

Supplemental Information

Table S1. Quality-filtering of 16S rRNA sequencing

Sample ID	Input Reads	Reads Post-DADA2 Filtering	Final OTU-Aligned Reads
ACV002	46104	32950	31454
ACV003	40072	28391	25845
ACV004	55517	39077	37931
ACV005	45614	31216	28107
ACV006	42618	30691	29726
ACV007	39663	28486	27120
ACV009	40045	29027	27359
ACV011	45406	31020	29327
ACV012	44914	32120	30520
ACV014	44172	31242	29844
ACV016	39007	27006	26316
ACV017	45282	31759	30360
ACV018	44274	31250	30327
ACV019	44997	31862	30401
ACV020	45105	31064	29003
ACV021	69979	49418	47393
ACV022	63098	44851	43064
ACV023	82068	57558	54767
ACV025	47151	32262	29769
ACV026	54304	37835	35467
ACV027	45634	31804	30570
ACV028	47385	33611	32477
ACV029	46869	32015	30214
ACV030	52128	37622	35938
ACV031	48993	35951	35180
ACV032	35361	24355	23632
ACV033	56100	40275	38125
ACV034	18513	10076	9349
ACV035	50345	35767	34314
ACV036	39860	28255	26175
ACV037	39229	26902	25317
ACV038	58827	42574	40615
ACV039	55461	41099	39076
ACV040	61699	43420	39973
ACV041	42516	29952	27922
ACV042	45314	32208	30156
ACV043	56761	41047	39297
ACV044	44425	33190	31413
ACV045	44026	31104	30366

ACV046	40428	28010	27014
ACV047	44342	31764	30481
ACV048	48952	35076	33937
ACV049	38551	27209	25847
ACV050	34153	23810	22099
ACV051	38538	26811	25257
ACV052	44843	32146	30400
ACV053	46922	31715	29792
ACV054	58930	41897	40481
ACV055	53560	37964	35571
ACV056	49264	34989	32603
ACV057	45366	31648	29481
ACV058	35988	25591	23683
ACV059	46487	32791	32152
ACV060	51704	37954	37186
ACV061	51887	36723	35901
ACV062	45969	33653	31341
ACV063	43094	31042	29357
ACV064	56800	40529	39413
ACV065	37973	26278	24655
ACV067	36246	25067	22980
ACV068	39969	28820	27141
ACV069	48138	33677	31933
ACV070	59926	42275	40273
ACV071	60234	43478	40811
ACV072	67810	47930	46360
ACV073	44813	30829	29939
ACV075	46879	33666	32898
ACV076	56680	39216	36957
ACV077	56253	39926	39434
ACV078	50587	36005	34315
ACV079	57249	38842	36979
ACV080	63389	44822	42889
ACV081	63304	42546	39439
ACV082	64382	45371	41295
ACV083	53130	37613	36177
ACV084	60476	43543	42096
ACV086	57107	41591	39739
ACV087	39118	28226	27201
ACV088	68107	47854	46215
ACV089	59339	42860	41008
ACV090	60376	42955	42331
ACV092	56137	40731	38516
ACV093	52795	37519	36776
ACV094	54301	38650	37954

ACV095	46239	33693	32539
ACV096	47934	32639	30910
ACV097	51220	36672	35200
ACV098	50124	36198	32243
ACV099	43782	30233	28234
ACV100	41823	29124	27750
ACV101	36452	25035	22717
ACV102	41817	29396	28752
ACV103	86311	62447	60366
ACV104	77418	55547	53593
ACV105	83095	60184	58526
ACV106	78735	56173	51101
ACV107	71815	51463	50311
ACV108	106765	77812	75849
ACV109	87128	62397	61442
ACV110	69469	50355	49287
ACV111	57972	41890	39771
ACV112	94587	69207	65661
ACV114	51582	37215	35939
ACV116	70403	51425	49077
ACV118	57312	41372	39036

Table S2. Diagnoses of COVID-19 negative patients

Patient ID	Age	Sex	Primary Diagnosis	Secondary Diagnosis
2	53	Male	Syncope	Metabolic acidosis from missing dialysis
3	34	Female	Vaginal bleeding	Retained products of conception
7	32	Male	Hypoxia	Community acquired pneumonia
9	80	Female	Poor oral Intake	Non-ST elevation myocardial infarction
12	65	Female	Pneumonia	
13	76	Female	Altered mental status	MSSA bacteremia
16	71	Male	Dizziness	Hypovolemia
18	41	Male	Weakness	Diabetic ketoacidosis
22	53	Male	GI bleed	
23	64	Female	Shortness of breath	CHF exacerbation
26	68	Female	Hypoxia	Pulmonary embolism
27	23	Male	Drainage from axillary wound	Anemia
31	52	Female	Placement of TDC for initiation of dialysis	
32	52	Female	Rectal bleeding	Sickle cell pain crisis
34	88	Male	Shortness of breath	CHF exacerbation
37	57	Male	Chest pain	Acute coronary syndrome
39	22	Female	Nausea/vomiting	Diabetic ketoacidosis
41	64	Male	Diarrhea	
49	85	Female	Pleuritic chest pain	CHF exacerbation
52	49	Male	Shortness of breath	CHF exacerbation
56	55	Female	Chest pain	
57	30	Female	Abdominal pain	Acute pancreatitis
60	68	Male	Dizziness	Hyperglycemia
61	67	Male	Pleural effusion	
62	66	Male	Chest pain	Non-ST elevation myocardial infarction
64	62	Male	Chest pain	CHF exacerbation
70	32	Male	Cough	Acute kidney injury
71	40	Male	Chest pain	Non-ST elevation myocardial infarction
72	83	Female	Fall	
73	66	Male	Sternal wound infection	
74	55	Male	Fall	L1 fracture
75	53	Male	Fatigue	Hypercalcemia from PTLD
76	22	Male	Shortness of breath	Asthma exacerbation
80	62	Male	Fatigue	Acute kidney injury
81	26	Female	Fatigue	Diabetic ketoacidosis
82	56	Female	Shortness of breath	COPD exacerbation
84	44	Female	Urosepsis	

85	71	Female	Abdominal pain	
87	51	Female	Fatigue	
90	51	Male	Cough	Pulmonary embolism
95	58	Male	Facial swelling	
96	72	Male	Weakness	Transient hypotension
97	35	Male	Lower extremity cellulitis	
98	30	Male	Sickle cell pain crisis	
99	65	Male	Cough	
100	77	Female	Syncope	Orthostatic hypotension
103	59	Male	Lower extremity pain	Deep vein thrombosis
104	75	Female	Failure to thrive	Urinary tract infection
105	64	Female	Palpitations	Non-ST elevation myocardial infarction
106	39	Male	Abdominal pain	HLH
107	71	Male	Weakness	
108	76	Male	Shortness of breath	CHF exacerbation
110	61	Female	Chronic hypoxia	Obstructive sleep apnea
111	43	Female	Fatigue	Anemia
113	54	Male	Cough	
114	47	Male	Cancer related pain	
115	67	Male	Back pain	Metastatic prostate cancer
116	76	Male	Shortness of breath	CHF exacerbation
118	56	Male	Transaminitis	

Abbreviations: MSSA – methicillin-sensitive *Staphylococcus aureus*; TDC – tunneled dialysis catheter; CHF – congestive heart failure; PTLN – post-transplant lymphoproliferative disorder; COPD – chronic obstructive pulmonary disease; HLH – hemophagocytic lymphohistiocytosis

Table S3. Demographic and clinical characteristics of COVID-19 patients stratified by saliva SARS-CoV-2 viral load.

	Negative ¹ (n=15)	Low viral load ¹ (n=14)	High viral load ¹ (n=14)	p ²
Saliva SARS-CoV-2 Ct (median [IQR]) ¹	-	34.7 [33.5-35.6]	24.8 [20.6-26.6]	
Age (mean (SD))	56.5 (17.6)	56.4 (15.6)	49.7 (15.9)	0.46
Male (%)	6 (40.0)	6 (42.9)	6 (42.9)	0.98
Race (%)				0.63
Black	7 (46.7)	3 (21.4)	6 (42.9)	
White	3 (20.0)	3 (21.4)	3 (21.4)	
Other/unreported	5 (33.3)	8 (57.1)	5 (35.7)	
Ethnicity (%)				0.07
Hispanic/Latinx	3 (20.0)	9 (64.3)	7 (50.0)	
Not Hispanic/Latinx	10 (66.7)	2 (14.3)	5 (35.7)	
Not specified	2 (13.3)	3 (21.4)	2 (14.3)	
BMI (median [IQR])	30.2 [25.0, 34.3]	27.3 [21.2, 37.0]	31.0 [27.2, 35.9]	0.37 ³
HTN (%)	7 (46.7)	8 (57.1)	7 (50.0)	0.85
DM (%)	5 (33.3)	5 (35.7)	6 (42.9)	0.86
Underlying kidney disease (%)	1 (6.7)	4 (28.6)	1 (7.1)	0.16
Any pulmonary disease (%)	4 (26.7)	3 (21.4)	2 (14.3)	0.71
Charlson Comorbidity Index (median [IQR])	2.0 [0.5, 4.0]	2.0 [1.0, 4.0]	2.0 [0.0, 3.0]	0.59 ³
Oxygen rank severity (%)				0.32 ⁴
No supplemental oxygen	12 (80.0)	9 (64.3)	7 (50.0)	
Nasal cannula	3 (20.0)	3 (21.4)	6 (42.9)	
Non-invasive ventilation	0 (0.0)	2 (14.3)	1 (7.1)	
IL-6 (median [IQR]) ⁵	10.4 [6.3, 25.9]	25.2 [20.4, 38.6]	17.9 [11.7, 24.2]	0.25 ³
ESR (median [IQR]) ⁵	56.5 [48.5, 109]	60.0 [50.0, 87.5]	67.0 [57.0, 83.0]	0.94 ³
CRP (median [IQR]) ⁵	63.8 [14.4, 129]	35.0 [17.2, 113]	104 [64.8, 176]	0.17 ³
Ferritin (median [IQR]) ⁵	560 [213, 911]	343 [262, 647]	567 [378, 1945]	0.45 ³
D-dimer (median [IQR]) ⁵	0.99 [0.72, 6.93]	0.92 [0.76, 1.31]	0.78 [0.53, 2.07]	0.61 ³
WBC (median [IQR]) ⁵	7.30 [5.75, 8.78]	6.91 [5.50, 9.11]	6.65 [4.61, 11.5]	0.93 ³
NLR (median [IQR]) ⁵	3.68 [3.19, 5.01]	3.67 [2.85, 6.16]	4.75 [2.19, 15.8]	0.78 ³
Symptom duration >3 d (%) ⁶	5 (33.3)	5 (35.7)	4 (28.6)	1.00 ⁴
Antibiotics ≤48 hrs prior to saliva collection (%) ⁷	7 (46.7)	6 (42.9)	8 (57.1)	0.74
Composite outcome (%)				0.54 ⁴
Deceased	1 (6.7)	1 (7.1)	1 (7.1)	
Decompensated (no death)	0 (0.0)	0 (0.0)	2 (14.3)	
Discharged (no death)	14 (93.3)	13 (92.9)	11 (78.6)	

¹ As determined via testing of saliva using qRT-PCR. Cycle threshold (Ct) values below 40 were considered positive, and median Ct value was used to stratify low (Ct>30) versus high (Ct<30) viral load

² Categorical variables were compared using the Chi-squared test, unless indicated as below. Continuous variables were assessed for normal or normal-like distribution and compared using t-tests, unless indicated as below.

³ Kruskal-Wallis test was used due to non-normal distribution

⁴ Fisher's exact test was used due to at least one expected value ≤ 5

⁵ Lab values as measured upon admission; not available for all patients (IL-6 n=30/43; ESR n=38/43; CRP n=41/43; Ferritin n=41/43; D-dimer n=37/43; WBC n=43/43; NLR n=39/43)

⁶ Reported duration of symptoms prior to hospitalization

⁷ Inpatient antibiotic use, determined through chart review

Abbreviations: BMI – body mass index; HTN – hypertension; DM – diabetes mellitus; CAD – coronary artery disease; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; WBC – white blood cell count; NLR – neutrophil-lymphocyte ratio

Table S4. Differentially abundant amplicon sequence variants (ASVs) across saliva viral load of SARS-CoV-2

ASV ID	baseMean	log2-FoldChange	lfcSE	stat	p-value	FDR	Taxon	Comparison
ASV3	8.01	-23.26	3.56	-6.54	6.32E-11	8.69E-09	<i>Streptococcus gordonii</i>	High Saliva Viral Load vs. Negative
ASV6	7.08	20.04	3.57	5.62	1.90E-08	1.67E-06	<i>Streptococcus sanguinis</i>	High Saliva Viral Load vs. Negative
ASV9	9.65	19.51	3.57	5.47	4.61E-08	3.90E-06	<i>Streptococcus infantis</i>	High Saliva Viral Load vs. Negative
ASV10	23.00	21.92	3.56	6.16	7.17E-10	7.51E-08	<i>Streptococcus infantis</i>	High Saliva Viral Load vs. Negative
ASV14	10.42	21.37	3.37	6.35	2.16E-10	2.50E-08	<i>Streptococcus anginosus</i>	High Saliva Viral Load vs. Negative
ASV19	13.93	20.85	3.56	5.86	4.73E-09	4.52E-07	<i>Actinomyces sp. HMT 172</i>	High Saliva Viral Load vs. Negative
ASV26	11.21	-27.51	3.56	-7.73	1.05E-14	4.63E-12	<i>Prevotella salivae</i>	High Saliva Viral Load vs. Negative
ASV27	14.98	-14.53	3.55	-4.09	4.25E-05	0.00346	<i>Prevotella histicola</i>	High Saliva Viral Load vs. Negative
ASV32	12.61	22.76	3.49	6.52	7.10E-11	9.18E-09	<i>Alloprevotella sp. HMT 473</i>	High Saliva Viral Load vs. Negative
ASV33	17.02	-23.31	3.05	-7.65	2.04E-14	7.47E-12	<i>Prevotella sp. HMT 304</i>	High Saliva Viral Load vs. Negative
ASV37	36.05	20.79	3.56	5.84	5.21E-09	4.77E-07	<i>Prevotella pallens</i>	High Saliva Viral Load vs. Negative
ASV39	24.91	-24.14	3.01	-8.03	9.94E-16	5.46E-13	<i>Fusobacterium nucleatum subsp. vincentii</i>	High Saliva Viral Load vs. Negative
ASV41	7.48	-26.63	3.56	-7.48	7.19E-14	2.26E-11	<i>Fusobacterium nucleatum subsp. vincentii</i>	High Saliva Viral Load vs. Negative
ASV42	28.48	-39.87	3.56	11.21	3.82E-29	8.40E-26	<i>Saccharibacteria (TM7) [G-5] bacterium HMT 356</i>	High Saliva Viral Load vs. Negative
ASV44	8.25	23.65	3.56	6.65	2.90E-11	4.56E-09	<i>Streptococcus parasanguinis clade 411</i>	High Saliva Viral Load vs. Negative
ASV45	43.22	-25.52	2.96	-8.63	6.24E-18	6.86E-15	<i>Streptococcus sp. HMT 066</i>	High Saliva Viral Load vs. Negative

ASV46	11.46	22.35	3.56	6.28	3.31E-10	3.64E-08	<i>Streptococcus sp. HMT 074</i>	High Saliva Viral Load vs. Negative
ASV48	5.73	-22.88	3.56	-6.43	1.28E-10	1.56E-08	<i>Streptococcus peroris</i>	High Saliva Viral Load vs. Negative
ASV50	5.96	-25.54	3.56	-7.18	7.12E-13	1.96E-10	<i>Prevotella oris</i>	High Saliva Viral Load vs. Negative
ASV53	12.06	-23.84	3.56	-6.70	2.10E-11	3.55E-09	<i>Prevotella denticola</i>	High Saliva Viral Load vs. Negative
ASV6	7.08	23.27	3.56	6.54	5.99E-11	6.92E-09	<i>Streptococcus sanguinis</i>	Low Saliva Viral Load vs. Negative
ASV9	9.65	23.74	3.56	6.68	2.45E-11	4.15E-09	<i>Streptococcus infantis</i>	Low Saliva Viral Load vs. Negative
ASV10	23.00	24.84	3.56	6.99	2.80E-12	6.84E-10	<i>Streptococcus infantis</i>	Low Saliva Viral Load vs. Negative
ASV14	10.42	23.68	3.36	7.04	1.90E-12	5.22E-10	<i>Streptococcus anginosus</i>	Low Saliva Viral Load vs. Negative
ASV19	13.93	24.17	3.56	6.80	1.05E-11	2.10E-09	<i>Actinomyces sp. HMT 172</i>	Low Saliva Viral Load vs. Negative
ASV22	12.10	24.19	3.35	7.23	4.99E-13	1.83E-10	<i>Actinomyces sp. HMT 180</i>	Low Saliva Viral Load vs. Negative
ASV23	20.42	-22.96	3.11	-7.39	1.46E-13	7.61E-11	<i>Actinomyces lingnae</i>	Low Saliva Viral Load vs. Negative
ASV24	11.86	-19.17	3.42	-5.60	2.12E-08	1.41E-06	<i>Bacteroidales [G-2] bacterium HMT 274</i>	Low Saliva Viral Load vs. Negative
ASV25	35.61	-21.89	2.97	-7.37	1.73E-13	7.61E-11	<i>Prevotella salivae</i>	Low Saliva Viral Load vs. Negative
ASV26	11.21	-23.44	3.56	-6.59	4.44E-11	5.45E-09	<i>Prevotella salivae</i>	Low Saliva Viral Load vs. Negative
ASV28	8.77	-20.39	3.56	-5.73	1.01E-08	6.93E-07	<i>Prevotella histicola</i>	Low Saliva Viral Load vs. Negative
ASV29	26.76	-21.13	3.56	-5.94	2.91E-09	2.13E-07	<i>Prevotella sp. HMT 306</i>	Low Saliva Viral Load vs. Negative
ASV30	7.73	-21.71	3.56	-6.10	1.06E-09	8.98E-08	<i>Prevotella melaninogenica</i>	Low Saliva Viral Load vs. Negative
ASV32	12.61	23.58	3.49	6.75	1.44E-11	2.64E-09	<i>Alloprevotella sp. HMT 473</i>	Low Saliva Viral Load vs. Negative

ASV37	36.05	25.58	3.55	7.19	6.25E-13	1.96E-10	<i>Prevotella pallens</i>	Low Saliva Viral Load vs. Negative
ASV38	11.37	-18.03	3.57	-5.05	4.33E-07	2.80E-05	<i>Prevotella pallens</i>	Low Saliva Viral Load vs. Negative
ASV40	8.68	24.24	3.56	6.82	9.21E-12	2.03E-09	<i>Fusobacterium periodonticum</i>	Low Saliva Viral Load vs. Negative
ASV41	7.48	-22.24	3.56	-6.25	4.09E-10	4.28E-08	<i>Fusobacterium nucleatum subsp. vincentii</i>	Low Saliva Viral Load vs. Negative
ASV42	28.48	-23.63	3.56	-6.64	3.09E-11	4.53E-09	<i>Saccharibacteria (TM7) [G-5] bacterium HMT 356</i>	Low Saliva Viral Load vs. Negative
ASV44	8.25	20.63	3.56	5.79	7.06E-09	5.01E-07	<i>Streptococcus parasanguinis clade 411</i>	Low Saliva Viral Load vs. Negative
ASV46	11.46	23.53	3.56	6.62	3.62E-11	4.97E-09	<i>Streptococcus sp. HMT 074</i>	Low Saliva Viral Load vs. Negative
ASV50	5.96	-21.98	3.56	-6.18	6.55E-10	6.26E-08	<i>Prevotella oris</i>	Low Saliva Viral Load vs. Negative
ASV51	23.68	-22.96	2.96	-7.75	8.89E-15	9.77E-12	<i>Prevotella oris</i>	Low Saliva Viral Load vs. Negative
ASV54	9.20	-21.30	3.48	-6.11	9.77E-10	8.59E-08	<i>Saccharibacteria (TM7) [G-3] bacterium HMT 351</i>	Low Saliva Viral Load vs. Negative
ASV5	16.79	22.58	2.67	8.45	2.97E-17	1.20E-14	<i>Streptococcus sanguinis</i>	Positive vs. Negative qRT-PCR
ASV8	14.80	22.66	2.88	7.86	3.86E-15	9.29E-13	<i>Streptococcus infantis</i>	Positive vs. Negative qRT-PCR
ASV13	17.23	22.89	2.67	8.58	9.39E-18	4.74E-15	<i>Streptococcus anginosus</i>	Positive vs. Negative qRT-PCR
ASV18	19.38	22.94	3.07	7.46	8.38E-14	1.13E-11	<i>Actinomyces sp. HMT 172</i>	Positive vs. Negative qRT-PCR
ASV21	13.93	22.59	2.86	7.91	2.65E-15	7.66E-13	<i>Actinomyces sp. HMT 180</i>	Positive vs. Negative qRT-PCR
ASV31	28.65	23.59	2.67	8.84	9.76E-19	6.57E-16	<i>Alloprevotella sp. HMT 473</i>	Positive vs. Negative qRT-PCR
ASV36	42.96	23.48	3.07	7.64	2.16E-14	3.11E-12	<i>Prevotella pallens</i>	Positive vs. Negative qRT-PCR
ASV42	28.48	-25.80	2.87	-8.98	2.59E-19	2.62E-16	<i>Saccharibacteria (TM7) [G-5] bacterium HMT 356</i>	Positive vs. Negative qRT-PCR

ASV43	18.95	23.02	2.93	7.85	4.14E-15	9.29E-13	<i>Streptococcus parasanguinis clade 411</i>	Positive vs. Negative qRT-PCR
ASV47	5.32	-23.52	3.05	-7.70	1.31E-14	2.21E-12	<i>Streptococcus peroris</i>	Positive vs. Negative qRT-PCR
ASV50	5.96	-23.67	3.05	-7.75	8.91E-15	1.64E-12	<i>Prevotella oris</i>	Positive vs. Negative qRT-PCR
ASV52	11.08	-24.52	3.05	-8.04	9.35E-16	3.15E-13	<i>Prevotella denticola</i>	Positive vs. Negative qRT-PCR

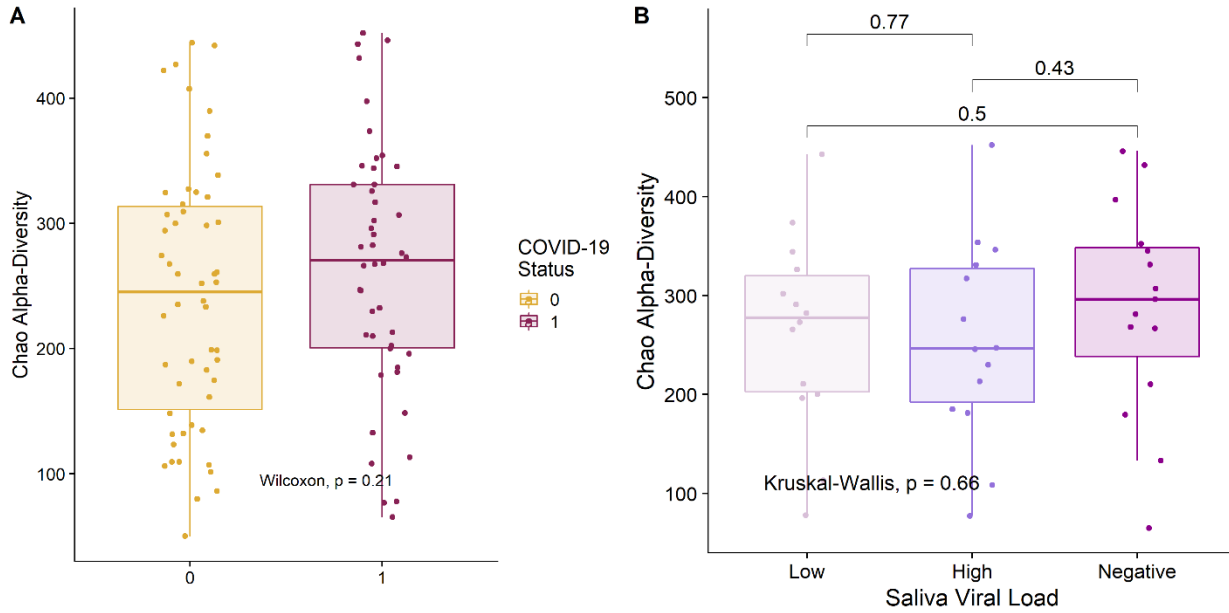


Figure S1. Saliva microbiome Chao α -diversity. (A) Chao α -diversity in patients with versus without COVID-19 (B) Chao α -diversity compared across SARS-CoV-2 saliva viral load. Saliva samples were stratified by SARS-CoV-2 RT-PCR cycle threshold (Ct) values into the following categories: negative (Ct>40), low viral load (Ct>30), and high viral load (Ct<30). Kruskal-Wallis test was used to compare Chao α -diversity across groups.