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博 士 論 文 の 要 旨 及 び 審 査 結 果 の 要 旨

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氏　　　　　名　　WINT Wint Phyu
学　　　　　位　　博士（医学）
学 位 記 番 号　　新大院博（医）第　1135　号
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博 士 論 文 名　　Epidemiology and genetic analysis of SARS-CoV-2 in Myanmar during the
　　　　　　　　　community outbreaks in 2020.
　　　　　　　　　　（2020年にミャンマーで発生したSARS-CoV-2流行時の疫学と遺伝学的解析）

論 文 審 査 委 員　　主査　教授　菊地　利明
　　　　　　　　　副査　特任教授　菖蒲川　由郷
　　　　　　　　　副査　准教授　茂呂　寛

博士論文の要旨

Background: The COVID-19 pandemic caused by SARS-CoV-2 continues to be a major global concern. In Myanmar, the first two confirmed cases of COVID-19 were reported on 23 March 2020, in people who had recently returned from the United States of America (USA) and the United Kingdom (UK). Subsequently, Myanmar experienced two community outbreaks in 2020. As of 31 December 2020, there were 33,917 confirmed cases and 741 deaths in Myanmar. We aimed to analyze the situation of the first two epidemic waves in Myanmar using the publicly available daily situation of COVID-19 and whole-genome sequencing data of SARS-CoV-2. This is the first comprehensive report to describe the epidemiological situation and genetic characteristics in Myanmar in 2020.
Methods: We retrieved publicly available data from the website of the Ministry of Health and Sports (MoHS), Coronavirus Disease 2019 (COVID-19) Surveillance Dashboard, Myanmar, of laboratory-confirmed cases and death cases between 23 March 2020, and 31 December 2020, which covered the daily situation of COVID-19. Then, we constructed epidemic curves using time-series surveillance data from the MoHS website to clarify the epidemic situation of COVID-19 in Myanmar. To investigate the COVID-19 transmission intensity throughout an epidemic, time-varying effective reproductive number (Rt) was estimated from the incidence time-series surveillance data. Our time-varying estimates were made with a seven-day sliding window. Statistical estimation was performed using R statistical programming software ver.3.6.3 with the EpiEstim package. For genetic analysis, nasopharyngeal and oropharyngeal swabs from suspected patients were collected at quarantine centers or hospitals. Each swab was placed in a viral transport medium and 10 sample were sent to the National Health Laboratory (NHL), Yangon, Myanmar for laboratory confirmation of COVID-19 infection. Whole-genome sequencing was performed at the NIID, Japan using the PrimalSeq protocol to enrich the cDNA of the SARS-CoV-2 genome using multiplex RT-PCR amplicons with a multiplexed

PCR primer set, as proposed by the Welcome Trust ARTIC Network. To clarify the genotypes of strains in Myanmar, 10 sequences in this study and an additional 31 sequences already registered in the public database were analyzed PANGOLIN lineage and Nextstrain classification by lineage assigner to find out Nextstrain and GISAID clades.

Results: In Myanmar, the first confirmed COVID-19 case was reported on 23 March 2020, and the first death case was reported on 31 March. The number of positive COVID-19 cases increased rapidly in April, forming the so-called first wave, after which the case occurrence dramatically decreased at the end of April until July in 2020. However, a community outbreak occurred in the middle of August in Rakhine State, then outbreaks spread nationwide, forming a second wave. The official surveillance data showed that the first wave was more related to international travels and local gatherings than the second wave. Case fatality rates of the two waves did not differ, at around 2%, despite the fact the second wave was bigger than the first. The estimated effective reproductive number (Rt) reached 6-8 at the beginning of each wave and gradually decreased as COVID-19 infections spread to the community. Whole-genome analysis showed that the genotypes of the viruses that caused the first and second waves in Myanmar were different. The previous report from the other group in Myanmar identified that nearly all of the sequences from the local cases in the early pandemic spread in April 2020 were PANGOLIN B.6 lineage (GISAID clade O and Nextstrain 19A). In contrast, during the second wave from August to September 2020, Myanmar sequences belonged to the clade GH (Nextstrain clade 20A or PANGOLIN lineage B1.36.1.

Our Nextstrain analysis and ML phylogenetic analysis showed that 29 SARS-CoV-2 viruses detected in Myanmar under the GH or PANGOLIN lineage B.1.36.16 clade in August and September were in close relationship with those in Bangladesh and India. The most prominent mutation in our selected sequenced genome was D614G in the spike protein. The initial strains in clade O in Myanmar retained D614, similar to the prototype Wuhan strain, but the subsequent strains in clades G, GR and GH changed to the D614G.

Conclusion: The phylogeographic analysis suggested that the Myanmar strains in the second wave had a close relationship with other south Asian strains, such as India and Bangladesh.

審査結果の要旨

ミャンマーにおける COVID-19 流行の第 1 波と第 2 波について、流行状況や SARS-CoV-2 ウイルスゲノムを公開されているデータも用いて解析した。ミャンマーでは、2020 年 3 月 23 日から 12 月 31 日まで、33,917 名の COVID-19 感染例と 741 名の COVID-19 死亡例が報告されている。その第 1 波は 2020 年 3 月から 7 月にかけてで、海外渡航者から始まった。第 2 波は 2020 年 8 月から 12 月にかけてで、西側国境沿いのラカイン州からミャンマー全土へ拡がった。いずれの流行においても実効再生産数は最大で 6-8 と推定された。ミャンマーで検出された SARS-CoV-2 ウイルス 10 株について全ゲノム解析を行い、31 株の登録されている SARS-CoV-2 ウイルスゲノムと合わせて解析したところ、第 1 波の SARS-CoV-2 ウイルスは GISAID clade O もしくは PANGOLIN lineage B.6 で、それが第 2 波の SARS-CoV-2 ウイルスでは clade GH or lineage B.1.36.16 へ変化していることがわかった。本論文は疫学データと原因ウイルスを合わせて解析することの有用性を示唆しており、この点において博士論文としての価値に値する。