Within-host diversity of SARS-CoV-2 in COVID-19 patients with variable disease severities

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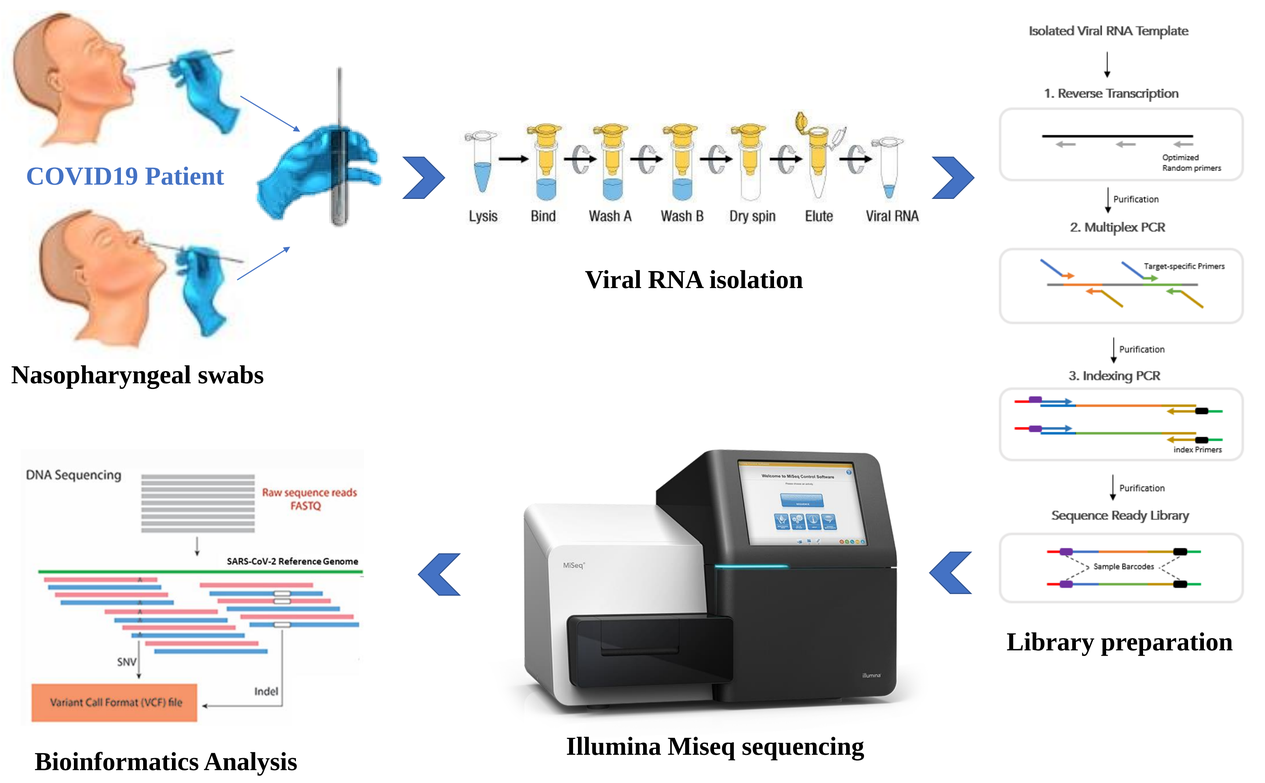
BACKGROUND

The ongoing pandemic of SARS-COV-2 has already infected millions of people worldwide. The majority of COVID-19 patients are either asymptomatic or have mild symptoms. Yet, about 15% of the cases experience severe complications and require intensive care. Factors determining disease severity are not yet fully characterized. The within-host diversity and their relation to severity were reported in infected patients during SARS-CoV-1 and MERS coronaviruses outbreaks; however, little is known about their effect on virus evolution, transmissibility and pathogenies. To date, thousands of SARS-CoV-2 sequences have been deposited in public databases; yet, we still lack fundamental information about the within-host diversity of SARS-CoV-2 and its possible role in disease severity.

OBJECTIVE

The aim of this study is to compare the SARS-CoV-2 diversity in COVID-19 patients with mild and severe manifestations and investigate its impact on clinical disease severity.

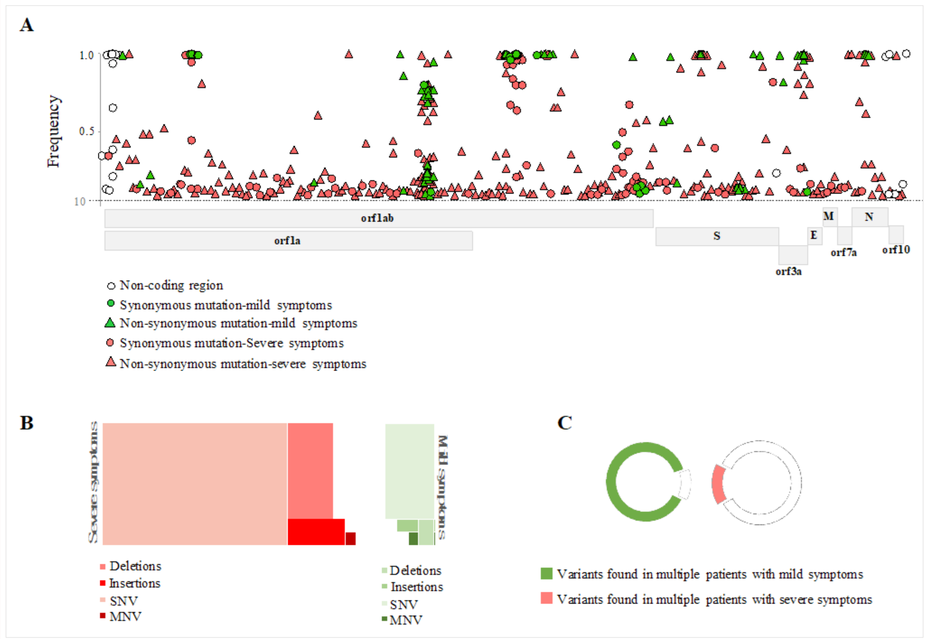
METHODS



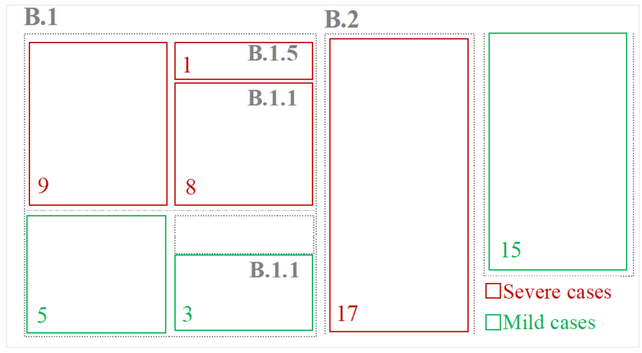
RESULTS

Summary of the main demographic and clinical characteristics of COVID-19 patients included in this study.

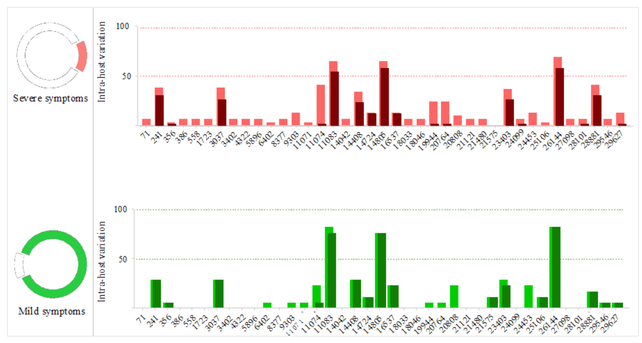
	Samples	Gender		Median Age (Age range)	Comorbidities				Severity score* (only severe cases)				
		F	M		0	1	2	>3	0	1	2	3	4
Mild cases	19	3	16	34 (20-54)	14	4	1	0	-				
Severe cases	27	6	21	51 (19-72)	9	6	5	7	4	3	6	8	6



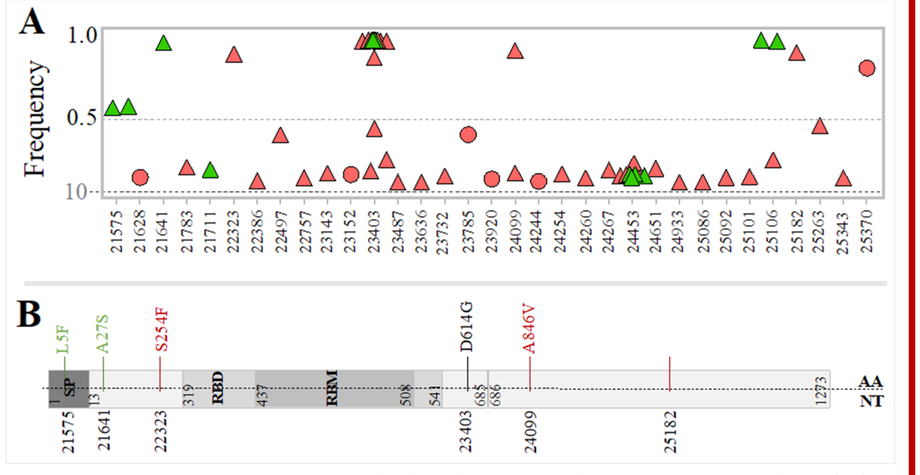
Nucleotide variation in SARS-CoV-2 genomes of all sequenced viruses. (A) Genomic positions and frequencies of variants found in the near-full genome (55-29640) of SARS-CoV-2 from all 46 patients. The y-axis represents the frequency of each variant and the x-axis represents the position of variants. **(B)** A treemap presenting types of variants found in SARS-CoV-2 genomes of mild (green) and severe (red) cases. (C) Colored parts of the circles represent varinats seen in more than one patient.



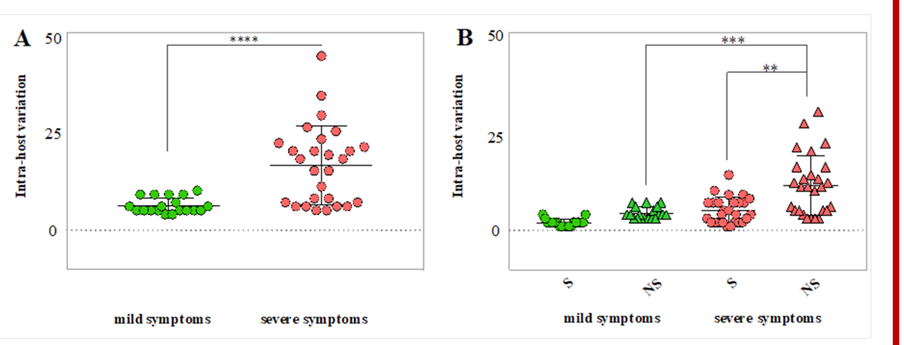
SARS-CoV-2 Lineage: Lineage are based on the nomenclature system proposed in Rambaut et al., 2020. Numbers inside the boxes indicates the number of samples within each lineage.



Comparison of variants found in mild cases (green) and severe cases (red). Colored parts of the circles (on the left) represent variants seen in more than one patient. Only variants found in more than one patients were used to generate bar charts. Bar charts demonstrate the prevalence of each variant in patients within each group (severe vs mild). Bars with darker colors demonstrate variants detected at the consensus sequence level.



Variants found in the SARS-CoV-2 spike glycoprotein. (A) Genomic position and frequency of S variants detected in all patients. **(B)** Schematic representation showing consensus mutations found in mild (green) and severe (red) cases. D614G mutation was found in both mild and severe cases.



Assessment of within-host SARS-CoV-2 diversity. (A) Total number of variants detected in each patient with mild (green) and severe (red) symptoms. **(B)** Comparsion of number of synonymous (S) and non-synonymous (NS) mutations found withih each patinet of the two groups (mild vs severe cases). P-values are indicated as follows: **** for p-value less than 0.0001, *** for p-value less than 0.001.

CONCLUSION

Exploring within-host diversity of this newly emerged virus, SARS-CoV-2, has revealed significant differences between mild and severe cases, particularly among older patients. Therefore, further investigation of within-host diversity role in disease severity is of significance at this stage of the pandemic and should be considered in future studies. It is also crucial to compare viral quasispecies in patients of different age groups as well as from different sample types. This would also help us better understand disease severity and transmission patterns.

ACKNOWLEDGEMENT

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