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REVIEW ARTICLE

Performance evaluation of estimated glomerular filtration rate (eGFR) equations in Asia: A systematic review

Ayra SIDDIQUI[1], Shan LAKHANI[1], Fatima Asad KHAN[2], Imran SIDDIQUI[2], Sibtain AHMED[2]*

[1]Medical College, The Aga Khan University, Karachi, Pakistan; [2]Section of Clinical Chemistry, Department of Pathology and Laboratory Medicine, The Aga Khan University, Karachi, Pakistan

Abstract

Introduction: Chronic kidney disease (CKD) poses a global public health challenge, necessitating accurate assessment of renal function for timely intervention. Glomerular filtration rate (GFR) is a crucial indicator, traditionally measured using creatinine-based equations. However, Cystatin C-based equations offer potential advantages. We aim to evaluate the performance of estimated GFR (eGFR) equations for accurate renal function assessment in diverse Asian populations. *Materials and Methods:* Following PRISMA guidelines, the systematic review covered studies from 1991 to 2023 across Asian populations, incorporating equations based on both creatinine and Cystatin C. Eligibility criteria included adults aged 18 or older, either healthy or with CKD. Data extraction included study details, population characteristics, disease conditions, and formulas used. Quality assessment was conducted using the QUADAS-2 tool. *Results:* The study analysed 26 studies focusing on South Asia and 66 on East Asia. In South Asia, the CKD-Epi-Pak equation demonstrated superior accuracy, achieving high percentages of eGFR values within specified ranges of measured GFR (P15: 70.39%, P30: 89.35%) with minimal bias (-1.33). The traditional MDRD equation exhibited poor performance, registering the lowest agreement percentages (P15: 7.8%, P30: 25.4%, P50: 71.1%) and the highest bias (-26.13). In East Asia, the CKD-Epi-2021 formula displayed the best accuracy, with high percentages of eGFR values within specified ranges (P15: 65.4%, P30: 97.6%). The simplified MDRD formula showed suboptimal performance, indicating lower agreement percentages (P15: 15.46%, P50: 56.59%). Variations of the MDRD formula in Japan exhibited bias while modified Gates Method demonstrated inferior precision. *Conclusion:* CKD-Epi-Pak and CKD-Epi-2021 show potential suitability in South and East Asia, respectively. Future research should prioritise ethnicity-specific equation development to enhance accuracy and clinical utility in Asian populations.

Keywords: Glomerular filtration rate, Estimated glomerular filtration rate, Chronic kidney disease, South Asia, East Asia

INTRODUCTION

Chronic kidney disease (CKD) is a global public health issue with increasing incidence and prevalence. It is associated with unfavourable outcomes, significant healthcare expenditure, and greater morbidity and mortality.[1] Not only does CKD lead to kidney failure, but also encompass complications arising from reduced kidney function, such as cardiovascular disease, hypertension, anaemia, mineral bone disorder, volume overload, electrolytes, and acid-base abnormalities.[2] Existing research indicates that early detection and timely intervention can potentially avert or postpone some of these adverse outcomes.[3] Therefore, timely diagnosis of CKD is of utmost importance.

Accurately assessing renal function is essential in the diagnosis, staging, and treatment of chronic kidney disease (CKD).[4] Glomerular filtration rate (GFR) is recognised as the most valuable indicator for assessing overall renal function, and its accurate estimation significantly contributes to the identification, progression and management of kidney diseases. Traditionally,

*Address for correspondence: Sibtain Ahmed, Aga Khan University Hospital, Stadium Road, Karachi, Pakistan. 74800. Tel: +92 21 111-911-911; Email: *sibtain.ahmed@aku.edu (SA)*

GFR measurement has relied on renal clearance using either exogenous filtration markers like inulin, iohexol, and 125I-iothalamate, or endogenous markers such as creatinine and Cystatin C. Inulin, although considered to be the "gold standard" method, is primarily utilised only in research due to its costliness, technical complexity, and the need for continuous infusion and repeated blood sampling.[5] Hence, nuclear medicine techniques, such as (99m) Tc-diethylenetriaminepentaacetic acid [(99m) Tc-DTPA] and (51) Cr-ethylenediaminetetraacetic acid [(51) Cr-EDTA], are the preferred methods for GFR measurement in both scientific research and routine clinical practice. These methods exhibit a strong correlation with inulin clearance.[6]

GFR can be computed using the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) study equations based on plasma or serum creatinine.[7,8] Creatinine production is proportional to muscle mass and is influenced by factors such as age, gender, race, and weight.[7,9] Nevertheless, relying on plasma or serum creatinine has notable drawbacks. One such limitation is that serum creatinine may remain within the normal range until GFR has declined by more than 50%, making it less reliable for detecting early stages of renal dysfunction.[7] Consequently, an elevation in serum creatinine may not become apparent until a substantial decrease in GFR has already taken place.

Cystatin C is a cysteine protease inhibitor with a molecular mass of 13 kDa.[10] Research has demonstrated that Cystatin C serves as a more sensitive indicator of GFR changes compared to serum creatinine, since it is unaffected by factors such as muscle mass, age, inflammation, fever, or external substances.[10,11] Numerous studies have consistently shown Cystatin C to outperform serum creatinine in predicting kidney function.[12-16] Consequently, Cystatin C has been adopted as an alternative endogenous serum marker for estimating GFR, leading to the development of multiple GFR estimation formulas based on serum Cystatin C measurements, such as Hoek, Flodin, Grubb and Larsson.[17-19] A Cystatin C-based equation developed by Hoek *et al*. demonstrated superior precision and accuracy when compared to the Cockcroft-Gault equation.[20] Newer equations based on Cystatin C include CAPA and full-Age Spectrum (FAS) equations.[21,22]

In 2012, the CKD-EPI consortium introduced equations based on standardised Cystatin C (CKD-EPI Cystatin C) or a combination of Cystatin C and creatinine (combined CKD-EPI equation).[23] More recently, the New European Kidney Function Consortium (EKFC) has developed an equation that modifies the FAS SCr-based equation by incorporating design elements from both the FAS and CKD-EPI equations.[24] Furthermore, the National Kidney Foundation and the American Society of Nephrology have recommended the immediate replacement of older estimated GFR equations based on serum creatinine (such as the MDRD Study and CKD-EPI 2009) with the new 2021 CKD-EPI equation.[25,26]

A notable disparity exists between the estimation of GFR using Cystatin C and creatinine-based methods when applying the CKD-EPI equation. Numerous clinical trials have sought to compare the efficacy of creatinine and Cystatin C in CKD-EPI equations for GFR estimation, but the findings have remained inconclusive. The Kidney Disease Improving Global Outcome (KDIGO) guidelines in 2012 recommended the use of the CKD-EPI-Cr-Cystatin C equation for adults whose estimated GFR (eGFR) falls within the range of 45–59 mL/min/1.73 m^2 and who exhibit no signs or markers of renal damage.[27] However, the use of Cystatin C is associated with higher medical costs since the reagents required for Cystatin C testing are more expensive compared to serum creatinine.[28]

Numerous studies have continually updated creatinine-based equations, tailoring them to different ethnicities. One example is the CKD-EPI Pak equation, which was found to have a better performance when compared to CKD-EPI 2021, CKD-EPI 2009, and MDRD equations taking CrCl as the gold standard.[29]

Cystatin C-based equations remain underutilised in the Asian population, contributing to a lack of knowledge regarding the most suitable eGFR equations for Asia. The challenge is compounded by regional variations in factors like diet, genetics, and lifestyle, making it essential to identify equations tailored to the diverse Asian population. This review aims not only to compile evidence on the most effective GFR equations for different age groups, ethnicities, and health status within Asian populations but also to emphasise their clinical implications. Additionally, the study explores whether equations combining creatinine and Cystatin C outperform those based on a single biomarker across diverse Asian subpopulations.

Beyond accuracy, practicality and ease of clinical implementation will be considered, along with the potential impact on public health and healthcare guidelines in the region. This research aims to guide clinical practice, facilitate better healthcare decision-making, and ultimately contribute to improved patient care in the region.

MATERIALS AND METHODS

Protocol:

The systematic review's protocol adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines and was registered with PROSPERO (International Prospective Register of Systematic Reviews; https://www.crd.york.ac.uk/prospero, registration number: CRD42024500144).[30] However, a meta-analysis could not be conducted due to the large amounts of heterogeneity between the studies. This can be attributed to the fact that the studies were carried out in different geographical locations amongst different patient populations. Hence, the data could not be pooled without introducing a large amount of bias. The PRISMA-P checklist was referred to assess the quality of our manuscript.

Eligibility Criteria:

In our systematic review, we included validation studies conducted in all Asian populations, which utilised equations based on both creatinine and Cystatin C to estimate GFR, either separately or in combination. The study participants had to be adults aged 18 years or older who were either healthy or had CKD. Additionally, only equations that were referenced in more than one research paper were considered. Moreover, only studies that compared the performance of the equations with measured GFR (mGFR), determined using established exogenous markers like 99mTc-DTPA, 51Cr-EDTA, and Inulin, were included. Furthermore, we considered only original validation studies that were written in the English language.

Conversely, we excluded studies that did not provide accurate results for evaluating equation performance. We also excluded studies carried out in the general population with other disease conditions, meta-analyses and review studies, studies involving children, and any studies conducted on animals.

Search Strategy and Study Selection:

A comprehensive systematic search was conducted across multiple databases including Pubmed, Cochrane, EBSCO CINAHL and ProQuest Dissertations and Theses, spanning from 1991 to 2023. Two independent reviewers (AS and SL) conducted this search.

The search strategy for PubMed incorporated a wide range of Medical Subject Headings (MeSH) and keywords as follows: "("Glomerular Filtration Rate"[Mesh] OR "Estimated glomerular filtration rate"[tiab] OR eGFR[tiab] OR "glomerular filtration rate"[tiab]) AND (estimated OR estimation OR estimating OR estimate) AND (equation) AND ("South Asia" OR Bangladesh OR Bhutan OR India OR Pakistan OR Nepal OR Sri Lanka OR Afghanistan OR China OR Taiwan OR Japan OR Thailand OR Singapore OR Korea OR Malaysia OR Arab)".

Cochrane' search strategy was as follows: ("Estimated glomerular filtration rate" OR eGFR OR "glomerular filtration rate") AND (estimated OR estimation OR estimating OR estimate) AND equation* AND ("South Asia" OR Bangladesh OR Bhutan OR India OR Pakistan OR Nepal OR Sri Lanka OR Afghanistan OR China OR Taiwan OR Japan OR Thailand OR Singapore OR Korea OR Malaysia OR Arab) in Title Abstract Keyword. EBSCO CINAHL complete search strategy was as follows: AB (("Estimated glomerular filtration rate" OR eGFR OR "glomerular filtration rate")) AND ((estimated OR estimation OR estimating OR estimate)) AND (equation) AND (("South Asia" OR Bangladesh OR Bhutan OR India OR Pakistan OR Nepal OR Sri Lanka OR Afghanistan OR China OR Taiwan OR Japan OR Thailand OR Singapore OR Korea OR Malaysia OR Arab)) Expanders - Apply equivalent subjects Narrow by Language: - English Search modes - Boolean/ Phrase. ProQuest Dissertations and Theses database search strategy was: ab (("Estimated glomerular filtration rate" OR eGFR OR "glomerular filtration rate")) AND ab ((estimated OR estimation OR estimating OR estimate)) AND ab(equation*) AND ("South Asia" OR Bangladesh OR Bhutan OR India OR Pakistan OR Nepal OR Sri Lanka OR Afghanistan OR China OR Taiwan OR Japan OR Thailand OR Singapore OR Korea OR Malaysia OR Arab).

In the initial screening, all identified records were assessed by the independent reviewers based on their titles and abstracts. Abstracts that did not meet the inclusion criteria or those that matched the exclusion criteria were excluded from further consideration. The remaining records, as well as those with abstracts providing

sufficient information for evaluation, were then subjected to full-text assessment. This evaluation was also performed independently by the same reviewers. Any disagreements that arose during the review process were resolved through consultation with a third reviewer (SA) to ensure consensus and accuracy in the selection of articles for inclusion in the review.

Search Results:
A total of 1,223 unique records were identified and screened after the removal of duplicates. Of these, 1,073 studies were excluded based on title screening, leaving 150 studies for full-text screening. Two studies had to be further excluded as their full texts were not available. The remaining 148 studies were carefully assessed. Of these, 26 studies were of the wrong study design, 18 reported data in the wrong population and 17 did not report the desired results, leading to their exclusion. This left us with 87 studies for our final review. The process of study identification and inclusion is represented in the PRISMA Flow diagram (FIG 1).

Data Collection and Extraction:
The selected studies were analysed, and their data was extracted, by two investigators (AS and SL). A standardised data extraction protocol was applied to systematically collect the following essential information. This included details such as: first author's name and publication year,

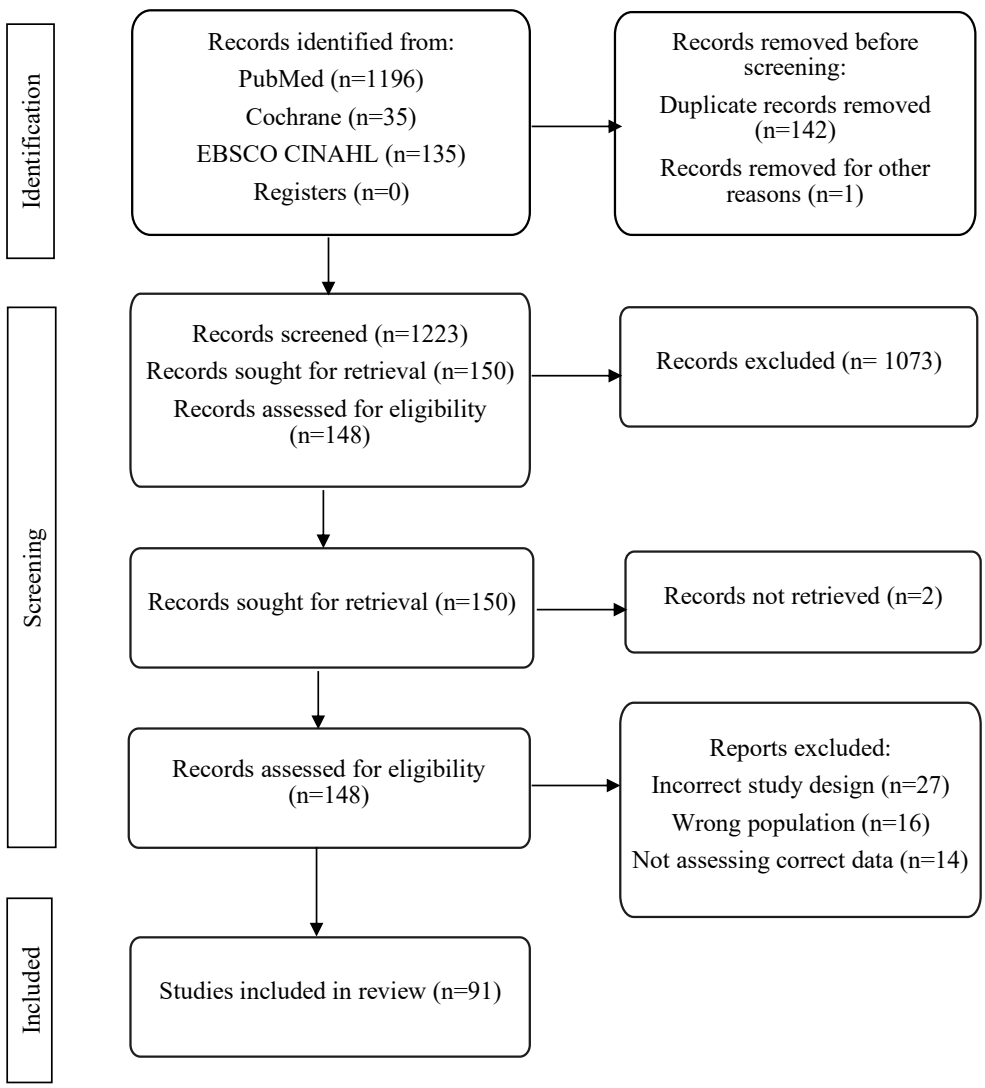

Figure 1: PRISMA Flow diagram showing the process of study identification, screening and inclusion

sample size, classification of the population into healthy and CKD groups, specific demographic characteristics of the study populations, which encompassed age groups and the proportion of males. Additionally, the disease conditions for which the equations were validated, along with the formulas used to estimate GFR were recorded.

Equation performance was assessed by comparing the bias, precision, accuracy and root mean squared error of the different formulas with the standard of mGFR. Bias represented the mean or median difference between mGFR and eGFR. Precision was represented by the Interquartile range (IQR) of the difference between mGFR and eGFR and was also represented by the coefficient of determination (R^2). Accuracy represented the percentage of people falling within a certain percentage difference of mGFR. RSME measured the square root of the square of the difference between mGFR and eGFR. Additional data, such as Pearson's correlation value, were also extracted where available.

Finally, the study aimed to offer practical suggestions for the clinical application of these optimal equations, projecting their suitability across CKD and healthy people, age groups, and various ethnicities, as approximated from the findings of the validation studies, and envisaging their potential utility within specific clinical settings based on the characteristics of the study populations from which these equations were derived.

Risk of Bias in Individual Studies and Quality of Systematic Review: The quality and risk of bias of studies were evaluated with the Quality of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.[31]

RESULTS

Tables 1 and 2 represent an overview of the studies conducted in South Asia and East Asia, respectively.

Results for South Asia

A total of 91 studies were included in this systematic review.[32-119] Twenty-six of them included South Asian populations (TABLE 1). The total population of this subgroup was found to be 10,838 out of which 4,997 (46.1%) were males. MDRD was the formula most represented in the data, appearing in 23 of the studies, followed by CG (15 studies), CKD-Epi-2009 (9 studies), CKD-Epi-Pak (6 studies) and CKD-Epi-CR (5 studies). Out of all the formulas used in these studies, CKD-Epi-Pak performed the best in multiple metrics. It secured the highest accuracy, with the highest P15 value (70.39%) and P30 value (89.35%) as well as the lowest degree of mean difference bias (-1.33).[55] CKD-Epi Cr-Cystatin C was another formula that performed well. It yielded the most precise results, having an IQR of 2.20.[34] MDRD was found to be the worst performing formula according to multiple metrics. It achieved the lowest P15, P30 and P50 accuracy values at 7.8%, 25.4% and 71.1% respectively.[46,33,44] MDRD was also found to have the highest degree of bias, achieving a mean difference of -26.13.[33] Gates method was found to have the least precise results, having an IQR of 33.30.[39] The coefficients of determination (R2) were not significant for any of the formulas, ranging from 0.016 in MDRD to 0.082 in 6 variable MDRD.[46,37] CKD-Epi Cr Cys equation was found to have the highest Pearson's correlation score, particularly in patients with late-stage disease. This formula was found to have an R=0.98 in this population.[42]

Results for East Asia

65 out of the 91 studies were included in this section of the study (TABLE 2). The total population of this geographical group was 35,019 with there being 17,149 reported males (49.0%). A total of 22 different formulas, including regional subtypes, were represented more than once in the review. The most studied formulas included MDRD 4 Variable which was used in 33 studies. Other commonly used formulas included CKD-Epi-2009 (25 studies), CKD-Epi-Cr (24 studies), CKD-Epi-Cys (21 studies) and CKD-Epi-CrCys (21 studies). The new CKD-Epi-2021 formula was found to accurately estimate GFR in these populations, managing to get the highest P15 and P30 values at 65.4% and 97.6% respectively.[79] MDRD was found to have the best coefficient of determination at 76.2.[80] CG was found to have the least bias, having a mean difference of -3.7.[82] BIS-2 had the most precise results in terms of IQR at 4.36.[107] The simplified MDRD formula was found to be the least accurate at predicting GFR, having the least P15 and P50 values at 15,46% and 56,59%.[84] The Japanese MDRD formulas were found to have the most bias at a mean difference of -38.5.[72] The modified Gates Method was found to be the least precise, having an IQR of 78.4.[116] IDMS-MDRD formulas results were found to be the have the strongest correlation, having a Pearson's correlation value of 0.95.[79]

Table 1: Evaluation of eGFR equations in South Asian populations

Author's Name	Country of Study	Sample Size	Number of males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Khalid *et al.*[43]	Pakistan	181	104	Creatinine learance	CKD-EPI Cr								0.689 Early / 0.896 Late
					CKD-EPI Cys								0.889 / 0.823
					CKD EPI Cr-Cys								0.904 / 0.977
					MDRD								0.677 (early stage) / .893 (late stage)
Ahmed S *et al.*[44]	Pakistan	670	373	Creatinine clearance	CKD-EPI								0.82
					CKD-EPI Pak								0.82
					MDRD								0.79
					CG								0.78
Jessani *et al.*[35]	Pakistan	581	251	Inulin clearance	CKD-EPI Cr		76.1 (72.7-79.5)		22.6 (19.9-25.3)		0.265 (.24 to .29)	-6.8 (-8.2 to -5.4)	
					MDRD		68.0 (64.3-71.7)		28.6 (25.8-31.5)		0.295 (0.269 to 0.321)	-8.5 (-10.1 to -6.8)	
					Pakistani CKD-EPI		81.6 (78.4-84.8)		22.8 (20.3 to 25.2)		0.265 (.24 to .29)		
Shaikh *et al.*[51]	Pakistan	140	99	99Tc-DTPA	MDRD	43	81	95				-1.9743	0.904
Zubairi *et al.*[49]	Pakistan	369	201	Creatinine clearance	CG							16.3	
					MDRD							15.22	
Wang *et al.*[34]	Pakistan	557	227	Inulin clearance	CKD-EPI Cr		76.1		22.6		0.29	-6.76	
					CKD EPI Pak		82.4		22.7		0.27		
					CKD-EPI Cys		73.3		25.6		0.32	12.7	
					CKD EPI Cr-Cys		83.1		21.2		0.25	2.73	

Author's Name	Country of Study	Sample Size	Number of males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Malik *et al.*[36]	Pakistan	92	49	99Tc-DTPA	CG							31.48	
					MDRD							27.37	
					EPI-CKD							23.38	
Safdar *et al.*[56]	Pakistan	385	184	Inulin clearance	CKD-EPI PK	70.39	89.35		2.33			-1.33	
Wang *et al.*[104]	Pakistan	557	-	Inulin clearance	CKD-EPI Cr		76.1		22.6		0.29	-6.76	
					CKD-EPI Pak		82.4		22.7		0.27		
					CKD-EPI Cys		73.3		25.6		0.32	12.7	
					CKD EPI Cr-Cys		83.1		2.2		0.25	2.73	
Ahmed S *et al.*[39]	Pakistan	2609	1419	Creatinine clearance	CKD EPI Pak							-2.8 (-3.5 to -2.1)	
					CKD EPI 2021							7.08 (6.1 to 8.2)	
Kumar V *et al.*[33]	India	130	72	Inulin clearance	CKD-EPI Cr		22.3		-27.90 to -21.95		30.22	-24.92	
					CKD-EPI Pk		39.2		-19.52 to -14.17		47.22	-16.84	
					CKD EPI Jap		51.5		-12.87 to -8.33		16.79	-10.62	
					MDRD		25.4		-30.09 to -22.17		34.63	-26.13	
					CKD-EPI Cys		74.6		-0.608 to -0.98		15.06	-3.53	
Kakde *et al.*[38]	India	336	121	99Tc-DTPA	CKD-EPI Cr							-10.3 (21.8)	
					CKD-EPI Cys							-0.86 (24.22)	
					CKD EPI Cr-Cys							-6.15 (21.71)	
					MDRD							-20.4 (22.2)	
					CG							N/A	

Table 2: Evaluation of eGFR equations in East Asian populations

Author's Name	Country of Study	Sample Size	Number of males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Mulay *et al.*[40]	India	105	65	99Tc-DTPA	CKD-EPI				26.6			1.4	0.7
					MDRD				28.9			7.6	0.64
					CG				32.7			3.1	0.63
					Gates method				33.3			6.7	0.57
Srinivas S *et al.*[37]	India	599	289	99Tc-DTPA	CG CrCl	50.50	80.10			0.082*		7.5	0.242*
					CG GFR	65.80	84			0.081		-9	0.287*
					MDRD 6V GFR	50	74			0.082		13.1	0.252*
					MDRD 4V GFR	54.3	80.1			0.081		7.5	0.245*
Mahajan *et al.*[50]	India	173	45	99Tc-DTPA	CG-CrCl		71.3			0.05		-14.14	
					CG GFR		85			0.05		1.47	
					MDRD 6V GFR		86			0.06		11.89	
					MDRD		76			0.06		17.7	
Bailey *et al.*[53]	India	917	484	Creatinine clearance	CG								0.33
					MDRD								0.284
					CKD EPI								0.314
Jafar *et al.*[54]	Pakistan	262	-	Creatinine clearance	CG-CrCl		72	91		0.05		-13.62	0.22
					CG GFR		85	96.5		0.05		1.34	0.22
					MDRD 1		86	98		0.07		10.73	0.26
					MDRD		76	95		0.05		17.16	0.25
Janjirala *et al.*[41]	India	579	300	Creatinine clearance	CG		64.9	79.4				6.1	
					MDRD		49.6	72.9				8.2	

Author's Name	Country of Study	Sample Size	Number of males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Kumar *et al.*[33]	India	66	14	99Tc-DTPA	CG		57.6					8.93	0.495
					MDRD		62.1					17	0.54
					Gates method		60.6					2.87	0.685
Prasad *et al.*[48]	India	202	90	99Tc-DTPA	MDRD					0.026			0.161
					Gates method					0.07			0.264
Mahajan *et al.*[52]	India	122	34	99Tc-DTPA	CKD-EPI								0.934 (all patients) r=0.848 (patients) 0.616(healthy)
					MDRD								0.913 (all patients) 0.841(patients) 0.568(healthy)
Das *et al.*[32]	Bangladesh	200	-	Creatinine clearance	CG		29.6					-19.39	
					MDRD		40.7					-6.47	
					CKD-EPI		42.6					0.33	
Mitra *et al.*[114]	Bangladesh	54	27	99Tc-DTPA	CG		29.6					-19.39	
					MDRD		40.7					-6.47	
					CKD-EPI		42.6					0.33	
Islam *et al.*[55]	Bangladesh	50	30	Creatinine clearance	MDRD								0.951
					CG								0.948
Weerakko *et al.*[45]	Sri Lanka	475	212	Creatinine clearance	MDRD Males	41	68.4	84	22.02		23.92	-9.34	0.633
					MDRD Females	25.5	47.1	71.1	24.97		34.39	-23.65	0.643
					CKD EPI Males	40.1	67	84.4	21.41		23.28	-9.15	0.625
					CKD EPI Females	44.5	79.5	91.6	20.45		20.45	0.04	0.651
Chaurasia *et al.*47	Nepal	51	18	99Tc-DTPA	CG	15.7	27.5			0.025		-18.83±3.41	0.157
					MDRD	7.8	29.4			0.016		-19.83±3.36	0.127

Table 2: Evaluation of eGFR equations in East Asian populations

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Xie *et al.*[105]	China	154	79	99Tc-DTPA	CKD-EPI		72.08						
					24 h CrCl		69.48						
					CG CrCl		58.44						
					eGFR		51.95						
					MDRD		70.13						
Kong *et al.*[82]	China	977	505	99Tc-DTPA	CKD-EPI two level race	42.2	73.4	90	20.5	0.05		0.2	-0.22
					CKD-EPI four level race	41.2	70.1	86.8	20.5	0.01		3	-0.11
					MDRD	38.7	69.8	92.1	23.4	0.09		-2.4	-0.3
Liu *et al.*[60]	China	702	417	99Tc-DTPA	CKD-EPI		Non-DM=66.7, DM=57.3					healthy= 2.9 (1.3,4.6) Diabetes= -3.7 (-6.7,-0.5)	
					Asian modified CKD-EPI		Non-DM=65, DM=53					healthy= 0.3 (-1.8,1.8) diabetes= -7.3 (-10.9,-2.2)	
					Re-expresed 4 variable MDRD		Non-DM=64.4, DM=51.3					healthy= 5.1 (3.2,7.6) diabetes= -2.2(-6.8,-0.8)	
Zhang *et al.*[89]	China	617	314	99Tc-DTPA	CKD EPI Cr	46.52	72.61	87.36				5.399	0.868
					CKD EPI Cys	43.27	72.12	89.3				4	0.848
					CKD EPI Cr Cys	47.49	76.66	92.06				2.614	0.887

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Xia *et al.*[58]	China	612	386	99Tc-DTPA	CKD EPI-2009		64.9		16.2		64.9	0.795	
					LMR		69.9		13.4		69.9	-3.015	
					BIS-1		73.9		12.7		73.9	-0.05	
					FAS		72.4		13.1		72.4	-1.765	
					EKFC		69		13.5		69	-1.97	
Hu *et al.*[59]	China	1471	916	99Tc-DTPA	CKD EPI Cys C		41.1		18.68		25.62	-5.61	
					MacIsaac		48.23		21.19		23.7	-0.55	
					Pei		49.73		18.89		21.13	2.11	
					Feng		50.82		19.22		21.5	1.31	
Liu *et al.*[60]	China	668	398	99Tc-DTPA	CKD- EPI	30.6	47.2	75.7	30.6			7.4	
Yang *et al.*[61]	China	843	476	99Tc-DTPA	CKD EPI Cr		37.1		59.85		1.47	13.20 (-21.87 to 74.45)	
					CKD EPI Cys		60.6		36.32		0.87	-1.87 (-24.28 to 36.61)	
					CKD EPI Cr Cys		47.6		45.43		1.02	2.86 (-21.57 to 47.63)	
					Chinese CKD EPI Cr		43.4		32.22		1.25	5.03 (-27.01 to 55.39)	
					Chinese CKD EPI Cys		62.3		15.45		0.8	-2.97 (25.11 to 31.59)	
					Chinese CKD EPI Cr Cys		55.3		21.12		0.89	-1.00 (-26.27 to 36.77)	

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Peng *et al.*[62]	China	187	-	Iohexol	CKD EPI Cr 2009		73 (63–82)		19.8 (14.0–23.5)		36.0 (27.1–45.5		
					CKD EPI Cr 2021		70 (58–80)		20.8 (15.0–24.6)		40.0 (30.3–50.4)		
					CKD EPI Cys 2012		***84 (75–91)***		15.4 (10.3–21.2)		***25.2 (19.9–31.5)***		
					CKD EPI Cr Cys 2012		***85 (76–92)***		15.6 (11.7–21.8)		27.2 (20.1–35.2)		
					CKD EPI Cr Cys 2021		80 (71–89)		17.6 (12.5–22.3)		28.9 (21.5–37.3)		
Ye *et al.*[63]	China	419	263	99Tc-DTPA	CKD-EPI Cr	48.45	79	92.84	21.49		15.7	-1.47	
					CKD-EPIcys	41.05	71.84	93.32	19.61		18.5	-9.05	
					CKD-EPI Cr-cys	51.55	78.76	95.23	18.74		15.3	-5.09	
					BIS Cr	47.26	79.71	95.7	21.58		17.2	-5.2	
					BIS Cr-cys	48.93	79.71	96.9	16.31		16.94	-8.65	
Liu *et al.*[65]	China	319	198	99Tc-DTPA	CG	31.3	57.7	81.5	13.9				
					6 Variable MDRD	29.5	53.6	76.5	16				
					4 variable MDRD	27.9	54.5	74.9	17.6				
					CKD EPI	27.6	54.9	75.5	16.7				
					Jelliffe equation	30.1	57.1	81.2	15.1				
					Hull equation	32.9	55.2	79.3	14.6				

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Li *et al.*[66]	China	2772	1407	99Tc-DTPA	CG		64.89		28.34		24.26	1.09	
					MDRD		66.46		26.21		22.93	–2.43	
					Chinese MDR		47.49		36.46		30.15	18.87	
					CDK EPI Cr		66.1		27.93		21.51	1.11	
					Chinese CKD EPI		58.21		31.14		23.55	8.32	
					Asian CKD EPI		52.43		35.18		24.94	12.57	
Ye *et al.*[67]	China	1522	923	99Tc-DTPA	CKD-EPI Cr	39.5	67.9	83.4	24.58		19.07	1.66	
					CKD-EPIcys	37.6	67.6	88.2	21.26		19.68	-6.68	
					CKD-EPI Cr-cys	44.2	71.6	88.9	19.97		17.25	-2.6	
Changjie *et al.*[69]	China	218	158	99Tc-DTPA	CG		64.67		12.73		13.56	-9	
					Chinese MDRD		62.84		21.41		16.77	5.19	
					CKD-EPI-Cr		75.69		13.67		10.33	-1.22	
					CKD-EPI-Cys		67.89		17.07		17.52	3.86	
					CKD-EPI-Cr-Cys		89.91		9.17		8.87	1.92	
					BIS-1 (Cr)		88.53		10.22		9.82	-3.81	
					BIS-2 (Cr and Cystatin C)		94.5		4.36		7.21	0.63	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Xia *et al.*[70]	China	359	226	99m-DTPA	CG		70.2		12.87		13.92	-2.26	
					CKD-EPICr		63		14.75		14.18	0.75	
					LMR		70.2		12.49		12.78	-2.36	
					BIS1		74.7		11.76		12.44	0.61	
					FASCr		72.4		12.06		12.61	-1.06	
					EKFC		68		12.89		12.92	-1.79	
					CKD-EPI-Cys		67.7		12.72		14.64	-3.34	
					FASCys		69.9		13.29		15.56	-1.54	
					CKD-EPI-Cr-Cys		69.4		12.33		12.7	-1.83	
					BIS2		78		10.34		12.64	-1.92	
Changjie *et al.*[108]	China	347	233	99m-DTPA	FASCr-Cys		78.3		10.65		12.51	-1.84	
					FAS-CR		63.98		17.57		17.29	– 3.62	
					EKFC		53.05		18.71		17.47	– 4.50	
					Asian CKD-EPI		50.72		22.08		18.62	– 1.50	
					Xiangya		51.87		20.62		16.57	2.69	
					LMR		55.62		18.69		17.42	– 4.28	
Chi *et al.*[71]	China	1296	814	99m-DTPA	CKD-EPI Cr		51.2	77.6				-4.8	
					CKD-EPI Cys		60.3	86.4				2.4	
					CKD- Epi Cr Cys		57.4	83.7				-0.3	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					abbreviated MDRD		52.1	76.4				-6	
					Chinese MDRD		47.1	71.3				-8.9	
					MDRD		49	73.5				-11.5	
Xie *et al.*[106]	China	-	-	99m-DTPA	MDRD		85.12	90.2	18.73	0.75		-6.86	0.866
					CKD-EPI Cr		86.39	90.2	17.4	0.786		5.91	0.886
Huang *et al.*[84]	China	551	225	99m-DTPA	FAS		75.31		15.69			-1.22	
Xie *et al.*[107]	China	162	78	99m-DTPA	FAS		75.31		15.69			-1.22	
Xie *et al.*[105]	China	154	73	99m-DTPA	CKD EPI		72.08		14.24	0.85		2.49	0.922
					24-hour CrCl		69.48		17.4	0.781		-0.035	0.884
					CG		58.44		23.02	0.546		2.79	0.739
					MDRD		51.95		23.2	0.587		0.97	0.766
					Modified MDRD		70.13		15.31	0.821		-0.64	0.906
Guo *et al.*[72]	China	252	138	99m-DTPA	CKD-EPI Cr	29.8	59.1	79	22.1			2.4	
					CKD-EPI Cys	38.9	64.3	83.3	18.4			-0.2	
					CKD-EPI Cr-cys	39.7	62.3	83.7	16.4			0.5	
					Feng Cys	38.9	61.9	79	19			3.3	
					Feng Cr-cys	36.1	62.7	86.6	17.3			5.6	

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Zhao *et al.*[73]	China	224	68	99m-DTPA	CG		78.6	98.2			26	-3.7	0.43
					Chinese MDRD1		80.4	96.4			22.6	6.5	0.52
					Chinese MDRD2		71.4	91.1			24.9	13.2	0.48
					Japanese MDRD		42.9	94.6			22.7	-38.5	0.48
Ma *et al.*[102]	China	482	254	99m-DTPA	modified Gate's method	32.4	56	79.1	78.4			933.1	
					modified abbrevi-ated MDRD equation estimated GFR	43.2	75.5	90.9	57			894.5	
Zhu, Ye, Zhu *et al.*[101]	China	788	478	99m-DTPA	C-MDRD		64.21		32.11		29.74	8.17	0.795
					CKD-EPI2009Scr		75.76		24.49		18.94	2.21	0.798
					CKD-EPI-2012cys		68.4		24.39		20.1	–9.23	0.802
					CKD-EPI2012Scr-cys		77.03		23.84		17.29	–4.11	0.829
Wang *et al.*[97]	China	195	93	99m-DTPA	CKD-EPI equation		74.36		18.48			3.45	
					Asian modified CKD-EPI equation		78.46		18.33			0.21	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Yang *et al.*[96]	China	632	478	99m-DTPA	C-MDRD		45.9		45.45		2.22	10.61	
					Cys		50.8		34.98		1.25	13.58	
					Cscr–cys		46.5		39.57		1.26	18.01	
					CKD-EPIscr		54.1		32.62		0.99	8.07	
					CKD-EPIcys		63.1		25.99		0.83	–1.34	
					CKD-EPIscr-cys		63.4		26.79		0.76	3.11	
Huang *et al.*[95]	China	151	66	99m-DTPA	CG		88.7		20.08			4.2	0.77
					MDRD		68		20.79			13.17	0.824
					Cystatin C		85.4		21.81			6.27	0.697
					Cystatin C-SCr		87.4		18.06			9.45	0.842
					CKD-EPI Cystatin C		89.4		20.79			6.44	0.741
					CKD-EPI Cystatin C-SC		88.7		19.13			8.6	0.849
Yong *et al.*[92]	China	1184	-	99m-DTPA	CKD-EPI-Cys		64.95		21.83		20.1	–7.2	
					CKD-EPI-Cr–Cys		70.35		20.18		17.56	–4.0	
					FASCys		70.1		21.01		20.18	–5.17	
					FASCr–Cys		74.16		19.01		17.84	–2.87	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Zhang *et al.*[89]	China	617	314	99m-DTPA	CKD-EPI Scr	46.52	72.61	87.36	20.636			5.399	0.868
					CKD-EPI cys C	43.27	72.12	89.3	23.87			4.417	0.848
					CKD-EPIS-cr-Cystatin C	47.49	76.66	92.06	20.078			2.614	0.887
Liu *et al.*[88]	China	431	233	99m-DTPA	CG		57.5		23.6		12.2	2.5	
					Re-expressed 4-variable MDRD		57.5		23.6		11.4	0.4	
					CKD EPI-Cr		55.5		23		11.6	0.5	
					CKD EPI-Cr cys		59.9		19.5		10.5	5.7	
Li *et al.*[87]	China	839	525	99m-DTPA	CKD-EPIcys	36.97	63.03		16.72		14.62	–7.46	
					modified CKD-EPIcys	43.03	80.61		8.02		11.5	–0.06	
					CKD-EPIs-cr–cys	34.15	63.41		15.22		14.61	–8.64	
					modified CKD-EPIs-cr–cys	49.39	77.44		9.42		11.07	0.3	
Li *et al.*[86]	China	450	211	99m-DTPA	CKD-EPI		72.22		63.8	0.78		-1.09	0.88
					Abbreviated MDRD		58.88		76.2	0.68		-7.88	0.81

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Liao *et al.*[76]	China	200	127	99m-DTPA	MDRD	36.18	61.81	78.39				–2.7788 (mean)	
					Chinese MDRD equation6	38.19	59.8	75.38				–7.1126 (mean)	
					Chinese MDRD equation 10	38.19	58.79	75.88				–7.8192 (mean)	
					CKD-EPI	40.2	66.83	79.9				–0.2744 (mean)	
Dou *et al.*[77]	China	122	69	99m-DTPA	CKD-EPI	41.8	50	56.6				0.92	
					C-MDRD	44.3	51.6	55.7				3.76	
					MDRD	44.3	51.6	55.7				3.53	
Xun *et al.*[81]	China	103	25	99m-DTPA	CG	35	59.2	80.6		71.9		-5.73 (-11.24 to 1.33)	
					Hull	37.9	56.3	78.6		65.3		-4.42 (-11.56 to 3.26)	
					MDRD1	30.1	60.2	73.8		76.2		1.69 (-7.37 to 12.81)	
					abbreviated MDRD	26.2	54.4	73.8				1.81 (-5.76 to 14.09)	
Zhao *et al.*[83]	China	160	65	99m-DTPA	Asian CKD-EPI		74.4 (61.6 to 89)		12.72 (9.88 to 14.67)			0.84 (–0.63–3.60)	
					EKFC		80.0 (66.7 to 95.1)		12.69 (10.38–16.61)			–1.64 (–3.17 to –0.25)	
Yang *et al.*[85]	China	744	452	99m-DTPA	CKD EPI Cr	15.72	32.12	55.78	12.65			-9.01	
					CDP Epi Cys	22.67	42.61	69.76	13.77			-4.18	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					CKD-EPIcr-cys	16.53	35.75	62.77	12.42			-7.9	
					MDRD simplified	15.46	32.39	56.59%	12.45			-9.26	
					MDRD chinese	15.46	30.24	55.24	12.95			-9.15	
					Feng Cys	23.52	46.51	68.15	14.03			3.77	
					Feng Cr-Cys	29.7	49.33	71.37	12.53			3.17	
					CG	20.56	41.8	63.31	17.84			-0.02	
Chen *et al.*[90]	China	220	137	99m-TcDTPA	MDRD		55.9		16.55		16.18	6.96	
					BIS1		72.3		12.62		6.57	3.45	
					CKD-EPI-cr		59.1		15.95		14.27	5.94	
					FAS-Cr		72.7		14.05		10.2	1.84	
Liu *et al.*[91]	China	327	-	99m-TcDTPA	CG		52.9	76.1				-3.03	
					Gate		45.3	69.1				-2.02	
					Hull		47.7	71.9				-3.21	
					6 variable MDRD		49.2	71.3				-3.55	
					4 variable MDRD		50.8	70				-2.27	
DU *et al.*[98]	China	111	65	99m-DTPA	CKD-EPI Cr		58.6					2.34 SD 18.18	
					CKD- Epi Cys c		56.8					1.19 SD 16.37	
					CKD-EPI Cr-Cys		63.6					1.32 SD 17.16	

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
Horio *et al.*[99]	Japan	763	463	Inulin clearance	Japanese MDRD		1.73						
					Japanese CKD-EPI		2.75						
Matsuo *et al.*[57]	Japan	350	203	Inulin clearance	IDMS-MDRD	34	72				19.9	-5.9 and SD 19	
					JSN-CKDI	36	73				20.3	-7.9 and SD 18.7	
					Jap CG	45	75				19.4	-1.7 and SD 19.6	
Guan *et al.*[103]	China	368	231	Inulin clearance	CKD-EPI-Cr-Cys		75.27%		18.42		16.3	1.57	
					BIS-2		79.08		13.21		14.75	3.36	
					MA-Cr-Cys		48.91%		27.38		27.27	9.51	
					FENG-Cr-Cys		38.04%		20.2		23.39	14.65	
Imai *et al.*[44]	Japan	248	-	Inulin clearance	MDRD	40	71	82				1.8 SD 16.4	
					0.881 times MDRD	47	73	93				–4.7 ± 17.2	
					0.84 times CG	43	74	93				–5.9 ± 16.6	
Horio *et al.*[116]	Japan	350	203	Inulin clearance	Japanese MDRD		73					1.3	
					Japanese CKD-EPI		75					0.4	
Hwang *et al.*[80]	Japan	211	100	Creatinine clearance	IDMS-MDRD	23.7	88.2				9.104		0.949 (0.933 to0.961)
					CKD-EPI	54	93.4				10.154		0.936 (0.916 to 0.951)

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						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					CKD-EPI 2021	65.4	97.6				10.419		0.932 (0.912 to 0.948)
					Kor-IDMS-MDRD	53.1	92.9				12.359		0.903 (0.875 to 0.925)
					Kor-CKD-EPI	48.8	92.9				9.424		0.945 (0.928 to 0.958)
					FAS-eGFR	58.8	94.8				10.417		0.932 (0.912 to 0.948)
Teo *et al.*[42]	Mixed	232 (94 Chinese, 74 Malays, and 64 Indians)	-	99m-TcDTPA	CKD-EPI	50.0 (43.6 to 56.4)	82.8 (77.9 to 87.6)	94.8 (92.0 to 97.7)		12.1 (9.0 to 15.1)	13.8a (11.3 to 16.4)	1.2 (2.7 to 0.3)	
					MDRD	50.0 (43.6 to 56.4)	79.7 (74.6 to 84.9)	95.3 (92.5 to 98.0)		12.2 (10.0 to 14.4)	15.2a (12.1 to 18.3)	3.0 (4.2 to 1.7)	
Pradit-pornsilpa *et al.*[110]	Thailand	350	193	99mTc-DTPA	CKD-EPI		68						
					MDRD		62.7						
					Chinese MDRD		N/A						
					Japanese MDRD		N/A						
					Thai MDRD		73.3						
					Thai eGFR		90						
Pradit-pornsilpa *et al.*[111]	Thailand	196	84	99mTc-DTPA	MDRD		1.74						

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					CKD-EPI		2.8						
					Thai MDRD		3.84						
					Thai eGFR		4.84						
					CG		5.53						
Townam-chai *et al.*[112]	Thailand	98	59	99mTc-DTPA	CKD-EPI		62.9						
					MDRD		62.9						
					Thai eGFR		54.6						
					Thai MDRD		55.7						
Jalalon-muhali *et al.*[100]	Malaysia	40	31	Cr-EDTA	CGBSA		85			10.68		–7.97	0.861
					4-MDRD		90			8.7		–2.76	0.889
					CKD-EPIcr		95			8.18		–3.09	0.902
					CKD-EPIcys		81			8.26		4.9	0.928
Jalalon-muhali *et al.*[113]	Malaysia	51	46	Cr-EDTA	CGBSA		85			10.68		–7.97	0.861
					4-MDRD		90			8.7		–2.76	0.889
					CKD-EPIcr		95			8.18		–3.09	0.902
					CKD-EPIcys		81			8.26		4.9	0.928
Chung *et al.*[119]	Korea	207	87	99 Tc DTPA	CGBSA		47.1			10.802		–1.573	0.877
					4-MDRD		54.9			12.058		–6.137	0.848
					CKD-EPI		49			11.697		–4.804	0.854

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					CKD-EPI		49			11.697		–4.804	0.854
Jeong *et al.*[78]	Korea	960	625	Cr-EDTA	CG		86					-0.73	
					MDRD		84.1					-9.6	
					CKD EPI		91.8					-1.6	
Jeong *et al.*[64]	Korea	1654	-	Cr-EDTA	MDRD		76.6				20.7	-2.2	0.923
					CKD EPI		82.8				13.7	-0.9	0.931
Jeong *et al.*[68]	Korea	1312	809	Cr-EDTA	CKD EPI Korea		85.9				13.5	-0.6	0.935
Oh *et al.*[93]	Korea	147	-	Inulin clearance	Abbreviated MDRD	21.1	50.3	74.8	20.7	0.67		15.0 (6.4 to 29.4)	
					6 variable MDRD	20.4	51	74.1	20.5	0.67		14.8 (6.3 to 32.1)	
					4 variable IDMS MDRD	32.7	61.9	82.3	17.9	0.65		10.2 (4.8 to 20.5)	
					6 variable IDMS MDRD	34	64.6	82.3	18	0.66		9.9 (5.2 to 19.8)	
Lee *et al.*[75]	Korea	120	-	Inulin clearance	4V IDMS MDRD		82.4	91.2	14.5			619.3	0.8
					6v IDMS MDRD		84.8	92	15.3			315.1	0.8
Chen *et al.*[121]	Taiwan	556	261	Inulin clearance	CKD-EPI		60.4						
					MDRD		63.3						
					Japanese MDRD		71.2						

Author's Name	Country of Study	Sample Size	Number of Males	Method of Measuring GFR	Formulas used	Accuracy			Precision		RSME	Bias	Pearson'sPearson's Correlation Coefficient (r)
						P15 (%)	P30 (%)	P50 (%)	IQR	R^2		Mean/median Difference	
					Japanese CKD-EPI		70.5						
					Thai MDRD		52.5						
					Taiwanese MDRD		73.4						
					Taiwanese CKD-EPI		73.4						
El-Min-shawy and El-bassu-oni[115]	Arabic	320	-	99m Tc DPTA	CKD-EPI		62						
					MDRD		65						
					Walser		59						
					Nankivell		59						
					CG		68						
Teo *et al.*[94]	Mixed	335	-	99m Tc DPTA	Creatinine equation		13.73 (10.05, 17.42)		15.37 (13.26, 17.69)			-0.036 (-1.23, 1.58)	
					Cystatin C		12.84 (9.25, 16.42)		14.03 (12.23, 16.83)			-2.93 (-3.82, -1.2)	
					Creatinine-Cystatin C		9.85 (6.66, 13.04)		13.74 (11.30, 15.92)			-1.21 (-2.77, -0.16)	
Teo *et al.*[79]	Mixed	232	-	99m Tc DPTA	CKD-EPI	50	82.8	94.8	12.1		13.8	-1.2	
					MDRD	50	79.7	95.3	12.2		15.2	-3	

The Japanese MDRD formulas were found to have the most bias at a mean difference of -38.5.[72] The modified Gates Method was found to be the least precise, having an IQR of 78.4.[116] IDMS-MDRD formulas results were found to be the have the strongest correlation, having a Pearson's correlation value of 0.95.[79]

DISCUSSION

This systematic review comprehensively evaluates the performance of GFR equations in various Asian populations, highlighting the nuances of regional disparities in the efficacy of eGFR formulas. These findings underscore the critical need for accurate renal function assessment in chronic kidney disease (CKD) management, while emphasising the challenges and potentials offered by creatinine and Cystatin C-based equations across diverse Asian subpopulations.

One of the key observations from this review is the significant heterogeneity in equation performance across different regions within Asia. In South Asia, the evaluation of various estimated GFR equations revealed CKD-Epi-Pak as a standout performer across multiple metrics. This equation demonstrated superior performance, securing high percentages of eGFR values within specific ranges of measured GFR (P15 = 70.39% and P3 0= 89.35%) and exhibiting minimal bias with the lowest degree of mean difference (mean bias= -1.33).[55] Conversely, the traditional MDRD formula displayed notably poor performance across metrics, registering the lowest agreement percentages. The P15 values for MDRD ranged from 7.80% to 50.30% while P30 ranged from 25.40% to 76.00%.[46,33,49,51] MDRD also had the highest bias for equations in the region, ranging from –26.13 to 7.5.[33,37]

In East Asia, the evaluation encompassed a more extensive array of equations, highlighting variations in performance across different formulas. Notably, the newly introduced CKD-Epi-2021 formula demonstrated commendable accuracy in estimating GFR, achieving high percentages of eGFR values within specified ranges of measured GFR. It was found to have a P15 of 65.4% and a P30 of 97.6%.[79] Conversely, the Chinese MDRD formula displayed suboptimal accuracy, indicating lower agreement percentages compared to other equations evaluated in this region. Its P15 value ranged from 15.46% to 38.19%.[84,75] Additionally, specific variations of the MDRD formula used in Japan exhibited considerable mean bias (mean bias = -38.5), suggesting limitations in accurately estimating GFR within this subgroup.[72] The modified Gates Method also demonstrated inferior precision in estimating GFR, characterized by a notably high IQR (IQR = 78.4).[101]

Interestingly, Liu *et al* reported a difference in equation performance between healthy people and CKD patients who had comorbid Diabetes Mellitus (DM). They found that the Asian Modified CKD-Epi formula had lower mean difference (0.3 in healthy vs -7.3 in DM CKD patients), as well as higher P30 values (65% in Healthy vs 53% in DM patients).[91] Another interesting finding was that there was differences in study performance between genders, as reported by Janjirala *et al*.[41] They found that MDRD had lower mean bias in females vs males (0.38 vs –1.07). Conversely, they found that the CG formula had lower mean bias in males vs females (0.06 vs 0.46).[41] In contrast to Janjrila's findings, Weerakkody *et al.* Found that MDRD was more precise in males. They found that compared to males, females had lower values of P15 (41.00% in males vs 21.50% in females) and P30 (68.40% in males vs 47.1%).[45] Correlation scores of the formulas present a critical insight into their predictive performance, particularly in specific population subgroups. In South Asian populations, the CKD-Epi Cr-Cys equation demonstrated the highest Pearson's correlation score (R = 0.98), especially in patients with late-stage CKD. This suggests a strong agreement between estimated and measured GFR in this group, making it a potentially reliable tool for clinical decision-making in advanced CKD cases.

In East Asian populations, the IDMS-MDRD formula showed the strongest Pearson's correlation value (R = 0.95), reflecting its consistency in estimating GFR across a diverse cohort. Interestingly, the new CKD-Epi-2021 formula also demonstrated high accuracy with the best P15 and P30 values, yet its correlation metrics were not explicitly highlighted. This points to the potential for future studies to further investigate its comparative performance against other established formulas in terms of correlation and agreement metrics.

The variability in correlation scores across formulas and regions underscores the importance of geographic and demographic tailoring in GFR estimation. Formulas with strong correlations, like CKD-Epi Cr-Cys in South Asia and IDMS-MDRD in East Asia, may serve as benchmarks for optimising CKD management in these populations.

The disparity in equation performances emphasises the need for ethnicity-specific equation validation and development. The complex interplay of genetic, dietary, and lifestyle factors in diverse Asian populations significantly influences renal function markers. As such, a one-size-fits-all approach to eGFR estimation equations may not be applicable across all ethnicities within the Asian continent.

While the performance metrics of eGFR equations are crucial, their clinical applicability and ease of implementation are equally significant. The selection of an appropriate equation for routine clinical use necessitates considerations beyond accuracy and precision. Factors such as cost-effectiveness, availability of resources, and ease of measurement are pivotal in real-world healthcare settings.

While Cystatin C-based equations, such as CKD-Epi-CrCys and CKD-Epi-Cys, proved to be a sensitive indicator of GFR changes, especially in East Asian populations, its higher cost than creatinine-based measurements pose a significant challenge in their widespread implementation, especially for routine use in clinical practice in resource-constrained healthcare systems.[120] Therefore, pragmatic considerations are essential in balancing equation performance with feasibility and cost-effectiveness.

Moreover, the availability and standardisation of measurement techniques for creatinine and Cystatin C across different laboratories and regions also impact equation performance. Variability in assay methods and calibration standards can introduce discrepancies in results, affecting the accuracy and comparability of eGFR equations. Standardisation efforts and quality assurance measures are imperative to ensure consistent and reliable measurements, facilitating accurate GFR estimation.

The findings of this review have implications for healthcare guidelines and recommendations concerning the assessment and management of CKD in Asian populations. The identification of equations exhibiting superior performance in specific regions can potentially influence guideline recommendations, guiding clinicians in selecting the most appropriate eGFR equation for accurate renal function assessment.

Furthermore, the recognition of equations that perform optimally in diverse age groups, health statuses, and ethnicities within Asia can aid in personalised patient-centred approaches. Tailoring equation selection based on patient characteristics and regional factors could enhance the precision of GFR estimation, consequently improving patient management and clinical outcomes.

Future research should focus on refining existing equations and developing new models that account for the complexities of Asian populations. This includes exploring the integration of additional biomarkers, enhancing accuracy across diverse ethnicities, and conducting multi-centre studies across different regions to develop ethnicity-specific equations. Longitudinal studies investigating the clinical impact of specific eGFR equations on treatment decisions and patient outcomes will provide valuable insights. Furthermore, robust validation studies across South Asian populations are necessary to confirm the accuracy of the CKD-EPI Pak equation, with an emphasis on collaboration, standardisation of measurement techniques, and regional data refinements to enhance its cross-border applicability.

Limitations:

The limitations encountered in conducting a meta-analysis due to significant heterogeneity between studies underscore the complexity of synthesising data from diverse populations. The diverse methodologies, patient demographics, and reference methods used in these validation studies underscore the challenge in drawing universally applicable conclusions regarding equation performance. This highlights the importance of cautious interpretation and individualised evaluation of equations based on specific patient characteristics and regional contexts.

The variability in measurement techniques and calibration standards for creatinine and Cystatin C is a critical factor influencing the performance of eGFR equations. While this systematic review acknowledges the potential impact of such variability on accuracy and comparability, it did not use this as an explicit exclusion criterion. Future studies should address assay variability by incorporating standardised measurement techniques as eligibility criteria and conducting subgroup analyses based on assay standardisation to assess its impact on eGFR performance. Transparent reporting of calibration methods and quality assurance data is essential.

CONCLUSION

In conclusion, this review provides valuable insights into the performance of eGFR equations

in Asian populations, emphasising the need for tailored equation development and cautious consideration of regional disparities. Across both regions, certain equations such as CKD-Epi-Pak in South Asia and CKD-Epi-2021 in East Asia emerged as promising performers, indicating their potential suitability for accurate GFR estimation within these populations. Conversely, traditional equations like MDRD exhibited consistent shortcomings, highlighting their limitations in accurately estimating GFR in both South and East Asian populations. Future research efforts should prioritise ethnicity-specific equation development to enhance the accuracy and clinical utility of GFR estimation in Asian populations.

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