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Characteristics, Outcomes and 60-Day Hospital Mortality of ICU Patients with COVID-19 and Acute Kidney Injury

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Abstract

Background AKI has been reported in patients with COVID-19 pneumonia and it is associated with higher mortality. The aim of our study is to describe characteristics, outcomes, and 60-day hospital mortality of patients with COVID-19 pneumonia and AKI in the intensive care unit (ICU).

Methods We conducted a retrospective study in which all adult patients with confirmed COVID-19 who were admitted to ICUs of Montefiore Medical Center and developing AKI were included. The study period ranged from March 10 to April 11, 2020. The 60-day follow-up data through June 11, 2020 were obtained.

Results Of 300 adults admitted to the ICUs with COVID-19 pneumonia, 224 patients (75%) presented with AKI or developed AKI subsequent to admission. A total of 218 (97%) patients required invasive mechanical ventilation for moderate to severe acute respiratory distress syndrome (ARDS). A total of 113 (50%) patients had AKI on day 1 of ICU admission. The peak AKI stages observed were stage 1 in 49 (22%), stage 2 in 35 (16%), and stage 3 in 140 (63%) patients, respectively. Among patients with AKI, 114 patients (51%) required RRT. The mortality rate of patients requiring RRT was 70%. Of the 34 patients who were survivors, 25 (74%) were able to be weaned off RRT completely before hospital discharge. Nonsurvivors were older and had significantly higher admission and peak creatinine levels, admission hemoglobin, and peak phosphate levels compared with survivors. The 60-day hospital mortality was 67%.

Conclusions COVID-19 requiring ICU admission is associated with high incidence of severe AKI, necessitating RRT in approximately half of such patients. The majority of patients with COVID-19 and AKI in ICU developed moderate to severe ARDS, requiring invasive mechanical ventilation. Timing or severity of AKI did not affect outcomes. The 60-day hospital mortality is high (67%). Patients with AKI requiring RRT have high mortality, but survivors have good rates of RRT recovery.

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Introduction

AKI is a marker of severe disease in patients with coronavirus disease 2019 (COVID-19) and is associated with higher mortality (1–3). Multiple studies have reported that the hospital incidence of AKI in patients with COVID-19 is between 0.5% and 37% (L. Chan *et al.*: Acute kidney injury in hospitalized patients with COVID-19. *medRxiv* 10.1101/2020.05.04.20090944) (3–5). In the intensive care units (ICUs), the incidence of AKI is much higher, ranging from 21% to as high as 78% (L. Chan *et al.*: Acute kidney injury in hospitalized patients with COVID-19. *medRxiv* 10.1101/2020.05.04.20090944) (6–8). The aim of our research is to study the clinical characteristics, complications, outcomes, and 60-day hospital mortality of patients with laboratory-confirmed COVID-19 who were admitted to the ICU with AKI or who developed AKI during their stay in ICU.

Materials and Methods

We conducted a retrospective, observational study in adult ICUs of the Montefiore Medical Center. All adult patients who were positive for COVID-19 in the ICU, who developed AKI at ICU admission or during the course of ICU stay, were included. The study period was March 10 to April 11, 2020. Patients with ESKD, pregnancy, and history of kidney transplant were excluded. The study was approved by the Montefiore Medical Center Institutional Review Board and a waiver of informed consent was granted.

AKI was defined using the Kidney Disease: Improving Global Outcomes (KDIGO) criteria: stage 1, increase in serum creatinine by 0.3 mg/dl within 48 hours or 1.5–1.9 times increase in serum creatinine from baseline within 7 days; stage 2, a two to 2.9 times increase in

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serum creatinine from baseline within 7 days; stage 3, a three times or more increase in serum creatinine within 7 days, increase in serum creatinine to ≥4 mg/dl, or initiation of RRT (9).

Baseline creatinine was defined using the last creatinine value in the electronic medical record between 7 and 365 days before the current admission (10). If no prehospital baseline creatinine value was available, we defined it as the lowest serum creatinine value during the current hospitalization. Baseline creatinine value was not known in 43% of our patients. Data were collected through June 11, 2020 to provide 60 days of follow-up. We excluded CKD as a comorbid condition because we did not know baseline creatinine in a high proportion of our patients, and the diagnosis of CKD using the electronic health record has low sensitivity and a low positive predictive value (11). In-hospital survivors at 60 days were defined as patients discharged alive or alive in hospital at 60 days, with censorship either at discharge or at the end of the 60-day follow-up period. In-hospital nonsurvivors at 60 days were the patients who died in the hospital by the end of follow-up period.

Descriptive statistics were reported as means, medians or counts, and percentages, and analyses were performed using the Fisher exact test, *t* test, or Wilcoxon rank sum test. The Fine and Gray multivariable model of risk of in-hospital mortality was created with discharge alive treated as a competing event.

Results

Baseline Characteristics

A total of 300 adults were admitted to our ICUs during the study period. Of these patients, 224 developed AKI, with a cumulative incidence of 75%. The mean (±SD) age was 60 (±11.78) years and 140 (62%) patients were males. By the end of our follow-up period on June 11, 149 (67%) patients died and 75 (34%) survived (67 discharged alive, eight still in hospital). Table 1 lists the baseline characteristics of our patients. Compared to 76 patients who did not develop AKI, patients with AKI were older, had higher body mass index, and had a statistically significant higher incidence of diabetes mellitus, hypertension, and history of smoking (Table 1).

ICU Course and Complications

Table 2 lists ICU complications and outcomes. A total of 218 (97%) patients needed invasive mechanical ventilation, with a median of 10 ventilator days, and 60% patients had severe and 36% had moderate acute respiratory distress syndrome (ARDS), respectively. Median (interquartile range) ICU length of stay was 11 (6–18) days and median hospital length of stay was 16 (9–28) days.

Table 1. Baseline characteristics of patients

Characteristics	Patients with AKI (*N*=224)	Patients with No AKI (*n*=76)	*P* Value	AKI in Hospital		*P* Value
				Survivor at 60 d (*N*=75)[a]	Nonsurvivor at 60 d (*N*=149)[b]	
Age (yr), mean (SD) (IQR)	60.1 (11.78) (26–97)	52.1 (13.30) (30–89)	<0.001[c]	55.9 (11.1) (26–93)	62.2 (11.6) (37–97)	<0.001[c]
Female, *n* (%)	84 (38)	33 (43)	0.36	37 (49)	47 (32)	0.01[c]
Race, *n* (%)			0.17 (omnibus)			0.96 (omnibus)
White	33 (15)	7 (9)		10 (13)	23 (15)	
Black	83 (37)	23 (30)		28 (37)	55 (37)	
Hispanic	84 (38)	32 (42)		28 (37)	56 (38)	
Other	24 (11)	14 (18)		9 (12)	15 (10)	
BMI (kg/m^2) (*n*=221), median (IQR)	31.12 (28.0–37.11)	29 (25.80–33.91)	0.02[c]	32.18 (27.1–35.9)	30.77 (28.0–38.35)	0.48
Diabetes, *n* (%)	107 (48)	23 (30)	0.008[c]	41 (55)	66 (44)	0.16
HTN, *n* (%)	154 (69)	41 (54)	0.02[c]	45 (60)	109 (73)	0.05[c]
CAD, *n* (%)	33 (15)	7 (9)	0.15	8 (11)	25 (17)	0.32
COPD, *n* (%)	15 (7)	4 (5)	0.44	4 (5)	11 (7)	0.78
HIV, *n* (%)	5 (2)	1 (1)	0.26	3 (4)	2 (1)	0.34
HFrEF, *n* (%)	12 (5)	4 (5)	0.58	3 (4)	9 (6)	0.76
HFpEF, *n* (%)	6 (3)	2 (3)	0.67	0 (0)	6 (4)	0.18
Cancer, *n* (%)	20 (9)	4 (5)	0.22	4 (5)	16 (11)	0.22
DVT history, *n* (%)	5 (2)	2 (3)	0.56	1 (1)	4 (3)	0.67
Smoker, *n* (%)	57 (25)	8 (11)	0.006[c]	14 (19)	43 (29)	0.11
NSAID, *n* (%)	47 (21)	17 (22)	0.79	15 (20)	32 (21)	0.86
ACE inhibitors, *n* (%)	39 (17)	14 (18)	0.84	10 (13)	29 (19)	0.35
ARBs, *n* (%)	46 (21)	17 (22)	0.73	13 (17)	33 (22)	0.48

IQR, interquartile range; BMI, body mass index; HTN, hypertension; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; DVT, deep vein thrombosis; NSAIDs, nonsteroidal anti-inflammatory drugs; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers.
[a]Patients discharged alive or alive in hospital with censorship at end of 60-d follow-up period.
[b]In-hospital death at the end of 60-d follow-up period.
[c]$P \leq 0.05$.

Table 2. AKI patient outcomes and admission and peak laboratory values

Outcomes	Overall (N=224)	In Hospital		P Value
		Survivors at 60 d (N=75)[a]	Nonsurvivors at 60 d (N=149)[b]	
ICU LOS (d), median (IQR)	11 (6–18)	14 (8–26)	9 (6–15)	<0.001[c]
Hospital LOS (d), median (IQR)	16 (9–28)	29 (17–42)	12 (7–20)	<0.001[c]
RRT (n=114), n (%)	114 (51)	34 (30)	80 (70)	0.26
RRT (d), median (IQR)	7 (4–16)	17.5 (8–26)	5 (3–10)	<0.001[c]
First RRT modality (n=114), n (%)				0.62 (omnibus)
CVVHD	33 (29)	11 (33)	22 (67)	
IHD	52 (46)	13 (25)	39 (75)	
PD	15 (13)	6 (40)	9 (60)	
SLED/SCUF	14 (12)	4 (29)	10 (72)	
Diuretics, n (%)	187 (83)	63 (84)	124 (83)	>0.99
Steroids, n (%)	131 (58)	46 (61)	85 (57)	0.57
Mechanical ventilation, n (%)	218 (97)	72 (96)	146 (98)	0.41
Days on ventilator, median (IQR)	10 (6–18)	11 (7.5–22.5)	9 (6–16)	0.02[c]
ARDS, n (%)				0.04 (omnibus)[c]
None	5 (2)	3 (4)	2 (1)	
Mild	4 (2)	3 (4)	1 (1)	
Moderate	82 (37)	32 (43)	50 (34)	
Severe	133 (59)	37 (49)	96 (64)	
Vasopressors, n (%)	190 (85)	53 (71)	137 (92)	<0.001
NE	185 (83)	53 (60)	132 (98)	(omnibus)[c]
Vasopressin	106 (47)	17 (23)	89 (60)	
Phenylephrine	76 (34)	17 (23)	59 (40)	
Epinephrine	26 (12)	4 (5)	22 (15)	
AKI at admission (day 1), n (%)	113 (50)	35 (46)	78 (52)	0.48
AKI postadmission, n (%)	111 (50)	40 (53)	71 (48)	0.42
Day 2	24 (11)	6 (8)	18 (12)	
Day 3	23 (10)	7 (9)	16 (11)	
Day 4	15 (7)	8 (11)	7 (5)	
Day 5	13 (6)	4 (5)	9 (6)	
Day 6	15 (7)	6 (8)	9 (6)	
Day 7	4 (2)	1 (1)	3 (2)	
>7 Days	17 (8)	8 (11)	9 (6)	
Peak AKI stage, n (%)				0.35 (omnibus)
1	49 (22)	19 (25)	30 (20)	
2	35 (16)	14 (19)	21 (14)	
3	140 (63)	42 (56)	98 (66)	
Liberation from RRT (n=114), n (%)[d]	36 (32)	25 (69)	11 (31)	<0.001[c]
Admission laboratory tests				
Creatinine (mg/dl), median (IQR)	1.27 (0.9–1.7)	1.1 (0.8–1.6)	1.3 (0.9–1.7)	0.04[c]
WBC (k/μl), median (IQR)	8.7 (6.1–12.0)	9.3 (5.8–13.1)	8.6 (6.2–11.0)	0.55
Lymphocyte (%), median (IQR)	11 (8.0–17.0)	12.0 (8.0–18.0)	11.0 (8.0–15.0)	0.32
Hemoglobin (g/dl), median (IQR)	13.5 (11.7–14.6)	13.0 (11.1–14.3)	13.6 (12.1–14.9)	0.03[c]
Platelet (k/μl), median (IQR)	209 (157–259)	214.5 (164.0–269.0)	204.0 (155.0–257.0)	0.63
BUN (mg/dl), median (IQR)	22.0 (14.0–33.5)	19.0 (12.0–35.0)	22.0 (15.0–33.0)	0.39
Na (mEq/L), median (IQR)	136.0 (133.0–139.0)	137.0 (133.0–140.0)	136.0 (133.0–139.0)	0.12
K (mEq/L), median (IQR)	4.4 (4–4.8)	4.3 (3.9–4.6)	4.5 (4.0–4.8)	0.11
Troponin (ng/ml), median (IQR)	0.01 (0.01–0.04)	0.01 (0.01–0.03)	0.01 (0.01–0.04)	0.29
Hematuria (≥3 RBCs/HPF), n (%)	121 (54)	40 (60)	81 (60)	>0.99
Proteinuria, n (%)				0.48
Normal/trace (up to 30 mg/dl)	34 (17)	13 (11)	21 (22)	
1+ (30–100 mg/dl)	53 (26)	19 (18)	34 (35)	
2+ (100–300 mg/dl)	78 (38)	27 (26)	51 (52)	
3+ (300–1000 mg/dl)	35 (17)	8 (12)	27 (23)	
4+ (>1000 mg/dl)	5 (2)	1 (2)	4 (3)	
Urine Na (mEq/L), median (IQR)	24.5 (20.0–51.0)	28.0 (20.0–56.0)	23.0 (20.0–49.0)	0.40
BUN/Cr ratio, median (IQR)	16.7 (13.25–20.75)	16.8 (13.1–22.5)	16.7 (13.4–20.4)	0.94
Peak laboratory values, median (IQR)[e]				
BUN (mg/dl)	104.0 (61.0–140.0)	106.0 (56.0–140.0)	103.5 (63.0–142.5)	0.37

Table 2. (Continued)

Outcomes	Overall (*N*=224)	In Hospital		*P* Value
		Survivors at 60 d (*N*=75)[a]	Nonsurvivors at 60 d (*N*=149)[b]	
Creatinine (mg/dl)	5.5 (2.95–8.56)	3.8 (1.8–8.5)	6.2 (3.9–8.6)	0.007[c]
Phosphate (mg/dl)	8 (5.5–11.1)	7.1 (4.9–10.9)	8.3 (5.8–11.8)	0.05[c]
Magnesium (mg/dl)	3.0 (2.1–4.4)	3.0 (2.6–3.3)	3.0 (2.7–3.4)	0.82
Lactate (mmol/L)	3.05 (2.2–4.65)	2.6 (1.9–3.5)	3.4 (2.3–5.6)	<0.001[c]
Procalcitonin (ng/ml)	4.6 (1.5–15.7)	2.6 (0.9–11.1)	6.0 (2.1–21.8)	0.01[c]
Ferritin (ng/ml)	1894.0 (1141.5–3581.0)	1835.0 (930.0–3852.0)	1909.0 (1154.0–3568.0)	0.96
LDH (U/L)	747.5 (570.0–993.0)	701.5 (601.0–922.0)	770.0 (567.0–1005.0)	0.45
CRP (mg/dl)	31.8 (20.7–41.5)	23.4 (16.1–36.5)	33.8 (23.9–44.3)	0.001[c]
D-Dimer (μg/ml)	14.85 (6.84–20.0)	12.1 (6.8–20.0)	17.6 (6.8–20.0)	0.16
Fibrinogen (mg/dl)	748.5 (629.0–895.0)	763.5 (659.5–924.0)	729.5 (579.5–875.0)	0.11
CPK (U/L)	733.0 (242.0–2273.0)	1162.0 (220.0–2466.0)	655.0 (261.0–1996.0)	0.23
Troponin (ng/ml)	0.06 (0.01–0.25)	0.06 (0.01–0.23)	0.06 (0.01–0.25)	0.70
Pro-BNP (pg/ml)	800.5 (230.0–3758.0)	715.0 (230.0–4455.0)	845.0 (234.0–3479.0)	0.95
AST (U/L)	113 (70–235)	92.0 (63.0–214.0)	118.0 (74.5–241.5)	0.12
ALT (U/L)	78 (42–157)	93.0 (41.0–161.0)	70.5 (43.5–133.0)	0.17
Bilirubin (mg/dl)	0.9 (0.5–2.0)	0.8 (0.5–1.9)	1.0 (0.6–2.0)	0.17
Creatinine before initiation of RRT (mg/dl)	7.05 (5.2–8.8)	7.07 (4.87–9.3)	7.05 (5.48–8.3)	0.86

ICU, intensive care unit; LOS, length of stay; IQR, interquartile range; CVVHD, continuous venovenous hemodialysis; IHD, intermittent hemodialysis; PD, peritoneal dialysis; SLED, sustained low-efficiency dialysis; SCUF, slow continuous ultrafiltration; ARDS, acute respiratory distress syndrome; WBC, white blood count; Na, sodium; K, potassium; LDH, lactate dehydrogenase; CRP, C-reactive protein; CPK, creatine phosphokinase; Pro-BNP, N-type probrain natriuretic peptide; AST, aspartate aminotransferase; ALT, alanine aminotransferase.
[a]Patients discharged alive or alive in hospital with censorship at end of 60-d follow-up period.
[b]In-hospital death at the end of 60-d follow-up period.
[c]$P<0.05$.
[d]Patients whose native kidney function improved such that they were able to be weaned off of RRT completely and no longer required it for clearance or volume removal.
[e]Peak laboratory values measured during entire hospitalization.

Laboratory Results

Table 2 summarizes admission and peak laboratory results during hospitalization for our patients. Nonsurvivors had significantly higher admission and peak creatinine levels, admission hemoglobin, and peak phosphate levels compared with survivors.

Renal Outcomes

Of the 224 patients with AKI, 113 (50%) presented with AKI on day 1 of ICU admission, with the remainder developing AKI during their ICU course. The peak AKI stage was stage 1 in 49 (22%), stage 2 in 35 (16%), and stage 3 in 140 (63%) patients. Mechanical ventilation was required in 96% of patients with stage-1 AKI, 91% of patients with stage-2 AKI, and 99% of patients with stage-3 AKI. Of the 134 (60%) patients with severe ARDS, 66% had stage-3 AKI, 13% had stage-2 AKI, and 21% had stage-1 AKI. A total of 114 patients (51%) required RRT; the median number of days of RRT overall was 7 days, with a median of 17.5 days in survivors compared with 5 days in nonsurvivors. Of the total of 114 patients requiring RRT, 80 (70%) died. Of the 34 (30%) survivors requiring initiation of RRT, 25 (74%) patients were able to be weaned from RRT completely before hospital discharge. The 60-day, in-hospital mortality was 67%. We did not observe any differences in mortality on the basis of timing of AKI development and severity of AKI. Using the Fine and Gray multivariable model, advancing age, serum potassium, and hemoglobin levels on admission were predictors of risk of in-hospital mortality. (Figure 1).

Discussion

Our study reports an extremely high incidence (75%) of AKI in patients with COVID-19 in the ICU setting, with a high 60-day mortality of 67%. Of our patients, 63% had severe stage-3 AKI. Similar findings were reported by Chan *et al.* (L. Chan *et al.*: Acute kidney injury in hospitalized patients with COVID-19. *medRxiv* 10.1101/2020.05.04.20090944) describing 3235 patients in hospital with an incidence of AKI of 68% among patients admitted to the ICU, with the majority having stage-3 AKI. They reported that 34% of patients in ICU required RRT, whereas 50% patients required RRT in our study. Their in-hospital mortality for patients with COVID-19 and AKI in ICU is 52% (study period of 49 days), compared with our in-hospital, 60-day mortality of 67%. Our higher mortality rate may reflect our longer, 60-day follow-up on all patients, and due to our population being mainly comprised of underserved socioeconomic groups (Black and Hispanic patients) who have been noted to have a higher burden of COVID-19–related AKI due to multiple

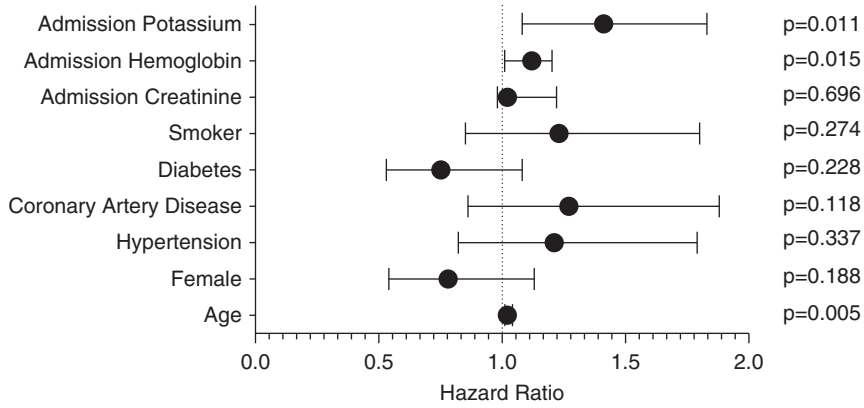

Figure 1. | **Predictors of risk of in-hospital mortality.** Fine and Gray competing-risk multivariate model with adjusted subdistributed hazard ratio. *N*=218; death events=144. Discharge alive was treated as a competing event; patients still in hospital at the end of follow-up were censored at last day of follow-up. Units of measure: admission potassium, mEq/L; admission hemoglobin, gm/dl; admission creatinine, mg/dl; age, years.

comorbidities and a higher mortality rate (12). In the previous cited study by Chan *et al.* (L. Chan *et al.*: Acute kidney injury in hospitalized patients with COVID-19. *medRxiv* 10.1101/2020.05.04.20090944), >40% of patients in hospital who were discharged alive did not recover kidney function. In our study, we did not report recovery of kidney function, however, weaning off of RRT was achieved in only 36 (32%) patients, 25 (69%) of them being survivors. Eleven patients weaned off of RRT still died due to worsening respiratory failure. Overall, RRT was associated with dismal outcomes because only 34 (30%) patients receiving RRT survived to 60 days of follow-up.

We did not observe any differences in outcomes on the basis of peak stage of AKI or the severity of AKI. This is in contrast to the study by Lim *et al.* (3) who reported that stage-3 AKI was associated with higher mortality compared with no AKI or stage-1 AKI. We hypothesize the likely reason for this disparity in findings is that severe ARDS and septic shock are a greater determinant of poor outcomes than peak stage of AKI in our patients. Also, inconsistencies in determination of peak AKI stage could be a reason, given that 43% of patients were missing a prehospital baseline creatinine value.

AKI in patients with COVID-19 is closely associated with the need for invasive mechanical ventilation. These findings are similar to a study by Hirsch *et al.* (4) who reported that 90% of patients on mechanical ventilation developed AKI. We found that patients who are obese, older in age, have a history of hypertension, diabetes mellitus, and who smoke are at greater risk of developing COVID-19–associated AKI in ICU, similar to the risk factors described by Hirsch *et al.* (4). Darmon *et al.* (13) described a 44% rate of AKI in ARDS, whereas we report that COVID-19–associated ARDS has a much higher rate of AKI of >70% in patients requiring ICU admission.

The major strength of our study is that we have a 60-day follow-up of outcomes for all patients and we report the 60-day hospital mortality. Our study had several important limitations. First, we did not include CKD as the comorbid condition because we did not know baseline creatinine in 43% of patients. This could also contribute to inaccuracies in the determination of peak AKI stages in our study. Second, we did not collect data on recovery of renal function because we felt it was too short of a period to report accurate renal recovery data. Third, we did not use KDIGO urinary output criteria in determination of AKI stage. In summary, COVID-19 requiring ICU admission is associated with an extremely high incidence of severe (stage 2 and 3) AKI, and requirement for RRT. The majority of patients with COVID-19 and severe AKI in ICU have moderate to severe ARDS and require invasive mechanical ventilation. Timing or severity of AKI did not affect outcomes. We report a high 60-day hospital mortality of 67% in our population. Patients with COVID-19 and AKI who require RRT have a high mortality, but survivors have good rates of liberation from RRT (74% in our study).

Disclosures

M.K. Abramowitz reports receiving consulting fees from Tricida, Inc., outside the submitted work. All remaining authors have nothing to disclose.

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Author Contributions

M. Aboodi was responsible for formal analysis; M. Aboodi, P. Dicpinigaitis, M. Ross, and D. Sharma provided supervision; M. Abramowitz, P. Dicpinigaitis, and M. Ross reviewed and edited the manuscript; E. Alahiri, S. Chand, A. Gone, D. Grand, S. Kapoor, D. Schecter, and J. Thakkar were responsible for investigation; E. Alahiri, S. Chand, A. Gone, D. Grand, and D. Schecter were responsible for data curation; S. Kapoor and D. Sharma were responsible for methodology; and S. Kapoor and J. Thakkar conceptualized the study and wrote the original draft.

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