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Burden of Diabetes Mellitus in a Community Resident in an Area Designated as "High Risk" for Chronic Kidney Disease of Unknown Origin in Sri Lanka

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Abstract

Chronic kidney disease (CKD) where etiology cannot be attributed to any known etiology is named CKD of uncertain etiology (CKDu). The main aims of this study were to assess the prevalence of diabetes mellitus (DM), treatment coverage, and glycemic control and its effect on renal function of patients with DM in a rural community affected by CKDu in Sri Lanka. A cross-sectional representative household survey (n = 4803) was conducted in Anuradhapura district. A random blood sugar (RBS), blood pressure, bio-impedance measurements, and renal profile were measured using standard instruments and protocols. Prevalence of DM based on self-reports verified by records was 7.9% (95% confidence interval [CI]: 7.1–8.7). Among the 4425 who did not give a history of being diagnosed ever as having DM, 2.1% (95% CI: 1.7–2.5) were classified as "possible diabetes" (RBS of more than 200 mg/dl with no history of DM). Although 76.2% were on treatment, glycemic control was poor in 40.2% (95% CI: 34.9–45.0). The presence of DM was associated with poor renal function. One in ten individuals in the rural district of Anuradhapura has possible DM. DM poses a significant burden to CKD even in populations affected by CKDu. Hence, public health initiatives should be implemented to control both CKDu and DM in these rural communities.

Keywords: Burden, Chronic kidney disease, Community, Diabetes mellitus, High risk

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Background

Diabetes mellitus (DM) is a major public health problem worldwide. A staggering 9.3% of the 20–79 years population (43 million adults) was affected globally in 2019 and is predicted to rise to 10.9% by 2045 (700 million adults).[1] The burden is significant in low and middle-income countries, which share 79.4% of the estimated diabetes population. The Southeast Asian region of the International Diabetes Federation, consisting of Mauritius, India, Bangladesh, Sri Lanka, and Bhutan, is one of the worst affected by the epidemic increase in cases recording the second-highest number of patients with 87.6 million being reported in 2019. Nearly 99% of this total diabetes population in the region live in India, Bangladesh, and Sri Lanka, with Sri Lanka recording the second-highest age-adjusted comparative diabetes prevalence of 10.7%.[1]

A systematic review on the diabetes epidemic in Sri Lanka reported a steady increase in the prevalence with 8.5% reported from a rural area in 2000 to 19.6% reported from an urban area in 2007. The analysis of secular trends in the different provinces of the country shows that from 2000 to 2006, the highest provincial increase in the prevalence of diabetes was observed in the Southern province (60.6%) followed by the North Central (27.1%) and Western province (6.4%).[2]

DM is a chronic disease characterized by hyperglycemia and increased risk of microvascular and macrovascular damage.[3] Chronic kidney disease (CKD) is a well-known microvascular complication of DM.[4] Several studies have demonstrated that good glycemic control could lower the risk of nephropathy among patients with DM.[5,6] With the high prevalence of DM observed in the North Central province of Sri Lanka,[2] it is expected that the prevalence of diabetes nephropathy, which could ultimately lead to CKD, should also be higher. However, a systematic assessment of the contribution of diabetes nephropathy to the total CKD burden has not been conducted so far neither in North Central province nor in Sri Lanka. This is of special importance in the backdrop where, since the early 1990's, there are records of an exponential increase in the number of cases of CKD, which are not attributed to any known etiology in Sri Lanka. The North Central province, one of the nine provinces in the country, has recorded the highest number of CKD of unknown etiology (CKDu).[7] This double burden of CKD, that is, CKDu and CKD due to diabetes nephropathy, has continued to affect the communities within this province despite a significant lack of studies on their burden. Recently, there have been attempts to quantify the prevalence of CKDu in the province, which has shown that 6% of adults suffering from CKDu.[8] However, the effect of diabetes control on renal function has not been carried out so far.

Considering diabetes to be a potential cause for CKD, our main aim of this analysis was to estimate the prevalence of

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diabetes, assess the status of glycemic control and its effect on renal function of patients with diabetes in North Central province of Sri Lanka. This will provide the information on the burden of diabetes and its potential effect to add on to the CKD burden in this CKDu affected population in North Central province, Sri Lanka. Given the primacy of the predominantly agricultural rural population in the North Central province, we also assessed how individual characteristics of the people affected the prevalence of diabetes in the province. The evidence generated from this paper will help to better understand the burden of DM in a rural CKDu-affected community in Sri Lanka. Furthermore, the evidence could be used to develop targeted interventions to reduce the burden of DM as well as CKD in this community.

MATERIALS AND METHODS

Study Design and Study Setting

We designed this cross-sectional community-based household survey primarily to estimate the extent of impaired kidney function in the district of Anuradhapura, Sri Lanka, which has the highest burden of CKDu in the country.[9] Anuradhapura district is an agricultural district and farming is the main occupation of its residents. Three Divisional Secretariat areas of the district were sampled and within each, five geographically demarcated locations comprising 2–4 villages adjacent to each other were selected as the study areas. The basis for the geographical demarcation was to include approximately 1000 potentially eligible adult residents.

Study Participants

We invited all adults above the age of 18 years, whose main place of residence (defined as living in the setting for at least 5 days of the week for the past 6 months) was in the study area. We excluded pregnant women and patients undergoing treatment for cancer.

Sample Size and Sampling Technique

The required sample size of 1000 from each of the five study areas, totaling 5000, was estimated to determine the population prevalence of impaired kidney function in the Anuradhapura district.[8] We confirmed that this sample size allows accurate estimation of the prevalence of DM with enough statistical power for comparisons between population subgroups.[10] Eligible adult residents from each of the five areas were selected from the official updated voters' lists of local administrative officers. Upon visiting the households of the selected participants information on the study was provided and written consent obtained before recruitment.

Data Collection

Graduates from a University located in the district were trained for data collection. The interviewer-administered questionnaire gathered data on a previous diagnosis of DM and its treatment coverage (i.e., whether they were prescribed oral hypoglycemic or insulin and their adherence to the prescription at the time of the study). The medical records were photographed and were used to validate the accuracy of the self-reported information. The questionnaire also inquired into the history of other non-communicable diseases (NCDs), socio-demographic, and lifestyle characteristics of the participants. Upon completion of the questionnaire, the study participants were given a container and an instruction sheet on collecting the early morning urine sample. They were requested to visit the "clinic" on the following day for the anthropometry measurements and blood sample collection. The "clinics" were held within the study areas in locations acceptable and accessible to study participants and around 100 were invited to each clinic. The data collectors revisited the houses to recruit any eligible study participants who were not available at the time of the first visit.

In the clinics, trained nurses performed the random capillary blood sugar measurements using a calibrated automated glucometer. Samples of 5 ml of blood were drawn for measurements of serum creatinine and samples of overnight urine were collected for measurement of urine proteins. The height and weight of the participants were measured to calculate the body mass index (BMI). Three blood pressure readings, 5 min apart from each measurement, were taken with the participant in a seated position using an electronic blood pressure apparatus.

We tested the serum creatinine and urine protein: Creatinine ratio in the laboratory of the Anuradhapura Teaching Hospital which is the tertiary level hospital that caters to the population of the district. Serum creatinine was measured using assays calibrated utilizing quality controls traceable to isotope dilution mass spectrometry standards.

We obtained Institutional Ethics Committee approval from the Ethics Review Committee of the Faculty of Medicine, University of Colombo (EC-17-031).

Data Analysis

The proportion of study units with DM at recruitment was estimated based on self-reports of diagnosis verified by medical records. Univariable and multivariable logistic regression analysis was applied to identify socio-demographic, lifestyle, biological, and comorbid factors associated with self-reported DM. In addition, those who recorded a random capillary plasma blood sugar of more than 200 mg/dl during the survey were categorized as cases of "possible diabetes."

We further developed multivariable logistic regression models to assess the independent association between DM and renal function, keeping estimated glomerular filtration rate (eGFR) level <60 ml/min/1.7 $m^2$and urine albumin-creatinine ratio (ACR) >30 mg/g as dependent variables. The other factors controlled in the models were age, sex, current smoking status, current alcohol consumption status, BMI, presence of hypertension, and ever occupied in farming.

A $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of the Study Participants

Of the 5000 individuals approached, 4803 consented to participate, giving an overall response rate of 88.7%. The majority were female (68.2%). Nearly half (46.3%) were in the age category of 31–50 years and were engaged in full-time farming (46.6%).

Prevalence of DM in the Population

Table 1 describes the prevalence of DM at recruitment, based on self-reports and verified by medical records. Overall prevalence of DM at recruitment was 7.9% (*n* = 378) (95% confidence interval [CI]: 7.1–8.7) and was higher among females (8.3%; 95% CI: 7.3–9.3) compared to males (6.9%; 95% CI: 5.7–8.2), though the difference was not statistically significant. The age group of 51–70 years (14.2%; 95% CI: 12.7–16.0) showed the highest prevalence among both males (10.7%; 95% CI: 8.4–13.2) and females (16.3%; 95% CI: 13.8–18.6).

Among the 4425 who did not give a history of being diagnosed ever as having DM, 2.1% (*n* = 92, 95% CI: 1.7–2.5) were classified as "possible diabetes" based on an RBS of more than 200 mg/dl [Table 2]. The proportions of "possible diabetes" were similar among males and females (males 2.5%; 95% CI: 1.7–3.3 and females 1.9%; 95% CI: 1.4–2.4). The proportions showed an increasing trend with age, though the differences were statistically not significant.

Prevalence of diabetes when those known to be diabetic at recruitment and those classified as "possible diabetes" combined was 9.8% (95% CI: 8.9–10.7) with no gender difference in prevalence (males– 9.2%; 95% CI: 7.8–10.7; females– 10.0; 95% CI: 9.1–11.1). The prevalence estimates increased with increasing age [Table 3]. Those classified as "possible diabetes" made up 19.5% of all diabetic individuals.

Table 1: Prevalence of known diabetes mellitus by sex and age category

	Prevalence (95% confidence interval)		
	All	*Male*	*Female*
Total population (*n*=4803)	7.9 (7.1–8.7)	6.9 (5.7–8.2)	8.3 (7.3–9.3)
Age categories			
18–30 (*n*=774)	0.8 (0.3–1.4)	0.5 (0.0–1.6)	0.8 (0.2–1.7)
31–50 (*n*=2225)	5.3 (4.4–6.2)	5.0 (3.5–6.6)	5.4 (4.4–6.5)
51–70 (*n*=1573)	14.2 (12.7–16.0)	10.7 (8.4–13.2)	16.3 (13.8–18.6)
>70 (*n*=231)	13.0 (8.7–17.3)	10.5 (4.2–17.9)	14.7 (9.6–20.6)

Table 2: Proportion of "possible diabetes" among those without a history of the disease by sex and age category

	Prevalence (95% confidence interval)		
	All	*Male*	*Female*
Total population (*n*=4425)	2.1 (1.7–2.5)	2.5 (1.7–3.3)	1.9 (1.4–2.4)
Age categories			
18–30 (*n*=768)	0.4 (0.0–0.9)	0.0	0.5 (0.0–1.2)
31–50 (*n*=2107)	2.0 (1.4–2.6)	2.6 (1.4–4.0)	1.7 (1.1–2.4)
51–70 (*n*=1349)	2.8 (2.0–3.7)	2.8 (1.4–4.3)	2.9 (1.8–4.3)
>70 (*n*=201)	4.5 (1.9–7.5)	4.7 (1.1–9.8)	4.3 (0.9–8.3)

Table 3: Prevalence of diabetes in the study population by sex and age category (*n*=470)

	Prevalence (95% confidence interval)		
	All	*Male*	*Female*
Total population (*n*=4803)	9.8 (8.9–10.7)	9.2 (7.8–10.7)	10.0 (9.1–11.1)
Age categories			
18–30 (*n*=774)	1.2 (0.5–1.9)	0.5 (0.0–1.6)	1.4 (0.5–2.5)
31–50 (*n*=2225)	7.2 (6.2–8.2)	7.5 (5.6–9.5)	7.1 (5.7–8.4)
51–70 (*n*=1573)	16.7 (14.7–18.4)	13.2 (10.4–16.0)	18.6 (16.3–21.0)
>70 (*n*=231)	16.9 (11.7–21.6)	14.7 (8.4–22.1)	18.4 (11.8–25.0)

Treatment Coverage and Glycemic Control

Treatment coverage of DM was based on the proportion of study units with DM at recruitment who reported that they adhered to the prescribed medication (oral hypoglycemic and/or insulin) in the prescribed frequency.

The majority among those who had been diagnosed as having diabetes at recruitment were on treatment with oral hypoglycemic or insulin (76.2%; 95% CI: 71.4–79.9). The treatment coverage was similar among females (77.2%; 95% CI: 72.1–82.4) and males (73.6%; 95% CI: 65.1–81.1) [Table 4]. Except those aged 18–30 years, the majority in other age categories reported that they were prescribed to be on medication and that they were adhering to the treatment.

The glycemic control of those with a history of diabetes was assessed using random blood sugar (RBS) test and values >200 g/dl were considered as indicative of uncontrolled diabetes. Accordingly, 40.2% (*n* = 152, 95% CI: 34.9–45.0) had poor control with males reporting a higher percentage of poor control though statistically not significant (males: 46.2%, 95% CI: 36.8–55.7; females: 37.9%, 95% CI: 32.4–43.8). Those in the age category of 31–50 years had the highest proportion with poor glycemic control [Table 5].

In the multivariable analysis, increasing age (adjusted odds ratio [aOR] 1.046, 95% CI: 1.036–1.056), having a family history of diabetes (aOR 4.504, 95% CI: 3.530–5.747), having high blood pressure (aOR 3.502, 95% CI: 2.727–4.496), and having a higher BMI were found to increase the risk of diabetes [Table 6].

Effect of DM on the Renal Profile

We further explored the effect of diabetes on the renal profile of patients with diabetes controlling for socio-demographic factors, behavioral factors, physical parameters, and prevalence of hypertension [Table 7].

The presence of DM was independently associated with renal function and urine ACR. Patients with diabetes had 1.51 times and 3.01 times the likelihood of having an e-GFR level <60 and urine ACR >30 mg/g, respectively, when controlled for age, sex, current smoking, current alcohol consumption, BMI, hypertension, and ever occupied in farming.

Discussion

We assessed the prevalence and control of DM and its effects on the renal profile of a rural population at risk for CKDu to assess the contribution of diabetes to the cumulative burden of kidney disease in the population. To the best of our knowledge, this is the first such attempt to conduct an in-depth analysis of a rural community severely affected by CKDu.

We found the prevalence of diabetes to be 9.8% (95% CI 8.9–10.7), including those already diagnosed with the disease or classified as "possible diabetes" from a high RBS test, which corresponded with the prevalence rate of 9.6% reported in a national survey for the North Central province in 2006.[11] Given the increasing trend in the prevalence of diabetes overall, this value may be an underestimation considering the lapse of 10 years since the 2006 study and could be attributed to the difference in the testing methods used to classify diabetes status in the two studies. The national survey in 2006 was conducted

Table 4: Treatment coverage among diagnosed diabetes mellitus by sex and age category (*n*=288)

	Prevalence (95% confidence interval)		
	All	*Male*	*Female*
Total population (*n*=378)	76.2 (71.4–79.9)	73.6 (65.1–81.1)	77.2 (72.1–82.4)
Age categories			
18–30 (*n*=6)	33.3 (0.0–66.7)		40.0 (0.0–80.0)
31–50 (*n*=118)	71.2 (62.7–79.7)	76.5 (61.8–88.2)	69.0 (58.4–78.6)
51–70 (*n*=224)	79.0 (73.2–83.9)	72.1 (60.7–82.0)	81.6 (75.5–87.1
>70 (*n*=30)	83.3 (70.0–93.3)	80.0 (50.0–100.0)	85.0 (70.0–100.0)

Table 5: Poor glycemic control (RBS >200 mg/dl) among known patients with diabetes mellitus at recruitment by sex and age category

	Prevalence (95% confidence interval)		
	All	*Male*	*Female*
Total population (*n*=378)	40.2 (34.9–45.0)	46.2 (36.8–55.7)	37.9 (32.4–43.8)
Age categories			
18–30 (*n*=6)	33.3 (0.0–66.7)		40.0 (0.0–80.0)
31–50 (*n*=118)	50.8 (41.5–59.3)	47.1 (29.4–61.8)	52.4 (41.7–63.1)
51–70 (*n*=224)	38.8 (33.0–45.1)	50.8 (37.7–63.9)	34.4 (26.4–41.7)
>70 (*n*=30)	10.0 (0.0–100.0)	20.0 (0.0–50.0)	5.0 (0.0–15.0)

Table 6: Factors associated with diabetes mellitus

Covariates	*Univariable logistic regression odds ratio (95% CI)*				*Multivariable logistic regression adjusted odds ratio (95% CI)*			
	OR	*95% CI*		*Sig.*	*aOR*	*95% CI*		*Sig.*
Age in years	1.06	1.05	1.07	<0.001	1.046	1.036	1.056	<0.001
Sex								
Male	1							
Female	1.21	0.95	1.53	0.53	1.136	.823	1.569	0.438
Ever occupied in farming								
No	1							
Part time farming	2.61	1.89	3.60	<0.001	1.193	.825	1.724	0.348
Full time farming	1.79	1.31	2.46	<0.001	.930	.657	1.316	0.682
Family history of diabetes								
Present	3.92	3.15	4.88	<0.001	4.504	3.530	5.747	<0.001
Absent	1							
Current use of alcohol								
Present	0.62	0.46	0.87	0.004	0.908	0.583	1.414	0.668
Absent	1							
Current smoking								
Present	0.51	0.31	0.82	0.006	0.665	0.376	1.175	0.160
Absent	1							
Hypertension								
Present	6.13	4.91	7.66	<0.001	3.502	2.727	4.496	<0.001
Absent	1							
Body mass index (kg/m^2)	1.06	1.04	1.08	<0.001	1.047	1.024	1.070	<0.001

Table 7: The effect of diabetes mellitus on the renal profile

Renal parameter (dependent variable in the multivariable logistic regression model)	*Diabetes status (self-reported diabetes mellitus)*	*Multivariate analysis adjusted odds ratio (95% CI)*			
		aOR	*95% CI*		*Sig.*
eGFR level <60	Presence of diabetes mellitus	1.51	1.13	2.01	0.004
	Absence of diabetes mellitus	1			
Urine albumin-creatinine ratio >30 mg/g	Presence of diabetes mellitus	3.01	1.65	5.51	0.001
	Absence of diabetes mellitus	1			

[a]Other independent variables controlled in the model: Age, sex, current smoking, current alcohol consumption, body mass index, hypertension, ever occupied in farming

to assess the prevalence of cardiovascular risk factors and the diabetes status was verified with the oral glucose tolerance test and fasting blood sugar. The proportion newly diagnosed was 36% of all diabetic subjects where "possible diabetes" in the current study only comprised 19.5% of all with diabetes.[12] This also indicates an improvement in access to diabetes care services where more people are screened and diagnosed with the disease. Given that since 2006, many novel service delivery platforms have been introduced in the backdrop of an alarming increase in CKDu in this region, including increased access to screening facilities, there is a higher likelihood of being detected for chronic conditions such as diabetes.[13]

Around 50% or less in each age group had poor control of diabetes, as indicated by random plasma glucose >200 ml. This finding contrasts with proportions reported in other studies in the country. Based on a cutoff of HbA1c of 6.5%, 76.2% of adults aged 35–64 years had poor control in an urban area in the Western province in 2007.[14] Similarly, in the Kalutara district of the Western province, which has urban, rural, and estate populations, 90.4% of adults of the same age group were found to have poor control 2 years later.[15] The lower rates of poor control reported in the current study could be due to the differences in the method used to classify diabetes control or may be a reflection of the improved health services over the years targeting NCDs which may have increased access to healthcare services delivered free at the point of care through government hospitals. Some of the targeted interventions are the introduction of a list of essential drugs at the primary level to improve access to NCD medicines, including antihyperglcemic agents, introduction of clinical practice guidelines for the primary level, and improving the awareness of disease control through health education nurses. The burgeoning private sector has also contributed to improving access to diabetes care services mainly through private practitioners. These private practitioners are government doctors working in the private sector during their off-work times.[16]

Family history of diabetes had the highest likelihood of predicting diabetes (OR: 4.5). Other risk factors associated with an increased risk of diabetes, age, presence of hypertension, and BMI were also well-known risk factors of the disease. We did not observe a relationship between diabetes and farming as an occupation in this predominantly agricultural community which was also not observed for CKDu in the main study.[8]

The presence of diabetes increased the likelihood of impaired kidney function as indicated by significant associations with the eGFR level <60 and urine ACR >30 mg/g. Given that one in ten adults is affected by diabetes, health authorities must be alerted to the contribution of diabetes to the cumulative burden of CKD in the region already significantly affected with CKDu. Health service delivery in the region should be strengthened to detect diabetes patients early, provide adequate treatment, and prevent complications without overly focusing on addressing only CKDu. In contrast to the management of CKDu, the cause of which is not known, there are risk factors that can be modified to reduce the impact of diabetes in the population.

Our study had a couple of limitations. First, blood glucose measurements and eGFR values were also measured only once; thus, misclassification is a possibility. Second, the classification of "possible DM" was made based on the random blood test, which could have resulted in either over or underestimate of the true diabetes prevalence in the study population.

Conclusion

We found that one in ten individuals in this rural community have DM. The treatment coverage is relatively good, though the glycemic control is unacceptable. Couple of modifiable risk factors was identified during the study and targeted primary preventive interventions are recommended. Uncontrolled diabetes mellitus seeming to be contributing significantly to the burden of CKD in this community, in addition to the hit by an epidemic of CKD of unknown etiology.

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Authors' Contributions

SS, PC, NG, NW: Research idea, study design. SS, PC, NG, NW: Statistical analysis and drafting of the manuscript SS, PC, NG, NW, TR: Data analysis/interpretation.

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