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Increase in hypoglycaemia and hyperglycaemia in people with diabetes admitted to hospital during COVID-19 pandemic

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ABSTRACT

Background: We used detailed information on patients with diabetes admitted to hospital to determine differences in clinical outcomes before and during the COVID-19 pandemic in the UK.
Methods: The study used electronic patient record data from Imperial College Healthcare NHS Trust. Hospital admission data for patients coded for diabetes was analysed over three time periods: pre-pandemic (31st January 2019–31st January 2020), Wave 1 (1st February 2020–30th June 2020), and Wave 2 (1st September 2020–30th April 2021). We compared clinical outcomes including glycaemia and length of stay.
Results: We analysed data obtained from 12,878, 4008 and 7189 hospital admissions during the three pre-specified time periods. The incidence of Level 1 and Level 2 hypoglycaemia was significantly higher during Waves 1 and 2 compared to the pre-pandemic period (25 % and 25.1 % vs. 22.9 % for Level 1 and 11.7 % and 11.5 % vs. 10.3 % for Level 2). The incidence of hyperglycaemia was also significantly higher during the two waves. The median hospital length of stay increased significantly (4.1[1.6, 9.8] and 4.0[1.4, 9.4] vs. 3.5[1.2, 9.2] days).
Conclusions: During the COVID-19 pandemic in the UK, hospital in-patients with diabetes had a greater number of hypoglycaemic/hyperglycaemic episodes and an increased length of stay when compared to the pre-pandemic period. This highlights the necessity for a focus on improved diabetes care during further significant disruptions to healthcare systems and ensuring minimisation of the impact on in-patient diabetes services.
Summary: Diabetes is associated with poorer outcomes from COVID-19. However the glycaemic control of in-patients before and during the COVID-19 pandemic is unknown. We found the incidence of hypoglycaemia and hyperglycaemia was significantly higher during the pandemic highlighting the necessity for a focus on improved diabetes care during further pandemics.

1. Introduction

Diabetes is associated with poorer outcomes from Coronavirus Disease 2019 (COVID-19)[1,2] especially in people admitted to hospital.[3–5] However, no quantitative analysis has been carried out to compare the clinical outcomes of hospital in-patients with diabetes. We analysed three years of data from the electronic patient record system of a large UK tertiary hospital and compared key clinical outcomes including glycaemia and length of stay in patients with diabetes before and during the COVID-19 pandemic.

2. Materials and methods

2.1. Dataset

The study was conducted using data from the electronic patient record system within Imperial College Healthcare NHS Trust. The data included demographics, admission information, blood test results

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including point-of-care testing, vital signs, and details of medications administered during the hospital stay. The dataset comprised data from 1st January 2019 to 30th April 2022 for all inpatients patients with diabetes.[6]

2.2. Ethics approval

Data access has been granted and the study has been approved by the NIHR Imperial Biomedical Research Centre Data Access and Prioritisation Committee. The study conforms to recognized standards.

2.3. Statistical analysis

When reporting the glycaemic outcomes, Level 1 and Level 2 hypoglycaemic episodes were defined as any blood glucose measurement <4 mmol/l and 3 mmol/l.[7] Two or more consecutive low blood glucose measurements within a two-hour time window were considered as one single hypoglycaemic episode. Hyperglycaemic episodes were defined as blood glucose measurement >12 mmol/l and 15 mmol/l.

The data was analysed over three periods: pre-pandemic (31st Jan 2019–31st Jan 2020), Wave 1 (1st Feb 2020–30th Jun 2020) and Wave 2 (1st Sep 2020–30th Apr 2021). Statistical analyses of clinical outcomes (proportions, mean and standard deviation or median and interquartile range) and between-group comparisons of key metrics were performed using R version 3.3. Point-biserial correlation was used to relate the binary variables (hypoglycaemia and hyperglycaemia) and the continuous variable (length of stay).

3. Results

We analysed data for 8084, 2990 and 5021 in-patients with diabetes who underwent 12,878, 4008 and 7189 hospital admissions during the pre-pandemic, Wave 1 and Wave 2 periods, respectively (Table 1).

The in-patient demographics were similar across the three time periods ($P > 0.05$). Blood pressure, creatinine levels, and haemoglobin levels were also similar ($P > 0.05$). The proportionate use of diabetes medications did not differ during the studied periods ($P > 0.05$).

Across Wave 2, there was a greater use of dexamethasone compared to the pre-pandemic and Wave 1. The incidence of Level 1 and Level 2 hypoglycaemia was significantly higher during Waves 1 and 2 compared to the pre-pandemic period (25 % and 25.1 % vs. 22.9 % for Level 1 and 11.7 % and 11.5 % vs. 10.3 % for Level 2). The incidence of hyperglycaemia was also significantly higher.

The median length of stay increased significantly during Waves 1 and 2 periods compared to the pre-pandemic period (4.1[1.6, 9.8] and 4.0 [1.4, 9.4] vs. 3.5[1.2, 9.2] days) (Boxplots shown in Supplementary file Fig. S1). The correlation coefficient between occurrence of Level 1 hypoglycaemia and length of stay was 0.30 ($P < 2.2e-16$) and that between occurrence of hyperglycaemia (>15 mmol/l) and length of stay was 0.25 ($P < 2.2e-16$).

4. Discussion

This is the first study to compare glycaemic outcomes and length of stay for hospital in-patients with diabetes before and during the COVID-19 pandemic.

We report a significantly higher incidence of both hypoglycaemia and hyperglycaemia during the two waves of the pandemic compared to the pre-COVID-19 period. As severe hypoglycaemic is associated with increased mortality,[8] this may have contributed to the higher mortality rate in inpatients with diabetes during the pandemic.

Putative reasons for these adverse glycaemic outcomes may include a change in the demographics of the in-patient cohort (e.g. fewer elective cases, more emergency admissions) caused by COVID-19. This is reflected by an increase in the proportion of inpatients with diabetes during the pandemic (pre-pandemic period, Wave 1 and Wave 2 being

Table 1
Baseline characteristics and glycaemic outcomes of the in-patients with diabetes before, during wave 1 and wave 2 of the COVID-19 pandemic.

Variables		Total in-patients with diabetes (N = 8084) Number of hospital admissions (n = 12878)	Total in-patients with diabetes (N = 2990) Number of hospital admissions (n = 4008)	Total in-patients with diabetes (N = 5021) Number of hospital admissions (n = 7189)
		Pre-COVID-19 31st Jan 2019–31st Jan 2020	COVID-19 Wave 1 1st Feb 2020–30th Jun 2020	COVID-19 Wave 2 1st Sep 2020–30th Apr 2021
Sex, N (%)				
	Male	4572 (57)	1738 (58)	2878 (57)
Age [years], mean (SD)		69.2 (14.5)	69.1 (14.4)	67.8 (14.5)
Ethnicity, N (%)				
	White	2840 (43)	1004 (40)	1686 (43)
	Asian	1414 (21)	490 (20)	861 (21)
	Black	1170 (18)	498 (20)	709 (18)
	Mixed	147 (2)	42 (2)	80 (2)
	Other	1083 (16)	452 (18)	630 (16)
Type of diabetes, N (%)				
	Type 1 diabetes	546 (7)	210 (7)	313 (6)
	Type 2 diabetes	7538 (93)	2780 (93)	4708 (94)
Vital signs and Laboratory test				
Systolic blood pressure [mmHg], mean (SD)		134 (18)	135 (18)	134 (18)
Creatinine [umol/l], median (IQR)		92 (70, 152)	96 (70, 174)	91 (69, 160)
Haemoglobin [g/l], mean (SD)		113 (19)	112 (19)	114 (20)
Albumin [g/l], mean (SD)		29.9 (5.8)	29.0 (6.3)	29.7 (6.0)
Neutrophils [x10^9/l], mean (SD)		6.4 (3.9)	6.2 (3.1)	6.4 (3.3)
Medication use				
Sulfonylurea, N (%)		1865 (14)	530 (13)	979 (14)
SGLT2, N (%)		333 (3)	123 (3)	325 (5)
DPP-4, N (%)		2675 (21)	863 (22)	1417 (20)
GLP-1, N (%)		73 (0)	12 (0)	11 (0)
Metformin, N (%)		4847 (38)	1362 (34)	2501 (35)
Intravenous insulin, N (%)		1225 (10)	339 (8)	583 (8)
Dexamethasone		312 (2)	80 (2)	780 (11)*
Glycaemic outcomes				
Hypoglycaemia, N (%)				
	Level 1 hypoglycaemia <4 mmol/l	2949 (22.9)	1000 (25.0)*	1804 (25.1)*

(continued on next page)

Table 1 (*continued*)

Variables	Total in-patients with diabetes (N = 8084) Number of hospital admissions (n = 12878)		Total in-patients with diabetes (N = 2990) Number of hospital admissions (n = 4008)	Total in-patients with diabetes (N = 5021) Number of hospital admissions (n = 7189)
	Pre-COVID-19 31st Jan 2019–31st Jan 2020		COVID-19 Wave 1 1st Feb 2020–30th Jun 2020	COVID-19 Wave 2 1st Sep 2020–30th Apr 2021
Hyperglycaemia, N (%)	Level 2 hypoglycaemia <3 mmol/l	1329 (10.3)	470 (11.7)*	828 (11.5)*
	>12 mmol/l	7794 (60.5)	2512 (62.7)*	4574 (63.6)*
	>15 mmol/l	5389 (41.8)	1780 (44.4)*	3269 (45.4)*
Blood glucose level [mmol/l], mean (SD)		10.0 (4.8)	10.1 (5.0)	10.2 (4.8)

N (%), number of patients and percentage over the total number of patients; n (%), number of admissions and percentage over the total number of admissions.
* Statistically significant difference compared to the pre-COVID-19 time period.

14.6 %, 16.8 % and 16.4 % respectfully). Similarly, COVID-19 infection itself may have led to greater hyperglycaemia and, indirectly, hypoglycaemia, through attempts to manage elevated blood glucose levels. However the increase in hypoglycaemia and hyperglycaemia was also seen in wave 1, prior to the widespread introduction of Dexamethasone (June 2020) as a treatment for COVID pneumonia. Other factors that may have led to the discrepancy in glycaemic control included the national healthcare regulations, that allowed only emergencies to be admitted; the fear of the patients for contracting Covid-19, that led to postponed appointments; and disruption of general and specialist diabetes services. A previous Diabetes UK study, interviewing healthcare professionals across the UK on their experiences of delivering in-patient diabetes care during the first wave of the pandemic, showed that some teams struggled to provide the same level of care, partly due to a lack of readily-available diabetes expertise where needed.[3]

In addition to changes in incidence of hyperglycaemia and hypoglycaemia, there was an increase in diabetic ketoacidosis in people with type 2 diabetes and newly diagnosed diabetes.[9]

Our study showed an increased length of stay for in-patients with diabetes during the pandemic. This was associated with the higher incidence of both hypoglycaemia and hyperglycaemia.

The strength of this study lies in the analysis of a unique dataset containing detailed information on the observation and treatment of in-patients with diabetes over a three-year period, before and during the COVID-19 pandemic.

The limitations stem from the nature of the dataset, which contains only information that is routinely collected within a hospital. It was not possible to determine, with sufficient reliability, the reason for hospitalisation, the severity of disease, or the medication taken by each patient prior to admission. However there was no significant difference in mean Albumin or Neutrophil levels which suggests a comparable degree of disease severity in the three time periods.

In conclusion, during the COVID-19 pandemic in the UK, we observed a higher incidence of both hypoglycaemia and hyperglycaemia which was associated with an increased length of stay for in-patients with diabetes. This highlights the need for a focus on improved diabetes care during further significant disruptions to healthcare systems and minimising the impact on in-patient diabetes services.

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CRediT authorship contribution statement

YR and RR co-designed the study analysis. YR carried out the data analysis. YR and RR drafted the manuscript. All authors contributed to the interpretation of the results and critical review of the paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Guarantor statement

YR and BG are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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