

COVID-19 IN PATIENTS WITH DIABETES:

real-world data on factors influencing outcome

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Introduction

Emerging data has shown associations between patients with diabetes (PwD) having excess mortality from Covid-19, but granularity is lacking.

Methods

We retrospectively audited all inpatients aged ≥ 18 yrs admitted to our trust with PCR-confirmed and/or clinical diagnosis of Covid-19 infection, between 31 January and 23 May 2020.

Data on baseline demographics, co-morbidities and admission outcome (ITU admission, respiratory support if required, 28-day mortality) were extracted from electronic patient records.

For PwD, we recorded background information (including type and duration of diabetes, HbA1c, diabetes treatment, diabetes-related complications) as well as admission-related parameters - admission capillary blood glucose (CBG) and ketone levels and episodes of hypoglycaemia (< 4.0 mmol/L) or hyperglycaemia (≥ 12 mmol/L).

Data was analysed using SPSS (v 26). The primary outcome (death within 28 days of admission) was analysed by binary logistic regression, with multivariate analysis of variables with $p < 0.05$ in univariate analysis. Patients not suitable for escalation beyond ward-based supportive care were excluded from secondary analyses of admission to ITU, or requirement for ventilatory support.

Results

Demographics

There were 405 adult patients admitted with Covid-19 between 31st January and 23rd May 2020 to our institution.

Demographic details are shown in Table 1, and overall outcomes in Figure 1. PwD had higher median BMI ($p = 0.022$), and were from areas with lower median Index of Multiple Deprivation (IMD) deciles ($p = 0.034$). They were also more likely to have a diagnosis of hypertension or chronic kidney disease ($p = 5.8 \times 10^{-5}$, $p = 6.5 \times 10^{-5}$).

108 (26.7%) patients had an existing diagnosis of diabetes mellitus (4 with Type 1 or secondary diabetes, the remainder with Type 2 diabetes). 36% of patients were managed with diet alone, and 24.1% were prescribed insulin.

Median HbA1c measured within 3 months of admission for PwD was 61 (35-117) mmol/mol ($n = 45$). 63.6% of patients had a duration of diabetes < 10 yrs.

Results

	Diabetes (n=108)	No diabetes (n=297)
Age years	74 (19-100)	74 (23-101)
Sex Male	67 (62%)	149 (50%)
Female	41 (38%)	148 (50%)
BMI kg/m ² (n= 38, n= 106)	28.9 (17.4-53.9)	25.1 (14.6-63.8)
IMD decile		
1-2 (most deprived)	55 (51%)	126 (43%)
3-4	23 (21%)	49 (17%)
5-6	7 (6%)	30 (10%)
7-8	15 (14%)	36 (12%)
9-10 (least deprived)	19 (18%)	56 (19%)
Ever smoker (n=77, n=222)	47 (64%)	109 (49%)
Comorbidities		
- Hypertension	63 (58%)	107 (36%)
- Microvascular disease (n=94)	41 (44%)	-
- Macrovascular disease	49 (45%)	67 (23%)
- Chronic Kidney Disease (eGFR < 60 ml/min)	42 (39%)	58 (20%)

Table 1. Demographic characteristics of inpatients with COVID-19 (n=405)

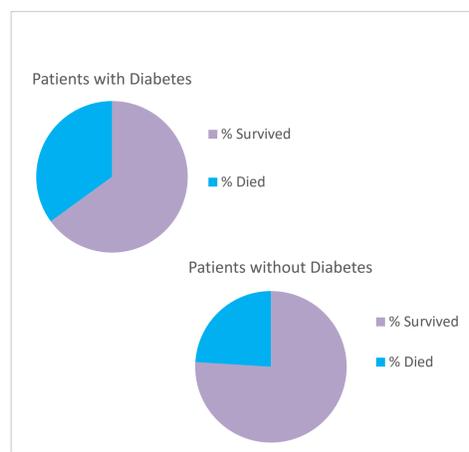


Figure 1. Overall outcomes of COVID-19 infection (within 28 days of admission)

In-hospital diabetes management

94.4% of PwD had capillary blood glucose (CBG) measured on admission, but only 3% capillary ketones, in contrast to national guidance¹. There were no cases of diabetic ketoacidosis or hyperglycaemic hyperosmolar syndrome. Two patients were taking sodium-glucose co-transporter 2 (SGLT2) inhibitors and these were not stopped, nor were ketones tested, however they were admitted prior to publication of national guidance.

24.1% of patients experienced hypoglycaemia (CBG < 4 mmol/L, range 1-9 episodes), and 53.7% had at least one episode of hyperglycaemia (CBG ≥ 12 mmol/L). Presence or frequency of hyper/hypoglycaemia did not correlate with outcome (*data not shown*).

Factors associated with outcome

A diagnosis of diabetes was associated with higher 28-day mortality (**35.2 v 23.9%** $p = 0.024$) and need for non-invasive ventilation (**35.9% v 19.8%** $p = 0.002$, $n = 350$) but not intubation or ITU admission.

Factors influencing 28-day mortality in PwD are shown in Table 2. There were no additional factors identified statistically associated with need for ventilatory support or ITU admission (*data not shown*).

	OR Death within 28 days (Univariate)	OR Death within 28 days (Multivariate)
Age < 70 yrs	Ref	Ref
> 70 yrs	6.8 (95%CI 2.2-21.1)	5.8 (95%CI 1.8-18.7)
Sex (M)	0.7 (95%CI 0.3-1.5)	-
HbA1c (within 3 months) (n= 45)	1.0 (95% CI 1.0- 1.0)	-
Admission CBG	0.9 (95% CI 0.8-1.0)	-
Duration of diabetes (n=88)	1.0 (95%CI 0.9-1.1)	-
Treatment for diabetes		
- Metformin	0.3 (95% CI 0.1-0.8)	0.4 (95%CI 0.2-1.0)
- Insulin	0.5 (95%CI 0.2-1.3)	-
Complications of diabetes		
- Microalbuminuria	2.6 (95%CI 0.6-13.1)	-
- Foot disease	1.3 (95%CI 0.2-8.0)	-
- Retinopathy	0.4 (95%CI 0.1-1.6)	-
- Neuropathy	0.6 (95%CI 0.1-3.2)	-
- Ischaemic heart disease	1.3 (95%CI 0.6-3.0)	-
- Cerebrovascular disease	1.0 (95%CI 0.3-3.0)	-
- Chronic kidney disease	2.9 (95%CI 1.3-6.5)	2.2 (95%CI 0.9-5.4)

Table 2. Factors affecting mortality in PwD (n=405 or as shown). Results of significance highlighted in bold.

Discussion

This data is consistent with published findings that diabetes and increasing age are risk factors for Covid-19 related death².

There were insufficient numbers of patients with type 1 diabetes to analyse effect of diabetes type on outcome.

Neither preceding nor inpatient glycaemic control appeared to influence mortality or severity of disease – similarly seen in the French CORONADO study³. As previous clinical trials on the effects of glycaemic control on mortality have shown conflicting results⁴, we suggest that tight inpatient glycaemic control in PwD with Covid-19 needs to be balanced with risk of hypoglycaemia.

Interestingly, PwD taking metformin had significantly lower mortality (22.4% v 45.8%, $p = 0.012$) compared to those not on metformin, although this was borderline in multivariate analysis. This may represent a true protective effect, or equally may be reflective of PwD on metformin having less advanced CKD which would preclude metformin use. This observation would benefit from further study in a larger cohort.

Of all diabetes-related co-morbidities, only CKD was associated with excess mortality in univariate analysis (50% v 25.8%, $p = 0.010$), as was also found in the national English study published earlier this year².

We were concerned that the risk of ketosis in PwD with Covid-19 infection taking SGLT2 inhibitors may not be well appreciated especially among non-diabetes specialists. This has been flagged in a trust-wide safety alert, and these medications have now been removed from routine drug stocks.

Conclusions

Our results reinforce the diverse and conflicting nature of observational data published thus far regarding associations between diabetes and Covid-19.

Increasing age, and a diagnosis of diabetes however, remain firm risk factors for mortality due to Covid-19, therefore these patient groups should continue to be considered high-risk and shielded during the ongoing pandemic.

References

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