SCREENING OF KIDNEY FUNCTION BIOMARKERS FOR CHRONIC KIDNEY DISEASE PREDICTION AND FINANCIAL HEALTH BENEFIT

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ABSTRACT

Introduction *Chronic kidney disease (CKD) is a significant public health problem, affecting more than 10% of the global population. This alarming increase is due to multiple factors, including an aging population worldwide and the increasing prevalence of metabolic diseases. Management of CKD and its associated complications is a major challenge of health systems due to the high cost of treating this catastrophic disease.* ***Method*** *A comprehensive search of the published literature in Scopus was conducted. The search strategy was designed to identify studies reporting the economic impact of CKD, as well as studies evaluating the cost-effectiveness of biomarkers for predicting CKD.* ***Results*** *The use of estimated glomerular filtration rate (eGFR) and microalbuminuria, as biomarkers for predicting progression of chronic kidney disease is a cost-effective strategy especially in people with high-risk CKD population. This may lead to a reduction in healthcare costs associated with End Stage Renal Disease (ESRD), including the need for expensive renal replacement therapies such as hemodialysis, Continuous Ambulatory Peritoneal Dialysis (CAPD), and kidney transplantation.* ***Discussion*** *The use of eGFR and microalbuminuria as biomarkers to predict CKD progression and patient outcomes appears to be a cost-effective strategy.* ***Conclusions*** *These biomarkers may improve early detection and management of CKD, potentially helping to reduce the substantial economic burden.*

Keywords: *Cost effectiveness; eGFR; microalbuminuria*

ABSTRAK

Pendahuluan *Penyakit ginjal kronis (PGK) merupakan masalah kesehatan masyarakat yang signifikan, yang mempengaruhi lebih dari 10% populasi global. Peningkatan yang mengkhawatirkan ini disebabkan oleh berbagai faktor, termasuk populasi yang menua di seluruh dunia dan meningkatnya prevalensi penyakit metabolik. Manajemen PGK dan komplikasi terkaitnya merupakan tantangan utama sistem kesehatan karena tingginya biaya pengobatan penyakit katastrofik ini.* ***Metode*** *Pencarian komprehensif literatur yang dipublikasikan di Scopus dilakukan. Strategi pencarian dirancang untuk mengidentifikasi studi yang melaporkan dampak ekonomi PGK, serta studi yang mengevaluasi efektivitas biaya biomarker untuk memprediksi PGK.* ***Hasil*** *Penggunaan estimasi laju filtrasi glomerulus (eGFR) dan mikroalbuminuria, sebagai biomarker untuk memprediksi perkembangan penyakit ginjal kronis merupakan strategi yang hemat biaya terutama pada orang dengan populasi PGK berisiko tinggi. Hal ini dapat menyebabkan pengurangan biaya perawatan kesehatan yang terkait dengan Penyakit Ginjal Stadium Akhir (ESRD), termasuk kebutuhan untuk terapi penggantian ginjal yang mahal seperti hemodialisis, Continuous Ambulatory Peritoneal Dialysis (CAPD), dan transplantasi ginjal.* ***Pembahasan*** *Penggunaan eGFR dan mikroalbuminuria sebagai biomarker untuk memprediksi perkembangan CKD dan hasil akhir pasien tampaknya merupakan strategi yang hemat biaya.* ***Kesimpulan*** *Biomarker ini dapat meningkatkan deteksi dini dan penanganan CKD, yang berpotensi membantu mengurangi beban ekonomi yang besar.*

Kata Kunci*: Efektivitas biaya, eGFR, mikroalbuminuria.*

INTRODUCTION

Chronic kidney disease has become a pressing global public health concern, with its prevalence steadily climbing driven by the rapid aging of populations worldwide and the growing epidemic of metabolic disorders like diabetes and hypertension. There are some markers for detecting CKD. Serum creatinine levels can provide an estimate of eGFR, while the albumin-to-creatinine ratio in urine can indicate the presence of elevated albumin, an early sign of kidney damage (Graziani et.al., 2015).

The cost-effectiveness of screening for CKD using GFR and albumin-to-creatinine ratio (ACR) varies based on the population and screening strategy (Wang et.al, 2017). Targeted screening of high-risk populations, such as those with diabetes or hypertension, has been shown to be more cost-effective than mass screening of the general population (Komenda et.al., 2014). Cost-effectiveness strategies are essential given the enormous financial burden of end-stage kidney disease, which requires expensive treatments such as dialysis and kidney transplantation (Foster, 2019). Therefore, this systematic review aims to evaluate the economic impact and cost-effectiveness of using eGFR and albumin-to-creatinine ratio as biomarkers to predict the progression of chronic kidney disease. The systematic review was conducted within the last 2 years because previous studies have explained the advantages of screening based on differences in population and risk factors. This article further explains the economic impacts caused by these chronic risk factors, which if handled immediately will benefit a country.

Estimated Glomerular Filtration Rate (eGFR)

Estimated glomerular filtration rate (eGFR) is considered the most accurate overall measure of kidney function, as it provides a quantitative assessment of the kidney's ability to filter waste products from the blood. CKD is typically defined as a persistent eGFR below 60 mL/min/1.73 m2 for 3 months or more, with or without evidence of kidney damage (Abraham et.al., 2018).

Albumin-to-creatinine ratio (ACR)

Albumin-to-creatinine ratio in urine can detect the presence of albumin, which is an indicator of kidney damage. Elevated levels of albumin in the urine suggest reduced kidney function and an increased risk of progression to end-stage renal disease (Muhamad et.al., 2024). Regular screening for albuminuria is recommended for individuals with diabetes or hypertension, as these conditions are major risk factors for the development and progression of chronic kidney disease (Critselis et.al., 2018).

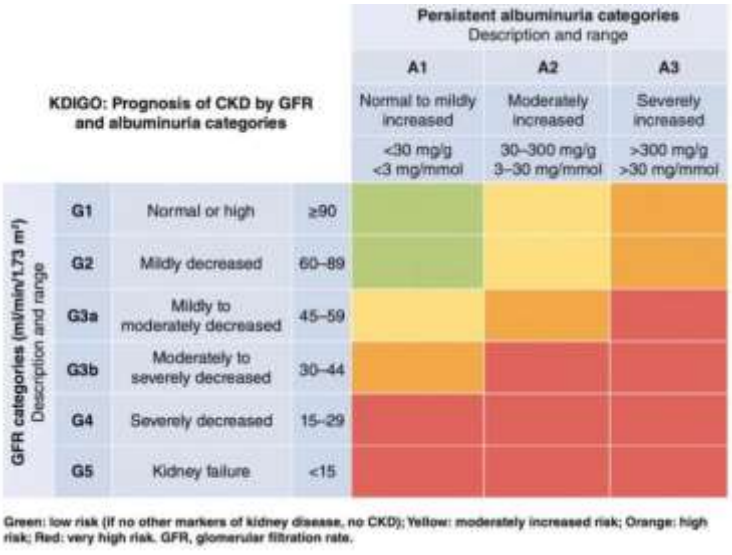
Table 1. Biomarkers for Predicting Chronic Kidney Disease Progression

Biomarker	Description	Role in CKD
Estimated Glomerular Filtration Rate (eGFR)	Estimates the kidney's filtration rate based on serum creatinine levels	Quantifies overall kidney function, with CKD defined as eGFR < 60 mL/min/1.73m2
Albumin-to-Creatinine Ratio/ Microalbuminuria	Measures the ratio of albumin to creatinine in urine	Indicates the presence of albumin, an early marker of kidney damage

Prognosis CKD

According to the Kidney Disease Improvement Global Outcome (KDIGO) guidelines, prognosis is divided based on risk level. Green means low risk, yellow means moderate risk, orange means high risk, and red means very high risk. The division of these criteria is based on Albuminuria and eGFR measurements. According to the Albuminuria range, the classification is divided into three A1, A2, and A3 where one is normal or slightly increased, two are moderately increased, and three are severely increased. The prognosis is based on GFR where the prognosis is divided based on stage, namely G1 to G5 (KDIGO, 2012).

Table 2. Risk Prediction of CKD by GFR and albuminuria categories



METHOD

A systematic literature review was conducted to assess the cost-effectiveness of utilizing eGFR and albumin-to-creatinine ratio as biomarkers for predicting and monitoring chronic kidney disease progression. The search strategy involved a comprehensive search of the Scopus database for relevant published literature. The search terms included various combinations of keywords related to cost-effectiveness, chronic kidney disease, eGFR and albumin-to-creatinine ratio. PRISMA guidelines, a widely recognized set of evidence-based

recommendations for the conduct of systematic reviews and meta-analyses, were strictly followed to ensure a robust and transparent article selection and data extraction process. At the start of selecting journals, they were selected based on keywords alone in Scopus without going through any set time limits. However, in the end, after selecting the contents of the journal, a time limit was set to avoid the effects of the COVID pandemic bias, therefore the journals used between 2023 and 2024.

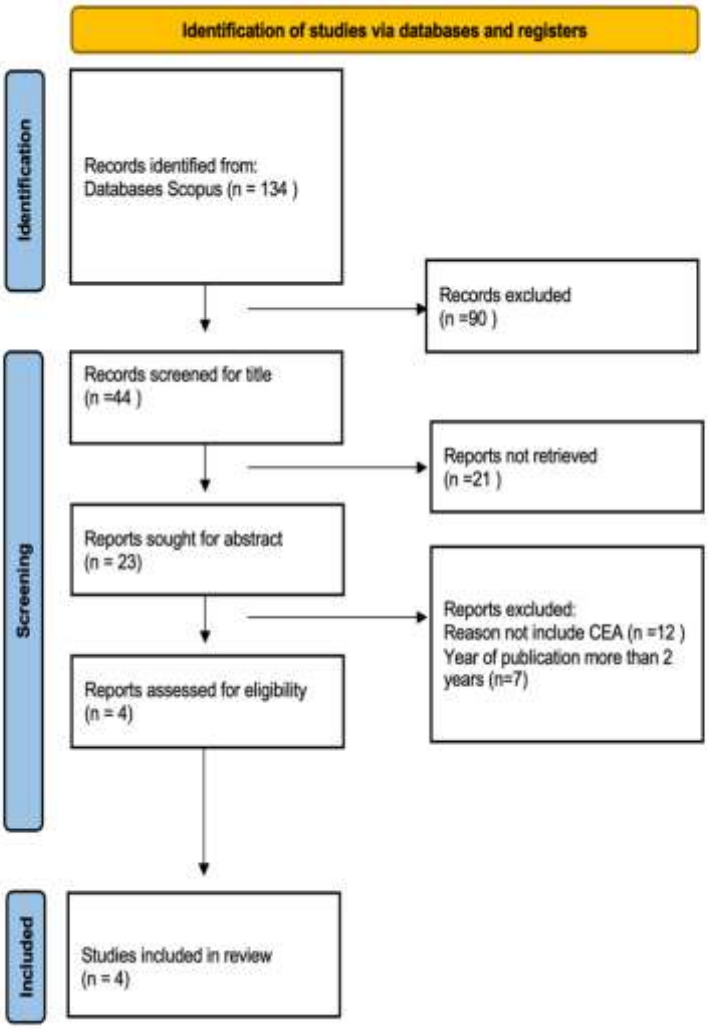


Figure 1. PRISMA flowchart

The key criteria for inclusion in this review were studies that evaluated the cost effectiveness of using biomarkers like eGFR and albumin-to-creatinine ratio for detecting and managing chronic kidney disease. The exclusion criteria included studies that lacked relevant economic data and studies that did not provide sufficient information to assess their findings.

RESULTS AND DISCUSSION

The systematic review identified 4 relevant studies that examined the cost-effectiveness of utilizing eGFR and albumin-to-creatinine ratio for the detection and management of chronic kidney disease.

Table 4. Summary of Selected Journals

Author/Year/ Title	Population	Intervention	Outcomes	ICER
(Rossing et al.,2023) **Estimated health economic impact of conducting urine albumin-to-creatinine ratio testing alongside estimated glomerular filtration rate testing in the early stages of chronic kidney disease in patients with type 2 diabetes**	The hypothetical cohort consisted of 1,000 modelled patients. Patients were aged 60 with a diagnosis of T2D. 41.8% of the cohort were male	ACR testing enables early diagnosis and treatment of CKD. Early intervention improves survival and reduces dialysis needs. Cost-effectiveness is demonstrated across various CKD stages.	Early ACR testing improved clinical outcomes significantly. Cost savings were observed with timely management initiation.	ICERs for A2 or A3 range from PS 4,407 to PS 6,208. Higher ICER for G3aA1 is PS 51,397 per LYg. ACR testing shows consistent cost-effectiveness across KDIGO groups. Cost-effectiveness improves with more efficacious treatments.
(Kumar et al.,2023) **Cost-effectiveness of population-based screening for microalbuminuria in people with type 2 diabetes mellitus in India**	The target population is normotensive type 2 diabetes patients over 40. Patients with hypertension were excluded from the screening. Screening aimed to reduce chronic kidney disease progression.	The intervention involves population-based ACR screening for diabetes patients. Two screening scenarios were evaluated: dipstick and spot urine ACR. Both screening scenarios were cost-effective at one GDP per capita.	ACR screening reduces ESRD cases. Scenario I reduces 180 ESRD cases per 100,000 population. Scenario II reduces 193 ESRD cases per 100,000 population. Cost savings of ₹12.3 crore in Scenario I over 10 years. Cost savings of ₹13.3 crore in Scenario II over 10 years. Screening is cost-effective at one-time GDP per capita threshold.	Scenario I ICER: ₹ 24,114 (US$ 308) per QALY. Scenario II ICER: ₹ 13,790 (US$ 176) per QALY. Both scenarios were cost-effective below India's GDP per capita threshold.
(Zafarnejad et al.,2024) **Cost-effectiveness of chronic kidney disease screening using cumulative eGFR-based statistics**	The study focuses on a synthetic cohort aged 30 years and older. The cohort represents diverse racial and ethnic groups in the US.	The intervention focuses on CKD screening policies. It utilizes GFR-based screening methods. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are integrated into treatment.	Routine CKD screening improves clinical and societal outcomes. GFR screening reduces DALYs. Annual screening starting at age 30 is cost-effective. Incorporating SGLT2 inhibitors enhances health outcomes and cost savings.	Lower ICER indicates more cost-effective screening strategy. Annual screening starting at age 30 has lowest ICER. ICER values range from 15,614 USD *to* 54,373 USD per DALY averted.
(Cusick et al.,2024) **Population-Wide Screening for Chronic Kidney Disease: a Cost-Effectiveness Analysis**	The study focuses on the U.S. adult population aged 35 and above. Approximately The analysis includes 158 million individuals aged 35 to 75 years.	Screening detects previously unrecognized chronic kidney disease. Patients initiate treatment based on albuminuria and eGFR levels.	Cost-effectiveness of screening varies by self-reported diabetes status. UACR-based screening is cost-effective for U.S. adults aged 35 and above.	For 55-year-olds, ICER was 86,300 QALY gained.

In a study conducted by Rossing, on the economic impact of conducting ACR screening on patients with diabetes mellitus, it was found that Incremental Cost-Effectiveness Ratio (ICER) would differ at each stage of CKD according to the KDIGO classification. Rossing explained that at stage A2 or A3, ICERs range from PS 4.407 to PS 6.208. This explains that with earlier ACR screening, it will have a significant impact on the results of improving CKD. Therefore, in this study, cost savings can be observed at each different level of CKD stage. The probabilistic sensitivity analysis showed cost-effectiveness results for a cohort of 1,000 individuals in KDIGO category G3aA2 receiving timely CKD treatment. The analysis included estimates of life years before kidney failure and number of dialyses avoided, varying for relative risk reduction rates (Rossing et.al., 2023).

In a study conducted by Kumar in 2023, ACR screening will reduce the incidence of ESRD. Kumar used two different scenarios, in the first scenario, Kumar used urine dipstick screening and in the second scenario used ACR screening. The results of scenario I ICER were ₹ 24,114 (US$ 308) per quality-adjusted life years (QALY). The results of scenario II ICER were ₹ 13,790 (US$ 176) per QALY. Both screenings are considered effective in reducing ESRD. This study was conducted in India on diabetic patients. The study assessed the cost effectiveness of population based screening for microalbuminuria in individuals with type 2 diabetes mellitus in India. Screening scenario I resulted in a total discounted cost of Rs 59,412 and a total discounted QALY of 6.88, showing an ICER of Rs 24,114 per QALY gained compared to no screening scenario. The study highlighted the importance of ACR testing in patients with chronic kidney disease, showing that as more efficacious treatments become available, the healtheconomic benefit provided by ACR testing is likely to improve. The analysis considered different scenarios with varying treatment effects to assess cost effectiveness across different KDIGO categories (Mathan Kumar et.al, 2023).

Zafarnejad (2024) wrote in his article about CKD screening using GFR-based screening methods. The study focused on a cohort over 30 years of age representing a diverse racial and ethnic group in the US. The intervention focused on CKD screening policies. In people with or without diabetes Sodium-glucose cotransporter-2 (SGLT2) inhibitors were integrated into treatment. Lower ICERs indicate a more cost-effective screening strategy. Annual screening starting at age 30 years had the lowest ICER. ICER values range from 15,614 USD to 54,373 USD per disability-adjusted life years (DALY) averted (Zafarnejad et.al., 2024).

In a study conducted by Cusick on Population-Wide CKD Screening, screening detected previously unrecognized chronic kidney disease. Patients were initiated on treatment based on albuminuria and eGFR levels. Cost-effectiveness of screening varied by self-reported

diabetes status. ACR-based screening was cost-effective for US adults aged 35 and older. For those aged 55, the ICER was 86,300 QALYs gained (Cusick et.al., 2023).

All journals explore research on the effectiveness of screening in patients using eGFR and microalbumiuria biomarkers that will benefit state payers and patients economically. All showed effective results with indicators of reducing costs incurred for kidney replacement therapy.

CONCLUSION

In summary, the use of these biomarkers, either alone or in combination, shows promise for early detection and management of CKD, potentially reducing the substantial medical and economic burden of this disease.

The potential use of eGFR and microalbuminuria as biomarkers could save government funding for kidney disease. These biomarkers may improve early detection and management of CKD, potentially helping to reduce the substantial economic burden.

The renal screening demonstrated significant cost-saving benefits and improved effectiveness compared to usual care. By focusing on systematic control of eGFR, microalbuminuria, comorbidities, and promoting healthy lifestyles, the progression of patients to dialysis and overall mortality **.** Costs were estimated from the payer perspective, considering direct medical costs like nephroprotection treatment, outpatient visits, and laboratory tests, with variations in costs across different CKD stages.

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