What is the clinical course of patients hospitalised for COVID-19 treatment Ireland: a retrospective cohort study in Dublin's North Inner City (the 'Mater 100')

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Research Article

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Abstract

Background: Since March 2020, Ireland has experienced an outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To date, while several cohorts from China have been described, our understanding is limited, with no data describing the epidemiological and clinical characteristics of patients with COVID-19 in Ireland. To improve our understanding of the clinical characteristics of this emerging infection we carried out a retrospective review of patient data to examine the clinical characteristics of patients admitted for COVID-19 hospital treatment.

Methods: Demographic, clinical and laboratory data on the first 100 adult patients admitted to Mater Misericordiae University Hospital (MMUH) for in-patient COVID-19 treatment after onset of the outbreak in March 2020 was extracted from clinical and administrative records. Missing data were excluded from the analysis.

Results: Fifty-eight per cent were male, 63% were Irish nationals, 29% were GMS eligible, and median age was 45 years (interquartile range [IQR] =34-64 years). Patients had symptoms for a median of five days before diagnosis (IQR=2.5-7 days), most commonly cough (72%), fever (65%), dyspnoea (37%), fatigue (28%), myalgia (27%) and headache (24%). Of all cases, 54 had at least one pre-existing chronic illness (most commonly hypertension, diabetes mellitus or asthma). At initial assessment, the most common abnormal findings were: C-reactive protein >7.0mg/L (74%), ferritin >247µg/L (women) or >275µg/L (men) (62%), D-dimer >0.5µg/dL (62%), chest imaging (59%), NEWS Score (modified) of ≥3 (55%) and heart rate >90/min (51%). Twenty-seven required supplemental oxygen, of which 17 were admitted to the intensive care unit - 14 requiring ventilation. Forty received antiviral treatment (most commonly hydroxychloroquine or lopinavir/ritonavir). Four died, 17 were admitted to intensive care, and 74 were discharged home, with nine days the median hospital stay (IQR=6-11).

C**onclusion:** Our findings reinforce the emerging consensus of COVID-19 as an acute life-threatening disease and highlights, the importance of laboratory (ferritin, C-reactive protein, D-dimer) and radiological parameters, in addition to clinical parameters. Further cohort studies involving larger samples followed longitudinally are a priority.

Background

Since March 2020, Ireland has experienced an outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To date, while several cohorts from China have been described, our understanding is limited, with no data describing the epidemiological and clinical characteristics of patients with COVID-19 in Ireland. COVID-19 was declared a global pandemic on 11/3/2020[1]. As of 18 April 2020, **2,197,593 cases** of COVID-19 (in accordance with the applied case definitions and testing strategies in the affected countries) have been reported and 153,090 deaths worldwide [2]. As of the same date, in Ireland, 14,758 confirmed cases and 571 deaths, have been reported

[3]. In Ireland, the median age of people infected with COVID-19 is 48 years, 44% of those infected are male, and 2168 (16% of case) have been hospitalised, of whom 296 have been treated in Intensive Care Unit [3].

Most people are susceptible to COVID-19 infection[4 5]. Patients present with fever, cough, dyspnoea and fatigue, with some developing acute respiratory distress syndrome (ARDS), multi-organ damage and secondary bacterial infections[6 7]. Manifestations of COVID-19 infection vary according to disease severity and a person's characteristics [4 5 8]. Many are asymptomatic[9], some show mild to moderate symptoms[4 5], and some develop a severe, potentially life threatening illness involving ARDS, myocardial injury, and / or secondary bacterial infection [4 8]. COVID-19 infection is linked to a range of blood, cellular, and genetic abnormalities[4 5]. Those most at risk of severe illness as a result of infection include elderly males and/or people with underlying health conditions (e.g. hypertension, chronic heart disease, chronic lung disease and diabetes mellitus) [4 8 9]. Older age, elevated lactate dehydrogenase (LDH) and elevated D-dimer levels are also associated with adverse outcomes [10]. Results of clinical trials will inform best treatment approaches but results of these are pending[4].

A lot is known about the epidemiology of COVID-19 at a whole-population level in Ireland, as from mid-March 2020 Ireland's Government has reported on deaths, numbers hospitalised and number infected on a daily basis[11].

However, little is known about those who are hospitalised and clinical outcomes. To address this knowledge gap, we examined the baseline clinical characteristics, treatments and clinical outcomes among patients with COVID-19 receiving in-patient hospital treatment under the care of the Infectious Diseases department at our institution.

Methods

Setting

The study was conducted at the Mater Misericordiae University Hospital (MMUH). In addition to the local services for the catchment area, the hospital provides a range of frontline and specialist services on a regional and national level, treating 24,750 inpatients, 221,956 outpatients and 82,307 emergency department visits last year. The hospital is located in Dublin's north inner city with many of Ireland's most deprived neighbourhoods are situated in the hospital's catchment area. Reflecting this demographic, infectious diseases care locally has involved addressing communicable diseases such as HIV and hepatitis C in partnership with local communities. Most recently this has involved initiatives involving prisoners[12], homeless populations[13] and patients attending General Practice [14].

The MMUH Infectious Diseases Department contains the National Isolation Unit (NIU), a six-bed unit with isolation rooms under negative–pressure ventilation, donning and doffing areas of a high specification. During the 'Containment Phase' (January to March 2020), our strategy was to contain suspected/confirmed cases of COVID-19 in the NIU. During the 'Delay Phase', with rising numbers of

cases, the hospital established a 'COVID pathway', whereby unscheduled admissions with possible COVID infection were streamed in a parallel system with patients managed on dedicated wards by the team. Once patients were fit for discharge and had appropriate accommodation to self-isolate, they were discharged utilising a mobile health platform (Patient-M-Power®) to monitor their progress.

As in most hospitals in Ireland, from late March, patients were admitted under the care of a 'COVID Team', whereby one or all of Infectious Diseases, Respiratory Medicine, Acute Medicine, and Intensive Care specialties, among others, would input to patient care based on the predominant issue requiring clinical intervention.

Subjects

Patients admitted to the COVID pathway with SARS-CoV-2 detected by PCR were included.

Data collection and study instrument

Anonymised data was collected on baseline demographics, clinical parameters and health outcome measures from clinical records, including: age; gender; type of health insurance; dates of presentation, admission and discharge; presence of pre-existing morbidity or other illnesses at admission; subsequent clinical care; and treatment outcomes. This data was collected by a member of the clinical team (CC, BOK, SC, EOC, and JL) and anonymised to allow data analysis by the research team (SC, TMH, GA, and WC).

Data analysis

Frequency counts were presented in respect of categorical and ordinal data, and median / interquartile range (IQR) in respect of numerical data where such data was not normally distributed. We examined patient characteristics (e.g. age, gender, pre-existing morbidity [any], pre-existing cardiorespiratory morbidity[15], GMS status), findings on clinical assessment [e.g. National Early Warning Score (NEWS)[16] / NEWS2 Score[17]]) and laboratory parameters (e.g. lymphopaenia[18], D-dimer, CRP, ferritin, abnormal chest imaging). For laboratory results, we also assessed whether the measurements were outside the normal range. We used SPSS (version 26.0) for all analyses. If it was not possible to find data on clinical parameters this 'missing data' was treated in accordance with 'STROBE Guidance'[19]. As such, when reporting proportions for specific variables, the observed finding is presented as a percent of the total number of cases on whom data was available.

Ethical issues

In designing this study we have taken cognisance of best practice in conducting health research during times of major disasters[20]. Data was collected from clinical and administrative records by a member of the clinical team. All data was anonymised at the time of data collection. All anonymised data was stored as password protected files on a secure server at the University College Dublin Catherine McAuley

Research Centre, where it was analysed by the research team. The study was approved by the MMUH Research Ethics Committee (8th April 2020; reference 1/3782141).

Patient and public involvement

Due to the pandemic nature of Covid-19 it was not feasible to include patient and public involvement. Patients were not invited to comment on any aspect of the study design nor were they invited to contribute to the drafting or editing of this manuscript.

Results

Participants

By mid-April, 352 patients had been admitted to the COVID pathway, 163 of whom received hospital treatment and 189 received outpatient treatment. We present data in the first 100 adult in-patients admitted to Mater Misericordiae University Hospital for in-patient treatment of COVID-19 infection from time of disease outbreak in March 2020 to 1st April 2020.

With regards to patient characteristics (see Table 1) 58 (58%) were male, 55 (63%) were Irish nationals, 29 (59%) were GMS eligible and median age was 45 years (IQR=34-64 years). Eighty-three (88%) were reported as having community-acquired infection; 24 (25%) acquired the infection from household contacts, 13 (14%) from foreign travel, 10 (10%) from their occupation and seven (7%) from working in a healthcare setting. Fourteen patients worked in healthcare (16%).

Table 1 Patient Characteristics

Variable	*Characteristic*	n (% of total, where recorded)
Gender	Male	58 (58%)
	Female	42 (42%)
Medical cover	General Medical Scheme	29 (29%)
	Private	17 (17%)
	Hospital staff billing	3 (3%)
	None documented	51 (51%)
Nationality	Irish	55 (63%)
	Other	32 (37%)
	Not recorded	13
Occupation	Retired	16 (17%)
	Service industry/ Hospitality/ Retail	16 (17%)
	Unemployed	12 (13%)
	Healthcare	12 (12%)
	Homemaker	9 (10%)
	Student	7 (7%)
	Finance/ Legal/ Administration	7 (7%)
	Construction	5 (5%)
	Other	10 (11%)
	Missing data	6
Smoking status	Current / previous	21 (25.6%)
	Never	61(74.4%)
	Not recorded	18
Route of infection	Household	24 (25%)
	Foreign travel	13 (14%)
	Occupational	10 (10%)
	Healthcare	7 (7%)
	Unknown	42 (43%)
	Missing data	4

Descriptive data

Patients had symptoms for a median of five days before diagnosis (IQR=2.5-7 days), most commonly cough (72%), fever (65%), dyspnoea (37%), fatigue (28%), myalgia (27%), headache (24%), sore throat (15%), nausea (15%), diarrhoea (11%) and abdominal pain (10%) (See figure 1).

Fifty-four patients had at least one pre-existing chronic illness, with hypertension (16%), diabetes mellitus (12%), asthma (11%), dyslipidaemia (11%), chronic obstructive pulmonary disease (8%) and a chronic mental health condition (8%) the most commonly observed comorbidities. With regards to presenting features and initial assessment 25% of patients had oxygen saturations <96%, 37% had respiratory rate >24/min, 51% had heart rate >90/min, 32% had temperature >38.0ºC and 14% had systolic BP <111mmHg (see Table 2).

Table 2. Findings at initial assessment.

Variable	*Characteristic*	*n (% of total where recorded)*	*Abnormal*
Oxygen saturation	96+%	58 (75%)	Low 19 (25%)
	94-95%	8 (10.4%	
	92-93%	6 (7.8%)	
	<92%	5 (6.5%)	
	Missing data or already on O2 when measured	23	
Respiratory rate	12-20/min	56 (62.9%)	High 33 (37%)
	21-24/min	21(23.6%)	
	>24/min	12 (13.5%)	
	Missing	11	
Heart rate	51-90/min	43 (43%)	High 45 (51%)
	91-110/min	33 (33%)	
	111-130/min	12 (12%)	
	Missing	12	
Temperature	36.1-38.0 degC	54 (61%)	High 28 (32%)
	35.1-36.0 deg C	6 (7%)	
	38.1-39.0 deg C	23 (26%)	
	>=39.1 deg C	5 (6%)	
	Missing	12 =	
Systolic BP	111-149mmHg	64 (73%)	12 (14%)
	101-110mmHg	6 (7%)	
	>149mmHg	12 (14%)	
	91-100mmHg	5 (6%)	
	<91mmHg	1 (1%)	
	Missing	12	
NEWS score[16]	0	16 (18%)	NEWS ≥3 45 (51%) NEWS ≥7 9 (10%)
	1	16 (18%)	
	2	11 (12%)	
	3	17 (19%)	
	4	8 (9%)	
	5	7 (8%)	
	6	4 (5%)	
	7+	9 (10%)	
	Insufficient data	12	
NEWS2 score[17]	0	15 (17%)	NEWS2 ≥3 47(53%) NEWS2 ≥7 10 (11%)
	1	16 (18%)	
	2	11 (12%)	
	3	14 (16%)	
	4	8 (9%)	
	5	7 (8%)	
	6	8 (9%)	
	7+	10 (11%)	
	Insufficient data	11	
Modified NEWS for COVID-19[21]	0	14 (16%)	NEWS (modified) ≥3 48(55%) COVID NEWS≥7 17 (19%)
	1	15 (17%)	
	2	11 (12%)	
	3	10 (11%)	
	4	7 (8%)	
	5	6 (7%)	

	6	8 (9%)	
	7+	17 (19%)	
	Insufficient data	12	
Chest imaging	Recorded as normal	41 (41%)	59 (59%)
	Recorded as abnormal	59 (59%)	
	Missing data	0	

A NEWS score16 of ≥3 was recorded in 51%, with a NEWS2 score17 of ≥3 documented in 53% and a modified NEWS21 score ≥3 observed in 55% of patients. With regards to laboratory findings commonly observed abnormalities were: elevated levels of C-Reactive Protein (74%), ferritin (63%) and D-dimer (62%); 42% had a neutrophil / lymphocyte ratio of >3.5, 38% had lymphopaenia; and 15% and 25% had elevated levels of sodium and creatinine, respectively (see Table 3). All 100 had chest imaging; 59 (59%) had an abnormality reported, with bilateral infiltrates documented in 32 (32%) and focal changes in 12 (12%).

Table 3. Laboratory parameters.

Variable	*Characteristic*	*N (%)*	*Abnormal*
Neutrophils	<2.0 x10^9/ L	15 (15%)	Elevated 12 (12%)
	2.0-8.0 x10^9/L	73 (73%)	
	>8.0 x10^9/ L	12(12%)	
	Missing data	0	
Lymphocytes	<1.0	38 (38%)	Lymphopaenic 38 (38%)
	1.0-4.0	60 (60%)	
	>4.0	2 (2%)	
	Missing data	0	
Neutrophil / lymphocyte ratio	<0.8	6 (6%)	Elevated >3.5 42 (42%) >7 20 (20%)
	0.8-3.5	52 (52%)	
	>3.5	42 (42%)	
	Missing data	0	
Platelets	<150	15 (15%)	Thrombocytopaenic 15 (15%)
	150-400	81 (81%)	
	>400	4 (4%)	
	Missing data	0	
Creatinine	(F)<46 or (M)<65µmol/L	7 (7%)	Elevated 25 (25%)
	(F)46-86 or (M)65-107µmol/L	68 (68%)	
	(F)>86 or (M)>107µmol/L	25 (25%)	
	Missing data	0	
Urea	<2.8 mmol/L	8 (8%)	Elevated 18 (18%)
	2.8-8.6 mmol/L	73 (73%)	
	>8.6 mmol/L	18 (18%)	
	Missing data	1	
Sodium	<133mmol/L	15 (15%)	Hyponatraemic 15 (15%)
	133-145mmol/L	81 (83%)	
	>145mmol/L	2 (2%)	
	Missing data	2	
Potassium	<3.3 mmol/L	4 (4%)	Abnormal 6 (6%)
	3.3-5.0 mmol/L	89 (94%)	
	>5.0 mmol/L	2 (2%)	
	Missing data	5	
C-Reactive Protein	=<7.0mg/L	26 (26%)	>7 mg/l 73 (74%) >50 mg/l 37 (37%) >100 mg/l 23 (23%)
	>7.0mg/L	73 (74%)	
	>50mg/L	37 (37%)	
	>100mg/L	23 (23%)	
	Missing data	1	
D-dimer	=<0.5mcg/dL	29	>0.5mcg/dL 47 (62%) > 1mcg/dL 19 (25%)
	>0.5mcg/dL	47(62%)	
	>1.0mcg/dL	19 (25.0%)	
	Missing data	24	
Highly-sensitive cardiac troponin T	<5ng/L	26 (44%)	Elevated 8 (13%)
	5-7ng/L	7 (12%)	
	8-34ng/L	18 (30%)	
	>34ng/L	8 (13%)	
	Missing data	41	

Ferritin	(F) <8 or (M) <22 µg/L	1 (1.3%)	Elevated (F) >247 or (M) >275µg/L 48 (63.2%) >1,000ug/L 21 (27.6%)
	(F) 8-247 or (M) 22-275µg/L	27 (35.5%)	
	(F) >247 or (M) >275µg/L	48 (63.2%)	
	Ferritin > 1000ug/L	21 (27.6%)	
	Missing data	24	
Alanine aminotransferase (ALT)	<55.0 iU/L	78 (80%)	Elevated 20 (20%)
	>=55.0 iU/L	20 (20%)	
	Missing data	2	

Outcomes

Twenty-seven required supplemental oxygen, of whom 17 were admitted to the intensive care unit - 14 requiring ventilation. Forty received antiviral treatment, most commonly hydroxychloroquine (35%) and lopinavir/ritonavir (16%). Complications documented in the clinical record included: ARDS, diarrhoea / gastrointestinal complaints and acute kidney injury. Four people died and 74 people were discharged home. The median length of hospital stay was nine days (IQR=6-11).

Discussion

Key results

Our findings reinforce the consensus that COVID-19 is an acute, life threatening disease that is associated with considerable mortality. The study highlights the importance of clinical, laboratory and radiological parameters in assessing disease severity. At admission, the most common abnormalities identified among our cohort were elevated levels of C-reactive protein, ferritin, D-dimer, abnormal chest imaging, a NEWS Score (Modified) of ≥3 and tachycardia.

Correlation with other centres' experiences

To date, most data on COVID-19 disease has been reported from China although in recent weeks literature has started to emerge from Europe and the United States (Table 4). The baseline clinical characteristics of our population show striking similarities to those reported in studies from China, with regards in particular to male predominance, high prevalence of cough and fever, blood test abnormalities (including lymphopenia and elevated CRP, ferritin and D-dimer levels) and high frequency of abnormalities on chest imaging[10 22-25]. Cohorts reported from outside of China (e.g. Korea, Europe and United States) also identified these findings [26-30].

Table 4. Summary of studies reporting cohorts of patients requiring in-patient hospital treatment (search conducted 15th April 2020)

Study	Population	Comorbidities	Presentation	Transmission	Labs	Treatment	Imaging	Severity/ Outcome
China (Wuhan)								
Zhou et al[9] Jin Yin-tan Hospital and Wuhan Pulmonary Hospital (Wuhan, China) Retrospective multicentre cohort study January 2020	N=191 Median age 56 (IQR 46-67) Female 72(38%) Male 119(62%)	91 (48%) HTN (30%) DM (19%) CAD (8%) Smoker 11(6%) COPD 6(3%)	Median 11 days (8-14) until hospital presentation Fever 180(94%) Cough 151(79%) Sputum 44(23%) Fatigue 44(23%) Myalgia 29(15%) Diarrhoea 9(5%) Nausea 7(4%)	No data	Lymphopenia (40%) Anaemia 29 (15%) Platelets <100 13 (7%) ALT >40 U/L 59 (31%) Troponin >28 pg/ml 24 (17%) D-dimer >0.5 to ≤1 45 (26%) >1 72 (42%) Ferritin >300 µ/L 102 (80%)	Antibiotics 181(95%) Antiviral treatment (LPV/r) 41(21%) Corticosteroids 57(30%) IVIG 46(24%) HFNC 41(21%) NIV 26(14%) IMV32(17%) ECMO 3(2%)	Consolidation 112 (59%) Ground-glass opacity 136 (71%) Bilateral pulmonary infiltration 143 (75%)	In-patient deaths n=54 Discharged n=137 (No active in-patients included) General 72 (38%) Severe 66 (35%) Critical 53 (28%) Sepsis 112(59%) Respiratory failure 103(54%) ARDS 59(31%) ICU 50(26%)
Wang et al[21] Zhongnan Hospital of Wuhan University (Wuhan, China) Retrospective single centre case series January 2020	N=138 Median age 56 (IQR 42-68) Female 63(45.7%) Male 75 (54.3%)	64 (46.4%) HTN 43(31.2%) CV disease 20(14.5%) DM 14(10.1%) Malignancy 10(7.2%) COPD 4(2.9%)	Median 7 days (4-8) until hospitalisation, 10 days (IQR 6-12) to ICU Fever 136(99%) Fatigue 96(70%) Dry cough 82(60%) Anorexia 55(40%) Myalgia 48(35%) Dyspnoea 43(31%)	Hospital acquired 57(41.3%) HCW 40(29%) Hospitalised patients 17(12.3%) Community acquired 81(58.7%)	Lymphopenia 97(70.3%) Prolonged PT 80(58%) Raised LDH 55(40%)	Antibiotics - moxifloxacin 89(64%) - ceftriaxone 34(24.6%) - azithromycin 25(18.1%) Antiviral treatment (oseltamivir) 124(90%)	Bilateral patchy shadows or ground glass opacity on CT imaging in all patients n=138	In-patient deaths n=6(4.3%) Discharged n=47(34%) Active in-patients n=85 acute cardiac injury 10(7.2%) Shock 11(30.6%)

			Sputum 37(27%) Pharyngitis 24(17%) Diarrhoea 14(10%) Nausea 14(10.1%)			Corticosteroids 62 (44.9%) OT 106(76.8%) NIV 15(10.9%) IMV 17(12.3%) ECMO 4(2.9%)		Arrythmia 16(44.4%) ARDS 22(61%) ICU 36(26%)
Guan et al[22] Multi-site, 552 hospitals Retrospective cohort study of hospitalised and OPD patients	N=1099 Median age 47 (35-58) Female 459(41.9%)	261 (21.3%) HTN 165(15%) DM 81(7.4%) CAD 27(2.5%) HepB 23(2.1%) COPD 12(1.1%) Cancer 10(0.9%) Smoker 137(12.6%)	Median incubation 4 days (IQR 2-7) Fever 975(88.7%) Cough 745(67.8%) Fatigue 419(38.1%) Sputum 370(33.7%) SOB 205(18.7%) Myalgia/arthralgia 164(14.9%) Headache 150(13.6%) Chills 126(11.5%)	Living in wuhan 483(43.9%) Contact with Wuhan resident 442(72.3%)	Lymphopenia (83.2%) Thrombocytopenia (36.2%) Leukopenia (33.7%) CRP >10mg/L 481/793(60.7%) Raised LDH 277/675(41%) Raised ALT 158/741(21.3%) Raised d-dimer 260/560(46.4%) Raised CK 90/657(13.7%)	Antibiotics 637(58%) Antiviral (oseltamivir) 393(35.8%) Corticosteroids 204(18.6%) IVIG 144(13.1%) OT 41.3% NIV 56(5.1%) IMV 25(2.3%) ECMO 5(0.5%)	CT in n=975 Abnormality (86.2%) Ground-glass change (56.4%) Bilateral infiltrates (51.8%) (Abnormalities detected on Xray in 59%)	Death n=15(1.4%) Discharged 55(5%) Active in-patients1029(93.6%) Non-severe 926 Severe 173 Septic shock 12(1.1%) Pneumonia 972/1067 (91.1%) ARDS 37(3.4%) ICU 55(5%)
China (Outside Wuhan)								
Yang et al[23] 3 hospitals	N=149 Mean age 45.11 ± 13.35	52(34.9%) Cardio-cerebrova	Median 6.8 days until hospitalisation	Hubei travel/residency 85	Lymphopenia 53(35.6%)	Antibiotics 34(22.8%)	CT abnormal in 137/149(91.9%)	Deaths 0(0%) Discharged 73(49%)

in Wenzhou, Zhejiang, China Retrospective multicentre cohort study Jan-Feb 2020	Female 68 Male 81(54.4%)	scular disease 28(18.8%) Malignancy 2(1.34%) Endocrine disease 9(6.04%) Respiratory disease 1(0.67%)	Fever 114(76.5%) Cough 87(58.4%) Sputum 48(32.2%) Sore throat 21(14%) Chills 21(14%) Chest tightness 16(10.74%) Headache 13(8.7%) Diarrhoea 11(7.38%)	Contact with those from Hubei 49(32.9%) No relation with Hubei 15(10%)	Leukopenia 22(24.2%) Raised CRP 82(55%) Thrombocytopenia 20(13.42%) Increased PT 17(11.41%) Raised d-dimer 21(14.1%) Raised ALT 18(12.1%) Raised LDH 45(30.2%)	Antiviral 140(94%) Interferon 144(96.6%) Corticosteroids 5(3.36%) IVIG 19(12.75%) OT 134(89.9%) NIV 2(1.34%) IMV 0(0%)		Active in-patients 76(51%) Septic shock 0(0%) ARDS 0(0%) ICU 0(0%)
Tian et al[24] Multicentre cohort study (Beijing) Jan-Feb 2020	N=262 Median age 47.5 Male 127(48.5%)	No data	Days of illness onset to hospitalisation 4.5 ±3.7 Fever 215(82.1%) Cough 120(45.8%) Fatigue 69(26.3%) Dyspnoea 18(6.9%) Headache 17(6.5%)	Residents of Beijing 192(73.3%),50(26%) of whom travelled to Wuhan. Residents of Wuhan 53(20.2%) Residents elsewhere 17(6.5%). Close contact with confirmed cases 116(60.4%) No contact	No data	No data	No data	Deaths 3(0.9%) Discharges 45(17.2%) Active in-patients 214(81.7%) Severe 46(17.6%) Non-severe 216(82.4%)

				with confirmed cases 21(10.9%)				
Korea								
COVID-19 National Emergency Response Centre[25]	N=28 Mean age 42.6 years (range 20-73) Female 13(46.4%) Male 15(53.6%)	N=10(35.7%) HTN, DM, Asthma, chronic rhinitis, dyspilidaemia, hypothyroidism	Fever 9(32.1%) Sore throat 9(32.1%) Cough/sputum 5(17.9%) Chills 5(17.9%) Myalgia 4(14.3%) Weakness 3(10.7%) Headache 3(10.7%)	Imported cases: Wuhan 11(68%) Zhuhai 1(6.3%) Japan 1(6.3%) Singapore 2(12.5%) Thailand 1(6.3%) Local transmission 10	No data	No data	No data	No data
Europe								
Spiteri et al[26] WHO, ECDC surveillance report	N=38 (35 hospitalised) Median age 42(range 2-81 years) Male 25	Cardiac disease 1 Obesity 1	Median days symptomatic before hospitalisation 3.7 (range 0-10) Of 31 patients: Fever 20 Cough 14 Weakness 8 headache 6 sore throat 2 rhinorrhoea 2 SOB 2	14 infected in China 21 infected in Europe	No data	IMV 3	No data	Death 1 Discharged 20 4 active in-patients ICU 3
Grasselli et al[27] Multi centre retrospec	N= 1591 Median age 63 (IQR 56-70)	N=709/1043(68%) HTN 509(49%)	No data	No data	No data	NIV 137(11%)	No data	Deaths 405(26%) Discharged from ICU

tive analysis in ICU patients (Lombardy, Italy)	Male 1304(82%)	CV disease 223(21%) DM 180(17%) Malignancy 81(8%) COPD 42(4%) CKD 36(3%) CLD 28(3%)				IMV 1150(88%)		256(16%) Active patients 920(58%)
Caruso et al[28] Single centre prospective cohort study (Rome, Italy)	N=158 Mean age 57±17 Female 75(47%) Male 83(52%)	No data	Fever 97(61%) Cough 88(56%) Dyspnoea 52(33%)	No data	Lymphopenia 95(60%) Raised CRP 139(88%) Raised LDH 128(81%)	No data	CT findings n=58 Ground glass opacification 58(100%) Consolidation 42(72%)	No data
US								
Arentz et al[29] Single centre retrospective cohort study (Washington)	N=21 (Critically ill patients in ICU) Mean age 70 (range 42-90) Male 52%	N=18(86%) CKD 10(47.6%) CCF 9(42.9%) COPD 7(33.3%) DM 7(33.3%) OSA 6(28.6%) Immunosuppression 3(14.3%)	Mean days of symptoms pre hospitalisation 3.5 (81% admitted to ICU within 24h of admission) SOB 17(76.2%) Fever 11(52.4%) Cough 11(47.6%)	No data	Lymphopenia 14(67%) Deranged LBTs 8(38%)	Vasopressors 14(67%) IMV 15(71%)	XR chest abnormal in 95% on admission Bilat. Reticulonodular opacities 11(52%) Ground glass opacities 10(48%)	Deaths 67% Discharged from ICU 9.5% Active cases 24% Cardiomyopathy 7(33%) ARDS 100% of IMV patients

HTN -hypertension, DM – diabetes mellitus, CAD – coronary artery disease, COPD - chronic obstructive pulmonary disease, CKD – chronic kidney disease, CLD – chronic liver disease, CCF – congestive cardiac failure,

OSA – obstructive sleep apnoea, HepB – hepatitis B, SOB- shortness of breath, ALT – alanine aminotransferase. IVIG – intravenous immunoglobulin, HFNC - high flow nasal canulae, NIV- non-invasive ventilation, IMV – invasive mechanical ventilation, ECMO – extra corporeal membrane oxygenation, OT – oxygen therapy, ARDS – acute respiratory distress syndrome, ICU – intensive care unit, CT computer tomography, PT – prothrombin time, CRP – C-reactive protein, LDH – lactate dehydrogenase, LBT- liver blood tests.

There is little consensus in the published literature to date regarding optimum therapeutic strategies. For example, the use of antibiotics has ranged from 23-95% [10 22-24]. Antiviral choice and use is also variable, with one study reporting use of lopinavir/ritonavir (LPV/r) in 21%[10], two studies describing oseltamivir in 90% and 35% of patients, respectively [22 23], and one study reporting 'antiviral' administration in 94% without specifying which drugs were used [24]. The reported rates of systemic corticosteroids has ranged from 3%[24] to 45%[22] and the reported rates of use of intravenous immunoglobulin (IVIG) has ranged from 13[24]-24%[10]. The reported rates requiring supplemental oxygenation for COVID-19 infection has ranged from 21%[10] to 90%[24] with reported rates of ventilation ranging from 0%[24] to 17%[10].

Spiteri et al describe the first 38 cases in Europe with comparable prevalence of IMV at 9% of hospitalized patients. Since the studies from the United States and Italy (see Table 4) primarily describe patients in an Intensive Care Unit (ICU) setting, the proportion of patients requiring ventilation is higher at 71-88% [28 30]. The median length of stay in studies from China has ranged from 10-12 days where such data was available [4 10 23]. This is comparable to our cohort who spent a median of nine days in hospital. Furthermore, the rate of complications including requirement for ICU admission, development of ARDS and death also appear comparable to that reported previously.

To date, the largest cohorts have been reported by Guan et al [23], who reported 1099 patients across multiple sites in China and Grasselli et al[28], who reported on 1591 patients admitted to ICUs in Lombardy, Italy. In terms of size, setting and population, the studies which report on a setting most similar to ours are Wang et al[22] (retrospective study of 138 patients attending Zhongnan Hospital of Wuhan University, China), Yang et al[24] (retrospective study of 149 patients attending three hospitals in Wenzhou, Zhejiang, China) and Caruso et al[29] (single centre prospective cohort study of 158 patients hospitalised in Rome, Italy). Our findings are comparable with these other centres with regard to male gender, age, symptoms at presentation, treatment requirements and laboratory abnormalities. Of our cohort, 75% have been discharged and this is higher than that reported by Wang et al[22] and Yang et al[24]. However, our observed mortality rate of 4% died is the same as that reported by Wang et al[22]. Finally, our cohort characteristics are consistent with those reported in Ireland overall, in terms of age and those most at risk of severe illness being those with an underlying health condition [3].

Our findings differ from that reported in other cohorts in that more people had a pre-existing chronic illness. While respiratory symptoms and fever were common among our sample, we also observed less specific symptoms such as myalgia, fatigue and gastrointestinal symptoms (e.g. nausea, diarrhoea) more commonly than has been previously reported.

In our sample, the application (albeit post hoc) of standard 'early warning scores' [16] [17] would have resulted in less than half of people who required admission actually being admitted (45% using NEWS and 48% using NEWS2 parameter, respectively). We therefore recommend against relying on these measures alone when assessing requirement for patient admission, since these scoring systems were developed to aid in decision making for patients with bacterial sepsis as opposed to viral pneumonitis due to COVID-19.

Methodological considerations

This paper reports on real world data from a University teaching hospital in Dublin with a high incidence of COVID-19 disease. As the disease has unfolded it has become apparent that communities living in our local catchment area are especially at risk of the infection and its deleterious consequences [31] and this finding has been reported in other large cities [32]. The data was collected as our understanding of the natural history of this disease was unfolding. In that regard, while we endeavoured to ensure that the dataset is as complete as possible, this was not always possible and some data points were therefore missing. Nonetheless, we strove to minimise the bias resulting from this by reviewing clinical and administrative records and treating such missing data in accordance with 'STROBE Guidance'[19].

We acknowledge a number of limitations in our study. Firstly, there may have been a low threshold to admit patients for hospital treatment due to an initial containment strategy and relative absence of capacity constraints at the outbreak's onset. This may continue to change as both hospital bed capacity and our understanding of the factors associated with worse outcomes evolves in the months ahead. The sample size, while small, is nonetheless, at the time of writing, one of the ten largest cohorts reported to date and to our knowledge the first such from Ireland or the UK.

Conclusion

Implications for clinical practice

COVID-19 is a new disease caused by an emergent virus and is not yet well characterised. Clinical manifestations are different to illness caused by other coronaviridae. Our findings provide a guide on the clinical predictors of patients requiring hospital treatment. The epidemiological characteristics and clinical manifestations of COVID-19 in our cohort appears consistent with findings in cohorts reported to date. Men in their fifth decade appear especially at risk, while elevated levels of C-reactive protein, ferritin and D-dimer, in addition to abnormalities on chest imaging, elevated NEWS Score (Modified) score and tachycardia appear to be important predictors of disease severity. Further research involving larger samples followed longitudinally is a priority and such research will be key to identifying those parameters which best predict disease outcomes and best allocate resources. For clinicians, our key message is that relying exclusively on clinical assessment and tools such as early warning scores alone may not identify those who require hospital care.

Abbreviations

Mater Misericordiae University Hospital (MMUH)

National Isolation Unit (NIU)

Polymerase chain reaction (PCR)

General Medical Scheme (GMS)

National Early Warning Score (NEWS)

Statistical Package for the Social Sciences (SPSS)

Acute respiratory distress syndrome (ARDS)

C-reactive Protein (CRP)

Intensive Care Unit (ICU)

Declarations

Ethics approval and consent to participate: Ethical approval was granted by the Institutional Review Board, Mater Misericordiae University Hospital, Dublin, Ireland. 8th April 2020 Reference No. 1/378/2141. The study team retrospectively reviewed clinical records and extracted anonymised data on patient demographics, baseline morbidity, and initial outcomes. Patient consent was not sought for this retrospective review.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interest statement: None declared.

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Author contributions

*B O'Kelly: Study conception, study design, data collection, data analysis, clinical care, manuscript drafting.

*C Cronin: Study conception, study design, data collection, data analysis, clinical care, manuscript drafting.

*SP Connolly: Study design, data collection, data analysis, clinical care, manuscript drafting.

* **Denotes equal contribution** from B O'Kelly, C Cronin and SP Connolly.

W Cullen: Study conception, study design, ethics approval, data analysis, manuscript drafting.

G Avramovic: Study design, ethics approval, data analysis, manuscript preparation.

T McHugh: Data analysis, manuscript drafting.

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A Cotter: Study design, clinical care, ethics approval, manuscript drafting.

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T McGinty: Study design, clinical care, manuscript drafting.

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Figures

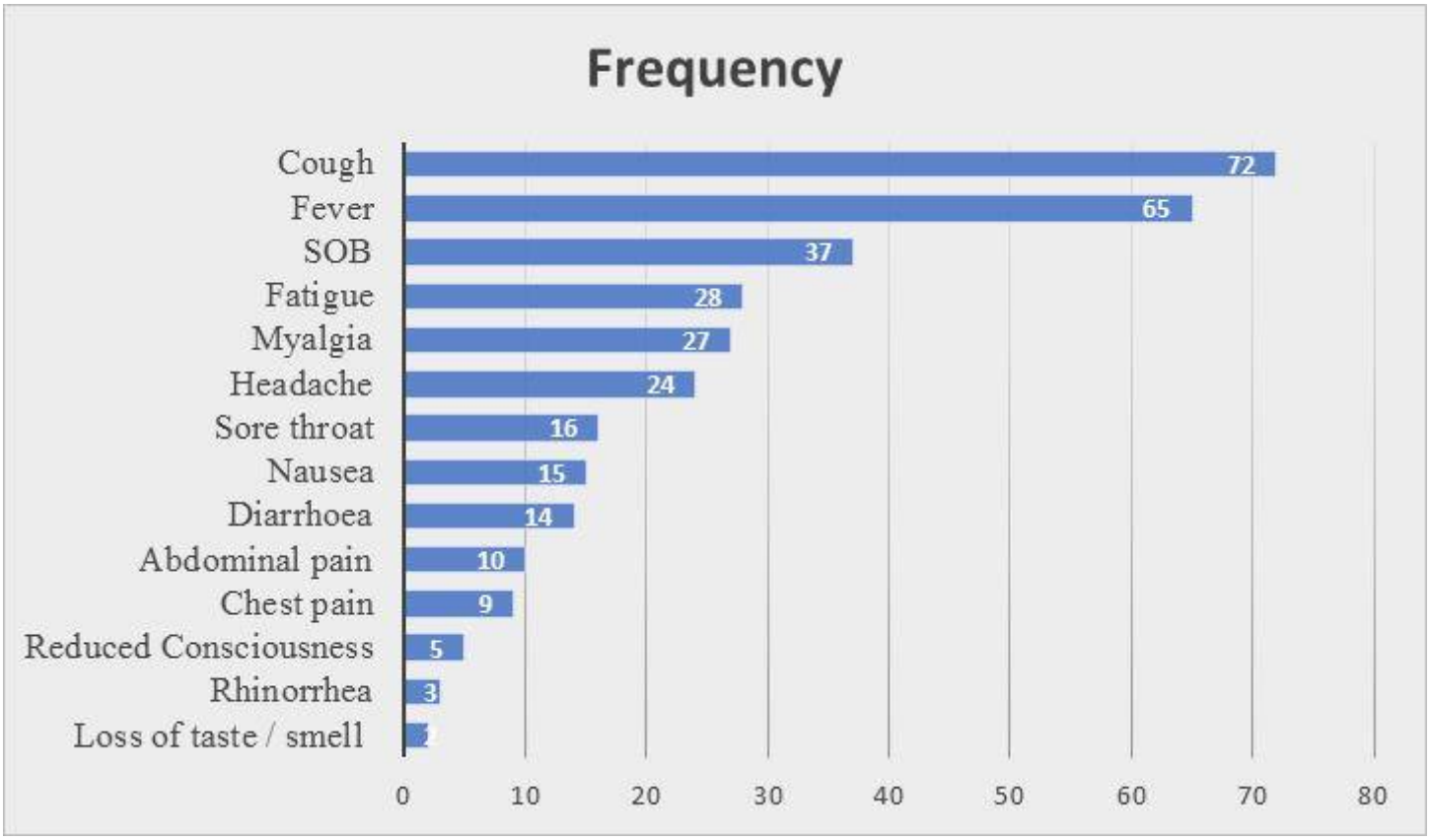

Figure 1

Presenting symptoms at time of admission.

Supplementary Files

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- STROBEchecklist.docx