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BRIEF REPORT

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Medical morbidity and risk of general hospital admission associated with concurrent anorexia nervosa and COVID-19: An observational study

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Abstract

Objective: Investigate medical morbidity and risk of general hospital admission for patients with concurrent coronavirus disease 2019 (COVID-19) and anorexia nervosa (AN) who have not received severe acute respiratory syndrome coronavirus 2 vaccination.

Methods: United Kingdom eating disorders clinicians contributed to a database of patients with an eating disorder and COVID-19. We used this to investigate demography, symptoms, hospitalization, treatment, and outcomes for those with AN.

Results: We describe data for 49 patients (median age 21.5 years [interquartile range 17.0–33.5], 46 female) including 36 adults and 13 under-18-year-olds. Three (6.1% [95% confidence interval 1.3%–17.9]) were admitted to a general hospital. For this sample, the expected age-standardized hospital admission rate per COVID-19 case (based on the general population of England) was 2.6% and therefore not significantly different to the hospitalization rate we observed. Three (including two of those admitted to hospital) contracted pneumonia. One had severe pneumonia and was admitted to an intensive care unit. No deaths or use of mechanical ventilation were recorded.

Discussion: To our knowledge, this represents the first study investigating medical morbidity or frequency of hospitalization for patients with COVID-19 and AN. We did not find evidence that patients with AN are at increased risk of severe COVID-19.

Public Significance: Medical morbidity and risk of hospitalization associated with concurrent COVID-19 and anorexia nervosa (AN) had not, to our knowledge, been studied before. We used a database of patients with eating disorders and COVID-19 (to which United Kingdom clinicians had contributed) to investigate presentation, treatment, outcomes, and COVID-19 severity for those with AN and COVID-19. We did not find evidence that patients with AN are at increased risk of severe COVID-19.

KEYWORDS
anorexia nervosa, COVID-19, eating disorders, SARS-CoV-2

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported at the end of 2019 (Huang et al., 2020). By May 6, 2022, there had been more than 22 million laboratory-confirmed cases in the United Kingdom (UK) and 176,000 deaths within 28 days of a positive test result. Infection risk varies markedly by age, with highest case rates seen in children and young adults. In December 2021, cumulative case rates in females in England were 26.1% of those aged 10–14 years, 26.3% of those aged 15–19 years, and 23.1% of those aged 20–24 years, compared to only 6.9% of females aged 80–84 years (Gov.uk, 2022). Infection may be asymptomatic; symptoms may be mild, often involving fever, cough and anosmia. Moderate-to-severe disease involves pneumonia and infection can lead to critical complications such as sepsis, thrombosis, and severe acute respiratory distress syndrome (World Health Organization, 2021).

Patients with anorexia nervosa (AN) have been reported to show a range of immunological abnormalities, including those relating to the number and function of specific immune cells and the concentrations of certain immunoglobulins and cytokines, which for some specific cytokines are increased (Allende et al., 1998; Brown et al., 2008; Dalton et al., 2018; Gibson & Mehler, 2019; Wyatt et al., 1982). However, many studies included few participants and results are sometimes contradictory; it is also unclear how closely the findings correlate with the degree of malnutrition (Brown et al., 2008).

At the beginning of the COVID-19 pandemic there was concern among eating disorders clinicians in the UK that patients with AN would be at increased risk of severe COVID-19 (DeSarbo & DeSarbo, 2020; Walsh & McNicholas, 2020) and they were eligible for vaccination at a higher priority than others of the same age (Royal College of Psychiatrists, 2022). The aim of the present study was to ascertain medical morbidity and risk of general hospital admission associated with concurrent AN and COVID-19.

2 | METHODS

Early in the pandemic, a database was established of adults and children with eating disorders who developed COVID-19. The database was hosted by NHS England/Improvement (NHSE/I) (NHS England, 2021) and an advisory group with clinical and technical expertise was established to oversee the project. Clinicians from eating disorders services in the UK were invited to submit anonymized patient data. Eating disorders services in England were invited directly via email by NHSE/I and eating disorders psychiatrists across the UK were sent an invitation email using a listserv (electronic mailing list) maintained by the Faculty of Eating Disorders of the Royal College of Psychiatrists. Announcements inviting eating disorders clinicians to submit data for the project were placed on the websites of the Royal College of Psychiatrists and the British Eating Disorders Society, with a subsequent reminder notice. Data were collected between May 20, 2020 and May 11, 2021. The start date was the earliest the data collection could commence, and the end date was chosen due to the introduction of COVID-19 vaccination.

Data were received from 19 services; each submitted data for between 1 and 10 patients (median 2, inter-quartile range 1–5). Seventeen services described their caseload, which ranged from 12 to 1185 (median 15, IQR 12–208); some comprised only inpatient beds, while others included numerous outpatients. The proportion of cases submitted per caseload ranged from .002 (1 in 600) to .45 (10 in 22). In all cases, COVID-19 was ascertained by polymerase chain reaction (PCR) tests and clinicians confirmed eating disorder diagnoses as per

TABLE 1 Outcome measures

Outcome category	Outcome measure
Demographics	Age
	Gender
	Ethnicity
	Smoking status
Body mass data	Body mass index for adults
	Percent median body mass index for under-18-year-olds[a]
Anorexia diagnosis	Anorexia nervosa subtype
Comorbidities	Medical comorbidities
	Psychiatric comorbidities
COVID-19 onset and severity	World Health Organization severity of disease classification
	Setting of COVID-19 onset
Symptoms	Dry cough
	Breathlessness
	Sore throat
	Change in smell
	Change in taste
	Rhinorrhoea
	Headache
	Confusion
	Myalgia
	Fatigue
	Gastrointestinal symptoms
Treatments	Oxygen mask
	Intravenous infusion
	Antimicrobials
	Continuous positive airway pressure
	Noninvasive ventilation
	High-flow nasal oxygen
	Intermittent mandatory ventilation
	Extracorporeal membrane oxygenation

[a]Percent median BMI (%mBMI) was recorded for those aged under 18 years in preference to BMI due to variation with sex and age in the ratio between weight and height in childhood and adolescence (Golden et al., 2015).

TABLE 2 Sample demographics, comorbidities, COVID-19 severity, signs, symptoms, treatments, and investigation results for the 49 patients

Outcome category	Variable (*n* of non-missing responses)	Proportion (*n*)[a], unless otherwise specified
Demographic data	Adult (aged ≥18 years, *n* = 49)	73.5% (36)
	Age (*n* = 48) [median (inter-quartile range)]	21.50 (17.00–33.50)
	Gender (% male, *n* = 49)	6.1% (3)
	Ethnicity (*n* = 48)	White: 89.6% (43), Mixed or multiple ethnic groups: 2.1% (1), Asian or Asian British: 4.2% (2), Black, African, Caribbean, or Black British: 4.2% (2)
	Smoking status (*n* = 25)	Never smoked: 68.0% (17), Past smoker: 24.0% (6), Current smoker: 8.0% (2).
Body mass data	Body mass index for the 36 adults (median, IQR)	15.5 (13.9–16.7)
	Percent median body mass index for the 13 under-18-year-olds (median, IQR)	95.2 (92.45–94.0)
	Anorexia nervosa subtype (*n* = 49)	Restrictive type: 77.6% (38), Binge/purging type: 20.4% (10), Atypical: 2.0% (1)
Comorbidities	Medical comorbidities (*n* = 49)	2.0% (1) each for: Type 1 diabetes; human immunodeficiency virus, cerebrovascular accident, asthma, aspergillosis, epilepsy
	Psychiatric comorbidities (*n* = 49)	Depression: 17.6% (9), Autistic spectrum disorder 7.8% (4), Emotionally unstable personality disorder 3.9% (2), Obsessive compulsive disorder 3.9% (2), Post-traumatic stress disorder 3.9% (2).
COVID-19 onset and severity	Setting of COVID-19 onset (*n* = 49)	Community: 14.3% (7), Specialist eating disorders unit: 67.4% (33), Acute psychiatric ward: 12.2% (6), General hospital: 6.1% (3).
	World Health Organization severity of disease classification (*n* = 43)	Asymptomatic: 2.3% (1), Mild illness: 90.7% (39), Non-severe pneumonia: 4.7% (2), Severe pneumonia: 2.3% (1)
Symptoms	Dry cough (*n* = 40)	50.0% (20)
	Breathlessness (*n* = 37)	18.9% (7)
	Sore throat (*n* = 38)	26.3% (10)
	Change in smell (*n* = 35)	31.4% (11)
	Change in taste (*n* = 35)	28.6% (10)
	Rhinorrhoea (*n* = 34)	11.8% (4)
	Headache (*n* = 36)	36.1% (13)
	Confusion (*n* = 34)	2.9% (1)
	Myalgia (*n* = 36)	22.2% (8)
	Fatigue (*n* = 36)	75.0% (27)
	Gastrointestinal symptoms (*n* = 33)	6.1% (2)
Treatment[b]	Oxygen by mask (*n* = 31)	3.2% (1)
	Intravenous infusion (*n* = 31)	6.5% (2)
	Antimicrobials (*n* = 31)	Antivirals: 3.2% (1) Antibiotics: 3.2% (1) Antifungals: 3.2% (1)

[a]All percentages are of non-missing responses.
[b]We asked whether patients received continuous positive airway pressure, noninvasive ventilation, high-flow nasal oxygen, intermittent mandatory ventilation, or extracorporeal membrane oxygenation. No patient was reported to have received any of these.

standard clinical practice. We used these data to investigate medical morbidity and frequency of hospitalization associated with concurrent AN and COVID-19 (see Table 1 for outcome measures).

The Word Health Organization COVID-19 classification system in use at the time (World Health Organisation, 2020) was used to classify COVID-19 severity as uncomplicated illness, pneumonia or severe

pneumonia. COVID-19 admissions were defined as those with a primary or secondary diagnosis of COVID-19. Rate of hospital admission per case was compared to that of admission per case in the general population of England between May 20, 2020 and May 11, 2021. General population data were obtained from the gov.uk COVID-19 dashboard (https://coronavirus.data.gov.uk/) and were broken down by 5-year age bands and COVID-19 diagnosis with or without pneumonia.

In the UK, patients with severe mental illness were eligible for SARS-CoV-2 vaccination from February 15, 2021 (NHS England and NHS Improvement, 2021) and the present cohort were therefore likely all eligible for vaccination from this date. Data for 11 patients with AN was submitted sufficiently late for some to have potentially been vaccinated; we contacted each of these services to enquire about these patients' vaccination status at the time of their SARS-CoV-2 infection. None were known to have received a vaccination but two patients with AN may have been diagnosed after 15th February and their vaccination status is unknown.

2.1 | Statistical analysis

Data are described using median and interquartile range. We carried out indirect standardization to calculate the Standardized Admission per Case Ratio for the study population compared to the general population of England.

2.2 | Ethics

All data were submitted in a non-identifiable form and only routine clinical data were supplied. No additional investigation or assessment was carried for the purposes of this study. We sought advice from the NHS Health Research Authority, who confirmed that approval from a research ethics committee was not required.

3 | RESULTS

Data were obtained for 51 patients with AN; two of these patients were removed from analysis due to their vaccination status being unknown and having been diagnosed with COVID-19 sufficiently late to have potentially benefited from a vaccination on or after 15th February. Results are presented for the remaining 49 patients (Table 2). The median age of this sample was 21.5 years (interquartile range 17.0–33.5), and 46 were female.

3.1 | Hospital admissions

In our sample, three adult patients were admitted to hospital following a positive SARS-CoV-2 PCR test. Two of these patients had pneumonia and a third patient who had mild COVID-19 illness subsequently developed diabetic ketoacidosis and was transferred to a general hospital for treatment of this.

Of the general population of England, those who tested positive for SARS-CoV-2 between May 20, 2020 and May 11, 2021 had a 7.7% chance of being admitted to hospital generally, and a 4.2% chance of being admitted with pneumonia. If our sample of 49 patients with AN had the same age-standardized rate of hospital admissions per COVID-19 case as the general population of England, we would expect there to have been 1.27 (2.6%) admissions, and .57 (1.2%) admissions with pneumonia. In comparison, within our patient sample, three (6.1% [95% confidence interval 1.3–17.9]) were admitted to a general hospital, of whom two (4.1% [95% CI .5%–14.7%]) had pneumonia. We, therefore, found no significant increased risk of admission for the AN patient group compared to the general population.

3.2 | Patients with moderate or severe pneumonia

Of the three patients who contracted pneumonia, one was treated in a specialist eating disorders unit (SEDU) and was not admitted to a general hospital. A second patient, who also had aspergillosis, was transferred from an SEDU to a general hospital after experiencing breathing difficulties and remained there for around 12 h before being returned to the SEDU; the extent to which the pneumonia was caused by COVID-19 rather than aspergillosis is unknown. A third patient developed COVID-19 while on an SEDU before being admitted to an intensive care unit with severe pneumonia and encephalitis; this patient recovered following treatment that included acyclovir and co-amoxiclav and did not require mechanical ventilation.

4 | DISCUSSION

We describe the characteristics, treatments, hospitalizations, and outcomes of 49 patients with AN who contracted COVID-19 before May 11, 2021. While over 80% had mild or asymptomatic disease, three were diagnosed with pneumonia (although one of these also had aspergillosis), of whom two received treatment in a general hospital. A third patient was treated in a general hospital due to developing diabetic ketoacidosis following SARS-CoV-2 infection. Although we did not observe a statistically significant increased general hospital admission risk per case within the patient sample, compared to the general population of England, our study was not powered to make this comparison. Most (67.4%) of our sample contracted COVID-19 on an SEDU; this may have been due to COVID-19 being more likely to be detected and tested for in inpatient units than in the community.

The susceptibility of patients with AN to viral infection and infectious complications is an under-researched area (Simeunovic Ostojic et al., 2021) but our results are consistent with limited evidence that suggests that underweight patients with AN are not necessarily at greater risk from viruses than the general population (Armstrong-Esther et al., 1978; Brown et al., 2008; Dobner & Kaser, 2018; Raevuori et al., 2016). It has been suggested that this may partially be

explained by patients with AN exhibiting fewer symptoms such as fever in response to viral infection (Dobner & Kaser, 2018) but the prevalence of asymptomatic viral infection in patients with AN has not previously been investigated (Simeunovic Ostojic et al., 2021).

It is uncertain why the immunological abnormalities reported in AN do not seem to lead to increased vulnerability to severe infection with SARS-CoV-2 or other viruses. It may be that these abnormalities are simply not significant or consistent enough to have an impact on clinical infection. Alternatively, it is possible that high concentrations of pro-inflammatory cytokines protect against viral infection or that an impaired immune response reduces the inflammatory processes which are responsible for much of the pathophysiology of severe COVID-19 disease.

Despite expectations at the beginning of the COVID-19 pandemic, this study did not find evidence that patients with AN are at increased risk of severe COVID-19 disease. This may provide qualified reassurance to professionals and patients. During the COVID-19 pandemic hospitals and social care facilities introduced severe restrictions on visiting, as part of measures to control the spread of the virus. It is likely that implementation of similar measures will be considered during the next pandemic, whether that is influenza or a novel virus. Given the importance to psychological health of human interaction (Eslinger et al., 2021; Orben et al., 2020), it is essential that policymakers strive to ensure any future potential restrictions on social contact with vulnerable patients are proportionate to the level of risk.

This study has a number of limitations. The most significant is that, despite extensive efforts to encourage recruitment, the number of patients in the study was small. Most of the cases reported occurred in specialist inpatient eating disorders units, where SARS-CoV-2 infection was more likely to be identified than in the community, and the effect of SARS-CoV-2 infection on community patients with less severe AN is unknown. Furthermore, although we tried to inform as many colleagues as possible about the study, some patients with AN who contracted COVID-19 might not have been entered onto the database. Clinicians may have tended to provide data relating to more severe SARS-CoV-2 infections, due to these potentially being more salient to them than milder cases. A further limitation is the lack of a control group of participants with low BMI without AN. A strength of this study, however, is that it was conducted before the introduction of SARS-CoV-2 vaccination and therefore provides data that are not confounded by the effect of vaccination or specific drug treatment.

We have some suggestions for future research. A possible explanation for our findings is that patients with AN mount a relatively normal immune response to SARS-CoV-2 infection and it would be beneficial to investigate whether this is the case. Further research is also required to investigate the immunogenicity of SARS-CoV-2 vaccines in patients with AN and the susceptibility of vaccinated patients with AN to infection. It would also be worthwhile to investigate the immune response to other viruses in this patient group. In contrast to adult participants, %mBMI values for under-18-year-olds within our sample were mostly within the normal range and it would be useful to investigate the severity of COVID-19 in children and young people with low %mBMI.

AUTHOR CONTRIBUTIONS

Anthony P. Winston: Conceptualization; investigation; methodology; writing – original draft; writing – review and editing. **Michael J. Taylor:** Data curation; formal analysis; investigation; methodology; writing – original draft; writing – review and editing. **Hubertus Himmerich:** Investigation; validation; writing – original draft; writing – review and editing. **Mohammad A. A. Ibrahim:** Investigation; methodology; validation; writing – original draft; writing – review and editing. **Uju Okereke:** Investigation; methodology; validation; writing – original draft; writing – review and editing. **Robert Wilson:** Conceptualization; investigation; methodology; supervision; validation; writing – original draft; writing – review and editing.

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No funding was received for this study.

CONFLICT OF INTEREST

The authors have no conflicting interests to declare.

DATA AVAILABILITY STATEMENT

We did not obtain consent from participants for their data to be shared, therefore we are not able to share our study data.

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