



# PRIME TRIGGER

Heat stress dominates debate on the causes of a mysterious chronic kidney disease that continues to baffle health experts and is on the rise globally

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**M**ORE THAN 30 years and 35 countries. These are the only definitive data available about the chronic kidney disease of unknown origin or CKDu—a condition whose mysterious nature is evident from its name.

Chronic kidney disease, which is characterised by progressive loss of kidney function, is usually reported among those suffering from diabetes, hypertension and glomerulonephritis (a type of kidney inflammation), or those who

have inherited genetic diseases that damage this key filter system of the body. But scientists have so far not been able to pinpoint what causes CKDu. This knowledge gap hampers efforts to prevent new cases and slow progression of the disease, which can be fatal. Doctors say the condition usually remains undiagnosed until kidney failure. What's alarming is that the prevalence of CKDu is on the rise globally.

CKDu was first identified in Sri Lanka and India in the 1990s.

Soon, the disease was also reported from Central American countries. According to a review paper published in *Environmental Geochemistry and Health* on September 12, 2022, CKDu was initially limited to tropical countries. But in the last three decades, it has been reported from 35 countries, including the US and UK. Though no data is available on the global burden of CKDu, the paper estimates that the disease could be responsible for over 30,000 deaths a year and that Sri Lanka



and India have the highest number of people affected by CKDu.

According to the Indian Chronic Kidney Disease Burden 2022, published in *Clinical Kidney Journal*, 19.5 per cent of all chronic kidney disease patients in the country are classified as CKDu. The rate is on par with chronic kidney disease triggered by diabetes (24.9 per cent) and by cervical intraepithelial neoplasia (23.2 per cent), characterised by abnormal growth of cells on cervix.

A great deal of research by governments, research institutes and even the World Health Organization (WHO) have tried to resolve the mystery of CKDu. They all point to varied as well as a combination of factors—from heat stress to strenuous labour to exposure to pesticides and heavy metals to the use of polluted water. However, an equal number of studies are also available that discredit the hypotheses, thus thickening the mystery.

In 2008, WHO conducted an extensive study of CKDu in Sri Lanka. Both the government and WHO received flak soon after the findings were published. One such finding linked CKDu in the endemic area to exposure to cadmium. It found that the level of cadmium in phosphate fertiliser was 30.8 µg/g, compared to the maximum acceptable limit of 4 µg/g. "If cadmium is the only causative factor, why is CKDu not prevalent in other agricultural areas where the same agrochemicals are used?" Oliver Ileperuma, professor of chemistry at University of Peradeniya in Sri Lanka, who studied the disease since 1990s, had told *Down To Earth* (see 'Kidney Conundrum', December 1-15, 2013).

At places, the authorities have

taken preventive measures based on suspected risk factors, but to little avail. Uddhanam, a coastal region in Andhra Pradesh, is a CKDu hotspot. To identify root cause of the disease, the state government in 2018 roped in two research institutes in Delhi—The Energy and Resources Institute and the George Institute for Global Health—that tested samples of groundwater from 40 villages in Uddhanam and compared the results with groundwater quality from 100 villages in adjoining districts. The study published in *Groundwater for Sustainable Development* in October 2020, showed that 35 per cent villages in Uddhanam had acidic groundwater, while the figure was 3 per cent for other districts. The study also found

### **FROM 2017 TO 2020, RESEARCHERS SURVEYED 352 WORKERS IN SEVEN SALT PANS IN TAMIL NADU'S VEDARANYAM AND MARAKKANAM TOWNS. THEY FOUND THAT HEAT STRESS AND DEHYDRATION ARE MAJOR DRIVING FORCES OF CKDU**

high levels of silica and lead in the groundwater of Uddhanam. Phthalates, known endocrine disruptors, were detected in all samples. Pesticides were not found in the groundwater samples even though the region is known for coconut and cashew plantations and most CKDu patients work in farms.

While the researchers have called for more studies to explore the synergic effects of lead, fluoride, silica and water hardness in acidic water on kidney function, the government has recommended clean water supply to villages in Uddhanam. Venkatramana, a 45-year-old resident of Uddhanam who was di-

agnosed with CKDu five years ago, tells DTE that the disease however continues to spread.

### **HEAT STRESS A KEY TRIGGER**

Amid the debate, a consensus appears to be building in recent years. Increasing number of studies suggest heat stress could be the root cause of CKDu—or accelerating it.

At salt pans in Tamil Nadu's Vedaranyam and Marakkanam towns, workers can be seen loading and crushing salt crystals during the summer and spring months. They work from 6 in the morning till afternoon, with a break that lasts from half an hour to an hour. On average, the workers consume one litre of water during the shift as the locations do not have toilet

facilities. There are also no shaded areas for resting. Since the salt pan workers do strenuous work in high temperatures, and are not exposed to pesticides or other toxicants, they provided an opportunity to study the role of heat stress alone in CKDu.

From 2017 to 2020, researchers surveyed 352 workers in seven salt pans and found that heat stress and dehydration are major driving forces of CKDu. The researchers measured heat stress in wet bulb globe temperature, which takes into account temperature, wind speed, cloud cover, sun angle and humidity, and found that the workers exceeded the threshold limit values by 87 per cent with frequent dehydration-related symptoms.

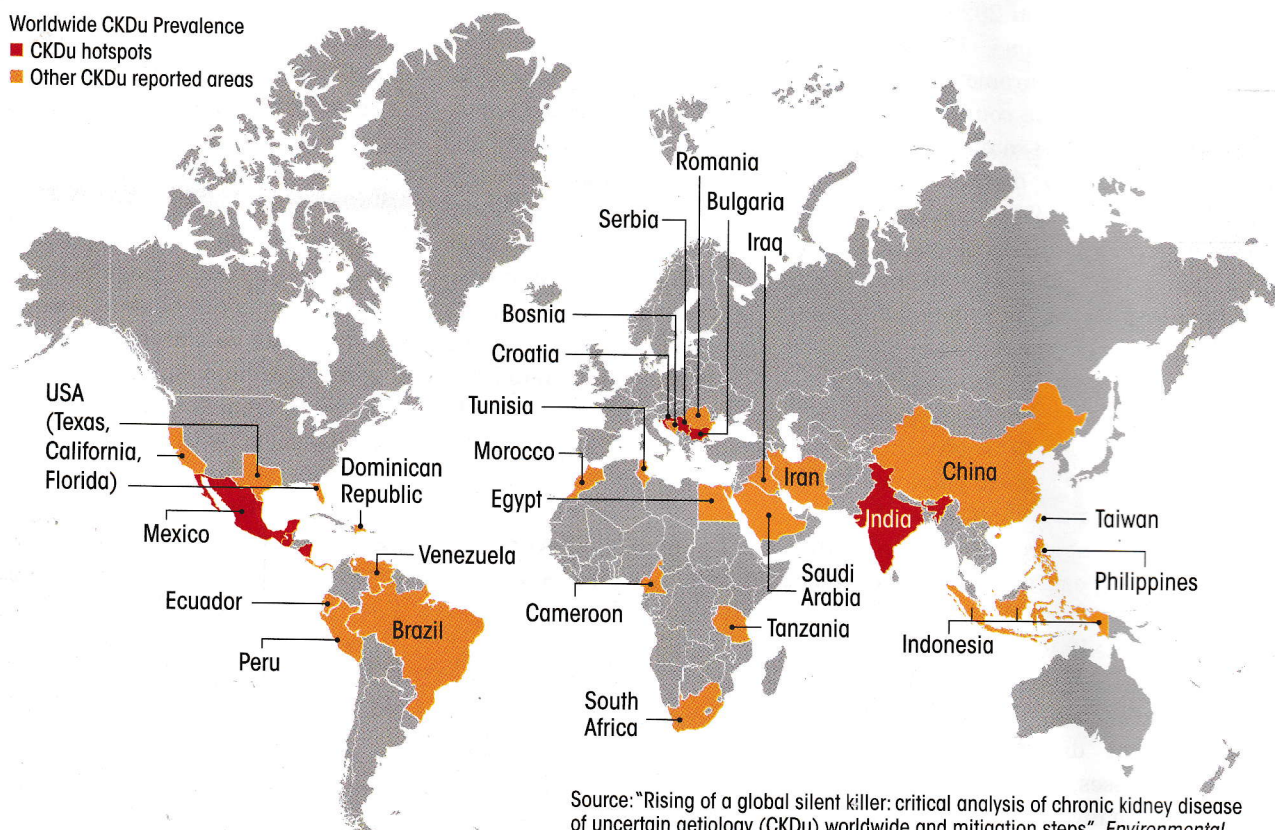
Vidhya Venugopal, professor of environmental health and industrial hygiene at Sri Ramachandra Institute of Higher Education and Research, Chennai, who led the



## Symptom of heat stress

Regions in which chronic kidney disease has been reported tend to be the hottest in their countries

Worldwide CKDu Prevalence  
 ■ CKDu hotspots  
 ■ Other CKDu reported areas



Source: "Rising of a global silent killer: critical analysis of chronic kidney disease of uncertain aetiology (CKDu) worldwide and mitigation steps", *Environmental Geochemistry and Health*, September 2022

study, tells DTE that when a worker is exposed to heat and is exerting himself with heavy work, dehydration may follow due to excessive sweating and lack of replenishment. Repetitive dehydration can cause a repetitive kidney injury preventing the kidney from filtering out waste. If this happens for years, it leads to chronic kidney disease, she says, adding that climate change could exacerbate the prevalence of CKDu.

In Central America, CKDu, which is known as Mesoamerican nephropathy, primarily afflicts agricultural workers from communities along the Pacific Coast, especially those working in sugarcane fields. "In general, these men have a

history of manual labour under very hot conditions in agricultural fields," notes a 2014 study published in *American Journal of Kidney Diseases*. Another study published in *The New England Journal of Medicine* in 2019, researchers from US find that CKDu is more likely to develop among those sugarcane workers engaged at sea level than in those who work at higher altitude, since the fields at low altitude have higher environmental heat. The study further notes that regions in which chronic kidney disease has been reported tend to be the hottest regions in the various countries.

To pinpoint the causes, medical research professionals from India, Central America and US have set

up a consortium, known as CKD of Unknown Etiology in Agricultural Communities or CURE Consortium. They plan to assess multiple potential causes of CKDu across the regions by following a uniform research protocol. Vivekanand Jha, executive director of The George Institute for Global Health, which is part of the consortium, says the study aims to offer a comprehensive view of the environment, air pollution, water contamination, food material and full genetic analysis. Several thousand people will be studied. "The assessment is yet to begin and will span many years. But it will not miss out on any factors," Jha says. **DTE**

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