COVID-19 and dexamethasone-induced hyperglycaemia: Workload implications for diabetes inpatient teams

The RECOVERY trial showed that mortality in patients requiring supplementary oxygen or ventilation for COVID-19 is reduced by administration of dexamethasone 6 mg daily for up to 10 days.1 This welcome finding led to an increased frequency of dexamethasone use at our district general hospital. However, high-dose glucocorticoid exposure is a well-recognised cause of hyperglycaemia, particularly in the presence of diabetes.2–7 Furthermore, glucocorticoid-induced hyperglycaemia is associated with an increased risk of mortality, infections, and cardiovascular events.8 Guidelines have been developed to address these risks, both in the general inpatient setting and specifically in the context of COVID-19.9,10

After observing an increase in referrals for dexamethasone-related inpatient hyperglycaemia, and related complications, during the extended second wave of the COVID-19 pandemic, we decided to quantify the impact of this change in clinical practice on the workload of the diabetes specialist team. We conducted a retrospective audit, using ICD-10 codes to identify every inpatient episode at East Surrey Hospital with a coded diagnosis of COVID-19 whose admission started between 2 December 2020 and 2 February 2021 inclusive.

Overall, 1178 episodes included a positive SARS-CoV-2 RNA PCR test. Of these, the combination of ICD-10 codes U07.1, J12.8 and B97.2 identified 829 episodes of care, for 791 individual patients, that were coded as COVID-19 pneumonia, and medical records were reviewed in each case. A total of 186 patients did not require oxygen or ventilatory support and did not receive dexamethasone.

The remaining 605 patients ranged in age from 20 to 100 years, and all received dexamethasone therapy in accordance with the RECOVERY trial findings. Their clinical characteristics and outcomes are presented in Table 1.

A total of 141 (23%) had a pre-existing diagnosis of diabetes mellitus, of whom 103 (17% of population receiving dexamethasone; 73% of those with known diabetes) experienced worsening hyperglycaemia, defined as either a requirement for additional antidiabetic medication, or for titration of existing medication. Three men developed ketoacidosis, and one man and one woman developed hyperosmolar hyperglycaemic state (HHS). Among these five individuals who experienced severe acute diabetic emergencies as inpatients, all were known to have diabetes, but none had been treated with insulin prior to admission with COVID-19. There was one death, after HHS.

Of the 464 patients without a prior diagnosis of diabetes mellitus, 52 (11%) developed hyperglycaemia, defined as capillary blood glucose ≥11.1 mmol/L on two or more occasions, but none experienced ketoacidosis or HHS.

Amongst those with pre-existing diabetes, the risk of worsening hyperglycaemia was greater for men than for women (odds ratio 2.55; 95% confidence intervals 1.18 to 5.59; Fisher’s exact test p = 0.027; GraphPad Prism 8.4.3).

Conversely, there was no statistically significant sex difference in risk of hyperglycaemia for patients without a prior diagnosis of diabetes (Fisher’s exact test p = 0.659).

A networked blood glucose monitoring system at our hospital allows the diabetes specialist inpatient team to identify patients with dysglycaemia without requiring direct referral between teams. A total of 128 separate visits by the inpatient diabetes team were triggered, to assist in the management of 59 patients. Other inpatients were managed by their existing teams. After discharge from hospital, 47 patients had persisting hyperglycaemia, 39 of whom were referred to primary care for follow-up. Another eight patients required a total of 14 clinic visits or telephone contacts with the diabetes specialist team to monitor and adjust antidiabetic medication.

Decisions on which individuals required specialist follow-up, and which could safely be managed in primary care, were based mainly on local knowledge of the resources available in each general practice surgery. An ongoing requirement for injectable therapy characterised most of the individuals followed up in the specialist clinic but did not preclude successful discharge to primary care. Age, HbA1c and estimated glomerular filtration rate were similar for both groups.

To the best of our knowledge, this brief study is the first published account of the increased workload experienced by diabetes specialist inpatient teams during the...
COVID-19 pandemic. In the 4 months prior to the data collection period, during which there were relatively few admissions with COVID-19, the average time spent per month on inpatient referrals was 56.4 h, whereas in the subsequent 4 months, the average was 73.7 h, representing an increase of 31%.

In addition to delivering direct inpatient care under difficult circumstances, we provided remote inpatient clinical advice, training for hospital colleagues and a modified outpatient service. We speculate that other centres have had similar experience of increased workload in recent months and offer these data for use in future pandemic planning.

**Note on codes used to identify cases:**
- U07.1: Emergency use of U07.1 [identifies every instance of SARS-CoV-2 RNA PCR positive test].
- J12.8: Other viral pneumonia.

**ACKNOWLEDGEMENTS**
We acknowledge the kind assistance of Clinton Krynie, Information Services Manager, Surrey & Sussex Healthcare NHS Trust, in compiling the list of patients.

**CONFLICT OF INTEREST**
None.

**TABLE 1**  Characteristics, outcomes and follow-up requirements of inpatients prescribed dexamethasone for COVID-19 pneumonia

| Inpatients prescribed dexamethasone for COVID-19 pneumonia | Total (N = 605) | Known diabetes (n = 141) | No known diabetes (n = 464) |
|----------------------------------------------------------|----------------|--------------------------|-----------------------------|
| Denominator                                              | 605            | 93                       | 251                         |
| **Outcome of admission**                                 |                |                          |                             |
| Discharged alive                                         | 429 (71)       | 61 (66)                  | 187 (75)                    |
| Deceased                                                 | 176 (29)       | 32 (34)                  | 64 (25)                     |
| New or worsening hyperglycaemia                          | 155 (26)       | 74 (80)                  | 30 (12)                     |
| **Acute hyperglycaemic complications**                   |                |                          |                             |
| Ketoacidosis                                             | 3 (0.5)        | 3 (3.2)                  | 0 (0.0)                     |
| Hyperosmolar hyperglycaemic state                        | 2 (0.3)        | 1 (1.1)                  | 1 (2.1)                     |
| **Hyperglycaemia outcome**                               |                |                          |                             |
| Resolved during admission                                | 155 (43)       | 74 (48)                  | 30 (25)                     |
| Unresolved by time of discharge                          | 67 (30)        | 24 (32)                  | 15 (50)                     |
| N/A (patient deceased)                                   | 40 (26)        | 23 (31)                  | 7 (23)                      |
| Unknown                                                  | 1 (0.6)        | 0 (0.0)                  | 0 (0.0)                     |
| **Additional medication for hyperglycaemia**             |                |                          |                             |
| Oral hypoglycaemic agent                                 | 14 (9.0)       | 6 (8.1)                  | 4 (13)                      |
| Insulin                                                  | 99 (64)        | 58 (78)                  | 15 (50)                     |
| Insulin and oral hypoglycaemic agent                     | 16 (10)        | 10 (14)                  | 1 (3.3)                     |
| Monitored without treatment                              | 26 (17)        | 0 (0.0)                  | 10 (33)                     |
| **Inpatient diabetes specialist team involvement**       |                |                          |                             |
| Patients requiring ward visits                           | 59 (38)        | 34 (46)                  | 6 (20)                      |
| Number of ward visits                                    | 128 (N/A)      | 83 (N/A)                 | 10 (N/A)                    |
| **Outpatient clinic follow-up**                          |                |                          |                             |
| Patients requiring outpatient appointments                | 8 (5.2)        | 6 (8.1)                  | 1 (3.3)                     |
| Number of outpatient appointments (remote and/or in person) | 14 (N/A) | 11 (N/A) | 2 (N/A) |

Note: Data are n (%); denominators for percentages are indicated in each column.

B97.2: Coronavirus as the cause of diseases classified to other chapters [attributes SARS-CoV-2 infection as the cause of J12.8].

Younes R. Younes
Susan Stockley
Lorna Keegan
Linda O’Donoghue
REFERENCES

1. RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med*. 2021;384:693-704.

2. Dashora UK, Taylor R. Maintaining glycaemic control during high-dose prednisolone administration for hyperemesis gravidarum in Type 1 diabetes. *Diabet Med*. 2003;21:298.

3. Kim SY, Yoo C-G, Lee CT, et al. Incidence and risk factors of steroid-induced diabetes in patients with respiratory disease. *J Korean Med Sci*. 2011;26:264-267.

4. Pilkey J, Streeter L, Beel A, Hiebert T, Li X. Corticosteroid-induced diabetes in palliative care. *J Palliat Med*. 2012;15:681-689.

5. Rowbottom L, Stinson J, McDonald R, et al. Retrospective review of the incidence of monitoring blood glucose levels in patients receiving corticosteroids with systemic anti-cancer therapy. *Ann Palliat Med*. 2015;4:70-77.

6. Breakey S, Sharp SJ, Adler AI, Challis BG. Glucocorticoid-induced hyperglycaemia in respiratory disease: a systematic review and meta-analysis. *Diabetes Obes Metab*. 2016;18:1274-1278.

7. Jeong Y, Han HS, Lee HD, et al. A pilot study evaluating steroid-induced diabetes after antiemetic dexamethasone therapy in chemotherapy-treated cancer patients. *Cancer Res Treat*. 2016;48:1429-1437.

8. Delfs N, Struja T, Gafner S, et al. Outcomes of hospitalized patients with glucocorticoid-induced hyperglycemia—a retrospective analysis. *J Clin Med*. 2020;9:4079.

9. James J, Roberts A, Dhatariya K, on behalf of the Joint British Diabetes Societies for Inpatient Care Group. *Management of hyperglycaemia and steroid (glucocorticoid) therapy, revised May 2021 (JBDS 08)*. Available at https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group. Accessed August 12, 2021.

10. Rayman G, Lumb AN, Kennon B, et al. Dexamethasone therapy in COVID-19 patients: implications and guidance for the management of blood glucose in people with and without diabetes. *Diabet Med*. 2021;38:e14378.