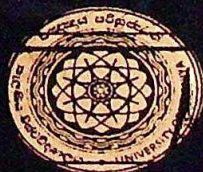


**BIOCHEMICAL, INFLAMMATORY, AND HISTOPATHOLOGICAL  
CHANGES IN WISTAR RATS GIVEN DUG WELL WATER FROM HIGH AND  
LOW DISEASE PREVALENT VILLAGES FOR CHRONIC KIDNEY DISEASE  
OF UNKNOWN ETIOLOGY (CKD<sub>U</sub>) IN NORTH CENTRAL PROVINCE OF  
SRI LANKA**

Submitted by  
**M.G. Thammitiyagodage**  
FGS/05/PhD/16/2014/01

A thesis submitted to the Faculty of Graduate Studies, University of Kelaniya, Sri Lanka in fulfillment of the requirements for the degree of Doctor of Philosophy in  
**Biochemistry**



April 2021

This thesis has been accepted by the University of Kelaniya for the award of the Degree of Doctor of Philosophy (.....) It is not allowed to Publish this as a thesis accepted for the Degree of Doctor of Philosophy without the authority of the University



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## DECLARATION

The work reported in this dissertation entitled “**Biochemical, Inflammatory, and Histopathological Changes in Wistar Rats Given Dug Well Water from High and Low Disease Prevalent Villages for Chronic Kidney Disease of unknown Etiology (CKDu) in the North-Central province of Sri Lanka**” is the result of the candidate’s investigation, carried out at the Medical Research Institute, Colombo 8, Sri Lanka. No part of this dissertation has been submitted to any other university or institute for any other degree or certificate. It doesn’t infringe upon anyone’s copyright nor violates any proprietary rights. Any ideas, techniques, quotations, or any other material from the work of other people included; published or otherwise, are fully acknowledged under the standard referencing practices.

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## ABSTRACT

Chronic Kidney Disease of unknown etiology (CKDu) is prevalent in the North Central Province (NCP) of Sri Lanka. Ingestion of groundwater is identified as one of the causative factors. The majority of the population consumes un-boiled dug well water. The objectives of the study were to find out the biochemical, haematological, and immunological changes in Wistar rats that ingested dug well water from high and low disease prevalent areas from the NCP and low disease prevalent Colombo and correlate the findings with their histopathological changes. Sex balance 3 months old Wistar rats (n=60) were used for the study. Their WBC/ DC, CD<sup>4+</sup>, CD<sup>8+</sup>, serum cytokines, creatinine, ALT, AST, BUN levels and Microalbumin: creatinine ratios were measured. Rats were randomly divided into 6 groups by assigning 10 rats per group.

Groups 1, 2, and 3 were given water from high disease prevalent New Town Medirigiriya (NTM), Bisobandaragama (BB), and Divuldamana (DD) respectively. Group 4 was given boiled water from NTM (NTMB). Groups 5 and 6 were given water from low disease prevalent Huruluwewa (HW) from NCP and tap water from low disease prevalent Colombo (CO) *adlibitum* quantity. Serum cytokines (IL1 $\beta$ ; IL6, TNF $\alpha$ ) were measured after 8 months and CD<sup>4+</sup> and CD<sup>8+</sup> counts were measured after 14 months. Histopathology was performed in kidney and liver tissues.

Serum TNF $\alpha$  levels were significantly elevated in rats from DD and BB (p<.0.05) but hepatic TNF $\alpha$  levels were significantly elevated only in rats from DD (p<.0.05)). Rats from high disease prevalent NTM had significantly high CD<sup>4+</sup> and CD<sup>8+</sup> cells than those from low disease prevalent HW and CO. Immunological findings were correlated with the histopathological changes. There was a correlation between the kidney Tubular Interstitial (TI) Lesion index and liver lesions. Serum TNF $\alpha$  and CD<sup>4+</sup>

and CD<sup>8+</sup> lymphocytes were closely correlated with renal damage. Rats with severe TI lesions reported a high percentage of portal tracts and parenchymal lesions in the liver and this expression was minimum in CO. It was evident that boiling water was effective against liver damage but not renal damage. The present study is supportive of an immune therapy targeting the CD<sup>4+</sup>, CD<sup>8+</sup>, and TNF $\alpha$  in reducing renal damage in the early stages of the disease.

In conclusion, peritubular nonsuppurative interstitial cell infiltrations in kidney tissues were common in all the experimental groups irrespective of the toxicant present in water bodies. Observed kidney damage may mediate via cytokine triggered immune response by high sodium, fluoride, calcium and some other unmeasured toxic agents present in NCP water. Some toxicant present in DD from NCP can directly damage the kidney tubules leading to fibrosis.

**Keywords:** CKDu, NCP in Sri Lanka, Renal and Hepatic Histopathology, Serum cytokine, Wistar rats.