

Risk Factor Distribution among Subjects with Declined Estimated-Glomerular Filtration Rate in Areas Endemic to Chronic Kidney Disease of Unknown Aetiology of Sri Lanka

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ABSTRACT

Objective: Risk factors among chronic kidney disease (CKD)/ chronic kidney disease of unknown aetiology (CKDu) patients were followed in Padaviya (PDV), and Girandurukotte/ Mahiyanganaya (GK/MH) of Sri Lanka, where CKDu was endemic. The studies profiled risk factor data pertaining to CKD and assessed risk factor association with renal dysfunction in the areas concerned.

Methods: Data of initiation risk factors (IRF) that existed prior to diagnosis, progression risk factors and demography were collected in cross sectional studies at PDV, and GK/MH separately. Subject participation was volunteer and preceded informed consent. Control and CKD/CKDu groups were identified using serum creatinine based estimated glomerular filtration rate followed by verification of renal status with urine albumin to creatinine ratio obtained from spot samples. Data were analysed as compared to control with chi-square goodness of fit test and odds ratio.

Results: Among IRF, both chi-square and odds ratio revealed ($p < 0.05$) that hypertension associated disease development in GK/MH. In PDV, autoimmune diseases, systemic infections mostly multiple episodes of malaria, and leptospirosis, urinary tract infections and family history of kidney disease associated it ($p < 0.05$). Nevertheless, IRF prevalence was higher in endemic control of PDV (85.7%), nonendemic control of PDV (71.4%), and endemic control of GK/MH (41.7%) as well. In PDV and GK/MH, 3.5% and 14.5% of CKD/CKDu patients did not report any IRF respectively. Odds of CKD/CKDu development increased among males and field farmers, and with low level of education, agrochemical usage, and with domestic usage of dug-well water.

Conclusion: The results suggest that the disease in Padaviya, and Girandurukotte/ Mahiyanganaya areas may not be explained by traditional risk factors alone, and certain demographic factors such as education level, occupational application of agrochemicals, and domestic usage of dug-well water appeared to be influencing it.

Keywords: Chronic kidney disease; Serum creatinine; Estimated glomerular filtration rate; Urine albumin to creatinine ratio; Chronic kidney disease risk factors; Demography; Padaviya; Girandurukotte; Mahiyanganaya; Sri Lanka

INTRODUCTION

The chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka is an endemic nephropathy marked by progressive tubulointerstitial damage in kidneys [1]. The disease has emerged

endemic in North Central, Uva and certain other provinces in Sri Lanka [2,3] and is enigmatic with the uncertainty over the causal factors involved. The medically relevant risk factors pertaining to CKD [4] do not appear to explain the disease development in the

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endemic areas of the country. The disease associates factors such as notable confinement to a geoclimatic region namely the dry zone of the island and to a particular socioeconomic stratum of the society. First emerged in 1990s, the disease has been predominantly seen in paddy farming communities with greater occurrence among males. A range of other demographic factors such as exposure to agrochemicals, contaminated drinking water, and genetic predisposition, as well as exposure to heavy metals [5] have been received the attention as causal but the issue remains without a finality. For this reason, the disease is termed CKD of unknown aetiology (CKDu) and more recently as CKD of multifactorial origin (CKDmfo) in Sri Lanka [6]. It implies aetiology beyond the medically established CKD risk factors. It is thus important that the contribution of both medically established and other suspected risk factors of the disease development be assessed in endemic areas.

The clinically pertinent risk factors of CKD have been listed by the National Kidney Foundation, USA [4]. Accordingly, initiation risk factors (IRF) may induce the kidney damage while progression risk factors (PRF) aggravate the already initiated disease. The rationale is that a history of an initiation risk factor may suggest a causal relation hence aetiology to the subsequent CKD of the individual. The approach may distinguish between CKDu fraction among total CKD in the areas affected as the former may not associate such history. The recognition of locally important CKD precursors and thereby the individuals at increased risk of renal disease potentially allows directed disease alleviation at community level by prior intervention. PRF management and treatment to modifiable risk factors may improve the wellbeing of the patients by compromising disease progression towards end stage renal disease (ESRD). These approaches in long run will ease the economic burden of the consequent public health expenditure. In this context, risk factor distribution among chronic kidney disease patients in the affected areas deserves attention.

METHODS

Two cross sectional studies were conducted in Padaviya (PDV, 2016-2017), and Girandurukotte/ Mahiyanganaya (GK/MH, 2017-2018) in North Central and Uva provinces respectively. The areas are known to be endemic to CKDu with high disease prevalence as compared to the rest of the country. The studies collected spot urine, whole blood and risk factor data from volunteer subjects to span all CKD stages and a control group with sufficient renal health. The subjects were subsequently sorted using estimated glomerular filtration rate (eGFR; mL/min per 1.73 m²) and urine albumin to creatinine ratio (UACR, mg/g) into CKD/CKDu and control groups as mentioned below in this section. Delineation between CKD and CKDu remains obscure in individual medical records and in local medical practice, thus a tendency to designate the disease as CKD/CKDu occurs [7]. Similarly, the study presumably involved CKD and CKDu cases and attempted to assess and compare between two using the history of initiation risk factors. Study areas were comparable in the contexts of climate, subculture and socioeconomics as the subjects were predominantly from rural paddy farming communities supported by irrigation water.

In Padaviya, patients undergoing treatments for chronic kidney disease at the renal clinic of the district hospital, and individuals who were presumably of renal health from the same general area participated in the study. The latter constituted the endemic control. Total subject participation was 178 (all male, age range:

36-79 yrs). The study also included a nonendemic control group from Padalangala (PDL) in Sabaragamuwa province which is geographically non-contiguous to the North Central Province. The area was not considered as CKDu endemic. In Girandurukotte and Mahiyanganaya, participants were either suspected or diagnosed CKD/ CKDu patients identified during community screening program conducted by the Renal Disease Prevention and Research Unit (RDPRU) of the Ministry of Health, Nutrition and Indigenous Medicine, Sri Lanka. An endemic control group with apparently good renal health was constituted from the general population of the area. Total subject participation was 172 (gender: random, age range: 19-86 yrs).

Subject participation was on volunteer basis following verbal and informed consent. Only males were recruited in PDV and PDL where as both males and females were involved randomly in GK/MH. Serum creatinine (mg/dL), urine albumin (mg/L) and urine creatinine (mg/dL) were measured by standard methods of clinical determination in compliance with respective producer-manuals and quality control (QC) standards at laboratories of Padaviya hospital (PDV samples), Padaviya and Venus Hospital (GK/MH samples), Polonnaruwa. Estimated glomerular filtration rate (eGFR; mL/min per 1.73 m²) was determined using serum creatinine. For the purpose, chronic kidney disease epidemiology collaboration (CKD-EPI) equation was used. Urine albumin to creatinine ratio (UACR mg/g) which is unaffected by urine concentration was estimated as the ratio of urine albumin to urine creatinine.

Subjects were verified and sorted into the CKD stages and control group in both studies using renal dysfunction markers, eGFR and UACR, in agreement with Stevens and Levin [8]. Briefly, the subjects were assigned to disease progression stages, G1, G2, G3a, G3b, G4 and G5 when they were within eGFR ranges of >89, 60-89, 45-59, 30-44, 15-29 and <15 respectively. However, subjects were confirmed to be at G1 or G2 only if they further had a UACR at or greater than 30. Individuals having an eGFR greater than or equal to 90 with UACR equal to or lower than 29 were considered to be with adequate renal health hence in the control. Provisional G2 subjects with eGFR equal to or lower than 29 were excluded from the study as their renal status was inconclusive with the dysfunction markers employed in the study. Finally, stages G1 through G5 were merged as total CKD and considered against respective control groups.

The study followed the established CKD risk factors (traditional risk factors) of each individual participant as put forward by the National Kidney Foundation of USA [4]. The risk factor data were collected by an authorized medical practitioner as answers to a questionnaire through subject interview. Subjects were gently cross-examined for verification and elimination of recall bias. Diabetes mellitus, hypertension, autoimmune diseases, systemic infections such as malaria and leptospirosis, urinary tract (UT) infections, urinary stones, lower UT obstructions, cardiovascular diseases, dyslipidemia, liver diseases, drug toxicity, snake bites, family history of kidney disease and history of acute kidney disease were considered as initiation risk factors (IRF) when those existed prior to initial diagnosis of the disease. Diabetes mellitus, high blood pressure, and smoking were considered as progression risk factors (PRF) if those emerged after diagnosis. Questionnaire also spanned demographic risk factors (non-traditional risk factors) suspected to be implicated in CKDu development in the areas, such as education, occupation and domestic water source.

Ethical clearance for the studies, RP/2015/04 dated November 02, 2015 and RP/2017/03 dated July 07, 2017, was obtained from the ethical review committee at the Faculty of Medicine, General Sir John Kotelawala Defence University, Sri Lanka.

Statistical analyses

Risk factor prevalence was compared between control and CKD groups using Chi square goodness of fit test. The hypothesis tested was, 'the occurrence of the IRF between CKD and non CKD groups was not different'. The test was conducted independently for each risk factor. The expected values were estimated according to McHugh [9]. Statistical significance ($p < 0.05$) suggested a known aetiology hence CKD rather than CKDu with regard to the IRF considered. Complementarily, odds ratio (OR) was determined with 95% confidence interval for IRF, and demographic factors. Odds > 1 at $p < 0.05$ pointed to an association.

RESULTS

The study followed medical (traditional) and demographic (non-traditional) risk factors pertaining to the chronic kidney disease in two areas endemic to the chronic kidney disease of unknown aetiology in North Central and Uva provinces of Sri Lanka. In both areas, substantial percentage of CKD subjects reported IRF that existed prior to medical diagnosis (Table 1 and Figure 1). However, IRF prevalence was higher among healthy subjects as well. In Padaviya (PDV), about 92% of the CKD affected had IRF as compared to 85.7% in the endemic control group from the same area while in the nonendemic control group from PDL had IRF in 71.4% of the subjects. In GK/MH, 69.5% reported IRF among the CKD affected while its endemic control group reported 41.7% (data not shown).

Chi square analyses showed that CKD development statistically associated only with hypertension ($p < 0.01$) in GK/MH and with systemic infections ($p < 0.01$), urinary tract infections ($p < 0.05$) and family history of kidney disease ($p < 0.05$) in PDV as IRF (Table 2). Odds Ratio estimation (Table 3) confirmed that likelihood of CKD development increased with systemic infections ($p < 0.01$) and urinary tract infections ($p < 0.05$) in PDV and with hypertension ($p < 0.01$) in GK/MH. Majority of IRF studied however were not associated with CKD development. Occurrence of hypertension at GK/MH was 38.2% among total CKD (data not presented). In PDV, systemic infections predominantly malaria, family history of kidney disease and urinary tract infections were reported by 79.6%, 28.2% and 48.6% CKD subjects respectively. On the other hand, 3.5% and 14.5% of CKD patients did not report any IRF of the study in PDV and GK/MH respectively. These percentage occurrences represent CKD cases excluding control subjects. Major fraction of CKD patients had one or more progression risk factors (PRF). Diabetes mellitus, hypertension and smoking habit occurred among 48.6% and 44.2% of the total CKD in PDV and GK/MH respectively with hypertension as the most common (PDV, 26.06% and GK/MH, 32.06%). About 2.7% of CKD subjects had two PRF each in PDV (data not shown).

The odds of CKD development was greater among males, the subjects with lesser education, and among the subjects who utilized dug-well water for drinking (Table 3). Risk also increased among field farmers by occupation and with agrochemical usage. All the enhanced risks were statistically significant ($p < 0.001$). The risk of CKD rendered by unemployment was 27% lesser compared to those with employment with true population effect between 13-57%.

DISCUSSION

Excluding the control, the volunteer subjects participated in the study at PDV were diagnosed CKD/CKDu patients who were receiving treatments at the renal clinic of the hospital. It was similar in GK/MH where the participants already had symptomatic decrease in eGFR and increase in UACR in serial measures over months in RDPRU screening programs and were patients referred to hospital treatments. Present study recruited the subjects among participants following verification of renal function and sorting into control and CKD/CKDu groups using eGFR and UACR generated from the whole blood and spot urine samples collected. For these reasons, a need for confirmation of the chronic kidney disease using biopsy or ultrasound scanning methods did not arise.

The study sorted subjects between poor renal outcomes and healthy (control) when eGFR and UACR estimates were made following later analyses. Classification did not depend on diagnostic history or subject responses. Subjects for control with both $eGFR \geq 90$ and $UACR \leq 29$ were found to be infrequent among participants in endemic PDV, endemic GK/MH and in nonendemic PDL rendering a statistical constraint. PDL control subjects were not compared with GK/MH patients as there was an unfavourable temporal gap between respective sampling visits, and non-comparable gender composition between two groups. Further, a relatively feasible sample size was emerged for endemic control of GK/MH. Male predominance in CKD/CKDu prevalence in CKDu endemic areas prompted a sampling regime spanning only males in PDV and PDL, which was not considered later in GK/MH with the need to have a quantitatively improved control.

Statistical analyses did not reveal ($p > 0.05$) associations between CKD development and majority of IRF studied (Tables 2 and 3) suggesting that the disease development in endemic PDV and GK/MH areas could not be totally explained by the traditional risk factors in the areas. Substantial and even comparable presence of IRF in both CKD and control groups in the study points to the fact that there could be other factors influencing the induction of the chronic renal failure. However, the involvement of certain medically established initiation risk factors in CKD development, such as hypertension, urinary tract infections, and family history of kidney disease as well as systemic infections was confirmed ($p < 0.05$) by both Chi square test and Odds ratio assessment in the study. IRF profiles apparently differ between PDV and GK/MH (Figure 1). The predominant systemic infections among CKD subjects at PDV were malaria (77.4%) and leptospirosis (2.1%). Multiple episodes of Malaria were reported by almost all subjects who had the infection. Among CKD affected in GK/MH, only 21.4% and 1% reported a history of malaria and leptospirosis respectively. It is known that chronic kidney disease may aetiologically associate with malaria particularly following serial infections [10] as reported in PDV subjects, and with Leptospirosis [11]. The major IRF in GK/MH were hypertension (38%) and family history of kidney disease (37%). With only a fraction of CKD affected traceable to traditional risk factors, the presence of CKD patients without a history of traditional IRF in both PDV (3.5%) and GK/MH (14.5%) remain consistent with the notion that CKD in the areas at least in part may have an unknown or uncertain aetiology (CKDu). Regional differences in IRF profiles are evident among CKDu endemic areas as PDV had more cases in systemic infections mostly malaria (56%), urinary tract infections (36%), and snake bites (27%) as percentage difference compared to GK/MH (Figure 1). Spatial differences of IRF among endemic areas may be expected and such tendencies should help in

Table 1: Risk factor distribution pertaining to chronic kidney disease development in CKDu endemic Padaviya, and Girandurukotte/ Mahiyanganaya areas of Sri Lanka

	NEC-PDL ¹	EC-PDV ²	PDV ³	EC-GK/MH ⁴	GK/MH ⁵
Initiation risk factors					
Diabetes mellitus	7.1	0	9.2	9.8	13
Hypertension	21.4	28.6	31	12.2	38.2
Autoimmune diseases	0	0	0	9.8	10.7
Systemic infections	28.6	64.3	77.5	19.5	21.4
Urinary tract infections	14.3	14.3	48.6	9.8	13
Urinary stones	7.1	0	6.3	4.9	13
Lower urinary tract obstructions	7.1	0	4.2	2.4	9.2
Cardiovascular diseases	7.1	0	7	2.4	12.2
Dyslipidemia	7.1	0	10.6	12.2	15.3
Liver diseases	0	0	0.7	0	1.5
Drug toxicities	0	0	4.9	2.4	2.3
Snake bites	28.6	14.3	38	4.9	11.5
Poisoning	7.1	0	4.2	0	0.8
Family history of any kidney disease	0	42.9	28.2	31.7	37.4
History of acute kidney disease	0	0	3.5	0	3.8
Progression risk factors					
Diabetes mellitus	7.1	0	13	9.8	13
Hypertension	0	7.1	39	12.2	38
Smoking	57.1	21.4	23	2.4	4
Demographic risk factors					
Gender					
Male	100	100	100	22	65
Female	-	-	-	78	35.1
Education					
Illiterate	0	14.3	2.6	2.4	13
Primary education	8.3	0	30.2	9.7	30.5
GCE ordinary level	41.6	14.3	13.1	51.2	19
GCE advance level	16.7	7.1	1.3	17	6.8
Occupation					
Labourer	0	0	1.3	9.7	3.8
Field farmer	91.7	42.8	98	5	55.7
Unemployment	0	0	0.6	58.5	28.2
agrochemical usage	91.7	92.8	94.7	22	61.8
Domestic water source					
Dug-well	91.7	100	81.6	31.7	88.5
Dug-well (purified)	0	0	9.9	none	none
Reservoir	0	0	0	24.4	1.5
Reservoir (purified)	none	none	none	none	none
Harvested rain water	0	0	0.6	2.4	0
ROP water	none	none	none	none	none

NEC: nonendemic control, EC: endemic control, PDL: Padalagala, PDV: Padaviya, & GK/MH: Girandurukotte/ Mahiyanganaya, GCE: General Certificate of Education, ROP: reverse osmosis plant; Data represent percentages from group total n= ¹ 12, ² 14, ³ 152, ⁴ 41, and ⁵ 131, none: not available before diagnosis with CKD

local disease management. IRF differences were reported between CKDu endemic and nonendemic areas in Sri Lanka [12].

The demographic risk factors that rendered significant risks of developing the disease showed over lapping but different patterns between the areas. The results in general confirmed

increased vulnerability of males, field farmers and those with lesser education in both endemic areas. CKD/CKDu predominance among male farmers with lesser education has been in agreement with previous reports [13]. Unemployment in fact tended to reduce the risk suggesting perhaps that CKD is

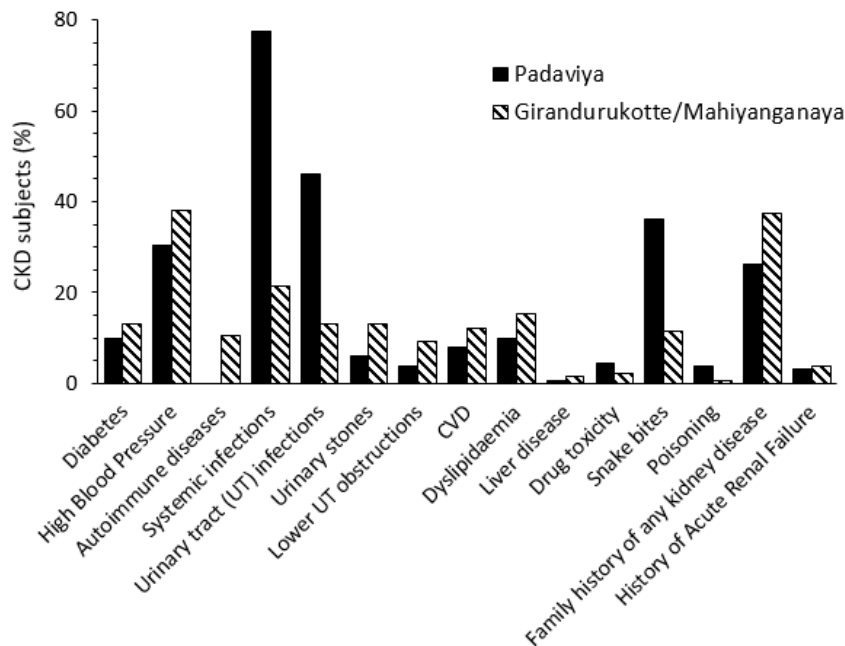


Figure 1: Initiation risk factors that existed prior to the development of chronic kidney disease in subjects of CKDu endemic areas of Sri Lanka. Data were obtained by interview n=152, and 131 in Padaviya, and Girandurukotte/ Mahiyanganaya respectively CKD subjects were identified as G1, G2, G3a, G3b, G4 and G5 by eGFR >89, 60-89, 45-59, 30-44, 15-29 and <15 respectively. Then, G1 or G2 were confirmed when UACR ≥ 30. eGFR ≥ 90 with UACR ≤ 29 was considered healthy and excluded. G2 with eGFR ≤ 29 were excluded as their renal status was inconclusive. Stages G1 through G5 were subsequently merged as total CKD (Stevens and Levin, 2013).

Table 2: Association of initiation risk factors with chronic kidney disease in CKDu endemic areas of Sri Lanka

	Padaviya ¹	Padaviya ²	Girandurukotte/ Mahiyanganaya ³
Diabetes mellitus	1.52	0.03	0.3
Hypertension	-	0.93	9.68**
Autoimmune diseases	-	-	0.03
Systemic infections	1.25	11.22**	0.06
Urinary tract infections	3.17	6.46*	0.3
Urinary stones	-	-	2.08
Lower urinary tract obstructions	-	-	2.01
Cardiovascular diseases	1.16	-	3.35
Dyslipidemia	1.52	0.04	0.23
Liver diseases	1.57	-	-
Drug toxicities	-	-	-
Snake bites	2.68	0.62	1.51
Poisoning	-	-	-
Family history of any kidney disease	1.85	4.21*	0.44
History of acute kidney disease	-	-	-

Data represent χ^2 . Chi square goodness of fit test tested the null hypothesis “the occurrence of the risk factor was not different between healthy and CKD subjects”, with degrees of freedom =1, n=152, and 131 in Padaviya, and Girandurukotte/ Mahiyanganaya respectively. In comparison to ¹ endemic control (n=14), ² nonendemic control (n=12) or ³ endemic control (n=41) * p <0.05, ** p <0.01, Subject sorting was done as in Figure 1 foot note. - Test requirements were not met.

linked to an occupational hazard or else has employment related aetiology. Agrochemical application and usage of dug-well water increased the risk of the disease in GK/MH in consistent with the fact that both practises have long been considered as CKD/CKDu risk factors in endemic areas of Sri Lanka [14]. However it should be noted that in the community and at individual level, these factors remain linked and the statistical associations noted could perhaps be incidental rather than causal. Likelihood of being unrelated in spite of coexistence ought to be a consideration in community based studies. Further, possibility of CKD development linked to consumption of unpurified reservoir-water

and harvested rain-water when the study subjects were presumably undergoing disease development was not considerable in both study areas (Table 3). Drinking water quality has often been a concern in relation to CKD/CKDu development in endemic areas so that numerous water borne factors were received attention in literature in relation to the chronic renal failure. Those include metals [15], fluorides [16], water hardness [17], agrochemicals, and local hydrogeochemistry [18]. The results hardly go beyond field associations and remain inconclusive mainly due to scarcity of mechanistic data that can reveal causal links to renal tissue damage as the endpoint.

Table 3: Odds of chronic kidney disease development with risk factors in CKDu endemic areas of Sri Lanka

	Padaviya ¹	Padaviya ²	Girandurukotte/ Mahiyanganaya ³
Initiation risk factors			
Diabetes mellitus	1.55 (0.18-12.3)	1.20 (0.14-9.99)	1.38 (0.43-4.36)
Hypertension	0.87 (0.25-3.03)	2.17 (0.46-10.3)	4.44 (1.63-12.1) **
Autoimmune diseases	0.09 (0.01-1.44)	0.04 (0.01-0.46) *	1.11 (0.34-3.57)
Systemic infections	1.15 (0.30-4.51)	6.94 (1.97-24.4) **	1.12 (0.47-2.70)
Urinary tract infections	2.56 (0.67-9.83)	9.39 (1.18-74.5) *	1.38 (0.43-4.36)
Urinary stones	0.90 (0.11-7.62)	0.69 (0.08-5.97)	2.91 (0.64-13.1)
Lower urinary tract obstructions	0.63 (0.07-5.54)	0.45 (0.05-4.10)	4.03 (0.51-32.0)
Cardiovascular diseases	1.20 (0.14-9.90)	1.20 (0.14-9.90)	5.56 (0.71-43.3)
Dyslipidemia	1.55 (0.18-12.3)	1.20 (0.14-9.99)	1.30 (0.45-3.70)
Liver diseases	1.17 (0.01-2.01)	0.08 (0.01-1.45)	1.60 (0.07-34.0)
Drug toxicities	0.71 (0.08-6.14)	0.71 (0.08-6.14)	0.94 (0.09-9.27)
Snake bites	2.83 (0.60-13.4)	1.70 (0.44-6.55)	2.52 (0.55-11.5)
Poisoning	0.62 (0.07-5.42)	0.45 (0.05-4.10)	0.95 (0.04-23.9)
Family history of any kidney disease	0.35 (0.11-1.17)	4.72 (0.60-37.2)	1.29 (0.61-2.72)
History of acute kidney disease	0.53 (0.06-4.72)	0.53 (0.06-4.72)	3.61 (0.19-66.7)
Demographic risk factors			
Gender			
Male	-	-	6.57 (2.29-14.9) ***
Female	-	-	0.15 (0.07-0.34) ***
Education			
Illiterate	0.16 (0.03-0.98)	0.44 (0.05-4.02)	5.56 (0.71-43.3)
Primary education	6.60 (0.84-51.3)	4.77 (0.60-38.1)	4.25 (1.93-9.37) ***
GCE ordinary level	0.91 (0.19-4.36)	0.21 (0.06-0.73)*	0.91 (0.31-2.69)
GCE advance level	0.17 (0.01-2.04)	0.07 (0.01-0.52)**	0.37 (0.03-4.23)
Occupation			
Labourer	0.30 (0.03-3.05)	0.26 (0.02-2.66)	1.16 (0.31-4.38)
Field farmer	66.2 (13.9-314)***	4.51 (0.43-47.1)	18.6 (5.47-63.5) ***
Unemployment	0.20 (0.02-2.31)	0.17 (0.01-2.01)	0.27 (0.13-0.57) ***
Agrochemical usage	1.38 (0.16-11.9)	1.64 (0.19-14.3)	6.15 (2.71-14.0) ***
Domestic water source			
Dug-well	2.09 (0.04-2.26)	0.40 (0.05-3.25)	42.6 (15.5-117.2)***
Dug-well (purified)	1.74 (0.21-14.0)	1.51 (0.18-12.3)	none
Reservoir	0.10 (0.01-1.65)	0.08 (0.01-1.44)	0.62 (0.05-7.02)
Reservoir (purified)	none	none	none
Harvested rain water	0.20 (0.02-2.31)	0.17 (0.01-2.01)	0.29 (0.02-4.80)
ROP water	none	none	none

n=152, and 131 in Padaviya, and Girandurukotte/ Mahiyanganaya respectively. In comparison to ¹ endemic control (n=14), ² nonendemic control (n=12) or ³ endemic control (n=41). Data represent Odds Ratio (95% confidence interval) and statistical significance * p <0.05, ** p <0.01 based on Z test. Subject sorting was done as in Figure 1 foot note. Acronyms are as in Table 1 foot note. -: did not assess, none: did not exist before diagnosis with CKD

Occurrence of one or more progression risk factors (PRF) in CKD/CKDu patients was substantial in both CKDu endemic areas studied. This raises the opportunity of PRF management for improvement of the patient wellbeing. It can be achieved by identification and correction of health related quality of life (HRQOL) determinants of CKD [19]. The context urges HRQOL assessment practices pertaining to the disease in PDV and GK/MH areas.

CONCLUSION

The results indicate that the disease chronic kidney development in

both PDV and GK/MH areas may not be explained by traditional risk factors alone, and certain non-traditional risk factors such as education level, occupational application of agrochemicals, and domestic usage of dug-well water appeared to be influencing it. Feasibility for enhanced patient wellbeing occurs in the endemic areas *via* PRF management.

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