

Table 1. (a) Clinical, demographic and laboratory characteristics of training cohort of 72 COVID and 66 MIS-C patients and validation cohort 1 (29 COVID-19, 43 MIS-C) and cohort 2 (30 COVID-19, 32 MIS-C). Categorical variables are expressed as frequencies or percentages, while continuous quantities are represented as median/interquartile range pairs. The variables that show significant differences between the COVID-19 and MIS-C cohorts at $p < 0.05$, using the Wilcoxon rank-sum test for continuous quantities and the chi-squared test for discrete quantities, are in italics. (b) Clinical, demographic and laboratory characteristics of the validation cohort 1 (29 COVID-19, 43 MIS-C), validation cohort 2 (30 COVID-19, 32 MIS-C) and validation cohort 3 (20 COVID-19, 46 MIS-C). Categorical variables are expressed as frequencies or percentages, while continuous quantities are represented as median/interquartile range pairs. (c) Cytokines/chemokines ordered by p-value of the Wilcoxon rank-sum univariate test for discriminating COVID-19 from MIS-C in the training cohort (72 COVID-19, 70 MIS-C). A total of 34 of the 45 cytokines/chemokines are statistically significant in a univariate sense. The specificity and sensitivity of each marker in a five-fold cross validation is also shown. All values are in pg/mL.

(a)			
	COVID-19 Training (N = 72)	MIS-C Training (N = 66)	<i>p</i> -Value
Age at sample collection Med/IQR (yrs)	14 (6–18)	9 (6–14)	<i>0.013</i>
BMI Med/IQR	20.8 (17.6–30.5)	19.4 (17.1–25.8)	0.4
Gender			<i>0.03</i>
M/F%	46/54	62/38	
Race			0.95
White%	65.7	63.7	
African American%	28.7	28.9	
Asian%	2.8	4.3	
Other%	2.8	2.9	
Ethnicity			0.65
Hispanic%	54	49	
not Hispanic%	46	51	
SARS-CoV-2 test			<i>1.3×10^{-11}</i>
PCR%	90	0	
Antibody%	10	100	
unknown%	0	0	
IVIg/steroids 7 dys before collection. %	33	46	0.08
IVIg/steroid from collection days	−8.5 (−41, −1)	0 (−2.75, 1)	<i>4.9×10^{-10}</i>
LOS in hospital day	5.5 (2.8, 12.3)	7.8 (5.3, 11.5)	<i>0.03</i>
ICU LOS days	0 (0, 4.5)	3.4 (1.5, 6.7)	<i>0.002</i>
ECMO%	1.4	4.6	0.36
Ventilator%	17.1	30.8	<i>0.035</i>
CPAP%	15.7	24.6	0.16
AKI%	11.4	35.3	<i>1.3×10^{-3}</i>
Labs			
Sodium mEq/L	138 (136, 140)	134 (131, 137)	<i>2.5×10^{-7}</i>
Albumin g/dL	4 (3.4, 4.6)	3.3 (3.0, 3.7)	<i>9.7×10^{-7}</i>
CO ₂ mEq/L	26 (23, 28)	24 (20, 26)	<i>3.8×10^{-3}</i>
BNP pg/mL	64.1 (18.5, 67.5)	221.6 (49.8, 589.2)	<i>1.5×10^{-7}</i>
TropI ng/mL	0.02 (0.01, 0.07)	0.02 (0.01, 0.08)	0.12

Table 1. Cont.

Platelets #/nL	280 (176, 404)	158 (123, 240)	7.0×10^{-7}			
Protime seconds	14.6 (14, 14.9)	15.4 (14.6, 16.5)	1.6×10^{-4}			
D-dimer µg/mL	1.1 (0.5, 2.04)	3.0 (1.7, 4.06)	1.4×10^{-7}			
Fibrinogen mg/dL	402 (317, 459)	513 (424, 600)	1.8×10^{-5}			
Procalcitonin ng/mL	1.6 (0.1, 2.1)	4.7 (1.6, 12.8)	4.6×10^{-9}			
CRP mg/dL	2.1 (0.5, 5.7)	15.9 (5.2, 24.3)	5.2×10^{-10}			
NLRatio	2.5 (1.3, 5.4)	8.0 (3.1, 14.6)	3.3×10^{-4}			
Ferritin ng/mL	254 (97, 377)	333 (166, 641)	7.2×10^{-3}			
(b)						
	COVID-19 Val Set 1 (N = 29)	MIS-C Val Set 1 (N = 43)	COVID-19 Val Set 2 (N = 30)	MIS-C Val Set 2 (N = 32)	COVID-19 Val Set 3 (N = 20)	MIS-C Val Set 3 (N = 46)
Age at sample collect. Med/IQR	13 (7, 19)	9 (6.5, 11)	14 (10, 20)	11 (7, 14)	11.5 (10, 15)	10.5 (7.3, 14)
BMI Med/IQR	21.2 (17.8, 28.7)	21.2 (16.9, 23.2)	26.2 (17.9, 32.1)	19.4 (16.2, 21.2)	18.9 (16.5, 31.4)	18.9 (16.4, 21.0)
Gender						
M/F%	44/56	58/42	45/55	48/52	56/44	50/50
Race						
White%	70.4	65.1	75.9	51.7	67.0	53.0
African American %	22.2	23.3	20.7	27.6	27.0	27.0
Asian%	7.4	7.0	3.4	13.8	6.0	13.0
Other%	0	4.6	0	6.9	0.0	7.0
Ethnicity						
Hispanic%	48	56	69	24.1	55.5	66.7
not Hispanic%	52	44	31	75.9	44.5	33.3
SARS-CoV-2						
PCR%	100	0	100	0	100	0
Antibody%	0	100	0	100	0	100
unknown%	0	0	0	0	0	0
LOS in hospital (days)	3.8 (1.7, 13.2)	6.7(5.6, 8.5)	3.8(1.7, 13.2)	6.0 (5.6, 8.5)	0.5(0.0, 8.0)	5.8 (4.1, 7.7)
ICU LOS (days)	0 (0, 3.3)	2.9 (0.8, 4.7)	0 (0, 0)	2.1 (1.3, 3.1)	0(0, 0)	1.9 (0.6, 3.0)
ECMO (%)	3.7	4.7	3.4	0.0	0.0	0.0
Ventilator (%)	25.9	11.6	13.8	3.4	3.3	3.3
CPAP (%)	22.2	39.5	17.2	20.7	10.0	19.0
AKI (%)	11.1	30.2	17.2	24.1	10.0	22.6
Labs						
Sodium Med/IQR mEq/L	138 (136, 140)	137 (135, 138)	137.5 (136, 139)	134 (132, 137)	137 (136, 139)	134 (130.5, 136)
Albumin Med/IQR g/dL	4.2 (3.4, 4.4)	3.3 (2.8, 3.7)	3.7 (3.1, 4.1)	3.5 (3.0, 3.9)	3.6 (3.1, 3.8)	3.3 (3.0, 3.8)
CO ₂ Med/IQR mEq/L	26 (24, 28)	24 (23, 26)	25.5 (23, 29)	25 (21.5, 26)	26 (23, 28)	24 (20.5, 25)
BNP Med/IQR pg/mL	105.2 (34.2, 169)	259.8 (124, 632)	201 (110, 228)	142.5 (55.3, 636)	169 (100, 231)	143 (65.3, 706)

Table 1. Cont.

Trop I Med/IQR ng/mL	0.02 (0.00, 0.03)	0.02 (0.01, 0.07)	0.01 (0.01, 0.01)	0.02 (0.01, 0.08)	0.01 (0.01, 0.01)	0.02 (0.01, 0.08)
Platelets Med/IQR #/nL	264 (194.5, 356)	177 (106, 265)	233.5 (199, 275)	199 (144, 267.5)	230 (198, 279)	199 (145, 270)
Protime Med/IQR sec	15 (14.4, 15.2)	15.1 (14.4, 15.6)	14.2 (13.6, 14.4)	14.9 (14.5, 15.6)	14.4 (13.8, 14.5)	14.9 (14.4, 15.5)
D-Dimer Med/IQR µg/mL	2.4 (1.3, 2.9)	2.9 (1.9, 3.8)	1.6 (0.7, 3.8)	2.8 (1.6, 3.8)	2.8 (0.7, 4.2)	2.7 (1.5, 3.6)
Fibrinogen Med/IQR mg/dL	448 (430, 457)	459 (359, 634)	416 (350, 532)	539 (393, 614)	455 (377, 494)	527 (393, 597)
Procalcitonin Med/IQR ng/mL	1.5 (1.2, 1.6)	4.6 (2.2, 14.2)	0.4 (0.1, 0.5)	2.2 (1.0, 4.8)	0.4 (0.2, 0.5)	1.8 (1.0, 4.8)
CRP Med/IQR mg/dL	3.8 (0.5, 5.5)	19.3 (5.1, 22.8)	13 (4.0, 13.5)	7.9 (4.3, 22.3)	13.9 (4.3, 14.5)	7.9 (4.8, 20.7)
NLRatio Med/IQR	2.3 (1.0, 3.7)	4.7 (2.9, 9.0)	3.7 (2.1, 5.2)	5.7 (2.7, 12.2)	3.5 (2.0, 4.6)	5.7 (2.3, 9.7)
Ferritin Med/IQR ng/mL	239 (100, 253)	282 (182, 472)	211 (38.8, 400)	334 (223.5, 597.5)	277 (44, 592)	302 (224, 532)
(c)						
Cytokine (Pg/mL)	COVID-19	MIS-C	p-Value	Specificity	Sensitivity	
sIL2R	491.8 (388.1, 782.2)	3576.6 (2270.0, 5475.0)	1.97×10^{19}	0.95 ± 0.07	0.8 ± 0.08	
IP-10	175.9 (91.4, 494.0)	9000.0 (1991.0, 15, 803.2)	2.57×10^{17}	0.93 ± 0.05	0.7 ± 0.08	
MIG	1395.0 (941.6, 2938.5)	27764.5 (12, 618.8, 43, 215.0)	2.71×10^{16}	0.35 ± 0.43	0.94 ± 0.08	
IL-10	25.6 (16.2, 59.2)	191.6 (85.3, 368.5)	6.77×10^{16}	0.87 ± 0.08	0.7 ± 0.15	
IL-15	15.7 (6.1, 23.8)	39.2 (30.5, 54.2)	4.55×10^{15}	0.79 ± 0.19	0.79 ± 0.06	
IL-3	1.2 (0.7, 1.9)	3.3 (2.3, 4.8)	4.19×10^{14}	0.85 ± 0.1	0.76 ± 0.17	
IL-1RA	38.7 (21.6, 143.3)	681.2 (155.9, 7816.2)	8.13×10^{13}	0.9 ± 0.13	0.54 ± 0.13	
TNFalpha	57.1 (44.3, 85.7)	132.3 (88.7, 225.6)	1.84×10^{11}	0.8 ± 0.2	0.59 ± 0.21	
IL-13	42.9 (37.4, 57.5)	63.7 (56.5, 74.3)	8.45×10^1	0.77 ± 0.14	0.64 ± 0.14	
IFNgamma	7.0 (5.7, 10.8)	17.2 (9.8, 32.0)	4.47×10^9	0.84 ± 0.21	0.37 ± 0.21	
IL-22	80.1 (68.2, 105.2)	109.8 (94.5, 125.2)	5.15×10^8	0.73 ± 0.18	0.6 ± 0.26	
IL-2	3.7 (3.1, 4.7)	5.0 (4.3, 5.9)	1.50×10^7	0.78 ± 0.15	0.56 ± 0.22	
TGF-a	11.5 (8.0, 15.8)	18.4 (14.0, 25.1)	5.75×10^7	0.82 ± 0.08	0.46 ± 0.1	
G-CSF	66.1 (46.2, 116.1)	155.7 (78.8, 339.3)	6.64×10^7	0.92 ± 0.05	0.31 ± 0.12	
IL-6	9.4 (4.5, 27.3)	48.4 (12.7, 188.8)	1.12×10^6	0.89 ± 0.07	0.41 ± 0.12	
IL-27	2216.5 (1368.8, 3763.5)	4241.5 (3043.2, 8846.8)	3.05×10^6	0.0 ± 0.0	1.0 ± 0.0	
MCP-3	48.4 (41.0, 57.6)	62.3 (49.2, 88.6)	4.14×10^6	0.83 ± 0.21	0.49 ± 0.22	
IL-4	3.3 (2.1, 4.6)	5.1 (3.5, 7.2)	8.27×10^6	0.85 ± 0.16	0.31 ± 0.17	
IL-1alpha	27.2 (22.8, 39.3)	39.0 (31.8, 50.8)	1.77×10^5	0.79 ± 0.18	0.31 ± 0.1	
TNFBeta	15.0 (12.4, 18.5)	18.8 (16.0, 22.3)	1.93×10^5	0.75 ± 0.13	0.34 ± 0.17	

Table 1. Cont.

IL-18	88.6 (54.2, 174.6)	180.5 (128.8, 380.0)	3.38×10^5	0.8 ± 0.12	0.37 ± 0.08
IL-12(p70)	8.8 (7.5, 11.9)	10.6 (9.4, 14.3)	4.03×10^5	0.75 ± 0.14	0.39 ± 0.17
MIP-1alpha	46.7 (40.3, 63.1)	54.9 (48.7, 67.2)	4.87×10^5	0.78 ± 0.25	0.1 ± 0.11
M-CSF	709.8 (461.7, 1071.8)	1073.0 (740.7, 1547.2)	5.04×10^5	0.75 ± 0.16	0.5 ± 0.15
MCP-1	350.7 (210.6, 689.1)	715.4 (316.7, 1423.0)	1.12×10^4	0.8 ± 0.21	0.49 ± 0.15
Fractalkine	191.1 (169.0, 240.4)	244.8 (191.2, 286.6)	1.16×10^4	0.76 ± 0.17	0.49 ± 0.14
IL-1beta	20.8 (16.0, 28.3)	26.1 (21.8, 35.1)	2.16×10^4	0.78 ± 0.12	0.34 ± 0.12
IL-5	9.2 (6.4, 17.8)	16.8 (9.1, 30.8)	5.81×10^4	0.84 ± 0.17	0.17 ± 0.21
PDGF-AB/BB	28685.5 (18, 716.2, 41, 657.2)	21208.0 (11, 836.0, 28, 590.2)	6.20×10^4	1.0 ± 0.0	0.0 ± 0.0
MIP-1beta	25.7 (20.2, 40.7)	37.1 (25.8, 48.3)	7.40×10^4	0.75 ± 0.2	0.34 ± 0.15
MDC	541.0 (294.7, 835.9)	345.9 (190.7, 583.0)	1.56×10^3	0.54 ± 0.1	0.7 ± 0.17
IFNalpha2	84.0 (73.1, 104.2)	91.0 (83.9, 119.8)	9.47×10^3	0.79 ± 0.16	0.3 ± 0.14
IL-17F	35.6 (24.2, 76.7)	46.5 (36.6, 96.2)	1.01×10^2	0.81 ± 0.18	0.14 ± 0.19
IL-7	6.3 (3.7, 8.9)	7.6 (5.3, 10.6)	2.72×10^2	0.55 ± 0.28	0.37 ± 0.25
FGF-2	144.3 (122.7, 192.0)	164.7 (131.7, 183.2)	7.23×10^2	0.66 ± 0.23	0.21 ± 0.2
sCD40L	2781.5 (928.0, 4929.8)	1651.0 (923.7, 3796.0)	7.34×10^2	0.68 ± 0.28	0.4 ± 0.33
IL-8	23.5 (11.4, 50.8)	26.8 (18.6, 45.0)	8.08×10^2	0.33 ± 0.13	0.59 ± 0.15
VEGF	142.7 (74.0, 224.3)	153.9 (114.5, 276.9)	8.81×10^2	0.78 ± 0.19	0.17 ± 0.12
IL-17A	17.9 (11.9, 23.0)	17.4 (14.9, 25.6)	1.03×10^1	0.68 ± 0.34	0.21 ± 0.26
IL-9	32.6 (26.0, 43.9)	36.8 (26.4, 50.4)	1.65×10^1	0.69 ± 0.18	0.4 ± 0.1
FLT-3L	40.5 (24.7, 63.9)	42.7 (32.5, 62.6)	1.80×10^1	0.54 ± 0.29	0.37 ± 0.25
IL-12(p40)	110.7 (72.0, 158.8)	107.3 (89.1, 162.6)	2.88×10^1	0.39 ± 0.11	0.63 ± 0.11
IL-17E/IL-25	1908.5 (1601.5, 2447.0)	1974.5 (1560.8, 2507.0)	3.75×10^1	0.96 ± 0.09	0.04 ± 0.09
GROa	55.4 (41.3, 76.3)	58.7 (38.6, 87.2)	3.98×10^1	0.68 ± 0.17	0.21 ± 0.13
PDGF-AA	3404.5 (1553.2, 4519.0)	2811.0 (1384.8, 4426.8)	4.81×10^1	0.56 ± 0.46	0.46 ± 0.46

3.2. Laboratory Characteristics of the Training Cohort and Validation Sets

Table 1b also summarizes statistics for all the measured laboratory markers for the training cohort, and Table 1c provides these statistics for validation sets 1, 2 and 3. Markers that were significantly elevated in the MIS-C training cohort compared to the COVID-19 training cohort are CRP (median 15.9 mg/dL, $p = 5.2 \times 10^{-10}$), ferritin (median 333.3 mg/L, $p = 7.2 \times 10^{-3}$), procalcitonin (median 4.7 ng/mL, $p = 4.6 \times 10^{-9}$), fibrinogen (median 513 mg/dL, $p = 1.8 \times 10^{-5}$), protime (median 15.4 s, $p = 1.6 \times 10^{-4}$), D-dimer (median 3.0 µg/mL, $p = 1.4 \times 10^{-7}$), BNP (median 221.6 pg/mL, $p = 1.5 \times 10^{-7}$) and the neutrophil to lymphocyte ratio (NLR), (median 8.0, $p = 3.3 \times 10^{-4}$). Markers that were significantly lowered in the MIS-C training cohort compared to the COVID-19 training cohort are albumin (median 3.3 g/dL, $p = 9.7 \times 10^{-7}$), platelet counts (median 158/µL, $p = 7.0 \times 10^{-7}$) and sodium (median 134, $p = 2.5 \times 10^{-7}$). Troponin I level between the two cohorts was not significantly different.

In the three validation sets, for the MIS-C cohort, ferritin, fibrinogen, protime, D-Dimer, albumin and sodium levels remain about the same as in the training set. However, other inflammation markers improve from the training MIS-C cohort (pre-alpha) to the MIS-C cohort in validation set 3 (delta and omicron variants): platelet counts increase from 158/µL in the training MIS-C cohort to 199/µL in validation set 3, CRP declines from 15.9 mg/dL