8.8 EFFECT OF CONCENTRATED WATER FROM RESERVOIRS OF HIGH PREVALENCE AREA FOR CKD OF UNKNOWN ORIGIN IN SRI LANKA ON MICE

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Abstract :

Introduction: There is threateningly high prevalence of chronic kidney disease due to tubulointerstitial disease ending as chronic renal failure in the North Central Region of Sri Lanka. The epidemiology of the disease shows distribution of these patients around the some water reservoirs and most of them are farmers. The lowprevalence of the disease among the in villagers who use water from the natural springs was observed. The aim of the study is to find the potential effects of concentrated water of the reservoirs in the high prevalent area by mouse bioassay.

Method: Water of Padaviya reservoir supplying water to a highdisease prevalent area was concentrated fifteen times by evaporation, exposing to sunlight. The test group of mice (20) and control group (15) were fed with concentrated reservoir water and water from non prevalence area respectively for a period of 6 months and the kidneys were examined histopathologically for the evidence of renal disease. Water samples were analyzed for Fluoride, Na +, K+ , heavy metals and for cyanobacterial toxins microcystin& cylindrospermopsin .

Results:

The analysis of concentrated water samplesfrom Padaviya reservoir showed significantly high content of fluoride (2.25 mg/L), Sodium (225 mg/L) ($p<0.05$) than control samples. However, no increased levels of heavy metals were detected. The analysis of water samples showed presence of Deoxy cylindrospermopsin(1.28 ug/L - DCYN) as the predominant isomer present over cylindrospermospsin (CYN) which is unusual. At the end of 6 months interstitial nephritis was detectedin 45% of test mice andonly6.5% of control group ($p< 0.001$)

Conclusion: The results show the ability of the water of this reservoir to induce interstitial nephritis that could be due to the high salinity, fluoride or due to DCYN. Although present in

Sample collected	F mg/L	Na ug/L	K ug/L.	Cr ug/L.	Mn ug/L.	Fe ug/L	Co ug/L	Ni ug/L	Cu ug/L	Zn ug/L	As ug/L	Cd ug/L	Hg ug/L	Tl ug/L	Pb ug/L

low levels, the possibility DCYN to induce interstitial nephritis needs to be investigated further as the epidemiological evidence is in favor of a cyanobacterial toxin. The long term effects and safe levels for DCYN in drinking water & the effect of salinity & high fluoride content of water needs to be studied.

Extended Abstract:

Introduction: There is threateningly high prevalence of chronic kidney disease due to tubulointerstitial disease ending as chronic renal failure in the North Central Region of Sri Lanka. The epidemiology of the disease shows distribution of these patients around the some water reservoirs and most of them are farmers. The lowprevalence of the disease among the in villagers who use water from the natural springs was observed.

Objectives: The aim of the study is to find the potential effects of concentrated water of the reservoirs in the high prevalent area by mouse bioassay.

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Results:

The analysis of concentrated water samplesfrom Padaviya reservoir showed significantly high content of fluoride (2.25 mg/L), Sodium (225 mg/L) ($p<0.05$) than control samples. However, no increased levels of heavy metals were detected. Table 1 shows the results of the analysis of water samples before concentration.

Table 1: analysis of water samples before concentration.

1: End May	0.172	16060	1483	0.04	9.69	1.57	0.65	0.29	0.51	167	0.19	0.00	0.00	0.00	0.19
: Early June	0.187	22367	2542	0.02	4.47	1.53	0.21	0.14	0.35	354	0.20	0.00	0.00	0.13	0.07
3: End June	0.108	10169	1009	0.01	3.86	1.06	0.06	0.11	0.29	128	0.08	0.00	0.00	0.04	0.02
4: Early July	0.152	16513	2015	0.02	16.71	2.26	0.12	0.38	0.71	295	0.15	0.00	0.00	0.07	0.12
5:End July	0.210	20340	1966	0.02	1.87	1.54	0.08	0.31	0.72	88	0.21	0.00	0.00	0.00	0.03
Control	0.0075	2624	1752	0.00	0.58	5.57	0.01	1.62	1.71	36.11	0.02	0.01	0.00	0.00	0.00

The analysis of water samples showed presence of Deoxy cylindrospermopsin(1.28 ug/L - DCYN) as the predominant isomer present over cylindrospermospsin (CYN) which is unusual (Table 2).

Table 2:Analysis of water samples for cyanobacterial toxin

	Cylindrospermopsin Micrograms/lire	**Deoxy-Cylindrospermopsin Micrograms/lire**	**Microcystin Micrograms/lire**
1: End May	Nil	0.80	Nil
2:Early June	Nil	0.84	Nil
3 End June	Nil	0.84	Nil
4: Earl Jul	Nil	0.71	Nil
: End Jul	Nil	3.75	Nil

At the end of 6 months interstitial nephritis was detectedin 45% of test mice andonly6.5% of control group ($p < 0.001$) (Table 3) .

	Test group (Padaviya water)	**Control group(Kandy water)**	**Total**
Normal	11	13	24
Inersiial Nephriis	9	2	11
total	20	15	35

Conclusion: The results show the ability of the water of this reservoir to induce interstitial nephritis that could be due to the high salinity, fluoride or due to DCYN. Although present in low levels, the possibility DCYN to induce interstitial nephritis needs to be investigated further as the epidemiological evidence is in favor of a cyanobacterial toxin. The long term effects and safe levels for DCYN in drinking water & the effect of salinity & high fluoride content of water needs to be studied.

8.9 THE ROLES OF ENVIRONMENTAL TOXINS IN THE PATHOGENESIS OF CHRONIC KIDNEY DISEASE OF UNKNOWN ORIGIN IN SRI LANKA

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Introduction :

The chronic Kidney Disease of Unknown origin (CKD-U) in Sri Lanka is a chronic tubulointerstial nephropathy affecting residents of villages located near the water reservoirs in the North Central Region of dry zone of Sri Lanka. The epidemiologic findings suggest that there is a possibility of involvement of an environmental toxin in the nephropathy. A variety of environmental factors have been explored during the last 15 years include heavy metals (Cadmium, Lead and Aluminium), fluoride and agrochemicals etc.

Objective:

Objective of the study is to identify likely aetiological agents using epidemiological and environmental information.

Method:

The information on the emergence of the disease was traced back to 30 years (1980-2010) using hospital statistics and statistics from death registers of this region. The information on live discharges and deaths due to different disease entities from General Hospital Anuradhapura and environmental data for this period was collected and analyzed.

Results:

Hospital based statistics showed that there is an increasing trend in the number of patients with diseases of the genito urinary system from 1980. CKD-U appeared in early nineties for the first time and then the incidence of the disease amplified gradually reaching highest in 2002. The incidence of the disease has been stable but at a lower level thereafter. Alcoholic liver disease reported to the general hospital Anuradhapura during the same time frame showed a similar distribution.

The water capacities of the reservoirs were relatively low from 1989-1997 in months of June-September when the temperature of environment and solar radiation is highest to the affected regions. It is likely that these conditions favored the formation or addition of the toxin to the environment.

Conclusion:

Similarity in the variations of incidence over time in CKD-U, alcoholic liver disease in the North Central Region indicates the possibility of common aetiological agent for both diseases. Literature reveals that cyanobacterial toxin present in stagnant water is one of the probable aetiological agents with well identified hepatotoxicity. The environmental conditions in the North Central Region is highly favourable for cyanobacterial blooming and toxin production. However, nephrotoxic effect of this toxin has not yet been identified.

Extended Abstract

Introduction:

The chronic Kidney Disease of Unknownorigin (CKDu) in Sri Lanka is a chronic tubulointerstial nepropathy affecting residents of villages located near the water reservoirs supplying water for paddy cultivation in the North Central region of Sri Lanka (Figure 1). All these affected villages are located in the dry zone of the country with anlower rainfall and higher solar radiationleading to high evaporation rate. Most of the affected patients are male paddy farmers in the age group of 40-60 years. The disease shows a marked similarity to Endemic (Balkan) nephropathy. The disease emerged in early nineties and showed a steady increase in numbers till 2008 and slightly lower numbers thereafter. The significant epidemiologic features of CKD-U include its focal occurrence in certain rice farming villages, a familial but not inherited pattern of disease, frequently affecting members of the same household; male preponderance and occurrence only in individuals who are older than 18 yrs. These epidemiologic findings suggest that there is a possibility of involvement of an environmental toxin in the nephropathy. A variety of environmental factors have been explored during the last 15 years include heavy metals (Cadmium, Lead and Aluminium), fluoride, Organophosphate etc.However, there are no clear explanations for the higher prevalence of the disease in male farmers in the agegroup of 40-60 years of age.

Objective:

Objective of the study is to identify likely aetiological agents using epidemiological and environmental information.

Method:

The information on the emergence of the disease was traced back to 30 years (1980-2010) using hospital statistics. The information on live discharges and deaths due to different disease entities from General Hospital Anuradhapura and environmental data for this period was collected and analyzed. Monthly statistics on mortality & morbidity from 1999-2008 was analyzed with the monthly information on the environmental conditions (temperature, rainfall etc) and farming activities collected from the Department of irrigation.

Results:

Hospital based statistics showed that there is an increasing trend in the number of patients with diseases of the genitor urinary system from 1980. CKD-U appeared in early nineties for the first time and then the incidence of the disease amplified gradually reaching highest in 2002. The incidence of the disease has been stable but at a lower level thereafter. Alcoholic liver disease reported to the general hospital Anuradhapura during the same time frame showed a similar distribution. The water capacities of the reservoirs were relatively low from 1989-1997 in months of June-September when the temperature of environment and solar radiation is highest to the affected regions. It is possible that these conditions favored the formation or addition of the toxin to the environment.

The monthly statistics on CKD-U from G. H. Anuradhapura showed that the mortality rate due to CKD-U is highest during the months of November to January every year when the rain fall to the area is maximum with slightly low temperatures. The mortality rate is minimum in the month of April when the physical exertion is minimum. The information on the water issues of the reservoirs indicate that the higher physical activity of the farmers due to farm land preparation is coinciding in the months of high mortality.

Conclusion:

Similarity in the variations of incidence over time in CKD-U, alcoholic liver disease and malignancies in the North Central Region indicates the possibility of common aetiological agent for all three diseases.

The monthly mortality data with cyclical pattern in the high mortality rates in November – January indicates that the possibility of a high level of toxin existing in the environment or possibility of high concentration of the toxin in the body due to dehydration with sweat loss in outdoor farming activities or both.

Literature reveals that cyanobacterial toxin present in stagnant water is one of the probable aetiological agents with well identified hepatotoxic properties. The environmental conditions in the North Central Region is highly favourable for cyanobacterial blooming and toxin production. However, nephrotoxic effect of this toxin has not yet been identified in the humans although it is demonstrated in the experimental animals.

The environmental conditions during the period of 1989-1997 shows that the low water levels of the reservoirs with prolong stagnation, long retention times with high temperatures due to global warming may have induced optimum conditions for the toxin production by the cyanobacteria.