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Trends and socioeconomic inequality of the burden of congenital abnormalities of the kidney and urinary tract among children and adolescents

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ABSTRACT

Background. Although congenital abnormalities of the kidney and urinary tract (CAKUT) is the leading cause of childhood-onset chronic kidney disease and kidney failure, comprehensive information on the disease burden among children and adolescents globally is lacking. We aim to report the trends and socioeconomic inequality of CAKUT burden for people aged 0–24 years from 1990 to 2019.

Methods. We reported the prevalence, mortality and disability-adjusted life-years (DALYs) for CAKUT based on the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, quantified the association of disease burden and socio-demographic index (SDI), and calculated the slope index of inequality, the relative index of inequality and concentration index.

Results. In 2019, the global prevalence, mortality and DALYs of CAKUT among individuals aged 0–24 years were 167.11 (95% confidence interval 166.97, 167.25), 0.30 (0.29, 0.30) and 32.22 (32.16, 32.29), respectively, per 100 000 population. The greatest prevalence, mortality and DALYs were recorded in the 0–4 years age group. The greatest mortality and DALYs were recorded in low SDI countries and territories. During 1990 to 2019, the prevalence, mortality and DALYs decreased globally, while in low and low-middle countries and territories the reduction was much less slower. India, Nigeria and Pakistan had the highest DALYs. Saudi Arabia and China exhibited a markedly decrease of CAKUT burden. Globally for every 0.1 increase in SDI, there was a 20.53% reduction in mortality and a 16.31% decrease in DALYs, but a 0.38% rise in prevalence.

Conclusions. Inequality for disease burden of varying SDI was increasing globally. Thus, specific preventive and health service measures are needed to reduce the global burden from CAKUT.

Keywords: congenital abnormalities of the kidney and urinary tract (CAKUT), disease burden, inequality

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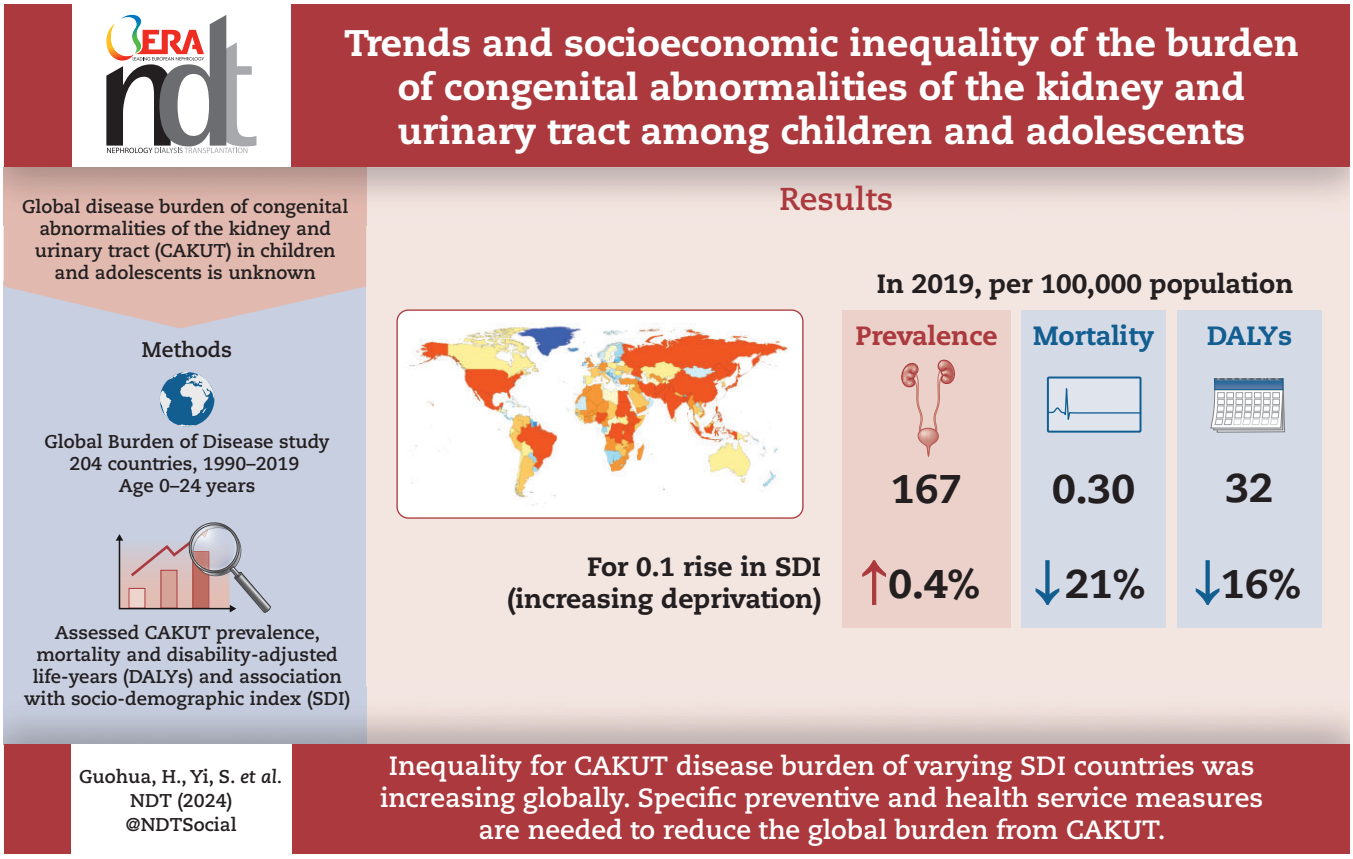
GRAPHICAL ABSTRACT



KEY LEARNING POINTS

What was known:

- Although congenital abnormalities of the kidney and urinary tract (CAKUT) is the leading cause of childhood onset chronic kidney disease and kidney failure worldwide, neither comprehensive and recent information on the disease burden among children and adolescents globally, nor its socioeconomic inequality status across countries and territories are available.

This study adds:

- In 2019, the global prevalence, mortality, and disability-adjusted life-years of CAKUT were 167.11, 0.30 and 32.22, respectively, per 100 000 population individuals aged 0–24 years.
- Low socio-demographic index (SDI) countries bearded the heaviest burden and the inequality of CAKUT burden between different SDI countries increased in the last 30 years.

Potential impact:

- Inequality in disease burden of CAKUT has increased across SDI groups.
- Specific preventive and health service measures—prenatal and postnatal ultrasound screening and health resources investment in low and low-middle SDI countries and territories, improved access to kidney replacement therapy globally—are needed to reduce the CAKUT burden.

INTRODUCTION

Chronic kidney disease (CKD), with a global prevalence of 9.1%, affecting 697.5 million people and causing 1.2 million death in 2017 [1], is the 18th leading cause of global disability-adjusted life-years (DALYs) lost with a 93% increase from 1990 to 2019 [2]. CKD is expected to become the fifth leading cause of death by 2040 globally [3]. Children and adolescents with CKD and kidney failure are facing a higher risk of mortality that is estimated at 30- to 1000-fold that of their healthy counterparts [4]. As the most important underlying cause of childhood onset CKD and kidney failure, congenital abnormalities of the kidney and urinary tract (CAKUT) attributes to 20%–59% of CKD cases among the pediatric population [5–10]. Comprehensive analyses of the global burden of CAKUT among children and adolescents remain scarce, other than data from single centers, single districts, specific disease populations or restricted to infancy [5–10].

Understanding of the current disease burden of CAKUT might accelerate policy actions to achieve progress for the United Nation's Sustainable Development Goals (SDGs) target to end avertable deaths in children under five and the World Health Organization Global Strategy for Women's, Children's and Adolescents' Health [11, 12], and aligns with the emphasis of World Kidney Day 2024 on promoting equitable kidney health, providing a structured pathway towards achieving targeted health outcomes for all [13]. However, the disease burden of adolescents has been overlooked in global health and social policy. Even though previous studies have revealed socioeconomic inequalities in CKD disease burden [1, 14, 15], they neither focused on CAKUT, nor explored its association with socioeconomic development. Although one study had described socioeconomic inequalities in urogenital congenital anomalies [16], it did not specifically focus on children and adolescents, nor did it explore the underlying cause or propose comprehensive strategies for amelioration on an international scale.

In the present study, we aimed to estimate the global, regional and national burden of CAKUT among children and adolescents in 204 countries and territories from 1990 to 2019 using estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019. We also aimed to quantify the magnitude and direction of temporal trends in exemplary countries and territories, and further explore CAKUT inequalities in socioeconomic development status, which might contribute to track progress, map resource requirements, and help in policy making and implementation towards prevention and tackling the growing burden of CAKUT.

MATERIALS AND METHODS

Overview and data definitions

The GBD 2019 provides a systematic scientific estimation of publicly available, published and contributed data with enhanced method performance and standardization on prevalence, mortality and DALYs of 369 injuries and diseases for 204 countries and territories from 1990 to 2019 by age, sex and country. In most studies, CAKUT can be sub-grouped into congenital obstructive uropathies, renal hypoplasia, dysplasia, oligonephronia and reflux nephropathy [5, 6, 17, 18], which is collectively reported under urogenital congenital anomalies in GBD 2019 dataset (Table S1). In this cross-sectional study, we encompassed all instances of CAKUT, not restricted to CAKUT instances associated with CKD. CAKUT was defined based on registered diagnoses, without considering estimated glomerular filtration rate or CKD stages as well. As a result, our study focus on CAKUT diagnosis without considering CKD stages. We studied CAKUT burden using the prevalence, mortality and DALYs of urogenital congenital anomalies to represent the disease burden of CAKUT among the 0–24 years age group included in the GBD 2019 database. (Details of data source description in Appendix Methods; for the Global Health Data Exchange see https://ghdx.healthdata.org/gbd-results-tool.) Cause of death data obtained from vital registration with medical certification using the International Classification of Diseases and Injuries, Ninth Revision were mapped to the GBD cause list [2].

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Data analysis

We calculated age-standardized prevalence and DALYs per 100 000 population and 95% confidence intervals (CI) from 1990 to 2019 applying the world standard population in the GBD 2019 (https://vizhub.healthdata.org/gbd-results/). We also calculated the average annual percentage change (AAPC) and 95% CI using log-transformed linear regression. We performed subgroup analyses stratified by age (0–4, 5–9, 10–14, 15–19, 20–24 years), sex (male and female) and socio-demographic index (SDI) (high, high-middle, middle, low-middle and low SDI categories). We used log-transformed fixed-effect panel data regression model to identify the association between SDI and disease burden, while country was used as the group variable and year was used as the time variable. We calculated the slope index of inequality (SII), the relative index of inequality (RII) and concentration index to measure the inequality between countries and territories. The SII represents the absolute age-standardized rates difference between the lowest SDI group and the highest SDI group. A negative SII value indicates higher age-standardized rates in the low SDI group. The RII represents the relative rate difference. We also plotted the concentration curve and calculated the concentration index to describe the differences. A negative concentration index reflects that there are higher age-standardized rates in the low SDI group. Statistical analyses were carried out using the R program version 4.2.1 (R Development Core Team, Vienna, Austria). *P*-values <.05 (two-tailed) were considered significant. (Details of the Methods description can be found in the Appendix Methods.)

Ethical approval and informed consent were waived because the GBD dataset was publicly available and no identifiable information was included in the analyses.

RESULTS

Overview of the global disease burden of CAKUT

A total of 5 313 105 people aged 0–24 years [2 661 405 male (50.96%); 2 651 700 female (49.91%)] were included in the analysis. In 2019, the global prevalence, mortality and DALYs of CAKUT among individuals aged 0–24 years were estimated at 167.11 (95% CI 166.97, 167.25), 0.30 (0.29, 0.30) and 32.22 (32.16, 32.29) per 100 000 population respectively (Table 1). The absolute number of prevalence, mortality and DALYs of CAKUT encompassed the sum of CKD caused by hypertension, diabetes mellitus, glomerulonephritis and other and unspecific cause in 0–4 years age group. Among five categories of SDI countries and territories, the low SDI countries and territories bearded the highest rates of prevalence, mortality and DALYs of CAKUT In children under 1 year old. (Fig. S1 and Table S2). From 1990 to 2019, the global age-standardized prevalence rate per 100 000 population showed little change, while the mortality and DALYs significantly declined (Table 1, Fig. 1).

Disease burden of CAKUT by age and sex

In 2019, the 0–4 years age group had the highest prevalence, mortality and DALYs at 402.28 (299.53, 527.67), 1.36 (0.97, 1.85), 134.79 (98.65, 178.58) per 100 000 population, respectively (Table 1, Fig. S1). In children under 1 year old, the absolute number of deaths [8639.12 (6239.00, 11 581.35)] and DALYs [797 114.04 (581 160.40, 1 061 837.54)] significantly exceeded the combined totals from all other age groups. (Fig. S2 and Table S2). In 2019, the

Table 1: The global age-standardized rate per 100 000 of prevalence, mortality and DALYs for CAKUT among those aged 0–24 years in 1990 and 2019, and AAPC 1990–2019.

	Prevalence			Mortality			DALYs		
Variables	ASR per 100 000 in 1990, *n* (95% CI)	ASR per 100 000 in 2019, *n* (95% CI)	AAPC between 1990 and 2019, % (95% CI)	ASR per 100 000 in 1990 (95% CI)	ASR per 100 000 in 2019 (95% CI)	AAPC between 1990 and 2019 (95% CI)	ASR per 100 000 in 1990 (95% CI)	ASR per 100 000 in 2019 (95% CI)	AAPC between 1990 and 2019 (95% CI)
Global	165.19 (165.04, 165.34)	167.11 (166.97, 167.25)	0.03 (–0.01, 0.07)	0.45 (0.45, 0.46)	0.30 (0.29, 0.30)	–1.26 (–1.35, –1.17)	45.73 (45.66, 45.81)	32.22 (32.16, 32.29)	–1.07 (–1.14, –1.00)
Male	159.77 (159.56, 159.97)	162.40 (162.21, 162.60)	0.09 (0.05, 0.14)	0.54 (0.53, 0.55)	0.36 (0.35, 0.37)	–1.13 (–1.24, –1.03)	53.26 (53.15, 53.37)	37.80 (37.71, 37.89)	–0.98 (–1.07, –0.88)
Female	170.89 (170.68, 171.11)	172.11 (171.90, 172.32)	–0.03 (–0.08, 0.02)	0.36 (0.36, 0.37)	0.23 (0.23, 0.24)	–1.47 (–1.54, –1.40)	37.72 (37.63, 37.82)	26.26 (26.18, 26.34)	–1.20 (–1.24, –1.16)
0–4 years	396.50 (294.57, 520.57)	402.28 (299.53, 527.67)	0.05 (–0.01, 0.12)	2.19 (1.25, 3.52)	1.36 (0.97, 1.85)	–1.39 (–1.50, –1.27)	207.52 (123.32, 325.47)	134.79 (98.65, 178.58)	–1.27 (–1.37, –1.17)
5–9 years	164.82 (124.05, 215.51)	165.04 (123.76, 217.54)	–0.02 (–0.07, 0.03)	0.04 (0.02, 0.06)	0.02 (0.02, 0.03)	–1.90 (–1.99, –1.81)	8.79 (5.97, 13.11)	7.62 (5.07, 11.75)	–0.54 (–0.60, –0.47)
10–14 years	108.18 (79.91, 140.39)	108.33 (79.55, 141.27)	–0.03 (–0.06, –0.00)	0.02 (0.02, 0.03)	0.02 (0.01, 0.02)	–1.03 (–1.09, –0.98)	5.74 (3.93, 8.34)	5.32 (3.52, 7.88)	–0.29 (–0.32, –0.26)
15–19 years	79.80 (58.39, 105.30)	80.00 (58.10, 105.92)	0.00 (–0.03, 0.03)	0.02 (0.01, 0.02)	0.02 (0.01, 0.02)	–0.17 (–0.27, –0.07)	4.21 (2.81, 6.24)	4.15 (2.70, 6.18)	–0.01 (–0.06, 0.03)
20–24 years	62.49 (45.40, 83.45)	62.44 (45.27, 83.64)	0.06 (–0.02, 0.15)	0.02 (0.01, 0.02)	0.02 (0.01, 0.02)	0.59 (0.51, 0.67)	3.39 (2.23, 5.00)	3.56 (2.30, 5.23)	0.26 (0.20, 0.32)
High SDI	177.89 (177.40, 178.38)	156.28 (155.81, 156.76)	–0.63 (–0.74, –0.51)	0.43 (0.41, 0.46)	0.21 (0.19, 0.23)	–2.34 (–2.42, –2.26)	44.86 (44.61, 45.11)	24.28 (24.09, 24.47)	–2.03 (–2.08, –1.98)
High-middle SDI	171.18 (170.82, 171.54)	163.36 (162.97, 163.76)	–0.09 (–0.17, –0.01)	0.43 (0.42, 0.45)	0.20 (0.19, 0.22)	–2.68 (–2.78, –2.58)	44.32 (44.13, 44.50)	23.35 (23.20, 23.50)	–2.21 (–2.29, –2.12)
Middle SDI	152.72 (152.48, 152.97)	160.04 (159.78, 160.31)	0.10 (0.02, 0.18)	0.44 (0.43, 0.45)	0.24 (0.23, 0.26)	–1.82 (–1.99, –1.64)	43.78 (43.65, 43.91)	26.98 (26.87, 27.09)	–1.53 (–1.66, –1.40)
Low-middle SDI	170.72 (170.42, 171.02)	178.57 (178.28, 178.85)	0.16 (0.11, 0.20)	0.48 (0.46, 0.49)	0.34 (0.32, 0.35)	–0.94 (–1.04, –0.83)	48.33 (48.18, 48.48)	36.19 (36.06, 36.32)	–0.77 (–0.86, –0.69)
Low SDI	165.35 (164.94, 165.75)	168.04 (167.75, 168.33)	0.11 (0.06, 0.16)	0.47 (0.45, 0.48)	0.38 (0.37, 0.40)	–0.48 (–0.56, –0.40)	46.88 (46.69, 47.07)	39.66 (39.53, 39.80)	–0.40 (–0.47, –0.33)

ASR = age-standardized rate.

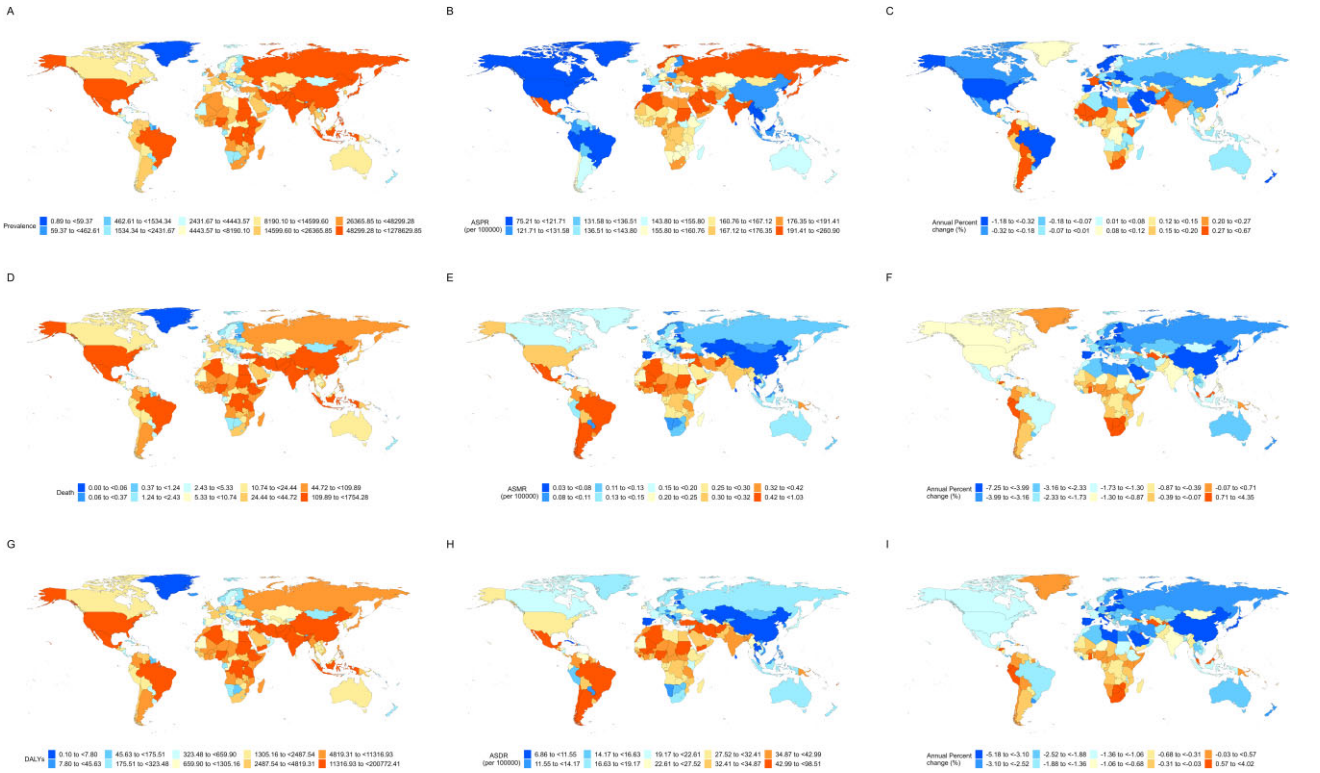


Figure 1: The numbers, ASPR and ASDR in 2019 and estimated annual percentage changes of rates during 1990–2019 for CAKUT in 204 countries and territories. (**A**) Numbers of prevalence for CAKUT in 2019. (**B**) ASPRs for CAKUT in 2019. (**C**) Estimated annual percentage changes of ASPRs from 1990 to 2019. (**D**) Numbers of death for CAKUT in 2019. (**E**) ASMRs for CAKUT in 2019. (**F**) Estimated annual percentage changes of ASMRs from 1990 to 2019. (**G**) Numbers of DALYs for CAKUT in 2019. (**H**) ASDRs for CAKUT in 2019. (**I**) Estimated annual percentage changes of ASDRs from 1990 to 2019. ASDR = age-standardized DALYs rate; ASPR = age-standardized prevalence rate.

mortality and DALYs of CAKUT were both higher in males than females (Table 1, Fig. S3).

Disease burden of CAKUT by SDI

In 2019, low SDI countries and territories bore the greatest mortality and DALYs, while low-middle SDI countries and territories bore the greatest prevalence (Table 1). All SDI categories showed a reduction in age-standardized DALYs rates from 1990 to 2019, with the highest relative reduction observed in high SDI [AAPC: –2.21% (–2.29, –2.12)]. Conversely, the relative reduction of DALYs rates in low SDI [AAPC: –0.40% (–0.47, –0.33)] and low-middle SDI countries and territories [AAPC: –0.77% (–0.86, –0.69)] was considerably less steep (Table 1, Fig. 2). There was a notable global reduction of 28.48% in the absolute number of DALYs but with a substantial increase of 41.07% only in low SDI countries and territories from 1990 to 2019 (Fig. 2, Table S3).

Changes of disease burden of CAKUT in exemplary countries and territories from 1990 to 2019

Among 204 countries, Saudi Arabia and China were two of the typical countries which showed the deepest rates changes of mortality and DALYs between 1990 and 2019. It could be witnessed obvious changes in Saudi Arabia, where had a substantial increase in SDI from 0.480 in 1990 to 0.805 in 2019, accompanied by a large reduction in mortality from 1.33 (1.14, 1.56) to 0.30 (0.21, 0.43) and DALYs from 125.45 (123.47, 127.45) to 33.95 (32.88, 35.05) (Tables S4–S6). Meanwhile, from 1990 to 2019, China exhibited markedly decrease in mortality with an AAPC of –5.66% (–6.00, –5.33), and DALYs with an AAPC of –4.10% (–4.37, –3.82) (Tables S4–S6). China exhibited a significant reduction in DALYs absolute numbers, which contributed to more than 25% of the global decline (absolute numbers decrease: 408 046.97 globally and 111 173.45 in China) over the three decades (Tables S3 and S6).

India, Pakistan and Nigeria topped the list for the highest disease burden of DALYs related to CAKUT in 2019. Nigeria experienced an increase in age-standardized prevalence, mortality and DALYs from 1990 to 2019. Conversely, both India and Pakistan saw slight declines in age-standardized DALYs rates, even though both countries experienced an increase in prevalence. Yet India and Pakistan still accounted for nearly a quarter of the global DALYs burden (Tables S4–S6).

Panel regression and inequality analysis of disease burden correlated with the SDI

For every 0.1 increase in SDI, there was a 20.53% reduction in age-standardized mortality and a 16.31% decrease in DALYs, but a 0.38% rise in prevalence rate among individuals aged 0–24 years. However, on subgroup analysis, after the age of 5 years, prevalence was positively correlated with SDI. After the age of 15 years, both mortality and DALYs were positively correlated with SDI. This means that in these ages groups, as SDI increases, the age-standardized rates also increased (Table 2, Fig. S4).

Significant absolute and relative SDI-related inequalities in the disease burden were observed, with a disproportionate higher burden shouldered by countries with lower SDI. As illustrated by the concentration index, the gap in prevalence, mortality and DALYs

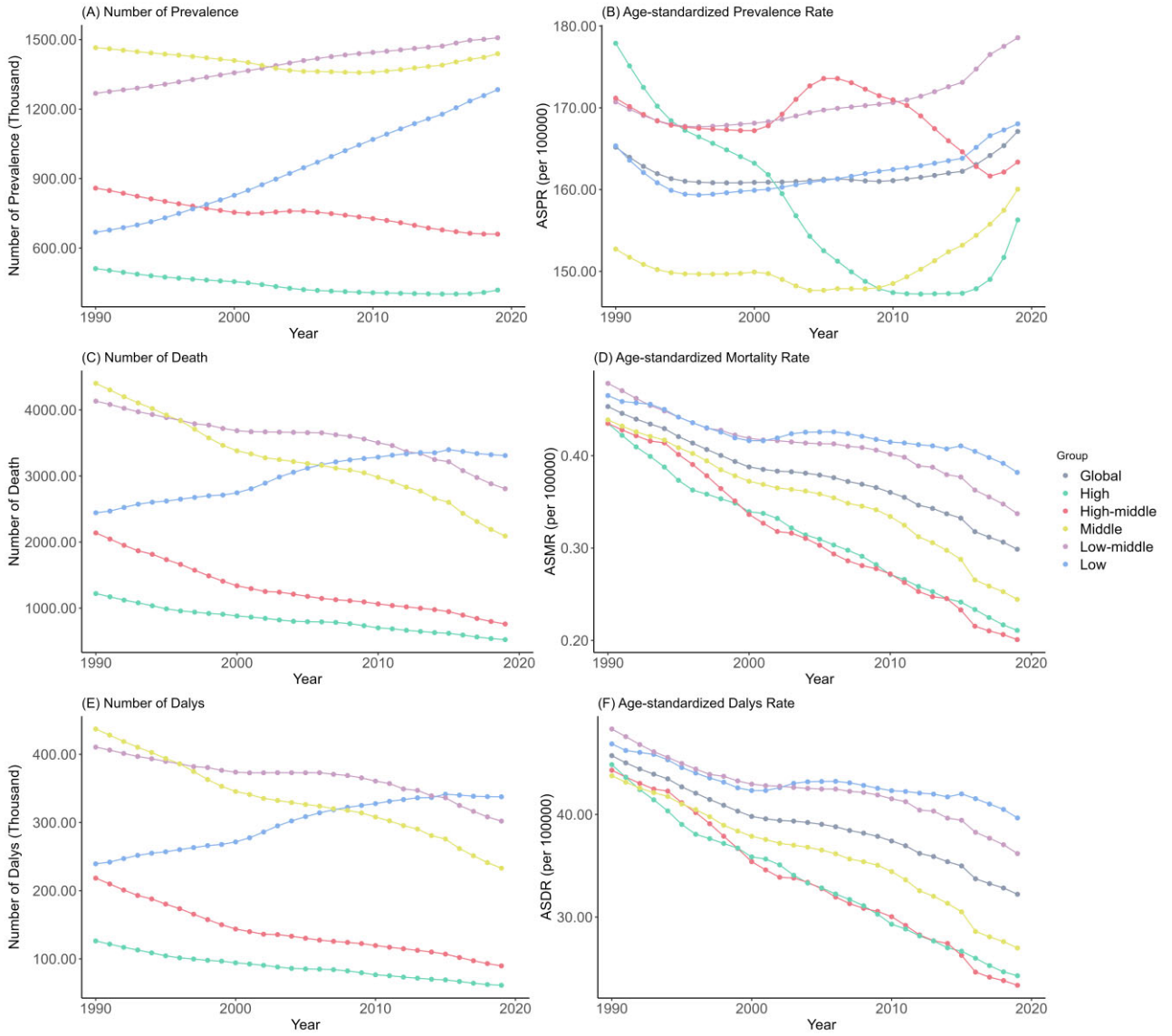


Figure 2: Trends of prevalence (**A**), ASPR (**B**), death (**C**) ASMR (**D**), DALY (**E**) and ASDR (**F**) of CAKUT by SDI quintiles,1990–2019. ASPR = age-standardized prevalence rate; ASMR = age-standardized mortality rate; ASDR = age-standardized DALYs rate.

Table 2: Association between age-standardized prevalence, mortality, DALYs rate of CAKUT and every 0.1 increase of SDI.

Subgroup	Prevalence (%)	Death (%)	DALY (%)
Global	0.38	−20.53	−16.31
Sex			
Male	0.01	−20.43	−16.97
Female	0.72	−20.00	−14.95
Age			
Neonatal	−1.44	−17.51	−17.40
1–11 months	−1.10	−28.65	−24.47
1–4 years	−0.20	−32.27	−14.83
5–9 years	0.77	−15.24	−4.09
10–14 years	1.28	−8.50	−1.71
15–19 years	1.61	4.33	2.51
20–24 years	1.88	5.94	3.11

Age-standardized rate was used for global and male/female subgroups, while crude rate was used for the remainder.

between the highest and the lowest SDI country all increased from 1990 to 2019. Moreover, most of the magnitudes of slope index of inequality the SII and RII in 2019 were higher than those in 1990. The overall results suggested that the SDI-related inequalities in the burden across countries exacerbated over time (Fig. 3).

DISCUSSION

CAKUT is the leading cause of CKD and kidney failure in children and adolescents, and aligns with two key United Nation SDGs because of its significantly impact on global health [11]. Previous reports had exhibited the disease burden of CKD and the relationship between SDI and CKD disease burden [1, 14–16]. Compared with earlier studies, the present report had three main findings. First, our study provided a comprehensive assessment of the global disease burden of CAKUT, including prevalence, mortality and DALYs, and its proportionate contribution to CKD. Second, we identified the association between the SDI and the disease burden. Finally, inequality of disease burden in across SDI groups from

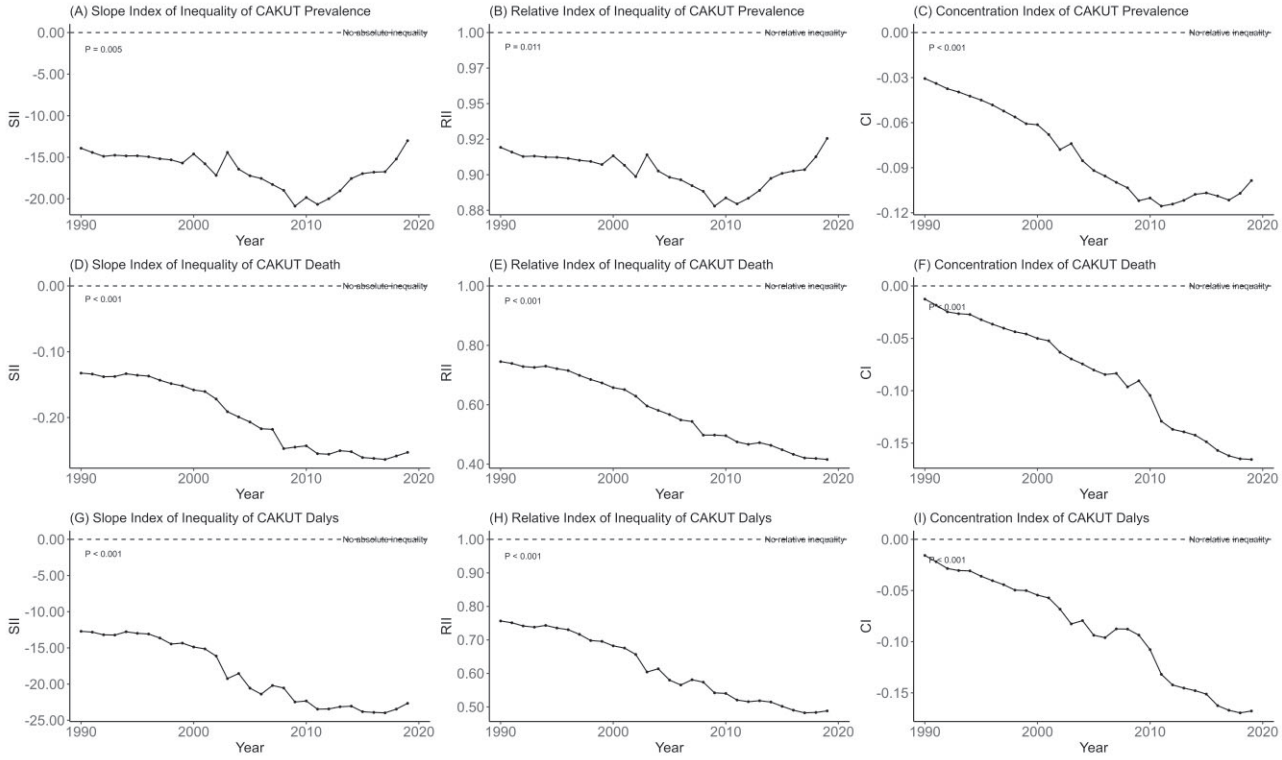


Figure 3: Trend for inequality during 1990–2019 for CAKUT in 204 countries and territories. ASDR = age-standardized DALYs rate; ASPR = age-standardized prevalence rate.

1990 to 2019 were significantly increased. Our investigation contributes to the call for action to improve the disease burden in low and low-middle SDI countries and territories in order to reduce the global burden of CAKUT.

Compared with previous studies which suggested a broad variation in CAKUT prevalence from different countries and territories [5–10], our study provided age-standardized prevalence, death and DALYs rates which will facilitate comparisons across nations in different periods. The reported CAKUT prevalence in previous studies is 2.0% in preterm infants [19], which is much higher compared with our reported prevalence in 0–24 years population (0.17%). The difference might be due to the various sample selection and different age span: for example, preterm infants have a significant higher prevalence rate of CAKUT compared with full-term infants [19], and the prevalence in those aged 0–4 years is the highest among all age groups in our study at 0.4%, which is comparable to previous CAKUT prevalence reported in other full-term infants (0.04%–1.1%) [20–28]. Moreover, our findings are consistent with a meta-analysis that included 104 572 screen subjects, 1.6% with antenatal hydronephrosis and 0.4% with postanal pathology-confirmed CAKUT [29]. In our study, the prevalence is highest in younger age group, and decreased in older age group. The underlying reason might be, firstly, the mortality was in younger age group, highest during infancy, highlighting the importance of prenatal and infancy diagnosis and management for CAKUT. The high mortality rate of CAKUT during infancy was also supported by a previous study, ranging from 17% [30] to as high as 60%–80% in different reports [31]. Secondly, CAKUT is often diagnosed in infancy or early childhood. As individuals age, unless there are significant clinical symptoms necessitating medical attention, the rate of new diagnoses may decrease. Thirdly, some CAKUT cases would be resolved or cured as patients age, so the prevalence in older age might drop [29]. Fourthly, the transition from pediatric to adult care systems might contribute to lower reported prevalence in older age groups, because mild cases of CAKUT might not require ongoing treatment.

By quantifying the relationship between SDI and CAKUT disease burden in children and adolescents across 204 countries, our findings highlight that low and low-middle SDI countries shoulder the majority of the disease burden. A prime example is India, contributing to nearly one-fifth of the global burden of DALY, underscoring the imperative to prioritize specific interventions in low and low-middle SDI nations to mitigate CAKUT impacts globally. Another example is among children under 1 year old, low SDI countries bearded the highest rates of prevalence, mortality and DALYs of CAKUT, whereas high SDI countries had a much lower rate compared with low SDI countries.

Increasing inequality across SDI groups in the disease burden of CAKUT was observed during the last three decades. The high and ever-increasing disease burden of CAKUT in low and low-middle SDI countries and territories, such as India, Pakistan and Nigeria, is attributable to multiple challenges, including delayed diagnosis of CAKUT in infancy, insufficient resources for managing young children with CKD, and limited availability of kidney replacement therapy [1, 14, 32, 33]. Early detection of CAKUT relies significantly on healthcare resources, chiefly the ability for antenatal and postnatal ultrasound screening by expert healthcare personnel, which is lacking in lower SDI countries such as India and Nigeria [34–38]. Moreover, the deficiency of health workers and medical resources in low and low-middle SDI countries and territories like Pakistan and Nigeria may obstruct the implementation of early CAKUT detection and subsequent kidney disease management [32, 39]. Lastly, CAKUT is the leading cause of kidney failure in children and adolescents, necessitating kidney

replacement therapy (KRT) for survival. The high cost and limited resources for KRT create barriers to access in low-income countries and remote regions [32, 33, 39].

Public health strategies and programs have significantly influenced the burden of CAKUT. For example, our findings showed that high and high-middle SDI countries like Japan and Saudi Arabia, despite high CAKUT prevalence, have successfully reduced related mortality and DALYs during last 30 years. This achievement is attributed to notable budget allocations, public health plans that ensure prenatal and postnatal check-ups, as well as universal access to KRT, which are commonly observed in wealthy countries [1, 40–42]. Furthermore, genetic screening projects for high-risk CAKUT patients have been undertaken in some prosperous nations [43]. However, these procedures come with relatively substantial costs and can exert a significant demand on medical resources. As a middle SDI country, China has achieved a remarkable reduction in CAKUT burden during the past three decades, which might serve as a reference for other middle and low SDI countries. The public health strategies and programs of universal antenatal ultrasound screening and a three-level prevention network contributed to this success, along with high insurance coverage for early CKD diagnosis and improved KRT access [44, 45]. Moreover, family planning contributes significantly to the prevention of children mortality [46]. Family planning in low-income countries might play an important role in reducing the strain on the healthcare system, thus reducing congenital disease burden, including CAKUT [46, 47].

Our study qualified the correlation between SDI and disease burden of CAKUT in different age groups. For every 0.1 increase in SDI, there was a 0.38% rise in prevalence rate among individuals aged 0–24 years. One potential explanation is that in wealthier countries and territories, early detection and management of CAKUT enable a portion of these patients to survive into adolescence. After 15 years of age, both mortality and DALYs were positively correlated with SDI. This findings might indicated that, as the disease progresses in older ages, the need for KRT intensifies, which may subsequently raise the DALYs in regions with higher prevalence. Kidney transplantation stands as the optimal KRT for kidney failure patients' survival. Many nations prioritize children on the transplant waitlist. Yet, the age cut-off for "children" varies from country to country, typically ranging from 15 to 18 years [48–52]. This variation in age categorization might contribute to the observed surge in mortality and DALYs over 15 years of age with increasing SDI. The difference in age-specific trends highlights the need for tailored health interventions in countries and territories with different SDI.

As World Kidney Day 2024 emphasizes equitable kidney health and optimal medication practices [13], we propose to integrate CAKUT preventive measures into SDGs, and advocate for the establishment of an International Action Target to eliminate deaths caused by CAKUT in children under five by 2030 (Table S7). Achieving these goals requires improving prenatal and postnatal ultrasound screenings in primary healthcare to enable early detection and intervention, and increase human resources for health, prioritizing prevention over high-cost KRT and enhancing access to KRT services.

The study has several limitations. Firstly, the definition of CAKUT varies among countries and territories [39, 53]. While CAKUT typically denotes urinary tract malformations, for the purposes of our analysis, we have utilized data on urogenital congenital anomalies from GBD dataset. This includes most of the common conditions such as bladder outlet obstruction, predominantly posterior urethral valves and other frequently reported urinary tract malformations. Nonetheless, it is important to acknowledge the potential for selection bias in our study's findings due to the variability in the definition of CAKUT and due to the inclusion of some female genital tract malformation in the GBD dataset. Given their limited proportion [54, 55], this does not affect the trend results of our CAKUT study. It may, to a minor extent, impact our estimates of regional differences in disease burden. Furthermore, more accurate data will be required for cross-validation in the future. More detailed classification of disease information are needed to further estimate the disease burden in future study. Secondly, the analyses relied on GBD models and estimates from higher-resource settings, due to limited primary data in low SDI countries and territories [1]. This may have affected trends estimates and overstate improvements in some low SDI countries and territories. We primary focused on the prevalence, death and estimated the CAKUT burden because there are fewer missing data. Thirdly, GBD uses mutually exclusive causes and a single underlying cause of death for CAKUT, potentially underestimating actual burden. Subtypes of CAKUT were not analyzed due to data unavailability, limiting the specificity of the analysis. As a result, we could not estimate the specific disease burden of every single cause of CAKUT. Similarly, a more detailed classification, distinguishing between glomerular and non-glomerular causes of CKD, is necessary for in-depth analysis, especially in the pediatric population. Fourthly, the GBD does not provide disease burden data for discrete age groups, which restricts further study from analyzing differences between the pediatric population and adolescents defined by the age threshold of 18 years. Fifthly, There is a possibility that the transition from pediatric to adult care systems might affect the tracking and reporting of CAKUT. The prevalence in older groups might be composed of more serious cases still receiving medical attention, which can affect prevalence figures. This selection bias towards more severe cases in healthcare data might not accurately reflect the true distribution of CAKUT severity in the general population.

CONCLUSIONS

Our investigation provided a comprehensive portrayal of disease burden of CAKUT. Countries with higher SDI had lower burden of CAKUT. The inequality in disease burden between countries and territories with different SDI levels has widened over last 30 years. We advocate for the establishment of an International Action Target to eliminate deaths caused by CAKUT in children under five by 2030. Low and low-middle SDI countries and territories should promote the prenatal and postnatal healthcare screening for CAKUT, increase human resources for health and enhance the accessibility of KRT. In high and high-middle SDI counties, access to kidney transplantation should be increased to reduce the burden of CAKUT.

SUPPLEMENTARY DATA

Supplementary data are available at *Nephrology Dialysis Transplantation* online.

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AUTHORS' CONTRIBUTIONS

Y.S. and X.J. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. G.H. and Y.L. are considered co-first authors. Concept and design: all authors. Acquisition, analysis or interpretation of data: G.H., Y.L., Y.S., X.J. and J.D. Drafting of the manuscript: G.H., Y.L., Y.S. and X.J. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: G.H., Y.L. and Y.S. Obtained funding: X.J., Y.S. and T.L. Administrative, technical or material support: A.B., C.U.O., F.S., Z.Z., W.E.S., N.X., T.L., A.A.L., H.G.K., S.P. and M.Z.W. Supervision: X.J., Y.S. and J.D. All of the authors approved the final submission of the study.

DATA AVAILABILITY STATEMENT

The data utilized for the displays and calculations presented in this manuscript can be downloaded at http://ghdx.healthdata.org/gbd-results-tool.

CONFLICT OF INTEREST STATEMENT

The authors declare to have no compelling interests in this article.

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