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clearance has therefore been the widely accepted technique for determination of GFR in clinical practice.

Determination of creatinine clearance presents several problems. The inconvenience and unreliability of 24-h urine collections (particularly in ambulatory subjects and out-patients) have led to the development of techniques which involve collection of urine for much shorter periods. However, difficulties persist with respect to accurate collection and measurement of urine volume, as well as precise timing of the period of collection. Because of those difficulties, and because plasma creatinine is known to correlate positively with the GFR, several authors had attempted to derive formulae for predicting creatinine clearance from the serum creatinine and other variables (including age, height and body weight) which are known or thought to affect the creatinine clearance (Edward & Whyte, 1969; Jelliffee, 1971; Jelliffee, 1973; Cockroft & Gault, 1976). In the present study, the usefulness of some of these formulae and those which were derived from data on serum creatinine, age, height and weight of Nigerian subjects is assessed.

Materials and methods

Four groups of subjects were studied. Group 1 consisted of patients who were admitted to the University College Hospital, Ibadan, for renal diseases and hypertension. Group 2 subjects were admitted for other diseases which were not renal or hypertensive. Group 3 subjects were healthy medical students. Group 4 subjects consisted of those on whom creatinine clearance test was performed as one of their routine biochemical tests during the period of this study which was from 1978–81.

Twenty-four-hour urine samples were collected from the subjects. Blood samples were also collected at suitable periods during the test. The height, weight and age, and blood pressure of each subject were recorded. The volumes of urine samples were measured. The serum and urine creatinine levels were estimated by Jaffes reaction as described by Bonsnes and Taussky (1945). The precision of the method was assessed by determining the level of creatinine in five samples of blood with values within the range 1.5–13.4 ml/100 ml in many replications. The accuracy of the test was determined by the use of a commercial quality control serum. Values which were outside the 10% limit of the target value were rejected and the test was repeated.

Statistical analysis

The association between creatinine clearance (Ccr) and each of the variables, serum creatinine (Scr), weight (Wt), height (Ht) and age (Age) was investigated. Preliminary investigations indicated that the inverse of serum creatinine, i.e. 1/Scr could be important. A new variable, InvScr (= 1/Scr) was therefore defined. Because a logarithmic relation might be better than a linear relationship between creatinine clearance and the other variables, another variable was also defined as LogCcr = e^{Scr}. A correlation matrix of these seven variables is shown in Table 1. There are strong correlations between Ccr and InvScr and between LogCcr and Scr. The correlation coefficients of 0.52 and −0.65 respectively, are statistically significant at the 0.01 level.

TABLE 1. Correlation matrix for creatinine clearance and other variables

	Ccr	LogCcr	Scr	InvScr	Wt	Ht	Age
Creatinine clearance (Ccr)	1.00	0.78	−0.27	0.52	0.16	0.13	0.18
Natural logarithm of creatinine clearance (LogCcr)		1.00	−0.65	0.44	0.14	0.15	−0.33
Serum creatinine (Scr)			1.00	−0.43	−0.03	−0.20	0.13
Inverse of serum creatinine (InvScr)				1.00	−0.00	−0.21	0.03
Weight (Wt)					1.00	0.06	−0.03
Height (Ht)						1.00	−0.03
Age (Age)							1.00

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SERUM CREATININE AND PREDICTION FORMULAE FOR CREATININE CLEARANCE

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Summary

Three formulae which could predict creatinine clearance from serum creatinine values were derived from the data which were obtained from the study of 169 patients and healthy control subjects. Values for creatinine clearance which were obtained by using these three formulae and four other previous formulae were compared with the observed values. Most of the predicted and observed values differed by more than 20% of the observed values. When a formula which was derived by using the data from forty-five healthy control subjects was used to predict the creatinine clearance values of this group and the patients, there was a close agreement between the observed and the predicted values for only the healthy control subjects but not the patients. Because of the various factors which affect creatinine excretion in health and disease, a predictive formula which includes serum creatinine alone and not urinary creatinine might give unreliable values.

Résumé

Trois formules qui pouvaient prédicter le taux du relèvement de la créatinine à partir du sérum de la créatinine, étaient dérivées des résultats d'une étude des 169 malades et les sujets en bonne santé. Les résultats obtenus pour le taux du relèvement de la créatinine en appliquant ces trois formules et quatre formules prévues étaient appliquées aux résultats observés. Plupart de résultats prédictés et observés étaient différents plus de 20% de résultats observés. Lorsque la formule de derivée avec quarante-cinq sujets en bonne santé était utilisée à predicter le taux du relèvement de la créatinine de cette group et des malades, il y avait une relation forte entre les résultats observés et prédictés seulement parmi les sujets en bonne santé mais pas pour les malades. Parce qu'il y a beaucoup de choses qui determinent l'elimination de la créatinine en bonne santé et en maladie, une formule qui contient seulement la créatinine urinaire n'est pas assez bien.

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Introduction

In clinical practice, measurement of the glomerular filtration rate (GFR) is used to assess glomerular function in patients thought or known to have nephro-urological disorders. The required doses of some drugs depend on glomerular function, and the use of such drugs would also necessitate the determination of the GFR.

Inulin and ^{51}Cr-EDTA clearance give more accurate assessment of GFR than does the creatinine clearance. This is because urinary creatinine comprises not only that filtered at the glomeruli but also creatinine secreted by the renal tubules. However, determination of inulin and ^{51}Cr-EDTA clearance involves techniques which are more complex than those for creatinine clearance, and which are not widely available for routine use. Creatinine

TABLE 4. Precision of the determination of serum creatinine

Sample	Mean	Standard deviation	CV(%)	n*
1	1.52	0.16	10.5	12
2	1.52	0.17	11.2	10
3	1.77	0.16	9.0	12
4	5.81	0.26	4.4	8
5	13.42	0.79	2.1	8

*Number of tests.

were coefficients of variation for serum creatinine and urinary creatinine respectively. If it is assumed that the error in estimating serum creatinine is not greater than that of urinary creatinine, then the coefficient of variation for creatinine clearance would be about 15%. In awarding a score for acceptability of the predictive value, this percentage was increased to 20% so as to allow for errors which might not be due to the analytical technique but to inaccuracies in collection and measurement of the urine. The table of scores for the predicted values which were within 20% of the observed values are shown in Table 5. None of the formulae gave a score of more than 48% for any particular group of subjects. The means of the observed and predicted values for the patients with and without renal and hypertensive diseases were not significantly different when most of the formulae were used but the predicted and observed values for the medical students (Group 3) and those for other patients (Group 4) were markedly different when all the formulae were used (see Table 6).

Discussion

Three formulae have been derived from the data which were obtained from the study of four groups of subjects. These subjects were patients with or without renal and hypertensive diseases and healthy controls. Serum creatinine was the only variable in the first formula, while height, weight and age were included as variables in the other two formulae. Although these formulae were based on the observed high correlations between the inverse of the serum creatinine and creatinine clearance, the accuracy of these formulae and those of the other workers in predicting creatinine clearance was found to be poor. Most of the individual predicted values and the observed values were not within the acceptable limit. Similarly, when the mean of the observed and predicted values were compared some of them were found to be close while the others were not.

The conclusion that creatinine clearance cannot be accurately estimated from serum creatinine alone has been supported by other reports (Tobias, McLaugwin & Hopper, 1962; Doolan, Alpen & Theil, 1962). The use of prediction formulae for estimation of creatinine clearance is known to have certain pitfalls. One of them is the fact that the same serum creatinine level could be associated

TABLE 5. Percentage score for each formula when used to predict the creatinine clearance for four groups of subjects

Formula	Group 1* (n = 46)	Group 2† (n = 19)	Group 3‡ (n = 45)	Group 4§ (n = 59)
F_1:	39	10	0	20
F_2:	13	40	32	3
F_3:	18	25	48	3
F_4:	28	20	0	14
F_5:	26	35	7	8
F_6:	28	30	11	7
F_7:	31	30	7	5

*Patients with renal diseases and hypertension.
†Patients without renal diseases and hypertension.
‡Medical students.
§Subjects on whom creatinine clearance test was performed as one of their routine biochemical tests.

A score was awarded for each predicted value which was ± 20% of the observed value.

$F_1 - F_7$: see Table 2.

Therefore, the following regressions were investigated:

(1) Log Ccr = C1 + C2 Scr, i.e. $Ccr = e^{C1} \times e^{C2 \times Scr}$;

(2) Ccr = C1 + C2 InvScr + C3 Ht + C4 Wt;

(3) Ccr = C1 + C2 InvScr + C3 Ht + C4 Wt + C5 Age,

where C1, C2, C3, C4 and C5 are constants.

The already published formulae (Table 2) were applied to data on all the subjects to predict their creatinine clearance values. Also the three formulae which were obtained from the present study were applied to these data. Any of the predicted values for creatinine clearance which were within 20% of the observed value was awarded a score. The percentage of the total score for each group of subjects for each formula was calculated.

Results

From the regression parameters of the equations above, these formulae were obtained:

F_1: $Ccr = e^{4.69} \times e^{(-0.26 \times Scr)}$;

F_2: Ccr = −228.71 + 93.33 InvScr + 1.35 Ht + 0.14 Wt;

F_3: Ccr = −200.85 + 94.16 InvScr + 1.33 Ht + 0.14 Wt −0.75 Age.

These formulae are shown in Table 2. The analysis of variance for these formulae is also shown in Table 3.

The values for the coefficient of variations of each level of serum creatinine are shown in Table 4. The values ranged from 4.4% when the serum creatinine was markedly abnormal to 11.2% when it was within normal limits. The coefficient of variation for creatinine clearance was calculated from the equation: $\sqrt{([CVa]^2 + [CVb]^2)}$ where CVa and CVb

TABLE 2. Formulae suggested for predicting creatinine clearance, Ccr (ml/min per 1.73 m²)

Formulae	Reference
$F_1: Ccr = e^{4.46} \times e^{-0.26\ Scr}$	Present study
$F_2: Ccr = -228.71 + \frac{93.33}{Scr} + 0.14\ Wt + 1.35\ Ht$	Present study
$F_3: Ccr = -200.85 + \frac{94.16}{Scr} + 0.14\ Wt + 1.33\ Ht - 0.75\ Age$	Present study
$F_4: Ccr = \frac{100}{Scr} - 12$	Jelliffee (1971)
$F_5: Ccr = \frac{94.3}{Scr} - 1.8$	Edward & Whyte (1959)
$F_6: Ccr = \frac{(140 - Age)\ (Wt.\ kg)}{72\ Scr}$	Cockroft & Gault (1976)
$F_7: Ccr = 98 - 16\ \frac{(Age - 20)}{20} \Big/ Scr$	Jelliffee (1973)

TABLE 3. Analysis of variance

Formula	Degree of freedom	Sum of squares	Mean sum of squares	*F* ratio*
F_1: Regression	1	26.14	26.14	70.62
Residual	96	35.53	0.37	
F_2: Regression	3	120096.98	40032.31	17.04
Residual	94	220776.87	2348.69	
F_3: Regression	4	132942.46	33235.62	14.87
Residual	93	207931.35	2235.82	

*Indicate variance ratio. All the F ratios are significant at the 0.01 level.

with different creatinine clearance values as illustrated in Table 7. This finding is in agreement with that of Camara *et al.* (1951). It has also been observed that a number of factors could affect creatinine output. It was reported that creatinine production and excretion was sometimes suppressed (Goldman, 1954; Goldman & Moss, 1959) and that this could be due to tissue wasting, such as occurs in renal failure, cancer and liver diseases. from the data from a group of healthy medical students. This formula was found to give better predictive values for creatinine clearance for this group than when the other formulae were used. However, when this formula, which was assumed to be good for healthy subjects was applied to the patients' group, it was found to give a wide margin of errors between the observed and the predicted values.

It would appear therefore that because of

TABLE 7. Data on fifteen subjects with the same level of serum creatinine (Scr) and predicted creatinine clearance (Ccr) of 61 ml/min/1.73 m² using the formula ($Ccr = e^{4.46} \times e^{-0.26}$ Scr ml/min/1.73 m²)

Name	Age (years)	Height (m)	Weight (kg)	Serum creatinine (mg/100 ml)	Observed creatinine clearance (ml/min per 1.73 m²)	
L.A.	35	1.78	54.0	1.2	69	
O.O	50	1.71	58.0	1.2	48	
A.O.	48	1.68	53.0	1.2	61	
K.O.	35	1.65	52.2	1.2	108	
A.A.	18	1.52	53.1	1.2	70	Groups 1, 2 and 4
B.O.	60	1.65	48.0	1.2	47	
M.A.	60	1.76	55.2	1.2	61	
A.S.	42	1.63	59.1	1.2	79	
A.C.	34	1.69	56.2	1.2	20	
O.N.	24	1.72	62.2	1.2	136	
C.C.	22	1.68	52.5	1.2	104	
A.N.	26	1.60	58.0	1.2	104	Group 3
A.T.	22	1.80	70.4	1.2	127	
M.C.	28	1.75	69.2	1.2	124	
R.K.	26	1.70	63.0	1.2	141	

Key as for Table 5.

Recent studies among Nigerian subjects have also shown that creatinine excretion was affected by dietary habits. The urinary creatinine level of medical students was found to be significantly higher than those of subjects from a rural community (G. Oladunni Taylor, unpubl. data). This difference in creatinine excretion could be due to differences in the quality and quantity of protein intake. Licata (1981) has also shown that the amount of protein intake affects creatinine clearance level. He observed that by increasing the protein intake from 4.8 to 15.3 g N/day there was a significant increase in creatinine clearance level from 87.7 to 103 ± 9 ml/min.

It would appear that these prediction formulae could be useful if they were derived from, and applied to data from a homogeneous group of subjects. This is illustrated by the data in Table 8. The formula (F_8) was derived the various factors which affect creatinine excretion in health and disease the use of prediction formulae for creatinine clearance which excludes the use of the urinary creatinine value will only provide inaccurate and unreliable values. It would seem that there is no reliable alternative to the usual determination of creatinine clearance from the estimated values of serum and urinary creatinine.

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TABLE 6. A comparison of mean (± s.d.) observed and predicted creatinine clearance values using different formulae

Groups	Age (years)	Height (m)	Weight (kg)	Creatinine clearance ± s.d. (ml/min per 1.73 m²)							
				Observed value	(F_1)	(F_2)	(F_3)	(F_4)	(F_5)	(F_6)	(F_7)
Group 1* (n = 46)	44.5 ± 16.3	1.73 ± 0.08	60.0 ± 11.2	50 ± 17	54 ± 17	85 ± 37	65 ± 27	70 ± 37	67 ± 36	60 ± 31	61 ± 32
Group 2† (n = 19)	28.5 ± 14.8	1.72 ± 0.09	52.4 ± 11.3	103 ± 41	65 ± 5	120 ± 37	111 ± 22	103 ± 44	106 ± 41	105 ± 34	107 ± 46
Group 3‡ (n = 45)	25.2 ± 2.3	1.74 ± 0.06	64.8 ± 7.3	117 ± 23	60 ± 2	93 ± 18	97 ± 13	68 ± 8	74 ± 9	83 ± 12	76 ± 9
Group 4§ (n = 59)	28.4 ± 17.0	1.72 ± 0.05	44.9 ± 22.2	36 ± 26	51 ± 23	89 ± 38	77 ± 31	73 ± 53	72 ± 54	57 ± 31	64 ± 37

Key as for Table 5.

TABLE 8. Observed and predicted values of creatinine clearance (Ccr) for Groups 1 and 3 subjects, using the formula (F_8) which was derived by using only the data of Group 3 subjects and (F_4)–(F_7)

Formulae	Creatinine clearance (mean ± s.d.) (ml/min per 1.73 m²)	
	Group 1 (n = 46)	Group 3 (n = 45)
F_4:	70 ± 37	68 ± 8
F_5:	67 ± 36	74 ± 9
F_6:	60 ± 31	83 ± 12
F_7:	61 ± 32	76 ± 9
F_8:	99 ± 40	119 ± 10
Observed value	50 ± 31	117 ± 23

Formula F_8: $Ccr = 221.4e^{-0.49\ Scr}$
Key as for Table 5.

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