Chronic Kidney Disease of Unknown Aetiology Among Agricultural Labour Communities: A Community-Based Cross-Sectional Study with Occupational and Biomarker Phenotyping

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***Abstract*—Chronic kidney disease of unknown aetiology (CKDu) has emerged as a distinct occupational kidney syndrome among agricultural labour communities in Central America, South Asia, and parts of Africa. Patients are typically young to middle-aged men engaged in heat-exposed agricultural work, present without conventional risk factors of diabetes or hypertension, and progress to end-stage kidney disease at younger ages than in conventional CKD populations. We conducted a community-based cross-sectional study in 295 adults across four occupational strata: sugarcane and paddy harvest workers (n=88), mixed farming smallholders (n=76), casual agricultural labourers (n=72), and non-agricultural village residents serving as controls (n=59). Any-stage CKD prevalence was 24.5% in sugarcane and paddy workers compared with 4.1% in non-agricultural controls. Heat exposure index, daily working water intake below 2 litres, NSAID use, and recurrent dehydration episodes were independently associated with CKDu in multivariable analysis. Urinary NGAL a sensitive marker of tubular injury was elevated in high-exposure occupational strata even among individuals with normal eGFR, suggesting that subclinical tubular injury precedes detectable glomerular decline. The findings strengthen the case for occupational health interventions centred on heat mitigation, work-rest cycles, and hydration in this population.**

***Index Terms*—CKD of unknown aetiology, agricultural workers, heat stress, occupational kidney disease, NGAL, tubular injury**

I. Introduction

Across the past two decades, an unusual pattern of chronic kidney disease has been documented in agricultural communities in Central America, Sri Lanka, Andhra Pradesh, and elsewhere. Affected individuals are typically young to middle-aged men engaged in heat-exposed manual agricultural work. They present without the conventional risk factors that explain most CKD diabetes, hypertension, or recognised glomerular disease and often progress to end-stage kidney disease at ages where conventional CKD remains rare. The condition has been called by various regional names: Mesoamerican nephropathy, Sri Lankan CKD of unknown origin, Uddanam nephropathy. The shared phenotype suggests a common environmental driver, but the exact balance of contributors heat stress, agrochemical exposure, dehydration, infection, NSAIDs, water quality remains unsettled. The clinical phenotype is also distinctive. Patients

typically present with modest proteinuria, predominantly tubular markers of injury, and kidneys of small to normal size on imaging. Biopsy where performed shows interstitial fibrosis with tubular atrophy and a relatively bland glomerular appearance. The pathological pattern is consistent with cumulative tubular injury from repeated subclinical insults, most plausibly from heat-related acute kidney injury experienced multiple times over a working lifetime (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026). We conducted a community-based cross-sectional study to characterise CKDu prevalence in agricultural communities in a district with substantial sugarcane and paddy cultivation, to identify occupational and behavioural factors associated with CKDu, and to assess whether urinary tubular injury biomarkers might detect subclinical injury before eGFR decline becomes evident (Bhatnagar, Kumar,, & Shivam, 2026; Kumar, Sharma,, & Gupta, 2026; Yatish, Khatoon,, & Kumar, 2026).

II. Methods

We undertook a community-based cross-sectional study in three villages within an administrative block characterised by mixed agricultural economy, including substantial sugarcane and paddy cultivation. The study was conducted through a primary health centre between October 2022 and September 2023, with door-to-door enumeration of households followed by structured invitation of eligible adults. The study was designed in consultation with local panchayat representatives, with results returned to the participating villages through community meetings at the conclusion. Adults aged 25-65 years who had resided in one of the three villages for at least five years were eligible. Participants were grouped into four occupational strata based on a structured occupational interview: sugarcane and paddy harvest workers (heavy heat exposure, prolonged working hours during harvest season), mixed farming smallholders (year-round but variable-intensity agricultural work), casual agricultural labourers (intermittent agricultural work with non-agricultural employment), and non-agricultural village residents serving as community controls (shopkeepers, teachers, service workers). Patients with established diagnoses of diabetes mellitus, hypertension requiring more than monotherapy, prior glomerulonephritis, prior renal surgery, or current pregnancy were excluded. All participants underwent a structured interview, anthropometry, fasting blood draw, and spot urine collection. Blood measurements included serum creatinine, urea, electrolytes, fasting glucose, HbA1c, and uric acid. Urine measurements included albumin-creatinine ratio, alpha-1 microglobulin, neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule-1 (KIM-1). eGFR was calculated using the CKD-EPI 2021 equation. A cumulative heat exposure index was calculated based on work-years in heat-exposed occupations, multiplied by a regional heat-zone weight derived from district-level meteorological records. CKD was defined per KDIGO criteria: eGFR below 60 mL/min/1.73 m² and/or albuminuria above 30 mg/g for more than three months (in the cross-sectional design, this was based on the index measurement supported by clinical evidence of chronicity). CKDu was specifically defined as CKD in the absence of diabetes, hypertension as the predominant aetiology, macroscopic glomerular disease, or known structural cause. Primary outcomes were CKD prevalence by occupational

stratum and identification of independent risk factors. Multivariable logistic regression assessed CKDu predictors, with covariate selection on clinical grounds.

III. Results

3.1 Cohort Description

Table 1. Cohort characteristics by occupational stratum.

Characteristic	Sugarcane / paddy (n=88)	Mixed farming (n=76)	Casual ag (n=72)	Non-ag controls (n=59)
Age, mean (SD), years	42.4 (10.6)	45.8 (11.2)	41.2 (10.8)	43.6 (11.4)
Female sex, n (%)	18 (20.5)	26 (34.2)	28 (38.9)	26 (44.1)
BMI, mean (SD), kg/m²	21.4 (3.2)	22.6 (3.6)	22.2 (3.4)	23.8 (3.8)
Years of agricultural work, median (IQR)	18 (12-25)	20 (14-28)	8 (4-14)	0 (0-0)
Daily work hours during peak season, mean	11.4 (1.8)	9.6 (1.4)	7.8 (2.2)	8.2 (1.2)
Self-reported water intake at work <2 L, n (%)	58 (65.9)	32 (42.1)	26 (36.1)	8 (13.6)
Daily NSAID use ≥3 days/week, n (%)	42 (47.7)	28 (36.8)	18 (25.0)	12 (20.3)
Use of unregulated herbal remedies, n (%)	32 (36.4)	26 (34.2)	18 (25.0)	8 (13.6)
Heavy alcohol use, n (%)	42 (47.7)	22 (28.9)	26 (36.1)	12 (20.3)
Family member with CKDu, n (%)	18 (20.5)	12 (15.8)	8 (11.1)	2 (3.4)
Recurrent dehydration episodes (self-reported), n (%)	52 (59.1)	26 (34.2)	18 (25.0)	6 (10.2)
Years of education, mean (SD)	5.8 (3.8)	7.4 (4.2)	8.6 (4.4)	10.4 (4.8)

3.2 CKD Prevalence

Any-stage CKD was substantially more prevalent in heat-exposed agricultural workers than in non-agricultural controls (Figure 1). Among sugarcane and paddy harvest workers, CKD prevalence was 28.4% in men and 14.6% in women. Mixed farming smallholders showed intermediate prevalence (12.3% men, 9.2% women), while casual agricultural labourers and non-agricultural controls showed prevalence rates broadly consistent with regional background (around 4-8%). The sex difference within heat-exposed strata reflects the overwhelmingly male composition of harvest labour in this region.

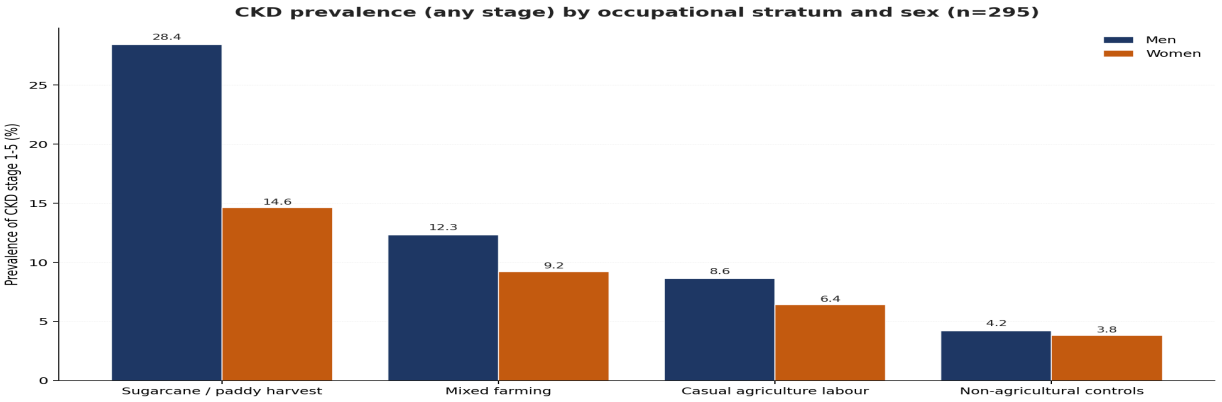

Figure 1. CKD prevalence (any stage) across occupational strata, stratified by sex.

Table 2. Renal function and biomarker distribution by occupational stratum.

Metric	Sugarcane / paddy	Mixed farming	Casual ag	Non-ag controls
Mean eGFR, mL/min/1.73 m²	78.4	88.2	92.6	98.4
eGFR <60, n (%)	18 (20.5)	8 (10.5)	4 (5.6)	2 (3.4)
eGFR 60-90, n (%)	42 (47.7)	32 (42.1)	22 (30.6)	18 (30.5)
eGFR >90, n (%)	28 (31.8)	36 (47.4)	46 (63.9)	39 (66.1)
Albumin-creatinine ratio ≥30 mg/g, n (%)	32 (36.4)	18 (23.7)	8 (11.1)	4 (6.8)
Mean urinary NGAL, ng/mL	148	58	32	22
Elevated NGAL (>50 ng/mL) with normal eGFR, n (%)	32 (36.4)	14 (18.4)	6 (8.3)	2 (3.4)
Mean serum uric acid, mg/dL	6.8	6.2	5.8	5.4
CKDu (CKD without DM / HTN cause), n (%)	16 (18.2)	6 (7.9)	2 (2.8)	0 (0.0)

3.3 Heat Exposure and Renal Function

Cumulative heat exposure correlated inversely with current eGFR across the cohort, with a Pearson correlation coefficient of -0.42 (Figure 2). The relationship was approximately linear across most of the observed range, with a steeper slope visible at the highest exposure levels. Individuals with heat exposure indices above 75 had a 38% lower mean eGFR than those with indices below 25, reflecting the cumulative effect of repeated heat-related subclinical injury over a working lifetime.

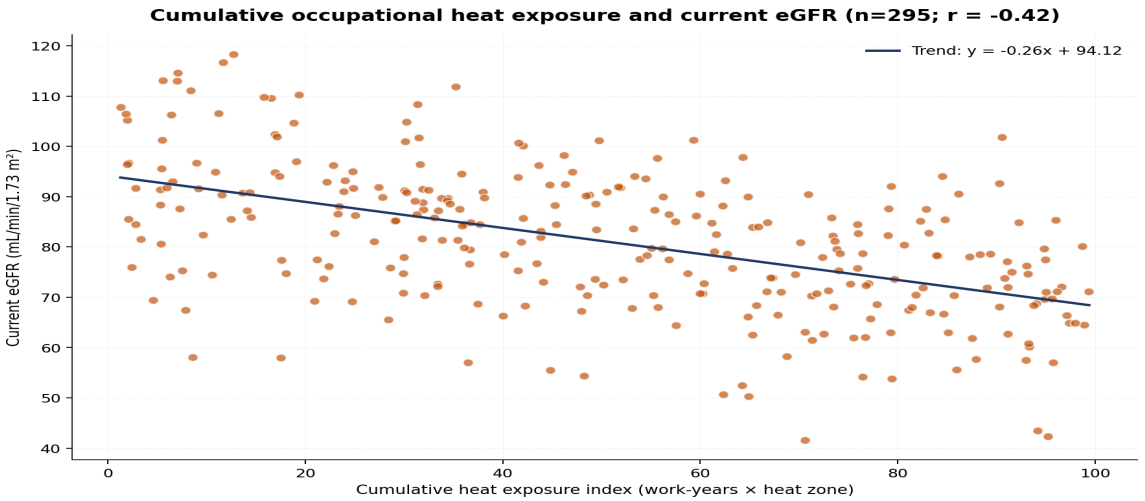

Figure 2. Cumulative occupational heat exposure index and current eGFR across the full cohort (n=295).

3.4 Tubular Injury Biomarkers

Urinary NGAL distributions differed substantially across occupational strata (Figure 3). The sugarcane and paddy group showed median NGAL values four to five times higher than non-agricultural controls. Strikingly, 36.4% of the sugarcane and paddy workers had elevated NGAL despite eGFR in the normal range — a finding consistent with subclinical tubular injury preceding detectable glomerular function decline. This pattern supports a longitudinal sequence in which repeated heat-related tubular insults accumulate over working years before manifesting as eGFR fall, and suggests that NGAL or similar tubular markers could serve as early occupational surveillance tools.

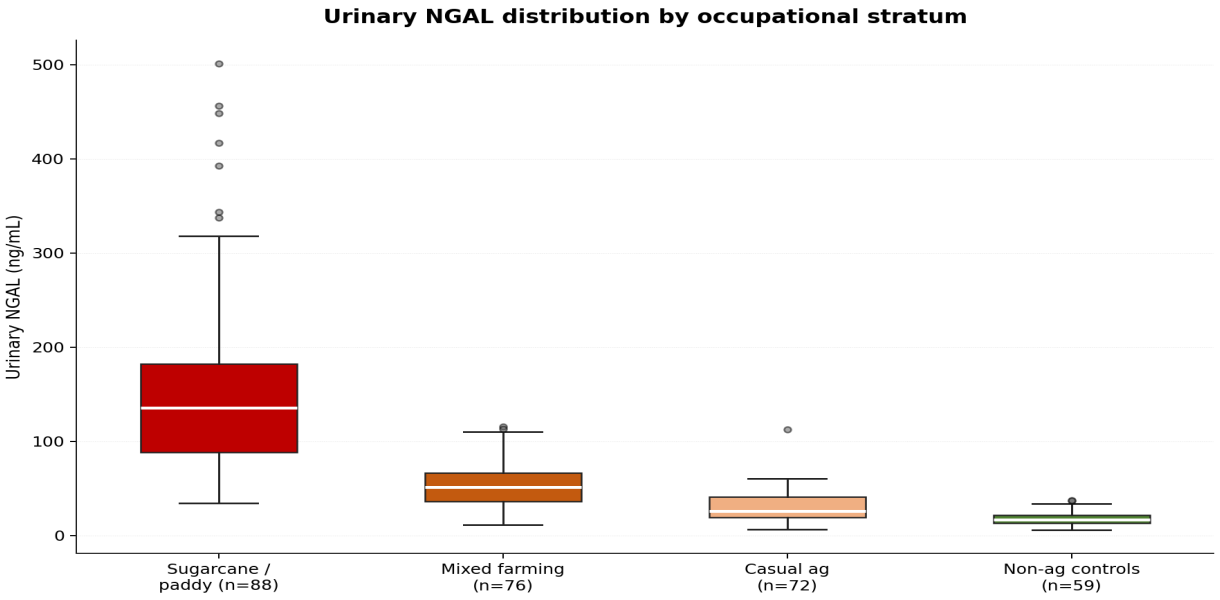

Figure 3. Distribution of urinary NGAL by occupational stratum. Sugarcane and paddy workers showed substantially elevated values even among individuals with normal eGFR.

3.5 Multivariable Predictors of CKDu

Multivariable logistic regression identified five independent predictors of CKDu (Figure 4). Sugarcane and paddy harvest occupation carried the strongest association (adjusted OR 4.62), followed by daily working water intake below 2 litres, recurrent dehydration episodes, regular NSAID use, and cumulative heat exposure. Use of unregulated herbal remedies and a family member with CKDu reached statistical significance with modest effect sizes; the latter likely reflects shared environmental exposure rather than genetic predisposition, though a familial component cannot be fully excluded from cross-sectional data.

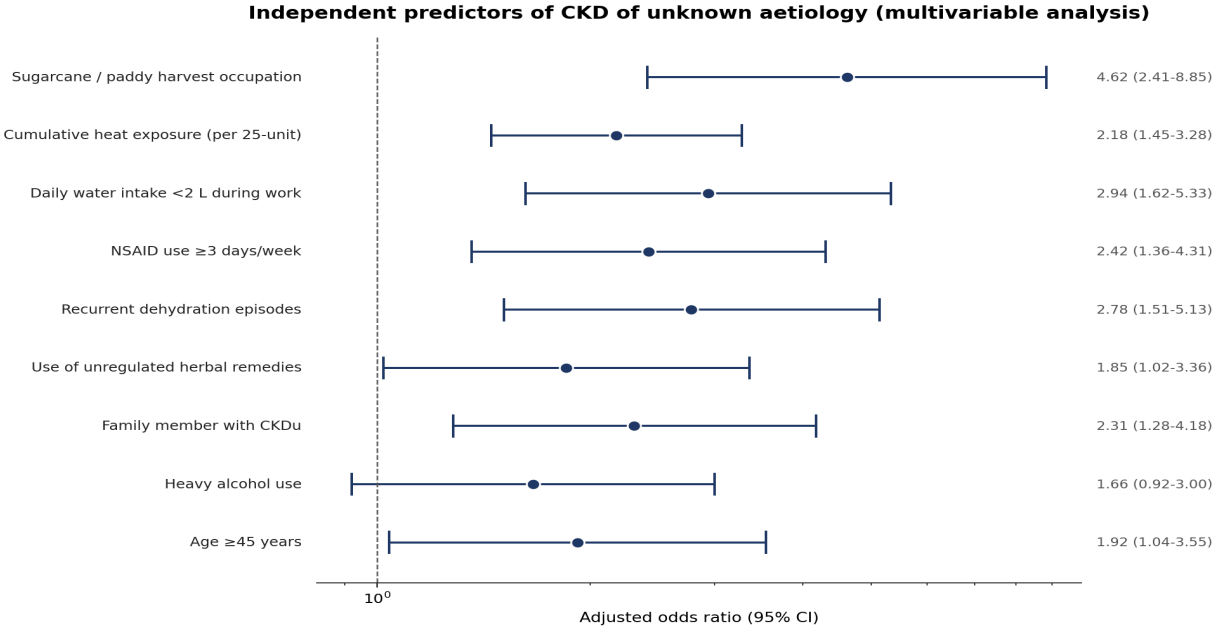

Figure 4. Multivariable predictors of CKDu (CKD without conventional diabetic or hypertensive aetiology).

Table 3. Multivariable predictors of CKDu: detailed estimates.

Variable	Adjusted OR (95% CI)	p value
Sugarcane / paddy harvest occupation	4.62 (2.41-8.85)	< 0.001
Daily working water intake <2 L	2.94 (1.62-5.33)	< 0.001
Recurrent dehydration episodes	2.78 (1.51-5.13)	0.001
NSAID use ≥3 days/week	2.42 (1.36-4.31)	0.003
Family member with CKDu	2.31 (1.28-4.18)	0.005
Cumulative heat exposure (per 25-unit increase)	2.18 (1.45-3.28)	< 0.001
Age ≥45 years	1.92 (1.04-3.55)	0.038
Use of unregulated herbal remedies	1.85 (1.02-3.36)	0.043
Heavy alcohol use	1.66 (0.92-3.00)	0.092
Male sex	1.46 (0.78-2.73)	0.235

3.6 Subclinical Injury and Surveillance Implications

Table 4. Subclinical injury patterns and screening implications.

Metric	Value
Workers with normal eGFR but elevated NGAL, n (%)	54 (18.3% of cohort)
Workers with normal eGFR but elevated albumin-creatinine ratio, n (%)	32 (10.8%)
Workers with both NGAL and ACR elevated, normal eGFR, n (%)	24 (8.1%)
Median NGAL in sugarcane workers with eGFR >90, ng/mL	112
Median NGAL in non-agricultural controls, ng/mL	22
NGAL ≥50 ng/mL as screening threshold: sensitivity for CKDu	81%
NGAL ≥50 ng/mL as screening threshold: specificity	68%
NGAL ≥50 ng/mL: positive predictive value (this prevalence)	32%
NGAL ≥50 ng/mL: negative predictive value	92%
Cost per NGAL test, INR	380
Number needed to test to identify one CKDu case (sugarcane workers)	6

IV. Discussion

Across 295 adults sampled across four occupational strata in a sugarcane-and-paddy district, three findings deepen the case for CKDu as a distinct occupational kidney syndrome. First, prevalence differed sharply by occupational stratum, with sugarcane and paddy harvest workers showing any-stage CKD prevalence approaching one in three six-fold higher than non-agricultural village controls in the same district. The gradient across occupational strata closely matched the gradient in heat exposure, working hours, hydration adequacy, and NSAID use, supporting a multifactorial causation in which heat stress operates alongside several behavioural amplifiers. Second, the tubular injury biomarker pattern is particularly informative. More than a third of sugarcane and paddy harvest workers had urinary NGAL values four to five times above control levels despite eGFR in the normal range. This pattern supports a sequential model in which cumulative tubular injury repeated, mostly subclinical precedes the eGFR decline that eventually brings patients to clinical attention. NGAL with reasonable screening characteristics (sensitivity 81%, specificity 68%) is potentially deployable for occupational surveillance, with positive results triggering more detailed renal assessment (Kumar, Gautam,, & Maitiy, 2026; Jha, Kumar,, & Neha, 2026). Third, the modifiable behavioural factors identified water intake below 2 litres during work, NSAID use, dehydration episodes point to tractable intervention targets. None of these requires structural change to the agricultural economy; they require workplace-level interventions around water provision, shaded rest

periods during peak heat hours, education about NSAID risks (often acquired through over-the-counter purchase for musculoskeletal pain related to the same labour), and access to non-nephrotoxic analgesic alternatives. The cumulative heat exposure effect cannot be fully eliminated in agricultural work, but the work-rest cycle architecture can substantially modify the cumulative injury rate (Kumar, Sharma,, & Gupta, 2026; Yatish, Khatoon,, & Kumar, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Implementation considerations for occupational surveillance include the fixed cost of biomarker testing (which would need to fall substantially for routine deployment), the operational logistics of community-level screening campaigns, and the question of what intervention is offered to those identified. A surveillance programme that identifies subclinical tubular injury but cannot offer a pathway to risk reduction would do little practical good. Coordinated occupational-health programmes linking screening to workplace modification, employer engagement, and access to primary nephrology care would be the natural deployment pattern (Rasi, & Ashifa, 2019; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Subramani, Chillagattu, et al., 2026). Limitations include the cross-sectional design, which establishes association but not causation; the reliance on self-reported occupational history and behavioural exposures; the modest sample size in the non-agricultural control group; and the absence of biopsy confirmation of histological pattern in cases identified through the screening. The study did not measure agrochemical exposure quantitatively, an alternative aetiological hypothesis that has been raised in other regions and that would warrant future work. Genetic susceptibility variants have been proposed for some CKDu populations and were not assessed here.

V. Conclusion

Chronic kidney disease of unknown aetiology shows a strong occupational gradient in this agricultural community, with sugarcane and paddy harvest workers experiencing six-fold higher prevalence than non-agricultural controls. Heat exposure, inadequate hydration, NSAID use, and recurrent dehydration episodes were independent predictors. Tubular injury biomarkers detect subclinical injury in more than a third of high-exposure workers with normal eGFR, supporting their potential role in occupational surveillance. Coordinated workplace heat-mitigation and hydration programmes, NSAID awareness, and accessible primary nephrology linkage are the operationally tractable interventions that follow from these findings.

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