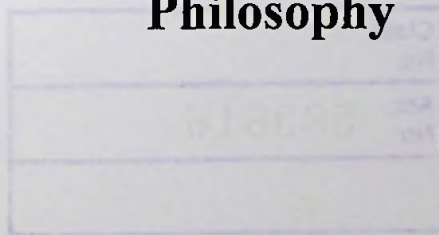




**Study on risk factors in transmission
of leptospirosis in the District of
Gampaha, Sri Lanka**

**A thesis submitted for the Degree of Doctor of
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ABSTRACT

Leptospirosis is a globally widespread, neglected and emerging zoonotic disease, posing important public health threats in humid, tropical and subtropical areas, where most developing countries are located. Leptospirosis is caused by a pathogenic species of the genus *Leptospira* which is transmitted directly or indirectly from animals to humans through contact with contaminated soil or water or with body fluids of infected animals. Most feral and domestic mammals may serve as major reservoir hosts. A large number of leptospirosis cases are recorded in Sri Lanka every year but it is probably grossly under-recognized due to difficulties in clinical diagnosis and lack of diagnostic laboratory services. Knowledge on reservoir animals and potential risk factors is lacking in Sri Lanka. Objectives of the present study were to establish laboratory diagnostic assays for early diagnosis of leptospirosis, identify potential risk factors and reservoir animals of leptospirosis and to analyze seasonal and spatial distribution of leptospirosis to prevent and control the disease in the District of Gampaha.

Paired blood samples of patients, kidney, blood and urine samples of reservoir animals were collected and tested by molecular and serological assays. Two molecular assays were established and evaluated using reference DNA samples. The analytical sensitivity of real-time PCR was approximately 60 genome copies and no cross-reactivity was observed with saprophytic *Leptospira spp.* and other pathogenic microorganisms. Of a total of 111 patients, 43% and 57% were diagnosed as positive and negative for leptospirosis by real-time PCR, respectively. Based on confirmation by Patoc-MAT on paired samples, diagnostic sensitivity and specificity were 67.7% and 90.0% respectively. The analytical sensitivity of conventional PCR was approximately 100 genome copies and no cross-reactivity was observed with saprophytic *Leptospira spp.* and other pathogenic microorganisms. Of a total of 111 patients, 20.7% and 79.3% were diagnosed as positive and negative for leptospirosis by conventional PCR, respectively. Based on confirmation by Patoc-MAT on paired samples, diagnostic sensitivity and specificity were 23.1% and 80.0% respectively. The results of this study showed that real-time PCR and conventional PCR have the potential to facilitate rapid and definitive diagnosis of leptospirosis during the early phase of infection in Sri Lanka.

Of the 38 rodent kidney samples, 11% were positive by real-time PCR. Of the 50 cattle/buffalo urine samples tested, 10% were positive by real-time PCR. Results of PCR and MAT indicate *Leptospira* are circulating among a significant proportion of rodents and farm animals tested in this study. This suggests that these (semi) domestic animals form an infection reservoir for *Leptospira*. Therefore, there is a threat to public health and a potential zoonotic risk to the population, notably farmers in this area.

Several significant risk factors were identified in this study. The identified potential risk factors would help understand the transmission dynamics of the disease and help formulate public health interventions. Findings of this study revealed a link between numbers of cases of leptospirosis with the meteorological parameters that were considered in the district. This study provides an evidence base for reducing disease burden by improving the understanding of the patterns, risk maps and case predicting model of the disease in the District of Gampaha, Sri Lanka. Intensified community awareness can be performed during monsoon seasons and several environmental management practices, educational campaigns can be launched to limit activities that contribute to the transmission of leptospirosis in the endemic areas of the district.