

A Retrospective Cohort Study of Treatment Patterns and Clinical Outcomes in Patients with COVID-19



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INTRODUCTION

- SARS-CoV-2 pneumonia (COVID-19) is a serious global health threat.
- Multiple agents were suggested as possible treatments early in the pandemic.
- These off-label treatments carried a significant risk of drug adverse events.

MATERIALS AND METHODS

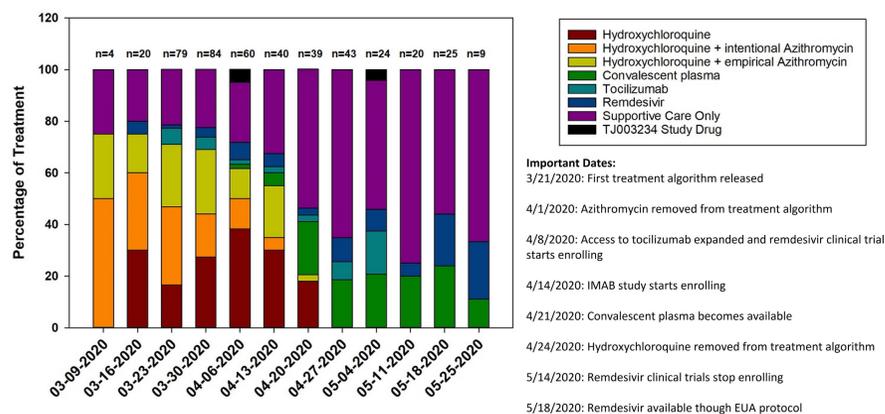
- Retrospective cohort study of all patients admitted to any IU Health hospital for >24hrs with positive SARS-CoV-2 polymerase chain reaction (PCR) from nasopharyngeal, oropharyngeal, and/or bronchoalveolar lavage sample
- Data extracted manually from review of the electronic medical record
- Primary outcome – in-hospital mortality
- Secondary outcomes – admission to the intensive care unit (ICU), endotracheal intubation, initiation of vasopressors, and drug-related adverse events

RESULTS

- Data collection was completed for 453 patients admitted between March 18, 2020 and May 8, 2020.
- All-cause in-hospital mortality was 14.3% (65/453) during this time. Mortality rates increased with age, up to 45% for patients over 80 years old.
- QTc interval prolongation occurred significantly more frequently in patients who received hydroxychloroquine (HCQ) with or without azithromycin (AZM) than those who did not (HCQ 6%, HCQ+AZM 7.8% vs all other patients, 0%, p<.0001).
- Review of treatment trends showed close adherence to the treatment recommendations at that time (Figure 1).

RESULTS

Figure 1. Treatment Choices Over Time, 3/9/2020-5/25/2020



RESULTS

Table 1. Patient Characteristics

Characteristic	Total n(%)
Age (years)	
0-17	14 (3.1)
18-40	82 (18.1)
41-50	51 (11.3)
51-60	100 (22.1)
61-70	90 (19.9)
71-80	65 (14.3)
≥81	51 (11.4)
Gender	
Male	230 (50.8)
Female	223 (49.2)
Treatment	
HCQ	222 (49)
HCQ + AZM	129 (28.5)
LPV/r	4 (0.8)
RDV	33 (7.2)
Tocilizumab	23 (5.1)
TJ003234 Study Drug	5 (1.1)
Convalescent Plasma	53 (11.7)
Supportive Care Only	112 (24.7)
Severity	
No supplemental oxygen	86 (19.2)
Supplemental oxygen, no ICU	178 (39.7)
ICU admission <48hrs after admission	61 (13.5)
ICU admission >48hrs after admission	64 (14.1)
Mechanical Ventilation	125 (27.6)
Vasopressors	91 (20.3)
ECMO	10 (2.2)
Death	65 (14.3)

AZM, azithromycin; ECMO, extracorporeal membrane oxygenation; HCQ, hydroxychloroquine; ICU, intensive care unit; LPV/r, lopinavir/ritonavir; RDV, remdesivir

RESULTS

Table 3. Incidence of Drug Adverse Events

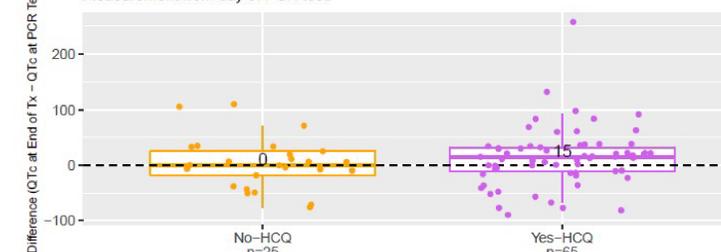
Treatment	Total n	None n(%)	GI Symptoms n(%)	QT Interval Prolongation n(%)	Allergic Reaction n(%)	Renal Injury n(%)	Liver Injury n(%)	Bacterial Infection n(%)	Other n(%)
HCQ	222	195 (87.8)	2 (0.9)	12 (5.4)	0	5 (2.3)	10 (4.5)	0	4 (1.9)
HCQ + AZM†	129	112 (86.2)	1 (0.8)	7 (5.4)	0	3 (2.3)	8 (6.2)	0	4 (3.1)
LPV/r	4	3 (75)	0	0	0	0	1 (25%)	0	0
RDV	33	25 (75.8)	1 (3)	1 (3)	0	2 (6.1)	5 (15.2)	0	2 (6.1)
Tocilizumab	23	10 (43.5)	0	0	0	1 (4.3)	2 (8.7)	11 (47.8)	0
TJ003234 Study Drug	5	3 (60)	0	0	0	0	1 (20)	1 (20)	0
Convalescent Plasma	53	47 (88.7)	1 (1.9)	0	0	1 (1.9)	4 (7.5)	0	1 (1.9)

AZM, azithromycin; GI, gastrointestinal; HCQ, hydroxychloroquine; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; LPV/r, lopinavir/ritonavir; RDV, remdesivir
 †All patients who received HCQ + at least 1 dose of AZM

RESULTS

Figure 2. QTc Interval Change and Hydroxychloroquine (HCQ) Use

Note: Y-axis shows difference from end of treatment relative to day of PCR test. Values above 0 show increase in measurement from day of PCR test. Values lower than 0 show decrease in measurement from day of PCR test.



	HCQ	HCQ+AZM	No HCQ or AZM	p-value
QTc prolongation	5 (6.0)	9 (7.8)	0 (0)	<.0001*
No QTc prolongation	79 (94.1)	106 (92.2)	249 (100)	

Values are frequencies (percentages) with p-value from Fisher's Exact test.

AZM, azithromycin; HCQ, hydroxychloroquine

RESULTS

Table 2. Primary and Secondary Outcomes

Treatment	Total n(%)	ICU Admission n (%)	Endotracheal Intubation n(%)	Hospital LOS (Days) Median(IQR)	ICU LOS (Days) Median (IQR)	Dead n(%)
Cases	453 (100)	190 (41.9)	125 (27.6)	9 (6, 16)	10 (5, 18)	65 (14.3)
HCQ	222 (49)	117 (52.7)	92 (41.4)	10 (7, 20)	12 (6, 18)	33 (14.9)
HCQ + AZM*	90 (19.9)	67 (74.4)	58 (64.4)	16 (8, 24)	14 (8, 19)	19 (21.1)
LPV/r	4 (0.9)	3 (75)	3 (75)	21.5 (17, 22)	17 (13, 18)	1 (25)
RDV	33 (7.3)	20 (60.6)	10 (30.3)	14 (9, 21)	8 (6, 17)	3 (9.1)
Tocilizumab	23 (5.1)	23 (100)	19 (82.6)	22 (15, 33)	18 (12, 28)	8 (34.8)
TJ003234 Study Drug	5 (1.1)	5 (100)	3 (60)	18 (12, 22)	12 (8, 16)	1 (20)
Convalescent Plasma	53 (11.7)	41 (77.4)	23 (43.4)	16 (10, 26)	12 (6, 24)	15 (28.3)
Supportive Care Only	112 (24.7)	16 (14.3)	6 (5.4)	6 (4, 10)	6 (3, 10)	12 (10.7)

AZM, azithromycin; HCQ, hydroxychloroquine; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; LPV/r, lopinavir/ritonavir; RDV, remdesivir

*All patients who received HCQ + at least 3 days of AZM

CONCLUSIONS

- Treatment choices changed rapidly over time as new literature became available
- Differences in hospital and ICU length of stay are likely attributable to differences in patient severity at the time of drug initiation
- Use of off-label treatments for COVID-19 was associated with a high incidence of drug-related adverse events
- Hydroxychloroquine use was associated with statistically significant prolongation of QTc interval.