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ESTIMATION OF GLOMERULAR FILTRATION RATE (GFR) FORMULAS: CKD EPI EQUATION, CKD EPI EQUATION MODIFIED FOR ASIAN, AND MODIFICATION OF DIET IN RENAL DISEASE (MDRD)

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Abstract

The selection of the right and efficient formula in estimating GFR is still an interesting topic in the medical world, especially nephrology. The CKD Epi and MDRD formulas have long been used in American, Australian and European populations. The results of GFR measurements from these two formulas in other populations such as Asia need further study. Differences in ethnicity, culture, diet, and so on can be biased factors in establishing the diagnosis of kidney disease. The existence of the CKD Epi Modified for Asian formula can be an option for Asian populations such as Indonesia. So based on these reasons, it is necessary to conduct a comparison test of the measurement results to the three (3) formulas. This study is comparative study between the formula CKD Epi Modified for Asian, CKD Epi, and MDRD. Serum creatinine data was taken from 30 men aged 19 years in Bengkulu who used purporsive sampling techniques. Data were analyzed univariate and bivariate using IBM SPSS 25.0 applications to see homogeneity and differences per formula. The mean value per GFR formula showed a significant difference (p-value=0.03), but with the same homogeneity value (p-value=0.86). The CKD Epi Modified for Asian formula has significant differences from the MDRD formula (p-value=0.02). There is a significant difference between the three formulas (p-value = 0.03), with the same homogeneity value (p-value = 0.86).

Keywords: CKD EPI, MDRD, GFR

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INTRODUCTION

Estimation of GFR provides information on the number of nephrons that function in both excretory and secretory processes. Estimated GFR measurement is an accurate method to assess kidney function and provide an overview of the development of kidney disease. GFR measurement is quite complicated and takes a relatively long time, as well as large costs. GFR values can be predicted using serum creatinine, although creatinine is filtration-free in the glomerulus and there is a small amount of creatinine secreted in the tubules (Betzler et al. 2022; Ebert et al. 2022; Irawan, Farizal, and Febrianto 2019; Luis-Lima and Porrini 2017).

There are several biomarkers to measure GFR, namely: endogenous and exogenous biomarkers. Exogenous biomarkers include: Cromium-51-EDTA, Inulin, etc. While commonly used endogenous biomarkers include: creatinine, cystatin C, B-trace protein, B-microglobulin, and others (Ebert et al. 2022; Irawan 2020; Irawan, Farizal, and Febrianto 2019; Luis-Lima and Porrini 2017; Yue et al. 2020).

Several studies have found equivalence and a strong correlation between creatinine levels and GFR. Based on the above, serum creatinine is often an alternative choice to be used as a biomarker and measure GFR values that are simpler and provide fast and precise results There are several GFR estimation formulas that have been revealed by researchers before. Three (3) of them: CKD EPI, ID-MS Traceable MDRD, and MDRD-4 Variable, etc. (Betzler et al. 2022; Ebert et al. 2022; Gao et al. 2021; Irawan 2020; Irawan, Farizal, and Febrianto 2019; Ji et al. 2017; Luis-Lima and Porrini 2017).

The CKD EPI Modified for Asian formula is a formula used to determine the glomerular filtration rate (GFR) in people of Asian descent who have or are suspected of having kidney problems. The modified version was adapted to Asian populations and had better accuracy than other common GFR formulas, such is the MDRD formula or the Cockcroft-Gault formula originally developed for Western populations. The CKD EPI Modified for Asian formula uses factors such as ethnicity, age, gender, and blood creatinine levels to calculate GFR. The results of these calculations can help monitor kidney health, diagnose kidney disease, and plan appropriate treatment (Ebert et al. 2022; Irawan, Farizal, and Febrianto 2019; Ji et al. 2017).

The CKD EPI and MDRD formulas tend to be frequently used in measuring GFR in Europe and America (Ebert et al. 2022; Irawan, Farizal, and Febrianto 2019; Levey and Inker 2023;

Luis-Lima and Porrini 2017). Differences in race and skin color are also weighed in the formula. The CKD EPI Modified for Asian formula is relatively new in the last decade (Gao et al. 2021; Ji et al. 2017; Teo et al. 2018). This is an interesting topic in determining the value of GFR when associated with Asian ethnicities that are different from European and American ethnicities (Ji et al. 2017; Kim et al. 2023; Teo et al. 2018). The similarities and differences in GFR measurement results are still a scientific discussion in the medical field, especially nephrology. So based on some of these things, it is necessary to study related to the problem.

MATERIALS AND METHODS

The study is a comparative study between three (3) practical formulas used in measuring glomerular filtration rate. The biomarker data used was serum creatinine sourced from 30 male respondents in 2015 taken by purporsive sampling technique. Respondents were homogenized to facilitate the analysis process and minimize bias. The data obtained were then analyzed univariately and bivariately using IBM SPSS 25.0 applications to see the homogeneity and differences of each formula. The process of examining the respondents' creatinine was approven by Reseach Ethic Commite (REC) Faculty of Medicine, Jenderal Soedirman University (Approval number Ref: 062/KEPK/IV/2015 29th April 2015).

The following are the three (3) GFR formulas used:

Formula Chronic Kidney Disease Epidemiology (CKD EPI**)** Equation (x 1,59 if black) (Gao et al. 2021; Irawan, Farizal, and Febrianto 2019; Yue et al. 2020; Zafari et al. 2019)

a) Serum Creatinine (S-Cr) ≤ 0,9 mg/dL→ GFR = 141 x $(S\text{-}Cr/0{,}9)^{-0.411}$ x $(0{,}993)^{age}$
b) Serum Creatinine (S-Cr) > 0,9 mg/dL→ GFR = 141 x $(S\text{-}Cr/0{,}9)^{-1{,}209}$x $(0{,}993)^{age}$

Formula Chronic Kidney Disease Epidemiology (CKD EPI) Equation Modified for Asian (Betzler et al. 2022; Gao et al. 2021; Ji et al. 2017; Liao et al. 2011; Liu et al. 2014; Teo et al. 2018)

a) Serum Creatinine (S-Cr) ≤ 0,9 mg/dL; 149 X $(S\text{-}Cr/0{,}9)^{-0{,}412}$ X $0{,}993^{Age}$
b) Serum Creatinine (S-Cr) > 0,9 mg/dL; 149 X $(S\text{-}Cr/0{,}9)^{-1{,}210}$ X $0{,}993^{Age}$

Formula Modification of Diet in Renal Disease (MDRD) with 4 variables (abbreviation or modification) (Andrew S. Levey, MD, Lesley A. Stevens, MD, MS, FRCP(C) 2009; Irawan, Farizal, and Febrianto 2019; Levey and Inker 2023).

GFR = 186,3 x Serum Creatinine (S-Cr) $^{-1{,}154}$ x age $^{-0{,}203}$ x 0,742 (female) x 1,212 (black)

RESULTS AND DISCUSSION

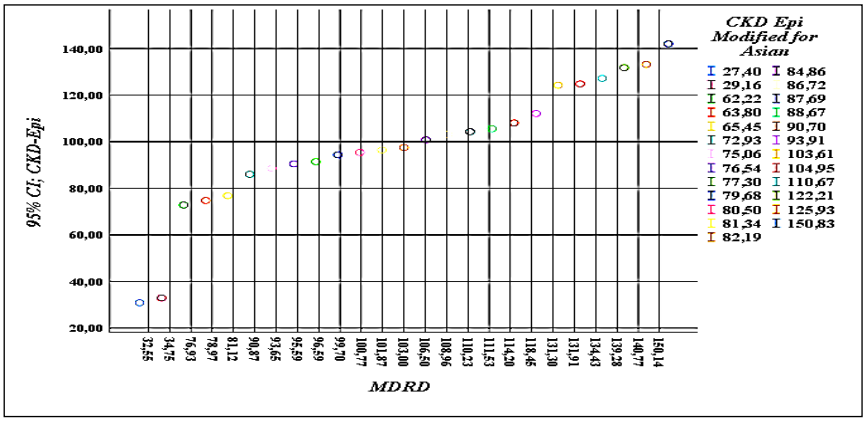
The data from the evaluation of the three (3) GFR formulas are as follows*:*

Table 1. Univariate test result data GFR value

Value (N=30)		Formula (mL/min/1,73 m^2)		
		CKD Epi	CKD Epi Modified for Asian	MDRD
Mean		95.20	82.43	100.58
Std. Deviation		25.94	25.34	27.43
Median		95.91	80.92	101.32
Min		30.84	27.40	32.55
Max		142.03	150.83	150.14
95% Confidence Interval for Mean	Lower Bound	85.51	72.96	90.34
	Upper Bound	104.88	91.89	110.82
5% Trimmed Mean		96.30	82.11	101.74
Variance		672.87	642.19	752.34
Range		111.19	123.43	117.59
Interquartile Range		32.80	26.47	34.68
Anova test, F; P-value =		**3.79; 0.03***		
Homogenity =		**0.86**		

Information: **CKD Epi** = Chronic Kidney Disease Epidemiology Equation; **CKD Epi Modified for Asian** = Chronic Kidney Disease Epidemiology Equation Modified for Asian; **MDRD** = Modification of Diet in Renal Disease

Based on the data in table 1, it is known that the three (3) have an average value, standard deviation. The minimum, maximum, and median are different from each other. The results of statistical analysis (Anova test) also show significant p-value = 0.03<0.05 confirms that there is a significant difference from the GFR measurement results to the three (3) formulas. The following is the distribution graph data of the GFR calculation results using the three (3) formulas:



Information: CKD Epi = Chronic Kidney Disease Epidemiology Equation; MDRD = Modification of Diet in Renal Disease; CKD Epi Modified for Asian = Chronic Kidney Disease Epidemiology Equation Modified for Asian

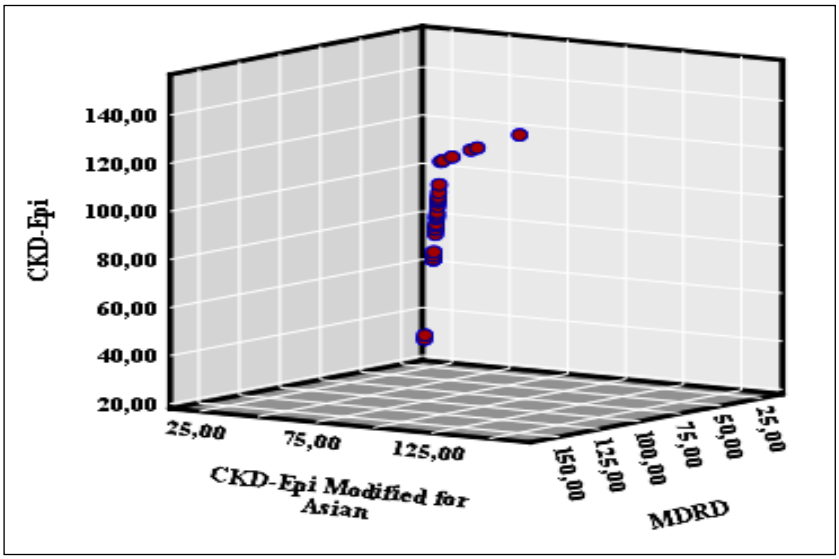
Figure 1. Distribution of GFR measurement data from three (3) formulas (n=30; p-value = 0.03) in units of mL/min/1.73 m^2

According to the Anova test's findings (table 2) shows a significant difference from the three formulas p-value = 0.03<0.05. However, the results of Tukey HSD's multiple comparisons test (Table 3) show that the GFR value with the CKD Epi Equation formula has no significant difference (p-value > 0.05) with two (2) other formulas. While the CKD Epi Equation Modified for Asian and MDRD formulas have very significant differences (p-value = 0.02; <0.05). The following are the results of the Tukey HSD multiple comparisons test and the results of the tukey uses harmonic mean sample size test to the three (3) GFR formulas:

Tabel 3. Test results multiple comparisons Tukey HSD to three (3) formulas GFR (n=30)

FORMULA		Mean Difference	Sig.	95% Confidence Interval Lower Bound	Upper Bound
CKD EPI	CKD EPI Modified for Asian	12.77	0.15	-3.39	28.93
	MDRD	-5.39	0.71	-21.55	10.78
CKD EPI Modified for Asian	CKD EPI	-12.77	0.15	-28.93	3.39
	MDRD	-18.157*	**0.02***	-34.32	-1.99
MDRD	CKD EPI	5.39	0.71	-10.78	21.55
	CKD EPI Modified for Asian	18.157*	**0.02***	1.99	34.32

Information: CKD Epi = Chronic Kidney Disease Epidemiology Equation; MDRD = Modification of Diet in Renal Disease; CKD Epi Modified for Asian = Chronic Kidney Disease Epidemiology Equation Modified for Asian



Information: CKD Epi = Chronic Kidney Disease Epidemiology Equation; MDRD = Modification of Diet in Renal Disease; CKD Epi Modified for Asian = Chronic Kidney Disease Epidemiology Equation Modified for Asian

Figure 2. Distribution of homogeneity of GFR value data (n=30; p-value homogeneity = 0.86) in units of mL/min/1.73 m^2

According to the homogeneity test's findings, the value of p-value = 0.86>0.05 is obtained, this can be interpreted that the third (3) variant of the GFR formula is the same or homogeneous. This can also be seen in the distribution of GFR value data based on the calculation of the three (3) formulas (graph.2).

The data in table 4 shows that the GFR calculation results using the CKD EPI Modified for Asian and CKD EPI formulas are not much different. Similarly, the MDRD formula and the CKD EPI formula tend to be the same. However, the CKD EPI Modified for Asian and MDRD differ significantly ($p<0.05$).

The National Kidney Foundation's suggested creatinine-based eGFR clinical laboratory reporting has contributed to increased awareness of CKD in the United States. Access to standardized creatinine techniques and eGFR equations has not only raised awareness of CKD but also facilitated the creation and application of several care metrics and medical decision points that depend on certain eGFR thresholds (Meeusen et al. 2022). Conventional GFR measurement methods generally require longer and more complicated when compared to using several practical formulas using either serum creatinine biomarkers or others. The use of formulas such as CKD EPI, and MDRD is very practical and efficient and makes it easier to determine the GFR value. The advantages and disadvantages of each formula are still not recommended in the physiological conditions of patients with extreme kidney disorders (Gao et al. 2021; Irawan, Farizal, and Febrianto 2019; Ji et al. 2017; Levey and Inker 2023; Liu et al. 2014; Teo et al. 2018).

Practical formulas such as CKD EPI and MDRD are often used in measuring GFR values. The formula is very suitable for calculating the GFR value of patients with end-stage chronic renal failure. The formula can also be used in patients with high GFR values and even without chronic renal failure. the use of the CKD EPI formula has results that are not much different from conventional GFR measurements (Irawan, Farizal, and Febrianto 2019; Teo et al. 2018).

MDRD formula is widely used in medical circles to measure glomerular filtration rate values in America and Europe to measure the prevalence of chronic kidney disease (CKD). However, the use of MDRD formula is still doubtful in patients with severe kidney damage. This is due to creatinine excretion contributed by tubule secretion and extrarenal pathways, besides that nutritional status also affects the validity of GFR values (Irawan, Farizal, and Febrianto 2019; Levey and Inker 2023; Teo et al. 2018).

Research conducted on Asian ethnicities in Japan, China, Hong Kong, Thailand, Taiwan, Singapore, and Pakistan in measuring GFR with MDRD and CKD EPI formulas revealed the need for a more accurate formula that considers the unique characteristics of Asian populations. This prompted some experts to develop a special formula for the Asian population (Kim et al. 2023; Teo et al. 2018). Every country certainly has etnic, culinary types, diverse regional cultures. In addition, consumption patterns, living habits, and adaptability to the environment such as survival in the wild in some ethnic worlds, are also concerns that need to be discussed. Many things are still a mystery and bias factor

related to the determination of GFR measurement results, especially with serum creatinine levels (National Kidney Fondation 2022; National Kidney Foundation 2021).

The existence of the CKD Epi Modified for Asian formula in the last decade is the first step in determining the right formula in measuring GFR, especially for the population in Indonesia. The results of GFR analysis conducted on 30 male respondents in Indonesia using the three (3) formulas showed a significant difference (p-value = 0.03<0.05). However, the homogeneity shown in the results of the data analysis of the three (3) formulas is not different or homogeneous.

The use of CKD Epi Modified for Asian formula is also recommended when associated with pre-clinical target organ damage (TOD) in elderly Chinese such as: Urinary albumin-creatinine ratio (uACR), Carotid-femoral pulse-wave velocity (cf-PWV), Carotid intima-media thickness (IMT), Ankle-brachial index (ABI), and Microalbuminuria. However, these studies were cross-sectional and required longitudinal analysis and clinical samples with a large prevalence of preclinical signs of kidney disease (Teo et al. 2018). The development of health transformation in the digital era has facilitated the process of implementing and modifying various GFR forms that are more precise, accurate, and efficient in accordance with the needs of establishing kidney disease diagnosis.

CONCLUSION

Considering the outcomes of the third (3) analysis, the formula shows a significant difference in GFR value (p-value = 0.03), but with homogeneity value of data distribution that is not much different or the same (p-value = 0.86). There is a significant difference only in the CKD Epi Modified for Asian and MDRD formulas (p-value = 0.02) from the three (3) formulas.

Declaration of Interest Statement

Authors have not declared any conflicts of interest.

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