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Variation in COVID-19 characteristics, treatment and outcomes in Michigan: an observational study in 32 hospitals

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ABSTRACT

Objective To describe patient characteristics, symptoms, patterns of care and outcomes for patients hospitalised with COVID-19 in Michigan.

Design Multicentre retrospective cohort study.

Setting 32 acute care hospitals in the state of Michigan.

Participants Patients discharged (16 March–11 May 2020) with suspected or confirmed COVID-19 were identified. Trained abstractors collected demographic information on all patients and detailed clinical data on a subset of COVID-19-positive patients.

Primary outcome measurements Patient characteristics, treatment and outcomes including cardiopulmonary resuscitation, mortality and venous thromboembolism within and across hospitals.

Results Demographic-only data from 1593 COVID-19-positive and 1259 persons under investigation discharges were collected. Among 1024 cases with detailed data, the median age was 63 years; median body mass index was 30.6; and 51.4% were black. Cough, fever and shortness of breath were the top symptoms. 37.2% reported a known COVID-19 contact; 7.0% were healthcare workers; and 16.1% presented from congregated living facilities. During hospitalisation, 232 (22.7%) patients were treated in an intensive care unit (ICU); 558 (54.9%) in a 'cohorted' unit; 161 (15.7%) received mechanical ventilation; and 90 (8.8%) received high-flow nasal cannula. ICU patients more often received hydroxychloroquine (66% vs 46%), corticosteroids (34% vs 18%) and antibiotic therapy (92% vs 71%) than general ward patients ($p<0.05$ for all). Overall, 219 (21.4%) patients died, with in-hospital mortality ranging from 7.9% to 45.7% across hospitals. 73% received at least one COVID-19-specific treatment, ranging from 32% to 96% across sites.
Across 14 hospitals, the proportion of patients admitted directly to an ICU ranged from 0% to 43.8%; mechanical ventilation on admission from 0% to 12.8%; mortality from 7.9% to 45.7%. Use of at least one COVID-19-specific therapy varied from 32% to 96.3% across sites.

Conclusions During the early days of the Michigan outbreak of COVID-19, patient characteristics, treatment and outcomes varied widely within and across hospitals.

Strengths and limitations of this study

- ► Using rigorous data collection including a well-defined sampling strategy and trained data abstractors, our paper is the largest multihospital study to examine clinical aspects related to COVID-19 in Michigan.
- ► This is the first study to examine variations in clinical care processes, treatment approaches and outcomes across hospitals.
- ► The high rate of use of non-evidence-based therapies for treating COVID-19 has significant safety, economic and policy implications for the most critically ill subsets in the hospital.
- ► Given the observational nature of the study and potential missing documentation on symptoms, comorbidities or treatments in the medical record, rationales for treatment or management decisions cannot be determined.
- ► Our sampling frame may be biased as patients who remain hospitalised may not be included in our cohort.

INTRODUCTION

Since detection in Wuhan, China,[1 2] over 4.5 million cases of COVID-19, caused by SARS-CoV-2, have been reported.[3] The USA leads the world in the total number of cases, with over 1.5 million cases and 92 000 deaths reported as of 20 May 2020.[4] Within the USA, Michigan remains one of the hardest hit states, with over 52 000 cases and 5000 deaths as of 20 May 2020.[5]

In the early days of the pandemic, data regarding patient characteristics, symptoms and signs and presentation and care strategies, including aspects such as oxygenation, laboratory testing and therapeutics, were unclear. As well, short-term and long-term outcomes of patients exposed to these varying approaches were unknown. Some studies reported substantial variation in patient characteristics and treatment modalities across hospitals. However, the extent of such variation and impact on outcomes remained unknown.

Michigan has a long history of collaborative quality improvement work that spans several disciplines including cardiovascular medicine, emergency medicine and hospital medicine, among others.[6] These consortia collect detailed clinical variables from hospitals to populate a central registry, allowing benchmarking and comparisons of care and outcomes. As the COVID-19 pandemic unfolded in Southeast Michigan, several consortia came together to focus data collection on patients hospitalised with COVID-19.

Using a well-established data collection strategy, we examined variations in clinical care processes, treatment approaches and clinical outcomes across Michigan hospitals.

METHODS

A retrospective cohort design was used. Data were collected from medical records of patients discharged between 16 March 2020 and 11 May 2020 from 1 of 32 Michigan hospitals who participated in collaborative quality initiatives sponsored by Blue Cross Blue Shield of Michigan and Blue Care Network. Trained abstractors at each hospital identified adult patients >18 years of age who underwent testing for COVID-19 via reverse-transcriptase PCR, including both positive cases and persons under investigation (PUIs) who eventually had a negative test. Abstractors were asked to abstract as many eligible cases as possible for their hospital. Demographic data (age, gender, race, ethnicity and payor) and in-hospital mortality were collected for all confirmed and PUI cases. A sample of COVID-19-positive cases from each hospital was selected for detailed abstraction. Positive cases were sorted by day of admission (eg, Monday–Sunday) and, for each day, a pseudo-random number (minute of hospital discharge) was used to select patients for detailed abstraction. Patients who were pregnant, transitioned to hospice within 3 hours of hospital admission or discharged against medical advice were excluded. All data were entered into a registry (Mi-COVID19) using a structured data collection template. Of the 92 non-critical access, non-federal hospitals in Michigan, data from 32 hospitals (34.8%) were included in the sample. Included hospitals are diverse in terms of size, teaching status and ownership structure (online supplemental appendix 1).

Patient characteristics including comorbidities, home medications, presenting symptoms and risk factors for COVID-19 (eg, exposure to sick contacts and healthcare workers) were collected. Clinical data during hospitalisation including location of care (ward vs intensive care unit (ICU), a 'cohorted' COVID-19 only unit), vital signs, body mass index, laboratory and radiology findings and therapeutics were abstracted. Organ supports such as mechanical ventilation and other respiratory support, vasopressor use and renal replacement therapy (continuous renal replacement therapy and intermittent haemodialysis were also collected.

The primary outcomes of interest included hospital mortality, receipt of cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric therapy for presumed thrombosis). In addition, we performed prespecified exploratory analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine variation in patient characteristics, management and outcomes. Specifically, we assessed variation in use of COVID-19-specific treatments (defined as hydroxychloroquine, combination hydroxychloroquine plus azithromycin, vitamin C (oral or intravenous), interleukin (IL)-6 inhibitors or remdesivir), antibiotic therapy, use of organ support (eg, use of vasopressors, mechanical ventilation and CPR), occurrence of venous thrombosis and in-hospital mortality.

Descriptive statistics (eg, mean, median and proportion) with measures of dispersion (eg, SE and IQR) were used to summarise data. Data that were not documented in medical records (eg, values of certain laboratory tests) were reported as missing. Pairwise comparisons were made using t-tests for continuous data and χ^2 tests for categorical data, respectively. Differences across hospitals were tested using the Kruskal-Wallis test for continuous variables and Pearson χ^2 test for categorical variables. All statistical tests were two-sided with $p<0.05$ considered statistically significant. It was not appropriate or possible to involve patients or the public in the design, conduct, reporting or dissemination plans of our research.

Patient and public involvement

Patients receiving care at a participating hospital were included in the study.

Data availability

All data relevant to the study are included in the article or uploaded as online supplemental information.

RESULTS

Demographic data

Demographic-only data from 1593 COVID-19-positive and 1259 PUI discharges from 32 Michigan hospitals were collected. PUIs had a median age of 64.4 years; 52.6% were male; and 32.0% were black. COVID-19-positive patients had similar age and gender as PUIs (63.9 years and 52.1% male, respectively) but were more commonly black (57.1% vs 32.0%, p<0.01). In the demographic-only cohort, 398 (25.0%) COVID-19-positive patients died during hospitalisation.

Detailed data were abstracted on 1024 (64.3%) randomly selected COVID-19-positive patients. The most prevalent comorbidities were hypertension (65.4%), diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%); 14.9% of the patients had no comorbidities. Though 12.8% of patients had a diagnosis of asthma and 11.2% had a diagnosis of chronic

Table 1 Demographic and clinical characteristics of COVID-19-positive patients (n=1024)

Residence prior to hospitalisation, n (%)	
Home	824 (80.5)
Congregated living facility*	165 (16.1)
Subacute rehabilitation facility	9 (0.9)
Unknown	18 (1.8)
Admission location, n (%)	
Emergency department	951 (92.9)
Transfer from another hospital	60 (5.9)
Direct admission	7 (0.7)
Median age (years) (IQR)	63.3 (50.9–74.4)
Male sex, n (%)	533 (52.1)
Race, n (%)	
Black	526 (51.4)
White	390 (38.1)
Unknown	45 (4.4)
Asian	30 (2.9)
Other	26 (2.5)
Native	4 (0.4)
Islander	3 (0.3)
Ethnicity, n (%)	
Non-Hispanic	873 (85.3)
Hispanic	30 (2.9)
Unknown	117 (11.4)
Insurance, n (%)	
Medicare	497 (48.5)
Commercial	251 (24.5)
Medicaid	128 (12.5)
Self-pay	29 (2.8%)
Other†	117 (11.4)
BMI, median (IQR)	30.6 (25.9–37.1)
Smoking history, n (%)	
Never	615 (60.2)
Former	279 (27.3)
Current	61 (6.0)
Unknown	65 (6.4)
Vaping history, n (%)	
Never	645 (63.2)
Former	366 (35.8)
Current	6 (0.6)
Unknown	3 (0.3)
Coexisting disorder, n (%)	
Hypertension	670 (65.4)
Diabetes	377 (36.8)
Cardiovascular disease	266 (26.0)
Moderate/severe kidney disease	239 (23.3)
Asthma	132 (12.9)
CHF/cardiomyopathy	131 (12.8)
Dementia	123 (12.0)
COPD	115 (11.2)
Cerebrovascular disease/paraplegia	97 (9.5)
Cancer‡	77 (7.5)
Peripheral vascular disorders	41 (4.0)
Chronic pulmonary disease (non-asthma/COPD)	35 (3.4)
Rheumatoid arthritis	29 (2.8)
Peptic ulcer disease	10 (1.0)
HIV/AIDS	7 (0.7)
Organ transplant	8 (0.8)
Inflammatory bowel disease	8 (0.8)
No reported comorbidities	152 (14.9)
Home medications	
ACE inhibitors	180 (17.6)
Steroids/immunosuppressive therapy	115 (11.3)
ARBs	136 (13.3)
NSAIDs	182 (17.8)
Statins	378 (37.0)
Beta blockers	298 (29.2)
Anticoagulants	149 (14.6)
Oral steroids§	62 (6.1)
Inhaled steroids	43 (4.2)
Inhaled long-acting beta agonist	30 (2.9)
Inhaled long-acting anticholinergic	5 (0.5)
Home oxygen therapy	36 (3.5)
Duration of symptoms before admission (days), median (IQR)	6 (3–9)
Respiratory symptoms, n (%)	
Cough (new or worsening)	751 (73.3)
Fever, n (%)	735 (71.8)
Fever (99.0°F–100.4°F)	151 (14.7)
Fever (>100.4°F)	390 (38.1)
Subjective fever	194 (18.9)
Dyspnoea/shortness of breath	739 (72.2)
Nausea/vomiting or diarrhoea	403 (39.4)
Fatigue	361 (35.3)
Myalgias	264 (25.8)
Weakness	253 (24.7)
Sputum production	146 (14.3)
Altered mental status	144 (14.1)
Non-pleuritic chest pain	100 (9.8)
Generalised malaise	91 (8.9)
Rhinorrhoea	75 (7.3)

Continued

Table 1 Continued	
Pleuritic chest pain	75 (7.3)
No reported symptoms	14 (1.4)
Sick contacts, n (%)	381 (37.2)
Known COVID-19 positive	244 (23.8)
Unknown COVID-19 status	236 (23.0)
Healthcare worker, n (%)	72 (7.0)
Service worker, n (%)¶	59 (5.8)
Initial location of admission, n (%)	
General medical/surgical ward	608 (59.5)
ICU	138 (13.5)
Step-down unit	160 (15.7)
Observation unit	115 (11.3)
Missing/uknown	3 (0.3)
Admitted to COVID-19-specific (ie, cohorted) unit	419 (40.9)
Advanced directives on admission	
DNR/DNI	64 (6.3)
No CPR (intubation OK)	19 (1.9)
No intubation (CPR OK)	3 (0.3)

*Includes assisted living, group home, skilled nursing facility, homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.
† Includes other payers, Michigan, out-of-state and government.
‡ Includes leukaemia, lymphoma, haematological cancer and any malignancy.
§ Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.
¶ Service workers include food service, transportation, postal/delivery and other related fields.
ARB, angiotensin receptor blocker; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; DNI, do not intubate; DNR, do not resuscitate; ICU, intensive care unit; NSAID, non-steroidal anti-inflammatory drug.

obstructive pulmonary disease, prehospital use of inhaled steroids, long-acting beta agonists and long-acting anti-muscarinic agents was low at 4.2%, 2.9% and 0.5%, respectively. Current smoking or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former vaping. A total of 115 (11.3%) patients were on immunosuppressive medications prior to hospitalisation, including 62 (6.1%) who were on oral steroids. Essential workers comprised 12.8% of the cohort, including healthcare workers (7.0%) and service workers (5.8%, eg, postal, food service and transportation). Prior to admission, 16.1% of patients resided in congregated living facilities, including nursing homes and homeless shelters (table 1).

Clinical presentation and initial evaluation

In the detailed abstraction cohort (n=1024), median duration of symptoms prior to hospitalisation was 6 days (IQR 3–9). The most common presenting symptoms

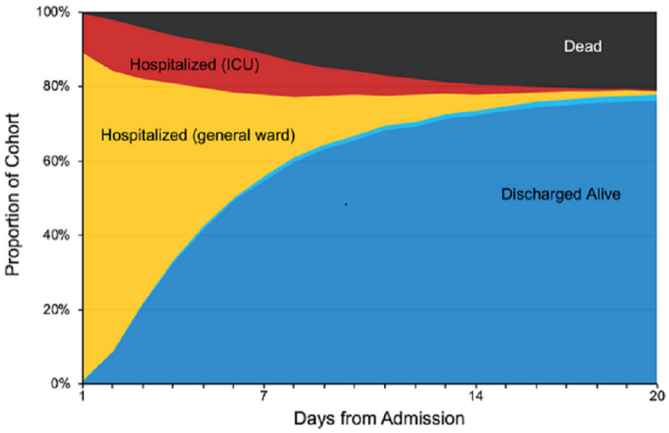

Figure 1 Depiction of the proportion of the N=1024 patient cohort who are hospitalised on general care/ward (yellow), hospitalised in ICU (red), discharged alive (blue), transferred to a new hospital (light blue) and deceased over time to day 20 of hospital admission. ICU, intensive care unit.

were cough (73.3%), fever (71.8%) and shortness of breath (72.2%); only 8% of patients did not report one of these three complaints (table 1). Gastrointestinal symptoms including nausea, vomiting and diarrhoea occurred in 39.4% of patients. Over a third of patients (37.2%) reported sick contacts at the time of admission, and 23.8% reported contact with a patient known to have COVID-19. The location of diagnostic testing for COVID-19 varied: 67.5% of patients were tested in hospital laboratories, 23.2% in commercial laboratories and 8.0% in the state laboratory. Patients were most commonly admitted to a general medical/surgical ward (59.5%), but 15.7% were admitted to intermediate care; 13.5% were admitted directly to the ICU; and 11.3% were admitted to an observation unit (figure 1). A total of 419 (40.9%) of patients were admitted to a cohorted (COVID-19 only) unit. At admission, 6.3% of patients had do not resuscitate/do not intubate orders, which increased to 13.8% by discharge.

Common laboratory testing on admission included white blood cell count (93.7%), absolute lymphocyte count (75.8%), troponin (57.4%), lactate (57.2%), C reactive protein (CRP) (44.9%) and procalcitonin (42.4%) (missingness by laboratory test are reported in the online supplemental e-appendix 2). Among those with available laboratory data, patients who received ICU treatment had higher levels of inflammatory markers at admission including d-dimer (2.88 mg/L vs 1.65 mg/L), ferritin (872 ng/mL vs 559 ng/mL), CRP (24.3 mg/dL vs 13.8 mg/dL) and lactate dehydrogenase (476 U/L vs 346 U/L) (table 2). Chest imaging (X-ray or CT) was performed in 528 (51.6%) patients within 1 day of admission and was more common in ICU than general care patients (59.9% vs 49.1%, p=0.004). ICU patients were more likely to have radiographic abnormalities on presentation. Viral respiratory panels, blood cultures and sputum cultures were collected in 722 (51.0%) patients but were positive in only 48 (4.7%) patients; 9.5% of ICU

Table 2 Clinical and laboratory data in COVID-19-positive patients by ICU status (n=1024)

	Ever ICU (n=232)	General ward (n=792)	P value
Vital signs on day of hospital admission, n (%)			
Fever (>100.4°F)	95 (40.9)	295 (37.2)	0.3073
Hypoxia/new or escalated O_2 requirement	142 (61.2)	257 (32.4)	<0.0001
Supplemental oxygen use	96 (41.4)	145 (18.3)	<0.0001
Respiratory rate>20 breaths/min	139 (59.9)	306 (38.6)	<0.0001
Heart rate>100 beats/min	99 (42.7)	321 (40.5)	0.5596
Systolic blood pressure<100 mm Hg	27 (11.6)	45 (5.7)	0.0018
Day 1 laboratory measures, median (IQR)			
Haemoglobin	13.2 (11.4–14.7)	13.2 (12.0–14.6)	0.4573
White blood cell count (K/µL)	7.3 (5.5–9.7)	6.5 (4.8–8.4)	<0.0001
Absolute lymphocyte count (K/µL)	0.80 (0.60–1.20)	1.00 (0.70–1.30)	0.3440
Platelet count (K/µL)	197 (149–256)	204 (159–268)	0.4875
ALT (IU/L)	32.0 (20.0–60.0)	27.0 (18.0–41.0)	0.2228
Lactate (mmol/L)	1.6 (1.2–2.5)	1.4 (1.0–1.8)	0.0010
Troponin (pg/mL)	9 (0–38)	0 (0–12)	0.5872
Brain natriuretic peptide (pg/mL)	79 (34–236)	49 (18–157)	0.0088
Procalcitonin (ng/mL)	0.30 (0.17–0.94)	0.12 (0.06–0.29)	0.5054
D-dimer (mg/L)	2.88 (1.19–35.00)	1.65 (0.59–368.00)	0.8240
Ferritin (ng/mL)	872 (379–1531)	559 (237–1019)	0.1074
CRP (mg/dL)	24.3 (12.0–107.1)	13.8 (5.8–66.2)	0.0031
LDH (IU/L)	476 (337–668)	346 (254–455)	<0.0001
Creatinine (mg/dL)	1.3 (1.0–2.0)	1.1 (0.8–1.5)	0.5736
Total bilirubin (mg/dL)	0.6 (0.4–0.9)	0.5 (0.4–0.8)	0.7147
Respiratory viral panel positive for non-COVID-19 respiratory virus, n (%)	2 (0.9)	7 (0.9)	0.9443
Positive blood culture within 1 day of admission, n (%)	7 (3.0)	9 (1.1)	0.0422
Positive respiratory culture within 1 day of admission, n (%)	4 (1.7)	4 (0.5)	0.0636
Any chest imaging*, n (%)	139 (59.9)	389 (49.1)	0.0038
Chest X-ray, n (%)	118 (50.9)	322 (40.7)	0.0058
Chest CT, n (%)	34 (14.7)	106 (13.4)	0.6201
Imaging findings, n (%)			
Pneumonia	61 (26.3)	100 (12.6)	<0.0001
Non-specified opacities/air-space disease	84 (36.2)	161 (20.3)	<0.0001
Pleural effusion	32 (13.8)	37 (4.7)	<0.0001
Normal/no abnormalities	5 (2.2)	30 (3.8)	0.2287
Pulmonary oedema	25 (10.8)	29 (3.7)	<0.0001
CT with ground-glass infiltrates	14 (6.0)	58 (7.3)	0.4995
Respiratory support on day of admission, n (%)			
Invasive mechanical ventilation	46 (19.8)	2 (0.3)	<0.0001
Non-invasive positive pressure	5 (2.2)	2 (0.3)	0.0020
HHFNC	5 (2.2)	5 (2.2)	0.1905
Oxygen mask (>40% FiO_2)	17 (7.3)	20 (2.6)	0.0006
Nasal cannula oxygen, 1–6 L	76 (32.8)	261 (33.0)	0.9555
No supplemental oxygen	83 (8.1)	502 (49.0)	<0.0001

Continued

Table 2 Continued

	Ever ICU (n=232)	General ward (n=792)	P value
Treatments during hospitalisation, n (%)			
COVID-19-specific treatment(s), n (%)			
Hydroxychloroquine	154 (66.4)	364 (46.0)	<0.0001
Hydroxychloroquine+azithromycin	112 (48.3)	260 (32.8)	<0.0001
Vitamin C (PO or intravenous)	35 (15.1)	68 (8.6)	0.0038
Remdesivir	7 (3.0)	10 (1.3)	0.0658
IL-6 receptor inhibitor	27 (11.6)	. (%)	<0.0001
Corticosteroids,†† n (%)	79 (34.1)	143 (18.1)	<0.0001
Antibiotics, n (%)	213 (91.8)	558 (70.5)	<0.0001
Azithromycin	149 (64.2)	415 (52.4)	0.0014
Ceftriaxone	124 (53.4)	345 (43.6%)	0.0079
Cefepime	90 (38.8)	79 (10.0)	<0.0001
Doxycycline	37 (15.9)	111 (14.0)	0.4615
Vancomycin	115 (49.6)	106 (13.4)	<0.0001
Linezolid	12 (5.2)	8 (1.0)	<0.0001
Antipseudomonals‡	123 (53.0)	115 (14.5)	<0.0001
Antivirals,§§ n (%)	1 (0.4)	13 (1.6)	0.1626
Enrolled in clinical trial	10 (4.3)	12 (1.5)	0.0098

*Includes chest imaging results 7 days before hospital encounter.
†Hydrocortisone, methylprednisolone, prednisolone or prednisone.
‡Cefepime, gentamicin, imipenem, meropenem, piperacillin–tazobactam, ceftazadime, aztreonam or tobramycin.
§Non-remdesivir antivirals including oseltamivir, lopinavir/ritonavir, ribavirin, others.
ALT, alanine transaminase; CRP, C reactive protein; FiO_2, fraction of inspired oxygen; HHFNC, heated high-flow nasal cannula; ICU, intensive care unit; IL, interleukin; LDH, lactate dehydrogenase.

patients vs 3.3% of general care patients had a viral or bacterial pathogen identified (p<0.001).

Critical care treatment

Overall, 232 patients (22.7%) were treated in an ICU, including 138 (13.5%) who were admitted directly to an ICU and 94 (9.2%) who were transferred to ICU within a median of 2 days following admission. Median length of ICU stay was 6 days (IQR 3–9), which was similar in survivors versus non-survivors (5 vs 6 days, p=0.790). Among 1024 patients with detailed abstraction, the maximum respiratory support received was invasive mechanical ventilation in 161 patients (15.7%), non-invasive positive pressure ventilation in 15 (1.5%), heated high-flow nasal cannula (HHFNC) in 60 (5.9%), oxygen mask (>40% fraction of inspired oxygen (FiO_2) or >6 L/min) in 88 (8.6%) and nasal cannula oxygen (1–6 L/min) in 441 (43.1%) (table 3). A total of 259 (25.3%) patients had no respiratory support or oxygen therapy during hospitalisation. Among 78 patients initiated on HHFNC, 13 (16.7%) progressed to invasive mechanical ventilation. Among 25 patients initiated on NIPPV, 10 (40.0%) progressed to invasive mechanical ventilation. An additional 12 patients and 2 patients, respectively, used HHFNC and NIPPV after extubation.

On initiation of mechanical ventilation, patients were predominantly treated with a volume control mode (75%), with high FiO_2 (≥80% in 49.1% of ventilated patients), and modest tidal volumes (median tidal volume 7.0 mL/kg predicted body weight, IQR 6.2–8.0). The median duration of mechanical ventilation was 6 days (IQR 3–8 days). Prone positioning was documented in 18 patients, pulmonary vasodilators in 2 patients and extracorporeal membrane oxygenation in 2 patients. CPR was administered to 41 patients (4.0%), with only 1 patient surviving to hospital discharge.

Vasopressors were used in 141 patients (13.8%); dialysis was performed in 53 (5.2%) and corticosteroids in 222 (21.7%) patients. A total of 771 (75.3%) patients received broad-spectrum antibiotics, with use being more common in the ICU than in general wards (91.8% vs 70.5%, p<0.001).

COVID-19-specific therapies

A total of 747 (72.9%) patients were treated with therapies targeting COVID-19, or the body's response to COVID-19, most commonly hydroxychloroquine (51%), hydroxychloroquine plus azithromycin (36%) and vitamin C (10%). Treatment with IL-6 inhibitors and remdesivir was infrequent (27 and 17 patients, respectively). Use of

Table 3 Organ support for COVID-19-positive patients by discharge status (n=1024)

	All patients (n=1024)	Discharged alive (n=805)	Died in hospital (n=219)
Treated in an ICU, n (%)	232 (22.7)	101 (12.5)	131 (59.8)
Respiratory support ever received, n (%)*			
Invasive mechanical ventilation	161 (15.7)	47 (5.8)	114 (52.1)
Non-invasive positive pressure ventilation	27 (2.6)	10 (1.2)	17 (7.8)
HHFNC	90 (8.8)	57 (7.1)	33 (15.1)
Oxygen mask (>40% FiO_2)	159 (15.5)	76 (9.4)	83 (37.9)
Maximum respiratory support received, n (%)†			
Invasive mechanical ventilation	161 (15.7)	47 (5.8)	114 (52.1)
Non-invasive positive pressure	15 (1.5)	6 (0.7)	9 (4.1)
HHFNC	60 (5.9)	40 (5.0)	20 (9.1)
Oxygen mask (>40% FiO_2)	88 (8.6)	48 (6.0)	40 (18.3)
Nasal canula oxygen, 1–6 L/min	441 (43.1)	415 (51.6)	26 (11.9)
No respiratory support	259 (25.3)	249 (30.9)	10 (4.6)
Max FiO_2 received, n (%)			
91%–100%	126 (12.3)	34 (4.2)	92 (42)
81%–90%	30 (2.9)	13 (1.6)	17 (7.8)
71%–80%	86 (8.4)	42 (5.2)	44 (20.1)
61%–70%	16 (1.6)	9 (1.1)	7 (3.2)
51%–60%	26 (2.5)	14 (1.7)	12 (5.5)
41%–50%	24 (2.3)	20 (2.5)	4 (1.8)
31%–40%	170 (16.6)	144 (17.9)	26 (11.9)
21%–30%	287 (28)	280 (34.8)	7 (3.2)
Non-respiratory organ support received, n (%)			
Vasopressor	141 (13.8)	35 (4.3)	106 (48.4)
Any dialysis‡	53 (5.2)	17 (2.1)	36 (16.4)
CRRT only	17 (1.7)	1 (0.1)	16 (7.3)
iHD only	28 (2.7)	15 (1.9)	13 (5.9)
CPR	41 (4.0)	1 (0.1)	40 (18.3)

*Represents any use of respiratory support. Numbers are greater than 100% as one patient may have received multiple treatments.
†Represents the highest level of respiratory support a patient has received during hospitalisation.
‡Includes iHD, dialysis and ultrafiltration.
CPR, cardiopulmonary resuscitation; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; FiO_2, fraction of inspired oxygen; HHFNC, heated high-flow nasal cannula; ICU, intensive care unit; iHD, intermittent haemodialysis.

COVID-19 treatments was more common in ICU than in general care patients (88% vs 69%, p<0.001). No patients in our sample received convalescent plasma. The proportion of patients treated with COVID-19-specific therapies decreased over time from 78.1% of patients admitted during 8–31 March to 65.0% of patients admitted during 1 April–11 May (p<0.001). Only 21 (2.0%) patients were enrolled in a clinical trial (table 2).

Clinical outcomes

The in-hospital mortality rate for the full cohort of COVID-19-positive patients (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age, ranging from 4.5% among patients aged 30–39% to 37.5% in patients aged 70–79 years (figure 2). Among 219 decedents with detailed abstraction, 134 (61.5%) died following ICU treatment and 114 (52.1%) died after undergoing mechanical ventilation. Of 219 decedents, 40 (18.3%) received CPR, and 91 (41.6%) were transitioned to comfort care prior to death. The most common causes of death were refractory hypoxaemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock (10.7%). Venous thromboembolism occurred in 32 (3.1%) patients, of which 9 experienced proximal lower-extremity

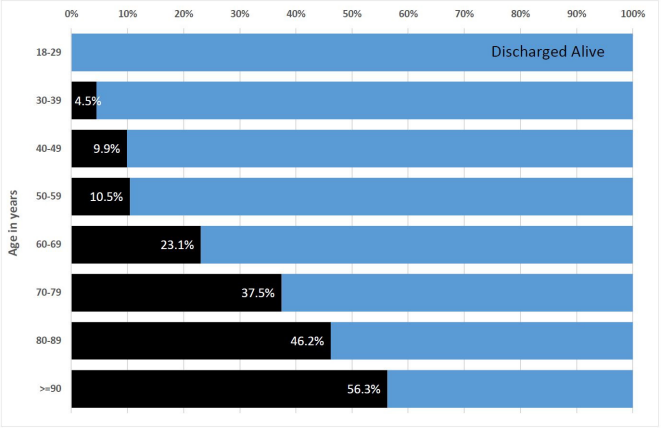

Figure 2 Graph depicting the proportion of the demographic cohort (n=1593) who died in the hospital by decade of age. Black shading indicates death, whereas blue shading indicates being discharged alive.

DVT; 21 experienced PE; and 2 experienced both DVT and PE.

Among the 805 patients that survived to hospital discharge, 86% were discharged home and 8% were discharged to a skilled nursing facility or rehabilitation centre. Only one patient (0.1%) was discharged to the Detroit field hospital (table 3).

Variation across hospitals

Among 14 hospitals with at least 25 detailed abstractions, substantial variation in demographics, illness severity, care processes, treatments and outcomes of COVID-19-positive patients was observed (table 4). The proportion of patients over 65 years of age ranged from 30.2% to 65.5%, while the proportion of black patients ranged from 0% to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from 0% to 43.8%, while the proportion of patients who were transferred to an ICU after admission ranged from 0% to 24.1%. Treatment in cohorted units ranged from 0% to 100%. Mechanical ventilation on admission ranged from 0% to 12.8%, while use of vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness on presentation (defined as admission to an ICU with receipt of vasopressors or mechanical ventilation on admission) varied from 0% to 7.7%.

Of the total number of patients, 72.9% received at least one COVID-19-specific therapy (eg, hydroxychloroquine, hydroxychloroquine plus azithromycin, IL-6 inhibitor and antiviral therapy), but use varied from 32% to 96.3% across sites. Similarly, 65% of patients received concurrent antibiotics and COVID-19-specific treatment during hospitalisation, with frequency varying from 50% to 100% in ICU patients versus 17% to 95% in general care patients.

Mortality across hospitals varied from 7.9% to 45.7% of patients, and rates of CPR before death ranged from 0% to 66.7%. Finally, rates of VTE also varied, occurring in 0%–11% of patients across hospitals.

DISCUSSION

While reports of patients with COVID-19 from New York, Washington and California exist,[7–9] this is the first multicentre study to examine epidemiology, treatment and outcomes of COVID-19 hospitalisations in Michigan. Also, in contrast to prior multihospital US cohorts, the Mi-COVID19 registry includes a large sample of patients treated at a diverse set of 32 academic and community hospitals.

The demographics of our cohort differ from those of other cohorts. First, patients with confirmed COVID-19 in Michigan are disproportionally black (over half of our cohort). This is in contrast to 32% of PUIs—indicating that the predominance of black patients with COVID-19 is not a reflection of local demographics, but rather a disproportionate impact of COVID-19 on black patients. Second, in contrast to prior studies,[1 7 10] our cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this difference are unclear.

Consistent with prior reports, the main presenting symptoms were cough, dyspnoea and fever. Similar to other studies,[11] a substantial proportion of patients had multiple comorbidities, but notably, 15% of our cohort had no known medical problems.[12] We found that a substantial proportion of patients reported contact with a known COVID-19-positive patient prior to developing symptoms. These findings mirror those of a study from Shenzen, China, where contacts of those with disease experienced a significantly higher rate of infection than the general public.[13] Additionally, patients underwent COVID-19 testing through a number of venues including hospital, commercial and state-run laboratories, illustrating the myriad ways in which diagnosis was obtained early in the outbreak when testing was limited.[14] Although only 14% of the sample was admitted directly to an ICU, an additional 9% was transferred to an ICU later in hospitalisation. Hospital mortality in cases with detailed abstractions was 21% but increased with age, consistent with prior studies.[15]

A key finding of our study is that a majority of patients hospitalised for COVID-19 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the body's immune response. More than half of patients were treated with hydroxychloroquine, and an additional 6% were treated with antivirals or immune modulating agents. Experts have increasingly questioned the use of unproven COVID-19 therapies outside of a clinical trial[16] and have argued that supportive care and trial enrolment are the best options until data regarding efficacy of therapies accrue.[17 18] Accumulating observational and trial data now suggest no benefit from hydroxychloroquine,[19–21] and concerns regarding harm from empiric use remain.[22] Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of experimental COVID-19 therapies outside empiric studies represents a lost opportunity for learning. It is also emblematic of the strong desire—particularly early in the pandemic—to use therapies with a theoretical potential to target the virus even

Table 4 Variation in clinical care and outcomes in COVID-19-positive patients across hospitals

	Range across hospitals							
	Min	10th Pctl	25th Pctl	Median	75th Pctl	90th Pctl	Max	P value*
Patient characteristics								
Age >65 years (%)	30.2	35.3	39.6	51.3	56.8	64.4	65.5	<0.0001
Black (%)	0.0	17.7	29.7	46.2	76.4	93.7	94.6	<0.0001
Male (%)	39.2	45.6	47.1	53.0	56.8	72.4	73.8	0.07
Charlson Comorbidity Index, median	0.0	1.0	1.0	1.0	1.0	2.0	2.0	0.01
BMI, median	24.3	28.4	29.5	31.1	33.3	36.5	36.9	0.09
Median age (years)	39.0	46.5	60.8	62.4	66.4	73.5	76.0	<0.0001
Admission information (%)								
Hospital-to-hospital transfer	0.0	0.0	0.0	0.00	2.8	10.7	20.9	<0.0001
Admitted directly to ICU	0.0	0.0	2.9	6.15	14.8	20.5	43.8	<0.0001
Transferred from floor to ICU	0.0	0.0	0.0	8.4	17.6	18.8	24.1	0.09
Admitted to a cohorted unit	0.0	2.1	18.6	67.9	85.71	96.3	97.1	<0.0001
Severe illness on presentation†	0.0	0.00	0.00	0.0	3.7	7.1	7.7	0.09
Vasopressor use on day 1	0.0	0.00	0.00	2.1	6.4	10.3	14.8	0.04
Mechanical ventilation on day 1	0.0	0.00	0.00	2.51	8.6	11.1	12.8	0.03
Treatment (%)								
Treated in a cohorted unit	0.0	0.00	6.3	57.1	90.9	100.0	100.0	<0.0001
Treated in an ICU	4.2	5.4	14.0	19.1	31.0	38.5	62.5	<0.0001
COVID-19-specific treatment	32.4	57.1	69.2	76.4	81.4	90.2	96.3	<0.0001
Concurrent antibiotic and COVID-19-specific treatment(s)	24.3	42.9	59.4	69.8	76.7	84.3	96.3	<0.0001
Hydroxychloroquine	13.5	31.4	42.3	59.7	65.5	81.5	82.4	<0.0001
Mechanical ventilation	2.1	2.7	6.4	10.9	31.0	38.5	40.6	<0.0001
Vasopressors	2.2	2.9	7.0	12.1	25.0	32.1	32.5	<0.0001
CPR before death	0.0	0.0	8.3	14.3	33.3	40.0	66.7	0.0102
Outcomes (%)								
Days of mechanical ventilation, median‡	1.0	1.0	1.0	5.0	8.0	8.0	9.0	0.01
Length of stay, median	2.0	3.0	3.0	4.5	6.0	8.0	8.5	<0.0001
ICU length of stay, median§	1.0	2.0	3.5	5.0	6.5	7.5	9.5	0.01
DVT	0.0	0.0	0.0	0.0	2.1	3.5	7.1	0.05
VTE	0.0	0.0	0.0	2.9	5.2	6.3	10.7	0.20
PE	0.0	0.0	0.0	1.8	3.9	6.3	7.1	0.72
Discharge status (%)								
Death	7.9	8.3	14.6	21.3	31.0	41.4	45.7	<0.0001
Transferred to another hospital	0.0	0.0	0.0	0.0	1.6	2.7	5.1	0.07
Discharged home	42.3	48.2	62.1	67.5	72.9	80.0	82.5	<0.0001

*Differences across hospitals were tested using the Kruskal-Wallis test for continuous variables and Pearson χ^2 test for categorical variables.
†Defined as admission to ICU on day 1 of hospitalisation and treatment with both mechanical ventilation and vasopressors.
‡For patients ever on mechanical ventilation.
§For patients ever in ICU.
¶Variables marked with asterisks represent variation from the demographic cohort.
BMI, body mass index; ICU, intensive care unit; CPR, cardiopulmonary resuscitation; DVT, deep vein thrombosis; VTE, venous thromboembolism; PE, pulmonary embolism

though improved survival from critical illness is largely attributed to improvements in supportive care.[23] Notably, we still do not have targeted therapies for sepsis or acute respiratory distress syndrome, which are the major mechanisms by which patients die from COVID-19 infection.

Another strength of our study is the variation in clinical presentation and outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19-specific treatments, corticosteroids and antibiotics varied markedly across hospitals. While we were unable to ascertain reasons for such variation, we anecdotally observed that practice evolved across hospitals over time. For example, at some Michigan hospitals, routine use of hydroxychloroquine was common in the first few weeks

of the pandemic but curbed as trial data became available. In contrast, use of hydroxychloroquine continues to be encouraged at other hospitals even today.[24] While it is unclear if these practice changes influenced outcomes, future studies exploring the rationale and impact of these changes on patients will be valuable.

Our findings provide corroboratory information regarding the first COVID-19 wave within Michigan. For example, in a single-centre retrospective study, Imam and colleagues found that advanced age and increasing number of comorbidities were independent predictors of in-hospital mortality in hospitalised Michigan patients, just as we did in our cohort.[25] Similarly, in two national population-level studies led by the Centers for Disease Control and Prevention, individuals over 65 years of age and those with ≥3 comorbidities experienced greater risk of hospitalisation and adverse outcomes, again consistent with our findings.[26 27] Our findings are also similar to others regarding disparities in COVID-19 care and outcomes, especially among minority populations.[28] Despite these findings, our study also differs from other national studies in important ways. For example, we observed a low rate of readmissions in our cohort. In contrast, Donnelly *et al* using Veterans Health Affairs data reported a readmission rate of 19.9% at 60 days.[29] While the reasons for this discrepancy are unclear, it is possible that practice pattern differences including variation in threshold for readmission and differences in patient characteristics may account for these discrepancies. As we begin to understand and manage the chronic sequelae of acute COVID-19,[30] studies understanding reasons for these pattern differences would be important. Another important difference lies in the use of therapeutics targeting COVID-19. For example, reports from New York City and Seattle show greater rates of use of remdesivir and IL-6 inhibitors.[8 31] Whether these differences were due to practice variation (which occurred widely in the early US waves of COVID-19) versus lack of access to therapeutics which was also reported is unclear.

Our study has limitations. First, given the observational nature of the study, rationales for treatment or management decisions cannot be determined. Second, because our sampling frame included patients who were discharged or deceased, our findings may be biased as patients who remain hospitalised may not be included in our cohort (potentially explaining lower duration of mechanical ventilation and hospital stay). However, COVID-19 hospitalisations in Southeastern Michigan have been declining since mid-April—limiting the degree of bias from exclusion of patients still in the hospital. Third, while variation in care was observed, the implications of such variability on clinical outcomes are unknown. Nevertheless, given that therapeutic modalities are scarce and not without risks, reducing variation may improve patient safety and resource use. Fourth, our study depends on available documentation, so symptoms, comorbidities or treatments not documented in the medical record may be omitted. For example, it is possible that the low use of prone positioning observed in our cohort may be due to incomplete documentation of this practice. Finally, we did not collect patient identifiers, so interhospital transfers could be reported as two separate hospitalisations. However, we did collect admission and discharge locations, and only 6% of the cohort was transferred from another hospital.

Our study also has strengths. First, ours is the first multihospital study to examine clinical aspects related to COVID-19 in Michigan. Through a rigorous data collection structure including a well-defined sampling strategy and trained data abstractors, we provide novel and detailed insights into clinical care during the pandemic. Second, we were able to examine variation across sites, finding substantial differences in clinical care and outcomes across hospitals. To our knowledge, this is the first study to examine differences in these important care processes, treatment approaches and outcomes across sites. Third, we report a high rate of use of non-evidence-based therapies for treating COVID-19. This finding has significant safety, economic and policy implications for the most critically ill subsets in the hospital. Finally, data collection for this effort remains ongoing, including longitudinal monitoring of patients after discharge. These data will help shed new light on the post hospital sequelae of COVID-19.

Michigan remains one of the regions most affected by COVID-19. This multicentre study provides granular clinical data regarding patients, care practices and clinical outcomes in the state. The wide variation in observed practices and outcomes suggests caution when interpreting findings from single-centre studies. Our study also demonstrates the value of hospital collaboratives to help inform best practices.

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