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Characteristics and Outcomes Among Hospitalized COVID-19-Positive Patients in a Nonurban Environment

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ABSTRACT

Introduction:

Virtually all hospitalized coronavirus disease-2019 (COVID-19) outcome data come from urban environments. The extent to which these findings are generalizable to other settings is unknown. Coronavirus disease-2019 data from large, urban settings may be particularly difficult to apply in military medicine, where practice environments are often semi-urban, rural, or austere. The purpose of this study is compare presenting characteristics and outcomes of U.S. patients with COVID-19 in a nonurban setting to similar patients in an urban setting.

Materials and Methods:

This is a retrospective case series of adults with laboratory-confirmed COVID-19 infection who were admitted to Hershey Medical Center (HMC), a 548-bed tertiary academic medical center in central Pennsylvania serving semi-urban and rural populations, from March 23, 2020, to April 20, 2020 (the first month of COVID-19 admissions at HMC). Patients and outcomes of this cohort were compared to published data on a cohort of similar patients from the New York City (NYC) area.

Results:

The cohorts had similar age, gender, comorbidities, need for intensive care or mechanical ventilation, and most vital sign and laboratory studies. The NYC's cohort had shorter hospital stays (4.1 versus 7.2 days, $P < .001$) but more African American patients (23% versus 12%, $P = .02$) and higher prevalence of abnormal alanine (>60U/L; 39.0% versus 5.9%, $P < .001$) and aspartate (>40U/L; 58.4% versus 42.4%, $P = .012$) aminotransferase, oxygen saturation <90% (20.4% versus 7.2%, $P = .004$), and mortality (21% versus 1.4%, $P < .001$).

Conclusions:

Hospitalists in nonurban environments would be prudent to use caution when considering the generalizability of results from dissimilar regions. Further investigation is needed to explore the possibility of reproducible causative systemic elements that may help improve COVID-19-related outcomes. Broader reports of these relationships across many settings will offer military medical planners greater ability to consider outcomes most relevant to their unique settings when considering COVID-19 planning.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease-2019 (COVID-19), has infected over 14 million persons in the USA, with over 275,000 deaths.[1] A case series ($N = 5{,}700$) from the New York City (NYC) area provided the first U.S. data on characteristics and outcomes of patients hospitalized with COVID-19.[2] The authors noted availability of outcome data for only 46.2% of hospitalized patients, a limitation which may affect generalizability.[2] Regional differences may also impact generalizability. For example, as of July 7, 2020, New York State accounted for over 13% of all U.S. COVID-19 cases and NYC for over 17% of all U.S. COVID-19-related deaths.[1] Coronavirus disease-2019 data from large, urban settings may be particularly difficult to apply in military medicine, where practice environments are often semi-urban, rural, or austere. For example, while the civilian world may simply shut down cruise ships, the military must maintain readiness at sea, which requires analytic models peculiar to that environment.[3] Numerous innovations have been reported across individual components of military medicine,[4] but there remains limited data on semi-urban/rural COVID-19 hospitalization outcomes that may be more relevant to inform military health policy.

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The objective of this study was to describe presenting characteristics and outcomes of patients hospitalized with a COVID-19 infection at a regional semi-urban/rural U.S. tertiary care facility and compare them to a similar cohort from an urban environment.

METHODS

This is a retrospective case series of adults with laboratory-confirmed COVID-19 infection who were admitted to Hershey Medical Center (HMC), a 548-bed tertiary academic medical center in central Pennsylvania, from March 23, 2020, to April 20, 2020 (the first month of COVID-19 admissions at HMC). This study conforms to the STrengthening the Reporting of OBservational studies in Epidemiology guidelines[5] and was deemed exempt by the Pennsylvania State College of Medicine Institutional Review Board.

Since the pandemic began, HMC has maintained a registry of HMC-hospitalized patients with COVID-19. Electronic health records of all adult COVID-19 patients on this registry during the study period were reviewed, with manual extraction of demographics; comorbidities defined using the Clinical Classification Software categories[6] (asthma, chronic obstructive pulmonary disease [COPD], diabetes mellitus [DM], cardiovascular disease or threshold body mass index (obesity, morbid obesity); admission vital signs; laboratory results from blood samples (collected within 24 h of presentation); length of stay; requirement for intensive care or mechanical ventilation; administration of COVID-19-specific medications; and discharge disposition. Published data on the NYC cohort were used for comparison.[2]

Mean, standard deviation (SD), median, and interquartile range (IQR) (the difference between 75th and 25th percentiles) described continuous variables; frequencies described binary variables. To compare HMC and NYC data,[2] either Fisher's exact test or chi-square test was used for binary variables, and two-sample *t*-test for continuous variables. The means and SDs of the NYC variables used were estimated from the published median and IQR values.[2] Missing data were deleted using the pairwise deletion method. Statistical analysis was completed using R statistical software, version 3.5.2.

RESULTS

All 69 patients hospitalized at HMC with laboratory-confirmed COVID-19 during the assessment window were analyzed. They were, on average, above middle-aged (median age: 63, IQR [52-75] and White [52%]; Table I). Almost half

TABLE I. Hershey Medical Center (HMC) Demographics, Comorbidities, and Vital Signs Comparison to New York Regional Patients

Measure	HMC ($n = 69$)	Missing[a] (HMC)	New York[2] ($n = 2{,}634$)	*P*-value[*]
Demographics				
Age (Median, IQR)	63 (43-72)	0	63 (52-75)	.17
Female Gender,[b] No. (%)	35 (51.5%)	1	3,437 (39.7%)	.06
Race,[b] No. (%)		11		
African American	7 (12.1%)		1,230 (23%)	.02[c]
Asian	9 (15.5%)		473 (9%)	
White	30 (51.7%)		2,164 (40%)	
Other	12 (20.7%)		1,574 (29%)	
Comorbidities[d], No. (%)				
Asthma	10 (14.5%)	0	9.0%	.13
COPD	4 (5.8%)	0	5.4%	.79
DM	26 (37.7%)	0	33.8%	.52
CVD	5 (7.2%)	0		
Any one of asthma, CVD, COPD, and DM	34 (49.3%)	0		
Obesity (BMI ≥ 30)	32 (49.2%)[e]	4		
Morbid obesity (BMI ≥ 35)	14 (21.5%)[e]	4		
Abnormal admission vital signs, No. (%)				
Temperature $> 38°C$	22 (31.9%)	0	1,734 (30.7%)	.9
Heart rate ≥ 100 beats per minute	27 (39.1%)	0	43.1%	.54
Respiratory rate ≥ 24 breaths per minute	17 (24.6%)	0	986 (17.3%)	.11
Oxygen saturation $\leq 90\%$	5 (7.2%)	0	1,162 (20.4%)	<.01

Abbreviations: BMI, body mass index in kg/m^2; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DM, diabetes mellitus; IQR, interquartile range; No. = number.

**P*-value was set at 95% confidence. Two-sample *t*-test, Chi-square test, and Fisher's exact test used in R version 3.5.2.

[a]Percentages based on present data (missing data excluded from denominator).

[b]As listed in medical chart. Patients were not asked regarding self-identification.

[c]Race was compared as a set.

[d]Comorbidities were defined using Clinical Classification Software categories [4] (asthma, COPD, DM, CVD) or threshold BMI in the chart (obesity, morbid obesity).

[e]The 14 morbidly obese patients are a subset of (not in addition to) the 32 obese patients listed.

TABLE II. Hershey Medical Center (HMC) Laboratory Studies, Treatments, and Outcomes Comparison to New York Regional Patients

Measure	HMC ($n = 69$)	Missing[a] (HMC)	New York[2] ($n = 2,634$)	P-value[*]
Laboratory studies, median (IQR) (reference range)				
Blood urea nitrogen (mmol/L) (2.5-7.1)	14 (10-21)	0		
Serum creatinine (mg/dL) (0.84-1.21)	0.93 (0.76-1.24)	0		
Platelets ($\times 10^3$/mL) (150-450)	194 (160-225)	1		
ALT (U/L) (10-45)	26 (18-42)	2		
AST (U/L) (10-40)	35 (26-59)	3		
ALT > 60 U/L, No. (%)	4 (5.9%)	1	2,176 (39.0%)	<.001
AST > 40 U/L, No. (%)	28 (42.4%)	3	3,263 (58.4%)	.012
Lactate dehydrogenase (U/L) (50-242)	296 (255-371)	25	404.0 (300-551.5	.08
CRP (mg/dL) (0.0-0.40)	4.9 (3, 9)	15	13.0 (6.4-26.9)	.74
Ferritin (ng/mL) (15-400)	569.6 (262, 803)	13	798 (411-1,515)	.064
White blood cell count ($\times 10^9$/L) (3.8-10.5)	6.47 (4.46, 8.51)	0	7.0 (5.2-9.5)	1
Lymphocyte % (20-40)	13 (8, 22)	4		
Neutrophil % (40-60)	76 (66, 84)	4		
COVID-19-specific treatments, No. (%)				
Hydroxychloroquine alone	33 (47.8%)	0		
Remdesivir alone	3 (4.4%)	0		
Hydroxychloroquine and remdesivir	3 (4.4%)	0		
Zinc alone	1 (1.4%)	0		
Hospital course				
Required intensive care, No. (%)	7 (10.1%)	1	373 (14.2%)	0.44
Required mechanical ventilation, No. %	3 (4.3%)	0	320 (12.2%)	0.057
Median length of stay (days) (IQR)	5.5 (3.1-8.9)	0	4.1 (2.3-6.8)	<0.001
Died, No. %	1 (1.4%)	0	553 (21%)	<0.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; IQR, interquartile range; No. = number.
*P-value was set at 95% confidence. Two-sample t-test, Chi-square test, and Fisher's exact test used in R version 3.5.2.
[a]Percentages based on present data (missing data excluded from denominator).

(49.3%) had at least one comorbidity, most commonly obesity (49.2%) and DM (37.7%).

Admission vital sign abnormalities were common, with 31.9% of patients febrile (temperature > 38°C), 39.1% tachycardic (heart rate ≥ 100 beats/minute), and 24.6% tachypneic (respiratory rate ≥ 20 breaths/minute); only 7.2% of patients had an oxygen saturation ≤ 90%. Median systolic and diastolic blood pressure was 135 mmHg (IQR 122-149) and 79 mmHg (IQR 70-88), respectively.

Median blood urea nitrogen was elevated (14 mmol/L, IQR [10-21]; Table II). Median creatinine, aminotransferases, and white blood cell count were within the normal range. Median lactate dehydrogenase, C-reactive protein, and ferritin concentrations were mildly elevated, but had several missing data points (Table II). Hydroxychloroquine alone was administered orally to 33 (48%) patients; remdesivir alone was administered intravenously to three (4%) patients, and their combination was administered to three (4%) patients. One patient received oral zinc alone.

Few patients required intensive care (10.1%) or mechanical ventilation (4.3%). The median length of hospitalization was 5.5 days (IQR 3.1, 8.9). Most patients were discharged home (78.3%) or to skilled nursing or rehabilitation (20.3). Only one patient (1.4%), an 84-year-old man with COPD and do-not-resuscitate preference, died.

Comparison to NYC Cohort

The cohorts had similar age, gender, and comorbidities (Table I). New York City's cohort included more African Americans (23% versus 12.1%, $P = .02$) and had a higher prevalence of patients with abnormal alanine (>60U/L; 39.0% versus 5.9%, $P < .001$) and aspartate (>40U/L; 58.4% versus 42.4%, $P = .012$) aminotransferase concentrations, and oxygen saturation ≤ 90% (20.4% versus 7.2%, $P < .01$). The cohorts did not differ in other vital signs, laboratory values, or need for intensive care or mechanical ventilation (Table II). Median length of hospital stay was longer for HMC patients (5.5 days versus 4.1 days, $P < .001$). The NYC mortality rate was higher than that at HMC (21% versus 1.4%, $P < .001$).

DISCUSSION

The 69 adult patients with COVID-19 hospitalized at HMC from March 23, 2020, to April 20, 2020 experienced a substantially lower mortality rate than that reported among the NYC cohort patients.[2] The HMC patients were similar in age, gender, and comorbidities, but less racially diverse compared to the NYC cohort.[2] Without a prospective study it is not possible to conclusively explain the reasons underlying these differences in mortality. However, there are several factors to consider.

New York City's first COVID-19 case was announced on March 1, 2020[7]; by the end of March, NYC was overwhelmed with cases,[8] about the time HMC reported its first case.[9] This gave HMC preparation time and knowledge about COVID-19. Hershey Medical Center, a designated Ebola Treatment Center, leveraged its expertise with special pathogens to develop COVID-19 protocols from phone triage through community discharge plans to minimize variability in care and viral transmission risk during care. Protocols also took advantage of early case reports showing better outcomes with noninvasive positive pressure ventilation and high flow oxygen (versus early intubation[10]) and self-proning when possible. Lower admission rates allowed care to be provided by a dedicated COVID-19 team of experienced hospitalists and intensivists.

The NYC patients appeared sicker than HMC patients on presentation, based on their liver-associated enzyme and oxygen saturation values. Population density may be related to viral load and, hence, disease severity.[11,12] Hershey Medical Center's lower population density (993 persons per square mile[13] versus NYC's 27,000[14]) may be protective; enough to overcome HMC's lower intent to comply with public health recommendations compared to NYC.[15] Other differences could be baseline disease burden, resources, or access to care. Access to care limitations could include a lower baseline access or could be related to limited inpatient beds[16]; patients who may have been sick enough to admit under normal circumstances may have been healthier than others presenting during the COVID-19 pandemic, such that they were sent home. Resource limitations could include bed space, equipment (i.e., ventilators), or medications (i.e., remdesivir or hydroxychloroquine).[16–18] Social determinants of health may also play a role. New York City had more African Americans, whose age-adjusted hospitalization rate is 4.7 times higher than Whites.[19]

CONCLUSIONS

This retrospective case series provides a contrast in characteristics and outcomes of patients hospitalized with COVID-19 infection at HMC, a semi-urban/rural tertiary clinical center in central Pennsylvania, and in the NYC area. Although results may not be generalizable to different environments, this comparison is directly relevant to military medicine. At a strategic level, the success of HMC may in part be attributed to its emphasis on infectious outbreak preparedness as a function of its role as an Ebola Treatment Center. Because the value of readiness is in the future, the cost of readiness is a tempting target for budget cuts—with disastrous, but future, consequences.[20] When arguing against readiness cuts, HMC's 93% lower mortality may prove a compelling example of the value of readiness. At a tactical level, the significant differences in outcomes between HMC and NYC suggest that military planners carefully consider how they construct screening and treatment protocols. Overreliance on NYC outcomes to drive more stringent treatment protocols would ignore that their outcomes were likely driven in part by their patients being sicker at presentation, in turn likely because of limited access to care. Under the military system, with free care provided to members and beneficiaries, early screening and support may be expected to substantially lessen the burden on inpatient facilities. Further, although most active duty populations will have a lower obesity and chronic disease rate than HMC patients, military planners may take advantage of the apparent benefit of HMC patients' natural social distancing through lower population density. Planners would do well to space traditionally high-density populations (i.e., barracks) to make their population mirror HMC. For populations challenged to distance (i.e., ships or submarines), planners may consider more stringent masking, contact, and handwashing protocols to gain the benefit of social distancing in settings where physical proximity is unavoidable.

Studies investigating the relationships between patient outcomes and comorbidities, social determinants, population density, and preparedness status are urgently needed to identify prognosticators of, and improve outcomes in, patients hospitalized with COVID-19 infection across differing practice environments. Broader reports of these relationships across many settings will offer military medical planners greater ability to consider outcomes most relevant to their unique settings when considering COVID-19 planning.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

ETHICAL APPROVAL

This research was deemed exempt from review with no requirement of consent by the Pennsylvania State College of Medicine Institutional Review Board.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

AUTHORS' CONTRIBUTIONS

R.P.L.: conception, design, acquisition, interpretation, and drafted the work. T.J.D.: acquisition, interpretation, and substantial revision. M.F.K.: acquisition, interpretation, and substantial revision. L.J.V.: analysis of data, interpretation, and substantial revision. E.M.: analysis of data, interpretation, and substantial revision. H.D.: analysis of data, interpretation, and substantial revision. A.Z.E.: analysis of data, interpretation, and substantial revision. All authors read and approved the final manuscript.

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