A Study to Assess Visit-to-Visit Blood Pressure Control and Its Correlation with Different Laboratory Parameters in Patients with Chronic Kidney Disease

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ABSTRACT

Introduction: Hypertension is related to chronic kidney disease (CKD) in a number of ways. The objective of this research was to assess visit-to-visit blood pressure control in patients of different stages of chronic kidney disease and to establish a relationship of the above observations with various biochemical parameters.

Material and methods: This study included patients with chronic kidney disease with blood pressure >140/90 mm of Hg at presentation. The patients were subjected hematological and biochemical investigations and were put on standard treatment protocol, respective of their stage of chronic kidney disease (CKD) at the discretion of attending physicians. Two follow up visits were planned at 2-week interval each.

Results: A total of 90 patients with chronic kidney disease were enrolled. Maximum number of cases were in CKD Stage V (n=46; 51.1%) followed by Stage IV (n=39; 43.3%). Overall the conversion to normotensive status was observed to be 36.6%. Though no statistically significant difference in blood pressure status of patients in different stages was observed yet for the overall as well as stages IV and V, the change was significant statistically ($p<0.001$). As compared to baseline, a significant decrease in mean urea, creatinine, BUN, K+ and blood sugar levels was observed ($p<0.05$). A significant increase in mean GFR was also observed ($p<0.001$). All the correlations were weak ($r<0.3$) except for the correlation of DBP with Urea, Creatinine and K+ levels.

Conclusion: This study suggests the non-existence of a relationship between stage of disease and blood pressure control in higher stages of CKD and existence of a poor correlation between extent of change in blood pressure to change in biochemical and laboratory parameters.

Keywords: visit-to-visit blood pressure control, laboratory parameters, chronic kidney disease

INTRODUCTION

Hypertension is related to chronic kidney disease (CKD) in a number of ways. Hypertension can independently cause CKD, contribute to its development in the setting of other potential causes or even be the result of CKD, as is the case in patients with polycystic kidney disease. Hypertension is present in approximately 80 percent of patients with CKD and it can also induce CKD, there are reports quoting the prevalence of CKD among hypertensive to be as high as 46.9%.[1-3] Hypertension may develop early in the course of CKD and can be associated with adverse outcomes such as worsening renal function and development of cardiovascular disease. Hypertension is a major promoter of the decline in GFR in both diabetic and nondiabetic kidney disease.[4,5] The objective of this research was to assess visit-to-visit blood pressure trend in patients of different stages of chronic kidney disease and to establish a relationship of the above observations with various biochemical parameters.

MATERIAL AND METHODS

This prospective observational study was performed from January 2011 to June 2012 after approval from the ethics committee of our institution. Study population included patients with chronic kidney disease (defined using National Kidney Foundation (NKF-KDOQI) working group criteria)[6] attending the outpatient and inpatient departments of General Medicine of either sex, aged between 18 years to 70 years with Systolic/ Diastolic blood pressure >140/90 mm of Hg at presentation. Patients on hemodialysis, Critically ill patients, and patients not willing to participate were excluded from the study. An informed consent was obtained from all the patients enrolled in the study. An informed consent was obtained from all the patients enrolled in the study.

Study Frame: It consisted of all the patients with chronic kidney disease attending the Medicine OPD, casualty ward and indoor patients, fulfilling the inclusion/ exclusion criteria.

After detailed physical examination, the patient was subjected hematological and biochemical investigations, which include complete blood count, Urine routine and microscopy, serum Urea, serum Creatinine, electrolytes, Random blood sugar, Fasting and Post prandial blood sugar, Glycosylated hemoglobin (in diabetic cases), Ultrasonography (KUB), Electrocardiogram, and Fundus examination.

All the patients were put on standard treatment protocol, respective of their stage of chronic kidney disease (CKD) at the discretion of attending physicians who was not part of this observational team. Cockcroft-Gault equation was used to estimate creatinine clearance. Blood pressure was measured by mercury sphygmomanometer in supine position. Appearance of first Korotkoff's sound and disappearance of fifth Korotkoff's sound was taken as systolic and diastolic blood pressure

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How to cite this article: Davendra Kumar, Ajay Kumar Mishra, Mehboob Subhani Siddiqui, Faraz Ul Islam. A study to assess visit-to-visit blood pressure control and its correlation with different laboratory parameters in patients with chronic kidney disease. International Journal of Contemporary Medical Research 2016;3(7):1935-1938.

respectively. Mean arterial pressure (MAP) was calculated by equation (SBP + 2DBP)/3.

In the present study, two follow up visits were planned at 2-week interval each, however, a variation of 2-3 days from the proposed time of follow up assessment was allowed due to practical exigency. Patients with a minimum of three different visits (each visit after two weeks of previous visit) were considered to be completing the study.

STATISTICAL ANALYSIS

Data so obtained was subjected to statistical analysis using Statistical Package for Social Sciences version 15.0. The data have been represented as number and percentage. Parametric data have been presented as mean ± SD. The chi - square test was used to evaluate the proportional data. Odds ratio/risk ratios have been calculated wherever necessary. Parametric data have been evaluated using Student "t"-test. The Confidence level of the study was kept at 95%, hence a "p" value less than 0.05 indicated a statistically significant difference.

RESULTS

A total of 90 patients with chronic kidney disease were enrolled in the study. Mean age of patients was 46.43±12.63 years. There were 47 (52.2%) and 43 (47.8%) females. (Table-1) Decrease urine output was the most common presentation followed by headache and decrease in appetite. A total of 16 (17.8%) were tobacco users, 15 (16.7%) were smokers and 6 (6.7%) were alcohol users. There were 3 (3.3%) patients who were regular analgesic users.

Maximum number of cases were in CKD Stage V (n=46; 51.1%) followed by Stage IV (n=39; 43.3%), stage III (n= 4; 4.4%), and stage I (n=1;1.1%). Mean heart rate, systolic blood pressure, diastolic blood pressure, arterial blood pressure and respiratory rate of patients were 93.56±9.13 bpm, 173.38±23.77 mm Hg, 102.86±10.73 mm Hg, 126.36±13.44 mm Hg and 21.87±3.66 per minute respectively. (Table-2) Mean SBP was found to be maximum among Stage III cases (182.5±9.57) followed by stage IV (179.3±21.32), stage V (168.3±25.26) and stage I (140±0) respectively. Mean DBP ranged from 90±0 mm of Hg in Stage I to 105.0±5.77 mm of Hg in Stage III and 104.1±11.91 mm of Hg in stage IV to 101.9±9.98 mm of Hg in stage V. Mean MAP also showed trends similar to SBP and DBP with maximum mean value in Stage III and minimum in Stage I.

At first follow up a total of 84 patients made a repeat visit. 6 patients were lost in follow up. The single case in Stage I and 2 (50%) out of 4 patients in stage II attained normotensive status. However, in stages IV and V only 11 out of 28 (31.7%) and 19/41 (31.7%) patients could attain normotensive status. Overall the conversion to normotensive status was observed to be 32.1%. Though no statistically significant difference in blood pressure status of patients in different stages was observed yet for the overall as well as stages IV and V, the change from hypertensive to normotensive status was highly significant statistically ($p<0.001$). Overall mean change in SBP and DBP was found to be -26.72±32.4 mm of Hg (14.5±17.2%) and -13.8±15.3 mm of Hg (12.8±14.3%) respectively. Although, there was no significant difference in mean SBP and DBP of different stages. However, the reduction in SBP and DBP was found to be significant statistically in Stages IV and V ($p<0.001$). Overall too, the reduction in SBP and DBP was significant statistically ($p<0.001$). Statistically, there was no significant difference in percentage reduction mean MAP among different stages ($p=0.816$). However, percentage reduction in MAP was found to be significant statistically for the overall as well as for stage IV and V ($p<0.001$).

At the second follow up, a total of 82 patients made a repeat visit. The single case in Stage I and 2 (50%) out of 4 patients in stage II had normotensive status. However, in stages IV and V only 12 out of 36 (33.3%) and 15/41 (36.6%) patients could attain normotensive status. Overall the conversion to normotensive status was observed to be 36.6%. Though no statistically significant difference in blood pressure status of patients in different stages was observed yet for the overall as well as stages IV and V, the change from hypertensive to normotensive status was significant statistically ($p<0.001$). (Table-3) Overall mean % reduction in SBP and DBP was observed to be 9.9±21.6% and 6.9±17.5% respectively. The reduction in SBP and DBP was found to be significant statistically in Stage IV only ($p<0.001$). However, percentage reduction in MAP was found to be significant statistically for the overall as well as for stage IV ($p<0.001$).

At the second follow up, change in different biochemical levels as compared to baseline has been shown in Table-4. As compared to baseline, a significant decrease in mean urea, creatinine, BUN, K+ and blood sugar levels was observed ($p<0.05$). An increase in mean GFR was also observed during this period, which was also significant statistically ($p<0.001$).

SN	Age	No. of cases	Percentages
1.	18-30 Years	9	10.0
2.	31-60 Years	70	77.8
3.	61-70 Years	11	12.2
SN	**Gender**	**No. of cases**	**Percentages**
1.	Male	47	52.2
2.	Female	43	47.8

Table-1: Age and gender wise distribution (n=90)

SN	Stage	SBP		DBP		MAP	
		Mean	SD	Mean	SD	Mean	SD
1.	I (n=1)	140	0	90	0	106.7	0
2.	II (n=0)	-	-	-	-	-	-
3.	III (n=4)	182.5	9.57	105.0	5.77	130.9	6.90
4.	IV (n=39)	179.3	21.32	104.1	11.91	129.1	13.0
5.	V (n=46)	168.3	25.26	101.9	9.98	124.0	13.70
ANOVA (F)		2.500		0.801		1.933	
"p"		0.065		0.497		0.130	

Table-2: Stage wise Comparison of Mean Blood Pressure levels (n=90)

SN	Stage	No. of hypertensives	%	Rate of conversion to Normotensive (%)	Significance of Change from baseline (Fisher exact test)
1.	I (n=1)	0	0	100	-
2.	II (n=0)				
3.	III (n=4)	2	50	50	0.429
4.	IV (n=36)	24	66.7	33.3	<0.001
5.	V (n=41)	26	63.4	36.6	<0.001
	Total (n=82)	52	63.4	36.6	<0.001
χ^2=2.208 (df=3); p=0.520; *All the cases were hypertensive at baseline					

Table-3: Distribution of cases in different stages according to their hypertensive status* at second follow up visit

SN	Parameter	Baseline		At 2nd follow up		Significance of change	
		Mean	SD	Mean	SD	"t"	"p"
1.	Urea	140.22	61.44	103.09	44.46	6.048	<0.001
2.	Creatinine	6.89	7.19	4.49	2.54	3.136	0.002
3.	GFR	14.86	7.90	20.85	12.85	-4.789	<0.001
4.	BUN	65.48	30.33	48.15	20.76	5.604	<0.001
5.	Na^+	139.68	6.10	140.00	4.93	-0.363	0.718
6.	K^+	4.88	1.11	4.51	0.83	2.866	0.005
7.	Blood sugar (mg/dl)	132.45	62.45	118.98	28.95	2.326	0.022

Table-4: Change in different biochemical levels as compared to baseline (n=82)

Table-4 shows the correlation between the % Change in blood pressure (from baseline to second follow up) and percentage change in different biochemical parameters. All the correlations were weak (r<0.3) except for the correlation of DBP with Urea, Creatinine and K+ levels.

DISCUSSION

The present study had enrolled patients with all etiologies and hence the relatively lower mean age of patients in the present study is consistent with the findings of Indian CKD registry. It has been reported that in Indian registry the mean age of patients with diabetic nephropathy as the origin is slightly higher (52.3±14.2 years) as compared to those with other/ undetermined etiologies (47.4±14.7 years).[7]

Although the prevalence of hypertension could be inferred to be higher among cases in higher stages of CKD owing to higher prevalence of higher stages of CKD cases in present study yet blood pressure levels did not show a significant linear relationship in different stages of CKD. This finding in the present study is in contrast with the findings of Wright-Nunes et al. who observed mean blood pressure levels among cases of lower stages (Stage 1 and 2) to be significantly lower as compared to those in higher stages (Stage 3 and 4).[8] The reason for this could be almost negligible representation of lower stages of CKD in present study owing to a strict inclusion criterion.

In present study, peak blood pressure levels were observed among cases of Stage III of CKD, while minimum levels (except for 1 case of CKD stage I) were observed in stage V. This might be because all the stage V patients were essentially on an intensive hypertension treatment protocol.[6,9]

With respect to categorical change in blood pressure levels from hypertensive to normotensive, evaluated in terms of conversion rate to normotensive status (as all the cases in present study were hypertensive at baseline), the conversion rate was higher in lower stages (Stage I and III) as compared to conversion rates in higher stages (Stages IV and V) at both the follow up intervals yet the change in status was significant only for higher stages (p<0.001) in both the follow up intervals whereas in lower stages it was not significantly statistically (p>0.05) despite being higher in proportional terms. Apart from that, despite proportional differences (100% conversion in stage I to 28.7% conversion in stage IV at first follow up and 100% conversion in stage I to 33.3% conversion in stage IV at second follow up) the difference in conversion rate among different stages was not significant statistically at either of the two time intervals (p>0.05). This problem is genuinely because of distorted representation of different stages of CKD in present study.

At the end of second follow up, a significant reduction in mean serum urea, creatinine, GFR, BUN, K+ and blood pressure was observed in 82 patients completing the study. On evaluating the percentage mean reduction in different parameters, maximum mean percentage change was observed for GFR (54.68±75.70%) while minimum change was observed for Na+ (0.41±5.60%). These percentage changes were correlated with percentage changes in blood pressure levels (SBP, DBP and MAP), it was observed that all the correlations were weak (r<0.3) and except for correlation of DBP with Urea, Creatinine and K+ and correlation of MAP with K+ level none of the correlations were significant statistically. These findings suggested that visit-to-visit blood pressure changes within the limitations of present study were independent of stage of CKD and did not show an impact on biochemical and laboratory parameters. The poor correlation of biochemical and laboratory parameters for renal function assessment with blood pressure changes is consistent with the previous studies by Agarwal R and Faqah A et al., who questioned the utility and benefit of achieving blood pressure levels far below than 140/90 mm of Hg.[10,11]

In present study, mean SBP, DBP and MAP levels at baseline were 168.3±25.26, 101.9±9.98 mm and 124.0±13.7 mm of Hg as compared to 154.6±36.8, 94.8±16.4 and 114.7±22.5 mm of Hg at second follow up, thus showing that despite achieving normotensive changes in 36.4% cases, in general mean blood pressure levels were indicative of hypertensive status of

the patients and this could be cited as one of the reasons for poor correlation between change in blood pressure levels and biochemical and laboratory parameters. Moreover, inclusion of a high proportion of patients in stage V which is termed to be characterized by irreversible renal functions has also a contributory role in this poor correlation.

CONCLUSION

This study suggests the non-existence of a relationship between stage of disease and blood pressure control in higher stages of CKD and existence of a poor correlation between extent of change in blood pressure to change in biochemical and laboratory parameters. It also provides an insight for future studies to be based on an equiproportional representation of all the stages.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 15-05-2016; **Published online**: 17-06-2016