

Status of chronic kidney disease of unknown aetiology in Pakistan

Salman Imtiaz, Ashar Alam

Abstract

The incidence of chronic kidney disease (CKD) is rising all over the world. Developing countries like Pakistan will be most affected due to the prevalence of risk factors associated with CKD, such as diabetes, hypertension, kidney stone, and infections. Chronic kidney disease of unknown aetiology (CKDu) is an emerging CKD recently recognised in agricultural communities all around the world. CKDu is recognised, mostly in men between 20 and 50 years of age, with no symptoms, having normal or borderline elevated blood pressure with normal blood glucose levels. Their ultrasonography manifests small kidneys. Urine examinations reveal no or minimal proteinuria, few red blood cells and leukocytes. The actual prevalence in Pakistan is unknown but it is not infrequent for nephrologists and physicians to see these patients in hospitals. There is a need to look into this entity at the community level.

Keywords: Pakistan, Chronic kidney disease, chronic kidney disease of unknown aetiology, chronic kidney disease in agricultural communities,

DOI: <https://doi.org/10.47391/JPMA.113>

Introduction

Chronic Kidney Disease (CKD) is an emerging health burden in all parts of the world, with many known and unknown causes. It is associated with diabetes and hypertension in developed countries. However, in developing countries, it has many other potential associations, with infectious diseases and environmental toxins. In the last 30 years, an epidemic of CKD has been observed in agricultural communities, first in the sugar cane workers in Central America and paddy farmers in Sri Lanka, and later from other regions with similar environments. The traditional causes of CKD were diabetes and longstanding hypertension. Now Nephrologists are increasingly seeing more and more patients, who are mostly men of 20-50 years of age, with no symptoms, having normal or borderline elevated blood pressure with normal blood glucose levels. Their ultrasonography manifests small kidneys and their kidney

.....
Department of Nephrology, The Indus Hospital, Karachi, Pakistan.

Correspondence: Salman Imtiaz. Email: salman_imtiaz@hotmail.com

histopathology shows tubulointerstitial nephropathy. Urine examinations shows no or minimal proteinuria, usually less than one gram in 24 hours, few red blood cells and leukocytes, and occasionally amorphous urate crystals. High uric acid levels is a frequent but not a persistent finding. This constellation of clinical presentation and laboratory markers is referred to as Mesoamerican Nephropathy (MEN) in Central America, and Chronic Kidney Disease of unknown aetiology (CKDu) in Sri Lanka. Now it is recognised as Chronic Interstitial Nephritis in Agricultural Communities (CINAC).¹

The mechanism that initiates the injury is not yet clear. Johnson et al proposed MEN is a dehydration disorder. Agricultural labourers, working in extreme climates, are likely to develop dehydration and heat, stress, rhabdomyolysis and hyperuricaemia which could all be potential factors responsible for this epidemic. They suggested a pathophysiological mechanism, that the recurrent dehydration may induce kidney injury through a fructokinase dependent mechanism likely from the generation of endogenous fructose and the polyol pathway.² On the contrary, Campese et al proposed that the injury is not precipitated by dehydration, but rather due to 'rehydration'. He suggested an alternative hypothesis that workers in rural areas of Nicaragua and Mesoamerica are exposed to very hot and humid climatic conditions. Due to the heat they perspire abundantly and drink more fluids resulting in increased uptake of toxins, or contaminants in the water such as heavy metals, pesticide and arsenic. In this environment, even if the contaminants of the drinking water are in normal range, the workers may end up in ingesting substantial quantities of toxic elements due to enormous amount of fluid intake on daily basis resulting in toxic concentration of these elements in blood and hence precipitating in the kidneys.³

In Pakistan, very few studies have been conducted to measure the prevalence of CKD and its causes. Ashar et al showed a prevalence of 16% in a community-based cohort.⁴ In reviewing the literature in reference to the epidemiology of CKD in Pakistan, Salman and Beena found that the prevalence ranges from 13% to 30% in different studies.⁵ Among various causes of CKD, diabetes was on the top while CKD of unknown aetiology was

nearly 12%, from which diabetic nephropathy and hypertensive nephropathy were more prevalent in urban, educated males with high socioeconomic background. On the other hand, CKD of unknown aetiology and stone diseases were more common in rural, uneducated, males with low socioeconomic background.⁶ The pathophysiology of underlying CKDu is controversial, and as we observe it, the cause is either due to water depletion, owing to heat stress, that causes acute tubular necrosis, which over the years progresses to CKD, and on the other hand it is perceived to be caused by drinking excessive amount of water which is contaminated with heavy metals, leading to acute interstitial nephritis and progress to CKD over the years. In this regard, in another study reviewing histopathology of more than 1,500 renal biopsies in a tertiary care unit, the prevalence of tubulointerstitial nephritis was around 15%, out of which most of the patients were from rural areas with no apparent aetiology.⁷

Water contamination with industrial effluent and agricultural pesticide is not uncommon in a country like Pakistan. Salman et al evaluated the water content of different nephrotoxic agents such as heavy metals and fungal contaminants in different parts of the country. In a review of different studies conducted in various urban and rural areas all over the country, with reference to poultry industry he found a significantly high level of arsenic, cadmium, ochratoxin and zearalenone that are known to cause renal and genitourinary damage.⁸ Pakistan is predominantly an agricultural country and heat stress is a problem in many parts of the country. In 2015, the country faced one of the worst heat waves that took the life of 2,000 people. There is a dire need to look into the matter. We have all the risk factors in our country that can cause CINAC, and what is being seen at tertiary care hospitals in urban areas is just the tip of the iceberg.

There may be many more cases in rural areas that have not been diagnosed yet. There is a need to conduct a population based study in our rural as well as in urban areas to see the exact prevalence and population at risk. Till that time, there is a pressing need to check drinking as well as agricultural water contents in these areas regularly, with provision of safe drinking water to all of the population at large and specifically to those who work in agricultural fields in hot climates.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Sources: None to declare.

References

1. Johnson RJ, Wesseling C, Newman LS. Chronic Kidney Disease of Unknown Cause in Agricultural Communities. *N Engl J Med* 2019; 380:1843-52.
2. Johnson RJ. Heat stress as a potential aetiology of Mesoamerican and Sri Lankan nephropathy: a late night consult with Sherlock Holmes. *Nephrol Dial Transplant* 2017; 32: 598-602.
3. Campese MV, Mesoamerican nephropathy: is the problem dehydration or rehydration? *Nephrol Dial Transplant* 2017; 32: 603-6.
4. Alam A, Amanullah F, Baig-Ansari N, Lotia-Farrukh I, Khan FS. Prevalence and risk factors of kidney disease in urban Karachi: baseline findings from a community cohort study. *BMC Res Notes*. 2014;7:179. doi: 10.1186/1756-0500-7-179.
5. Imtiaz S, Salman B, Qureshi R, Drohliya MF, Ahmad A. A review of the epidemiology of chronic kidney disease in Pakistan: A global and regional perspective. *Saudi J Kidney Dis Transplant* 2018;29:1441-51.
6. Salman B, Imtiaz S, Qureshi R, Drohliya MF, Ahmad A. The Causes of Chronic Kidney Disease in Adults in a Developing Country. *J Nephrol Ren Dis* 2017; 1:1. ISSN: 2576-3962.
7. Qureshi R, Salman B, Imtiaz S. Frequency and etiology of Tubulo-Interstitial Nephritis in adult renal biopsies in a tertiary renal care hospital: A single center study. *Saudi J Kidney Dis Transplant* 2020;31:335-41.
8. Imtiaz S, Alam A, Salman B. The role of the poultry industry on kidney and genitourinary health in Pakistan. *Pak J Med Sci*. 2020 Jan; 36: S67-S74.