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Title	Studies on rodent-borne zoonotic diseases circulating among small mammals and humans in urban and rural settings in Sri Lanka : hantavirus infection and leptospirosis [an abstract of dissertation and a summary of dissertation review]
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Degree Grantor	北海道大学
Degree Name	博士(感染症学)
Dissertation Number	甲第15049号
Issue Date	2022-03-24
Doc URL	https://hdl.handle.net/2115/86009
Rights(URL)	https://creativecommons.org/licenses/by/4.0/
Type	doctoral thesis
File Information	MUTHUSINGHE_Bungiriye_Devinda_Shameera_abstract.pdf, 論文内容の要旨

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学位論文内容の要旨
Abstract of the dissertation

博士の専攻分野の名称：博士（感染症学）　　氏名：MUTHUSINGHE Bungiriye Devinda Shameera
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学位論文題名
The title of the doctoral dissertation

Studies on rodent-borne zoonotic diseases circulating among small mammals and humans in urban and rural settings in Sri Lanka: hantavirus infection and leptospirosis.

（スリランカ都市部および農村部で小型哺乳類とヒトの間で循環しているげっ歯類媒介性人獣共通感染症に関する研究：ハンタウイルス感染症とレプトスピラ症）

In Sri Lanka, hantavirus infection and leptospirosis are recognized as important rodent-borne zoonotic diseases. High seroprevalence of anti-hantavirus antibodies against Thailand orthohantavirus (THAIV) related hantaviruses has been reported among chronic kidney disease of unknown etiology (CKDu) patients and rodents in Sri Lankan CKDu hotspots and febrile patients from several urban areas were also shown to be seropositive. Leptospirosis have been recorded from many areas as seasonal outbreaks among humans, while pathogenic *Leptospira* species have been detected in many animal species also. The studies described herein were carried out to obtain genomic and serologic evidence for these two diseases from selected rural and urban settings in Sri Lanka.

In chapter I, a small mammal survey to identify the hantavirus species and their reservoir hosts is described. Small mammals were captured from a CKDu-endemic region of Sri Lanka to estimate the anti-hantavirus antibody seroprevalence and genome detection by PCR and Mi-Seq analysis. Two hantaviruses from *Mus booduga* and *Rattus rattus* were identified. The rat-borne virus was an Anjozorobe virus variant (SA108), while the *Mus*-borne sequences were found to be from a novel virus (Lanka virus) in the THAIV lineage. The analysis of

nucleotide and protein sequences suggested that Lanka virus could be a novel orthohantavirus species while *M. booduga* could be a novel reservoir host.

In chapter II, development of specific diagnostics based on the hantaviral sequences detected in chapter I to retrospectively serotype the human hantavirus infections in CKDu areas is described. Pseudotyped recombinant vesicular stomatitis virus (rVSV-△G*)-based cross-neutralization assay and serotyping IFA based on the recombinant glycoprotein n (rGn) were developed and used to analyse THAIV-seropositive human sera from several CKDu-endemic areas. The rVSV-△G*-based cross-neutralization assay failed while the rGn-based IFA assay was successful in distinguishing the virus infections. The serotyping assay revealed that over 87% of human sera including both CKDu patients and healthy people showed Lanka virus infection pattern, indicating that these individuals had been infected with Lanka virus. Also, this provides the first serological evidence for a widespread human infection caused by a hantavirus of THAIV lineage.

In chapter III, urban market survey carried out to detect the infections by *Leptospira* and hantaviruses is described. Small mammal samples and market workers' blood samples were collected from the municipal public market of Kandy city, Sri Lanka. Serological evidence for the presence of both *Leptospira* and hantavirus infections were identified from small mammals and market workers. *Leptospira borgpetersenii* was isolated and novel *Leptospira* sequence types were identified from small mammals. The hantavirus species in humans were serotyped as Lanka virus and one worker seropositive for both infections was identified.

The results suggest that both hantavirus and *Leptospira* infections are found in both rural and urban settings in the country. Furthermore, the Sri Lankan unique Lanka virus has been infecting the human populations for at least a decade and can be possible zoonotic risk for CKDu in Sri Lanka. The findings of this study could be important for implementing effective control measures against these infections.