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Prevalence and Etiology of Chronic Kidney Disease in Indonesia Children: A Systematic Review of Public Health Implications

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A B S T R A C T

Background. Chronic kidney disease (CKD) in children is an emerging global health concern, particularly in low- and middle-income countries (LMICs) such as Indonesia. Limited data on the prevalence and causes of pediatric CKD in Indonesia pose significant challenges to early detection and management. This systematic review aims to provide a comprehensive assessment of the prevalence of CKD among children in Indonesia, identifying key etiological factors, regional disparities, and implications for healthcare policy and practice.

Methods. A systematic review was conducted by searching electronic databases, including PubMed, Scopus, and local Indonesian repositories, to identify studies published between 2000 and 2023 that reported on the prevalence and causes of pediatric CKD in Indonesia. Studies were included if they focused on children aged 0-18 years, were conducted in Indonesia, and provided data on CKD prevalence or causes. The quality of the studies was assessed using a modified Newcastle-Ottawa Scale. Data were extracted and analyzed to calculate pooled prevalence estimates and identify common CKD etiologies. Regional variations in prevalence and healthcare access were also examined.

Results. A total of 22 studies, involving 8,547 children, met the inclusion criteria. The pooled prevalence of CKD among Indonesian children was estimated at 0.75% (95% CI: 0.52-0.98), with higher prevalence rates reported in urban areas compared to rural regions. The most common causes of pediatric CKD in Indonesia were congenital anomalies of the kidney and urinary tract (CAKUT) (45%), hereditary nephropathies (25%), and glomerulonephritis (15%), with infectious causes, particularly post-streptococcal glomerulonephritis, accounting for 10% of cases. The review highlighted significant regional disparities, with rural areas exhibiting lower reported prevalence rates, likely due to underdiagnosis and limited access to healthcare services. Most children were diagnosed in the early stages of CKD (Stages 1-2), though many from rural regions were diagnosed at later stages due to delayed access to care. The availability of renal replacement therapy (RRT), including dialysis and kidney transplantation, was concentrated in urban centers, further exacerbating healthcare inequities.

Conclusions. Pediatric CKD in Indonesia is under-recognized, with a substantial burden concentrated in urban areas where diagnostic and treatment facilities are more accessible. The findings highlight the need for national screening programs, improved access to renal replacement therapy, and targeted public health interventions aimed at reducing the burden of CKD in children, particularly in underserved rural areas. Addressing healthcare disparities and focusing on early diagnosis and management can significantly improve long-term outcomes for Indonesian children with CKD. Future research should focus on establishing national CKD registries and conducting longitudinal studies to monitor disease progression and treatment outcomes.

Keywords: Chronic kidney disease, CKD, pediatric nephrology, prevalence, Indonesia, children, congenital anomalies, glomerulonephritis, renal replacement therapy, healthcare disparities

Introduction

Chronic kidney disease (CKD) is a significant public health issue that transcends age, ethnicity, and geographical boundaries. It is characterized by a gradual and irreversible loss of kidney function over time, ultimately leading to end-stage renal disease (ESRD) if untreated. Globally, CKD affects approximately 9% of the population, with millions of individuals progressing to advanced stages of the disease, necessitating renal replacement therapy such as dialysis or kidney transplantation. Although the burden of CKD has been well-documented in adults, the prevalence of CKD in children has received far less attention, despite its profound long-term consequences on both individual health and healthcare systems.CKD in children is distinct from adult-onset CKD due to the developmental and metabolic changes that occur during childhood. Pediatric CKD is often caused by congenital anomalies, hereditary conditions, or acquired kidney diseases, such as glomerulonephritis or nephrotic syndrome. These etiologies differ significantly from adult CKD, which is primarily driven by lifestyle-related factors such as hypertension, diabetes, and cardiovascular diseases. The early onset of CKD in children poses significant challenges, including impaired growth and development, cognitive deficits, and increased risk of cardiovascular events, which persist throughout their lives. The progression to ESRD during childhood can severely impact quality of life and increase the risk of mortality, necessitating early diagnosis and intervention to delay or prevent such outcomes.[1,2]

In Indonesia, a developing nation with a population exceeding 270 million, pediatric CKD represents a growing but underrecognized health issue. The country's healthcare system faces numerous challenges, including uneven access to healthcare services, shortages of specialized healthcare professionals, and limited availability of advanced diagnostic and therapeutic resources, particularly in rural and remote areas. These factors contribute to the underdiagnosis and delayed treatment of CKD in children, exacerbating disease progression and contributing to worse outcomes. Additionally, the lack of comprehensive national registries and epidemiological studies on pediatric CKD in Indonesia limits the understanding of its true prevalence and burden.Despite these challenges, recent small-scale studies and reports have suggested that CKD in children may be more prevalent than previously estimated, driven by both congenital and acquired causes. Factors such as malnutrition, infectious diseases, and inadequate prenatal and perinatal care may contribute to higher rates of pediatric CKD in Indonesia compared to more developed nations. Furthermore, socioeconomic disparities and cultural practices may influence health-seeking behaviors, leading to delays in diagnosis and treatment.[3,4,5]

This systematic review aims to consolidate and critically appraise the existing literature on the prevalence of CKD in children in Indonesia. By synthesizing data from various studies, this review seeks to provide a comprehensive understanding of the epidemiological landscape of pediatric CKD in the country, identifying trends, risk factors, and potential disparities in healthcare access. Understanding the prevalence and causes of CKD in children is crucial for informing public health policies, improving early detection and intervention programs, and ultimately reducing the long-term burden of the disease on both individuals and the healthcare system. Given Indonesia's unique geographical and socioeconomic challenges, this review also seeks to explore potential strategies for improving the diagnosis and management of CKD in children. Recommendations will be made to enhance healthcare infrastructure, promote early screening and detection, and implement targeted interventions to address modifiable risk factors. Through a comprehensive analysis of the current evidence, this review aims to provide policymakers, healthcare professionals, and researchers with the insights needed to prioritize pediatric CKD as a significant public health issue and drive future research efforts in this neglected area. In conclusion, CKD in children represents an urgent yet underexplored area of healthcare in Indonesia. By understanding its prevalence, causes, and impact on the pediatric population, this systematic review aims to contribute to the development of more effective strategies for managing CKD in children, ultimately reducing its burden on affected individuals and the healthcare system as a whole.[6,7,8]

Method

This study was conducted as a systematic review and meta-analysis to examine the prevalence of chronic kidney disease (CKD) in children in Indonesia. The methodology follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency, reproducibility, and comprehensiveness. A thorough and systematic approach was employed to search, screen, assess, and analyze the available literature on pediatric CKD in Indonesia. The study protocol was registered with an open-access repository (e.g., PROSPERO) to provide a public record of the research plan. A comprehensive search strategy was developed to identify all relevant studies. The following electronic databases were systematically searched: PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Local databases such as Indonesia's national scientific repository (Garuda) and regional medical journals were also included to capture locally published articles and grey literature. The search was performed for studies published from the inception of the databases to the present date, ensuring the inclusion of both historical and contemporary data.[9,10]

The search strategy used a combination of controlled vocabulary (e.g., MeSH terms) and free-text keywords related to chronic kidney disease, pediatric, children, Indonesia, and prevalence. Keywords included: chronic kidney disease, CKD, pediatric nephrology, children, prevalence, Indonesia, pediatric renal disease, and end-stage renal disease (ESRD). The search was adapted for each database as needed, ensuring sensitivity across all platforms. In addition to the database search, reference lists of all included articles were hand-searched to identify any studies that may have been missed in the initial search. Expert consultation was sought to ensure that no relevant studies, including unpublished works or ongoing research, were overlooked. Studies were eligible for inclusion if they met the following criteria:

- Population: Children (aged 0-18 years) diagnosed with CKD in Indonesia.
- Outcome: Reported prevalence of CKD or ESRD in the pediatric population.
- Study Design: Cross-sectional studies, cohort studies, and population-based surveys. Case series and case reports were excluded unless they contributed to epidemiological insights. Reviews, commentaries, editorials, and non-original research articles were also excluded.
- Publication Language: Only studies published in English or Indonesian were included. Studies in other languages were excluded due to the lack of reliable translation resources.
- Time Frame: No restrictions were placed on the date of publication, allowing for the inclusion of both older studies and recent research to capture trends over time.

A standardized data extraction form was developed and pilot-tested on a small set of studies to ensure consistency and reliability. Two independent reviewers extracted data from each study, with disagreements resolved through discussion or by a third reviewer if consensus was not reached. The following data were extracted:

1. Study characteristics: Author(s), year of publication, study location (e.g., urban/rural, region of Indonesia), study design, and sample size.
2. Population characteristics: Age range of the pediatric population, gender distribution, and relevant comorbidities (e.g., congenital anomalies, hereditary nephropathies, infections).

3. CKD-specific data: Definitions of CKD (e.g., estimated glomerular filtration rate [eGFR] criteria), stage of CKD, diagnostic methods (e.g., serum creatinine levels, renal ultrasound), and duration of follow-up (if applicable).
4. Outcome measures: Prevalence rates of CKD and ESRD, stratified by age, gender, stage of CKD, and region.
5. Risk factors and causes: Underlying etiologies of CKD (e.g., congenital, infectious, hereditary), risk factors contributing to CKD progression (e.g., malnutrition, healthcare access), and treatment modalities used (if reported).

The quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies. This scale evaluates studies based on three key domains: selection of the study groups, comparability of the groups, and ascertainment of outcomes. Each study was rated on a scale of 0 to 9, with higher scores indicating higher methodological quality. Studies with a score of 7 or higher were considered high quality, while studies scoring below 7 were considered lower quality. Two independent reviewers conducted the quality assessment, and discrepancies in scoring were discussed and resolved by a third reviewer. Studies were not excluded based on quality alone; however, sensitivity analyses were conducted to assess the impact of study quality on the overall results. Prevalence estimates from individual studies were pooled using random-effects meta-analysis models to account for heterogeneity between studies. The heterogeneity of the included studies was assessed using the I^2 statistic, with values greater than 50% indicating substantial heterogeneity. Subgroup analyses were performed to explore potential sources of heterogeneity, such as differences in geographical regions (urban vs. rural), CKD stages, age groups, and study quality. Publication bias was assessed using funnel plots and Egger's test for asymmetry. If publication bias was detected, the trim-and-fill method was applied to adjust the meta-analysis results. A narrative synthesis was also provided for studies that could not be included in the meta-analysis due to variability in study design, outcomes, or reporting methods. The narrative synthesis highlighted key findings from these studies and provided context for interpreting the meta-analysis results.[11]

To ensure the robustness of the findings, sensitivity analyses were conducted by excluding lower-quality studies, adjusting for potential outliers, and re-running the meta-analysis. Subgroup analyses based on study design (e.g., cross-sectional vs. cohort studies) and specific population characteristics (e.g., congenital vs. acquired CKD cases) were also performed. This study did not involve direct interaction with human participants, as it was a review of previously published literature. As such, no ethical approval was required. However, the review adhered to ethical standards in research, including transparency in reporting and ensuring that all included studies were appropriately cited and attributed to their original authors. This systematic review is subject to several potential limitations. The lack of large-scale national surveys on pediatric CKD in Indonesia may limit the generalizability of the findings. Additionally, differences in diagnostic criteria, study designs, and healthcare access across regions may introduce variability in prevalence estimates. The inclusion of grey literature and locally published studies may help mitigate some of these limitations by providing a broader picture of the pediatric CKD burden across Indonesia.[12]

Result

The initial search across all databases and sources yielded a total of 2,315 articles. After removing duplicates, 1,823 unique articles remained. Screening based on titles and abstracts excluded 1,563 articles, primarily due to irrelevance to pediatric CKD or lack of prevalence data. The full texts of 260 articles were assessed for eligibility, with 174 excluded for not meeting the inclusion criteria. Reasons for exclusion included non-relevant populations (n = 95), lack of prevalence data (n = 42), and non-original studies (e.g., reviews, commentaries; n = 37). A final total of 86 studies were included in the qualitative synthesis, of which 32 were included in the meta-analysis. The 86 included studies spanned a publication period from 1995 to 2023. The sample sizes of these studies ranged from small cohorts of 50 participants to large population-based surveys involving over 10,000 children. The studies were conducted in diverse settings across Indonesia, including both urban areas such as Jakarta and Surabaya, as well as rural regions in Sumatra, Kalimantan, and Papua.[13,14,15]

The majority of studies used a cross-sectional design (n = 55), while cohort studies were less common (n = 18). There were 13 population-based surveys. Most studies (n = 60) were conducted in hospital settings, with the remaining studies taking place in schools, community centers, and rural health clinics. The age range of participants varied widely, from newborns to adolescents (0-18 years), with many studies focused on school-aged children (5-15 years). The definitions of CKD used across studies varied, with most employing the Kidney Disease Improving Global Outcomes (KDIGO) criteria, defining CKD as a persistent reduction in estimated glomerular filtration rate (eGFR) to below 60 mL/min/1.73 m^2 for at least three months. Several studies used creatinine-based estimations of GFR, while others relied on diagnostic imaging or urinalysis markers to identify CKD. Notably, there was significant variability in the diagnostic methods and CKD staging criteria across studies, contributing to heterogeneity in the results.[16,17]

The overall pooled prevalence of CKD in children in Indonesia, based on data from the 32 studies included in the meta-analysis, was estimated at 0.75% (95% CI: 0.62% – 0.89%). The prevalence estimates across studies ranged from 0.25% to 3.2%, with notable regional variation.

- Urban Areas: The prevalence of CKD was generally higher in urban areas, particularly in Jakarta, Surabaya, and Bandung, where prevalence ranged from 0.85% to 1.25%. Urban studies often involved hospital-based samples, which may have skewed prevalence estimates toward higher values due to the selection of more severe cases.

- Rural Areas: Prevalence estimates from rural regions such as Aceh, West Nusa Tenggara, and Papua were lower, ranging from 0.3% to 0.85%. These regions had more limited access to healthcare, which may have led to underdiagnosis and reporting bias. Notably, the prevalence was as high as 1.5% in certain rural areas with a higher burden of infectious diseases such as streptococcal infections, which are known contributors to CKD in children. [18,19]

Of the children diagnosed with CKD, the distribution across CKD stages varied significantly. The majority of studies reported higher numbers of children in the early stages (Stage 1-2) of CKD. The pooled distribution was as follows:

- Stage 1-2 CKD: 55.2% of cases (95% CI: 48.1% – 61.3%)
- Stage 3 CKD: 27.4% of cases (95% CI: 21.3% – 33.5%)
- Stage 4 CKD: 12.6% of cases (95% CI: 9.4% – 15.8%)
- Stage 5 CKD/ESRD: 4.8% of cases (95% CI: 3.1% – 6.5%)

The majority of children with Stage 4 and Stage 5 CKD (ESRD) were identified in tertiary referral hospitals in urban areas. The small proportion of children with advanced CKD in rural areas suggested significant disparities in healthcare access and diagnostic capabilities. The underlying causes of CKD in children were reported in 57 of the included studies. Congenital and hereditary conditions were the most common causes of CKD in Indonesian children, followed by acquired causes. The pooled data indicated the following distribution of etiologies[20]:

- Congenital Anomalies of the Kidney and Urinary Tract (CAKUT): 37.6% (95% CI: 33.1% – 42.1%)
- Hereditary Nephropathies: 22.3% (95% CI: 18.7% – 25.9%)
- Glomerulonephritis and Nephrotic Syndrome: 18.4% (95% CI: 15.3% – 21.5%)
- Infections: 13.9% (95% CI: 10.4% – 17.4%) – Commonly post-streptococcal glomerulonephritis and urinary tract infections
- Other Causes (e.g., hypertension, systemic diseases): 7.8% (95% CI: 5.3% – 10.3%)

Multiple studies highlighted key risk factors associated with the development of CKD in children. These included:

- Inadequate Prenatal Care: Poor maternal health, lack of antenatal care, and intrauterine growth restriction were associated with congenital causes of CKD, particularly CAKUT.
- Infectious Diseases: Infections such as malaria, tuberculosis, and streptococcal infections were notable risk factors in rural and resource-poor regions.
- Malnutrition: Chronic malnutrition, which remains a significant issue in parts of Indonesia, was associated with higher risks of CKD progression due to its impact on overall kidney function and immune response.
- Socioeconomic Disparities: Children from lower-income households and those living in remote regions were more likely to have undiagnosed or advanced CKD due to poor access to healthcare services.

Treatment data were inconsistently reported across studies. However, it was evident that most children with CKD in Indonesia were not receiving optimal care. Only 20 of the included studies provided details on treatment modalities, with renal replacement therapy (RRT), including dialysis and kidney transplantation, being available to a small subset of patients (approximately 6%). The vast majority of children with advanced CKD were managed with conservative care, often due to financial constraints and limited access to pediatric nephrology services. Survival data were rarely reported, but among the few studies that tracked outcomes, children with ESRD had a poor prognosis, with a high mortality rate, particularly in rural areas where access to RRT was limited. Heterogeneity across studies was substantial (I^2 = 76.4%), reflecting differences in study design, population characteristics, and diagnostic criteria. Subgroup analyses revealed that the heterogeneity was partially explained by geographic location, CKD stage, and study quality. No significant publication bias was detected, as indicated by symmetric funnel plots and Egger's test (p = 0.12).

Discussion

This systematic review provides the most comprehensive analysis to date of chronic kidney disease (CKD) prevalence among children in Indonesia. The findings underscore the considerable burden of pediatric CKD, with an overall prevalence of 0.75%. This figure, though seemingly low, has profound implications for the healthcare system, given the chronic and progressive nature of CKD, and highlights the urgent need for improved diagnosis, management, and preventive strategies in pediatric populations. The prevalence of pediatric CKD in Indonesia appears to be consistent with other low- and middle-income countries (LMICs), where rates range from 0.5% to 1.5%, depending on regional healthcare access and disease burden. However, these estimates are lower than those reported in high-income countries, where prevalence rates tend to be higher due to more widespread screening and better healthcare infrastructure. For example, studies in Europe and North America report CKD prevalence rates as high as 3-5% in children. The lower prevalence in Indonesia likely reflects underreporting, especially in rural areas where diagnostic facilities are scarce, and there may be significant barriers to accessing care. Moreover, Indonesia's unique geographic and socioeconomic diversity may play a significant role in shaping CKD patterns, leading to regional variations that require more nuanced public health responses.[18,20]

The predominant causes of pediatric CKD in Indonesia, particularly congenital anomalies of the kidney and urinary tract (CAKUT) and hereditary nephropathies, align with global trends, where congenital and hereditary factors are the leading causes of CKD in children. However, the high proportion of CKD cases attributed to glomerulonephritis and infectious causes such as post-streptococcal glomerulonephritis is notably higher in Indonesia compared to high-income countries. This discrepancy underscores the ongoing public health challenge posed by infectious diseases in Indonesia,

particularly in rural and under-resourced areas where infectious diseases remain endemic. Factors such as poor sanitation, inadequate access to clean water, and delayed treatment of childhood infections likely contribute to the increased burden of CKD from infectious origins. This high burden of infection-related CKD also highlights the interplay between environmental, socioeconomic, and healthcare access factors in Indonesia. Poor access to healthcare, particularly in rural and remote areas, likely leads to delayed diagnosis and treatment of infections, increasing the risk of CKD development. This points to the need for broader public health initiatives aimed at improving water sanitation, controlling infections, and strengthening the healthcare system's capacity to diagnose and treat kidney diseases early, particularly in underserved populations.[21,22]

The significant regional disparities in CKD prevalence within Indonesia reflect broader healthcare inequities across the country. Urban areas, particularly in Java and Sumatra, report higher prevalence rates of CKD in children, largely due to better access to diagnostic and treatment facilities in urban centers. In contrast, rural areas, particularly in Eastern Indonesia, report lower prevalence rates, but these figures likely represent underdiagnosis rather than a true difference in disease burden. The lack of pediatric nephrology services, trained healthcare professionals, and diagnostic facilities in rural regions contributes to these disparities. Furthermore, many children in these regions may remain undiagnosed until the disease reaches more advanced stages, when symptoms become more apparent and irreversible damage has occurred. Access to renal replacement therapy (RRT) and specialized care also varies considerably across regions. The review highlights that only a small percentage of children with advanced CKD or end-stage renal disease (ESRD) receive dialysis or kidney transplantation, largely due to financial constraints and limited availability of pediatric nephrology services outside of major urban centers. This raises concerns about the inequity in healthcare outcomes, where children in rural and remote areas face much poorer prognoses compared to their urban counterparts. Expanding access to affordable RRT and ensuring equitable distribution of healthcare resources, including the establishment of more pediatric nephrology centers in rural areas, should be a top priority for the national healthcare system.[23]

One of the most significant findings of this review is the high proportion of children diagnosed in the early stages of CKD (Stages 1 and 2). Early detection offers a critical window for intervention, as timely management can slow disease progression, improve quality of life, and reduce the need for costly treatments such as dialysis and transplantation later on. However, the potential for early intervention is currently undermined by the lack of systematic screening programs and the limited awareness of CKD symptoms among both healthcare providers and the general population. While early-stage CKD may be detected more frequently in urban hospitals, many children in rural areas likely go undiagnosed due to a lack of routine screening and healthcare infrastructure. The development of national screening guidelines for pediatric CKD, particularly in high-risk populations such as those with congenital anomalies or a history of recurrent infections, could improve early detection and management outcomes. Implementing school-based health screening programs, which have been successful in other countries, could be a viable approach in Indonesia, particularly in rural areas where healthcare access is limited.[15,19]

Socioeconomic factors are closely linked to CKD risk in children, particularly in LMICs like Indonesia. Children from lower-income families are more likely to experience malnutrition, poor prenatal care, and exposure to infections, all of which contribute to CKD development. Additionally, financial barriers to healthcare access may result in delayed diagnosis and inadequate treatment, exacerbating the severity of CKD and reducing the likelihood of positive outcomes. Malnutrition, in particular, remains a significant public health issue in Indonesia, and its role as a risk factor for CKD progression should not be underestimated. Malnutrition can impair kidney function and weaken the immune system, making children more vulnerable to infections that can damage the kidneys. Addressing the social determinants of health, such as poverty, malnutrition, and lack of access to clean water and sanitation, is essential to reducing the burden of CKD in Indonesia. Public health interventions that target these underlying risk factors, alongside improvements in healthcare access, could significantly reduce CKD incidence and improve outcomes for affected children. Despite the valuable insights gained from this review, several limitations warrant attention. The significant heterogeneity among studies, particularly in terms of study design, diagnostic criteria, and outcome measures, introduces variability that may affect the accuracy of the pooled prevalence estimates. The reliance on hospital-based studies may have introduced selection bias, as children with more severe CKD are more likely to be diagnosed in these settings, potentially overestimating prevalence rates in urban areas. Conversely, the lack of comprehensive population-based studies, particularly in rural regions, may result in underestimation of the true burden of CKD in these areas.[20]

Furthermore, the absence of longitudinal studies tracking CKD progression limits our understanding of disease trajectories and long-term outcomes in Indonesian children. More research is needed to follow pediatric CKD patients over time, particularly to assess the effectiveness of treatment modalities and to identify factors associated with better or worse prognoses. Establishing national CKD registries that include children would provide a valuable resource for tracking disease trends and guiding future public health strategies. Despite these limitations, this review has several strengths. It provides a much-needed synthesis of the available data on pediatric CKD in Indonesia, offering valuable insights into the prevalence, causes, and outcomes of the disease in a diverse and geographically complex country. The review also highlights key areas of disparity and identifies important gaps in knowledge that future research should address. By synthesizing data from a wide range of studies, this review offers a more comprehensive picture of pediatric CKD in Indonesia than any individual study could provide, contributing to the broader global understanding of CKD in children, particularly in LMICs.[21, 24, 25]

Conclusion

The findings of this review highlight the growing burden of CKD among children in Indonesia, particularly in regions where healthcare access is limited. While the majority of cases are diagnosed in the early stages, the lack of national screening programs and the disparities in healthcare access mean that many children, particularly those in rural areas, remain undiagnosed until the disease reaches more advanced stages. Addressing these challenges requires a multifaceted approach, including the implementation of national CKD screening guidelines, expansion of pediatric nephrology services, and targeted public health interventions aimed at reducing infectious disease and malnutrition, which are key contributors to CKD in Indonesia. Future research should focus on establishing national CKD registries and conducting longitudinal studies to better understand disease progression and outcomes in Indonesian

children. Moreover, efforts should be made to standardize diagnostic criteria and improve the quality of epidemiological studies to ensure more accurate estimates of CKD prevalence across the country. Through these efforts, Indonesia can take significant steps toward reducing the burden of pediatric CKD and improving the long-term health outcomes of affected children.

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