Evaluation of Kidney Function in Hypertensive Patients in Quetta

N. TARIQ, N. BAJWA, N. ALI, S. SADOZAI, H. ALI, R. IQBAL[++*]

Zoology Department, Sardar Bahadur Khan Women's University, Quetta, Pakistan

Abstract: The study was conducted in Balochistan Institute of Nephro-Urology Quetta (BINUQ). One hundred (n=100) subjects were included amongst fifty were hypertensive and fifty were normal healthy. Demographic data was collected by questionnaire from all the participants. Venous blood samples were collected to analyze serum creatinine and uric acid by using semi-automated analyzer and estimated Glomerular Filtration rate (eFGR) was calculated by using Modification of Diet in Renal Disease (MDRD) study estimating equation. SPSS was used for statistical analysis.

The data shows that levels of serum creatinine and serum uric acid was found significantly high in hypertensive patients as compared to normal subjects (P=0.00). During study different risk factors like age, Body Mass Index (BMI), diabetes, smoking, alcohol consumption, exercise, occupation, salt intake were also analyzed in both normotensive and hypertensive patients. It was found a strong association of these risk factors with high blood pressure (P=0.00). A significant association of creatinine, eFGR and uric acid is found with hypertension and Choronic kidney disease (CKD). It was also found that due to increased creatinine count, 46% hypertensive patients have kidney disease(P=0.00). The individuals with normal levels of BP have normal level of creatinine. So it is concluded that Creatinine, eFGR and Uric acid are the important bio chemical markers to identify the kidneys dysfunction in hypertensive patients.

Keywords: Chronic Kidney Disease (CKD), Creatinine, eFGR, Hypertension, Quetta

1. INTRODUCTION

Hypertension is a noteworthy medical issue all through the world as a result of its high commonness and its relationship with expanded danger of cardiovascular malady. Advances in the finding and treatment of hypertension have assumed a noteworthy part in late emotional decreases in coronary illness and stroke mortality in industrialized nations. Be that as it may, in a considerable lot of these nations, the control rates for hypertension have really hindered over the most recent couple of years. It is assessed that by 2010, 1.2 billion individuals will be enduring hypertension around the world (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of HBP, 1997).

Pakistan, a nation with an aggregate populace of over 150 million individuals, has one of the most exceedingly awful wellbeing markers in South Asia, a locale confronting the developing plague of cardiovascular ailment and hypertension (Chaturvedi, 2003). Pakistan National Health Survey (PNHS) demonstrated that the predominance of hypertension expanded from <10% of every 18 to 19 years of age to > 60% in more than 70 a long time age in guys and also in females it expanded from <5% at 18 to 19 years to a

pinnacle of 70% in 60 to 69y age, the commonness being higher in the female contrasted with male. In the two guys and females the commonness rate expanded greatly after 20 to 29yars (Aziz *et al.,* 2005).

Chronic kidney disease (CKD) is recognized as a major health problem as it is progressive loss of renal function. It is estimated that the annual incidence of new cases of kidney disease (CKD) is >100 per million population in Pakistan (Ullah *et al,* 2015). The decreased renal function shown by glomerular filtration rate (GFR) of less than 60 mL/min per 1·73 m2, or markers of kidney damage, or both, of at least 3 months duration, regardless of the underlying cause (Thomas *et al*, 2008).

Hypertension is one of the main sources of kidney disappointment. Hypertension may harm the vessels in the body specially kidney and impact the emission of waste item. Extra-fluid and wastes stop emitting by the kidneys and further ascent the circulatory strain in the long run prompting end stage renal disease (Wulandari *et al.,* 2013).

The start and improvement of hypertension related to constant kidney ailment is multifactorial and

[++]Corresponding Author: rehanaiqbal82@gmail.com
[*]Institute of Pure and Applied Biology, Bahauddin Zakariya University, Multan. 60800

complex, basically in late periods of renal sickness. Presently withstanding the built up components for instance extended volume of intra vasculature and pointless activity of rennin angiotensin framework. There are likewise new understood players for instance endothelial brokenness, extended development of sympathetic nervous system (SNS) and alteration of neural and humeral factors that propel an extension of BP. Hypertension is significantly common in incessant kidney sickness, being associated with the renal function, patient's age and reason for renal ailment (Ridao *et al.,* 2001).

Kidney disease either acute or chronic attributed to hypertension, has become a public and economic health burden. There are several markers to evaluate kidney functions. The present study was designed to find out the association between kidney function and hypertension by using biochemical markers creatinine, estimated Glomerular filtration rate (eGFR) and uric acid. They are the reliable indicators of renal function. Increased level of creatinine and uric acid while low levels of estimated Glomerular filtration rate (eGFR) signifies kidney disease or impaired function of kidneys. Keeping in view the above discussion, a study was designed to investigate the correlation between hypertension and kidney function especially in hypertensive patients.

2. MATERIAL AND METHODS

The study was conducted in Balochistan Institute of Nephro-Urology Quetta (BINUQ) to compare the kidney function in hypertensive and healthy participants. One hundred subjects were included in the study. Of which 50% were hypertensive (clinically analyzed as hypertensive under normal OPD visits) and 50% were normal healthy. Among the both hypertensive and healthy subjects, 50% male and 50% female were selected from each subject. Demographic data was collected by questionnaire from all the participants. Venous blood samples were collected from patients and then analyzed by using semi-automated analyzer. The anthropometric measurements were taken by the following methods:

3. ANTHROPOMETRIC MEASUREMENTS
Measurement of Blood Pressure (BP)

Measurement of circulatory strain(BP) was done by proposals of Americans Heart Association (Perloff, *et al.,* 1993). The measurements were done with auscultator technique utilizing aligned mercury sphygmomanometers.

Measurement of Hypertension (HPT)

Hypertension was characterized As per seventh report of Joint National Committee on Prevention,

Detection, Evaluation and Treatment of High Blood Pressure (JNC-7), It is a normal SBP higher than or equivalent to 140mm/Hg and DBPs higher than or equivalent to 90mm/Hg (Chabonian, *et al.,* 2003). What's more, was organized by JNC7.

Measurement of Body Mass Index (BMI)

It was figured by proportion of weight in kg to height in m^2 (Aguilar-Salinas *et al.,* 2001). As indicated by WHO, a person is lean having a BMI of 18.5-24.9 kg/m^2, and over-weight with a BMI of 25.0-29.9kg/m^2 and a man is obese evaluating BMI noteworthy than 30.0 kg/m^2 (Nuttall, 2015).

SAMPLE COLLECTION

3ml venous blood was drawn from the hypertensive patients as well as the healthy subjects in disposable syringes. Blood was collected in plain tubes. The sample was centrifuged by HuMax 4k centrifugation machine at 5000 rpm for 3 minutes. The serum was separated for the analysis on the same day for the analysis for serum creatinine and serum uric acid.

BIO-CHEMICAL SERUM ANALYSIS

The sample analysis was carried out on a compact semi-automated clinical chemistry analyzer "Humalyzer 3500" by using reagent kits of HUMAN Company.

Measurement of Serum Creatinine

Measurement of serum creatinine was done by Jaffe Kinetic method. The standard strategy for estimation of creatinine utilizes the Jaffe response (Jaffe, 1886) in which creatinine forms in alkaline solution an orange-red colored complex with picric acid. Its red-orange color is effectively identified and measured. This response is very much portrayed with respect to its properties and confinements (Bonsnes and Taussky, 1945). The upsides of strategies utilizing the Jaffe response are their effortlessness and the wide clinical acknowledgment increased over right around 80 years of utilization (Mandell and Jones, 1953). The intensity of produced color is directly proportional to the amount of creatinine in the sample.

Measurement of Estimated Glomerular Filtration Rate (eGFR)

A more precise measure of the kidney function can be estimated by calculating how much creatinine is cleared from the body by the kidneys. This is referred to as creatinine clearance and it estimates the rate of filtration by kidneys (estimated glomerular filtration rate, or eGFR). The Glomerular Filtration Rateis estimated by using Modification of Diet in Renal Disease (MDRD) study estimating equation from the serum creatinine concentration by web-based tool (http://www.nkdep.nih.gov/professionals/gfr_calculators/index.htm).

Assessment of Chronic Kidney disease (CKD)

Severity of Chronic Kidney disease was assessed following the criteria developed by National Kidney Foundation, USA based on Kidney Disease Outcome Quality Initiative (K/DOQI) (Coresh *et al*, 2003).

Measurement of Serum Uric Acid

Assurance of uric acid in serum perform a vital role in research facility medication and along these lines is everyday determined in the lab(Zhao and Liao, 2007; Becker and Jolly, 2006).Most common method for serum uric acid is the uricase based strategies, utilizing the particular enzymatic oxidation of uric acid by oxygen to produce allantoin, hydrogen peroxide, and carbon dioxide (Sanders, *et al.,* 1980; Moss, 1980). Peroxidase undergoes catalysis with 4-amino-phenazoneand 3,5-dichloro-2-hydrobenzene-sulfonic acid(DHBS). It gives violet red color (Fossati *et al.,* 1980).

ANALYSIS OF DATA

The data was analyzed by using Statistical Package for Social Sciences (SPSS).

4. <u>**RESULTS AND DISCUSSION**</u>

a) **Baseline characteristics of participants**

The**(Table 1)** represents the demographic data of 100 subjects including 50 normotensive (control) and 50 hypertensive (case) were recorded which shows strong association of these parameters with hypertension.

Collectively 38% of subjects were observed to be hypertensive among the age group of 40-60 and above 60, this validate the results of study done by Khealani *et al.,* (2008) in Pakistan. In case of marital status one third of married subjects (74.0%) found to be hypertensive and occupation also shows a drastic percentage (60.0 %) of jobless who are living with hypertension. Association of exercise with hypertension shown to be positive as, 78.0 % of case subjects did not do exercise. According to Nogueria (2010) smoking increase hypertension and a similar result (40.0%) shows by present study. A very strong and positive association of BMI and diabetes were found with hypertension 74.0% & 26% respectively, which is in an agreement with (Bays *et al.,* 2007) and (Sampanis and Zamboulis, 2008) who also reported the association of hypertension with Increase BMI and diabetes respectively.

It was also found16% of healthy participants were not taking the salt, followed by6%(occasionally), 10%(often) and 68%(with each meal). In hypertensive patients, its percentage was as 6%(no salt), 18%(occasionally), 22%(often) and 54%(with each meal). It means that hypertensive patients consume high intake of salt. Similar to a study directed by Kofi (2011) affirmed that high admission of salt straightforwardly connected with hypertension. Majority of healthy subjects (98%) and hypertensive patients (96%) were non alcoholic.

Table 1: *Distribution of the participants according to their general characteristics*, Multan.
Systolic and diastolic blood pressure and CKD

Characteristics	*Category*	*Normotensive*		*Hypertensive*		*Total*	
		No of individuals	*%*	*No of individuals*	*%*	*%*	*No of individuals*
Age (years)	16-30	16	32.0	9	18.0	25	25.0
	31-45	28	56.0	22	44.0	50	50.0
	46-60	5	10.0	14	28.0	19	19.0
	Above 60	1	2.0	5	10.0	6	6.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Marital status	Married	32	64.0	37	74.0	69	69.0
	Unmarried	16	32.0	7	14.0	23	23.0
	Divorced	-	-	1	2.0	1	1.0
	Widow	2	4.0	5	10.0	7	7.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Occupation	Public sector	30	60.0	12	24.0	42	42.0
	Private sector	8	16.0	8	16.0	16	16.0
	Jobless	12	24.0	30	60.0	42	42.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Exercise	Yes	23	46.0	11	22.0	34	34.0
	No	27	54.0	39	78.0	66	66.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Salt intake	Not	8	16.0	3	6.0	11	11.0
	Occasionally	3	6.0	9	18.0	12	12.0
	Often	5	10.0	11	22.0	16	16.0
	With each meal	34	68.0	27	54.0	61	61.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**

Smoking	Yes	12	24.0	20	40.0	32	32.0
	No	38	76.0	30	60.0	68	68.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Alcohol consumption	Yes	1	2.0	2	4.0	3	3.0
	No	49	98.0	48	96.0	97	97.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Ethnicity	Punjabi	12	24.0	12	24.0	24	24.0
	Pathan	15	30.0	15	30.0	30	30.0
	Baloch	9	18.0	13	26.0	22	22.0
	Hazara	14	28.0	10	20.0	24	24.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Body Mass Index (BMI)	Under weight	7	14.0	1	2.0	8	8.0
	Normal weight	29	58.0	12	24.0	41	41.0
	Over weight	11	22.0	31	62.0	42	42.0
	Obesity	3	6.0	6	12.0	9	9.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Diabetes	Yes	-	-	13	26.0	13	13.0
	No	50	100.0	37	74.0	87	87.0
	Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**

Table 2: *Cross tabulation (Kidney disease and Systolic and diastolic blood pressure)* **Serum creatinine and uric acid**

Systolic Blood Pressure Count (mm of Hg)		Creatinine Count						P-value
		0.1-2	2.1-4	4.1-6	6.1-8	8.1-10	10.1-12	
Normal <120		48	2	-	-	-	-	0.00
Pre-hypertension 120-139		4	2	15	10	4	3	0.00
Hypertension stage I 140-159 Hypertension stage II >160		0	3	4	1	-	4	0.00

The hypertensive patients have high blood pressure and it reach at (160/100mm/Hg) as compared to healthy subjects because of kidney ailments. Mostly patients stated the symptoms of hypertension like headache and blur eye sight. Same was found by Marshal *et al.* (2012) who stated that high blood pressure patients complained blur eye sight, vertigo and headache. It has been shown in **(Table 2-3)** that statistically there is a significant association (x^2= 45.689[a], df $_=$ 5, P=0.00) between kidney disease and diastolic blood pressure (DBP). At normal values of DBP, only 1 individual has kidney disease and 29 have no disease. In pre-hypertension, 28 have kidney disease. In hypertension stage I, 17 patients have kidney disease while in stage II only 4 patients have kidney disease. Significant association (x^2=100.000[a],df$_=$ 5, P=0.00) is also found between kidney disease and systolic blood pressure (SBP). At normal values of SBP, no individual has kidney disease. In pre-hypertension, 38 patients have kidney disease while in hypertension stage I and II, 7 and 5 patients have kidney disease respectively.

Table 3: *Cross tabulation (Kidney disease and creatinine)*

Choronic Kidney Disease CKD	Systolic Blood Pressure mm of Hg				Diastolic Blood Pressure mm of Hg			
	Normal	Pre-hypertension	Hypertension Stage I	Hypertension Stage II	Normal	Pre-hypertension	Hypertension Stage I	Hypertension Stage II
Yes	0	38	7	5	1	28	17	4
No	50	0	0	0	29	20	1	0
P value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

In this study creatinine and uric acid has been considered as a representative to assess the renal function. The values of creatinine and uric acid of hypertensive patients were significantly higher as compared to values of normal healthy subjects. This is an agreement with Mahammad and Hammad (2012) showed that the mean creatinine estimations was high in hypertensive (141.3±39.0) than healthy controls (52.4±18.0µmol/l) and the distinction was factually critical.

Table 4: Cross tabulation (Systolic blood pressure and creatinine

Creatinine Count mg/dl	Chronic Kidney disease (CKD)				P-value
	Yes		No		
	f	%	f	%	
0.1-2	4	4.0	48	48.0	0.00
2.1-4	5	5.0	2	2.0	0.00
4.1-6	19	19.0	-	-	0.00
6.1-8	11	11.0	-	-	0.00
8.1-10	4	4.0	-	-	0.00
10.1-12	7	7.0	-	-	0.00

In the present research, 50 hypertensive patients have kidney disease. It has been found a statistically significant association (x^2=79.516[a]df =5, P=0.00) between kidney disease and creatinine. The data presented in **(Table 4)** shows that at normal values of creatinine (0.6-1.1 for men and 0.5-0.9mg/dl for women.), only 4 participants have kidney disease while 48 have no disease. In mild increase of creatinine value (2.1-4mg/dl), 5 have kidney disease. 41 Patients have kidney disease as they have high level of creatinine values (4.1-12mg/dl).

It has been shown in Table 4 that there is a significant association (x^2 = 120.033[a], df=25, P=0.00) between creatinine and systolic BP. The patients who have normal levels of BP have normal level of creatinine. At creatinine level (4.1-6mg/dl) 15 patients were in pre hypertension(120-139 mm/Hg) and 4 were in stage I and II. At 6.1-8mg/dl, 10 patients were in pre-hypertension. At 10.1-12 mg/dl 3 were in pre-hypertension and 4 were in stage I and II.

Table 5: Cross tabulation (Hypertension and eFGR)

Estimated Glomerular Filteration Rate (eFGR)	Blood Pressure mm of Hg				P-Value
	Normal	Pre-hypertension	Hypertension Stage I	Hypertension Stage II	
Stage I ≥90mL/minper1.73m²	46	4	0	0	0.00
Stage II 60-89mL/minper1.73m²	2	2	21	8	0.00
Stage III 30-59mL/minper1.73m²	0	0	2	15	0.00

Table 6: *Cross tabulation (Systolic blood pressure and uric acid)*

blood pressure count (mm of Hg)	Uric acid count mg/dl					P-value
	0.1-2	2.1-4	4..1-6	6.1-8	8.1-10	
Normal	2	3	34	11	-	0.00
Pre-hypertension	-	-	3	14	18	0.00
Hypertension stage I Hypertension stage II	-	-	1	1	10	0.00

(Table 5) shows that there is a statistically significant association (x^2=58.372[a], df = 4, P=0.00) between Hypertension and estimated Glomerular filtration Rate (eFGR). Among hypertensive patients 31 were in CKD Stage II with eFGR 60-8960-89mL/minper1.73m² while 17 were in CKD Stage III with eFGR 30-59mL/minper1.73m². The normotensive individuals have normal eFGR at Stage I (≥90mL/minper1.73m²).

The **(Table 6)** depicts that there is a significant association (x^2 = 71.766[a], df=20, P=0.00) between uric acid and systolic BP. Normal values of uric acid for men is 3.4-7.0mg/dl and 2.4-5.7mg/dl for women The patients who have normal levels of BP have normal level of uric acid. In pre-hypertension (120-139 mm/Hg) 18 patients and in stage I and II, 10 patients have increased level of uric acid (8.1-10mg/dl). This as an agreement with (Razak *et al.* 2010) who demonstrated that high BP patients had noteworthy increment in serum levels of uric acid when contrasted with control.

The results are agreement with Mazzali *et al*. (2001) who explained that increased Uric acid level brings down the levels of nitric oxide(N2O) which ultimately in the kidney lower the neuronal N2O synthase and then stimulated reninangiotens in framework. This system was demonstrated in a study on rat where hypertension was developed within 3-5 weeks after the increased level of uric acid by the admission of oxonic acid (uricase inhibitor). They also stated that there was a connection between high uric acid level and kidney ailment and obesity.

The findings of this research told that all hypertensive patients have kidney problems either acute or chronic both. Serum uric acid and creatinine are the important markers for the evaluation of kidney function. Muhammad and Hammad *et al.,* 2012 reported similarly that the mean estimations of creatinine was high in hypertensive patients and discovered this increased level due to direct impact of hypertension and its complications on kidney functions. In another contemplate study done by Rosansky *et al*(1990)and demonstrated that hypertensive patients have significantly higher rate of less kidney capacity as contrasted to normal subjects.

5. CONCLUSION

Hypertension and Chronic Kidney Disease are major health care problems in Pakistan. A significant association is found between Hypertension, a preventable risk factor, and CKD. Serum creatinine, eFGRand uric acid are the important bio chemical markers to identify the kidneys dysfunction in hypertensive patients.

6. ACKNOWLWDGEMENT

Statement of conflict of interest
The authors declare that they have no conflicting interests.

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