



## “AN EPIDEMIOLOGIC REVIEW OF CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY (CKDu)”

### Nephrology

<b>Nihar Nalini Senapati</b>	Associate Professor Anesthesiology RML PGI, New Delhi
<b>Debjanee Lenka</b>	Field Investigator in ICMR Project, SCB Medical College, Cuttack
<b>Supriyadarshini Behera</b>	Field Investigator in ICMR, Project, SCB Medical College, Cuttack
<b>Dr. Amarendra Mahapatra</b>	Co-Principal Investigator, RMRC, BHUBANESWAR
<b>Dr. Chittaranjan Kar*</b>	Principal Investigator, Prof. Nephrology SCB Medical College, Cuttack *Corresponding Author

### ABSTRACT

The impact of high prevalence of Chronic Kidney Disease (CKD) is now considered as a public health problem of epidemic proportion. It is also the leading factor for increased mortality every year Globally. According to World Health Records 2002, the highest contribution of Kidney Disease is accounted as the Global burden issue. Diabetes Mellitus, Hypertension and Chronic Glomerul Nephritis are the traditional responsible causes for increased burden of renal failure in developed as well as developing countries. The intend of this review is to explore some unidentified causes of increase the kidney disease (CKDu) and CKD in certain geographical areas of the world due to environment or other unknown factors.

### KEYWORDS

CKD, CKDu, Diabetes Mellitus, Hypertension

### Introduction

Globally Diabetes and Hypertension have been accounted for increase of CKD. In India 40-60% patients entering ESRD are due to Diabetes, Hypertension and Chronic Glomerul Nephritis. As per Indian Council of Medical Research (ICMR) data the prevalence of Diabetes in Indian adult population has increased to 7.1% and in Urban areas the prevalence is as high as 28% and high prevalence of CKD related to hypertension has been detected in Rural population also It is observed that most of the renal failure patients may have both diabetes and Hypertensi.<sup>1</sup> The commonest cause of End Stage Renal Disease (ESRD) is Diabetic Nephropathy in India.<sup>2</sup> Therefore, Diabetes and Hypertension are the significant traditional causes of CKD. The existing figure on mortality in CKD is increasing every year all over the World due to high expenditure of treatment, inaccessibility to health care facility and this leads to unsatisfactory outcome.

Although Diabetes, Hypertension and chronic glomerulonephritis are the important contributing causes of CKD, it is identified that some patients are develop CKD due to unknown etiology. To examine this International Society of Nephrology screening programme in china, Nepal and Mongolia revealed that 43% of CKD patients do not have diabetes and Hypertension. An epidemic of CKDu is highly recognised in some Countries such as Sri Lanka, Central America, Nicaragua, El-Salvador, India and Egypt.<sup>4</sup> The emerging Concept of CKDu varies among different authors. So it is difficult to define this unknown etiology of CKD. In literature the concomitant unknown causes of kidney disease are explained. The asymptomatic disease of CKD is progressively manifested among the young adults of 35-40yrs, male are more vulnerable than Female and Children, Indian agricultural workers/wage labors and coastal belt farmers are at higher risk.<sup>5</sup>

From review it is evident that; CKDu is frequently associated with risk factors such as heat stress in work place, exposure to pesticides, consuming contaminated water with heavy metals and industrial waste contaminated water or crop; these factors contribute to clusters of CKD epidemic. Scanty researches have been conducted in certain geographical zone of different countries on CKDu. Hence available literature of CKDu reviewed to understand the associated risk factors according to geographical location and environmental condition of specific region. Among these identified countries where CKDu was first recognized in 1990 is North Central province of Sri Lanka.<sup>6</sup> In 2001-2002 a cohort study recognised it in Sri Lanka and efforts made to identify the risk factors by multi stage cluster sampling and calculated

prevalence of CKDu in three endemic zones of North Central of Sri Lanka. High prevalence was found among the paddy farmers in Anuradhapura (15.1%), Polonnaruba (20.6%) and Badulla (22.9%).<sup>7</sup> It was predicted that in Sri Lanka, an agrochemical pesticide increased CKDu among the farmers.

CKDu is a Geo-environmental disease therefore distribution of CKDu is not uniform.<sup>8</sup> Since last two decades roughly it was estimated that 20,000 deaths have occurred due to CKDu in Central America.<sup>9</sup> Unlikely in Central America prevalence of CKDu was found to be high in Young adults below the age of 60. In El-Salvador the observed causes were use of harmful agrochemical pesticide (in sugarcane field), physical heat stress and heavy metal exposure. In year 2009, Bajo Iempa of El-Salvador, reported CKDu prevalence to be 25.7% in men and 11.8% in women due to occupational exposure, another cause was found in people living in hotter coastal areas (18%) than part of cooler high land (1%).<sup>10</sup> In Costa Rica, Nicaragua and Southern Honduras of Central America, Laborers affected by CKDu were working under high Ambient temperature. Thus, high temperature was considered as another potential risk factor leading renal failure. Hence, the burden of CKDu increases due to occupational heat stress and particular exposure to pesticide in Central America, the kidney disease has been labeled as “Mesoamerican Nephropathy”(MeN), it was coined by Richard Comea Rotter in International Society Of Nephrology meeting in 2011.<sup>11</sup>

In 2009 CKD prevalence in Nicaragua was found to be high as well as mortality. In 13yrs it has risen from 4.5 to 10.9% per 10,000 populations. The high prevalence of CKDu was among farmers growing sugarcane, Banana and mining workers.<sup>6</sup> It was revealed by the workers that, prolonged working in hot and humid climate above 40°C with minimal protection resulted this situation.<sup>9</sup> Dehydration, hypertension and drinking local alcohol *liza* and family history were other contributory factors.<sup>12</sup>

The prevalence of CKDu in high altitude of coffee cultivating zone of Nicaragua was not found increased they found incidence in men (0%) and women (1.4%). But high prevalence was reported among Sugar cane workers living in nearby town of Chichigalpa of Northwestern of Nicaragua.<sup>15</sup> Other studies conducted in Costa Rica north western region, where sugarcane cutting is the commonest occupation. It was revealed that there is increase in incidence of renal failure among cultivators since 1970s. In summary, the available evidence on

incidence if CKDu found almost all agricultural workers were high. Relatively thousands death of Young men working in plantation were due to some sorts of occupational exposure and maybe particularly due to exposure to pesticides.

In India, Prakasham district of Andhra Pradesh, researchers postulated high silica level in drinking water to be a possible cause of CKDu. Another study in Coastal Uddanam and Inland of Chimkurty Mandal, Andhra Pradesh reported high prevalence of CKDu in Young adult farmers involved in cultivation of coconut, rice, jackfruit and cashewnut. because of prolonged exposure to pesticides and occupational heat exposure.<sup>16</sup> In comparison to other countries India contribute 20% CKDu patients world wide.<sup>17</sup> Another study conducted in Odisha by SHARP (Social Action Human for Rural Poor) found 100 new cases of CKDu in Rautabhuin Village in Narsinghpur Block, Cuttack and none was attributable to any known cause of CKD; the result of this study again prompted ICMR (RMRC) in Bhubaneswar to carry out a survey in Narsinghpur, Cuttack and found 8-12% of the population suffer from CKDu. Besides Cuttack, the high incidence is reported from Bhubaneswar, Jajpur, Bolangir, Kalahandi, Jharsuguda and koraput.<sup>17</sup> Experts postulate that, CKDu might be occurring in Odisha due to Environmental heat exposure, and others such factors as in other places So in India, Odisha is considered as one of the hotspot endemic zone for CKDu.<sup>4</sup>

### Environmental Analysis

Environment is also responsible to increase of CKDu because of Climate change and rising temperature increasing dehydration and another factor may be Glyphosate; which is a herbicide it can be absorbed in water and soil easily, therefore the contamination of this non organic herbicide indirectly affect the people who are not using contaminated drinking water.<sup>16</sup> if we considered about geographical location of identified CKDu endemic Zones; then Nicaragua is situated near equator at 13.06°N latitude and 85° W longitude and average temperature is 25°C to 27°C. In year 2015 the highest temperature was recorded in this region. Since last 4yrs the temperature is increasing. So scientists foresee if this pattern of increase in temperature continues then sugarcane workers and health of the all population's will be at risk.<sup>18</sup> Similarly in Odisha, is lying south of the tropic cancer and has tropical climate. So throughout year it's warm in the central western part geographical zones. The temperature ranges average 40-42°C in March- May and it is also increasing every year. According to India Meteorological Department report the effect of global warming the rate of rain fall has been decreasing; in 2012 it was 106.7mm but in 2016 it reached 96.4mm. Therefore experts are expecting population of heat Zones of Odisha are at risk of renal failure.<sup>19</sup>

### Conclusion

So it may be conclude that, frequent exposure to pesticide or agrochemicals, heat stress contaminated heavy metal are the contributing causes of the globally increased burden of CKDu. "The young adult males are more prone to severe CKDu than the females" as reported by many authors. It is also perceived that the populations of CKDu are from very low socio-economic strata, farming or mining workers and working in low altitude and exposed to high. Although In India, Odisha is considered as a hot Spot endemic Zone of CKDu by ICMR; we suggest further epidemiological community based studies should be conducted to identify causes, risk factors in those suspected and reported geographical zones for further clarity in this regard.

### References:

1. Varma P.P; "Prevalence of Chronic Kidney Disease in India: Where are we heading?"; Indian J Nephrol, 2015 May-June 25(3):133-155
2. Jha Vivekananda et al; "Current Status of End-Stage Renal Disease care in India and Pakistan"; International Society of Nephrology (2013) 3, 157-160
3. Goonerate et al; "Epidemiology Of chronic Kidney Disease in a Srilanka Population"; Int. J Diab Dev Ctries; April 2008; Vol.28; Issue 2.
4. Kulkarni Sudhir and Gadekar Kshitija; "Chronic Kidney Disease of Unknown Etiology" Book- Nephrology, Chapter- 128, pp- 603-606.
5. Charlos M. Oranates et al; "Chronic Kidney disease and associated risk Factors In the Bajo Lempa region of El salvador: Nephrolempa Study 2009"; MEDICC rev. vol.13 no.4 Oakland Oct. 2011.
6. Almaguer et al; "Chronic Kidney Disease of Unknown Etiology in Agricultural Communities"; MEDICC Review; April 2014, Vol.16, No.2
7. Channa Jaysumanna, Ranil Gajanayaka; "Importance of Arsenic and Pesticide in Epidemic Chronic Disease in Srilanka"; BMC Nephrology 2014; 15:124
8. Chandrajit R., Nayakkara S et al; "A Chronic Kidney Disease of Unknown Etiology (CKDu) in Srilanka; Geographical Distribution and Environmental Implications"; Environ Geochem Health 2011, 33: 267-278
9. Clark P.A. et al; "Chronic Kidney Disease in Nicaraguan Sugarcane workers: A Historical, Medical, Environmental analysis and Ethical Analysis."; The Internate Journal of third World Medicine, 2016 Vol.12 No.1
10. Van Dervort R. Darey, Lopez L. Dina et al; "Spatial Distribution of Unspecified CKD in

- El-Salvador by Crop Area Cultivated and Ambient temperature"; MEDICC Review; April 2014, Vol.16 No.2
11. Elinder CG, Wernerson A, Wijkström J; "Mesoamerican Nephropathy (MeN): A 'New' Chronic Kidney Disease related to Occupational Heat Exposure with Repeated Deprivation of Salts and Water."; Int J Nephrol Kidney Failure (2015)
  12. Brooks D. Final Scoping Study Report, "Epidemiology of Chronic Kidney Disease in Nicaragua" [Internet]. Boston: Boston University School of Public Health; 2009 Dec [cited 2013 Sep 25]. (Available from: [http://www.cao-ombudsman.org/cases/document-links/documents/03H\\_BU\\_FINAL\\_report\\_scopestudyCRI\\_18.Dec.2009.pdf](http://www.cao-ombudsman.org/cases/document-links/documents/03H_BU_FINAL_report_scopestudyCRI_18.Dec.2009.pdf))
  13. Raines N, González M, Wyatt C, Kurzrok M, Pool C, Lemma T, et al. Risk factors for reduced glomerular filtration rate in a Nicaraguan community affected by Mesoamerican nephropathy. MEDICC Rev. 2014;16:16-22
  14. McClean M, Laws R, Ramirez Rubio O, Brooks D.; "Industrial hygiene/ occupational health assessment: Evaluating potential hazards associated with chemicals and work practices at the Ingenio San Antonio (Chichigalpa, Nicaragua)"; Boston University School of Public Health; 2010. <http://www.cao-ombudsman.org/cases/document-links/documents/FINALIHRreportAUG302010-ENGLISH.pdf>. Accessed 16 May 2016
  15. Wijkstrom Julia; "Chronic Kidney Disease of unknown etiology in Central America and Srilanka- Renal Morphology and Clinical Characteristics"; Karolinska Institute; Stockholm 2017.
  16. Valcke et al; "Pesticide exposure and Chronic Kidney Disease of Unknown Etiology: An Epidemiologic Review"; Environmental Health (2017) 16:49
  17. Mohapatra Richard, Varshneyand , Suchita M; "Kidney Conundrum" December 2013.
  18. Gillis J; "2015 was Hottest year in historical record, Scientist say"; The New York Times; Jan 20, 2016 (Retrieved from [http://www.nytimes.com/2016/01/21/science/earth/2015\\_hottest\\_year\\_global\\_warming.html](http://www.nytimes.com/2016/01/21/science/earth/2015_hottest_year_global_warming.html).)
  19. [www.imd.gov.in/2017](http://www.imd.gov.in/2017) (available source:-Online)