

**Table S4. Viral single nucleotide polymorphisms (SNPs) associated with longitudinal levels of viral load that are listed according to the sequence order of the polymerase region, stratified by HBV subgenotypes.**

Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P	Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P	Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P
<b>Entire, subgenotype Ba</b>					nt287	1.74	-0.81	(-1.61,-0.01)	0.0473	nt1080	19.13	-0.56	(-0.82,-0.29)	<0.0001
nt2439	8.91	-0.59	(-0.96,-0.22)	0.0019	nt294	8.26	-0.78	(-1.16,-0.40)	0.0001	nt1101	1.74	-1.19	(-1.95,-0.43)	0.0022
nt2441	24.78	-0.31	(-0.56,-0.07)	0.0120	nt327	2.17	-0.81	(-1.56,-0.06)	0.0351	nt1104	3.70	-0.69	(-1.24,-0.14)	0.0147
nt2452	6.09	-0.48	(-0.93,-0.02)	0.0393	nt330	6.30	-0.52	(-0.96,-0.07)	0.0229	nt1113	2.17	0.76	(0.03,1.49)	0.0419
nt2507	1.74	-0.88	(-1.74,-0.03)	0.0429	nt355	4.78	-0.72	(-1.21,-0.23)	0.0042	nt1123	38.70	-0.43	(-0.65,-0.21)	0.0001
nt2549	6.74	0.55	(0.12,0.97)	0.0113	nt357	9.57	-0.74	(-1.10,-0.37)	0.0001	nt1126	21.52	-0.61	(-0.87,-0.35)	<0.0001
nt2583	29.13	-0.36	(-0.59,-0.12)	0.0028	nt358	1.30	-0.98	(-1.87,-0.09)	0.0305	nt1138	8.91	-0.79	(-1.16,-0.42)	<0.0001
nt2617	13.70	-0.31	(-0.62,-0.00)	0.0483	nt390	2.39	-0.85	(-1.50,-0.19)	0.0115	nt1139	4.57	-0.52	(-1.02,-0.02)	0.0419
nt2618	24.35	-0.34	(-0.59,-0.09)	0.0070	nt400	15.22	-0.32	(-0.61,-0.03)	0.0312	nt1165	61.96	0.29	(0.07,0.50)	0.0103
nt2645	2.61	1.19	(0.43,1.95)	0.0023	nt408	4.35	-0.68	(-1.22,-0.14)	0.0131	nt1242	19.35	-0.37	(-0.64,-0.10)	0.0071
nt2659	1.30	1.06	(0.07,2.04)	0.0362	nt429	1.30	-1.02	(-1.98,-0.07)	0.0357	nt1290	5.22	-0.52	(-0.99,-0.05)	0.0286
nt2678	5.43	-0.55	(-1.03,-0.07)	0.0258	nt436	1.74	-0.94	(-1.70,-0.18)	0.0149	nt1320	18.04	-0.38	(-0.66,-0.10)	0.0070
nt2684	6.09	-0.65	(-1.09,-0.21)	0.0036	nt438	1.74	-1.09	(-1.92,-0.26)	0.0105	nt1332	2.83	-0.90	(-1.53,-0.27)	0.0054
nt2690	8.48	-0.51	(-0.90,-0.13)	0.0089	nt441	1.74	-1.10	(-1.90,-0.31)	0.0063	nt1341	3.26	-0.86	(-1.45,-0.27)	0.0044
nt2699	53.70	-0.29	(-0.50,-0.07)	0.0085	nt533	3.26	-0.74	(-1.33,-0.14)	0.0151	nt1353	1.74	-1.39	(-2.15,-0.62)	0.0004
nt2712	43.70	0.39	(0.18,0.60)	0.0003	nt551	3.91	-0.58	(-1.14,-0.01)	0.0446	nt1359	3.91	-0.60	(-1.14,-0.06)	0.0296
nt2739	51.74	0.25	(0.03,0.46)	0.0238	nt554	1.74	-1.13	(-1.93,-0.33)	0.0056	nt1368	28.70	-0.29	(-0.52,-0.05)	0.0167
nt2753	4.13	-0.57	(-1.11,-0.03)	0.0386	nt624	1.30	-0.98	(-1.96,-0.00)	0.0500	nt1371	27.39	-0.41	(-0.64,-0.17)	0.0008
nt2771	51.74	-0.28	(-0.49,-0.07)	0.0101	nt627	2.83	-0.88	(-1.53,-0.22)	0.0085	nt1407	6.30	-0.54	(-0.97,-0.10)	0.0161
nt2792	3.04	-0.66	(-1.31,-0.01)	0.0461	nt705	4.78	-0.58	(-1.10,-0.06)	0.0283	nt1509	3.91	-0.69	(-1.22,-0.16)	0.0114
nt2962	5.87	-0.73	(-1.19,-0.28)	0.0015	nt732	3.04	-1.01	(-1.60,-0.41)	0.0009					
nt3027	5.43	0.85	(0.39,1.32)	0.0003	nt753	53.26	0.26	(0.04,0.47)	0.0191	<b>Entire, subgenotype Ce</b>				
nt3067	9.13	0.66	(0.30,1.03)	0.0004	nt754	1.52	-1.13	(-1.98,-0.28)	0.0092	nt2441	12.63	-1.42	(-2.59,-0.25)	0.0177
nt3097	51.30	0.26	(0.04,0.47)	0.0185	nt762	1.74	-0.96	(-1.73,-0.19)	0.0143	nt2443	13.68	-1.30	(-2.44,-0.15)	0.0273
nt3153	2.83	-0.80	(-1.45,-0.15)	0.0155	nt765	19.57	-0.45	(-0.72,-0.18)	0.0011	nt2522	28.42	1.25	(0.39,2.11)	0.0049
nt3157	4.35	-0.62	(-1.17,-0.08)	0.0255	nt766	7.61	-0.52	(-0.92,-0.12)	0.0104	nt2574	73.68	0.93	(0.04,1.83)	0.0404
nt3158	2.61	-0.84	(-1.52,-0.16)	0.0160	nt771	4.78	-1.41	(-1.89,-0.92)	<0.0001	nt2608	7.37	-1.77	(-3.21,-0.34)	0.0160
nt3192	8.26	-0.39	(-0.77,-0.01)	0.0466	nt774	6.09	-1.05	(-1.48,-0.62)	<0.0001	nt2699	55.79	-1.40	(-2.17,-0.63)	0.0005
nt3195	1.74	0.89	(0.03,1.76)	0.0425	nt802	1.30	-0.91	(-1.82,-0.00)	0.0498	nt2898	11.58	-1.39	(-2.59,-0.19)	0.0240
nt3201	8.26	-0.54	(-0.94,-0.14)	0.0079	nt804	1.52	-1.29	(-2.15,-0.44)	0.0032	nt2946	93.68	1.69	(0.12,3.26)	0.0357
nt3211	2.39	0.73	(0.02,1.43)	0.0441	nt813	1.74	-0.97	(-1.77,-0.18)	0.0168	nt3084	7.37	-1.60	(-3.10,-0.09)	0.0382
nt3213	1.52	1.13	(0.19,2.06)	0.0182	nt849	5.87	-0.78	(-1.23,-0.34)	0.0006	nt3116	31.58	-0.95	(-1.81,-0.10)	0.0291
nt11	3.48	0.69	(0.10,1.28)	0.0214	nt915	15.00	0.40	(0.10,0.69)	0.0091	nt16	9.47	-1.58	(-2.91,-0.25)	0.0200
nt23	1.74	0.93	(0.03,1.83)	0.0437	nt925	3.26	-0.64	(-1.22,-0.05)	0.0332	nt28	9.47	-1.67	(-3.01,-0.33)	0.0150
nt27	3.04	0.83	(0.15,1.50)	0.0162	nt927	3.26	-1.00	(-1.59,-0.40)	0.0010	nt29	10.53	-1.77	(-3.01,-0.52)	0.0059
nt110	6.74	-0.74	(-1.18,-0.31)	0.0009	nt941	2.61	-0.77	(-1.46,-0.07)	0.0312	nt30	6.32	-1.69	(-3.28,-0.09)	0.0384
nt114	6.74	-0.69	(-1.12,-0.26)	0.0016	nt951	19.13	-0.38	(-0.65,-0.11)	0.0056	nt31	35.79	-1.38	(-2.18,-0.58)	0.0009
nt123	8.04	-0.73	(-1.12,-0.33)	0.0003	nt987	13.26	-0.38	(-0.70,-0.06)	0.0192	nt32	8.42	-1.72	(-3.13,-0.31)	0.0175
nt126	14.57	-0.43	(-0.73,-0.12)	0.0057	nt1005	1.30	-1.10	(-2.03,-0.17)	0.0205	nt33	8.42	-1.72	(-3.13,-0.31)	0.0175
nt154	2.61	-0.69	(-1.35,-0.03)	0.0406	nt1011	3.26	-0.79	(-1.37,-0.21)	0.0075	nt34	8.42	-1.49	(-2.92,-0.06)	0.0414
nt219	2.39	-0.88	(-1.61,-0.15)	0.0181	nt1017	1.96	-0.99	(-1.75,-0.23)	0.0107	nt35	8.42	-1.49	(-2.92,-0.06)	0.0414
nt255	3.26	-0.78	(-1.38,-0.17)	0.0122	nt1029	14.35	-0.32	(-0.62,-0.03)	0.0335	nt36	15.79	-1.57	(-2.64,-0.50)	0.0046
nt273	39.78	-0.44	(-0.66,-0.23)	0.0001	nt1077	3.04	-0.95	(-1.57,-0.33)	0.0028	nt37	10.53	-1.34	(-2.62,-0.07)	0.0387
nt285	35.43	-0.45	(-0.67,-0.23)	0.0001	nt1078	2.39	1.29	(0.59,1.99)	0.0003	nt38	10.53	-1.34	(-2.62,-0.07)	0.0387

Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P	Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P	Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P
nt39	11.58	-1.28	(-2.50,-0.05)	0.0418	nt2708	4.03	0.52	(0.05,0.99)	0.0293	nt355	5.54	-0.58	(-0.95,-0.20)	0.0025
nt41	10.53	-1.35	(-2.63,-0.07)	0.0384	nt2712	41.06	0.18	(0.00,0.36)	0.0439	nt357	9.82	-0.59	(-0.88,-0.29)	0.0001
nt42	13.68	-1.18	(-2.33,-0.03)	0.0440	nt2721	7.56	0.39	(0.06,0.73)	0.0204	nt358	1.51	-0.75	(-1.43,-0.08)	0.0284
nt44	14.74	-1.23	(-2.34,-0.13)	0.0294	nt2733	2.27	-0.60	(-1.19,-0.01)	0.0472	nt381	17.88	0.35	(0.12,0.57)	0.0024
nt47	11.58	-1.39	(-2.60,-0.17)	0.0258	nt2753	4.28	-0.63	(-1.05,-0.20)	0.0038	nt390	2.77	-0.59	(-1.09,-0.09)	0.0209
nt48	13.68	-1.40	(-2.53,-0.28)	0.0153	nt2763	1.76	0.77	(0.13,1.41)	0.0186	nt408	5.04	-0.55	(-0.96,-0.14)	0.0093
nt50	11.58	-1.39	(-2.60,-0.17)	0.0258	nt2790	2.52	-0.60	(-1.18,-0.02)	0.0433	nt429	1.51	-0.93	(-1.66,-0.21)	0.0121
nt51	11.58	-1.39	(-2.60,-0.17)	0.0258	nt2837	4.53	0.48	(0.05,0.91)	0.0302	nt436	1.76	-0.63	(-1.22,-0.03)	0.0396
nt52	69.47	1.12	(0.27,1.97)	0.0101	nt2860	4.79	0.46	(0.05,0.87)	0.0288	nt438	2.02	-0.92	(-1.56,-0.29)	0.0044
nt55	11.58	-1.60	(-2.84,-0.36)	0.0117	nt2892	1.51	0.91	(0.09,1.73)	0.0297	nt441	2.02	-0.98	(-1.58,-0.38)	0.0015
nt285	14.74	-1.41	(-2.50,-0.32)	0.0118	nt2944	4.79	0.45	(0.03,0.88)	0.0373	nt533	3.53	-0.54	(-1.01,-0.08)	0.0216
nt393	6.32	-1.77	(-3.38,-0.16)	0.0313	nt2945	4.79	0.45	(0.03,0.88)	0.0373	nt554	1.76	-0.84	(-1.50,-0.18)	0.0130
nt511	35.79	1.39	(0.58,2.19)	0.0009	nt2962	6.05	-0.53	(-0.89,-0.16)	0.0045	nt624	1.51	-0.79	(-1.54,-0.03)	0.0406
nt796	80.00	1.08	(0.10,2.06)	0.0304	nt2986	3.78	0.73	(0.26,1.19)	0.0022	nt627	3.27	-0.75	(-1.25,-0.25)	0.0031
nt834	60.00	-1.20	(-1.99,-0.40)	0.0035	nt2993	1.51	1.08	(0.29,1.88)	0.0075	nt678	1.76	-0.68	(-1.32,-0.04)	0.0370
nt841	91.58	1.64	(0.28,3.00)	0.0188	nt2997	2.02	0.76	(0.09,1.43)	0.0269	nt705	4.79	-0.42	(-0.84,-0.01)	0.0465
nt915	32.63	-1.17	(-2.02,-0.33)	0.0067	nt3004	1.76	0.71	(0.04,1.38)	0.0388	nt706	1.51	1.22	(0.48,1.96)	0.0014
nt934	54.74	1.83	(1.09,2.57)	<0.0001	nt3013	3.27	0.79	(0.28,1.29)	0.0024	nt732	3.53	-0.88	(-1.33,-0.43)	0.0001
nt951	90.53	-1.61	(-2.99,-0.23)	0.0227	nt3018	1.76	0.78	(0.06,1.50)	0.0344	nt754	1.51	-1.12	(-1.83,-0.40)	0.0022
nt955	38.95	1.38	(0.59,2.17)	0.0008	nt3026	4.28	0.49	(0.05,0.93)	0.0304	nt762	1.76	-0.91	(-1.54,-0.28)	0.0045
nt993	31.58	-1.12	(-1.97,-0.27)	0.0106	nt3027	5.54	0.71	(0.33,1.09)	0.0003	nt766	8.31	-0.36	(-0.67,-0.05)	0.0240
nt1053	54.74	1.20	(0.42,1.98)	0.0028	nt3031	1.76	0.78	(0.00,1.55)	0.0494	nt771	5.54	-1.30	(-1.67,-0.93)	<0.0001
nt1126	8.42	-1.85	(-3.22,-0.48)	0.0086	nt3067	9.32	0.48	(0.18,0.78)	0.0017	nt774	6.55	-0.92	(-1.26,-0.58)	<0.0001
nt1218	33.68	-1.09	(-1.94,-0.24)	0.0123	nt3150	4.03	0.47	(0.01,0.93)	0.0432	nt802	1.51	-0.70	(-1.39,-0.01)	0.0476
nt1221	42.11	-1.44	(-2.22,-0.66)	0.0004	nt3153	3.27	-0.69	(-1.19,-0.19)	0.0067	nt804	1.76	-1.06	(-1.72,-0.40)	0.0016
nt1230	30.53	-1.31	(-2.16,-0.47)	0.0027	nt3157	4.79	-0.47	(-0.89,-0.04)	0.0317	nt813	2.02	-0.88	(-1.48,-0.28)	0.0044
nt1323	78.95	1.06	(0.10,2.02)	0.0308	nt3158	2.77	-0.73	(-1.26,-0.19)	0.0080	nt831	2.52	-0.64	(-1.21,-0.08)	0.0263
nt1332	90.53	1.71	(0.42,2.99)	0.0097	nt3201	9.07	-0.51	(-0.83,-0.20)	0.0015	nt849	6.55	-0.61	(-0.95,-0.27)	0.0005
nt1479	62.11	-0.82	(-1.64,-0.01)	0.0483	nt3211	2.52	0.65	(0.08,1.22)	0.0257	nt897	2.02	-0.66	(-1.27,-0.04)	0.0356
nt1485	25.26	-1.00	(-1.92,-0.08)	0.0339	nt3213	1.51	0.82	(0.03,1.61)	0.0419	nt904	3.02	-0.75	(-1.26,-0.25)	0.0037
nt1574	25.26	-1.90	(-2.74,-1.07)	<0.0001	nt1	10.58	0.34	(0.05,0.63)	0.0223	nt915	14.11	0.34	(0.09,0.59)	0.0078
					nt27	3.02	0.55	(-0.02,1.11)	0.0588	nt927	3.53	-0.70	(-1.17,-0.23)	0.0034
					nt46	5.79	-0.39	(-0.77,-0.00)	0.0492	nt941	2.77	-0.61	(-1.17,-0.04)	0.0353
<b>HBeAg-negative, subgenotype Ba</b>														
nt2439	9.57	-0.36	(-0.66,-0.07)	0.0155	nt53	31.99	0.20	(0.02,0.39)	0.0309	nt950	3.02	-0.63	(-1.14,-0.11)	0.0170
nt2452	6.55	-0.41	(-0.77,-0.05)	0.0275	nt110	6.80	-0.70	(-1.06,-0.34)	0.0001	nt1005	1.51	-0.97	(-1.68,-0.26)	0.0075
nt2507	2.02	-0.74	(-1.39,-0.08)	0.0272	nt114	6.30	-0.59	(-0.95,-0.23)	0.0014	nt1008	2.52	0.76	(0.18,1.34)	0.0102
nt2511	3.53	-0.51	(-1.01,-0.01)	0.0472	nt123	8.82	-0.48	(-0.79,-0.17)	0.0024	nt1011	3.53	-0.79	(-1.25,-0.33)	0.0008
nt2549	6.80	0.52	(0.17,0.87)	0.0040	nt126	15.62	-0.25	(-0.49,-0.01)	0.0404	nt1017	2.27	-0.71	(-1.30,-0.13)	0.0163
nt2559	11.08	-0.32	(-0.60,-0.04)	0.0241	nt166	3.53	-0.51	(-0.99,-0.04)	0.0332	nt1059	2.77	-0.58	(-1.11,-0.05)	0.0320
nt2564	2.27	0.75	(0.07,1.42)	0.0301	nt219	2.52	-0.74	(-1.33,-0.15)	0.0148	nt1077	3.53	-0.68	(-1.15,-0.20)	0.0054
nt2603	3.78	-0.66	(-1.11,-0.20)	0.0048	nt246	2.27	-0.59	(-1.18,-0.01)	0.0458	nt1078	1.76	0.83	(0.16,1.50)	0.0148
nt2645	2.02	0.89	(0.14,1.65)	0.0200	nt255	3.78	-0.65	(-1.11,-0.18)	0.0065	nt1080	20.91	-0.31	(-0.52,-0.10)	0.0043
nt2678	6.05	-0.48	(-0.85,-0.10)	0.0135	nt285	37.78	-0.23	(-0.41,-0.05)	0.0117	nt1101	1.51	-1.06	(-1.73,-0.40)	0.0019
nt2684	6.55	-0.68	(-1.02,-0.33)	0.0001	nt287	2.02	-0.70	(-1.31,-0.09)	0.0246	nt1123	41.31	-0.22	(-0.40,-0.04)	0.0147
nt2690	9.57	-0.34	(-0.64,-0.04)	0.0268	nt294	9.07	-0.52	(-0.82,-0.22)	0.0007	nt1126	22.17	-0.52	(-0.73,-0.31)	<0.0001
nt2699	55.67	-0.23	(-0.40,-0.05)	0.0114	nt327	2.52	-0.73	(-1.31,-0.15)	0.0134	nt1138	9.07	-0.64	(-0.94,-0.33)	<0.0001

Nucleotide (nt) position	Freq. of variant SNP	$\beta$	95% CI	P
nt1139	4.79	-0.48	(-0.87,-0.08)	0.0184
nt1239	1.51	0.86	(0.16,1.55)	0.0154
nt1242	19.14	-0.38	(-0.61,-0.16)	0.0007
nt1243	1.76	-0.74	(-1.38,-0.10)	0.0242
nt1332	3.27	-0.70	(-1.19,-0.22)	0.0044
nt1341	3.53	-0.53	(-0.99,-0.07)	0.0234
nt1353	1.76	-1.24	(-1.84,-0.64)	0.0001
nt1359	3.78	-0.46	(-0.91,-0.01)	0.0443
nt1362	2.02	0.69	(0.10,1.27)	0.0215
nt1371	28.97	-0.22	(-0.41,-0.03)	0.0247
nt1479	3.02	-0.71	(-1.23,-0.19)	0.0075
nt1485	2.27	-0.55	(-1.10,-0.00)	0.0499
nt1509	3.78	-0.60	(-1.04,-0.16)	0.0072
nt1512	1.76	0.73	(0.07,1.38)	0.0296
nt1518	3.02	-0.58	(-1.08,-0.09)	0.0217
<b>HBeAg-negative, subgenotype Ce</b>				
nt2441	16.42	-0.74	(-1.44,-0.04)	0.0378
nt2607	11.94	-0.99	(-1.79,-0.20)	0.0155
nt2666	89.55	0.85	(0.03,1.68)	0.0425
nt2889	88.06	0.94	(0.15,1.73)	0.0206
nt53	32.84	0.77	(0.21,1.34)	0.0082
nt293	88.06	-1.10	(-1.93,-0.26)	0.0112
nt552	10.45	1.00	(0.11,1.90)	0.0291
nt592	22.39	0.75	(0.10,1.39)	0.0234
nt791	89.55	-1.25	(-2.24,-0.27)	0.0135
nt852	8.96	1.14	(0.22,2.05)	0.0159
nt921	10.45	0.93	(0.08,1.77)	0.0324
nt951	91.04	-1.43	(-2.30,-0.56)	0.0017
nt1126	11.94	-0.94	(-1.73,-0.15)	0.0198
nt1221	50.75	-0.68	(-1.21,-0.15)	0.0128
nt1229	43.28	-0.66	(-1.19,-0.12)	0.0167
nt1230	37.31	-0.59	(-1.14,-0.03)	0.0389
nt1383	10.45	1.17	(0.25,2.09)	0.0131
nt1574	31.34	-1.06	(-1.59,-0.52)	0.0002

CI, confidence interval; Freq, frequency; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.