

Review Article

Mesoamerican nephropathy: a narrative review

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ABSTRACT

Mesoamerican nephropathy (MeN) also known as chronic kidney disease of unknown etiology (CKDu) is prevalent in agriculturally rich areas. The most widely accepted pathophysiological explanation for MeN is chronic dehydration caused by prolonged exposure to the sun. Other theories include oxidative stress, chronic inflammation, infection and tubulointerstitial fibrosis. The clinical presentation is quite vague and is diagnosed similar to CKD from any cause using blood, urine analysis and ultrasound. The study highlights the need for interdisciplinary cooperation among physicians, epidemiologists, toxicologists, and geneticists while identifying significant research gaps and future objectives. Occupational health related to agriculture is not emphasised enough especially in third world countries where a large chunk of population heavily depend on farming. To safeguard the population at risk, the significance of community-based initiatives, occupational health measures, and regulatory changes is emphasised.

Keywords: Mesoamerican nephropathy, Sugarcane farmers, Chronic kidney disease of unknown etiology, Narrative review, Heat, Dehydration

INTRODUCTION

Mesoamerican nephropathy (MeN), a widespread type of chronic kidney disease (CKD), affects people living in rural areas of Central America.¹ Cross sectional studies conducted in Nicaragua and El Salvador have revealed a high prevalence of CKD in communities close to the Pacific coast, where physical labour and agricultural work are the main sources of employment.^{2,3}

The disease may progress to chronic kidney failure, a devastating diagnosis in most Central American countries where the resources for renal replacement therapy are limited. Men working in sugarcane fields are frequently affected. Although the leading theory for MeN's cause and

pathogenesis is repeated dehydration due to the extreme occupational conditions of sugarcane workers.^{1,4}

EPIDEMIOLOGY

Mesoamerica, includes Southeast Mexico, Guatemala, El Salvador, Western Nicaragua, and North-western Costa Rica. Mesoamerica has seen the occurrence of this mysterious and seriously fatal nephropathy that evolves into CKD.^{5,6} Majority of MeN patients in the coastal regions work in agriculture. Countries with low or middle incomes with this entity are struggling to diagnose cases and get accurate epidemiologic data because they lack institutional end stage kidney disease (ESKD) registries, suitable infrastructure, and a sufficient number of

nephrologists. Due to a lack of credible data and nephrology services, which just recently began to emerge in the region's major cities around the 1970s, the exact point at when the epidemic began is unknown.⁵

The typical Mesoamerican nephropathy (MeN) patient is usually a hispanic male between the ages of 20 and 60 who resides or works along Central America's Pacific coast.⁷ Nearly 40% of male of age group 20- 40 who participated in a research in chichigalpa, Nicaragua had less than 60 ml/min/1.73 m² eGFR (estimated gfr).⁸ The average yearly incidence rate of ESKD in the El Salvador (Bajo lampa region) was 1,409 per million people and out of which males were 89% and annual mortality rate was 128 per 100000 population.^{9,10}

When diabetic and hypertensive patients are eliminated, the male predominance in ESKD incidence and mortality increased noticeably, up to 97% in the above region.^{6,10-13} In CKD hotspots, reports from the local community and hospitals indicate that 70% to 80% of those affected are farmers.

ETIOPATHOGENESIS

Unlike the traditional CKD that commonly occurs secondary to diabetes and hypertension, the risk factors for MeN are quite different. It has been found that male agricultural workers from the pacific coast who are exposed to strenuous working conditions such as high heat stress, environmental pollutants and agrochemicals are more likely to develop MeN.^{11,14} Social determinants such as poverty, inadequate access to healthcare, malnutrition, low birth weight and high rates of social violence further increase the risk of development and progression of the disease.¹⁴ A possibility of infectious etiology from Hantavirus and leptospira is also considered as the pattern of epidemic curve which fits the curve that would be expected when a new pathogen is introduced into a naive population.¹⁵ Workers had higher seroprevalence for leptospira than non-field workers among sugarcane farmers which further raises the possibility of its etiological role in MEN.¹⁶

Madero et al proposed two possible theories for the pathogenesis of MeN. The first states that the cumulative effect of risk factors such as heat stress and dehydration would lead to constantly activated RAAS (renin-angiotensin-aldosterone system) and polyol-fructokinase pathway in the kidney. The risk factors can also cause subclinical rhabdomyolysis, induce uricosuria and exacerbate systemic inflammation. The usage of nephrotoxic drugs on top this would make the situation even worse.¹⁷

Asymptomatic exposure to leptospira infection bears the risk for CKD, in its chronic carrier stage, which is now thought to be a probable cause of MeN because leptospira may colonize in the proximal tubule and cause chronic tubulointerstitial nephritis and fibrosis.¹⁸

CLINICAL PRESENTATION

The presentation of Mesoamerican nephropathy can be either acute or chronic. An acute case presents with blood pressure (120/80 mmHg), BMI>25 kg/m², fever, chills, nausea, vomiting, back pain, headache, debility, paraesthesia, cramps, abdominal pain, myalgia, arthralgia, dizziness, urinary symptoms, fatigue, decreased loss of appetite, tremors, diarrhoea, cough, chest pain, blurred vision.¹⁹ There are several lab parameters changes that are evident in mesonephric nephropathy, they are as shown in Table 1.

Table 1: Laboratory parameters.

Variables	Values
Creatinine	>2 mg/dl
Leucocytosis	>10000 cells/mm ³
Neutrophilia	> 67%
Lymphopenia	<20%E
Eosinophilia	>4%
Haemoglobin	<13 g/dl in male, <12 g/dl in female
Haematocrit anaemia	<38.8 male, <34.9 female
RBC	<4.3×10 ⁶ cells
Hyperuricemia	>7 mg/dl male, >6 mg/dl
Hypocalcemia	<1.1 mmol/l
Hypomagnesemia	<1.9 mg/dl
Hypokalemia	<3.5 mmol/dl
Hyponatremia	<135
CPK	>336 u/l male, >1786 u/l female
BUN	>23.3 mg/dl
BCR	<10
CRP	>6 mg/dl

DIAGNOSIS

Parameters that are changed in patient are urea, blood urea nitrogen, creatinine, uric acid, calcium, phosphorus, sodium, potassium, chloride, bun/creatinine ratio, urea/creatinine ratio and urine albumin-to-creatinine ratio (UACR) of more than 30 milligrams per gram could be a warning sign of kidney disease. eGFR (estimated glomerular filtration rate) estimates the kidney function. Ultrasound of kidneys would show the changes in size and morphological features. Rarely, a kidney biopsy is ordered. A wide range of histologic features are observed on biopsy including tubular atrophy and fibrosis coupled with chronic glomerular changes, including glomerulosclerosis, hypertrophy, and collapse of glomerular tufts indicative of glomerular ischemia.²¹

Definition of CKDu (Chronic kidney disease of unknown etiology)

A type of chronic kidney disease (CKD) that is common in some rural populations around the world is chronic kidney

disease of unknown aetiology (CKDu). Its clinicopathologic traits set it apart, and its multifactorial etiology- which is primarily linked to a number of environmental toxins- has multiple causes.²²

Types of CKDu are as follows: suspected CKDu is said when: (a) eGFR <60 ml/min/1.73 m²; (b) and/or albuminuria >30 mg/g; (c) and/or proteinuria >150 mg/g.

All any of the above in the absence of HT, DM, AKI.

If proteinuria greater than 2 gm can exclude CKDu

Probable CKDu

Patient is said to have probable CKD when it (a) has all the features of suspected CKD; (b) hypokalemia and/or hyperuricemia; and (c) a and b in the absence of any kidney disorder

If all the above criteria are present even after 12 week it is said to confirmed CKD.

Confirmed CKDu

All probable CKD criteria and in addition, kidney biopsy results with histopathological characteristics that are consistent with CKDu (pyelonephritis and interstitial nephritis caused by specific aetiologies should be excluded from the definition).

TREATMENTS

There are no established standards for treating MeN patients due to a lack of strong evidence. However, medical professionals in Mesoamerica employ similar strategies for MeN as conventional CKD. Nephrologists frequently prescribe allopurinol, potassium supplements, potassium-sparing diuretics, bicarbonate, steroids, and even low doses of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in Mesoamerica. Due to the likelihood of AKI with dehydration and simultaneous Renin-angiotensin-aldosterone system (RAAS) blockade, the use of these medications is still controversial.²³ El Salvadorian nephrologists rarely used corticosteroids whenever biopsies revealed a lymphocytic infiltrate indicative of a potential tubulointerstitial nephritis. Interestingly, it has been found that CKD progression can be slowed down with sodium bicarbonate.²⁴⁻²⁶

PREVENTION

The focus of current preventive measures is on dealing with the risk factors associated with the emergence of MeN.^{27,28} Protection of worker from dehydration and thermal stress in endemic areas has been implemented due to the potentially harmful effects that thermal stress may have on the kidney. A set of interventional studies showed

that providing sugar cane workers with adequate access to water, rest in shaded areas was a good idea.²⁹

Oral rehydration salts and water should be made accessible at all times for proper hydration and rehydration. In accordance with some protocols, water should be provided to farm workers riding through animals such as camels so that they can consume roughly one litre every day.

The worker hydration status can be assessed through determining their body weight before and after a workday; the weight loss represents the volume lost throughout the day.²⁹ On the other hand, primary care physicians must be educated regarding MeN screening programs and screen for those at risk, kidney disorder diagnosis, and ensuring a prompt referral to a nephrologist if necessary.³⁰

LITERATURE SEARCH

At the end of the narrative review total 30 papers were used as a reference and they are mentioned below. The primary questioning line of our search was how Mesoamerican nephropathy would affect the farmers and how to effectively diagnose and manage them. Then all the relevant information was extracted from different study materials. All the below mentioned papers are from PubMed or PubMed indexed journals and were thoroughly read and analysed by all the author panel.

CONCLUSION

The above narrative review explains why farmers from Mesoamerica suffer from the CKDu and how to diagnose it on the basis of clinical presentation and laboratory markers. There are several treatments recommended which go hand in hand with CKD treatment but also we found some controversial treatments which some nephrologists are reluctant to use. Overall CKDu can pose a threat to the world if precautionary measures are not taken. Improved working conditions, cautious agrochemical management, etc. are some examples of preventive measures that should be put in place to lessen the harm that CKDu causes to agricultural workers. To measure impact and develop the evidence base, more high-quality research is required.

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