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A prospective study of the impact of glycaemic status on clinical outcomes and anti-SARS-CoV-2 antibody responses among patients with predominantly non-severe COVID-19

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Introduction

- Diabetes is a risk factor for severe COVID-19[1], less is known about impact of prediabetes on COVID-19 outcomes
- There are concerns about influence of impaired glucose metabolism on antibody response to COVID-19 vaccine[2]
- We carried out this **prospective study of COVID-19 patients**, predominantly of non-severe disease, to evaluate the influence of **glycaemic status** on **clinical outcomes** and **neutralising antibody (Nab) responses**, potentially relevant to the COVID-19 vaccination programme

Methodology

- Consecutive adults admitted to Queen Mary Hospital for COVID-19 from July 2020 to May 2021 were included (a representative cohort of COVID-19 patients in Hong Kong[3])
- Glycaemic status defined using admission HbA1c
  Diabetes: HbA1c≥6.5%, on anti-diabetic Rx, or known Dx
  Prediabetes: HbA1c 5.7-6.4%
  Normoglycaemia: HbA1c <5.7%
- **Clinical deterioration** defined by radiological progression, new oxygen requirement, intensive care unit admission, or death
- **Nab** measured among COVID-19 survivors at 1-, 2-, 3- and 6-month post-discharge

Results

- **605 patients included** (age 50.2±17.1 years; 45.1% men; 96.9% non-severe COVID-19): 325 had normoglycaemia, 185 had prediabetes and 95 had diabetes (**Table 1**)
- **74** patients (**12.2%**) had **clinical deterioration**: 16 required intensive care, and 4 died
- **Clinical deterioration** more likely with worse glycaemic status (p<0.001) and higher HbA1c (unadjusted OR 1.403, p<0.001) (**Figure 1**)
- Older age (p<0.001), higher viral loads (p<0.001), higher C-reactive protein (CRP) (p<0.001) and symptomatic presentation (p=0.008), but **NOT** glycaemic status/HbA1c, **independently predicted clinical deterioration**
- Older age (p=0.001), higher CRP levels (p=0.038), interferon treatment (p=0.001) and elevated lactate dehydrogenase levels (p=0.046), but **NOT** glycaemic status/HbA1c, were the **independent determinants of Nab titres**
- **Nab titres** were comparable across glycaemic status throughout the 6-month follow-up (p=0.280) (**Figure 2**)

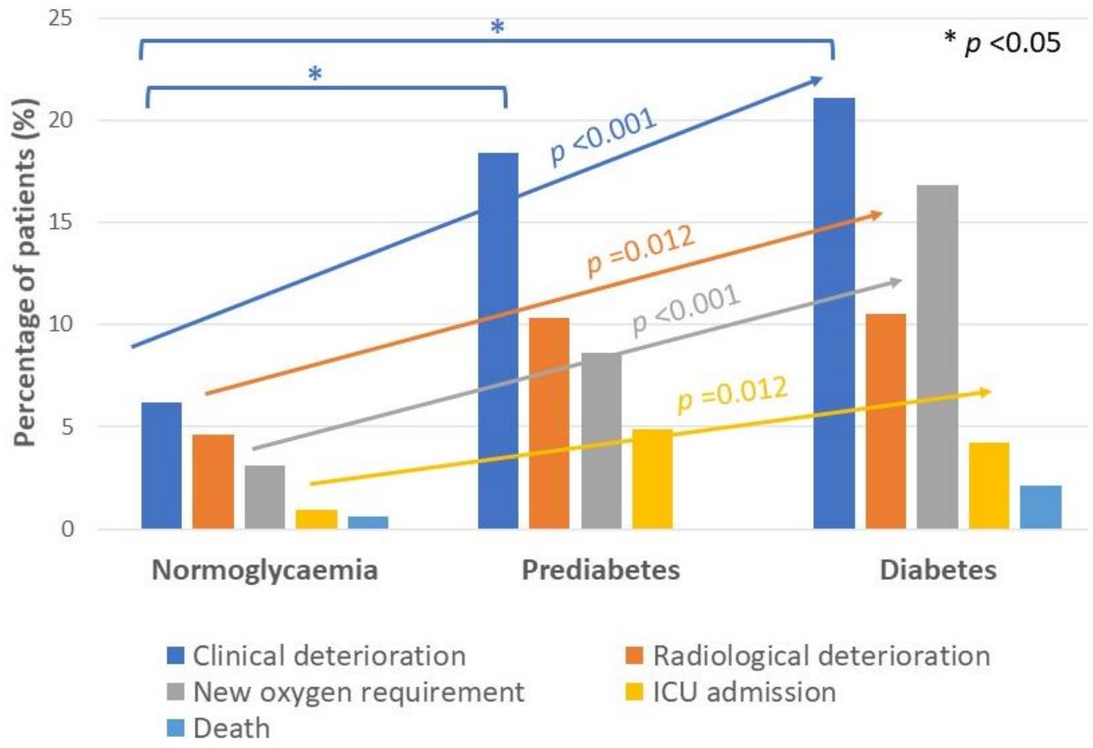

Figure 1. Rate of clinical deterioration

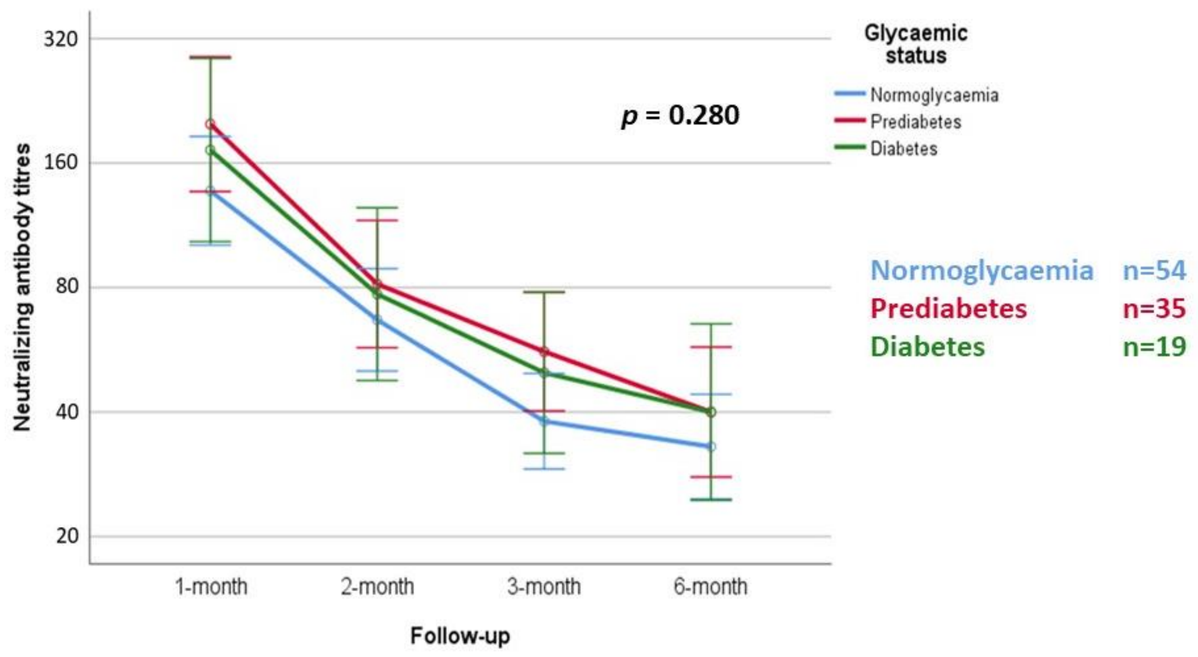

Figure 2. Nab titres according to glycaemic status (n=108)

	All	Normoglycaemia	Prediabetes	Diabetes	p-value
Number of patients	605	325	185	95	---
HbA1c (%)	5.84±1.00	5.30±0.29	5.93±0.19[a]	7.51±1.49[a,b]	<0.001
RG, mmol/L	5.91 (5.13–7.35)	5.45 (4.88–6.35)	6.18 (5.44–7.36)[a]	8.98 (6.88–12.66)[a,b]	<0.001
Age (years)	50.2±17.1	42.4±15.8	57.0±14.0[a]	63.3±13.0[a,b]	<0.001
Male (%)	273 (45.1%)	134 (41.2%)	91 (49.2%)	48 (50.5%)	0.050
Comorbidities					
Hypertension	127 (21.0%)	31 (9.5%)	46 (24.9%)[a]	50 (52.6%)[a,b]	<0.001
Obesity	28 (4.6%)	8 (2.5%)	9 (4.9%)	11 (11.6%)[a]	0.005
IHD/CHF	28 (4.6%)	4 (1.2%)	9 (4.9%)[a]	15 (15.8%)[a,b]	<0.001
Stroke/TIA	14 (2.3%)	3 (0.9%)	6 (3.2%)	5 (5.3%)[a]	0.021
Cancer	28 (4.6%)	10 (3.1%)	10 (5.4%)	8 (8.4%)	0.045
Symptomatic	422 (69.8%)	215 (66.2%)	136 (73.5%)	71 (74.7%)	0.066
COVID-19 severity					<0.001
Mild	445 (73.6%)	273 (84.0%)	116 (62.7%)[a]	56 (58.9%)[a]	
Moderate	142 (23.5%)	48 (14.8%)	57 (30.8%)[a]	37 (38.9%)[a]	
Severe	9 (1.5%)	4 (1.2%)	2 (1.1%)[a]	3 (3.2%)[a]	
Ct value	24.62 (18.20–31.39)	24.90 (17.62–31.65)	25.59 (19.94–31.42)	21.30 (17.50–28.19)[b]	0.038

[a]p<0.05 compared with normoglycaemia; [b]p<0.05 compared with prediabetes

Table 1. Baseline characteristics

Discussion

- **Our data enhanced the existing literature: while risk of clinical deterioration was higher among dysglycaemia, there was no significant impairment in antibody response among dysglycaemia**
- Results generalizable to COVID-19 patients at large
- Our cohort comprised mainly mild to moderate COVID-19 patients and thus had a low mortality rate: not powered to identify predictors of mortality
- SARS-CoV-2 viral loads were represented by Ct values: despite a good correlation, direct quantitative measurements of viral loads would have been preferred if available

Conclusion

In this cohort of predominantly non-severe COVID-19 patients

- We observed **a higher likelihood of clinical deterioration** in those with dysglycaemia, **starting from prediabetes**
- Likely secondary to the association of dysglycaemia with older age, symptomatic COVID-19, higher viral loads and levels of inflammation, which independently predicted clinical deterioration
- **Glycaemic status did not adversely impact anti-SARS-CoV-2 antibody responses upon 6 months of follow-up**

Reference

1. Landstra CP, et al. Front Endocrinol (Lausanne). 2021;12:649525.
2. Pal R, et al. Diabetes Metab Syndr. 2021;15(1):193-196.
3. Lui DTW, et al. Endocr Pract. 2021;27(9):894-902.

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