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# Characteristics of patients with diabetes hospitalised for COVID-19 infection-a brief case series report

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ABSTRACT

*Objectives:* Diabetes has been shown to be a risk factor for corona virus disease-2019 (COVID-19) infection. The characteristics of patients with diabetes vulnerable to this infection are less specified. We aim to present the characteristics of patients with diabetes admitted to hospital with COVID-19.
*Design:* A retrospective case series.
*Setting:* A single clinical centre in the UK.
*Methods:* We have retrospectively collected the demographics, medical characteristics and outcome of all patients with diabetes admitted to hospital over two-week period with COVID-19 infection. All cases were diagnosed by a reverse transcription polymerase chain reaction (RT-PCR) of pharyngeal and nasal swabs.
*Results:* A total of 71 COVID-19 patients were admitted during the study period of whom 16 (22.5%) patients had diabetes and were included in this case series. There was no significant difference between patients with compared to those without diabetes regarding age, gender or clinical presentation. However, comorbidities were more common in patients with diabetes specially hypertension {75% v 36.4%, a difference of 38.6%, 95% confidence interval (CI) 6.5–58.3} and chronic kidney disease (37.5 v 5.5, a difference of 32% (1.6–51.6). Patients with diabetes were significantly more obese than those without diabetes (56.2% v 21.8% a difference of 34.4%, 95% CI 7.7–61.1). About one third (31.3%) of patients with diabetes were frail. Mean {standard deviation (SD)} duration of diabetes was 10 (2.8) years and mean (SD) HbA1c was 60.3 (15.6) mmol/mol. The use of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and non-steroidal

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anti-inflammatory drugs (NSAIDs) was common (37.5%, 25% and 18.8% respectively). There was no significant difference in the outcomes between patients with compared to those without diabetes.

*Conclusion:* Patients with diabetes hospitalised for COVID-19 were significantly more obese and had high prevalence of comorbidities than those without diabetes. Other features of patients with diabetes and COVID-19 infection included long duration of diabetes, less tight glycaemic control and common use of ACE inhibitors, ARBs and NSAIDs.



## 1. Introduction

In December 2019, a pneumonia like illness was first reported in Wuhan-China caused by a new coronavirus named corona virus disease-2019 (COVID-19) which then spread to cause a global pandemic [1]. In the Chinese cohorts, diabetes mellitus appeared to be a risk factor for COVID-19 infection. A meta-analysis of 8 Chinese studies to assess the prevalence of comorbidities in 46,248 infected patients with COVID-19, median age 46.0 years (51.6%) men, diabetes mellitus was the second most prevalent comorbidity (8%) after hypertension (17%) and higher than cardiovascular (5%) and respiratory diseases (2%) [2]. Also diabetes appeared to be detrimental in predicting worse outcomes. Patients infected with COVID-19 who required intensive care unit (ICU) treatment were more likely to have diabetes (22.2% V 5.9%) compared to those who did not require ICU admission [3]. Presence of diabetes increased mortality from COVID-19 compared to patients without comorbidities (7.3% V 0.9%) [4]. In addition to the Chinese studies, subsequent international studies have demonstrated that diabetes was a frequent comorbidity and a risk factor for adverse outcomes of COVID-19 infection such as higher rates of ICU admissions and refractoriness to anti-viral and anti-inflammatory therapies [5–8]. The high risk of COVID-19 infection in patients with combined hypertension and diabetes has been now highlighted in the literature which may be related to the fact that the severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is a cause of endothelial dysfunction and endothelial dysfunction could represent a common link between hypertension, diabetes and COVID-19 [9]. The criteria of patients with diabetes infected with the COVID-19 virus are less specified. In this brief analysis, we report the characteristics of 16 patients with diabetes admitted to hospital in the UK with COVID-19 infection.

## 2. Methods

### 2.1. Design

A retrospective single-centre case report enrolling consecutive patients with diabetes admitted to a District General Hospital in the UK with COVID-19 infection from the period of 23rd of March to 4th of April 2020. Identification of cases with diabetes was verified by the confirmed diagnosis in medical records or by the use of hypoglycaemic medications. Identification of COVID-19 status was undertaken in line with Public Health England (PHE) which recommends screening of cases if they present with clinical or radiological evidence of pneumonia, acute respiratory distress syndrome or influenza like illness associated with fever and additional respiratory symptom of persistent cough, hoarseness of voice, nasal discharge, shortness of breath, sore throat, wheezing and sneezing [10].

### 2.2. Case confirmation

Patients meeting the above criteria then had nasopharyngeal and oropharyngeal swabs sent to our local laboratory for identification of 2019-nCoV nucleic acid by reverse transcription polymerase chain reaction (RT-PCR). Patients who tested negative by RT-PCR but still have a high index of clinical suspicion were re-tested with a further swab for RT-PCR.

### 2.3. Data collection

Medical records were reviewed and patients' demographic, medical and social history was collected. Laboratory and radiological information were available in the electronic records. We used a standardised data collection sheet which was used by the authors to capture all the relevant information for each patient. To assess frailty, we used the clinical frailty score (CFS) which classifies patients in a range of very fit (score 1) to terminally ill (score 9) [11]. As the study was retrospective, only available data in medical records were collected but other relevant tests, which are not routinely done in our practice, such as IL-6 and cardiac enzymes were not available and this was a limitation of this study. We used descriptive statistics and calculated 95% confidence interval for comparison between proportions. Patients outcomes such as discharged alive from hospital, died or required ICU admission were extracted from electronic medical records. Study was approved by our local research and development department.

## 3. Results

A total of 71 consecutive patients with COVID-19 infection were admitted to hospital during data collection over two-week period, of whom 16 (22.5) patients had diabetes mellitus. Demographics of patients with diabetes are displayed in Table 1. All patients were White British, had type 2 diabetes, mean (SD) age 70.5 (16.6) years, majority (12 patients, 75%) were ≥65 years old and predominantly men (9, 56.3%). Source of infection was not very clear in most patients, but no

**Table 1 – Patients characteristics.**

| | |
|---|---|
| Total number | 16 |
| Duration of diabetes | |
| *Mean (SD)* | 10 (2.8) |
| *Range* | 5–15 |
| HbA1c | |
| *Mean (SD)* | 60.3 (15.6) |
| *Range* | 40–88 |
| *Patients (%) > 58.5 mmol/mol* | 10 (63) |
| Total cholesterol | |
| *Mean (SD)* | 3.7 (1.1) |
| *Range* | 1.2–5.8 |
| HDL | |
| *Mean (SD)* | 1.2 (0.5) |
| *Range* | 0.47–1.9 |
| Triglycerides | |
| *Mean (SD)* | 1.9 (1.0) |
| *Range* | 0.47–3.8 |
| LDL | |
| *Mean (SD)* | 1.8 (0.6) |
| *Range* | 0.5–3.4 |
| RBG on admission | |
| *Mean (SD)* | 10.2 (2.9) |
| *Range* | 4.9–15.4 |
| SBP on admission | |
| *Mean (SD)* | 141.8 mmHg |
| *Range* | 97–198 mmHg |
| Number of medications | |
| *Mean (SD)* | 9.9 (3.9) |
| *range* | 4–16 |
| Hypoglycaemic therapy (%) | |
| *Oral only* | 11 (68.7) |
| *Insulin plus oral* | 5 (31.3) |
| Use of RAAS inhibitors (%) | |
| *ACEI* | 6 (37.5) |
| *ARBs* | 4 (25) |
| *NSAIDs* | 3 (18.8) |
| Oral hypoglycaemic medications | |
| *Metformin* | 6 (37.5) |
| *Gliclazide* | 4 (25.0) |
| *Linagliptin* | 3 (18.8) |
| *Sitagliptin* | 2 (12.5) |
| *Empagliflozin* | 2 (12.5) |

SD = Standard deviation, RBG = Random blood glucose, SBP = Systolic blood pressure.

patient reported animal contact, which may suggest that all infections were due to human to human transmission. Two patients reported recent travel to Spain and to a Mediterranean cruise respectively. Pre-existing comorbidities were present in 100% of patients with diabetes with a mean (SD) of 4.4 (1.8). All patients with diabetes were either overweight (7, 43.7%) or obese (9, 56.3%). About one third of patients (5, 31.3%) scored $\geq$ 5 in CFS indicating frailty. Mean (SD) duration of diabetes was 10 (2.8) years and about one third of patients (5, 31.3%) were on insulin treatment in addition to oral hypoglycaemic therapy. The use of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and non-steroidal anti-inflammatory drugs (NSAIDs) was common {6 (37.5%), 4 (25%) and 3 (18.8%) respectively}. Diabetes tended to be uncontrolled with a mean (SD) HbA1c of 60.3 (15.6) mmol/mol and 10 (63%) patients had HbA1c > 58.5 mmol/mol. Common presenting symptoms were fever (11 patients, 68.8%), general fatigue (10, 62.5%), cough (9, 56.3%), shortness of breath (8, 50%), gastrointestinal symptoms (7, 43.7%) and acute confusion (3, 18.8%). One patient presented with diabetic ketoacidosis. In comparison to those without diabetes, patients with diabetes had significantly higher prevalence of hypertension (75% v 36.4%, a difference of 38.6%, 95% CI 6.5–58.3) and chronic kidney disease (37.5 v 5.5, a difference of 32% (1.6–51.6). Patients with diabetes were significantly more obese than those without diabetes (56.2% v 21.8% a difference of 34.4%, 95% CI 7.7–61.1). Majority of patients had abnormal opacifications in the chest X-ray and abnormal systemic laboratory results. Comparison of patients with to those without diabetes is summarised in Table 2. All patients with diabetes were treated in acute medical wards and no patients were escalated to ICU. Supportive care was the only therapy given and no specific antiviral treatment was tried in this cohort. Most patients (12, 75%) had recovered fully and discharged home but 4 (25%) patients have died. The patients who died were not considered for ICU admission or escalation plans due to the severity of illness and their comorbidity burden.

## 4. Discussion

We present 16 case series with type 2 diabetes admitted to hospital with COVID-19 infection. In the Chinese COVID-19 affected patients, diabetes was found to be a risk factor for infection but the characteristics of patients with diabetes vulnerable to this infection have not been specified. Our cohort represented 22.5% of all COVID-19 patients admitted during study period. Diabetes prevalence has been shown to be 16% in one study and 12% in another [12,13]. We aimed to collect clinical data on these patients including their clinical presentations, laboratory findings, metabolic profile and their progression. Our cohort had a mean age of 70.5 years and 75% of patients were $\geq$65 years, which appears to be older than the Chinses cases that have a median age of 46.0 years and only 44.1% of them were above the age of 60 years [4]. About half of our patients presented with respiratory symptoms (fever 68.8%, cough 56.3% and shortness of breath 50%). Most prominent was the general non-specific symptoms of being generally unwell or fatigued (62.5%) and gastrointestinal symptoms (43.7%). Of note, gastrointestinal symptoms were not common in the Chinese population for example only 3.8% had diarrhoea [12]. Although in another Chinese study by Wang et al, 10% of patients initially presented with nausea and diarrhoea 1–2 days before the onset of fever and dyspnoea [3]. Metabolic profile showed that our patients had uncontrolled and long duration of diabetes. Poor glycaemic control may be associated with impairment of the immune response to viral infections and may predispose to potential secondary bacterial infections [14]. The most striking feature was that all patients were either overweight or obese. Obesity is a risk factor for severe infection [15]. It has been shown that obesity is associated with the severity and the longer duration of viral infections [16]. Central obesity, which is the predominant type in persons with diabetes, is particularly associated with higher risk. The increased

**Table 2 – Characteristics of patients with compared to those without diabetes.**

| Parameter (%) | Patients with diabetes (%) | Patients without diabetes (%) | Difference (95% CI) |
|---|---|---|---|
| Number of patients | 16 (22.5) | 55 (77.5) | |
| Age (Y) | | | |
| ● Range | 35–90 | 26–97 | |
| ● ≥65 | 12 (75) | 40 (72.7) | 2.3% (−20.9 to 25.5) |
| Gender, male | 9 (56.3) | 32 (58.2) | −1.9% (−25.8 to 29.4) |
| Comorbidities (%) | | | |
| ● Any comorbidity | 16 (100) | 44 (80) | 20.0% (15.5–39.1)* |
| ● Hypertension | 12 (75) | 20 (36.4) | 38.6% (6.5–58.3)* |
| ● COPD | 7 (43.8) | 17 (30.9) | 12.9% (−25.5–26.1) |
| ● CVD | 6 (37.5) | 18 (32.7) | 4.8% (−33.2 to 21.0) |
| ● CKD | 6 (37.5) | 3 (5.5) | 32% (1.6–51.6)* |
| ● CLD | 3 (18.8) | 3 (5.5) | 13.3% (−12.4 to 22.8) |
| ● Dementia | 3 (18.8) | 7 (12.7) | 6.1% (−15.0 to 27.2) |
| ● CFS | | | |
| ○ Range | 2–7 | 1–7 | |
| ○ ≥5 | 5 (31.3) | 22 (40) | −8.7% (−23.6 to 28.0) |
| BMI (%) | | | ○ |
| 25–30 | 7 (43.7) | 13 (23.6) | |
| >30 | 9 (56.3) | 12 (21.8) | |
| Presentation (%) | | | |
| ● Fever | 11 (68.8) | 31 (56.4) | 12.4% (−22.8 to 31.4) |
| ● Hypoxia | 10 (62.5) | 37 (67.3) | −4.8% (−28.0 to 25.8) |
| ● Tachypnoea | 12 (75) | 41 (74.6) | 0.4% (−26.9 to 28.7) |
| ● Tachycardia | 6 (37.5) | 17 (27.3) | 10.2% (−16.3 to 36.7) |
| ● AKI | 6 (37.5) | 16 (29.1) | 8.4% (−18.5 to 34.3) |
| ● Acute hepatic impairment | 4 (25.0) | 22 (40) | 15% (−16.9 to 32.3) |
| ● High CRP | 12 (75) | 45 (81.8) | −6.8% (−16.7 to 20.7) |
| ● Leucocytosis | 2 (12.5) | 13 (23.6) | −10.1% (−29.8 to 9.6) |
| ● Lymphopenia | 11 (68.8) | 41 (74.6) | −5.8% (−31.9 to 31.9) |
| ● CXR opacification | 10 (62.5) | 24 (43.6) | 18.9% (−8.2 to 46.0) |
| Outcomes | | | |
| ● Discharged home | 12 (75) | 36 (65.5) | 9.5% (−15.2% to 34.2) |
| ● ICU admission | 0 | 9 (15) | −9% (−18.4 to 0.4) |
| ● Died | 4 (25) | 19 (34.6) | −9.6% (−34.3 to 15.1) |

CI = Confidence interval, COPD = Chronic obstructive pulmonary disease, CVD = Cardiovascular disease, CKD = Chronic kidney disease, CLD = Chronic liver disease, CFS = Clinical frailty score, BMI = Body mass index, AKI = Acute kidney injury, CRP = C-reactive protein, CXR = Chest X-ray, ICU = Intensive care unit. *Significant difference.

secretion of cytokines characterises a chronic low-grade inflammation in central obesity and may induce an impaired immune response [15]. Other factors may be related to the fact that obesity may mechanically impair ventilation with reduced aeration of the lung bases that leads to accumulation of secretions and increased risk of infections [17]. Similar to our case series, a study from New Jersey has demonstrated that COVID-19 infection is associated with hyperglycaemia and obesity [18]. Also, in a small study of 49 outpatients with diabetes and COVID-19, the reported median BMI was 33.9 and a range that reaches as high as 63.9 Kg/m$^2$ [19]. The prevalence of hypertension was a common finding in our cohort (12 patients, 75%) and most patients used either ACE inhibitors or ARBs. Hypertension was also the most common (17%) comorbidity found in the Chinese population infected with COVID-19 [2]. Although less prevalent than in our cohort, but this is likely to be due to the fact that all our patients are diabetic and diabetes usually coexists with other cardiovascular diseases especially hypertension which has been shown to be associated with worse outcomes in COVID-19 [20–23]. Is not clear whether hypertension itself increases the risk of infection or it is due to the fact that many hypertensive patients are using ACE inhibitors or ARBs. The COVID-19 virus gains entry to the pulmonary cells through binding to membrane ACE2 receptors. The ACE inhibitors and ARBs appear to increase ACE2 receptors expression and may increase COVID-19 infectivity and illness severity [24]. The concentration of glycated SARS-CoV-2 viral particles and glycated ACE2 in the lung epithelium may explain the severity of COVID-19 infection. Binding of ACE2 by SARS-CoV-2 in COVID-19 also suggests that prolonged uncontrolled hyperglycaemia, and not just a history of diabetes mellitus, may be important in the pathogenesis of the disease [25]. On the contrary to this, these medications may reduce the pulmonary and systemic inflammatory response by decreasing cytokines and therefore may be beneficial [26]. Recent data from a small Italian study of 62 patients with COVID-19 has demonstrated that antihypertensive therapy of ACE inhibitors, ARBs or calcium channel blockers did not affect the outcome. Therefore, this issue remains needing further exploration in future larger studies [27]. We did not demonstrate higher mortality in our diabetes cohort compared to those without diabetes. This could be due to the small study sample. Also our cohort, although had overall less tightly controlled diabetes, their

admission random blood glucose was not grossly elevated. Data from the US showed that mortality rate was higher for patients with uncontrolled hyperglycaemia compared to those without hyperglycaemia. Also, hyperglycaemia related mortality was 41.7% compared to 14.8% for patients with diabetes but no hyperglycaemia suggesting that hyperglycaemia itself, rather than diabetes, played a crucial role in adverse outcome [28]. Also, a recent study has shown that insulin infusion to tighten blood glucose control in the immediate post-admission period was associated with a significant reduction of inflammatory cytokines and pro-coagulant state which may reduce the risk of disease progression [6]. About one third of our cohort was frail. Frailty is a syndrome that is characterised by multisystem dysregulation that leads to reduced physiologic reserve and increased risk of adverse health outcomes. Dysregulation in the innate and adaptive immunity also leads to chronic inflammation, increase in inflammatory markers and increased susceptibility to sever infections [29]. In a recent multicentre European cohort study, frailty, assessed by CFS, proportionately predicted mortality [30]. A limitations of this study is the small number of population included which may limit its generalisability. Also, no patients in our cohort was admitted to ICU, which may be just a reflection of the small study sample. Also of note, the cause of death in patients who died in this cohort was severe sepsis and these patients were not considered for further escalation to ICU treatment due to the perceived poor prognosis of their high comorbidity burden.

## 5. Conclusion

Patients with diabetes hospitalised for COVID-19 were significantly more obese and had higher prevalence of comorbidities, in particular hypertension and chronic kidney disease, than those without diabetes. Other features of patients with diabetes and COVID-19 infection include long duration of diabetes, less tight glycaemic control and the common use of ACE inhibitors, ARBs and NSAIDs.

## 6. Future perspectives

Preventative measures should continue to develop to improve the metabolic profile of people with diabetes to reduce their risk of infection. Overweight and obesity appeared to be a striking feature affecting all patients in this cohort. It is not yet clear whether the new weight reducing hypoglycaemic therapy will have an effect in reducing risk of infections in people with diabetes. Although a specific anti-viral drug is urgently required, a multi-target agent is also required to help regulate the dysregulated neuro-endocrine-immune system that is common in metabolic diseases including diabetes, cardiovascular disease, atherosclerosis, insulin resistance, hypertension, dyslipidaemia and obesity. Research is urgently required to develop protective vaccination. Due to vulnerability of the characterised group in our cohort these criteria should be considered in future vaccination programmes. The viral entry into the cell membrane through the ACE2 receptors needs further exploration and future trials are needed to investigate the role of the current blockers of angiotensin aldosterone pathway in viral infections. The role of hypoglycaemic medications such as dipeptidyl peptidase-4 (DPP-4) inhibitors, which may act as receptor for COVID-19 and the glucagon-like peptide-1 receptor agonist (GLP-1 RA), that may reduce inflammation, will need further investigation [31,32].

## 7. Key points

- Patients with diabetes hospitalised for COVID-19 are significantly more obese and had higher prevalence of comorbidities, in particular hypertension and chronic kidney disease, compared to those without diabetes.
- Other features of patients with diabetes at risk of COVID-19 infection include long duration of diabetes, less tight glycaemic control and common use of ACE inhibitors, ARBs and NSAIDs.
- Future research is still required to explore the role of hypoglycaemic medications in viral cell entry and relation to infection.

## Conflict of interest

No conflict of interest.

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