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SARS-CoV-2 Associated Mutations, Strain Variations and Mortality During the First Epidemic Wave in India: A Study.

Neha Sharma

University Institute of Biotechnology, Chandigarh University, Gharuan, Mohali, Punjab, 140413.
* Corresponding author : n.sharma137@gmail.com

Abstract

India is no different to global health havoc created by SARS-COV-2 outbreak, although the appearance of different waves and the magnitude of losses varied. The study of the first wave on timeline is of utmost importance due to the alarming emergency and lack of preparedness to deal with the new virus which entered the gene pool. Besides, population density and RNA virus mutation rate might have led to more strain variants. In the present study, comparative analysis of thirty-nine complete or nearly-complete genomes of SARS-COV-2 during the first wave of COVID-19 in India was made and a number of mutations were observed. These observations further supported the evidence for genetic basis of rapid evolution of the virus.

Keywords: Coronavirus, First wave, India, Mutation, SARS-COV-2, Variants.

The magnitude of toll on the health and lives of millions of people across the globe by RNA coronavirus SARS-CoV2 is massive and distressing[1,2]. The RNA viruses mutate at much higher rates (of the order of 10^{-6} to 10^{-4} substitutions per nucleotide per infection cell) than their host[3,4]. Since the case of its first incidence to notice in Wuhan, the capital of Hubei Province in the People's Republic of China and thereafter, the inexplicable mortality and fleeting rate of infection intrigued the scientists to draw the correlation between the viral genomic variations and its spread[5,6]. Consequently, it led to a marathon of scientific efforts in the direction to deduce its structure and find vaccine.

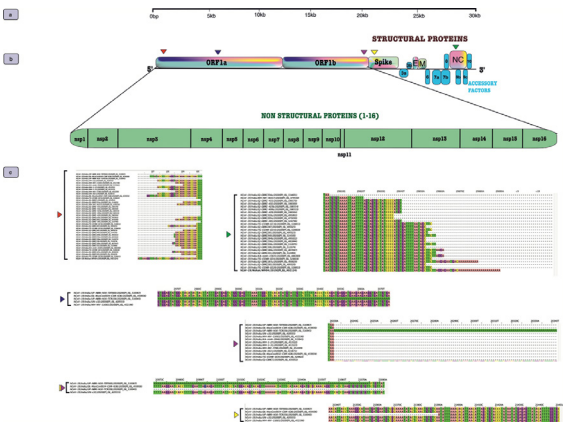

Figure 1: Polycistronic genome of SARS-CoV-2 (a) SARS-COV-2 genome representing individual ORFs. (b) 16 non-structural proteins (NSPS) are embedded in polyprotein 1ab (PP1ab) while structural proteins include S (spike), E (envelope), M (membrane), NC (nucleocapsid) (c) pairwise nucleotide sequence alignment of the strains showing mutations in NSPS, S and NC parts of the SARS-CoV-2 genome. Coloured arrows in part b and c depict mutations and are corelated with respect to position and strains, respectively.

Table 1: Mutations found in the genome of SARS-CoV-2 strains isolated from thirty-nine patients during the first wave of COVID-19 in India. The number in the parenthesis indicated the location of amino acid in its protein.

Month	S.No.	STRAIN		PATIENT DETAILS						MUTATIONS		
		Number	Lineage (Clade)	Location, India	Gender	Travel History	Age	Status	Sample collection date	Nucleotide*	Genomic region*	Missense*
January	1.	hCoV-19/India/MH-1-27/2020	B (L)	Maharashtra	Female	Wuhan, China	20	Recovered	2020-01-27	Gap of 3 nucleotides	NSP2 NSP3 NSP12 Spike	I(491)T P(1326)S A(406)V Y(145)del, R(408)I
	2.	hCoV-19/India/MH-1-31/2020	A (S)	Maharashtra	Male	China	23	Recovered	2020-01-31	-	NSP2 NSP3 NSP13 Spike NS8	I(296)V P(1261)L T(214)I A(930)V L(84)S
March	1.	hCoV-19/India/UN-c32/2020	B.1.1 (GR)	Unknown	Female	Italy	37	Unknown	2020-03-03	-	NSP12 Spike N	P(323)L D(614)G R(203)K, G(204)R
	2.	hCoV-19/India/UN-1621/2020	B.4 (O)	Unknown	Female	Indian citizen sampled at Iran	55	Unknown	2020-03-12	-	NSP2 NSP4 NSP6 Spike	R(27)C, V(198)I M(33)I L(37)F V(622)I

April	1.	hCoV-19/India/GJ-GBRC5/2020	B.1 (GH)	Ahmedabad	Female	-	66	Released, Alive	2020-04-13	-	NSP2 NSP3 NSP12 NSP13 Spike NS3 NS7a NS8 N	T(85)I, I(295)X, I(296)X, L(297)X, A(298)X, S(299)X, F(300)X, S(301)X S(371)T, C(417)X, V(418)X, G(1217)E, V(1434)X, L(1435)X, M(1436)X, S(1437)X, N(1438)X, L(1439)X, G(1440)X, M(1441)X, P(1442)X, S(1443)X P(323)L P(504)L D(614)G Q(57)H I(107)X, V(108)X, F(109)X, I(110)X, T(111)X, L(112)X, C(113)X E(110)stop S(33)I
	2.	hCoV-19/India/MH-NIV-11683/2020	B.1 (G)	Maharashtra	Female	-	12	Mild	2020-04-19	-	NSP5 NSP12 NSP16 Spike	A(116)V P(323)L G(39)C T(22)I, D(614)G
	3.	hCoV-19/	B.6 (O)	Maharashtra	Male	-	25	Mild	2020-	-	NSP3	S(1197)

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												X, A(264) X, Y(265) X, Y(266) X, V(267) X, G(268) X, Y(269) X, L(270) X, Q(271) X, P(272)X S(31)L P(13)L
May	1.	hCoV-19/ India/DL-Max-Cov0032-CSIR-IGIB/2020	B.6 (O)	Delhi	Female	-	23	Hospital-ized	2020-05-05	-	NSP2 NSP3 NSP6 NSP12 NSP15 NSP16 N	T(85)X, S(301)X S(1197)X, T(1198) K, W(1414)X L(37)F F(70)X, A(97)V Q(152)X, K(180) X, H(242)X, P(270) D(246)X, G(256) X, N(286)X P(13)L
	2.	hCoV-19/ India/DL-Max-Cov0034-CSIR-IGIB/2020	B.6 (O)	Delhi	Female	-	26	Hospital-ized	2020-05-10	-	NSP2 NSP3 NSP6 NSP12 NSP15 NSP16 NS7a N	S(301)X S(1197)X, T (1198)K, S(1428)X L(37)F A(97)V Q(188)X, E(202) X, K(204)X, D(219) X, E(266)X I(171)X, T(172) X, E(173)X, H(174) X, S(175)X, W(176) X, N(177)X, A(178) X, M(184)X, W(190) X, N(198)X, P(215) X, Y(228)X, R(255) X, N(268)X, E(284) X, D(293)X E(92)X, I(100) X, F(101)X, L(102)X P(13)L

	3.	hCoV-19/ India/KA-nimh-15835/2020	B.6 (O)	Karnataka	Female	-	15	Asymp-tomatic	2020-05-10	-	NSP3 NSP6 NSP12 Spike NS3 N	T(1198)K L(37)F A(97)V K(77)M, D(1084)Y L(52)I P(13)L
	4.	hCoV-19/India/UP-NBRI-N38-TDT660/2020	B.1.1.32 (GR)	Uttar Pradesh	Female	-	86	Suspect-ed coro-navirus infection	2020-05-14	-	NSP2 NSP3 NSP12 Spike N	E(66)X, A(192)V S(848)X, I(849)X, K(850)X, W(851)X, A(852)X, D(853)X, N(854)X, N(855)X, C(856)X, A(994)D P(323)L D(614)G R(203)K, G(204)R

However, the situation was more tensed in India during the first wave of its outbreak due to lack of unpreparedness in all facets of medical and health care artillery[7]. The population density in India is multiple times higher than those of developed countries making the precautionary step of social distancing more challenging to follow and implement. Moreover, significance of face masks was more taxing with the illiterate section of the society mostly the daily wage workers[8,9]. These factors led to the multitude of strain mutations of the RNA virus and consequentially challenged the available medical facilities, which led to heavy loss of lives. To work strategically in the direction to find a vaccine amid this health chaos, it was imperative to deduce the structure of the RNA virus and the strain mutations accompanying its infection rate. The marathon began in this direction and a number of authorized laboratories actively participated over the country[10].

In the present study an effort to evaluate the correlation of virus evolution and infection rate, SARS-CoV-2 genomes (complete or nearly complete) isolated from thirty-nine patients infected at different time period during the first wave of COVID-19 in India, were collected from Global Initiative on Sharing All Influenza Data (GISAID) [https://www.gisaid. org/]. These sequences were analysed on the basis of different parameters viz., detail(s) of patient and type(s) of mutation (Table 1). These sequences were also multiple aligned using the reference strain, hCoV-19/Wuhan/WIV04/2019(Accession number: EPI_ISL_402124) and were found with missense mutations, nucleotide gaps, intermittent stop codons, long stretch of N nucleotides and many other alterations (Figure 1c). Most of the mutations were found in the non-structural proteins (NSPS), Spike (S) polyproteins and nucleocapsid (NC) proteins (Table 1; Figure 1b,c). The known role of position equivalent to most of these mutation(s) are antibody recognition sites, ligand binding and viral oligomerization interfaces[11,12]. To date, there is lack of information on the viral protein

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Conflicts of interest

The authors declare no conflicts of interest/ competing interests.

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