

# Nonmedical Factors and Health-Related Quality of Life in CKD in India

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## Abstract

**Background and objectives** Patient-reported outcomes have gained prominence in the management of chronic noncommunicable diseases. Measurement of health-related quality of life is being increasingly incorporated into medical decision making and health care delivery processes.

**Design, setting, participants, & measurements** The Indian Chronic Kidney Disease Study is a prospective cohort of participants with mild to moderate CKD. Baseline health-related quality of life scores, determined by the standardized Kidney Disease Quality of Life 36 item instrument, are presented for the inception cohort ( $n=2919$ ). Scores are presented on five subscales: mental component summary, physical component summary, burden, effect of kidney disease, and symptom and problems; each is scored 0–100. The associations of socioeconomic and clinical parameters with the five subscale scores and lower quality of life (defined as subscale score  $<1$  SD of the sample mean) were examined. The main socioeconomic factors studied were sex, education, occupation, and income. The key medical factors studied were age, eGFR, diabetes, hypertension, and albuminuria.

**Results** The mean (SD) subscale scores were physical component summary score,  $43 \pm 9$ ; mental component summary score,  $48 \pm 10$ ; burden,  $61 \pm 33$ ; effects,  $87 \pm 13$ ; and symptoms,  $90 \pm 20$ . Among the socioeconomic variables, women, lower education, and lower income were negatively associated with reduced scores across all subscales. For instance, the respective  $\beta$ -coefficients (SD) for association with the physical component summary subscale were  $-2.6$  ( $-3.4$  to  $-1.8$ ),  $-1.5$  ( $-2.2$  to  $-0.7$ ), and  $-1.6$  ( $-2.7$  to  $-0.5$ ). Medical factors had inconsistent or no association with subscale scores. The quality of life scores also displayed regional variations.

**Conclusions** In this first of its kind analysis from India, predominantly socioeconomic factors were associated with quality of life scores in patients with CKD.

CJASN 15: 191–199, 2020. doi: <https://doi.org/10.2215/CJN.06510619>

## Introduction

Patient-reported outcomes have gained prominence to assess the effect of care on chronic noncommunicable diseases (1). Health-related quality of life is one such outcome measure. Patients with CKD give more importance to health-related quality of life than mere extension of life. According to an international survey on the hemodialysis population (2), patients and caregivers accorded value to ability to travel, dialysis-free time, dialysis adequacy, and feeling washed out after dialysis over disease-related parameters, hospitalizations, and mortality.

The long course of CKD necessitates understanding of longitudinal changes in health-related quality of life, underscoring the value of quantifying it early in disease course so that the effect of interventions can be evaluated. Health-related quality of life is not, however, an absolute measure, and combinations of patient-related and sociocultural variables will be identified across cultures, countries, and timescales. Recent studies

(3–6) from North America, Australia, Europe, China, and Korea have reported on quality of life in patients with nondialysis CKD. There are few studies from low- and middle-income countries, including those from South or Southeast Asia.

The Indian Chronic Kidney Disease (ICKD) study is a country-wide prospective cohort study recruiting participants with mild to moderate CKD (7). Here, we report on the baseline health-related quality of life in the inception cohort and its correlates with socioeconomic and clinical variables.

## Materials and Methods

### Study Design and Setting

The details of the study design have been published (7). Briefly, the ICKD study is recruiting participants from 11 tertiary care kidney hospitals from all parts of India to capture heterogeneities in terms of ethnicities, regions, and development status. The inclusion criteria are age 18–70 years old and stable CKD with eGFR

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of 30–60 or >60 ml/min per 1.73 m<sup>2</sup> with proteinuria. Organ transplant recipients, those with malignancy, those on immunosuppressive drugs therapy, and those with poor functional status are excluded. Demographic details, diagnosis, comorbidities, clinical details, laboratory details, and treatment details are recorded and stored anonymously in a secure database. Collection of biologic specimens (plasma, serum, urine, and buffy coat) and quality of life assessment are done at baseline and annually. The baseline data collection is completed within 2 weeks of enrolment.

The primary objectives of the study are to elucidate the natural history of CKD and understand the risk factors for progression, complications, hospitalizations, and mortality. The other broad areas being evaluated are sex differences, biomarkers, quality of life, and cost of care. This analysis explores the data on baseline health-related quality of life and its correlates.

The study has approval from the institutional review board at each center, and all participants provide a written informed consent.

### Study Variables

GFR is estimated using the Chronic Kidney Disease Epidemiology Collaboration equation with serum creatinine measured using assays traceable to isotope dilution mass spectrometry reference standards (8). Albuminuria is defined by dipstick positivity. Educational status is categorized as per prevalent educational tiers. Participants who never attended school were categorized as uneducated, those who did not complete 12 years of schooling were categorized as below high school, and those who completed 12 years of education were categorized as completed school. Economic status is categorized into quartiles. Quartile 1 broadly captures usual minimum wage. The second, and third quartiles capture the remuneration of semi-skilled workers, small farmers, or small-time self-employed individuals, while the upper quartile reflects the earnings of white collar workers or successful self-employed individuals. Rural residents were defined as participants residing in villages, and urban residents are those living in areas designated as towns and cities. Hazardous occupational exposure is defined as regular exposure to sand, dust, chemicals, or animals or working barefoot in fields. Participants in white collar jobs or with employment linked to a certain level of education, skill, or training were defined as professionals. Alternative medication use is defined as use of indigenous, ayurvedic, or other unregulated medications, and it is recorded as a binary outcome. Diabetes is defined as fasting plasma glucose  $\geq 126$  mg/dl, glycated hemoglobin  $\geq 6.5\%$ , or use of glucose-lowering drugs. Hypertension is defined as BP  $>140/90$  mm Hg or use of antihypertensive therapy. Presence of cardiovascular disease is defined as history of heart failure, coronary artery disease, prior revascularization, stroke, or peripheral vascular disease. All comorbidities are either self-reported or on the basis of chart review when available. Body mass index (BMI) is categorized as underweight ( $<18$  kg/m<sup>2</sup>), normal (18–25 kg/m<sup>2</sup>), and overweight ( $>25$  kg/m<sup>2</sup>).

### Quality of Life Assessment

The health-related quality of life is assessed by using the Kidney Disease Quality of Life 36 item questionnaire

(KDQOL-36), a validated KDQOL instrument (RAND Corporation, Santa Monica, CA) that is available free for noncommercial purposes (9).

The raw scores are converted to five subscale scores (mental component summary, physical component summary, burden of kidney disease [burden], symptoms and problems of kidney disease [symptoms], and effects of kidney disease [effect]) using the Microsoft Excel tool (KDQOL-36 Scoring Program, v 2.0; UCLA Division of General Internal Medicine and Health Services Research 2001). The first 12 items on the questionnaire are measures of physical and mental functioning, with items about general health, activity limits, ability to accomplish desired tasks, depression and anxiety, energy level, and social activities. The burden of kidney disease subscale (items 13–16) elicits how kidney disease interferes with daily life, takes up time, causes frustration, or makes the respondent feel like a burden. The symptoms and problems subscale (items 17–28) evaluates how bothered a respondent feels by sore muscles, chest pain, cramps, itchy or dry skin, shortness of breath, faintness/dizziness, lack of appetite, feeling washed out or drained, numbness in the hands or feet, nausea, or problems with dialysis access. The effects subscale (items 29–36) elicits information about how bothered the respondent feels by fluid limits, diet restrictions, ability to work around the house or travel, feeling dependent on doctors and other medical staff, stress or worries, sex life, and personal appearance.

Because only participants with predialysis CKD are enrolled in the ICKD study, item number 28a/b (for patients on dialysis) is not applicable and hence, was omitted as per recommendations. Each subscale category is scored between 0 and 100, with higher scores indicating better quality of life. Lower quality of life was defined as score  $>1$  SD below the mean score of the study population.

The KDQOL-36 survey is administered through face-to-face interviews by trained interviewers in local language. All interviewers are health care providers well versed in local languages as well as English, and they were trained before the start of the study. The administration of questionnaire was standardized, and the accuracy of interpretation of participant's responses was independently validated. The training is reinforced in periodic reviews by the project manager and center investigator.

### Study Population and Data

The study was initiated in April 2016. This paper describes all participants who had been enrolled until October 2018.

### Statistical Analyses

We used two types of outcome variables—the continuous subscale scores and the binary lower quality of life for each subscale. Summary statistics are presented as mean and SD or median (25th, 75th percentile) for the continuous variables and percentage for the categorical ones. The KDQOL-36 subscale scores were compared between groups using two-sample *t* tests or ANOVA depending on the number of groups. The prevalence of lower quality of life was compared between different groups using the

**Table 1. Characteristics of participants in the Indian Chronic Kidney Disease study (n=2919)**

Characteristics	Mean±SD, Median (25th, 75th Percentile) or N (%)	Missing N (%)
<b>Socioeconomic factors</b>		
Center-wise distribution		0 (0)
<i>Chandigarh and Shimla<sup>a</sup></i>	596 (20)	
<i>Lucknow</i>	392 (13)	
<i>Varanasi</i>	118 (4)	
<i>Kolkata</i>	216 (7)	
<i>Bhopal</i>	242 (8)	
<i>Nadiad</i>	202 (7)	
<i>Hyderabad</i>	392 (13)	
<i>Chennai</i>	83 (3)	
<i>Vellore</i>	284 (9)	
<i>Pondicherry</i>	394 (13)	
Sex (men)	2009 (69)	0 (0)
Age, yr	50±12	0 (0)
Education		13 (0.4)
<i>Uneducated</i>	747 (26)	
<i>Below high school</i>	911 (31)	
<i>Completed school</i>	421 (14)	
<i>College and above</i>	827 (28)	
Rural residence	1916 (65)	47 (2)
Hazardous occupational exposure <sup>b</sup>	1241 (42)	13 (0.4)
Vegetarian diet	1094 (37)	45 (1)
History of hypertension	2101 (72)	22 (0.8)
History of diabetes	998 (34)	22 (0.8)
History of cardiovascular disease	416 (14)	18 (0.6)
History of use of alternative drugs or medicines	722 (25)	30 (1)
Tobacco use	917 (31)	31 (1)
Medical insurance available	781 (27)	40 (1)
Annual income (United States dollars)	2000 (1000, 5000)	24 (0.8)
<b>Medical characteristics</b>		
BMI, kg/m <sup>2</sup>	25±5	99 (3)
<17.9	1189 (41)	
18–24.9	1458 (50)	
>25	173 (6)	
Systolic BP, mm Hg	134±20	162 (5)
Diastolic BP, mm Hg	84±12	168 (6)
eGFR, ml/min per 1.73 m <sup>2</sup>	41.9 (35, 52)	
30–44.9	1738 (59)	
>45–59.9	810 (28)	
>60	371 (13)	
Albuminuria (dipstick positive)	1049 (36)	148 (5)
<i>Nil</i>	1722 (59)	148 (5)
<i>Trace</i>	281 (10)	
1+	287 (10)	
2+	228 (8)	
3+	173 (6)	
4+	80 (3)	
<b>Causes of CKD</b>		
<i>Unknown</i>	727 (25)	
<i>Diabetic kidney disease</i>	593 (20)	
<i>Chronic interstitial nephritis</i>	581 (20)	
<i>GN</i>	368 (13)	
<i>Polycystic kidney disease</i>	90 (3)	
<i>Hypertensive nephrosclerosis</i>	213 (7)	
<i>Others</i>	347 (12)	

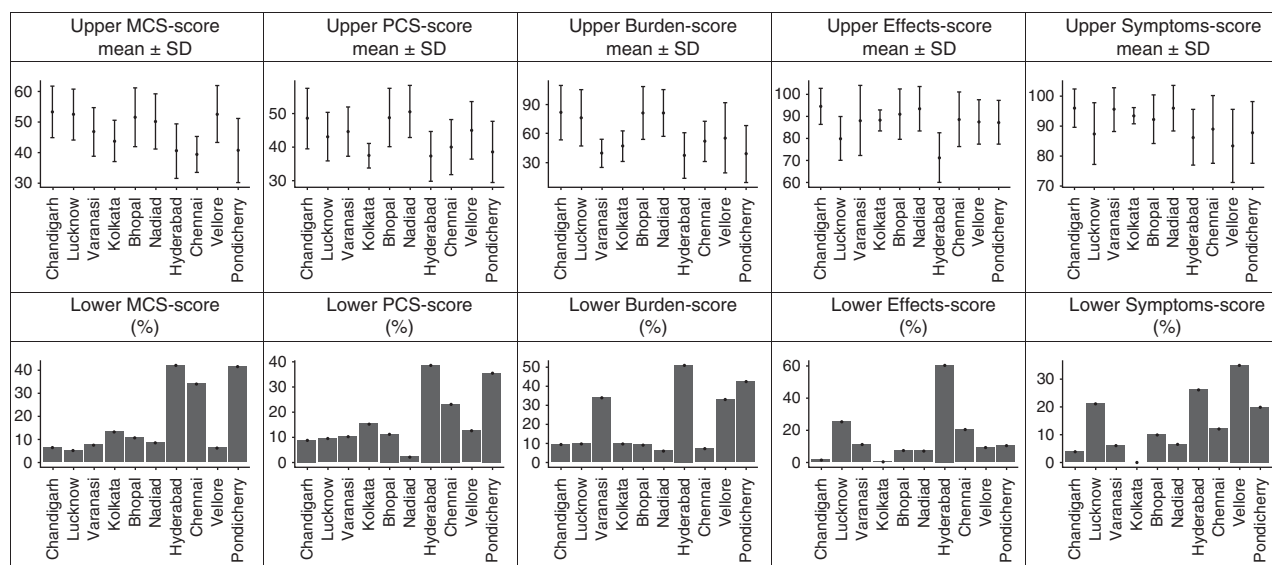
Rural residents are defined as participants residing in villages. Vegetarian indicates the consumption of plant-based food and milk/milk products. BMI, body mass index.

<sup>a</sup>Participants from Shimla and Chandigarh are presented together because of geographic certainty and small numbers of participants from Shimla.

<sup>b</sup>Occupational exposure: work amid sand, dust, chemicals, or animals or working barefoot in fields.

chi-squared test. Multivariable linear and logistic regressions were carried out for the subscale scores and lower quality of life variables, respectively, to identify independent risk factors associated with health-related quality of

life. The risk factors considered in the multivariable regressions were age, sex, rural/urban residence, educational attainment, occupation, dietary habits, tobacco use, alternative drug use, household income, BMI, hypertension,



**Figure 1. | Distribution of Kidney Disease Quality of Life scores and lower quality of life subscale scores across different centers.** Lower quality of life defined as score 1 SD below the mean. MCS, mental component summary; PCS, physical component summary.

diabetes, cardiovascular disease, albuminuria, and eGFR. We also adjusted for center in the linear and logistic regressions to account for differences across centers. Individuals with missing covariates were automatically dropped from the regressions, because we conducted a complete patient analysis. For ease of comparison between risk factors, we present in Supplemental Tables 1–4 the standardized  $\beta$ -coefficients from the linear regression along with unstandardized  $\beta$ -coefficients in the text that are more easily interpretable. Two-sided  $P$  value  $<0.05$  was considered to be significant. Analyses were carried out using the SPSS for Macintosh, version 21.0 (IBM SPSS, Chicago, IL) and Microsoft Excel for Macintosh, version 15.36 (Microsoft Corporation, Washington, WA).

## Results

### Participant Characteristics

Of the 3073 patients who had been enrolled in the ICKD study until October 31, 2018, KDQOL-36 data were available for 2919 participants. Data specific to mental component summary and physical component summary subscales were missing in 101 (3.5%) participants. Table 1 presents the socioeconomic and clinical characteristics. The mean age was 50 years old; 69% were men, and 66% came from rural areas. About 26% were illiterate, and 31% had not completed schooling; 63% of participants reported being nonvegetarian (average meat intake: 4.8 times per month). Engagement in hazardous occupations was recorded in 43% of participants. About 72% were hypertensive, 34% were diabetic, and 14% had a history of cardiovascular disease. Around 31% were tobacco users, and 25% had used alternative drugs. The baseline characteristics of participants with missing data were similar to those of participants with complete data (Supplemental Table 1). Figure 1 presents the distribution of KDQOL-36 subscale scores across different centers.

### Health-Related Quality of Life Scores and Their Associations

The KDQOL-36 subscale scores were physical component summary score,  $43 \pm 9$ ; mental component summary score,  $48 \pm 10$ ; burden,  $61 \pm 33$ ; effects,  $87 \pm 13$ ; and symptoms,  $90 \pm 10$ . Table 2 presents the distribution of the subscale scores.

**Socioeconomic Correlates.** Women, rural residence, education below high school, nonvegetarian dietary pattern, being a nonprofessional, and lower income were associated with lower quality of life scores across all five subscales. Participants engaged in hazardous occupations had lower scores on the mental component summary, physical component summary, and burden subscales. Those who used alternative drugs had better scores on mental component summary, physical component summary, and burden scales and worse scores on the symptoms scale.

**Clinical Correlates.** Lower BMI and diabetes were associated with worse quality of life scores across all of the subscales. Albuminuria, on the contrary, showed positive association on all subscale scores. Age  $>50$  years old, cardiovascular disease, and lower eGFR were associated with worse scores on the mental component summary, physical component summary, and burden subscales. In contrast, participants with hypertension had higher scores in all subscales except the symptoms subscale (Table 2).

### Health-Related Quality of Life Scores and Adjusted Analyses

In multiple linear regression analyses, lower education and lower incomes were significantly associated with lower scores across all subscales. Women showed significant negative association with mental component summary, physical component summary, effects, and symptoms subscales (Table 3). Age  $>50$  years old was positively associated with the burden subscale score but negatively associated with physical component summary and symptoms scores. Diabetes was negatively associated with the physical component summary score, and

**Table 2. Quality of life scores according to participant characteristics**

Variables	Mental Component Summary, <i>n</i> =2815		Physical Component Summary, <i>n</i> =2815		Burden, <i>n</i> =2919		Effects, <i>n</i> =2919		Symptoms, <i>n</i> =2919	
	Mean±SD	<i>P</i> Value	Mean±SD	<i>P</i> Value	Mean±SD	<i>P</i> Value	Mean±SD	<i>P</i> Value	Mean±SD	<i>P</i> Value
<b>Socioeconomic characteristics</b>										
Overall	48.0±10.4	—	43.4±9.3	—	61.5±32.8	—	86.6±12.6	—	90.5±9.9	—
Sex										
Women	47.2±10.7	0.007	41.7±9.2	<0.001	59.7±32.9	0.05	84.5±13.2	<0.001	89.0±10.7	<0.001
Men	48.3±10.3		44.2±9.3		62.2±32.7		87.5±12.2		91.2±9.5	
Age, yr										
≥50	47.5±10.6	0.01	42.3±9.3	<0.001	60.7±33.2	0.21	86.7±12.6	0.44	89.8±10.3	<0.001
<50	48.5±10.2		44.6±9.2		62.2±32.3		86.4±12.6		91.3±9.4	
Education										
Below high school	45.4±10.5	<0.001	41.0±9.1	<0.001	53.3±31.8	<0.001	84.7±12.9	<0.001	89.2±10.3	<0.001
High school and above	51.5±9.3		46.8±8.6		72.3±31.0		89.1±11.7		92.4±9.1	
Residence										
Rural	46.8±10.6	<0.001	42.1±9.3	<0.001	55.8±32.6	<0.001	85.4±12.9	<0.001	89.8±10.0	<0.001
Urban	50.6±9.6		46.1±8.9		73.2±30.1		89.2±11.1		92.0±9.5	
Occupational exposure										
Yes	46.7±10.2	<0.001	42.5±9.2	<0.001	59.2±30.8	0.001	86.6±12.5	0.93	90.7±9.6	0.35
No	49.0±10.5		44.1±9.4		63.1±34.2		86.6±12.6		90.4±10.2	
Diet										
Nonvegetarian	46.4±10.6	<0.001	41.7±9.1	<0.001	55.7±32.3	<0.001	85.0±12.4	<0.001	89.1±10.1	<0.001
Vegetarian	50.8±9.5		46.2±9.1		71.2±31.6		89.4±12.2		92.8±9.3	
Occupation										
Nonprofessional	46.9±10.6	<0.001	42.2±9.2	<0.001	58.3±32.6	<0.001	85.6±13.0	<0.001	90.2±9.8	0.004
Professional	51.1±9.4		47.1±8.7		71.0±31.6		89.6±10.6		91.5±10.3	
Tobacco use										
Current or past	47.5±10.8	0.07	43.2±9.5	0.52	60.5±33.9	0.22	86.6±12.3	0.84	89.7±10.1	0.003
Never	48.3±10.2		43.5±9.3		62.1±32.4		86.7±12.5		90.9±9.9	
Annual income (USD) <sup>a</sup>										
Quartile 1	44.0±10.1	<0.001	39.9±8.7	<0.001	50.7±30.5	<0.001	83.8±13.0	<0.001	89.3±9.7	<0.001
Quartile 2	45.8±10.5		41.6±8.9		53.2±32.1		84.4±12.5		89.8±9.4	
Quartile 3	49.5±10.0		45.0±9.3		66.3±32.0		88.4±12.1		90.2±10.4	
Quartile 4	53.3±8.4		47.7±8.5		77.7±26.7		90.4±11.4		92.1±10.0	
<b>Medical characteristics</b>										
BMI, kg/m <sup>2a</sup>										
<17.9	43.5±11.3	<0.001	40.1±9.0	<0.001	47.6±32.4	<0.001	82.3±13.7	<0.001	88.3±10.1	0.004
18–24.9	47.4±10.5		43.0±9.4		59.0±32.8		85.8±12.8		90.4±9.8	
>25	49.3±9.9		44.5±9.2		66.8±31.9		88.2±11.9		91.0±10.1	
Hypertension history										
Yes	48.3±10.3	0.005	43.7±9.3	0.02	63.6±32.8	<0.001	86.9±12.5	0.04	90.7±9.7	0.10
No	47.1±10.6		42.8±9.3		55.9±32.4		85.8±12.9		90.0±10.5	
Diabetes history										
Yes	46.7±10.5	<0.001	42.0±9.2	<0.001	59.2±33.2	0.01	85.5±13.0	<0.001	89.4±10.3	<0.001
No	48.7±10.3		44.2±9.3		62.7±32.6		87.2±12.3		91.1±9.7	
Cardiovascular disease history										
Yes	46.6±10.5	0.004	40.3±9.1	<0.001	58.2±31.2	0.03	86.6±12.5	0.95	89.7±9.9	0.07
No	48.2±10.4		43.9±9.3		62.1±33.3		86.6±12.6		90.7±10.0	
Alternative drug use										
Yes	49.3±10.8	<0.001	44.4±9.5	0.001	66.5±33.2	<0.001	87.3±12.4	0.09	89.4±11.2	0.001
No	47.6±10.3		43.1±9.3		60.0±32.6		86.4±12.7		90.9±9.5	
Albuminuria (dipstick)										
Yes	49.2±10.0	0.001	44.6±9.3	<0.001	65.9±31.8	<0.001	89.3±11.0	<0.001	91.5±9.5	<0.001
No	47.7±10.5		43.1±9.3		60.8±32.8		85.6±12.9		90.0±10.0	
eGFR, ml/min per 1.73 m <sup>2a</sup>										
30–44.9	47.4±10.5	<0.001	42.7±9.3	<0.001	58.5±32.8	<0.001	86.2±12.5	0.07	90.2±10.0	0.06
>45–55.9	48.2±10.6		44.5±9.5		64.0±32.5		87.5±12.3		90.9±9.7	
>60	50.3±9.6		44.7±8.9		69.3±32.0		86.3±13.5		91.3±10.0	

Annual income: quartile 1, <1000 USD; quartile 2, 1000–2000 USD; quartile 3, >2000–5000 USD; and quartile 4, >5000 USD. USD, United States dollars; BMI, body mass index.

<sup>a</sup>*P* values for these variable were obtained using one-way ANOVA.

**Table 3. Adjusted associations of participant characteristics with quality of life scores**

Variables <sup>a</sup>	Difference in Score (95% Confidence Interval)				
	Mental Component Summary, <i>n</i> =2564	Physical Component Summary, <i>n</i> =2564	Burden, <i>n</i> =2657	Effects, <i>n</i> =2657	Symptoms, <i>n</i> =2657
<b>Socioeconomic characteristics</b>					
Sex					
Women versus men	−1.1 (−1.9 to −0.2)	−2.6 (−3.4 to −1.8)	−2.0 (−4.7 to 0.6)	−2.1 (−3.0 to −1.1)	−3.1 (−3.9 to −2.2)
Age					
≥50 versus <50 yr	0.0 (−0.8 to 0.8)	−1.7 (−2.4 to −1.0)	2.4 (0.1 to 4.7)	0.2 (−0.7 to 1.0)	−1.0 (−1.8 to −0.3)
Education					
Below high school versus high school and above	−1.2 (−2.1 to −0.4)	−1.5 (−2.2 to −0.7)	−3.0 (−5.6 to −0.4)	−1.1 (−2.0 to −0.1)	−1.6 (−2.4 to −0.7)
Place of residence					
Rural versus urban	−0.4 (−1.2 to 0.4)	−0.7 (−1.4 to 0.0)	−2.6 (−5.0 to −0.2)	0.1 (−0.8 to 1.0)	0.2 (−0.6 to 1.0)
Occupational exposure					
Yes versus no	0.4 (−0.3 to 1.2)	−0.1 (−0.8 to 0.6)	3.1 (0.8 to 5.4)	0.8 (−0.1 to 1.7)	−1.2 (−1.9 to −0.4)
Diet					
Nonvegetarian versus vegetarian	−0.1 (−1.0 to 0.7)	−0.1 (−0.8 to 0.7)	−1.0 (−3.5 to 1.5)	−0.1 (−1.0 to 0.9)	0.5 (−0.4 to 1.2)
Occupation					
Nonprofessional versus professional	0.3 (−0.6 to 1.2)	−1.1 (−1.9 to −0.2)	−0.7 (−3.4 to 2.1)	−0.6 (−1.6 to 0.5)	0.5 (−0.0 to 1.4)
Tobacco use					
Yes versus no	−0.2 (−1.0 to 0.6)	−0.7 (−1.4 to 0.1)	−1.5 (−4.0 to 0.9)	−0.4 (−1.3 to 0.5)	−1.3 (−2.1 to −0.5)
Annual income (USD)					
Q1 versus Q4	−2.4 (−3.7 to −1.2)	−1.7 (−2.7 to −0.6)	−4.8 (−8.5 to −1.1)	−1.8 (−3.2 to −0.5)	−1.3 (−2.5 to −0.1)
Q2 versus Q4	−1.5 (−2.7 to −0.4)	−1.0 (−2.0 to 0.1)	−4.7 (−8.2 to −1.2)	−1.9 (−3.2 to −0.6)	−1.1 (−2.2 to 0.1)
Q3 versus Q4	−1.6 (−2.6 to −0.6)	−1.0 (−1.9 to −0.1)	−3.4 (−6.5 to −0.4)	−0.6 (−1.7 to 0.6)	−1.1 (−2.0 to −0.1)
<b>Medical characteristics</b>					
BMI, kg/m <sup>2</sup>					
<17.9 versus 18–24.9	−2.0 (−3.5 to −0.5)	−1.3 (−2.7 to 0.0)	−4.7 (−9.2 to −0.1)	−0.8 (−2.5 to 0.9)	−1.3 (−2.8 to 0.2)
>25 versus 18–24.9	0.6 (−0.2 to 1.3)	0.3 (−0.3 to 1.0)	2.1 (−0.2 to 4.3)	0.6 (−0.3 to 1.4)	−0.2 (−0.9 to 0.5)
Hypertension					
Yes versus no	0.0 (−0.9 to 0.8)	−0.1 (−0.9 to 0.6)	1.1 (−1.4 to 3.7)	−0.8 (−1.7 to 0.1)	0.0 (−0.8 to 0.8)
Diabetes					
Yes versus no	−0.6 (−1.5 to 0.2)	−0.8 (−1.5 to −0.1)	−0.19 (−2.5 to 2.3)	−0.7 (−1.6 to 0.2)	−0.6 (−1.4 to 0.2)
Cardiovascular disease					
Yes versus no	0.5 (−0.6 to 1.5)	−1.7 (−2.6 to −0.8)	2.6 (−0.5 to 5.7)	0.8 (−0.4 to 1.9)	−1.0 (−2.0 to −0.1)
Alternative drug use					
Yes versus no	−0.7 (−1.5 to 0.1)	−0.9 (−1.6 to −0.2)	−1.3 (−3.8 to 1.2)	−0.1 (−1.0 to 0.9)	−1.9 (−2.7 to −1.1)
Albuminuria					
Yes versus no	0.1 (−0.8 to 0.8)	0.0 (−0.7 to 0.7)	−0.9 (−3.3 to 1.5)	0.3 (−0.6 to 1.2)	−0.1 (−0.9 to 0.7)
eGFR, ml/min per 1.73 m <sup>2</sup>					
30–44.9 versus >60	−0.8 (−1.9 to 0.4)	−0.6 (−1.6 to 0.4)	−1.9 (−5.2 to 1.4)	−0.7 (−1.9 to 0.5)	−0.5 (−1.6 to 0.6)
45–59.9 versus >60	−1.0 (−2.2 to 0.2)	0.2 (−0.9 to 1.2)	0.2 (−3.3 to 3.8)	−0.5 (−1.8 to 0.8)	−0.3 (−1.4 to 0.9)

Income Qs are Q1: ≤1000 USD; Q2: >1000 and ≤2000 USD; Q3: >2000 and ≤5000 USD; and Q4: >5000 USD. USD, United States dollars; Q, quartile; BMI, body mass index.

<sup>a</sup>The fully adjusted model includes center, place of residence, sex, age, educational attainment, annual household income, occupation, occupational exposure (to sand, dust, working barefoot in field, animals, chemicals, etc.), current diet, tobacco use, BMI, history of hypertension, diabetes status, history of cardiovascular disease, alternative drug use, albuminuria, and eGFR. The estimates represent the  $\beta$ -coefficients interpreted as difference in score from the multivariable linear regression adjusted for center fixed effects and all other factors in the table.

cardiovascular disease was associated with lower physical component summary and symptoms subscale scores. The standardized  $\beta$ -coefficients of the multivariable regression analysis are presented in Supplemental Table 2.

### Lower Quality of Life and Its Associations

The prevalence rates of lower quality of life (score >1 SD below mean) were physical component summary, 17%; mental component summary, 17%; burden, 22%; effects, 16%; and symptoms, 15%. The distribution of lower quality of life across variables is shown in Supplemental Table 3. The results of multivariable logistic regression for the associations of lower quality of life with study variables are shown in Figure 2 and Supplemental Table 4.

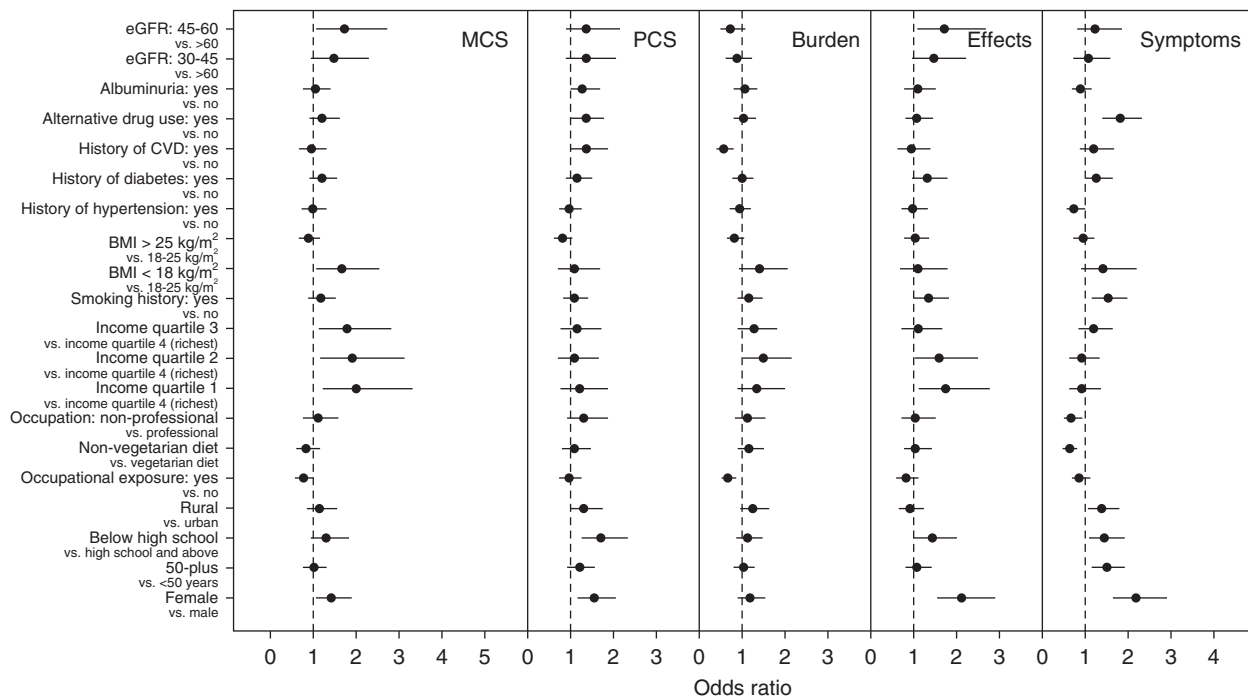
**Socioeconomic Correlates.** Women were associated with lower quality of life across all subscales. Participants with lower income had higher odds of worse mental component summary, burden, and effects subscale scores, and those with lower education had lower scores on physical component summary and symptoms subscales.

**Clinical Correlates.** Albuminuria, diabetes, and eGFR were not associated with lower quality of life on any subscale. Cardiovascular disease was associated with lower quality of life only on the burden subscale.

### Discussion

The ICKD study is the largest study examining health-related quality of life in patients with mild to moderate CKD in South Asia. The striking—albeit not altogether





**Figure 2. | Forest plot showing the association of lower quality of life with socioeconomic and clinical characteristics.** The odds ratios are from a multivariable logistic regression including the factors center (except for impaired symptoms score), place of residence, sex, age, educational attainment, annual household income, occupation, occupational exposure (to sand, dust, working barefoot in field, animals, chemicals, etc.), current diet, tobacco use, body mass index (BMI), history of hypertension, diabetes status, history of cardiovascular disease (CVD), alternative drug use, albuminuria, and eGFR.

surprising—finding is that socioeconomic parameters (low income, rural residence, poor education, women, and age) are more strongly associated with multiple quality of life domains than medical factors.

Patient-reported outcomes are being positioned as important end points in health care interventions. The importance on health-related quality of life assessment in patients with CKD not on dialysis is being highlighted by reporting from prospective cohorts of patients with CKD around the world (4–6,10–13). The ICKD study is an important addition to this evolving corpus of information. The mean scores in various subscales from our

study and other important studies (3,5,12,13) are shown in Table 4.

The Chronic Renal Insufficiency Cohort (CRIC) study (12) from the United States found younger age, women, low education, diabetes, vascular disease, congestive heart failure, obesity, and lower eGFR to be associated with low health-related quality of life scores. In another study of 1186 patients, lower scores were associated with the severity of CKD, women, diabetes, and a history of cardiovascular comorbidities. Furthermore, decline in scores over time correlated with age, albumin level, and comorbidities (11). A Brazilian report found worse quality

**Table 4. Kidney Disease Quality of Life subscale scores in major studies on participants with CKD not on dialysis**

Study	CKD Stage or Mean eGFR	Physical Component Summary	Mental Component Summary	Burden	Effect	Symptoms
ICKD, <i>n</i> =2919	46 (17)	43 (9)	48 (10)	61 (33)	87 (13)	90 (10)
KNOW CKD (3), <i>n</i> =1294 <sup>a</sup>	50 (0.86)	71 (0.5)	69 (0.5)	59 (1)	85 (0.4)	71 (0.3)
CRIC (12), <i>n</i> =3837	45 (17)	41 (11)	50 (10)	82 (24)	89 (16)	83 (15)
C STRIDE (5), <i>n</i> =778	3b	44 (9)	50 (9)	52 (28)	86 (13)	89 (11)
C STRIDE (5), <i>n</i> =499	3a	46 (8)	51 (8)	56 (26)	88 (12)	91 (11)
Zimbudzi <i>et al.</i> (13), <i>n</i> =308	3–5	36 (11)	47 (11)	66 (29)	76 (23)	74 (18)

Data are presented as mean (SD). ICKD, Indian Chronic Kidney Disease; KNOW CKD, Korean cohort study for outcome in patients with chronic kidney disease; CRIC, Chronic Renal Insufficiency Cohort; C STRIDE, Chinese cohort study of chronic kidney disease.

<sup>a</sup>KNOW-CKD: The data were abstracted for the control arm of the study that examined correlation between vitamin D deficiency and HRQOL.

of life with old age, women, lower education, lower income, being professionally inactive, and anemia. Interestingly, stage of CKD, even being on dialysis, was not found to have a major effect (14). A study from Australia (13) found younger age, women, obesity, and smoking to be associated with lower quality of life, whereas a Swedish study (4) found lower eGFR, older age, cardiovascular disease, diabetes, high C-reactive protein, anemia, and overweight to be associated with impaired health-related quality of life. In a Korean study, older age, women, lower education level, rural residence, living without a spouse, smoking, obesity, diabetes, ischemic heart disease, stroke, arthritis, and anemia were associated with lower quality of life (15).

The only previous study from India in patients with CKD not on dialysis revealed low quality of life scores in patients with eGFR < 30 ml/min per 1.73 m<sup>2</sup>, diabetes, cardiovascular disease, elevated C-reactive protein, anemia, and low BP (16).

This study highlights socioeconomic variables as the key determinants of quality of life in this part of world. Our findings are similar to the Brazilian study (14) while using a more robust adjusted analysis. In contrast, the developed world studies show clinical variables (eGFR, diabetes, cardiovascular disease, anemia, and obesity) to be negatively associated with quality of life. The finding of women being associated with worse scores has been seen uniformly. The effect of age is not consistent, with our study and the one from Brazil showing old age to be associated with worse quality of life, whereas younger age has this effect in developed economies.

We noticed differences in quality of life scores between centers, suggesting the contribution of unmeasured sociocultural or ethnic attributes that require further exploration. Several differences lost their significance after adjustment for centers. It is likely that the center-level differences are confounded by interlinked socioeconomic variables. With respect to the lower quality of life scores for nonvegetarians, meat eaters in India are more often poor and belong to minority and/or lower socially ranked communities. Similarly, the association with rural residence could be related to poor social welfare systems, lower incomes, lack of specialized CKD care, and the distance to the health care facility.

The association of high BMI with better quality of life is a new finding. It is possible that higher BMI in our study is a surrogate of better nutrition and income against the backdrop of widespread malnutrition and impoverishment.

Our study has several strengths. It is a large prospective study with annual quality of life assessment and multicentric recruitment that represents the diverse and large population of the country. Furthermore, all of the quality of life assessments are done by trained personnel with independent validation and supervision, assuring participation, accuracy in responses, and minimization of heterogeneity across centers. Lastly, the study is recording a wide array of clinical outcomes over several years and has a repository of biosamples for exploring future hypotheses. Longitudinal changes in quality of life scores and their association with various parameters and outcomes will

provide valuable insights for holistic management of CKD in this region.

The study has some limitations too, which include the large number of variables being evaluated, some of which are subjective and given to variability. Standardized training and validation of interviewer performance should have helped to minimize this variability. It would have been ideal to evaluate individual parameters (*e.g.*, income, occupational exposure, *etc.*) in greater detail, but effort invested has to be pragmatized for feasibility. Also, the observational cross-sectional design of the study makes it susceptible to the effect of unmeasured confounding factors and biases. These effects cannot be eliminated completely despite attempts to ensure uniformity and comprehensive evaluation. Most of the findings are, therefore, associative and thus, become hypothesis generating. Although our patients were recruited in tertiary care centers, the mean age and sex distributions of our study cohort are similar to those of the CKD Registry of India data that analyzed >50,000 participants (17).

Quality of life measurements have been shown to be associated with adverse outcomes. In the CRIC study, low physical component summary, effects, and symptoms subscales were independently associated with a higher risk of incident cardiovascular events and death, whereas low mental component summary was independently associated with a higher mortality (18). The ICKD study and other cohorts will shed more light on this in future.

Our study reiterates the need for a more inclusive approach to CKD management with attention to social determinants of care and incorporation and strengthening of supportive disciplines, like physical medicine, psychology, health care systems management, financial support, and attention to environment and occupation. Interventions targeting quality of life would need to address system-level factors in addition to medical management.

In conclusion, this large study has established baseline health-related quality of life scores for patients with CKD in India. The predominant association of quality of life scores with socioeconomic factors lays grounds for a more comprehensive and cost-analytic approach for investments in the care of CKD.

#### Acknowledgments

We acknowledge the contributions of Dr. R. Sakthirajan, Dr. T. Dineshkumar, and Dr. J. Dhanapriya from Rajiv Gandhi Government General Hospital, Chennai, India.

#### Disclosures

Dr. Gang reports receiving a grant from Novartis and personal fees from Roche and Sanofi outside of the submitted work. Dr. Gopalakrishnan reports receiving speakers' fees from Cipla and Roche. Dr. Jha reports receiving consultancy fees from Biocon, NephroPlus, and Zydus Cadilla outside of the submitted work. Dr. Modi reports receiving consultancy fees from Intas Pharmaceuticals and Vyapitus Life Sciences out of the submitted work. Dr. Yadav, Dr. Ghosh, Ms. Kamboj, Dr. Kaur, Dr. Kumar, Dr. Bhansali, Dr. Prasad, Dr. Sahay, Dr. Parameswaran, Dr. Varuguese, Dr. Singh, Dr. Sircar, Dr. Jaryal, Dr. Vikrant, and Dr. Agarwal have nothing to disclose.



## Funding

Dr. Jha is supported by grants from Baxter Healthcare Corporation; Department of Biotechnology, Ministry of Science and Technology; Department of Science and Technology, India; GlaxoSmithKline; Indian Council of Medical Research; and UK Medical Research Council. This study was funded by Department of Biotechnology, Ministry of Science and Technology grant BT/PR3150/MED/97/345/2016. The funding agency had no role in design and conduct of this study.

## Supplemental Material

This article contains the following supplemental material online at doi: <http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.06510619/-/DCSupplemental>.

Supplemental Table 1. Baseline characteristics of participants with missing Kidney Disease Quality of Life data.

Supplemental Table 2. Effect of background characteristics on scores from adjusted analyses—standardized  $\beta$ -coefficients.

Supplemental Table 3. Distribution of baseline characteristics by lower quality of life.

Supplemental Table 4. Association of low quality of life with individual baseline characteristics.

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Received: June 3, 2019 Accepted: November 7, 2019

Published online ahead of print. Publication date available at [www.cjasn.org](http://www.cjasn.org).

See related Patient Voice, “Patient Perspective on CKD in India,” and editorial, “Socioeconomic Determinants of Quality of Life in Patients with Kidney Diseases,” on pages 161 and 162–164, respectively.

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