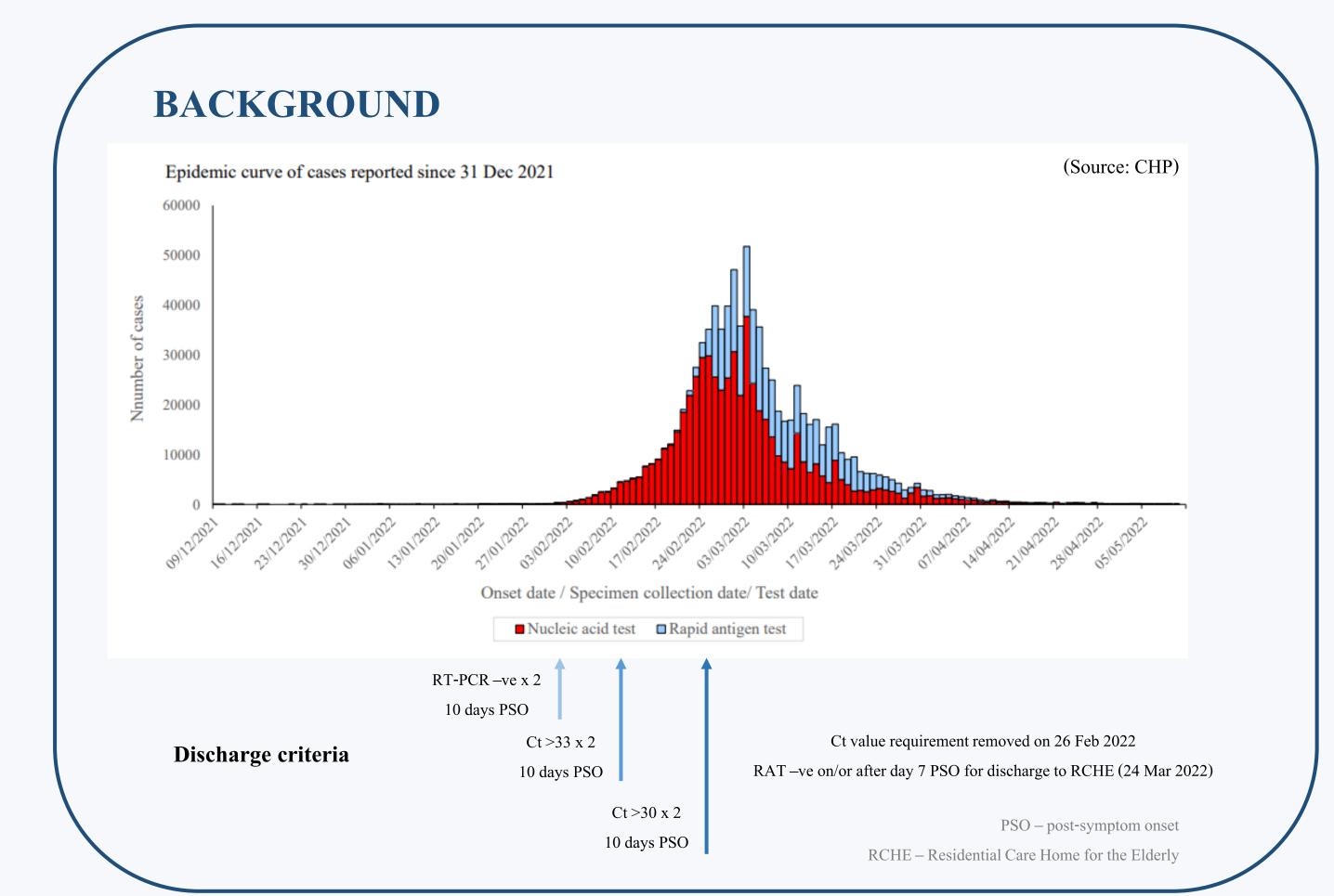
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METHODS

Patients

Adult patients admitted to Queen Mary Hospital for laboratory-confirmed COVID-19 between 20 January and 25 February 2022.

Inclusion criteria:

- ✓ Aged 18 years or above.
- ✓ At least one saliva tested positive by RT-PCR. ✓ At least one saliva specimen on or after day 7.

Exclusion criteria:

- χ Clinical information not available.
- χ COVID-19 vaccination status unknown.

Definition

Fully vaccinated – at least 2 doses of COVID-19 vaccines at least 14 days prior to symptom onset or first positive test.

Day 0 – the day of symptom onset or first positive SARS-CoV-2 test for asymptomatic patients.

Slow viral decline (SVD) – Ct value <30 for any specimen collected on or after day 7 PSO (SVD-7) or day 10 PSO (SVD-10).

Rapid viral decline (RVD) – at least one specimen on or after day 7 (or 10) and did not fulfil the criteria for SVD.

SARS-CoV-2 RT-PCR and lineage determination

Urgent request – GeneXpert XVI system (Cepheid, Sunnyvale, CA, USA).

Routine request – commercial real-time RT-PCR targeting the E gene (TIB Molbiol, Berlin, Germany).

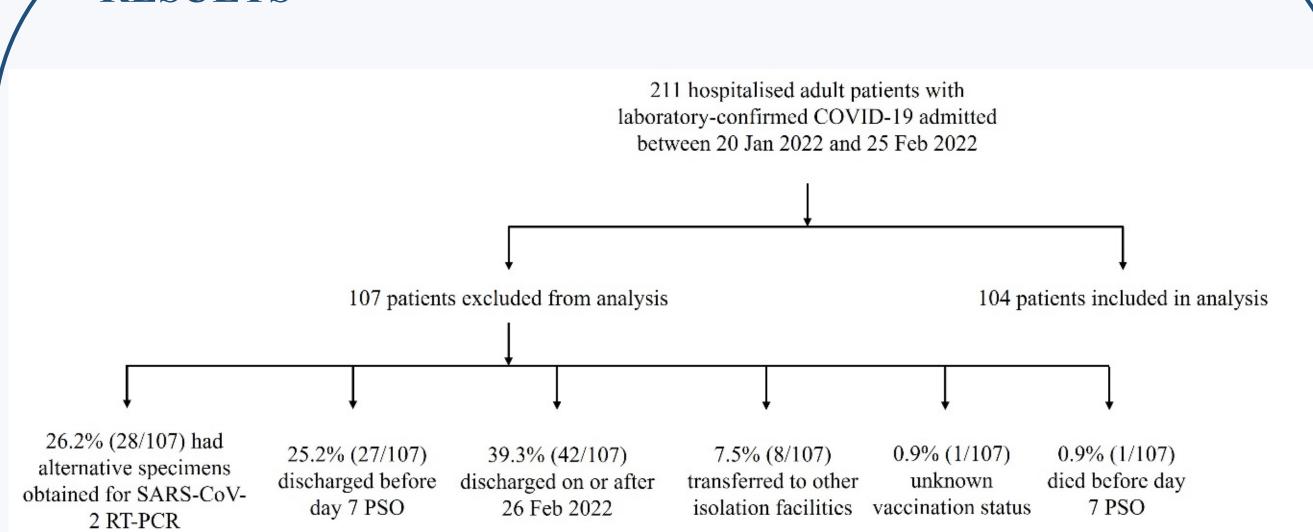
Whole genome sequencing - Oxford Nanopore MinION (Oxford Nanopore Technologies, Oxford, UK).

IBM SPSS Statistics 28.0.1.0 or PRISM version 9.1.2 (GraphPad Software, San Diego, CA, USA).

Statistical analysis

Ethical approval Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW 22-052).

RESULTS



- Viral load was highest (Ct value lowest) on days 1 PSO and gradually declined (Figure 1).
- O No significant difference in the median peak viral loads between older and younger individuals and between fully vaccinated and non-fully vaccinated patients. However, on or after day 2 PSO, the viral load was generally lower in younger adults (<60 years old) than older adults (≥60 years old), and in fully vaccinated than non-fully vaccinated individuals.
- Older age, hypertension, hyperlipidaemia, and chronic kidney disease were associated with slow viral decline in univariate analysis on both day 7 and day 10 PSO, while incomplete or no vaccination was associated with slow viral decline on day 7 PSO only (Table 1).
- Older age was the only risk factor that remained statistically significant in multivariate analysis (Table 2).

Table 2. Result of multivariate analysis

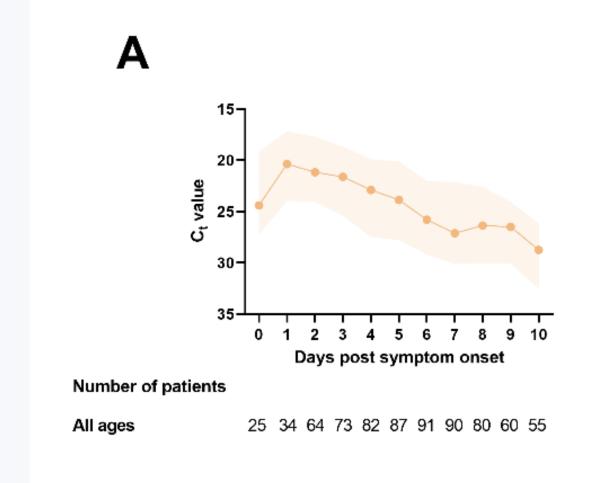
| | P value | | | |
|-----------------------------------|-----------|------------|--|--|
| Variable | Day 7 PSO | Day 10 PSO | | |
| Age | 0.016 | 0.018 | | |
| Presence of chronic comorbidities | 0.423 | 0.219 | | |
| Hypertension | 0.404 | 0.261 | | |
| Hyperlipidaemia | 0.377 | 0.370 | | |
| Chronic kidney disease | 0.998 | 0.109 | | |
| Connective tissue disease | N.A. | 0.999 | | |
| Fully vaccinated | 0.210 | 0.933 | | |

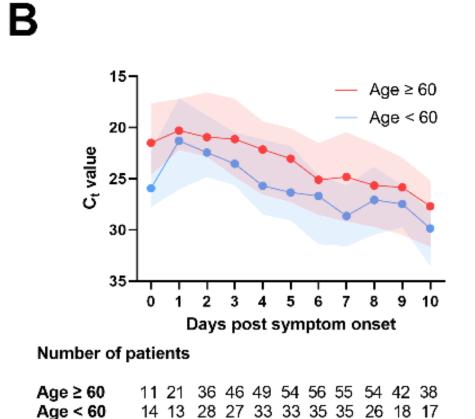
CONCLUSIONS

- Old age is an independent risk factor associated with slow viral decline in this retrospective cohort study conducted during the Omicron-dominant 2022 COVID-19 wave.
- Fransmission-based precaution guidelines should take age into consideration when determining the timing of termination of isolation, especially in resource limited settings where testing capacity is limited.

Table 1. Comparison between patients with SVD and RVD on day 7 and day 10 PSO.

| | Day 7 PSO | | | | Day 10 PSO | | | |
|------------------------------|----------------------|---------------|---------------|---------|------------------------|---------------|---------------|---------|
| | All patients (n=104) | SVD (n=84) | RVD (n=20) | P value | All patients (n=79) | SVD (n=45) | RVD (n=34) | P value |
| Demographics | | | | | | | | |
| | 68 (47-76) | 69 (53-76) | 47 (34-74) | | 68 (45-76) | 70 (55-80) | 53 (36-74) | |
| | 66 (63.5) | 58 (69) | 8 (40) | | 48 (60.8) | 33 (73.3) | 15 (44.1) | |
| Female sex | 58 (55.8) | 50 (59.5) | 8 (40) | 0.137 | 41 (51.9) | 27 (60) | 14 (41.2) | 0.155 |
| Chronic comorbidities | | | | | | | | |
| | 73 (70.2) | 64 (76.2) | 9 (45) | | 52 (65.8) | 36 (80) | 16 (47.1) | |
| | 48 (46.2) | 44 (52.4) | 4 (20) | | 34 (43) | 25 (55.6) | 9 (26.5) | |
| | 41 (39.4) | 38 (45.2) | 3 (15) | | 28 (35.4) | 21 (46.7) | 7 (20.6) | |
| Diabetes mellitus | 26 (25) | 24 (28.6) | 2 (10) | 0.148 | 15 (19) | 11 (24.4) | 4 (11.8) | 0.246 |
| Neurologic/cognitive disease | 22 (21.2) | 19 (22.6) | 3 (15) | 0.555 | 15 (19) | 11 (24.4) | 4 (11.8) | 0.246 |
| Chronic heart disease | 16 (15.4) | 14 (16.7) | 2 (10) | 0.731 | 11 (13.9) | 8 (17.8) | 3 (8.8) | 0.335 |
| | 17 (16.3) | 17 (20.2) | 0 (0) | 0.038 | 10 (12.7) | 9 (20) | 1 (2.9) | |
| Immunocompromised state | 5 (4.8) | 4 (4.8) | 1 (5) | 1.000 | 3 (3.8) | 1 (2.2) | 2 (5.9) | 0.574 |
| Chronic liver disease | 6 (5.8) | 6 (7.1) | 0 (0) | 0.593 | 4 (5.1) | 3 (6.7) | 1 (2.9) | 0.630 |
| | 6 (5.8) | 6 (7.1) | 0 (0) | 0.593 | 6 (7.6) | 6 (13.3) | 0 (0) | |
| Pulmonary disease | 8 (7.7) | 6 (7.1) | 2 (10) | 0.648 | 6 (7.6) | 3 (6.7) | 3 (8.8) | 1.000 |
| OVID-19 vaccination history | | | | | | | | |
| | 51 (49) | 37 (44) | 14 (70) | | 46 (58.2) | 24 (53.3) | 22 (64.7) | 0.362 |
| BNT162b2 | 51 (100) | 25 (67.6) | 8 (57.1) | 0.525 | 28 (60.9) | 16 (66.7) | 12 (54.5) | 0.547 |
| Booster dose | 7 (13.7) | 6 (16.2) | 1 (7.1) | 0.657 | 6 (13) | 5 (20.8) | 1 (4.5) | 0.190 |
| ineage | | | | | | | | |
| Omicron | 94 (90.4) | 75 (89.3) | 19 (95) | 0.683 | 69 (87.3) | 38 (84.4) | 31 (91.2) | 0.502 |
| reatment | | | | | | | | |
| Remdesivir | 29 (27.9) | 22 (26.2) | 7 (35) | 0.421 | 24 (30.4) | 15 (33.3) | 9 (26.5) | 0.623 |
| everity of disease | | | | | | | | |
| Symptomatic | 78 (75) | 63 (75) | 15 (75) | 1.000 | | | | |
| Require O2 | 3 (2.9) | 3 (3.6) | 0 (0) | 1.000 | 2 (2.5) | 1 (2.2) | 1 (2.9) | 1.000 |





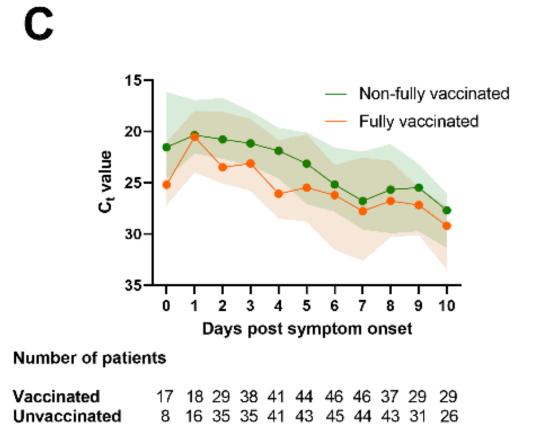


Figure 1. Serial changes of Ct value in saliva specimens. (A) All patients; (B) according to age; (C) according to vaccination status. Each dot represents the median viral load, and the shading represents the interquartile range.

Li, X., Tam, A. R., Chu, W. M., Chan, W. M., Ip, J. D., Chu, A. W., Abdullah, S. M. U., Yip, C. C., Chan, K. H., Wong, S. S., Cheng, V. C., Yuen, K. Y., Hung, I. F., & To, K. K. (2022). Risk Factors for Slow Viral Decline in COVID-19 Patients during the 2022 Omicron Wave. Viruses, 14(8). doi:10.3390/v14081714