Using the Abbreviated Version of Modification of Diet in Renal Disease Formula as A Primary Estimate for the Prevalence of Undiagnosed Chronic Kidney Disease in Patients with Acute Stroke

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Abstract

Introduction: The association between acute stroke and renal function is well known. The aim of this study is to know which group of patients with acute stroke is more likely to have undiagnosed Chronic Kidney Disease and which risk factors are more likely to be associated with.

Methods: We studied 77 patients who were diagnosed to have an acute stroke.Patients were selected between April2011andJune 2011 using the " 4-variable Modification of

Diet in Renal Disease Formula " which estimates Glomerular Filtration Rate using four variables :serum creatinine ,age ,race and gender.

Results : The study included 38 male and 39 females patients ,aged (35-95) years. Glomerular Filtration Rate in patients with acute stroke was calculated and showed 37.6% , 28.5% , 25.6% , 6.4% and 2.5% (Chronic Kidney Disease stage 0, 1,2,3,4,5 respectively.)

Conclusion : One Third of patients with acute stroke had Glomerular Filtration Rate less than 60ml/min per 1.73m² patients who had more than 2 risk factors of Chronic Kidney Disease are about 3 times more likely to have Glomerular Filtration Rate less than 60 ml/min per 1.73m² to those with 2 or less risk factors .

Key words : Formula ,Chronic Kidney Disease ,Acute Stroke

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Introduction

Cerebrovascular diseases include some of the most common and devastating disorders: ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysms and arteriovenous malformations (AVMs)[(1)]. Focal ischemia or infarction, on the other hand, is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart[(2)]. Intracranial hemorrhage is caused by bleeding directly into or around the brain[(3)]; it produces neurologic symptoms by producing a mass effect on neural structures, from the toxic effects of blood itself, or by increasing intracranial pressure [(4)].

Chronic kidney disease (CKD) is a worldwide public health problemwith an estimated prevalence of 11% of adults in the UnitedStates and higher prevalence among patients with cardiovasculardisease[(5)]. Renal dysfunction, even to a subtle degree, has been noted tobe a prognostic indicator of overall mortality in the presenceof co morbidities such as diabetes[(6).] Also renal function has provedto be prognostic in many patients groups, so subtle renal impairmentappears to be a marker of increased risk ofCerebrovascular disease in both normotensive and hypertensive subjects[(7)].

An association between renal function and stroke has previouslybeen noted in a study designed to assess the relationship betweenhypertension and fatality rates and its determinants in blackpatients with recent stroke, survivors of acute stroke had lowerplasma urea on admission than those who died[(6)].

Aim of the Study

To know which group of patients with acute stroke are more likely to have undiagnosed CKD & which risk factors are more likely to be associated with.

Methods

Seventy seven patients [38 male, 39 female] , diagnosed to have an acute stroke had been included in this cross-sectional study. Patients were selected betweenApril 2011 and June 2011, they were taken from four major teaching hospitals in Baghdad (**Table 1) .**Age of patients in this study ranged from 35 to 95 years (**Table 2**) . The mean age ± standard deviationfor them was (65.7±12.67) year.

Table (1) :The four major teaching hospital from which patients had been included .

Name of the hospital	No. of patients
Medical City/Baghdad Teaching Hospital [neurology & general medical wards]	65 patients
Alkhadimiyia Teaching Hospital [neurology & general medical wards]	5 patients
Alkindi Teaching Hospital [general medical wards]	6 patients
Alyarmook Teaching Hospital [general medical wards]	1 patient

Table (2): Age distribution of patients with acute stroke .

Age Limit	No. Of Patients	Percentage
35-39 Years	2	2.59 %
40-49 Years	7	9.09 %
50-59 Years	14	18.18 %
60-69 Years	22	28.57 %
70-79 Years	17	22.07 %
80-89 Years	13	16.88 %
90-95 Years	2	2.59 %

Patients with acute stroke were included in the study while patients who are known to have CKD were excluded .MDRD formula estimates GFR using four variables: serum creatinine, age, race, and gender .Using the "4-variable MDRD,"(Modification Of Diet In Renal Disease Formula) GFR, in ml/min per 1.73 m^2 =186.3 x ((serum creatinine) exp[-1.154]) x (Age exp[-0.203]) x (0.742 if female) x (1.21 if black)where exp is the exponential[8]. We calculated GFR in patients presented with features of acute stroke who were diagnosed on clinical and radiological bases(brain CT scan was done for all patients in the 1st 24 hours of presentation) . Based on guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)], in which stages of CKD are defined according to the estimated Glomerualar Filtration Rate (eGFR) [9]:

• Stage 0 disease is defined by a normal GFR (greater than 90 ml/min per 1.73m^2) and risk factors for CKD.

• Stage 1 disease is defined by a normal GFR (greater than 90 ml/min per 1.73m^2) and persistent albuminuria .

• Stage 2 disease is a GFR between 60 to 89 ml/min per 1.73 m^2 and persistent albuminuria .

• Stage 3 disease is a GFR between 30 and 59 ml/min per 1.73 m^2 .

• Stage 4 disease is a GFR between 15 and 29 ml/min per 1.73 m^2 .

• Stage 5 disease is a GFR of less than 15 ml/min per 1.73 m^2 or end-stage renal disease .

Patients were classified using an inquiry (history taking) searching for the presence of any risk factor of CKD such as hypertension,diabetes mellitus ,older age(being older than 60 years) , a family history of renal disease , autoimmune disease , previous episode of acute renal failure , structural abnormalities of the urinary tract, & obesity (central) (waist circumference for male more than 94 cm[37 inch] & more than 80 cm [31.5 inch] for female). Patients also were classified according to their gender , pathological type of stroke (ischemic or hemorrhagic) using brain CT scan and consciousness (conscious or unconscious).

Male patients with history of benign prostatic hypertrophy (BPH) had ultra sound examination of the prostate.

Results

"4-variable MDRD,"(Modification Of Diet In Renal Disease Formula)had been used to calculate GFR for patients with acute stroke included in this study & the results were as follows : (**Table 3**)

Table (3):Number & percentage of patients for each stage of CKD.

Stages of Chronic Kidney Disease	No. of patients	Percentage of patients
Stage 0 & 1	29	37.66%
Stage 2	22	28.57%
Stage 3	19	25.67%
Stage 4	5	6.49%
Stage 5	2	2.59%
Total	77	100%

Table (4):Prevalence's& percentages of risk factors of CKD in all patients with acute stroke included in this study.

Risk factors	Prevalence	Percentage	Male	Female
Hypertension	55/77	71.42%	25/55	30/55
Age more than 60 years	54/77	70.12%	23/54	31/54
Central Obesity	57/77	74.02%	21/57	36/57
Diabetes Mellitus(DM)	27/77	35.06%	12/27	15/27
Obstructive Uropathy*	5/77	6.49 %	5/5	Nil

*All patients were male with history of Benign Prostatic Hypertrophy(BPH).

Table (5) : Patients were classified according to their gender in addition to consciousness level & pathological type of their stroke .

Other factors to be studied		Prevalence	Percentage
Gender	Male	38/77	49.35%
	Female	39/77	50.64%
Level of consciousness	Conscious	53/77	68.83%
	Unconscious	24/77	31.16%
Pathological type of stroke	Ischemic *	51/77	66.23%
	Hemorrhagic	26/77	33.76%

* Ischemic strokes were diagnosed in (13) patients with focal neurological deficit & normal CT scan in this study .

Table (6) : According to "4-variable MDRD formula", patients with risk factors of (CKD) were staged as follows.

		GFR less than 60 ml/min per 1.73 m^2	GFR more than 60 ml/min per 1.73 m^2	Total	Odds	Odds Ratio & 95% Confidence Interval
Risk factors of Chronic Kidney Disease(CKD)	**Diabetes Mellitus**	**11**	16	27	**68.75%**	**OR = 1.6 CI=0.6 to 4.26**
	No Diabetes Mellitus	**15**	35	50	**42.85%**	
	Hypertension	**21**	34	55	**61.76%**	**OR = 2.1 CI=0.67 to 6.53**
	No Hypertension	**5**	17	22	**29.41%**	
	Age > 60 years	**19**	35	54	**54.28%**	**OR = 1.24 CI=0.43 to 3.54**
	Age < 60 years	**7**	16	23	**43.75%**	
	Obstructive Uropathy	**2**	3	5	**66.66 %**	**OR = 1.33 CI=0.٢ to 8.52**
	No Obstructive Uropathy	**24**	48	72	**٥٠%**	
	Centrally Obese	**20**	37	57	**54.05%**	**OR = 1.26 CI=0.41 to 3.79**
	Non Obese	**6**	14	20	**42.85%**	

Table (7) : According to " 4-variable MDRD formula", patients with other factors of interest were staged as follows : odds Ratios for having GRF less than 60 ml /min per 1.73 m^2in patients with acute stroke & risk factor of Chronic Kidney Disease(CKD) were as follows .

		Stage 0 & 1	Stage 2	Stage 3	Stage 4	Stage 5
		29 patients	22 patients	19 patients	5 patients	2 patients
Risk factors of Chronic Kidney Disease (CKD)	**Diabetes Mellitus**	8	8	**9**	**1**	**1**
	No Diabetes Mellitus	21	14	**10**	**4**	**1**
	Hypertension	20	14	**15**	**4**	**2**
	No Hypertension	9	8	**4**	**1**	**Nil**
	Age less than 60 years	14	2	**7**	**nil**	**Nil**
	Age more than 60 years	15	20	**12**	**5**	**2**
	Obstructive Uropathy	2	1	**1**	**1**	**nil**
	No Obstructive Uropathy	27	21	**18**	**4**	**2**
	Centrally Obese	21	16	**14**	**4**	**2**
	Non Obese	8	6	**5**	**1**	**Nil**

Table (8): **Odds Ratios for havingGFR less than 60 ml/min per 1.73 m^2in patients with acute stroke & other factors of interest were as follows .**

		GFR less than 60 ml/min per 1.73 m^2	GFR more than 60 ml/min per 1.73 m^2	Total	Odds	Odds Ratio & 95% Confidence Interval
Gender	**Male**	**8**	30	38	**26.66%**	**OR= 0.31** CI= 0.11 to 0.84
	Female	**18**	21	39	**85.71%**	
Level of consciousness	**conscious**	**13**	40	53	**32.50%**	**OR= 0.27** CI=0.09 to 0.76
	unconscious	**13**	11	24	**118.18%**	
Pathological type of stroke	**Ischemic**	**19**	32	51	**59.37%**	**OR=1.61** CI=0.57 to 4.54
	Hemorrhagic	**7**	19	26	**36.84%**	

Table (9) : Some patients have at least one of the 5 prevalent risk factors of (CKD) in this study i.e.(hypertension, diabetes mellitus, age more than 60 years ,central obesity & obstructive uropathy) while others have 2 or more up to a maximum of 4 risk factors (but in different combination) as follows .

No. of risk factors	Prevalence	Percentage
1 risk factor	18/77	(23.37%)
2 risk factors	18/77	(23.37%)
3 risk factors	24/77	(33.76%)
4 risk factors	17/77	(22.07%)

Table (10) : **Odds Ratio (OR) comparing patients with more than 2 risk factors to those with 2 or less risk factors were as follows** .

No. of risk factors	GFR less than 60 ml/min per 1.73 m^2	GFR more than 60 ml/min per 1.73 m^2	Total	Odds	Odds Ratio & 95% Confidence Interval
>2 risk factors	18	23	41	**78.26%**	**OR=2.73** CI=1.008 to 7.437
≤ 2 risk factors	8	28	36	**28.57%**	

Discussion

In this study, **(26/77 , 33.76%)** patients had(GFR)less than 60 ml/min per 1.73 m^2 according to Modification Of Diet in Renal Disease Formula (4-variable MDRD)**(Table 3)** . This was nearly similar to an American study in 2009

Although no similar studies were found , such prevalence was nearly similar to the prevalence of CKD in a study entitled ' Chronic kidney disease and clinical outcome in patients with acute stroke' published in 2009 by American heart association , stroke journal[5].

Patients with Diabetes Mellitus with GFR less than 60 ml/min per 1.73 m^2**(11/26,42.3%)**(**Table 6**) who had sustained acute stroke & were included in this study.

The Odds Ratio for those with acute stroke to have GFR less than 60 ml/min per 1.73 m^2 in this study was **(1.6 , CI=0.6 to 4.26)** (**Table 7**), so diabetic patients are at increased risk for CKD [10,11] and cardiovascular events[11].

Hypertension was obviously prevalent among patients with GFR less than 60 ml/min per 1.73 m^2 **(21/26 ,80.76%)** (**Table6**) who had sustained acute stroke and were included in this study

The Odds Ratio for hypertensive patients with acute stroke who have GFR less than 60 ml/min per 1.73 m^2 in this study was **(2.1, CI=0.67 to 6.53)** (**Table 7**), the explanation is that hypertension is the second most common cause of CKD [12] ,furthermore, hypertension is present in 75% - 80% of patients with CKD[13], i.e. hypertension is a cause and a complication of CKD [9,11].

The age distribution for patients with GFR less than 60 ml/min per 1.73 m^2 in this study , (**19/26,73.07%**)(**Table 6**) patients more than 60 years old , the Odds Ratio for patients older than 60 years with acute stroke who have GFR less than 60 ml/min per 1.73 m^2 in this study was (**1.24 , CI=0.43 to**

3.54) (**Table 7**) , so patients above sixty yearsare at increase risk of developing CKD[10,12].

Central obesity body mass index (BMI) more than 30 Kg/ m^2 was also clearly predominant among patients with GFR less than 60 ml/min per 1.73 m^2 , **(20/26,76.92%)**(**Table 6**) most obese patients were females (**18/20, 90%**), patients with GFR less than 15 ml/min per 1.73 m^2 **(2/2 ,100%)**and **(4/5,80%)** and patients with GFR less

than 30 ml/min per 1.73 m^2 were centrally obese .

The Odds Ratio for centrally obese patients with acute stroke to have GFR less than 60 ml/min per 1.73 m^2 in this study was **(1.26, CI=0.41 to 3.79)** (**Table 7**) .

This increase in CKD odds in centrally obese in comparison to those who are non obese patients may be due to an increase in the metabolic demands on the kidney, which leads to higher glomerular capillary pressures and glomerular hypertrophy,the hyperinsulinemia frequently linked with obesity may also accelerate structural damage by interacting with angiotensin II and increasing collagen production and deposition, and the histologic changes in the kidney noted in some obese, especially morbidly obese , adults frequently mimic those changes associated with secondary focal segmental glomerulosclerosis ,which may occur in disease states such as severely reduced nephron mass and hemodynamic stress, so given the presence of genetic susceptibility and/or reduced nephron mass, obesity may potentiate the development and progression of secondary focal segmental glomerulosclerosis[14,15,16].

Obstructive uropathywas the least prevalent risk factor of CKD among patients with acute stroke in this study **(5/77,6.49 %)**(all patients were male with history of benign prostatic hypertrophy) **.** (**Table 4**) & also for those with GFR less than 60 ml/min per 1.73 m^2**(2/26,7.69%)**(**Table 6**), the Odds Ratio for patients with acute stroke to have GFR less than 60 ml/min per 1.73 m^2 in this study was **(1.33 , CI=0.٢ to 8.52)** (**Table 7**),as lower urinary tract obstruction is one of initiative risk factors for CKD[9].

Although all above confidence intervals embrace the value of no difference i.e.non-significance , but this does not mean 'no effect'. Small studies will often report non-significance even when there are important , real effects which a large study would have detected[17].

Looking to the above 5 prevalent risk factors of CKD in another way by grouping the patients according to the number of risk factors which they have(**Table 9**).

So, broadly speaking , patients with GFR less than 60 ml/min per 1.73 m^2had been categorized into 2 classes , the first one includes patients with more than 2 risk factors(in any combination) **(18/26,69.23%)**& the other one includes patients with less than or equal to (any combination) 2 risk factors**(8/26,30.76%) (Table 10)** . The resultant odds ratio for patients with more than 2 risk factors to have GFR less than 60 ml/min per 1.73 m^2 was **(2.73,CI=1.008 to 7.43)** (**Table 10**) compared to that of patients with less than or equal to 2 risk factors .

Gender distribution for patients with GFR less than 60 ml/min per 1.73 m^2 in this study had revealed that **(18/26,69.23%)** are female patients &**(8/26,30.76%)** are male patients (**Table 8**).

The Odds Ratio for male patients with acute stroke who had GFR less than 60 ml/min per 1.73 m^2 in this study compared to female was **(0.31 , CI= 0.11 to 0.84)** (**Table 8**)**.**

Such clear shift towards female gender may be explained by knowing that percentage for female patients aging more than 60 years in this study is **(79.48%,31/39)** while that for male patients is **(60.52%,23/38)**, also higher percentage of hypertensive and or diabetic female patients in this study **(30/39,76.92%),(15/39,38.46%)**respectively, compared to that of male patients who were hypertensive **(65.78%,25/38)**and or diabetic **(31.57%,12/38)(Table 4).**Furthermorefemales were by far more centrally obese than male patients with mean waist circumference of **(100.97±13cm)** for female &**(95.36±14.55 cm)** for male, also more number of female patients have central obesity **(36/39,92.3%)** than male patients **(21/38,55.26%)(Table 4)**

Considering consciousness level for patients with GFR less than 60 ml/min per 1.73 m^2 in this study , **(13/26,50%)** were conscious &**(13/26,50%)** were unconscious patients(**Table 8**) , The Odds Ratio for conscious patients with acute stroke to have GFR less than 60 ml/min per 1.73 m^2 in this study compared to those who were unconscious was **(0.27, CI=0.09 to 0.76)** (**Table 8**).

Coming to pathological type of stroke for patients with GFR less than 60 ml/min per 1.73 m^2 in this study , ischemic **(19/26,73.07%),**hemorrhagic **(9/26,34.61%)**(**Table 8**)**.** The Odds Ratio for patients with ischemic stroke who had GFR less than 60 ml/min per 1.73 m^2 in this study compared to those with hemorrhagic stroke was **(1.61, CI=0.57 to 4.54)** (**Table 8**)**.**This can be explained that ischemic stroke is more prevalent than hemorrhagic stroke in patients with CKD[18].

Conclusion

About one third of patients with acute stroke have GFR less than 60 ml/min per 1.73 m^2

.Patients with acute stroke who have more than 2 risk factors of the 5 prevalent risk factors of CKD in this study (hypertension, diabetes mellitus, age more than 60 years , central obesity & obstructive uropathy, in any combination) are about 3 times (statistically significant) more likely to have GFR less than 60 ml/min per 1.73 m^2 to those with 2 or less risk factors. Taking each one of the above risk factors of CKD individually, there is an increased probability for having GFR less than 60 ml/min per 1.73 m^2 in this study but withstatistical non significance . Female gender , unconscious patients also are more likely (statistically significant) to have GFR less than 60 ml/min per 1.73 m^2 than male gender or conscious patients , respectively. In this study, pathological type of stroke shows higher probability for ischemic stroke to have GFR less than 60 ml/min per 1.73 m^2 than hemorrhagic one but with statistical non significance .

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