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Etiological agents causing leptospirosis in Sri Lanka: A review

Chamidri Naotunna, Suneth Buddhika Agampodi*, Thilini Chanchala Agampodi

Department of Community Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura 50008, Sri Lanka

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ABSTRACT

Objective: To systematically review the etiological agent causing human leptospirosis in Sri Lanka.

Methods: Published articles on leptospirosis and *Leptospira* in Sri Lanka were all reviewed to determine serovar, strain and species level identification of *Leptospira*. After screening process, 74 full text articles/reports were reviewed and among of them, 12 published papers describing isolation of *Leptospira* from Sri Lankan patients/animals, 5 molecular epidemiology papers on newer typing methods citing Sri Lanka isolates, with a descriptions of the isolates and 6 published papers reporting PCR based species level identification were identified.

Results: Published literature showed that more than 40 strains classified under at least 20 serovars and 10 serogroups have been isolated from Sri Lanka. These isolates belong to four species, namely, *Leptospira interrogans*, *Leptospira kirschneri*, *Leptospira borgpetersenii*, and *Leptospira santarosai*. In addition, recent studies on direct patient samples without culture and isolation showed *Leptospira* from *Leptospira weilli* is also circulating in Sri Lanka. Multi locus sequence typing showed 13 genotypes of *Leptospira* from Sri Lankan isolates.

Conclusions: This review shows the diversity of *Leptospira* in Sri Lanka, but culture isolation data has not been published in Sri Lanka during last 30 years.

1. Introduction

Leptospirosis is one of the most widely spread zoonotic disease in the world with an estimated 1.03 million annual cases and 58 999 deaths [1]. Control and prevention of leptospirosis are often limited due to knowledge gaps on disease agent, hosts and environment enabling the disease transmission in local settings. The disease is caused by spirochetes belonging to genus *Leptospira*, which has more than 230 serovars classified in to 31 serogroups based on the serology. Based on the DNA hybridization methods, 21 species has been identified to date [2–12]. Because of the diversity of *Leptospira*, management and control of leptospirosis is a challenge especially for countries in tropical setting where the facilities for isolation and typing are limited.

Sri Lanka is having one of the highest incidence of leptospirosis and considered as a leptospirosis high endemic country [13]. During the five year period from 2004 to 2008, the total number of cases reported to the Epidemiology Unit (National surveillance Centre) was around 4000 cases [14]. In 2008, Sri Lanka experienced the worst recent outbreak of leptospirosis with more than 7000 reported cases [15]. Cumulative annual incidence of leptospirosis during 2008–2014 period in Sri Lanka was more than 25 per 100 000 and during the last 6 years, an average of more than 5000 cases were reported annually to the Epidemiology unit [16–20]. Despite all control measures taken by the national control programme, leptospirosis continues to affect lives of people in Sri Lanka. This could be partly attributed to the knowledge gap in leptospirosis transmission. There were considerable numbers of research carried out since 2008, however investigations on disease causing agents are limited.

The present standard diagnostic method for leptospirosis is microscopic agglutination test (MAT) [21]. Several extensive studies showed that MAT could not be considered as the gold standard due to its very low sensitivity [22]. We experienced same in Sri Lanka in 2008 [15] and 2011 [23]. Though imperfect, MAT is still the standard test for leptospirosis

*Corresponding author: Suneth Buddhika Agampodi, Department of Community Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura 50008, Sri Lanka.

Tel: +94 777880096;

Fax: +94 252226252

E-mail: sunethagampodi@yahoo.com

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diagnosis due to lack of other diagnostic facilities. Standard MAT panel should be based on the local knowledge on circulating serovars or it should be a broad MAT panel to cover all pathogenic serogroups. In high burden countries in South East Asia, including Sri Lanka, these standard MAT diagnostic facilities are still not available. As an example, till 2014 Sri Lankan diagnostic laboratory used genes specific Patoc serovar for MAT and still the MAT panel used in Sri Lanka reference center include only 11 serovars. This lack of diagnostic facilities are attributed due to lack of knowledge on circulating serovars or lack of resources to maintain labor intensive MAT diagnosis facilities. However, this may be partly due to lack of knowledge synthesis within the country. The purpose of this review is to identify the locally prevalent serovars of *Leptospira* in Sri Lanka based on published literature to fill this knowledge gap.

2. Materials and methods

We carried out a comprehensive search of literature to identify studies related to leptospirosis and *Leptospira* in Sri Lanka. Two main search platforms were used for internet based search: Pubmed and Google Scholar. The search strategies were as follows: Pubmed search string (56) (((“Leptospirosis”(Mesh) OR ‘Weil Disease’(Mesh) OR “*Leptospira*”(Mesh) OR ‘*Leptospira interrogans* (*L. interrogans*) serovar Pomona’(Mesh) OR ‘*L. interrogans* serovar Icterohaemorrhagiae’(Mesh) OR ‘*L. interrogans* serovar Hebdomadis’(Mesh) OR ‘*L. interrogans* serovar Canicola’(Mesh) OR ‘*L. interrogans* serovar Autumnalis’(Mesh) OR ‘*L. interrogans* serovar Australis’ (Mesh) OR ‘*L. interrogans*’(Mesh)))) OR (((‘Leptospirosis’ OR ‘*Leptospira*’ OR ‘Weils disease’ OR ‘Weil’s syndrome’))) AND ((‘Sri Lanka’ OR ‘Ceylon’)); Google Scholar search (2320)

(“Leptospirosis” OR “*Leptospira*”) AND (“Sri Lanka” OR “Ceylon”).

In PubMed search, we used a specific search strategy. However, in Google Scholar, we manually screened all titles appeared after the initial search to include grey literature and articles that are not listed in PubMed.

We also carried out manual search, specially to retrieve data from non-indexed local publications. For this purpose we used three bibliographic references: a Bibliography of medical publications related to Sri Lanka 1811–1976 [24] and its supplement Bibliography on health in Sri Lanka, 1977–1980 [25] by Peiris and Urugoda and Bibliography of Medical Literature 1980–2005 compiled by Post Graduate Institute of Medicine (PGIM) Library, Colombo. In addition, we hand searched titles of theses and dissertations, and casebooks submitted to PGIM, all issues of Ceylon Medical Journals prior to 2008 and archived issues of Sri Lanka Journal of Medical Sciences and Kandy Medical Journal in four libraries (Sri Lanka Medical Association Library, PGIM library and Colombo and Peradeniya Medical School libraries). Further, we searched technical reports published by Medical Research Institute during 1960–1980 period and Quarterly Epidemiological Bulletins of Epidemiology Unit 1980–2014. Reference lists of relevant articles were also searched to identify any missing article. In addition, we searched for publications which included global collection of *Leptospira* isolates for typing to get information on Sri Lankan isolates.

The search was done in several steps. First we selected all Sri Lankan publications and publications on Sri Lankan patients or animals related to leptospirosis and *Leptospira*. This was done by three investigators. A title and abstract search was done to eliminate review articles or articles without primary data. Once the articles with original data were identified, we searched the full text for any article reporting culture isolation or inoculation of patient

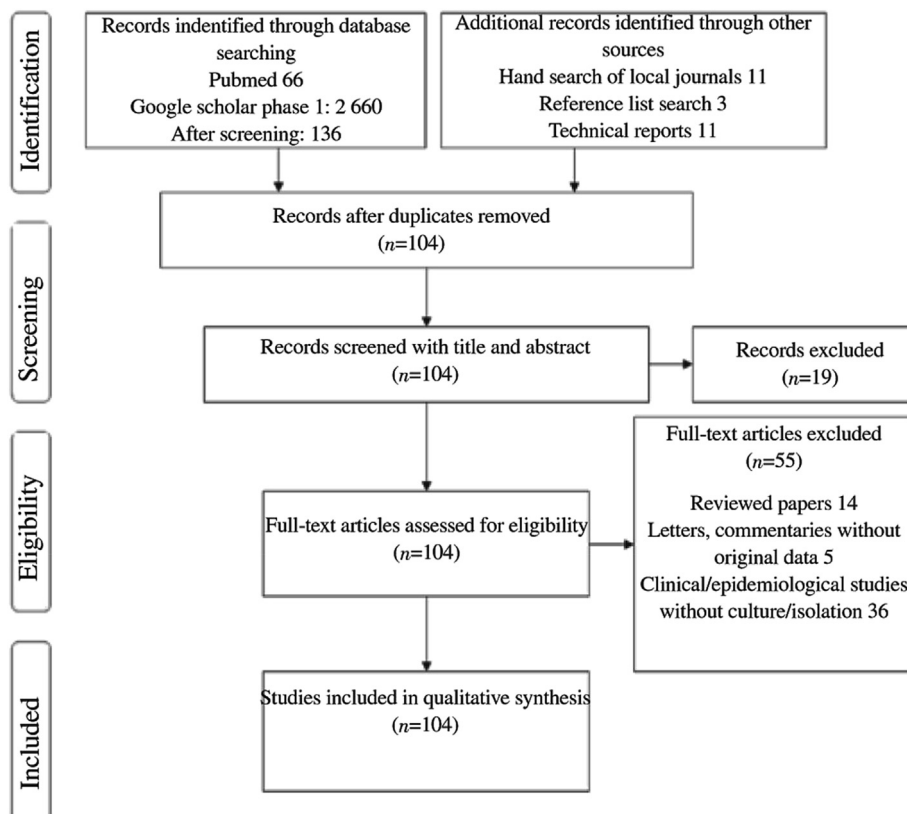


Figure 1. Flow diagram.

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