

High early neutralizing antibody titres in patients with acute Puumala orthohantavirus infection do not associate with reduced disease severity

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Supplementary materials

Table S1. Descriptive statistics table showing clinical and laboratory parameters of NE patients included in the study. Variable abbreviations are Dt = Overall disease duration, Df = Fever duration, FDBH = Fever days before hospitalization, eGFR = estimated glomerular filtration rate, WBC = white blood cell count, HCT = Hematocrit, TC = thrombocyte count, CRP = C-reactive protein, NAb = PUUV neutralizing antibodies, VL = PUUV viral load, IL-8 = Interleukin-8, H3 = Histone H3, cH3 = Citrullinated histone H3, MPO = Myeloperoxidase, hNE = Neutrophil elastase, FLCκ = Free light chain κ, FLCλ = Free light chain λ, MAP = mean arterial pressure, Sev(scale) = Severity scale. A) Scaled data with all missing data excluded B) the basic data.

(A) Scaled Data Descriptive Statistics																										
	Age	sex	FDBH	Df	Dt	WBCmax	HCTmin	TCmin	CRPmax	Nab	VL	IL8	H3	cH3	MPO	FLCκ/FLCλ	MAPmin	SEVscore	PUUV-N-IgG	hNE	FLCκ	FLCλ	Hmax	eGFRmin	eGFR	
N	Valid	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	49	
Missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Normal range	NA	NA	NA	NA	NA	11 x 10 ⁹ /L	0.36-0.41	150x10 ⁹ /L	35.2mmol/L	NA	NA	80.062ng/ml	0.2-2.7ng/ml	866-1887ng/ml	4285ng/ml	0.26-1.65	350mmHg	NA	NA	74-413ng/ml	0.3-19.4mg/L	0.71-26.3mg/L	0.45-0.48	30ml/min/1.73m ²	30ml/min/1.73m ²	
Mean	42.74		4.57	8.12	9.63	11.39	0.35	59.71	97.58	1020	84.85	0.28	5.70	336.06	157.57	1.16	83.74	3	0.57	115.36	34.19	29.56	0.44	49.88	67.53	
Median	40.80	0	4.00	8.00	9.00	10.30	0.36	53.00	91.60	640	26.81	0.13	4.79	325.73	131.59	1.04	83.33	3	0.17	98.71	24.44	24.26	0.44	38.00	73.00	
Mode	27.50*	0	4.00	8.00	8.00	8.80	0.36	35*	91.60	640	0.00	0.00*	4.72	214.690*	126.490*	35*	82.00	2	0.10*	57.280*	87.02	24.04	0.44	5.00*	7.00*	
Range	51.10		7.00	11.00	14.00	18.40	0.19	103.00	250.90	5040	717.50	1.45	20.07	379.89	286.13	2.19	52.00	7	3.73	419.27	77.72	62.54	0.26	120.00	120.00	
Minimum	22.40	Male = 0	2.00	4.00	4.00	5.60	0.25	15.00	15.90	80	0.00	0.00	1.16	214.69	46.04	0.35	51.33	0	0.00	11.84	9.30	8.80	0.33	3.00	7.00	
Maximum	73.50	Female = 1	9.00	15.00	18.00	24.00	0.44	118.00	266.80	5120	717.50	1.45	21.23	594.58	332.17	2.55	103.33	7	3.73	431.11	87.02	71.34	0.59	123.00	127.00	
a. Multiple modes exist. The smallest value is shown																										
(B) Basic Data Descriptive Statistics																										
	Age	sex	FDBH	Df	Dt	WBCmax	HCTmin	TCmin	CRPmax	Nab	VL	IL8	H3	cH3	MPO	FLCκ/FLCλ	MAPmin	SEVscore	PUUV-N-IgG	hNE	FLCκ	FLCλ	Hmax	eGFRmin	eGFR	
N	Valid	116	116	116	114	114	115	115	114	115	116	55	52	93	52	85	55	116	99	83	55	55	114	116	110	
Missing	0	0	0	2	2	1	1	2	1	0	61	64	23	64	31	61	1	0	17	33	61	61	2	0	6	
Mean	44.21		4.41	8.17	10.68	11.48	0.36	68.80	92.43	1082	77.82	0.27	6.32	335.83	135.51	1.16	84.86	3	1.01	148.71	34.04	29.31	0.44	49.31	65.23	
Median	41.10	0	4.00	8.00	10.00	10.80	0.36	61.00	80.70	640	23.88	0.13	6.75	322.81	117.39	1.06	84.87	3	1.11	131.80	24.44	24.28	0.44	41.00	72.00	
Mode	27.50*	0	4.00	8.00	8.00	8.800*	0.36	50.00	91.60	640	0.00	0.00*	4.72	214.690*	126.490*	35*	82.00*	2	0.10*	57.280*	87.02	24.04	0.44	7.00	7.00	
Range	55.30		14.00	15.00	17.00	27.30	0.19	229.00	253.30	5080	717.50	1.45	28.59	379.89	286.13	2.19	71.34	8	3.73	517.53	77.72	62.54	0.26	124.00	124.00	
Minimum	21.50	Male = 0	1.00	3.00	4.00	3.90	0.25	9.00	15.90	40	0.00	0.00	1.16	214.69	46.04	0.35	49.33	0	0.00	11.84	9.30	8.80	0.33	3.00	4.00	
Maximum	76.80	Female = 1	15.00	18.00	21.00	31.20	0.44	238.00	269.20	5120	717.50	1.45	29.75	594.58	332.17	2.55	120.67	8	3.73	529.37	87.02	71.34	0.59	127.00	128.00	
a. Multiple modes exist. The smallest value is shown																										

Table S2. Spearman correlation table for all the variables for both basic and scaled data. For abbreviations, see Supplementary Table S1.

Basic dataset	Variable	Age	sex	DUI	DUI2	DUI3	DRH	egR(min)	egR	WBC(max)	HCT(min)	HCT(max)	TC(min)	CRP(max)	NAB	IL	IL-R	H3	CH3	MPO	NHE	FLC	FLC2	FLC3	FLC4	FLC5	MAP(min)	PUUV-N-IgG	Sev(scale)
	Age	sex	DUI	DUI2	DUI3	DRH	egR(min)	egR	WBC(max)	HCT(min)	HCT(max)	TC(min)	CRP(max)	NAB	IL	IL-R	H3	CH3	MPO	NHE	FLC	FLC2	FLC3	FLC4	FLC5	MAP(min)	PUUV-N-IgG	Sev(scale)	
Basic dataset	Age	0.019	0.019	-0.042	0.096	0.165	-0.127	-0.352	0.176	-0.351	-0.213	0.176	-0.023	0.184	-0.016	0.176	-0.023	0.184	-0.016	0.176	-0.023	0.184	-0.016	0.176	-0.023	0.184	-0.016	0.176	-0.023
	sex	0.019	0.019	-0.082	0.015	-0.080	0.197	0.115	-0.205	-0.257	-0.209	-0.134	-0.025	0.157	0.057	0.123	-0.142	0.184	0.065	0.290	-0.058	-0.089	0.036	-0.229	-0.060	-0.075	-0.083	-0.075	-0.083
	DUI	0.402	-0.082	0.388	0.523	-0.624	0.537	0.324	-0.535	0.205	-0.047	0.064	0.045	0.024	0.026	0.351	-0.039	-0.021	0.453	0.232	0.252	0.045	-0.047	0.047	0.175	0.078	0.175	0.078	0.175
	DUI2	0.096	0.015	0.388	0.288	0.265	-0.026	0.054	0.018	-0.133	0.007	0.013	0.269	-0.041	0.153	-0.177	0.047	-0.023	0.039	-0.020	-0.039	-0.056	-0.045	-0.102	-0.030	-0.100	-0.030	-0.100	
	DRH	0.165	-0.080	0.523	0.265	-0.265	-0.389	-0.019	-0.111	-0.193	0.293	-0.261	0.117	-0.207	-0.324	0.260	-0.17	-0.290	0.138	0.174	0.185	0.001	0.095	0.241	0.062	0.241	0.062	0.241	
	egR(min)	-0.297	-0.197	-0.624	-0.026	-0.265	0.870	0.870	-0.504	-0.495	-0.026	0.028	0.031	-0.027	0.093	0.049	-0.239	0.057	-0.145	-0.307	-0.296	-0.322	-0.119	-0.081	-0.036	-0.577	-0.081	-0.036	-0.577
	egR	-0.395	0.115	-0.537	0.054	-0.389	0.870	0.870	-0.336	0.500	0.094	-0.025	0.107	-0.119	0.080	0.01	-0.260	0.000	-0.309	-0.298	-0.427	-0.430	-0.191	-0.021	-0.033	-0.577	-0.021	-0.033	-0.577
	WBC(max)	-0.020	-0.205	0.234	-0.018	-0.019	-0.504	-0.336	-0.225	0.140	-0.342	-0.302	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040
	HCT(min)	-0.357	-0.257	-0.533	-0.133	-0.111	0.495	0.500	-0.225	0.264	0.178	-0.251	-0.043	0.066	0.125	-0.019	0.071	-0.017	-0.226	-0.248	-0.256	-0.134	0.138	0.025	-0.162	0.138	0.025	-0.162	0.138
	HCT(max)	-0.020	-0.205	0.234	-0.018	-0.019	-0.504	-0.336	-0.225	0.140	-0.342	-0.302	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040	0.032	-0.040
	TC(min)	0.161	-0.134	-0.047	0.013	0.293	0.028	-0.025	-0.342	0.178	-0.481	-0.002	-0.002	-0.002	-0.259	-0.111	-0.003	-0.205	-0.551	-0.068	-0.116	-0.100	-0.139	-0.088	-0.116	-0.139	-0.088	-0.116	-0.139
	CRP(max)	0.176	0.025	0.064	0.269	0.261	0.031	0.107	0.032	-0.251	-0.082	-0.202	-0.082	-0.184	-0.033	-0.003	-0.164	0.090	-0.049	-0.090	-0.049	-0.136	-0.064	-0.132	-0.172	-0.132	-0.172	-0.132	-0.172
	NAB	-0.073	0.157	0.045	-0.041	0.117	-0.027	-0.119	-0.040	-0.043	-0.015	0.002	-0.082	-0.226	0.182	-0.117	-0.087	-0.124	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064	-0.064
	IL	0.084	0.057	0.024	0.153	-0.207	0.093	0.080	0.032	0.066	0.121	-0.259	0.184	-0.226	-0.070	0.223	0.087	0.373	0.120	0.154	0.024	0.024	0.024	0.024	0.024	0.024	0.024	0.024	0.024
	IL-R	-0.115	-0.123	0.026	-0.177	-0.324	0.049	0.011	0.085	0.125	0.132	-0.111	-0.033	0.182	-0.070	-0.020	-0.039	0.214	0.041	0.133	0.074	0.133	0.074	0.133	0.074	0.133	0.074	0.133	0.074
	H3	0.097	-0.142	0.351	0.067	0.260	-0.239	-0.260	0.262	-0.219	0.083	-0.003	-0.010	-0.117	0.223	-0.020	0.394	-0.037	0.530	0.303	0.170	0.239	0.185	0.224	0.155	0.239	0.185	0.224	0.155
	CH3	0.151	0.184	-0.039	-0.023	0.017	0.057	0.000	-0.064	0.071	0.176	-0.205	-0.164	-0.087	0.087	0.309	0.394	0.394	0.216	0.064	0.195	0.042	0.183	-0.068	-0.117	0.116	0.116	0.116	0.116
	MPO	-0.018	0.065	-0.021	0.039	-0.290	-0.145	-0.039	0.374	0.017	-0.481	-0.551	-0.090	-0.124	0.373	0.214	0.037	0.216	0.002	0.165	0.050	0.190	-0.220	-0.386	0.200	-0.386	0.200	-0.386	0.200
	NHE	-0.290	0.451	-0.002	0.318	-0.012	0.211	-0.226	0.015	-0.069	-0.159	-0.069	-0.159	-0.069	-0.159	-0.069	-0.159	-0.069	0.002	0.100	0.014	0.014	0.014	0.014	0.014	0.014	0.014	0.014	0.014
	FLC	0.207	-0.058	0.232	-0.039	0.174	-0.296	-0.427	0.239	-0.284	0.092	-0.196	-0.136	0.024	0.153	0.133	0.303	0.195	0.165	0.100	0.748	0.582	0.164	0.067	0.424	0.164	0.067	0.424	0.164
FLC2	-0.198	-0.089	-0.252	-0.056	-0.185	-0.322	-0.430	0.107	-0.256	0.011	-0.110	-0.064	0.040	-0.014	0.074	0.170	0.042	0.050	0.014	0.748	-0.031	-0.138	0.004	0.332	-0.138	0.004	0.332	-0.138	
FLC3	0.093	0.036	0.045	-0.045	0.001	-0.119	-0.191	0.186	-0.114	0.068	-0.098	-0.132	-0.021	0.231	0.119	0.233	0.183	0.190	0.129	0.582	-0.031	-0.137	0.055	0.226	-0.137	0.055	0.226	-0.137	
FLC4	-0.106	-0.229	-0.047	-0.102	0.095	-0.081	-0.021	-0.081	0.138	-0.051	0.186	-0.172	-0.055	-0.326	-0.159	-0.085	-0.068	-0.220	-0.064	-0.164	-0.138	-0.137	-0.137	-0.137	-0.137	-0.137	-0.137	-0.137	
FLC5	-0.085	-0.060	0.175	-0.030	0.241	-0.036	-0.033	0.097	0.025	0.073	0.116	-0.137	-0.208	-0.040	0.033	0.224	-0.117	-0.386	0.372	0.067	0.004	0.055	0.184	-0.007	0.055	0.184	-0.007	0.055	
MAP(min)	-0.106	-0.076	-0.283	-0.106	0.062	-0.577	-0.652	-0.447	-0.362	0.127	-0.375	-0.096	-0.104	-0.042	-0.061	0.155	0.116	0.320	0.324	0.424	0.322	0.226	0.113	-0.075	0.226	0.113	-0.075	0.226	
Scaled dataset	Age	-0.211	-0.322	-0.058	0.141	-0.337	-0.455	-0.028	-0.323	-0.197	0.333	-0.095	-0.133	0.061	-0.134	0.077	0.088	-0.078	-0.039	0.243	0.254	0.100	-0.003	-0.167	-0.088	0.254	0.100	-0.003	-0.167
	sex	-0.211	-0.173	-0.015	-0.032	0.326	-0.298	-0.276	-0.161	-0.420	0.075	-0.170	-0.174	0.062	-0.160	-0.192	0.123	-0.018	-0.151	-0.021	0.032	-0.198	-0.072	-0.086	-0.072	-0.086	-0.072	-0.086	
	DUI	-0.122	-0.173	0.257	0.257	-0.738	0.624	-0.683	-0.667	0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	-0.063	
	DUI2	-0.055	-0.015	0.257	0.173	-0.027	0.153	0.003	-0.087	-0.047	0.115	0.185	-0.237	0.103	-0.223	0.088	-0.034	0.003	0.024	-0.038	0.027	0.001	-0.364	-0.055	-0.364	-0.055	-0.364		
	DRH	-0.141	-0.032	-0.482	0.173	-0.376	-0.466	0.136	-0.332	-0.227	0.132	-0.253	-0.026	-0.179	-0.322	0.119	-0.102	-0.173	0.162	0.198	-0.257	-0.038	-0.129	0.157	-0.038	-0.129	0.157	0.322	
	egR(min)	-0.337	-0.326	-0.739	-0.027	-0.376	0.854	0.854	-0.443	-0.503	-0.084	0.022	0.185	-0.154	0.090	-0.106	-0.306	0.053	-0.184	-0.391	-0.260	-0.286	-0.135	-0.231	-0.098	-0.519	-0.098	-0.519	
	egR	-0.455	0.298	-0.624	0.153	-0.466	0.854	0.854	-0.325	0.519	0.015	0.047	0.320	-0.120	0.072	-0.144	-0.365	-0.066	-0.070	-0.242	-0.361	-0.401	-0.168	-0.203	-0.401	-0.168	-0.203	-0.401	
	WBC(max)	-0.028	-0.276	0.403	-0.001	0.136	-0.443	-0.325	-0.211	-0.211	0.505	-0.374	0.011	0.186	0.071	0.104	0.259	-0.409	0.401	0.301	0.184	0.304	0.176	0.037	0.170	0.044	0.304	0.176	
	HCT(min)	-0.323	-0.161	-0.667	-0.087	-0.332	0.503	0.519	-0.211	-0.248	0.098	0.081	-0.122	0.117	0.152	-0.186	0.066	-0.014	-0.153	-0.381	-0.341	-0.180	-0.123	-0.103	-0.153	-0.103	-0.153	-0.103	
	HCT(max)	-0.197	-0.420	0.006	-0.047	-0.227	-0.084	0.015	0.505	0.248	-0.096	-0.496	0.125	-0.066	0.143	0.152	-0.247	0.147	0.507	0.339	0.039	-0.060	0.057	-0.015	-0.060	0.057	-0.015	-0.060	
	TC(min)	0.333	0.075	-0.128	0.115	0.332	0.022	0.047	-0.374	0.098	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	-0.066	
	CRP(max)	-0.095	-0.107	-0.066	0.185	-0.253	0.185	0.320	0.011	0.081	0.125	-0.061	-0.168	0.130	-0.039	-0.039	-0.209	0.101	-0.075	-0.149	-0.093	-0.098	-0.360	-0.222	-0.107	-0.360	-0.222	-0.107	
	NAB	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	0.174	
	IL	0.061	0.062	-0.052	0.103	-0.179	0.090	0.072	0.071	0.117	-0.143	-0.238	0.130	-0.168	-0.267	-0.110	0.224	0.078	0.371	0.099	0.180	-0.029	0.299	-0.345	-0.029	0.299	-0.345	-0.029	
	IL-R	-0.134	0.160	-0.036	-0.232	-0.322	0.106	0.144	0.104	-0.152	0.152	-0.109	-0.039	-0.197	-0.110	-0.056	0.290	0.208	-0.047	0.128	0.068	0.112	-0.05	-0.037	0.008	-0.037	0.008	-0.037	
	H3	0.077	-0.192	0.164	-0.288	0.119	-0.306	-0.365	0.259	-0.186	0.247	-0.237	-0.093	-0.284	-0.224	-0.056	0.380	0.380	0.345	0.123	0.316	0.178	0.237	-0.058	-0.290	0.245	-0.058	-0.290	
	CH3	0.088	0.123	-0.073	-0.034	-0.012	0.051	0.006	-0.049	0.066	-0.147	-0.168	-0.209	-0.106	0.078	0.290	0.380	0.198	0.077	0									

Table S3. p-Values for the correlation for all variables for both the basic and scaled data. For abbreviations, see Supplementary Table S1.

	Variable	Age	sex	D(t)	D(f)	FDH	eGR(min)	eGR	WBC(max)	HCT(min)	HCT(max)	TC(min)	CRP(max)	Nab	VL	IL	H3	ch3	MPO	NNE	FLCx	FLCA	FLC/FLCA	MMP(min)	PUUV-NgG	Sev(scale)		
Basic dataset	Age	sex	0.841	0.841	0.000	0.311	0.079	0.001	0.000	0.832	0.000	0.023	0.088	0.060	0.437	0.543	0.153	0.285	0.873	0.655	0.129	0.146	0.500	0.258	0.401	0.257		
	sex		0.841	0.385	0.785	0.397	0.034	0.233	0.028	0.006	0.026	0.154	0.795	0.092	0.677	0.386	0.174	0.191	0.556	0.008	0.672	0.519	0.793	0.014	0.555	0.416		
	D(t)			0.000	0.385	0.000	0.000	0.000	0.000	0.000	0.000	0.795	0.626	0.501	0.634	0.864	0.854	0.001	0.781	0.851	0.000	0.088	0.063	0.743	0.617	0.084	0.002	
	D(f)			0.311	0.875	0.000	0.004	0.784	0.581	0.846	0.161	0.942	0.888	0.004	0.667	0.244	0.120	0.658	0.872	0.723	0.985	0.776	0.685	0.745	0.281	0.771	0.262	
	FDH			0.397	0.000	0.000	0.004	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	eGR(min)			0.001	0.034	0.000	0.784	0.004	0.000	0.000	0.000	0.000	0.788	0.766	0.741	0.774	0.500	0.728	0.212	0.687	0.186	0.005	0.028	0.116	0.388	0.932	0.723	
	eGR			0.000	0.233	0.000	0.581	0.000	0.000	0.000	0.000	0.000	0.329	0.795	0.270	0.217	0.569	0.484	0.014	0.000	0.732	0.008	0.001	0.001	0.170	0.828	0.754	
	WBC(max)			0.832	0.028	0.000	0.864	0.840	0.000	0.000	0.000	0.016	0.000	0.000	0.732	0.763	0.816	0.554	0.011	0.650	0.008	0.058	0.042	0.439	0.178	0.393	0.340	
	HCT(min)			0.000	0.006	0.000	0.161	0.241	0.000	0.000	0.016	0.005	0.058	0.007	0.645	0.636	0.380	0.035	0.617	0.879	0.001	0.037	0.062	0.411	1.142	0.809	0.000	
	HCT(max)			0.023	0.026	0.795	0.842	0.041	0.788	0.329	0.000	0.005	0.000	0.000	0.383	0.870	0.384	0.355	0.427	0.212	0.000	0.895	0.506	0.937	0.628	0.591	0.477	0.178
	TC(min)			0.088	0.154	0.626	0.988	0.002	0.766	0.795	0.000	0.008	0.058	0.000	0.031	0.982	0.059	0.439	0.976	0.144	0.000	0.549	0.156	0.427	0.482	0.049	0.258	0.000
	CRP(max)			0.047	0.795	0.501	0.004	0.005	0.741	0.270	0.732	0.007	0.383	0.031	0.382	0.183	0.816	0.921	0.245	0.413	0.663	0.326	0.044	0.341	0.067	0.001	0.308	
	NAb			0.630	0.092	0.534	0.667	0.216	0.776	0.217	0.673	0.645	0.870	0.982	0.383	0.097	0.197	0.264	0.319	0.259	0.881	0.661	0.770	0.381	0.500	0.859	0.265	0.000
	IL			0.543	0.677	0.864	0.164	0.129	0.569	0.000	0.016	0.639	0.196	0.384	0.559	0.883	0.097	0.126	0.629	0.366	0.000	0.917	0.262	0.000	0.912	0.767	0.000	0.000
	ch3			0.415	0.386	0.854	0.210	0.019	0.728	0.484	0.554	0.380	0.355	0.439	0.816	0.197	0.621	0.821	0.889	0.027	0.128	0.772	0.347	0.602	0.400	0.261	0.816	0.667
	ch3			0.353	0.174	0.001	0.658	0.012	0.021	0.014	0.011	0.035	0.427	0.976	0.921	0.264	0.112	0.889	0.004	0.004	0.739	0.000	0.029	0.229	0.096	0.422	0.039	0.138
	ch3			0.285	0.191	0.781	0.872	0.905	0.687	1.000	0.650	0.617	0.212	0.144	0.245	0.539	0.538	0.027	0.004	0.124	0.652	0.166	0.767	0.195	0.634	0.407	0.413	
	MPO			0.873	0.556	0.851	0.723	0.007	0.186	0.732	0.000	0.879	0.000	0.000	0.413	0.259	0.006	0.128	0.739	0.124	0.988	0.327	0.720	0.173	0.045	0.000	0.003	
	hNE			0.655	0.008	0.000	0.985	0.004	0.005	0.008	0.058	0.041	0.895	0.549	0.663	0.681	0.391	0.772	0.000	0.652	0.988	0.476	0.923	0.356	0.566	0.001	0.003	
FLCx			0.129	0.672	0.088	0.776	0.204	0.028	0.001	0.082	0.037	0.506	0.156	0.326	0.861	0.264	0.347	0.029	0.166	0.237	0.476	0.000	0.000	0.263	0.629	0.001	0.000	
FLCA			0.146	0.519	0.063	0.281	0.176	0.016	0.001	0.439	0.062	0.937	0.427	0.644	0.770	0.917	0.602	0.229	0.767	0.720	0.923	0.000	0.820	0.314	0.975	0.036		
FLC/FLCA			0.500	0.793	0.744	0.465	0.295	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.820	0.914	0.317	0.667	0.000	0.000		
NAB(min)			0.258	0.014	0.617	0.281	0.319	0.392	0.828	0.399	0.342	0.591	0.490	0.067	0.560	0.015	0.261	0.422	0.634	0.045	0.566	0.233	0.114	0.068	0.268	0.300	0.000	
PUUV-NgG			0.401	0.555	0.084	0.771	0.017	0.723	0.754	0.340	0.809	0.477	0.258	0.001	0.039	0.002	0.816	0.399	0.407	0.000	0.001	0.629	0.975	0.691	0.068	0.459		
Sev(scale)			0.257	0.416	0.002	0.262	0.515	0.000	0.000	0.000	0.178	0.000	0.308	0.265	0.763	0.667	0.138	0.413	0.003	0.003	0.001	0.016	0.097	0.230	0.459			
Scaled dataset	Age	sex	0.145	0.224	0.034	0.693	0.335	0.018	0.001	0.851	0.024	0.176	0.020	0.516	0.364	0.677	0.358	0.600	0.447	0.593	0.790	0.093	0.079	0.485	0.985	0.251	0.544	
	sex		0.145	0.234	0.019	0.828	0.022	0.037	0.055	0.269	0.003	0.609	0.242	0.231	0.673	0.272	0.186	0.399	0.904	0.300	0.888	0.795	0.826	0.172	0.393	0.284	0.000	
	D(t)		0.024	0.234	0.034	0.075	0.000	0.000	0.000	0.967	0.380	0.650	0.346	0.721	0.805	0.260	0.202	0.581	0.021	0.074	0.067	0.546	0.623	0.546	0.002	0.000		
	D(f)		0.693	0.919	0.075	0.235	0.852	0.293	0.000	0.551	0.747	0.432	0.204	0.102	0.482	0.124	0.547	0.816	0.983	0.868	0.796	0.591	0.993	0.067	0.560	0.072	0.000	
	FDH		0.335	0.828	0.000	0.235	0.000	0.001	0.000	0.351	0.020	0.117	0.365	0.079	0.860	0.220	0.028	0.417	0.313	0.235	0.677	0.192	0.774	0.794	0.376	0.282	0.004	
	FDH		0.001	0.022	0.000	0.852	0.008	0.000	0.000	0.000	0.000	0.568	0.881	0.204	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	eGR		0.001	0.037	0.000	0.293	0.001	0.000	0.000	0.023	0.000	0.921	0.746	0.025	0.410	0.624	0.123	0.100	0.966	0.364	0.094	0.005	0.004	0.249	0.162	0.784	0.000	
	eGR		0.001	0.037	0.000	0.293	0.001	0.000	0.000	0.023	0.000	0.921	0.746	0.025	0.410	0.624	0.123	0.100	0.966	0.364	0.094	0.005	0.004	0.249	0.162	0.784	0.000	
	WBC(max)		0.851	0.055	0.004	1.000	0.351	0.001	0.023	0.146	0.000	0.008	0.941	0.200	0.627	0.477	0.072	0.737	0.004	0.036	0.204	0.816	0.226	0.802	0.243	0.001	0.000	
	HCT(min)		0.024	0.269	0.000	0.551	0.020	0.000	0.000	0.146	0.005	0.052	0.507	0.144	0.424	0.298	0.201	0.651	0.923	0.295	0.007	0.017	0.217	0.400	0.483	0.012	0.000	
	HCT(max)		0.176	0.003	0.967	0.747	0.117	0.568	0.921	0.000	0.008	0.005	0.000	0.393	0.652	0.327	0.296	0.088	0.315	0.000	0.071	0.814	0.681	0.700	0.919	0.680	0.046	
	TC(min)		0.020	0.609	0.380	0.432	0.365	0.881	0.746	0.008	0.058	0.000	0.678	0.762	0.100	0.454	0.101	0.248	0.000	0.001	0.818	0.528	0.346	0.225	0.872	0.000	0.000	
	CRP(max)		0.516	0.242	0.650	0.204	0.079	0.204	0.025	0.941	0.579	0.393	0.678	0.249	0.373	0.792	0.525	0.419	0.490	0.609	0.308	0.526	0.501	0.011	0.126	0.242	0.000	
	NAb		0.364	0.231	0.346	0.102	0.860	0.292	0.410	0.200	0.144	0.652	0.762	0.249	0.063	0.174	0.048	0.468	0.380	0.798	0.801	0.625	0.923	0.100	0.002	0.108	0.000	
	IL		0.673	0.713	0.782	0.230	0.261	0.731	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	IL		0.358	0.272	0.805	0.124	0.024	0.469	0.323	0.477	0.298	0.296	0.454	0.792	0.174	0.451	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	H3		0.600	0.186	0.260	0.547	0.417	0.032	0.100	0.072	0.201	0.088	0.101	0.525	0.048	0.132	0.700	0.007	0.015	0.401	0.027	0.222	0.011	0.691	0.043	0.990	0.000	
	ch3		0.547	0.399	0.620	0.816	0.933	0.717	0.966	0.737	0.651	0.315	0.248	0.149	0.468	0.592	0.043	0.007	0.173	0.598	0.139	0.626	0.244	0.638	0.598	0.698	0.000	
	MPO		0.593	0.904	0.581	0.983	0.235	0.206	0.634	0.004	0.923	0.000	0.490	0.380	0.009	0.152	0.015	0.173	0.009	0.009	0.377	0.942	0.126	0.116	0.052	0.103	0.000	
hNE		0.790	0.300	0.021	0.868	0.267	0.025	0.094	0.036	0.295	0.017	0.009	0.298	0.498	0.750	0.401	0.598	0.009	0.009	0.453	0.922	0.382	0.871	0.299	0.001	0.000		
FLCx		0.093	0.888	0.074	0.796	0.172	0.071	0.005	0.204	0.007	0.814	0.181	0.308	0.801	0.215	0.381	0.027	0.139	0.377	0.453	0.000	0.000	0.430	0.842	0.004	0.000		
FLCA		0.079	0.795	0.667	0.591	0.074	0.044	0.																				

Table S4. Kruskal-Wallis test and general liner modelling (GLM) – analysis. The Kruskal-Wallis test included 4 levels of PUUV-NAb1 categories as the dependent variable (NAb≤320 = 29, NAb = 640 = 38, NAb = 1280 = 28, NAb ≥ 2560 = 21). GLM analysis was performed separately to PUUV-N-IgG1, PUUV-VL1, eGFRmin and eGFR as dependent variables. Variables of predictive significance marked in bold font.

		Kruskal-Wallis test			General linear model (GLM) analyses																			
		NAb			VL	eGFR(min)								eGFR				PUUV-N-IgG						
Variable		DF	Chisq	p	DF	MS ¹	F	p	Est	DF	MS ¹	F	p	Est	DF	MS ¹	F	p	Est	DF	MS ¹	F	p	Est
Basic dataset	Age	3	3.15	0.37	1	563.16	0.03	0.87	-0.27	1	13255.30	10.81	0.00	-0.85	1	17392.61	13.44	0.00	-1.00	1	1.33	1.99	0.16	-0.01
	sex	3	3.75	0.29	1	34518.30	1.67	0.20	51.14	1	4956.96	3.81	0.05	14.08	1	1191.49	0.82	0.37	7.15	1	0.03	0.05	0.83	-0.04
	D(t)	3	0.50	0.92	1	289.26	0.01	0.91	-0.95	1	42888.35	44.72	0.00	-7.17	1	27473.69	22.93	0.00	-5.87	1	0.02	0.03	0.87	0.00
	D(f)	3	0.51	0.92	1	45337.18	2.21	0.14	14.18	1	67.15	0.05	0.82	-0.36	1	2601.21	1.81	0.18	2.25	1	0.62	0.91	0.34	-0.04
	FDBH	3	5.59	0.13	1	10297.89	0.49	0.49	-10.23	1	10321.16	7.74	0.01	-5.86	1	21320.65	14.74	0.00	-8.79	1	2.48	3.67	0.06	0.10
	eGFR(min)	3	3.75	0.29	1	7686.76	0.36	0.55	0.32	1					1	106806.55	241.28	0.00	0.86	1	0.42	0.61	0.44	0.00
	eGFR	3	6.67	0.08	1	9079.82	0.41	0.52	0.36	1	99548.05	241.28	0.00	0.81	1					1	0.27	0.38	0.54	0.00
	WBC(max)	3	0.48	0.92	1	2701.26	0.12	0.73	-1.59	1	35639.11	35.67	0.00	-3.70	1	26618.44	22.20	0.00	-3.26	1	0.40	0.59	0.45	0.01
	HCT(min)	3	0.66	0.88	1	9349.24	0.43	0.51	-360.40	1	37397.55	38.03	0.00	458.73	1	40660.76	38.22	0.00	491.78	1	0.68	1.01	0.32	2.14
	HCT(max)	3	1.20	0.75	1	10460.35	0.49	0.49	-284.29	1	1558.62	1.21	0.27	-74.23	1	3.22	0.00	0.96	-3.52	1	0.36	0.53	0.47	1.18
	TC(min)	3	7.41	0.06	1	61347.78	2.99	0.09	-1.28	1	402.48	0.31	0.58	0.05	1	61.52	0.04	0.84	-0.02	1	0.70	1.03	0.31	0.00
	CRP(max)	3	7.10	0.07	1	2969.50	0.14	0.71	0.15	1	987.00	0.75	0.39	-0.05	1	227.80	0.16	0.69	0.03	1	2.88	4.42	0.04	0.00
	NAb	3			1	25601.13	1.23	0.27	-0.02	1	368.49	0.27	0.60	0.00	1	6781.17	4.86	0.03	-0.01	1	1.71	2.57	0.11	0.00
	VL	3	9.17	0.03	1					1	527.11	0.36	0.55	0.02	1	569.42	0.41	0.52	0.02	1	1.88	2.51	0.12	0.00
	IL-8	3	1.62	0.65	1	69140.17	3.29	0.08	-0.27	1	341.49	0.23	0.63	8.63	1	71.04	0.05	0.82	3.96	1	0.10	0.13	0.72	0.14
	H3	3	1.66	0.65	1	285.52	0.01	0.91	0.64	1	2764.34	2.10	0.15	-0.99	1	3071.05	2.08	0.15	-1.06	1	1.61	2.42	0.12	0.03
	cH3	3	8.15	0.04	1	5050.80	0.23	0.64	-0.12	1	2.63	0.00	0.97	0.00	1	86.53	0.06	0.80	0.02	1	0.07	0.09	0.76	0.00
	MPO	3	7.91	0.05	1	22628.83	1.05	0.31	0.30	1	7447.60	6.12	0.02	-0.15	1	3536.27	2.56	0.11	-0.11	1	5.53	8.48	0.00	0.00
	hNE	3	3.22	0.36	1	3430.81	0.16	0.69	-0.10	1	7024.49	5.19	0.03	-0.10	1	6705.45	4.60	0.04	-0.10	1	2.55	3.62	0.06	0.00
	FLCk	3	2.03	0.57	1	65473.80	3.26	0.08	1.46	1	7521.71	5.69	0.02	-0.50	1	16151.62	15.17	0.00	-0.73	1	0.09	0.12	0.74	0.00
	FLCA	3	0.58	0.90	1	24783.89	1.19	0.28	1.44	1	4989.96	3.64	0.06	-0.64	1	8103.20	6.61	0.01	-0.85	1	0.00	0.01	0.94	0.00
	FLCk/FLCA	3	1.60	0.66	1	115977.68	6.06	0.02	93.85	1	634.47	0.44	0.51	-6.94	1	4387.85	3.37	0.07	-18.40	1	0.02	0.02	0.88	0.04
	MAP(min)	3	1.24	0.74	1	18441.19	0.88	0.35	-1.79	1	95.92	0.07	0.79	-0.08	1	411.75	0.28	0.60	0.18	1	1.79	2.70	0.10	0.01
	PUUV-N-IgG	3	7.37	0.06	1	51265.57	2.51	0.12	-35.47	1	822.35	0.61	0.44	3.56	1	568.56	0.38	0.54	2.98	1				
	Sev(scale)	3	1.78	0.62	1	968.00	0.05	0.83	-2.48	1	44345.69	46.89	0.00	-10.92	1	71966.47	92.92	0.00	-14.92	1	0.46	0.68	0.41	-0.04
Scaled dataset	Age	3	6.17	0.10	1	0.00	0.10	0.75	-0.04	1	0.45	4.90	0.03	-0.40	1	0.82	10.74	0.00	-0.54	1	0.06	1.18	0.28	-0.15
	sex	3	2.35	0.50	1	0.07	1.55	0.22	0.08	1	0.47	5.15	0.03	0.20	1	0.36	4.14	0.05	0.17	1	0.07	1.30	0.26	0.08
	D(t)	3	0.88	0.83	1	0.01	0.24	0.63	-0.09	1	1.43	20.09	0.00	-1.01	1	0.84	11.11	0.00	-0.78	1	0.06	1.15	0.29	-0.21
	D(f)	3	4.41	0.22	1	0.06	1.33	0.25	0.20	1	0.07	0.73	0.40	0.22	1	0.76	9.85	0.00	0.70	1	0.00	0.00	1.00	0.00
	FDBH	3	2.51	0.47	1	0.01	0.32	0.58	-0.09	1	0.74	7.40	0.01	-0.62	1	1.11	12.08	0.00	-0.76	1	0.01	0.21	0.65	-0.08
	eGFR(min)	3	2.78	0.43	1	0.03	0.63	0.43	0.08	1					1	2.66	72.63	0.00	0.75	1	0.04	0.66	0.42	0.09
	eGFR	3	3.82	0.28	1	0.02	0.54	0.46	0.08	1	2.88	72.63	0.00	0.82	1					1	0.04	0.69	0.41	0.09
	WBC(max)	3	1.15	0.76	1	0.00	0.05	0.82	-0.03	1	0.97	12.02	0.00	-0.64	1	0.79	10.30	0.00	-0.57	1	0.00	0.01	0.92	0.02
	HCT(min)	3	2.29	0.51	1	0.01	0.19	0.67	-0.07	1	0.91	11.07	0.00	0.73	1	0.97	13.23	0.00	0.75	1	0.01	0.15	0.70	0.07
	HCT(max)	3	3.38	0.34	1	0.02	0.37	0.55	-0.10	1	0.27	2.79	0.10	-0.39	1	0.07	0.72	0.40	-0.20	1	0.02	0.35	0.56	-0.11
	TC(min)	3	6.36	0.10	1	0.13	2.94	0.09	-0.20	1	0.01	0.09	0.77	0.05	1	0.01	0.12	0.73	0.06	1	0.01	0.17	0.68	0.05
	CRP(max)	3	4.23	0.24	1	0.00	0.02	0.89	0.02	1	0.01	0.08	0.78	0.07	1	0.32	3.62	0.06	0.41	1	0.22	4.25	0.04	-0.34
	NAb	3			1	0.04	1.00	0.32	-0.16	1	0.16	1.65	0.21	-0.31	1	0.43	5.07	0.03	-0.51	1	0.26	5.25	0.03	0.40
	VL	3	7.01	0.07	1					1	0.06	0.63	0.43	0.17	1	0.05	0.54	0.46	0.15	1	0.10	1.90	0.17	-0.22
	IL-8	3	2.01	0.57	1	0.15	3.55	0.07	-0.27	1	0.05	0.51	0.48	0.16	1	0.01	0.15	0.70	0.08	1	0.01	0.11	0.75	0.05
	H3	3	4.62	0.20	1	0.00	0.00	0.99	0.00	1	0.09	0.85	0.36	-0.23	1	0.17	1.87	0.18	-0.32	1	0.12	2.26	0.14	-0.27
	cH3	3	7.12	0.07	1	0.01	0.25	0.62	-0.07	1	0.00	0.04	0.85	-0.04	1	0.00	0.00	0.99	0.00	1	0.00	0.00	0.98	0.00
	MPO	3	3.65	0.30	1	0.04	0.78	0.38	0.11	1	0.31	3.22	0.08	-0.32	1	0.11	1.20	0.28	-0.19	1	0.23	4.44	0.04	-0.28
	hNE	3	3.67	0.30	1	0.01	0.33	0.57	-0.09	1	0.33	3.46	0.07	-0.43	1	0.24	2.69	0.11	-0.36	1	0.01	0.09	0.76	-0.05
	FLCk	3	3.57	0.31	1	0.15	3.44	0.07	0.18	1	0.30	3.16	0.08	-0.26	1	0.82	10.71	0.00	-0.43	1	0.00	0.01	0.91	-0.01
	FLCA	3	2.75	0.43	1	0.05	1.10	0.30	0.14	1	0.18	1.80	0.19	-0.26	1	0.37	4.24	0.05	-0.37	1	0.01	0.11	0.75	-0.05
	FLCk/FLCA	3	1.19	0.75	1	0.25	6.27	0.02	0.32	1	0.02	0.22	0.64	-0.09	1	0.22	2.40	0.13	-0.29	1	0.00	0.03	0.86	-0.03
	MAP(min)	3	5.33	0.15	1	0.03	0.65	0.42	-0.12	1	0.09	0.89	0.35	-0.21	1	0.08	0.84	0.36	-0.20	1	0.32	6.49	0.01	0.40
	PUUV-N-IgG	3	10.74	0.01	1	0.08	1.90	0.17	-0.18	1	0.07	0.66	0.42	0.16	1	0.06	0.69	0.41	0.16	1				
	Sev(scale)	3	3.60	0.31	1	0.01	0.20	0.66	-0.06	1	0.83	9.89	0.00	-0.57	1	1.69	29.40	0.00	-0.81	1	0.00	0.02	0.90	-0.02

¹MS=Mean square

Table S5. Mixed model-analysis. The NAb was divided into 4 categories $\text{NAb} \leq 320 = 29$, $\text{NAb} = 640 = 38$, $\text{NAb} = 1280 = 28$, $\text{NAb} \geq 2560 = 21$. VL had 3 categories: $\text{VL} < 10$, $10 \leq \text{VL} < 80$ and $\text{VL} \geq 80$. The 3 categories of PUUV-N-IgG were < 0.15 , $0.15 \leq \text{PUUV-N-IgG} < 0.9$ and $\text{PUUV-N-IgG} \geq 0.9$. In the analyses, we utilized mixed models with eGFR, HCT, WBC, TC or CRP as dependent variables, and time, the categorized variable, and the interaction of time and the categorized variable serving as the independent variables. There were 54 patients' observations in the time series.

	Variable	N nonmiss	Fit Statistics	time*NAb ⁴		time ¹		NAb ¹	
			AIC	F Value	Pr > F	F Value	Pr > F	F Value	Pr > F
NAb	eGFR	195	1659,6	0,86	0,565	1,37	0,254	1,80	0,158
	HCT	191	-609,5	0,59	0,802	48,35	<.0001	0,89	0,451
	WBC	191	886,8	0,70	0,705	5,28	0,002	0,55	0,649
	TC	191	1742,7	2,95	0,003	50,60	<.0001	2,58	0,064
	CRP	190	1679,2	0,72	0,691	25,31	<.0001	2,03	0,122
	Variable	N nonmiss	Fit Statistics	time*VL ³		time ¹		VL ²	
			AIC	F Value	Pr > F	F Value	Pr > F	F Value	Pr > F
VL	eGFR	195	1688,5	1,12	0,352	1,78	0,153	1,70	0,194
	HCT	191	-638,4	1,61	0,149	49,54	<.0001	1,08	0,348
	WBC	191	891,0	1,94	0,078	5,03	0,003	0,77	0,468
	TC	191	1796,2	0,81	0,562	44,97	<.0001	0,74	0,482
	CRP	190	1709,8	1,52	0,178	28,79	<.0001	0,08	0,920
	Variable	N nonmiss	Fit Statistics	time*PUUV-N-IgG ³		time ¹		PUUV-N-IgG ²	
			AIC	F Value	Pr > F	F Value	Pr > F	F Value	Pr > F
PUUV-N-IgG	eGFR	195	1695,4	0,27	0,952	1,89	0,134	0,38	0,686
	HCT	191	-629,5	0,36	0,903	41,03	<.0001	0,04	0,964
	WBC	191	900,7	0,08	0,998	3,97	0,010	1,04	0,362
	TC	191	1773,7	5,01	0,000	52,19	<.0001	0,69	0,505
	CRP	190	1713,4	0,31	0,933	25,64	<.0001	1,50	0,233

Number of all observations in all models 216.

¹DF=3, ²DF=2, ³DF=6, ⁴DF=9.

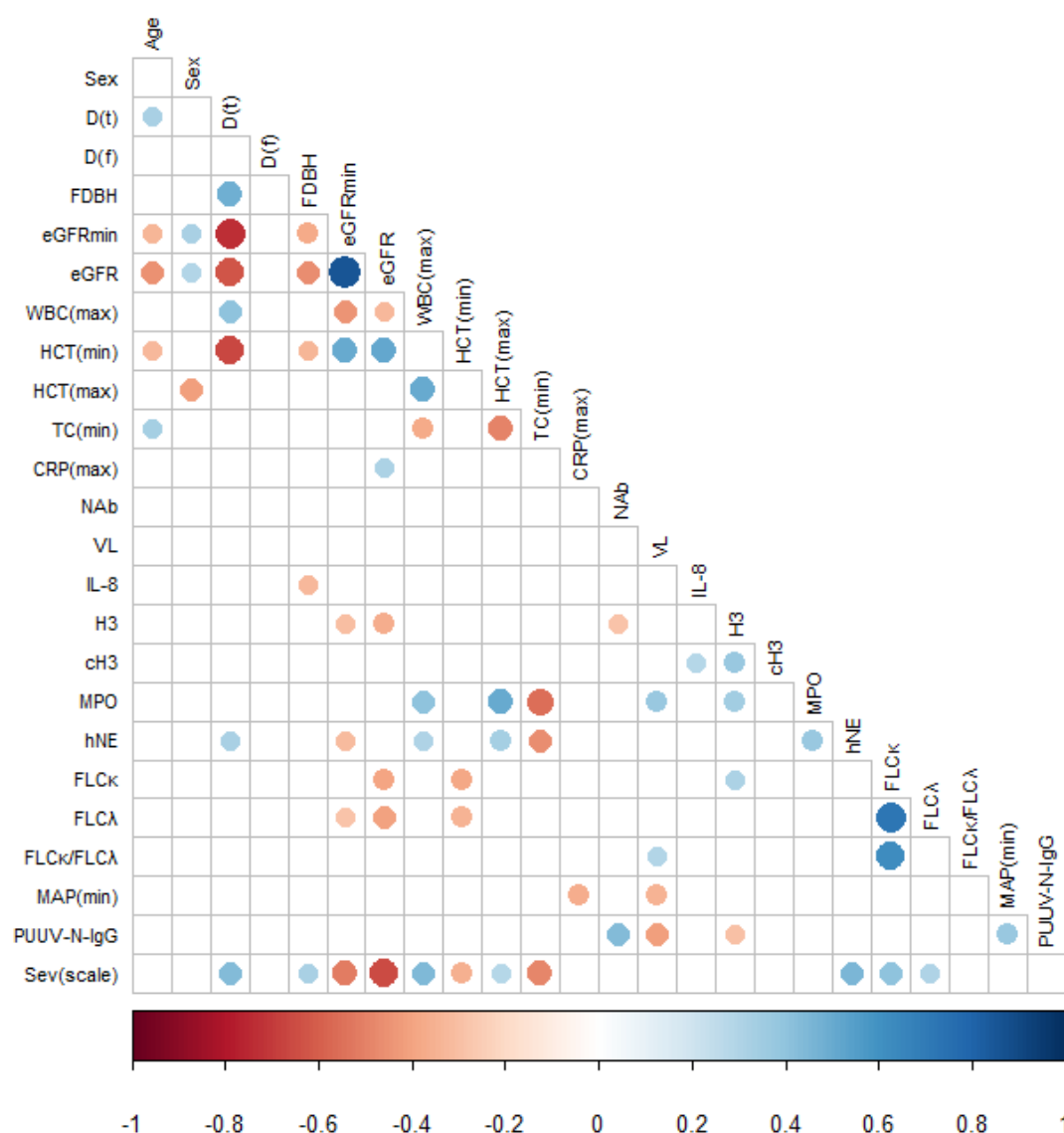


Figure S1. Spearman correlation plot of scaled dataset where missing data points in variables were excluded pairwise. Variable abbreviations are D(t) = Overall disease duration, D(F) = overall duration of fever, FDBH = Fever days before hospitalization, eGFR = estimated glomerular filtration rate, WBC = white blood cell count, HCT = Hematocrit, TC = thrombocyte count, CRP = C-reactive protein, NAb = PUUV neutralizing antibodies, VL = PUUV viral load, IL-8 = Interleukin-8, H3 = Histone H3, cH3 = Citrullinated histone H3, MPO = Myeloperoxidase, hNE = Neutrophil elastase, FLC κ = Free light chain κ , FLC λ = Free light chain λ , MAP = mean arterial pressure, Sev(scale) = Severity scale. The maximum or minimum values during the hospitalization are indicated as min or max, respectively and all other parameters are measured from 1st day of hospitalization. Only significant correlations at $p \leq 0.05$ are shown and the size of the dots are equivalent to the significance.

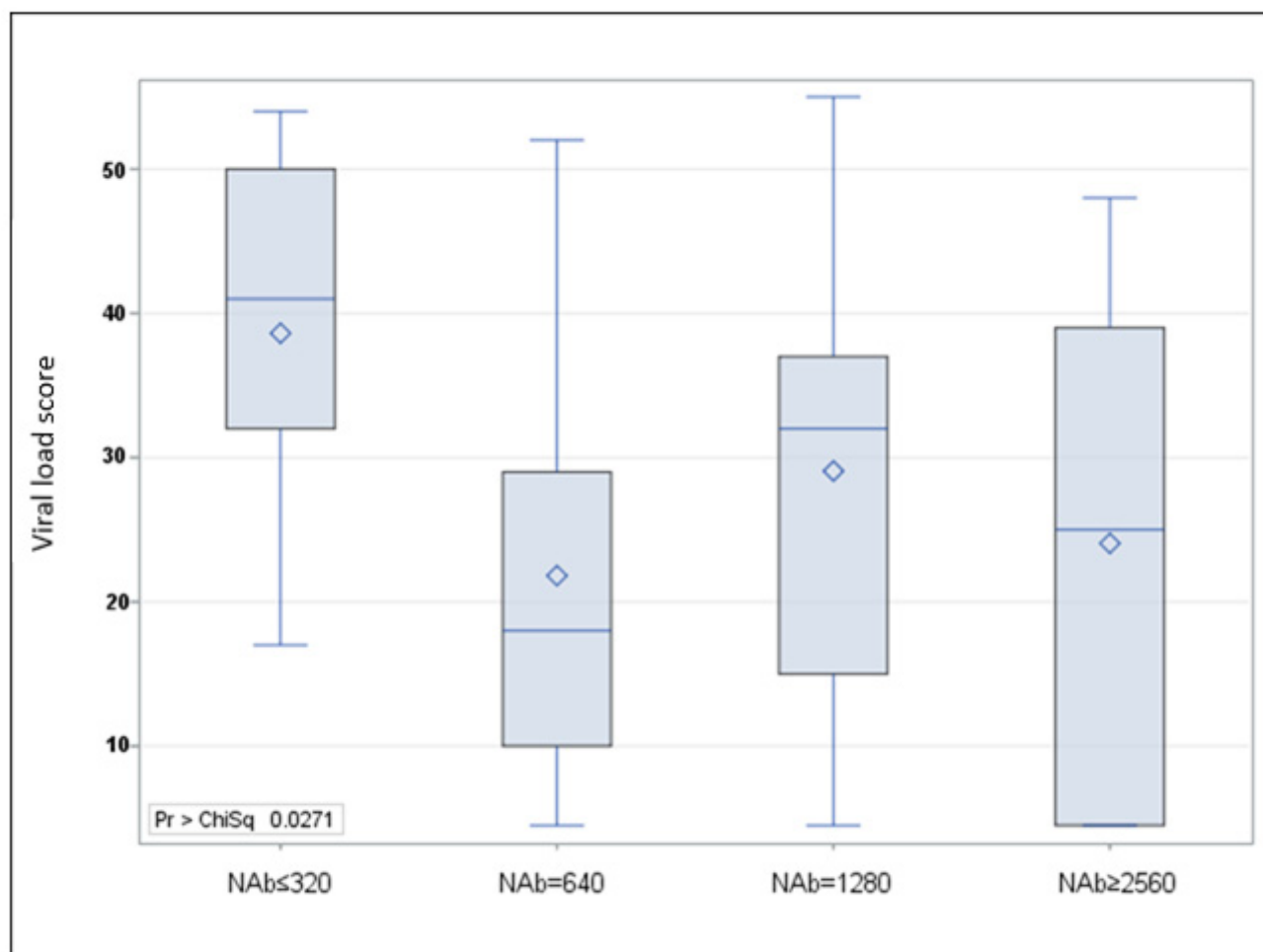


Figure S2. Distribution of Wilcoxon scores for VL in four groups of Nab. The group sizes are as follows: NAb ≤ 320 = 29, NAb = 640 = 38, NAb = 1280 = 28, NAb ≥ 2560 = 21

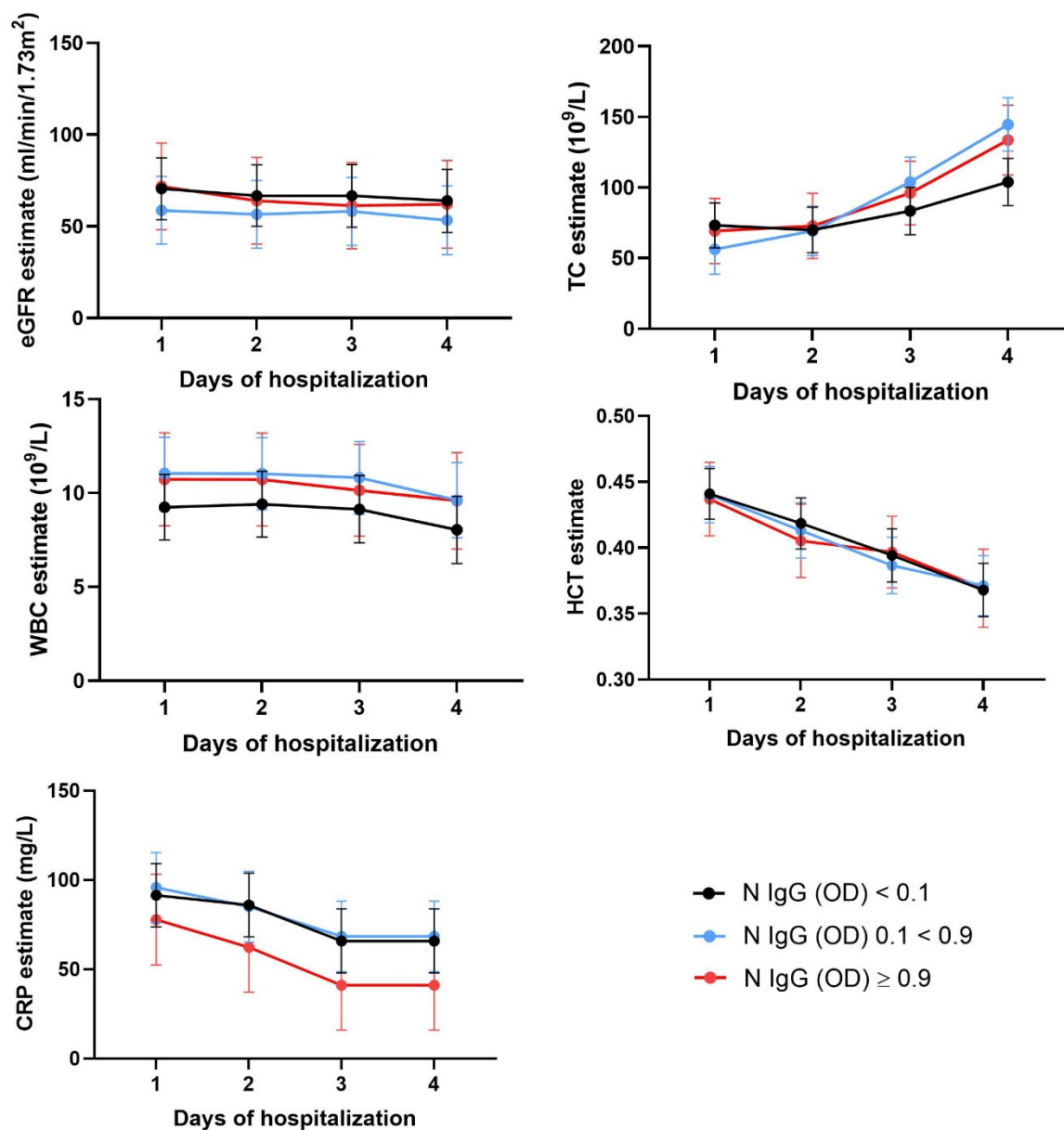


Figure S3. Time series graphs showing the impact of different categories of PUUV N-IgG at 1st day of hospitalization on eGFR, TC, WBC, HCT and CRP. The variables eGFR, TC, WBC, HCT and CRP were followed over time (the first 4 days of hospitalization) and reported as mean estimates from the mixed model analysis. The error bars indicate upper and lower limits of the estimates.

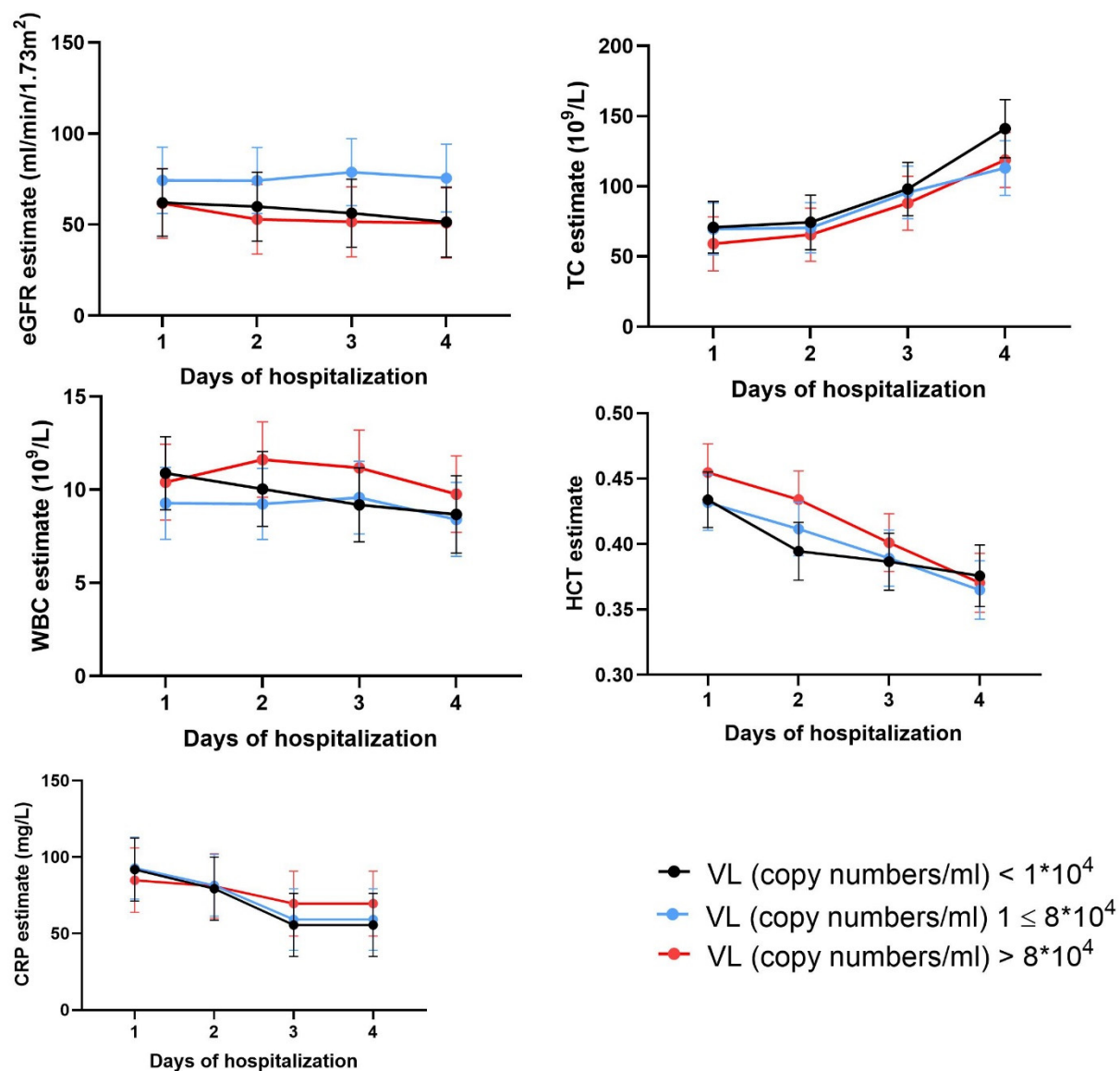


Figure S4. Time series graphs showing the impact of different categories of PUUV VL at 1st day of hospitalization on eGFR, TC, WBC, HCT and CRP. The variables eGFR, TC, WBC, HCT and CRP were followed over time (the first 4 days of hospitalization) and reported as mean estimates from the mixed model analysis. The error bars indicate upper and lower limits of the estimates.

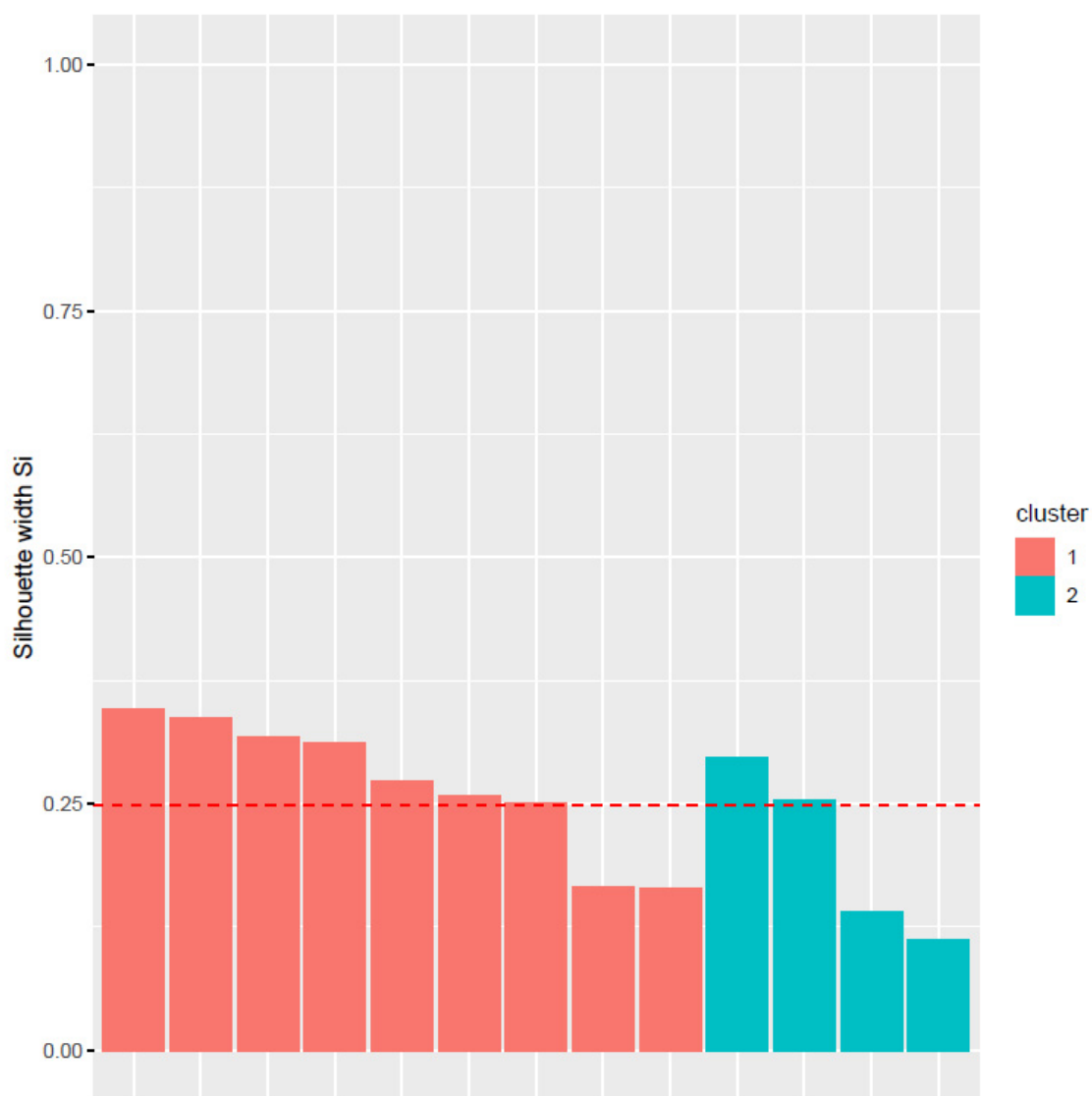


Figure S5. Silhouette plot of hierarchical cluster analysis. Average silhouette width 0.25. Cluster 1: 9 clusters, average silhouette width 0.27. Cluster 2: 4 clusters, average silhouette width 0.20. The clustering with the highest average silhouette width is considered to present the most appropriate clustering of the data points.