Addis Ababa University  
Collage of Health Science  
School of Post Graduate studies  
Department of Physiology

Comparison of GFR Estimating Equations with Creatinine Clearance among Patients who Visit Renal Unit of Tikur Anbessa Specialized Hospital

A Thesis Submitted to the School of Graduate Studies, Addis Ababa University in Partial Fulfillment of the Requirements for a Degree of Master of Science in Medical Physiology

by

Kassa Setegn Addisu

Advisors

Dr. Tewabech Zewde

Dr. Addisu Melkea

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by

Kassa Setegn Addisu

Approved by Examining Board

1. Dr. Tesfaye Tolessa

Chairman

Signature

Date

2. Dr. Tewabech Zewde

Advisor

Signature

Date

3. Dr. Wondyefraw Mekonen

Examiner

Signature

Date
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 Lists of Acronyms

1. ARC-Augmented Renal Clearance
2. 99mTc-DTPA- Technetium 99m Diethylenetriaminepenta Acetic Acid
3. BSA- Body Surface Area
4. Ccr - Creatinine clearance
5. CG-Cockcroft -Gualt
6. Ci – Clearance of inulin
7. CI-Confidence Interval
8. CKD -Chronic Kidney Disease
9. CKD- EPI-Chronic Kidney Disease Epidemiology Collaboration
10. CVD- cardiovascular disease
11. CysC - Cystatin C
12. eGFR- estimated Glomerular Filtration Rate
13. eGFR\textsubscript{CG} – GFR estimated with Cockcroft -Gualt
14. eGFR\textsubscript{CKD-EPI} – GFR estimated with CKD- EPI
15. eGFR\textsubscript{MDRD} – GFR estimated with MDRD
16. GFR - Glomerular Filtration Rate
17. IQR-Inter Quartile Range
18. KDOQI- Kidney Disease Outcomes Quality Initiative
19. Kg-Kilogram
20. m-meter
21. MDRD- Modification of Diet in Renal Disease
22. mGFR- measured Glomerular Filtration Rate
23. mGFR\textsubscript{CCR} - GFR measured with creatinine clearance
24. Max-maximum
25. Min – minimum or minute
26. ml – milliliter
27. mg/dl-milligram per deciliter
28. N = number of participants
29. NKF - National Kidney Foundation
30. Q3-Third quartile
31. $r = \text{pearson's correlation coefficient}$
32. Scr – Serum Creatine Concentration
33. SD – Standard Deviation
34. sGFR - Glomerular Filtration Rate measured by standard techniques
35. IBM SPSS = International Business Machine Statistical package service solution
36. TASH - Tikur Anbessa Specialized Hospital
37. Ucr - urine creatine concentration
38. Ui – Urine inulin concentration
39. USA – United states of America
40. V – Rate of urine flow
41. Vs. = Versus
Abstract

Background: Glomerular Filtration Rate (GFR) is the amount of plasma filtered through glomerular capillaries of both kidneys per minute. It is used to measure the function of kidney and to know its status. GFR measurement can be done by using endogenous and exogenous filtration markers. But this measurement is expensive, time consuming and inconvenient to patients. To alleviate these problem we can estimate GFR by using Cockcroft- Gault, MDRD and CKD–EPI equations. GFR estimating equations are affected by sex, age, race, muscle mass, weight and height of an individual. However, the relation GFR estimating equations with creatinine clearance using these physiologic variables have not been clearly evaluated in Ethiopia.

Hypothesis: The current study hypothesized that there will be a difference between GFR estimating equations (CG, MDRD and CKD-EPI) and creatinine clearance.

Objective: The objective of study was to compare GFR estimating equations with creatinine clearance among patients who visit renal unit of Tikur Anbessa Specialized Hospital.

Materials and Methods: Cross sectional study was conducted to compare GFR estimating equations with that of creatinine clearance among 123 patients who visit renal unit of TASH from May 20 to April 16 / 2013. A convenient sampling was used in the study to select the study participants. Data was collected by using questionnaire, test tube, 5ml syringe with needle, urine collecting bag, balance and meter. Five ml of venous blood and 24 hour urine were taken from each participant to determine serum and urine creatinine concentration respectively. Serum creatinine was determined by using fully automated HITACHI 902 chemistry analyzer. Whereas, urine creatinine concentration was determined by using automated autolab 18 chemistry analyzer. Descriptive statistic, Paired sample t test, Bland-Altman analysis and correlation were carried out. P-value < 0.05 was considered as statistical significant and 95% CI used.

Result: Of 123 study participants 52 (42.3%) were males and 71 (57.7%) were females. Their mean age was 39.9 ± 16.7 years. Mean GFR were 49.59± 32.40, 56.15±33.70, 65.53±52.80 and
80.52±80.52 ml/min with creatinine clearance, Cockroft-Gault, MDRD and CKD-EPI respectively. GFR estimating equations significantly overestimate mGFR$_{Ccr}$ by 6.56, 15.94 and 30.93 ml/min with CG, MDRD and CKD- EPI respectively ($p <0.05$). Strong, positive and significant correlations were observed between Ccr and GFR estimating equations. The Pearson’s correlation coefficients (r) were 0.719, 0.760 and 0.771 with CG, MDRD and CKD-EPI vs. Ccr respectively ($P = 0.00$). Accuracy of participants classification at lower GFR levels (GFR <30 ml/min ) with MDRD was ranged from 0.98-1 and with CG at higher GFR levels (GFR >30 ml/min) was from 0.94-0.98.Limit of agreement were from -43.03 -48.59,-53- 85.30 and -42.04 - 103.90 with CG, MDRD and CKD-EPI vs. Ccr respectively.

**Conclusion:** Overall comparison of the three GFR estimating equations with creatinine clearance showed that CG estimate GFR better than MDRD and CKD-EPI equations. Furthermore, better GFR estimation with MDRD was observed next to CG. In the current study strong, positive and significant correlation and good measurement agreement were observed between Ccr and CKD-EPI. However; it is less effective to estimate GFR as compared with CG and MDRD.
1. Introduction

1.1. Background of the Study

Kidneys perform multiple excretory and endocrine functions. The most important of its function is the filtration of body waste. Kidneys filter approximately 180 liters of plasma per day (125 ml plasma /min). Glomerular Filtration Rate (GFR) is the amount of plasma filtered through glomerular capillaries of both kidneys per minute. Its normal value is about 130 and 120 ml/min/1.73 m$^2$ in young men and women respectively, with considerable variation even among normal individual. Causes of normal GFR variation include age, sex, fluid intake, physical activity, drug etc. (1, 2). For example: Normally GFR decline with age from the peak GFR (120 ml/min) attained during the third decade of life is about 1 ml/min per year, reaching a mean value of 70 ml/min at the age of 70 years (3,4).

The first step in the assessment of kidney function is determination of glomerular filtration rate either by measurement or estimation. GFR can be measured by using exogenous filtration marker like radioisotope and inulin or endogenous filtration marker like cystatin C and creatinine. Except cystatin C and in some extent creatinine, these filtration markers are filtered at the glomerular capillary but they are neither reabsorbed nor secreted throughout the kidney tubules. We can measure GFR accurately by using radioactive labeled molecules such as Technetium 99m Diethylene Triamine penta Acetic Acid ($^{99m}$Tc-DTPA), $^{125}$I-iothalamate, Ethylene Diamine Tetra Acetic Acid (EDTA) and Chromium-Ethylene Diamine Tetra Acetic Acid ($^{51}$Cr-EDTA).However, radionucleotide measurements of GFR are expensive and impractical in the clinical area (5,6,7,8).

Inulin is a polysaccharide, made up of fructose in the roots and tubers of certain plants. It is a gold standard (ideal) filtration marker. Since inulin clearance equals to GFR, it can be used to measure GFR. GFR is calculated from the rate of inulin removal from the blood and its appearance in the urine over several hours. GFR measured by using inulin is calculated by using the following formula.
\[
\text{GFR} = \frac{U_i \times V}{P_i}
\]

Where:
1. GFR - Glomerular Filtration Rate
2. \(U_i\) - Urine inulin concentration
3. \(V\) – Urine flow rate
4. \(P_i\) – Plasma inulin concentration

Inulin is not produced in the human body and must be administered intravenously into a person to measure his or her GFR. The classic protocol for inulin clearance requires a continuous intravenous infusion, multiple blood sample, and bladder catheterization or 24 hours urine collection. This GFR measurement technique is inconvenient to the patients, time consuming procedure and rarely used today, even in the research setting (2, 4, 5, 9, 10, 12, 13).

Since 1985, cystatin C (CysC) has been described as a promising endogenous filtration marker of GFR for both adults and children. It has low molecular weight and is a member of cysteine protease inhibitors superfamily. Gene of CysC is expressed in all nucleated cells and is thought to be produced and secreted at a constant rate. CysC is a protein which is freely filtered at the glomerular capillary. It is almost completely reabsorbed and catabolized but not secreted by the tubular epithelial cells. Since only small amounts are excreted into the urine, its urinary clearance cannot be measured. Therefore, the blood concentration of CysC depends almost entirely on the GFR and is not substantially affected by diet or nutritional status. It is also independent of muscle mass, age or sex and does not have a circadian rhythm in its secretion. Because of these properties, many investigators have proposed that serum concentrations of CysC could serve as an improved indicator of GFR as compared with Scr. It is also a good real time GFR marker in unstable critically ill patients. However, the accuracy of measuring GFR by using cystatin C is affected with some circumstances. Large dose of glucocorticoids have been shown to increase serum CysC concentration. Additionally, thyroid gland function has an impact on CysC production. CysC levels are lower in the hypothyroid and higher in the hyperthyroid state. Therefore, thyroid function has to be considered when CysC is used as a marker of renal function. Similarly; the half life of serum cystatin C is three times shorter than
creatinine (5, 9, 14). Some of Cystatin C based equations for the measurement of glomerular filtration rate in adults are:

1. \[ \text{GFR} = \frac{80.35}{\text{PCysC (mg/l)}} - 4.32 \]
2. \[ \text{GFR} = \frac{86.7}{\text{PCysC (mg/l)}} - 4.2 \]
3. \[ \text{GFR} = 77.239 \times \text{PCys C (mg/l)}^{-1.2623}, \text{where: pCyst C plasma Cystatin C concentration (8, 14).} \]

The most widely used clinical marker of kidney function is creatinine. It is a nitrogenous substance which is formed in the muscle from creatine phosphate by irreversible, nonenzymatic dehydration and loss of phosphate. Creatinine is a small, freely filtered solute that varies slightly from day to day (since it is derived from muscle metabolism of creatine phosphate) is used to measure GFR. But Creatinine is now recognized as an unreliable GFR measurement technique because of its serum concentration is affected by age, muscle mass, race, various medications and dietary ingestion of meat. Serum creatinine is primarily determined by muscle mass and dietary intake of meat, which probably accounts for the variations in Scr levels observed among different age, geographic, ethnic, and racial groups. Furthermore, proximal tubular cell secretion plays an important role in creatinine elimination with decline GFR. Even though it has such limitations creatinine is widely used to measure GFR clinically. Since measurement of creatinine clearance does not require intravenous infusion into the patient, this method is much more widely used than inulin clearance. Creatinine clearance is equal to GFR and calculated as follow (5, 10, 13, 14).

\[ \text{GFR} = \frac{\text{Ucr x V}}{\text{Scr}} \]

Where:

1. GFR - Glomerular Filtration Rate (ml/min)
2. Ucr - Urine creatine concentration (mg/dl)
3. V - Urine flow rate (ml/min)
4. Scr - Serum creatinine concentration (mg/dl)

The gradual loss of muscle from chronic illness, chronic use of glucocorticoids, or malnutrition can mask significantly GFR measurement with creatinine clearance. However, in the absence of above determinant factors, creatinine clearance is sufficiently accurate to measure GFR. But; it
requires 24 hour urine collection. This is too difficult and time consuming to use frequently in the clinical setting and carried out GFR related studies in the community.

As we have seen earlier the methods which used to measure GFR have their own limitations or difficulties to apply. This problem can be alleviated by using GFR estimating equations (formulas). GFR estimating equations use age, sex, race correction factor, weight, height and muscle mass, in addition to serum creatinine. Therefore, they can overcome some of the limitations of using serum creatinine alone. GFR estimating equation includes: Cockcroft-Gault (CG) Equation, Modification of Diet in Renal Disease (MDRD) equation, Chronic Kidney Disease Epidemiology Collaboration (CKD –EPI) equation, Mayo clinic Quadratic equation, white methods, Larsson equation, MacDonald equation, Jelliffe-1973 equation, Hull equation, Rule formula and Schwartz equation. The most commonly used GFR estimating equations are CG, MDRD and CKD – EPI equation (5, 11, 15, 16, 17, 18).

Cockcroft-Gault equation was developed in 1973. It was developed from 249 men with a range of creatinine clearance between 30 to 130 ml/min. The primary objective of the formula wasn’t to estimate GFR, rather to estimate creatinine clearance, which is inherently less accurate to measure GFR since it contains some component of tubular secretion.

1. \[ eGFR_{CG} = \frac{(140-\text{age}) \times \text{weight}}{72 \times \text{Scr}} \]

Key:

1. \( eGFR_{CG} \) - GFR estimated with CG
2. Scr - Serum creatinine

Multiply the result by 0.85 if females; where age is in year, weight in kg and serum creatinine in mg/dl. GFR can be also estimated with a modified Cockcroft-Gault formula by taking body surface area (BSA) into consideration.

2. Body surface area adjusted Cockcroft-Gault formula = \( (\text{GFR by CG equation}) \times 1.73m^2 \) / BSA
Multiply by 0.85 if female, because females have 15% lower muscle mass than males. As a limitation, Cockcroft-Gault equation systematically overestimate GFR (11, 18, 20, 21, 22, 23, 24).

The MDRD was presented in 1999 by using data from 1628 CKD patients (mean GFR of 40 ml/min/1.73 m²) who were predominantly Caucasian and they did not have diabetic kidney disease or kidney transplants. The 4-variable MDRD equation estimate GFR by using serum creatinine, age, sex and race correction factor.

\[ eGFR_{MDRD} = 186 \times (Scr)^{-1.154} \times (age)^{-0.203} \times 0.742 \times \text{female} \times 1.21 \text{ if back} \]

Where:
1. \( eGFR_{MDRD} = \) GFR estimated with MDRD equation
2. \( Scr = \) Serum creatinine concentration

The MDRD includes a race correction factor of 1.21 for black people based on a 21% higher GFR in Afro-Americans than in whites. The South African renal society CKD guidelines, adopted in 2006, recommend using the Cockcroft-Gault (CG) or MDRD equations with inclusion of the race correction factor 1.212 for black patients, while the correction factor 1.0 for other races (27). GFR is expressed in ml/min/1.73 m², Scr in mg/dl, age in years, and race as African American or black. The terms age, sex, and race reflect differences in creatinine generation related to changes in muscle mass associated with age, sex and race. Unlike GFR measured with creatinine clearance, the MDRD equation does not require 24 hours urine collection, which is prone to errors and inconvenient for patients. Instead MDRD equation relies entirely on serum creatinine (5, 6, 11, 14).

Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) is a research group which is formed to develop and validate improved GFR estimating equations by using data from research and clinical population. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was developed from study conducted by Levey et al. from 1999-2006 in United States of America (USA) among 8,254 people with and without kidney disease (mean measured GFR of 68 ml/min/1.73 m²). The CKD-EPI equation is found to be as accurate as the MDRD for estimated GFR <60 ml/min/1.73 m² and considerably more accurate than MDRD in the group.
with GFR >60 ml/min/1.73 m$^2$. Levey et al. recommended that the CKD-EPI equation should replace the MDRD in the routine clinical use. The basis for this new equation provides a more accurate estimation of GFR, especially at higher levels. In addition, CKD-EPI equation uses the same 4 variables as the MDRD equation and it does not require additional variables to be collected by clinical laboratories (7, 9, 14, 19, 24).

$$eGFR_{CKD-EPI} = 141 \times (\text{Scr/} \kappa)^{\alpha} \times (0.993)^{\text{age}} \times (1.018 \text{ if female}) \times (1.159 \text{ if black})$$

**Key:**

1. $eGFR_{CKD-EPI}$ = GFR estimated with CKD-EPI
2. Scr = serum creatinine
3. $\kappa$ = 0.7 for females and 0.9 for males
4. $\alpha = -0.329$ if females and Scr $\leq$ 0.7mg/dl
5. $\alpha = -1.209$ if females and Scr $> 0.7$mg/dl
6. $\alpha = -0.411$ if male and Scr $\leq$ 0.9mg/dl
7. $\alpha = -1.209$ if males and Scr $> 0.9$ mg/dl

The CKD-EPI equation estimation of GFR has lower bias, especially at GFR greater than 60 ml/min per 1.73 m$^2$. The improved accuracy of the CKD-EPI equation overcome some of the limitations of the MDRD equation and has important implications for public health and clinical practice. However, its precision remains limited (23, 24, 25, 26).

Kidneys have different ranges of function in homeostasis; GFR remains the most widely accepted indicator of renal function in both health and disease. Largely, any assessment of GFR in clinical area is focused on the identification of renal impairment, where serum creatinine concentrations are typically employed as a key biomarker (2, 4).

A kidney disease outcome Quality Initiative (KDOQI) guideline which was developed by National Kidney Foundation (NKF) of USA provides a staging system for CKD based on the level of GFR. Lower levels of GFR (higher CKD stages) are associated with a higher prevalence of a wide range of symptoms and complications, including hypertension, anemia, malnutrition, bone disease, and neuropathy. There is a cumulative evidence for an increased risk of cardiovascular disease (CVD) and mortality with decreasing levels of GFR. The central role of GFR in this guideline reflects a consensus that the level of GFR is the best overall
measurement of kidney function, as well as the measurement that is most easily understood by physicians and patients. Using GFR, public health campaigns can focus on messages such as “know your GFR number” or “save your GFR,” a strategy analogous to those used for hypertension or hyperlipidemia. Based on this rationale, national and international organizations recommend the clinicians to use GFR estimating equation to assess kidney function (2,4).

Table A: The 5 stages of adult kidney function (CKD stages) as determined by GFR levels (19)

<table>
<thead>
<tr>
<th>CKD stages</th>
<th>GFR levels (ml/min/1.73 m²)</th>
<th>Clinical Implication</th>
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<tr>
<td>1</td>
<td>≥90</td>
<td>Normal kidney function</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Mild impairment</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
<td>Moderate impairment</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severe impairment</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>End stage Kidney disease</td>
</tr>
</tbody>
</table>

According to KDOQI guideline individuals with persistent 3 or more month reduction in GFR (<60 ml/min/1.73 m²) are defined as having CKD. Individuals with a GFR 60 ml/min/1.73 m² and markers of kidney damage (Eg. proteinuria), also are defined as having CKD. Individuals with a GFR 60 ml/min/1.73 m², but without any markers of kidney damage, do not have CKD (2, 4, 6, 14,19).
1.2. **Statement of the problem**

Glomerular filtration rate is considered as the best overall indicator of kidney function in healthy people and patients. However, GFR can’t be measured easily in the clinical setting; instead, it is estimated with GFR estimating equations. Most commonly used GFR estimating equations are CG, MDRD and CKD-EPI. These GFR estimating equations are affected by physiologic variables (age, race, sex, muscle mass, weight and height) of an individual. They have different qualities and significant limitations in the estimation of GFR. Furthermore, they are not accurate in the population that are different from those in which the equations were developed (white and Africa American people). Therefore to get more accurate result and to choose the best GFR estimating equation they should be evaluated by using physiologic variables of a population it intended to be used for. GFR estimating equations do not account for all determinants of serum creatinine, such as alterations in muscle mass not related to age, sex, race, diet and tubular secretion. Therefore, in people with muscle disorders, amputees, body builders, or those on very low protein diets, these equations will not be accurate. Since GFR estimating equations are not also accurate in patients with rapidly changing kidney function, patients must be in a steady state to obtain accurate GFR estimation (13, 19, 26).

Limited numbers of research were conducted in the comparison of GFR estimating equations with creatinine clearance in Sub Saharan African countries (19, 27). Moreover, study has not been done in Ethiopia. Thus the present study was carried out to compare GFR estimating equations with that of creatinine clearance in patients attended the renal unit of Tikur Anbessa Specialized hospital.
1.3. Significance of the Study

The present study compared CG, MDRD and CKD-EPI equations with creatinine clearance by taking the physiologic variables of the local community. Furthermore, it identified the most useful GFR estimating equation. This might serve as starting point to choose GFR estimating equation in the clinical setting. The relationships of these equations with creatinine clearance have also been reported from limited numbers of studies which were conducted in Sub Saharan Africa (19, 26, 27). However, study has not been carried out in Ethiopia to compare the GFR estimating equations with creatinine clearance. Thus the current study will fill this gap and the results also provide an insight to carry out similar study at larger population in Ethiopia.
2. Literature Review

Many different studies were conducted across the globe regarding measurement and estimation of GFR. Although the number of studies in this area is relatively high, its number is limited in sub Saharan Africa (19, 26, 27) and we can say almost nil in Ethiopia. Some of the researches conducted across the world which have direct relation with present study are as follow:

A prospective study was carried out by Baptista et al. at tertiary level ICUs in Portugal and Australia from 2005 to 2009. In the beginning two hundred nine patients were enrolled in study at each centre. Of these, 86 (Australia n = 43, Portugal n = 43) patients with augmented renal clearance or increased GFR (GFR >130 ml/min/1.73 m²) were included in the final study. Eight hour collected urine was utilized in Australia, while a 24 hour collected urine was employed in Portugal. The objective of the study was to compare CG and MDRD with Ccr. In this study median GFR (IQR) were 162 (45), 135 (55), 93 (27), 124 (52) and 108 (48) ml/min/1.73 m² with Ccr, CG, modified CG, 4-variable MDRD, 5-Variable MDRD respectively. Baptista et al reported that the linear relation between Ccr and CG were significant and weak. Pearson’s correlation coefficient (P-values) were 0.26 (0.017), 0.22 (0.044), 0.22 (0.161) and 0.25 (0.105) with CG, modified CG, 4-variable MDRD, 5-Variable MDRD vs. Ccr respectively (8).

Using a cut off for ARC of more than 130 ml/min/1.73 m² their sensitivity (correctly identifying ARC) were 53 (62) %, 47 % and 29 % with CG, 4-variable and 6-variable MDRD equations as it can be seen from the data GG was more accurate whereas, 6-variable MDRD was less accurate. Their bias (precision) were 39 (75%), 84 (70%), 48 (76%) and 68 (76%) CG modified CG, 4-variable MDRD, 5-Variable MDRD vs. Ccr respectively. Finally, Baptista et al. concluded that CG and MDRD equations were inaccurate in quantifying GFR in a sub-group of critically ill patients with ARC. Both of them significantly underestimate GFR measured by creatinine clearance (8).

A study was conducted by Franka et al. in internal medicine wards of two secondary care hospitals, south Switzerland (Regional Hospitals of Locarno and Bellinzona). This study was done on 69 hospitalized CKD Caucasian patients and published on December 19 /2012. The objective of the study was to investigate the reliability of GFR obtained by using CG, MDRD,
Larsson equation (use serum cystatin C), white methods (use beta trace protein, serum creatine and sex) and McDonald equation (use muscle mass, serum creatine and weight) in comparison with inulin clearance. The mean GFR with these six methods were $34.9 \pm 20.0$, $46.7 \pm 18.5$, $49 \pm 15.9$, $47.2 \pm 23.0$, $54.4 \pm 18.2$, and $67.99 \pm 27.2$ ml/min with inulin clearance, CG, MDRD, Larsson, white methods and McDonald equation respectively. In this study significant overestimation of GFR by 11.8, 14.1, 12.4, 19.5 and 32.29 ml/min with CG, MDRD, Larsson, white method and McDonald equation respectively as compared with inulin clearance was reported ($p$-value = 0.001 for all). Finally, Franka et al. concluded that the best GFR estimation was obtained with the Larsson equation which is characterized by lowest median error, provide more accurate classification. Furthermore CG provides better estimation next to Larsson equation (lowest mean difference, accurate classification) (9).

Another study was conducted by Liu et al. from January 2005 to December 2009 in Sun yet Sun University Hospital, China among 319 elderly CKD patients (>70 years). The intention of study was to compare GFR estimating equations with $^{99m}$Tc-DTPA. Technetium 99m Diethylene Triamine Penta Acetic Acid ($^{99m}$Tc-DTPA) renal dynamic imaging method was used as standard GFR measuring technique and CG, MDRD, CKD-EPI, Jelliffe-1973 (use age, sex and Scr) and Hull equations (use age, sex, Scr and weight) were used to estimate GFR. Mean GFR measured by $^{99m}$Tc-DTPA was $39.4 \pm 21.8$ ml/min. The mean difference between eGFR equations and mGFR were -3, 2.4, -0.6, 0.8 and -1.9 ml/min with CG, MDRD CKD-EPI, Jelliffe-1973 and Hull equations respectively (25).

The medians difference with four variable MDRD equation was less than those of the other GFR estimating equations (0.3 ml/min). The CKD-EPI equation demonstrated less mean difference from GFR measured with $^{99m}$Tc-DTPA than the other equations (0.6 ml/min). None of the equations had accuracies that reached 70% while differing less than 30% from $^{99m}$Tc-DTPA. Chronic kidney disease stages misclassifications by the four-variable MDRD equation was less than that of the other equations. All of the equations had CKD stages misclassification higher than 42%. The precisions of the GFR estimated by the CG equation and the CKD-EPI equation were better than the other equations. Liu et al. finally concluded that none of these GFR estimating equations were suitable for estimating GFR in the elderly Chinese population. But based on comparison of overall performance and accuracy, CG equation provided better
estimation than the above mentioned GFR estimating equations to estimate GFR of elderly Chinese patients with CKD (provide more accurate classification, lowest limits of agreement and more precise) (25).

An investigation was carried out by Chung et al. from March 2009 to September 2011 in South Korea among 207 healthy Korean adults who underwent the kidney donation workup. The objective of the study was to compare Ccr, CG, MDRD, CKD-EPI equations with that of $^{99m}$Tc-DTPA in kidney donors before and after kidney donation. In this study GFR was measured by using $^{99m}$Tc-DTPA and creatinine clearance and the value of mean GFR were $110.3 \pm 20.7$, $97.4 \pm 31.5$ ml/min respectively. Whereas, mean estimated GFR were $109.6 \pm 27.9$, $100.7 \pm 20.4$ and $108.7 \pm 18.0$ with Cockcroft–Gault, MDRD and CKD-EPI respectively. Mean difference (bias) between estimated GFR and GFR measured with $^{99m}$Tc-DTPA were $-12.5 \pm 29.4$, $-0.73 \pm 22.9$, $-9.6 \pm 20.8$ and $-1.6 \pm 19.1$ with Ccr, MDRD and CKD-EPI respectively. As we can noticed easily from the data CG and CKD-EPI showed minimal bias from $^{99m}$Tc-DTPA ($P<0.05$), while Ccr and MDRD significantly underestimated GFR ($P = 0.001$). Chung et al. determine precision of GFR estimating equations by taking their SD of mean difference (bias). Estimation with CKD-EPI showed highest precision (lowest SD of bias) among three equations before kidney donation study. In addition, the accuracy of CKD-EPI was 91.8%, which is significantly higher than that of creatinine clearance (71.5%) and MDRD (84.1%) ($P<0.001$ in each case) and it showed a higher tendency compared with CG (86.0%) ($P= 0.06$) (28).

In 170 participants with normal renal function (mGFR > 90 ml/min /1.73 m$^2$) mean GFR were $116.3 \pm 17.7$, $102.0 \pm 32.1$, $114.7 \pm 27.5$, $103.7 \pm 20.1$ and $111.8 \pm 17.3$ with $^{99m}$Tc-DTPA, Ccr, CG, MDRD and CKD-EPI respectively. In this group of participant both creatinine clearance and MDRD significantly underestimated mGFR ($P < 0.001$ in each case), but CKD-EPI gives better estimation. Mean difference (accuracy) were $-14.3 \pm 31.4$ (68.0%), $-1.5 \pm 24.4$ (84.6%), $-12.5 \pm 21.0$ (82.2%), and $-4.5 \pm 19.1$ (94.7%) Ccr, CG, MDRD and CKD-EPI respectively and accuracy of GFR estimated with CKD-EPI showed higher precision and accuracy ($P< 0.05$ in each case) than the other 3 equations as well (28).

In 37 subjects with decreased renal function (mGFR $\leq$ 90 ml/min/1.73 m$^2$) mean GFR were $83.16 \pm 6.4$, $78.7 \pm 16.5$, $86.0 \pm 15.1$, $86.8 \pm 15.1$ and $94.7 \pm 14.4$ with $^{99m}$Tc-DTPA, Ccr, CG, MDRD and CKD-EPI respectively. Mean difference and accuracy were also $24.5 \pm 15.7$ and 89.2%, $2.91 \pm 13.9$ and 81.1%, $3.6 \pm 13.9$ and 94.6%), $11.6 \pm 12.6$ and 81.1% Ccr, CG, MDRD and CKD-EPI respectively. As the data showed, CKD-EPI significantly overestimated GFR ($P<$
Ccr, CG and MDRD did not show significant difference from mGFR (P= 0.094, P= 0.211 and P= 0.123 vs. mGFR, respectively). In precision and accuracy no significant differences were detected in any comparisons between equations. Finally, Chung et al. reported that better GFR estimation was observed with CKD-EPI as compared with the other eGFR equations before donation. After donation, however, MDRD was reported as better GFR estimating equations (more accurate and precise) than CKD-EPI (28).

A retrospective study was conducted by Madala et al. in the adult renal clinic at King Edward VIII Hospital, Durban, South Africa to compare CG and MDRD with $^{99m}$Tc-DTPA. The study was done among 148 kidney patients of African and Indian ancestry from January 2004 to December 2006. In this study two thirds of patients (67.57%) had mGFR < 60 ml/min/1.73 m$^2$ in keeping this, the prevalence of CKD stages 3–5 of 70.3% and 63.2% in African and in Indian patients respectively. Overall median GFR (IQR) with $^{99m}$Tc-DTPA was 38.5 (44) ml/min/1.73 m$^2$ (27). The comparison between mGFR and eGFR were reported as follow:

In the African group (n=91) the median GFR (IQR) were 37 (38), 45 (77) and 48 (58) and 40 (48.5) ml/min with $^{99m}$Tc-DTPA, CG and MDRD with ethnicity correction factor 1.212 and MDRD without ethnicity correction factor respectively. A strong statistically significant linear relationship between estimated and measured GFR were reported in both African and Indian groups. The Spearman correlation coefficients (r) in the African group were 0.86 and 0.86 and 0.87 for CG, MDRD with correction factor and MDRD without correction factor respectively. Whereas, the “r” values for Indian group were 0.77 and 0.82 for CG and MDRD, respectively. In both group Bland–Altman plots showed greater measurement agreement between eGFR and mGFR when GFR was < 60 ml/min/1.73 m$^2$ for all equations, while concordance was poorer at higher GFR levels (27).

In African group with advanced CKD (stages 4–5 or GFR < 30 ml/min/1.73 m$^2$), all the three GFR estimating equations underestimated mGFR. Median difference between eGFR and mGFR were -1, -7 and -10 with CG, MDRD with race correction factor and MDRD without correction factor respectively. CG provided better estimation with the smallest median difference of -1.0 ml/min/1.73 m$^2$. In those with stage 3 CKD (GFR 30–59 ml/min/1.73 m$^2$), nearly similar estimation was observed when CG and MDRD with race correction factor were used with a median difference 6 ml/min/1.73. And the median difference with MDRD without correction
was lowest (2 ml/min/1.73m²). All equations overestimate mGFR when mGFR was > 60 ml/min/1.73 m² (stages 1–2 CKD) with the better GFR estimation observed when the MDRD equation was used. The median differences were 37, 27, 14 ml/min with CG and MDRD with correction factor and MDRD without race correction factor respectively (27).

In Indian group (n=57) the median GFR (IQR) were 41 (49), 40.5 (46) and 42.2 (60.7) ml/min/1.73m² with ⁹⁹ᵐTc-DTPA, CG and MDRD without race correction factor respectively. In this group of participants, both CG and MDRD without race correction factor underestimate mGFR in those with CKD stages 3–5 with median difference -6.5 and -12 respectively. This showed that CG outperforming MDRD. In CKD stage 3 CKD (GFR 30–59 ml/min/1.73 m²), median difference were -2 and -21 ml/min with CG and MDRD without race correction factor respectively and CG provided better estimation. Both equations overestimated mGFR in patients with CKD stages 1–2 (median difference 12 with CG and 5 with MDRD without correction) (27).

Finally Madala et al. concluded that MDRD calculated without the race correction factor (1.212) improved GFR prediction in African CKD patients and using the MDRD correction factor of 1.0 in Indian patients as in Caucasians may be inappropriate (27).

A community based study was conducted by Eastwood et al. in Ashanti, Ghana among 1013 adult people to assess their GFR by using creatinine clearance, Cockcroft- Gualt, MDRD and CKD -EPI. It was published on January 25/ 2010 with the report of the following results. The mean weight of participant was 56.4 ± 9.7kg. The mean serum creatinine (ml/dl) were 1.01 ± 0.21 (in male), 0.82 ±0.15 (in females) and 0.89 ± 0.20 (in both males and females). Serum creatinine had significant relation with sex (p<0.001). Mean GFR measured with creatinine clearance were 82.3 ± 22.4, 85.3 ± 22.7 and 84.1 ± 22.6 in males, females and both sexes respectively. 86.8% of participants had a GFR of ≥60 ml/min/1.73 m². Mean eGFRCG whereas, were 72.1± 15.6, 76.2 ± 20.0 and 74.7 ± 18.6, in males, females and both sexes respectively. The mean GFR estimated with CG was 9.4 (95% CI 8.3 to 10.6) ml/min/1.73 m² lower than the mGFRCcr. This indicates that CG underestimated GFR as compared with Ccr (19).
GFR Estimated with MDRD were 104.7 ± 23.0, 100.9 ± 22.6 and 102.3 ± 22.8 in males, females and both sexes respectively. GFR estimated with MDRD without race correction factors were also 86.5 ±19.0, 83.4± 18.6, and 84.6+ 18.8 in males, females and both sexes respectively. Estimated GFR_{CKD-EPI} were 103.6 ± 18.2, 102.8 ± 19.0 and 103.1± 18.7 ml/min in males, females and both sexes respectively. Estimated GFR_{CKD-EPI} without race correction factors were 89.6+ 15.8, 89.2 ±16.5 and 89.4 ±16.2 ml/min in males, females and both sexes respectively. As it can be easily notice that, without race correction factor GFR estimation values with MDRD and CKD-EPI become much closer to Ccr (19).

The mean GFR with MDRD and CKD-EPI were 18.2 (16.8 to 19.5) and 19.0 (17.8 to 20.2) ml/min/1.73 m², respectively higher than mGFR_{CCr}. Unlike CG, MDRD and CKD-EPI overestimate GFR in this study. Bland–Altman plots for MDRD, CKD-EPI and Cockcroft–Gault vs. Ccr indicates better concordance at the middle GFR stages and it was poor at the higher and lower GFR. Limits of agreement between GFR estimating equations and Ccr were −44.7 to 25.8, −23.6 to 59.9 and −17.9 to 53.8 with CG, MDRD and CKD-EPI respectively. A limit of agreement is narrower with Cockcroft–Gault equation than either MDRD or CKD-EPI (19). This narrow limit of agreement and low mean difference with CG suggest its better quality in the estimation of GFR as compared with MDRD and CKD-EPI. Finally Eastwood et al. has been reported that the CKD-EPI equation without black race correction factors appears to be the most useful.
3. Hypothesis

The current study hypothesized that there will be a difference between GFR estimating equations (CG, MDRD and CKD- EPI) and creatinine clearance.
4. Objective

4.1. General Objective
The general objective of the study was to compare GFR estimating equations with creatinine clearance among patients who visit renal unit of Tikur Anbessa Specialized Hospital.

4.2. Specific Objectives
1. To measure GFR with creatinine clearance
2. To estimate GFR by using CG equation
3. To determine GFR with MDRD equation
4. To calculate GFR by using CKD – EPI equation
5. To compare CG, MDRD and CKD – EPI equations with creatinine clearance
5. Materials and Methods

5.1. Study Area
The study was conducted in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

5.2. Study and Data Collection Period
The study was conducted from May 20 / 2013 to April 16 / 2014 and data was collected from September 14 to November 18 / 2013.

5.3. Study Design
A cross sectional study was used in this study. Data was collected at one time from each participant.

5.4. Target population
All patients who visit renal unit of TASH.

5.5. Study population
All patients who visit renal unit of TASH during data collection period.

**Inclusion criteria:** patients who visit renal unit of TASH during data collection period and who give informed consent, 24 hour urine and blood sample were included.

**Exclusion criteria:** Patients who do not give informed consent, 24 hours urine and blood sample were excluded.

5.6. Sampling Method and Sample Size Determination
A convenient sampling technique was used in the study and sample size was calculated by using the following formula which used to estimate sample size to determine single population mean.

\[ n = \frac{Z^2 \sigma^2}{\delta^2} \]

Where:
1. n - Is the minimum sample size required for the study
2. Z - value of confidence interval, Z = 1.96 (95% confident, interval) –commonly used as well as researchers interest
3. \( \sigma \) - Is the expected SD of measured GFR = 22.6 ml/ni/1.73/ m², taken from previous study
4. \( \delta \) – Is the margin of error (tolerable error) = 4ml/mi/1.73 m\(^2\) which is a researcher’s interest (29)

\[
n = \frac{(1.96)^2 (22.6)^2}{(4)^2}
\]

\[n = 123\]

5.7. Study Variables

5.7.1. Dependent study Variables

- Measured GFR
- Estimated GFR
- Urine creatine
- Serum creatinine

5.7.2. Independent study Variables

- Height
- Weight
- Age
- Sex
- Race

5.8. Data Collection

5.8.1. Data Collection Instrument

Questionnaire, 5 ml syringe with needle, urine collecting materials, balance, meter and different laboratory instruments were used in the study to collect the data.

5.8.2. Data Collection Procedure

Weight and height were measured by using Seca 761 weight scales and height ruler (meter) which is attached with it respectively (made in Germany). 5ml venous blood sample was taken from each participant then the serum was separated from the blood by centrifugation. Serum creatinine was analyzed by HITACHI 902 chemistry analyzer at TASH chemistry laboratory. 24 hour urine collected from each participant was sent to Bithania higher clinic’s laboratory. Then about 5 ml of urine was centrifuged at 3000 RPM for 3 minute at room temperature and urine creatinine level was determined by using auto lab 18 chemistry analyzer. In addition to these 24 hours urine volume was also measured.
5.9. Validity and Reliability

Validity and reliability ensured by checking each filled questionnaires and laboratory results for their correctness and completeness during each data collection day.

5.10. Statistical Analysis

International Business Machine Statistical Product and Service Solutions (IBM SPSS) version 21 and Microsoft excel 2007 were used to analyze the data. Descriptive statistic was used to calculate mean, median, range, IQR and standard deviation of estimated and measured GFR. Paired sample t test was used to compare mean of estimated and measured GFR. Bland-Altman analysis was also carried out to check whether measurement agreement was present or not between eGFR and mGFR (30). Sensitivity and specificity was calculated to determine accuracy of eGFR equations to classify participants at different GFR strata as compare to Ccr (31, 32, 33, 34).The mean difference between estimated GFR and measured GFR was used to determine the bias. Precision of the GFR estimating equations was determined as SD of the mean difference between estimated GFR and measured GFR as well as by using 95% CI (24, 29,31).Pearson’s correlation coefficient was calculated to quantify degree of linear relation between GFR estimating equations (CG, MDRD and CKD -EPI ) and creatinine clearance (34). Furthermore Box and Whisker plot was used to display and compared centering, spread, and distribution of measured and estimated GFR (36, 37). P-Value < 0.05 was considered as statistical significant and 95% CI was used in the current study. Finally the result summarized and presented by using tables and diagrams.

5.11 Ethical Consideration

Ethical clearance was obtained from both the research and ethics committee of physiology and Internal medicine departments of college of health, Addis Ababa University and TASH. Data was collected only from those participants who gave their informed consent.
6. Result

6.1. Sociodemographic Profile of participants

Table 1 shows the sociodemographic characteristics of participants of the study. A total of 145 patients who visited TASH from September 14 to November 18 / 2013 were participated in the study. Out of this, 123 participants completed the study by providing necessary data and the response rate was 85%.

Table 1: Socio demographic characteristics of participants

<table>
<thead>
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<th>Demographic variables</th>
<th>Category</th>
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<th>Percentage</th>
</tr>
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<tr>
<td>801 – 1600 Birr</td>
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<tr>
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### 6.2. Clinical Data

Table 2 shows the distribution of participants by their weight. The mean weight of participants was $61 \pm 13.34$ kg. Weight ranged from 35-98 kg and modal weight was 55 and 75 Kg.

Table 2: Distribution of participants by their weight

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<td></td>
<td></td>
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<td>Percentage</td>
<td>Frequency</td>
<td>Percentage</td>
<td>Frequency</td>
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<td>2.82</td>
<td>3</td>
<td>2.43</td>
</tr>
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</table>

Table 3 shows the distribution of participants by their height. The average height of participants was $1.63 \pm 0.087$ meter. The minimum and maximum heights were 1.40 and 1.83 meter respectively. Whereas, the mode was 1.60 & 1.68 meter.
Table 3: Distribution of patients by their height

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<td>Percentage</td>
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<td>1.92</td>
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<td>10</td>
<td>19.23</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>1.60-1.69</td>
<td>19</td>
<td>36.54</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>1.70-1.79</td>
<td>18</td>
<td>34.62</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>1.80-1.89</td>
<td>4</td>
<td>7.69</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>100.00</td>
<td>71</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Figure 1 shows the distribution of participant by their serum creatinine level. Out of 123 participants 42 (34.15 %) had serum creatinine 0.5-0.9 mg /dl in females and 0.6–1.2 mg/dl in males. About two third 81  (65.85 %) of participants had serum creatinine 0.9 -10.5 ml/dl in females and 1.2 - 9 mg/dl in males. Mean Ser was 2.23 ± 2.13 mg/dl. The median (IQR) serum creatinine were 1.3 (1.2) mg/dl and mode was 1.1mg/dl. The serum creatinine was ranged from 0.5- 10.5  mg/dl.
Figure 1: Distribution of participants by their serum creatinine level

Table 4 indicates distribution of participants by their 24 hour urine output. As shown in the table the urine output of 63 (51.22%) participants were 1000 - 2000ml / 24 hours and from 3001 - 3800 ml/24 hours in 7 (5.59%) of the participants. The average 24 hour urine output was 1870± 652.58 .It ranged from 500 to 3800 ml/24 hours and the mode was 1500ml.

Table 4: Distribution of patients by their 24 hours urine output

<table>
<thead>
<tr>
<th>No.</th>
<th>24 hour urine Output (ml)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percentage</td>
<td>Frequency</td>
<td>percentage</td>
</tr>
<tr>
<td>1</td>
<td>500-1000</td>
<td>4</td>
<td>7.69</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>1001-2000</td>
<td>25</td>
<td>48.08</td>
<td>38</td>
</tr>
<tr>
<td>3</td>
<td>2001-3000</td>
<td>22</td>
<td>42.31</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>3001-3800</td>
<td>1</td>
<td>1.92</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>100.00</td>
<td>71</td>
<td>100.00</td>
</tr>
</tbody>
</table>
Figure 2 shows the distribution of participants with their urine creatinine concentration. More than half 70 (56.91 %) of participants had urine creatinine concentration 15-50 mg /dl in females and 28 -100 mg/dl in males. 53 (43.10 %) of participants had Ucr levels from 50- 150 ml/dl in females and 100 -160 mg/dl in males. The mean urine creatinine level was 65.53 ± 27.96 mg/dl. The minimum and maximum Ucr were 15 and 160 mg/dl respectively and its mode was 50 mg/dl.

Table 5 show the distributions of participants by their GFR which was measured with creatinine clearance and estimated with CG, MDRD and CKD- EPI equations.

In 40 (32.52 %) of the participants the GFR measured by creatinine clearance lies between 30 and 59 ml/min and in 15 (12.20 %) participants the GFR were found to be ≥ 90 ml/min and the rest were between these two figures. The mean GFR measured by creatinine clearance was 49.59± 32.40 ml/min / 1.65 m². Median (IQR) were 42.17 (49.2) ml/min. The minimum and maximum mGFR_{Ccr} were 3.79 and 145.29 ml/min respectively. The mean mGFR_{Ccr} was 46.31 ± 30.19 ml / min/1.71m² and 52.00 ±33.93 ml/min/1.61 m² in males and females respectively.
In 44 (35.77 %) of the participants GFR estimated by using CG equation falls between 30 to 59 ml/min and in 22 (17.89 %) participants their GFR were found to be $\geq 90$ ml/min and the rest were between these two figures. The mean GFR estimated by CG was $56.15 \pm 33.68$ ml/min/1.65 m$^2$. The median (IQR) were 53.42 (46.6) ml/min. The minimum and maximum eGFR$_{CG}$ were 1.19 and 144.35 ml/min respectively. The mean eGFR$_{CG}$ was $54.55 \pm 34.51$ ml/min/1.71 m$^2$ and $58.10 \pm 32.57$ ml/min/1.61 m$^2$ in males and females respectively.

In 36 (29.27 %) of the participants the eGFR$_{MDRD}$ were $\geq 90$ ml/min and in 13 (10.57 %) the GFR lies between 15-29 ml/min and the rest were between these two figures. The average GFR estimated by MDRD was $65.53 \pm 52.84$ ml/min/1.65 m$^2$ and the median (IQR) was 49.99 (72.9) ml/min. GFR estimated by MDRD was ranged from 2.06 to 256.96 ml/min. The mean eGFR$_{MDRD}$ was $63.87 \pm 52.19$ ml/min/1.71 m$^2$ and $66.78 \pm 53.66$ ml/min/1.61 m$^2$ in male and female respectively.

45 (36.59 %) of the participants had eGFR$_{CKD-EPI}$ $\geq 90$ ml/min and 9 (7.32 %) had GFR between 15-29 ml/min and the rest were between these two figures. The mean of GFR estimated by CKD-EPI was $80.52 \pm 55.95$ ml/min. The median (IQR) were 68.74 (74.7) ml/min respectively. The minimum and maximum eGFR$_{CKD-EPI}$ were 6.11 and 282.98 ml/min respectively. The mean mGFR$_{CCr}$ was $92.30 \pm 29.81$ ml/min/1.71 m$^2$ and $68.13 \pm 45.40$ ml/min/1.61 m$^2$ in males and females respectively.
Table 5: Distribution of participants by their GFR

<table>
<thead>
<tr>
<th>Methods</th>
<th>Frequency (percentage) of participants at different GFR stage</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15</td>
<td>15-29</td>
</tr>
<tr>
<td>Ccr</td>
<td>23 (18.70)</td>
<td>15 (12.20)</td>
</tr>
<tr>
<td>CG</td>
<td>18 (14.63)</td>
<td>8 (6.50)</td>
</tr>
<tr>
<td>MDRD</td>
<td>23 (18.70)</td>
<td>13 (10.57)</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>15 (12.20)</td>
<td>9 (7.32)</td>
</tr>
</tbody>
</table>

6.3. Comparison of GFR Estimating Equations with Creatinine Clearance

6.3.1. Comparison by using Classification of Participants

As shown in the figure 3 there was substantial variation between creatinine clearance and GFR estimating equations in the classification of participants at different GFR levels. Out of the three GFR estimating equations better classification concordance was observed between CG and Ccr at GFR level ≥30 ml/min. At GFR below 30 ml/min better classification concordance was also demonstrated between MDRD and Ccr. Unlike the two equations relatively high classification discrepancy was observed between CKD-EPI and Ccr. This comparison based on sex was given under figure 4 and 5.
Figure 3: Comparison of eGFR equations with Ccr by their total participants classification
Figure 4: Comparison of eGFR equations with Ccr by their male participants classification

Figure 5: Comparison of eGFR equations with Ccr by their female participants classification
6.3.2. Accuracy of GFR Estimating Equations in the Classification of Participants

Table 6 shows the sensitivity, specificity and accuracy of GFR estimating equations in the classification of participants at different GFR strata as compared with creatinine clearance.

Table 6: Accuracy of the three GFR estimating equations in the classification of participants as compare with creatinine clearance

<table>
<thead>
<tr>
<th>Methods</th>
<th>GFR strata (ml/min)</th>
<th>&lt;15</th>
<th>15-29</th>
<th>30-59</th>
<th>60-89</th>
<th>&gt;90</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>Sensitivity</td>
<td>0.8</td>
<td>0.53</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>1</td>
<td>1</td>
<td>0.96</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>Accuracy</td>
<td>0.96</td>
<td>0.94</td>
<td>0.98</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td>MDRD</td>
<td>Sensitivity</td>
<td>1</td>
<td>0.87</td>
<td>0.78</td>
<td>0.67</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>Accuracy</td>
<td>1</td>
<td>0.98</td>
<td>0.92</td>
<td>0.91</td>
<td>0.83</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>Sensitivity</td>
<td>0.65</td>
<td>0.6</td>
<td>0.73</td>
<td>0.76</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>Accuracy</td>
<td>0.93</td>
<td>0.95</td>
<td>0.91</td>
<td>0.94</td>
<td>0.74</td>
</tr>
</tbody>
</table>

6.3.3. Comparison by using Mean and Median

Table 7 shows comparison of GFR estimating equations with creatinine clearance by using their mean, median and range of GFR. As we can see from the table the mean difference between GFR estimated by the three GFR estimating equations and GFR measured with creatinine clearance was statistically significant. Furthermore, lowest median difference was observed between MDRD and Ccr.
Table 7: Comparison of GFR estimating equations with creatinine clearance by using their mean and median GFR

<table>
<thead>
<tr>
<th>Methods</th>
<th>Mean GFR ± SD (ml/min)</th>
<th>Median GFR (IQR) (ml/min)</th>
<th>GFR range (ml/min)</th>
<th>Mean Difference With 95% CI</th>
<th>Median Difference</th>
<th>mGFR Vs. eGFR p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ccr</td>
<td>49.59±32.4</td>
<td>42.17 (49.2)</td>
<td>3.79-145.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CG</td>
<td>56.15±33.7</td>
<td>53.42 (46.6)</td>
<td>1.19-144.35</td>
<td>6.56 (2.14-10.98)</td>
<td>11.25</td>
<td>0.004</td>
</tr>
<tr>
<td>MDRD</td>
<td>65.53±52.8</td>
<td>49.99 (72.9)</td>
<td>2.06-256.96</td>
<td>15.94 (9.66-22.23)</td>
<td>7.82</td>
<td>0.000</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>80.52±56.0</td>
<td>68.74 (74.7)</td>
<td>6.11-282.98</td>
<td>30.93 (24.29-37.58)</td>
<td>26.57</td>
<td>0.000</td>
</tr>
</tbody>
</table>

As indicated under figure 6 Box and Whisker plot reveals that CG and Ccr are more agreed than MDRD and CKD-EPI. This is characterized by similar variation of GFR measurement as measured by range and IQR. Unlike CG and Ccr the GFR estimated with MDRD and CKD-EPI were more dispersed and accompanied by outliers (dots).

Figure 6: Box and Whisker plot between GFR estimating equations and creatinine clearance
6.3.4. Correlation between GFR Estimating Equation and Creatinine Clearance

The correlations between the three GFR estimating equations with creatinine clearance are shown from figure 7 to 9. As can be seen from these figures strong, positive and statistically significant correlations were observed between the three GFR estimating equations and creatinine clearance.

Figure 7: Correlation between Ccr and CG
Figure 8: Correlation between Ccr and MDRD

Figure 9: Correlation between Ccr and CKD-EPI
6.3.5. Agreement between GFR Estimating Equations and Creatinine Clearance

Table 8 shows limits of agreement between GFR estimating equations and creatinine clearance. Lowest bias and narrow limit of agreement was observed between CG and Ccr.

Table 8: Bias and limits of agreement between GFR estimating equations and creatinine clearance

<table>
<thead>
<tr>
<th>Methods</th>
<th>Bias ± SD</th>
<th>Limits of agreement with 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>6.56 ± 24.79</td>
<td>-43.03 – 48.59</td>
<td>.004</td>
</tr>
<tr>
<td>MDRD</td>
<td>15.94 ± 35.30</td>
<td>-53 - 85.30</td>
<td>.000</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>30.93 ± 37.23</td>
<td>-42.04 - 103.90</td>
<td>.000</td>
</tr>
</tbody>
</table>

Figure 10 to 12 shows the Bland-Altman plots between the three GFR estimating equations and that of creatinine clearance.

Figure 10: Bland–Altman plot between Ccr and CG
Figure 11: Bland–Altman plot between Ccr and MDRD

Figure 12: Bland–Altman plots between Ccr and CKD-EPI
7. Discussion

In the current study GFR was measured by using creatinine clearance which is one of the standard methods used to measure GFR. It is also estimated with Cockcroft – Gault, MDRD and CDK-EPI equations. These are the three novel equations which used to estimate GFR. CG, MDRD and CKD-EPI equations were compared with creatinine clearance by using five parameters. These include: participants classification, range, mean, correlation and Bland-Altman Analysis.

The first parameter used to compare GFR estimating equation (CG, MDRD and CKD-EPI) with standard GFR measurement technique (creatinine clearance) was number of participants classified at different GFR levels. When the current study compared the number of participants classified at different GFR strata with eGFR equation and Ccr substantial variations were observed (table 5 and Figure 3). Even though there was miss classification with GFR estimating equations in comparison with Ccr, better classification concordance between CG and Ccr was observed than the other two equations. For example with both Ccr and CG large number of participants classified having GFR between 30- 59 ml/min; 40 (32.52%), 43 (34.96%) with Ccr and CG respectively. In general with GFR > 30ml/min more accurate classification concordance was observed between CG and creatinine clearance as the number of participants falling under GFR strata 30-59, 60-89 and > 90 than the two equations (table 6).

On the other hand more accurate classification concordance was observed between MDRD and Ccr at lower GFR stages (GFR < 30 ml/min) than the other two GFR estimating equations. That means in GFR strata <15 and 15-29 ml/min the number of participants classified with MDRD was more similar with that of Ccr than CG and CKD-EPI equations. For instance, with both Ccr and MDRD the number of participants classified GFR having < 15ml/min which is interpreted as end stage renal failure was 23 (18.67 %) (table 5). Similar findings has been reported by Baptista et al. where GG was more accurate than MDRD in the identification of augmented renal clearance (8). The findings of the present study is also consistence with reports of Fauci & Jemson where MDRD equation has poorer accuracy when GFR > 60 ml/min per 1.73 m² (3).

In the current study classification concordance between CKD-EPI and Ccr was poor as compared with CG and MDRD in both lower and higher GFR levels. In line with the present
study, CKD misclassification with GFR estimating equations in comparison with standard GFR measurement techniques have been reported by Eastwood et al. and Liu et al. from Ghana and China respectively (19, 25).

In the current study the mean of GFR measured with creatinine clearance was 49.59 ± 32.4 ml/min/1.65 m$^2$. Whereas, the mean of estimated GFR with CG, MDRD and CKD-EPI were 56.15 ± 33.7, 65.53 ± 52.8 and 80.52 ± 56.0 ml/min/1.65 m$^2$ respectively. As it can be noticed easily, all estimated GFR were higher than that of GFR measured with Creatinine clearance. This indicates that GFR estimating equations overestimate GFR at clinical or research setting. The mean difference between GFR estimating equations and Ccr with 95 CI were 6.56 (2.14-10.98), 15.94 (9.66-22.23) and 30.93 (24.29-37.58) ml/min with CG, MDRD and CKD-EPI respectively (p-value <0.05 for all) (table 7).

In line with reports of Baptista et al. (8) in the current study the lowest mean difference was observed between CG and Ccr and the highest between CKD-EPI. This might suggest that CG outperforms the other two GFR estimating equations. However, all mean differences were significant. In addition to this CG is more precise than the two estimates. The narrower the confidence interval of mean difference, the more precise the estimate is (32).

As indicated under figure 6 Box and Whisker plot reveals that CG and Ccr are more agreed than MDRD and CKD-EPI. This is characterized by similar variation of measurement as measured by range and IQR. The ranges of participants’ GFR were from 3.79 - 145.29, 1.19 - 144.35, 2.06 - 256.96 and 6.11 - 282.98 ml/min with Ccr, CG, MDRD and CKD-EPI respectively (table 7). Unlike MDRD and CKD-EPI the range of estimated GFR with Cockcroft-Gault equation was roughly the same with that of creatinine clearance. Furthermore, the widest range was observed with that of CKD-EPI. This might suggest that CG provided better GFR estimation than the other two equations. Unlike CG and Ccr the GFR estimated with MDRD and CKD-EPI were more dispersed which is accompanied by outliers (figure 6). Outliers are represented by dots which are greater than third quartile (Q3) from 1.5 times IQR to 3 times IQR (36, 37). However, the lowest median difference was observed between MDRD and creatinine clearance. This might suggest the presence of agreement in some extent between MDRD and Ccr.
The finding of current study was comparable with that of results obtained from study conducted by Franka et al. in Switzerland where mean and median difference between CG and MDRD with inulin clearance was significant and the lowest mean difference was observed with CG (9). But the mean difference of current study disagreed with that of reports of Liu et al. where the lowest mean difference was observed with CKD-EPI (25). The probable reseason for this difference could be related to race of participants and their older age in China.

Over estimation of these GFR estimating equations as evidenced by higher mean and wide GFR range and other finding of the current study have been also reported from a community based study conducted in Ghana by Eastwood et al. A mean GFR obtained from this study were 84.1± 22.6, 74.7± 18.6, 102.3± 22.8, and 103.1± 18.7 ml/min/1.73m² with creatinine clearance, CG, MDRD and CKD- EPI respectively (19). This is consistent with the present study where GFR estimated by MDRD and CKD-EPI in both studies were found to be higher than that of creatinine clearance. Furthermore, lowest mean difference was observed between Cockcroft – Gault and creatinine clearance.

Study conducted on 69 hospitalized CKD Caucasian patients by Franka et al. in Switzerland to compare GFR estimating equations with GFR measured using inulin clearance has consistency with current study. The mean GFR obtained from this study were 34.9 ± 20.0, 46.7 ± 18.5, and 49.0 ± 15.9 ml/min using inulin clearance, CG and MDRD respectively (9). As shown from the data in both study over estimation of GFR with GFR estimating equations was observed. Comparison of GFR estimating equations with that of creatinine clearance was also done by Bouchard et al. in New Zealand (35). In this study, the mean GFR was reported as 15.4, 21.4, 17.3 ml /min with creatinine clearance, Cockcroft- Gault and MDRD respectively. These findings were similar with findings of current study where in both studies the mean GFR estimated by CG and MDRD were higher than that of creatinine clearance. It should however be noted that the mean GFR in the present study was lower than that of reports of Eastwood et al (19) and higher than that of Franka et al. and Bouchard et al (9,19,35). This could be due to difference in participants selection. A study done in Ashanti, Ghana by Eastwood et al. was a community based study which involves healthy individuals and that Franka et al. and Bouchard et al. involves CKD and critically ill kidney patients. Whereas, the present study involves all
type of kidney patients who were under treatment and follow up. Like the findings of current study, overestimation of GFR estimating equations were also reported from studies was conducted in South Africa, India and Korea by Madala et al. Bailey et al. and Chung et al. respectively (18, 27, 28).

The fourth parameter used in the present study to compare GFR estimating equations with Ccr was correlation. In the current study strong, positive and statistically significant correlation were observed between GFR estimating equations and creatinine clearance. The Pearson’s correlation coefficients \( r \) were 0.719 for Ccr vs. CG, 0.760 for Ccr vs. MDRD and 0.771 Ccr vs. CKD-EPI (Figure 7-9). The corresponding \( r \) values were 0.778, 0.818 and 0.824 in men and, 0.701, 0.726 and 0.746 in women (\( p < 0.05 \) for all). This finding is in line with that of other studies where similar correlations were reported between creatinine clearance and Cockcroft–Gault and MDRD (9, 27). The findings of current study are slightly different from the reports of Baptista et al. where the linear relation between Ccr and CG were significant and weak but it is weak and insignificant with MDRD (8). This could be due to higher GFR in Baptista et al. because MDRD is less accurate at higher GFR (3).

In addition to using participants classification, mean, range and correlation to compare GFR estimating equations with creatinine clearance, Bland-Altman analysis was also carried out in the current study to check whether there was measurement agreement exist between them or not. As shown from Bland–Altman plots (figure 10 -12), CG, MDRD and CKD-EPI equations had strong measurement agreement with that of Ccr at lower GFR and it become weaker at higher GFR stages. This is agreed with the results study conducted by Madala et al. in Durban, South Africa (27). The current finding is slightly different from reports of Eastwood et al. (19) where the agreement was better at the middle of GFR stage and it was poor at the higher and lower GFR.

Limit of agreement was from -43.03 – 48.59, -53 - 85.30 and -42.04 - 103.90 with CG, MDRD and CKD-EPI vs. Ccr respectively (table 8). The Lowest bias with CG which is closer to zero suggests that CG and Ccr measure similar results than the other two methods. In other words CG provides better GFR estimation than MDRD and CKD-EPI. CG was also more precise as indicated by narrow limit of agreement and lowest SD (28, 30). Even though Altman-Bland plot showed good agreement between the three eGFR equations and Ccr, the agreement between CG
and Ccr was better than MDRD and CKD-EPI as we have seen the evidence earlier. This finding is agreed with of reports Eastwood et al. and Madala et al. (19, 27)

Generally comparison between eGFR equations and Ccr by using different comparison parameters in the current study showed that the estimating performance of CG was better than the other two GFR estimating equations. This finding is consistent with reports of Franka et al., Eastwood et .and Liu et al. (9, 19, 25). On the contrary study was conducted by Bailey et al. in India, Chung et al. in Korea and Levey et al.USA have been reported that MDRD and CKD-EPI provides better GFR estimation (18, 24, 28).The current study also find out that MDRD next to CG and at lower GFR estimate GFR better than the other two GFR estimating equations. The probable reason for this difference could be related to participants selection and their difference in race. In relation to this effectiveness of CG and MDRD to estimate GFR in the European and American population respectively has been previously reported (19).

The CG and MDRD equations are the recommended methods for estimating GFR in the South African CKD early detection and management guidelines (27).This is in line with findings of present study. A review done by Salgado et al. in Brazil has been reported that Cockcroft-Gault and MDRD are widely used in clinical practice for adults (14).Similar findings also reported by Baptista et al. (8). This is consistent with current findings which indicate their better GFR estimating performance over CKD-EPI and might suggests them for clinical application in local community.
8. Conclusion

Out of the three GFR estimating equations more accurate participants classification concordance was observed between CG and Ccr at GFR level ≥30 ml/min and with MDRD at GFR <30 ml/min. Unlike the two equations relatively high classification discrepancy was observed between CKD-EPI and Ccr. Box and Whisker plot reveals that CG and Ccr are more agreed than MDRD and CKD-EPI. GFR estimating equations significantly overestimate GFR as compared with creatinine clearance. Strong, positive and significant correlations were observed between CG, MDRD and CKD-EPI and creatinine clearance. On top of these, all the three GFR estimating equations had strong measurement agreement with that of Ccr at lower GFR and it become weaker at higher GFR levels. Furthermore, the agreement between CG and Ccr was more precise.

Generally, overall comparison of the three GFR estimating equations with creatinine clearance showed that CG estimate GFR better than MDRD and CKD-EPI equations. Furthermore, better GFR estimation with MDRD was observed next to CG. In the current study significant correlation and good measurement agreement were observed between Ccr and CKD-EPI. However, it is less effective to estimate GFR as compared with CG and MDRD.
9. Limitation of the Study

The following were limitations of the study.

1. Serum creatinine was not determined in the same laboratory.

2. The study doesn’t involve healthy individuals and the sample size was small to generalize the finding to the Ethiopian population.

3. Since the study was cross sectional, it could not identify those patients with CKD.
10. Recommendation

Based on the findings of the present study the following recommendations were given:

1. Extensive community based study in the future is required to establish baseline GFR and to compare different GFR estimating equations with standard GFR measurement techniques.
2. Further study is also essential to either strengthen or modify the findings of current study.
11. References


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Annexes

Annex I

English Version of Consent Form

Addis Ababa University
College of Health Science
Post Graduate Studies
School of medicine
Department of physiology

Informed consent form prepared to compare GFR estimating equation with creatinine clearance among patients who visit renal unit of TASH.

Part I: Information about the Study

My name is Kassa Setegn Addisu; currently I am a graduate student at the department of physiology, College of health science, Addis Ababa University. I am conducting a study entitled “Comparison of GFR Estimating Equations with Creatinine Clearance among Patients who Visit Renal of TASH”. If you participate in the study, you will know your GFR level and kidneys status. Furthermore, the result of these researches is important to identify the most applicable GFR estimating equation. The information which obtained from the study will also contribute for the betterment of kidney treatment which is given in TASH as well as in Ethiopia at large. I kindly request you to participate in this study by providing response for all the following questions and giving ordered blood and urine sample. If you are voluntary to participate in the study, 5 ml of blood and 24 hour collected urine will be taken from you. The information you gave will be use only for research purpose. Your participation in this study is completely on voluntary bases and you have a right to refuse or interrupt the participation at any time. You will not loss any treatments because of you aren’t participating in the study. But your genuine participation is very important for the outcome of the research and all information you give are kept confidentially. If you need clarification you can ask questions. I would like appreciate your participation.
Part II consent

Are you volunteer to participate in the study  1. Yes——  2. No——

In signing this document, I am giving my informed consent to participate in the study entitled “Comparison of GFR Estimating Equations with Creatinine Clearance among Patients who Visit Renal Unit of TASH”. I have been informed that the purpose of this research project and I understand that I am selected to participate in this study randomly. I have been informed that my participation in this study is willing full and voluntary even. I have right to refuse or interrupt from participating in the study any time and my name will not be mentioned on the questionnaire. I undersigned, have understood the purpose of the study & fully agreed to participate in the study.

Participant’s
Name ____________________ Signature __________ Date __________

Data Collector’s
Name ____________________ Signature _____________ Date ________

Supervisor’s
Name ______________________ Signature _____________ Date _____
Annex II

English Version of Questionnaire

Addis Ababa University
College of Health Science
Post Graduate Studies
School of Medicine
Department of physiology

This questionnaire is designed to compare GFR estimating equations (CG, MDRD and CKD-EPI) with creatinine clearance among patients who visit renal unit of TASH. If you participate in the study, you will know your GFR level and kidneys status. Furthermore, the result of these researches is important to identify the most applicable GFR estimating equation. The information which obtained from the study will also contribute for the betterment of kidney treatment which is given in TASH as well as in Ethiopia at large. I kindly request you to participate in this study by providing response for all the following questions and giving ordered blood and urine sample. If you are voluntary to participate in the study, 5 ml of blood and 24 hour collected urine will be taken from you. The information you give will be use only for research purpose. Your participation in this study is completely on voluntary bases and you have a right to refuse, or to interrupt the participation at any time. You will not loss any treatments because of you aren’t participating in the study. But your genuine participation is very important to the outcome of the research and all information you give are kept confidentially. If you need clarification you can ask questions. I would like appreciate your participation.

Are you volunteer to participate in the study? 1. Yes, thank you: ________, No. Never mind, don’t worry ________

Note for Data Collector:
If the answer of participant’s is yes, you have to thank the participant and conduct the interview. If the answer is no, leave the participants kindly and proceeded to the next respondent.

Data Collector’s

Name ______________ Signature __________ Date __________

Supervisor’s

Name __________________________ Signature __________ Date __________

Instruction:
Please indicate the response of the participant by putting “✓” in the space provided.

Patient’s Card Number: ______________

Part: I Socio-demographic data of participants

1.1 Sex: Male _______ Female_______

1.2 Age (in year)_________

1.3 Ethnicity:

1. Amhara — 3. Oromo —
2. Tigre — 4. Other, specify ______________


4. Catholic — 5. Other, please specify ______________

1.4 Marital status:


1.6 Educational level:

1. Illiterate — 4. Secondary School —
2. Can read and write — 5. Higher Education —
3. Primary School —

1.7 Occupation: Please specify ______________

1.8 Monthly income
1. ≤800 Birr ——— 4. 2401 – 3200 ———
2.801–600 Birr ——— 5. ≥3201 ———
3.601 – 2400 ———

1.9 Weight (kg) ———— 1.10 Height (cm) ————

Part II: Laboratory Test

2.1 Laboratory Order 1: Serum creatine concentration: ————

2.2 Laboratory Order 1 result: : ————

2.3 Laboratory Order 2: Urine creatine concentration: ————

2.4 Laboratory Order 2 result: ————

2.5 24 hours collected urine volume: ————
Annex III

እንደ santa ፈልጭ የልካ ነዎች

እውቅ ገዳጋ እስላት ሁኔታ ከኔ ከመኖሩ ያለቸው የሚያድርጉ

አስፈላጊ ያለው እኔ ያላልች ያለባቸው ከሆናቸው ያለን ያስፈራ ከሚያጠቂ የመልስ ያለባቸው ታምህርት ከሆናቸው ሙስ ከላይ በባካሬ ያላች ያለባቸው ያላልች ያለባቸው ከእስራት ከሆናቸው ያለን ያስፈራ ከሚያጠቂ ያለባቸው ታምህርት ከሆናቸው ያለን

ከስ ይ የምት ምክንያት

እግወ ከሳ ያለን ምክንያት እንዳ ያላልች ያለባቸው ያላልች ያለባቸው ከሚያጠቂ ያለባቸው ከሆናቸው ያለን ያስፈራ ከሚያጠቂ ያለባቸው ያለባቸው ከእስራት ከሆናቸው ያለን ያስፈራ ከሚያጠቂ ያለባቸው ታምህርት ከሆናቸው ያለን

1. እም በአሰራች ያለባቸው
2. ከተጨማሪ ያለባቸው ያለባቸው ከሆናቸው ያለን ከሚያጠቂ ያለባቸው ታምህርት ከሆናቸው ያለን

ስሮ ለማሇት ያለባቸው ጊዜ ከሚያጠቂ ያለባቸው ያለባቸው ከሆናቸው ያለን ያስፈራ ከሚያጠቂ ያለባቸው ታምህርት ከሆናቸው ያለን

1. እም በአሰራች ያለባቸው ያለባቸው ከሆናቸው ያለን ከሚያጠቂ ያለባቸው ታምህርት ከሆናቸው ያለን

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Annex IV

የአማርኛ ይህን ተስጥዎቹ እና ይህን ተስጥዎቹ ይህን ተስጥዎቹ እና

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የህመምተኛው አርዲ

1. የተሳታፉዎች በአጠቃሊይ መረጃ

1.1 ወንድ: ወንድ: ______ ለ_____

1.2 እድሜ (በአመት) ___________

1.3 ይርር:

1. እኔዛ — 3. እርም —
2. ለንወ — 4.ለ: እስከናት ይቻች

1.4 ይግ.ም: 1.እርጆች— 2. እለአመሥ — 3.የ ለመሆኔ —
4. እወለት — 5. ለ: እስከናት ይቻች

1.5 ይርክ መንጋት:

1. ይሆነ/ት — 3. ይሆነ / ቷ —
2. ይታት ሆ — 4. ይሚው ሆ/ት —

1.6 ይግ.ማርት ይርች:

1. ይሆነ/ት /ት — 3. ይሆነ ይርች ይሆነርてる
2. ይፋን ይቀድ ይሚገኝ ይሚገኝ ይሚገኝ — 4. ይሆነት ይሆነርてる

3.የ ለመሆኔ ይሆነርてる

1.7 እር: እስከናት ይቻች

1.8 ይርን ይህ,

1. ለ800 እር — 4. 2401 — 3200 እር —
2. 801 — 1600 እር — 5. ለ3201 እር —
3. 1601 — 2400 እር —

1.9 ይወለት (ገ.ት) ——— 1.10 ይወለት (ለ.ም) ———

የ ለመሆኔ ይርመራ

2. 1 ይወለት ይርመራ ከም ይህ: ለም ለመሆኔ ይወለት ይቻች መንቷት:
2.2 ይወለት ይርመራ ከመልት:

2.3 ይወለት ይርመራ ከም ይህ: ለም ለመሆኔ ይወለት ይቻች መንቷት:
2.4 ይወለት ይርመራ ከመልት:

2.5 እስት ይወለት መንቷት: