Evaluation of control of blood pressure in chronic kidney disease patients with hypertension attending echo-lab of Nepal Medical College Teaching Hospital

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ABSTRACT

Hypertension and Chronic kidney disease (CKD) are common in Nepal. Control of blood pressure (BP) in general hypertensive patients is poor. Evaluation of adequacy of BP control in CKD patients with hypertension is rare. All consecutive indoor patients (52) with CKD and hypertension, attending echo-lab of Nepal Medical College Teaching Hospital during prospective study of 3 years period from 16th April 2008 to 15th April 2011, were evaluted. Mean age was 45.3 ± 16.7 years. Male female ratio was 8:5. Brahman and Chhetri (22, 42.3%) were the usual sufferers. There were two peaks in the age group wise distribution; one in age group 20-29 years and the next in 50-59 years. One hypertensive patient's BP was normalized after starting hemodialysis without antihypertensive therapy and was excluded from this study. Others' BP (n= 51) were followed up during admission for the evaluation of the adequacy of their BP control and their antihypertensive medications were reviewed. The control of hypertension in CKD patients was difficult. More than two third of the patients (68.6%) had BP >140/90 mm Hg. Intensive BP control was present in less than one tenth (7.9%) of the patients. In comparison to intensive group, uncontrolled group received more antihypertensive agents (3.0 ± 1.3 vs. 2.0 ± 0.8, $p < 0.05$). Amlodipine (39, 76.5%) and frusemide (39, 76.5%) were very popular antihypertensives used followed by Prazocin (20, 39.2%) and Metoprolol (11, 21.6%). Despite good efforts, BP control of Nepalese CKD patients with hypertension, were poor.

Keywords: Chronic kidney disease (CKD, Hypertension, blood pressure (BP), adequacy of control.

INTRODUCTION

Overall prevalence of hypertension in various parts of Nepal in recent years seems to range in between 19.7 and 22.7%.[1-4] Prevalence of hypertension seems rapidly increasing. Initial studies in Nepal showed the prevalence of hypertension to be around 5 to 10%.[5] There has been tripling (33.8%) of prevalence of hypertension in a Nepalese community during 25 years of period in a repeat cross-sectional study in rural Kathmandu.[6] Among the hospitalized medical patients, about one tenth (9.4%) of total medical patients of Nepal Medical College Teaching Hospital (NMCTH) were found to have hypertension.[7]

Hypertension doubles the risk of cardiovascular diseases including coronary heart disease (CHD), congestive heart failure, ischemic and hemorrhagic stroke, renal failure and peripheral arterial disease.[8] So, adequate control of BP in hypertensive patient is a must to prevent several of its complications. However, control of BP in Nepalese hypertensive patients were very poor[3] ranging in between 6%[1] and 9.5%. [6]Among the admitted hypertensive patients, BP control rates were variable with range in between 19 % and 72.4%.[7,9]

Renal diseases are quite common in Nepal. With a population of 27 million people the estimated incidence of ESRD is around 2700 /year if we take 100 cases of ESRD /million population at par with India and Pakistan.[10] Renal diseases seem increasing in Nepal. It was present in 5.6% of total medical admission in 1998 and in 16% in 2005 as analyzed in eight years of data of renal disorders in a tertiary care hospital in Nepal.[11]

Significant proportion of hypertensive patients had chronic kidney disease (CKD). Out of all admitted hypertensive patients, 14% had renal impairment.[7] However, evaluation of adequacy of control of BP in patients with chronic kidney disease and hypertension is very rare.[9,12] Here, we report our prospective evaluation of adequacy of BP control in a group of indoor CKD patients with hypertension in NMCTH.

MATERIALS AND METHODS

All consecutive indoor patients (52) with CKD and hypertension, attending echo-lab of Nepal Medical College Teaching Hospital for under going echocardiographic evaluation during 3 years period from Baisakh 2065 (April 16, 2008) to Chaitra 2067

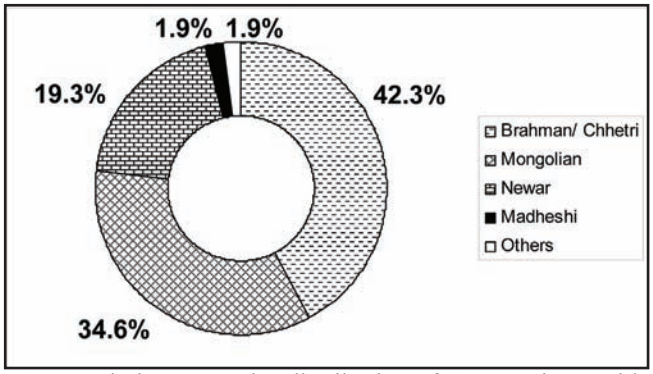

Fig. 1. Ethnic group wise distribution of CKD patients with hypertension

(April 15, 2011) in Nephrology Unit of NMCTH, were enrolled for this study. Mean age was 45.3 ± 16.7 years. Male female ratio was 8:5. Diagnosis of CKD has been done as per previous recommendation.[13] One patient's BP was normalized after starting hemodialysis without any use of antihypertensive medicine and was excluded from this study. Other's BP (n= 51) were followed up during admission for the evaluation of the adequacy of their BP control and their antihypertensive medications were reviewed.

BP measurement was performed as recommended previously. The auscultatory technique with a trained observer and mercury sphygmomanometer continues to be the method of choice for measurement in the office, using the first and fifth phases of the Korotkoff sounds. The use of mercury in sphygmomanometer is declining. Aneroid devices are suitable, but they require frequent calibration.[14,15] Doctor ® or ALPK2® aneroid sphygmomanometer (Japan) was used to measure BP in this study.

The National Kidney Foundation clinical practice guidelines (1997) recommend a blood pressure goal of<130 mmHg systolic and <80 mmHg diastolic for all CKD patients.[16] BP < 130/80 mm Hg is considered as intensive control of BP and BP control <140/90 mm Hg as usual (standard) control BP.[16] For the purpose of treatment, diagnosis of hypertension was made when the BP recording belonged to stage 1 hypertension (≥140/90 mm Hg) or more.[8] BP ≥140/90 mm Hg is considered as uncontrolled. Data are presented as numbers and percentages. Unpaired t-test was performed where appropriate and $p < 0.05$ was considered as statistically significant.

RESULTS

All consecutive indoor patients (52) with CKD and hypertension, attending echo-lab of Nepal Medical College Teaching Hospital for undergoing echocardiography in this prespective study of 3 years period from Baisakh 2065 (April 16, 2008) to Chaitra 2067 (April 15, 2011) in Nephrology unit of Nepal Medical College Teaching Hospital, were evaluated. Mean age was 45.3 ± 16.7 years. Male female ratio was 8:5.

Ethnic group-wise distribution is shown in Fig. 1. Brahman and chhetri (22, 42.3%) were the usual sufferers followed by mongolian (18, 34.6%) and newar (10, 19.3%).

Age group-wise distribution is shown in Fig. 2. There were two peaks in the age group wise distribution; one in 20-29 years age group (12, 23.1%) and the next in 50-59 years age group (12, 23.1%).

Adequacy of control of BP: The degree of BP control is shown in Table-1. Control of hypertension in CKD patients was difficult. More than two third of the patients (68.6%) had BP >140/90 mm Hg. About one third of the patients (31.4%) had BP control <140/90 mm Hg. Intensive BP control was present in less than one tenth of total patients (7.9%). Despite more efforts with use of more antihypertensive agents (3.0 ± 1.3 vs. 2.0 ± 0.8, $p<0.05$), uncontrolled group had BP > 140/90 mm Hg in comparison to intensive control group with BP <130/80 mm Hg.

Antihypertensive agents used: Antihypertensive medicines used in this study are shown in Table-2. Collectively, Diuretics (45, 88.2%), calcium channel blocker (44, 86.3%) and beta-blocker (25, 49%) were the common antihypertensives used. Amlodipine (39, 76.5%) and frusemide (39, 76.5%) were very popular antihypertensive agents used followed by alfa blocker, Prazocin (20, 39.2%) and beta-blocker, Metoprolol (11, 21.6%). Use of hydrochlorothiazide (e.g., Metolazone) was rare as a companion a drug only (2, 3.9%)

DISCUSSION

As of 2000, nearly one billion people or approximately 26% of the adult population of the world had hypertension.[16] It was common in both developed (333 million) and underdeveloped (639 million) countries.[17]

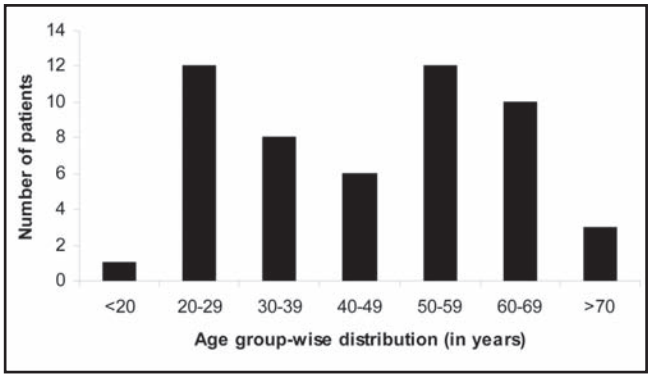

Fig. 2. Age group wise distribution of CKD patients with hypertension attending echo-lab of NMCTH

Table-1: Adequacy of BP control in hypertensive CKD patients

BP control	Number	%	Medicines used for BP control	p value*
<130/80 mm Hg	4	7.9	2.0 ± 0.8	
<140/90 to >130/80 mm Hg	12	23.5	2.7 ± 1.1	0.11
>140/90 mm Hg	35	68.6	3.0 ± 1.3	0.04
Total	51	100	2.8 ±1.2	

*p values compares number of medicines used in each group in comparison to BP<130/80 mm Hg

However rates vary markedly in different regions with rates as low as 3.4% (men) and 6.8% (women) in rural India to as high as 68.9% (men) and 72.5% (women) in Poland.[18] Because of escalating obesity and population aging, the global burden of hypertension is rising and is projected to affect 1.5 billion people or one third of the world's population, by the year 2025.

The prevalence of hypertension in urban Asian adult population varied between 15-35%.[19] Overall prevalence of hypertension in various parts of Nepal in recent years seems to range was 19.7 to 22.7%.[1-4] Prevalence of hypertension seems rapidly increasing in Nepal tripling (33.8%) in a Nepalese community during 25 years of period in a repeat cross-sectional study in rural Kathmandu.[6] The prevalence rate would be more if present criteria for diagnosis of HTN (>140/90 mm Hg) is accepted in stead of > 160/95 mm Hg.[6]

Hypertension doubles the risk of cardiovascular diseases including coronary heart disease, CHD, congestive heart failure, ischemic and hemorrhagic stroke, renal failure and peripheral arterial disease.[8] Currently high blood pressure (BP) causes about 54% of stroke and 47% of ischemic heart disease worldwide.[20] Lowering systolic BP by 10-12 mm Hg and diastolic BP by 5-6 mm Hg confer relative risk reductions of 35-40% for stroke and 12-16% for CHD within 5 years of the initiation of treatment. Risk of heart failure is reduced by >50%. So, adequate control of BP in hypertensive patient is a must to prevent several of its complications. Therapy with antihypertensive drugs reduces the incidence of all strokes 38% in women, by 34% in men, by 36% in older persons, and by 34% in persons older than 80 years.[21]

Kidney related diseases are quite common in Nepal. It is estimated to be around 10% of the country's 27 million inhabitants.[10] Over 10,000 Nepalese suffer from CKD due to increasing cases of hypertension and diabetes - the primary causes of kidney malfunction according to nephrologists of Nepal.[10] In a CKD and risk factors screening program in more than 3000 apparently healthy subjects at the community level in Eastern Nepal, Dharan, the burden of CKD risk factors such as diabetes (9.3%), hypertension (27%), overweight (25%) and smoking (35%) were high. In a subset group, CKD was detected in 10.6% of screened subjects.[22]

Renal diseases seem increasing in Nepal. It was present in 5.6% of total medical admission in the 1998 and in 16% in the 2005 as observed during 8 years evaluation in a tertiary care hospital in Nepal in the analysis of eight years of data of renal disorders. CKD was present in 56.0% of renal patients.[11]

In the ethnic group wise distribution of CKD patients with hypertension, Brahman and chhetri (22, 42.3%) were the usual sufferers followed by mongolian (18, 34.6%) and newar (10, 19.3%) (Fig. 1). These data were similar to ethnic group wise distribution of total CKD patients admitted in NMCTH during that period (Unpublished data). Similar data has been reported previously.[23] The cause may be the fact that these ethnic groups are mainly immigrated people to Kathmandu and stay in crowded places. Streptococcal infection (tonsillitis, skin infections) may be more common in these ethnic groups (e.g. Mongolians and Brahmans / chhetris). Poverty may have compounded the problem as trivial looking throat or skin infections may be ignored and

Table-2: Antihypertensive agents used

Antihypertensive	Number	Use in total patients (%)
Amlodipine	39	76.5
Nifedipine	4	7.8
Diltiazem	1	2
Frusenamide	39	76.5
Torsemide	4	7.8
Metolazone	2	3.9
Prozocin	20	39.2
Metoprolol	11	21.6
Atenolol	9	17.6
Carvidilol	5	9.8
Losartan	4	7.8
Enalapril/ Ramipril	3	5.9
Methyldopa	2	3.9
Clonidine	1	2
Total patients	51	
Total number of medicines	144	
Number of medicines/patient	2.8 ±1.2	

not treated. Khakurel *et al* have previously reported 41% of CKD were due to chronic glomerulonephritis.[10]

Male female ratio was 8:5. This finding is similar to gender-wise distribution of total admitted CKD patients in NMCTH (unpublished data) during the same period. Similar data has been reported previously.[23] The cause for more male involvement is not known. One cause may be the tradition of males receiving more and better treatment in our male dominated Nepalese society.

Mean age, 45.3 ± 16.7 years is similar to previous paper.[23,24] There were two peaks in the age group wise distribution (Fig.2); one in 20-29 years age group (12, 23.1%) and the next in 50-59 years age group (12, 23.1%). These data are similar to age group-wise distribution of total CKD patients admitted in NMCTH during this period (Unpublished data). Similar data has been reported previously.[23] The reason for two peaks in age group-wise distribution may be related with chronic glomerulonephritis caseing CKD in younger age group and hypertension/ diabetic nephropathy related CKD in elderly age group. Previous paper also indicated chronic glomerulonephritis as a common cause of end stage renal disease in Nepal.[10] Hypertension has been found to cause CKD in 13.7% to 54% patients.[10,23,24]

Our data (unpublished data) showed presence of hypertension in 158 patients (48.3%) which is similar to previous data.[23] It is higher than the community based data[10,23,24] Diabetes was detected in 74 (22.6%) patients (unpublished data). It is higher than previous data.[23] It is natural to have lower burden of hypertension and diabetes in community based study in comparison to the hospital based study.

Control of BP: The degree of BP control is shown in Table-1. Control of hypertension in CKD patients are terribly poor with more than two third of the patients (68.6%) have BP >140/90 mm Hg. About one third of the patients (31.4%) had BP control <140/90 mm Hg. Intensive BP control was present in less than one tenth of total patients (7.9%). This control rate is however better than previous BP control from the same centre with 19%[7] control of BP < 140/90 mm Hg in general hypertensive patients. The control of hypertension in admitted CKD patients may be difficult and challenging than in general hypertensive patient. Renal replacement therapy is usually necessary to support good control of BP in them. One hypertensive CKD patient had good control of BP simply by initiating hemodialysis.

Adhikary *et al* has reported far better intensive control of BP (72.4%) in CKD patients than our data of 7.9% with BP < 130/80 mm Hg.[9] They may have enrolled lots of milder CKD/hypertensive patients whose BP were easily controlled in the out patient department, OPD setting. In contrast, our patients were more difficult cases, who were admitted probably due to some other confounding problems (e.g. LVH, heart failure, valvular lesions, difficulty in controlling hypertension etc.) and underwent echocardiographic evaluation. OPD patients were not enrolled in this study. One cause may also be that their patients may be financially better affording than our patients. Their hospital is situated in a densely populated urban area near the only international airport of Nepal, The Tribhuvan International Airport. However, our hospital is situated in a semirural area of Kathmandu (Jorpati Village Development Committee) with lots of poor immigrated carpet factory workers residing in the surroundings of our hospital.

High poor control rates were not due to use of less antihypertensive medicines in inadequate dosages. Despite use of more antihypertensive agents (3.0 ± 1.3 vs. 2.0 ± 0.8, $p<0.05$), uncontrolled group had BP > 140/90 mm Hg in comparison to intensive control group with BP <130/80 mm Hg. It seems, some CKD patients are more sensitive and some were less sensitive to antihypertensive agents. Further study is necessary to better identify the sensitivity of Nepalese CKD/ hypertensive patients to available antihypertensive agents in a larger study population.

In our study, in average 2.8 ±1.2 medicines (1-6) were used to control BP, however Adhikary *et al* had used combination of three anti-hypertensive drugs in 51.4% patients and two drugs in 21% patients for the control of BP in hypertensive CKD patients. Number of medicines used was similar to the study by Minutolo *et al*. (2.5 ±1.1 in tertiary care and 1.9 ±1.1 in primary care.[12] In the antihypertensive and Lipid- Lowering Treatment to Prevent Heart Attack, ALLHAT trial, average number of antihypertensive agents used were two drugs and 40% of patients required more than one drug.[25] In another study, half of the patients in the tight-control group were taking 3 or more antihypertensive drugs, whereas more than two thirds of patients in the usual-control and uncontrolled groups were taking 3 or more antihypertensive agents.

Our approach for antihypertensive therapy is similar to the recommendation that drug therapy should be initiated with 2 antihypertensive drugs[27,28] if the BP is more than 20/10 mm Hg above the target BP. Considering the outcomes of various randomized clinical trials, our approach for antihypertensive therapy in CKD patients has been not too intensive, attempting to control BP within the range of 130/80 to 140/90 mm Hg but not too aggressively below 130/80 mm Hg.

Our control rate of BP (31.4%) is slightly better than previous studies of control of BP in Nepalese general hypertensive patients[3,29] with control percentage ranging from 6%[1] to 9.5%.[6] Among the admitted hypertensive patients, BP control rates were variable with range in between 19 % to 72.4%.[7,9] This control rate is quite reasonable in comparison to western data with poor control rate of 38% among patients,[30] who have to pay on their own for their antihypertensive therapy similar to Nepalese patients having no health insurance facility in general. Hypertensive patients with health insurance to pay their bills, had better control rate of BP of 70%. When aggressive antihypertensive therapy is attempted, better BP control has been reported up to 66%.[26] In the ALLHAT trial, One third of the patients did not reach the goal blood pressure of 140/90 mm Hg or less and had similar BP control rates.[25] Minutolo *et al* have also reported poor control of BP in hypertensive CKD patients in other international centre as well (5.8% in primary care centre and 21.5% in tertiary care centre).[12] That finding is similar to that of ours. A recent study in Nepalese CKD patients with hypertension, showed very high control rates of 72.4%.[9] This may mean aggressive approach in antihypertensive therapy may result in better control of BP however, there is strong debate about the usefulness of intensive BP control whether it is beneficial,[31-33] not beneficial[26,34,35] or harmful.[36,37] Some studies reported partly beneficial results of intensive BP control.[38,39]

The more aggressive control of BP among patients at high risk for CHD such as those with diabetes mellitus, chronic kidney disease, CHD or coronary artery risk equivalent, or a 10-year Framingham risk score ≥10% with maintenance of the BP below 130/80 mm Hg and below 120/80 mm Hg in patients with left ventricular dysfunction has been recommended by the AHA Task Force scientific statement in 2007.[40] It was based upon expert medical opinion at that time, not on prospective, randomized, adequately controlled trial data.[41]

Antihypertensive agents used: Among the antihypertensive medicines used in this study (Table-2), Amlodipine (39, 76.5%) and frusemide (39, 76.5%) were very popular antihypertensive agents used followed by alfa blocker, Prazocin (20, 39.2%) and beta blocker, Metoprolol (11, 21.6%). Despite being metabolized in liver and effective in renal failure torsemide[45] was less popular (4, 7.8%) in comparison to fruse mide. ARB (4, 7.8%) and ACE inhibitor (3, 5.9%) were also less preferred in our CKD patients.

ALLHAT trial have shown the degree of control BP rather than preference of one medicine or the other have stronger effect in reducing mortality and morbidity outcomes. Amlodipine had similar primary out come (fatal and nonfatal CHD as diuretics and ACE inhibitor but had increased heart failure and decreased new diabetes.[25] Use of amlodipine as the most popular antihypertensive agent may have been due to some influence of ALLHAT trial. Unexpectedly amlodipine also slowed renal deterioration better than other agents. Amlodipine is not nephrotoxic and a safe molecule as an initial choice or companion antihypertensive agent.

Among beta blockers, Metoprolol has been used in good number of patients (11, 21.6%). It is pharmacologically sound idea because it is chiefly metabolized in liver[42] in comparison to once upon a time very commonly used beta-blocker atenolol (9, 17.6%), which is mainly metabolized in kidney and may not be preferred in CKD patients. Some physicians still may be preferring atenolol. After understanding of the report of increased mortality noticed in the Losartan Intervention for Endpoint reduction in hypertension, LIFE trial, popularity of Atenolol has fallen drastically in clinical practice.[43] Despite reports of renoprotective effects of ARB[44] and ACE inhibitors,[45] they have been used in minimal proportion of the hypertensive CKD patients in this study. The cause of nonpreference of ARB and ACE inhibitor in this study may have been a matter of personal choice of treating nephrologists with the fear of the possibility of increment of serum potassium and creatinine in patients with CKD and hypertension.

In general hypertensive patients, ACE inhibitors / ARB were used in reasonable amount (30.4%)[29] which is more than that in CKD patients with hypertension. In a study by Minutolo *et al* ACE inhibitor and ARB were the main antihypertensive agent used (> 84%) for the control of BP in hypertensive CKD patients. [12] Cooper-DeHoff *et al* reported 75% or more of patients in all 3 groups were taking a renin angiotensin-system blocking agent.[26] We should also be a bit more liberal in using ARB and ACE inhibitor for their renoprotective effects in CKD/ hypertensive patients.

The main limitation of this study is not evaluating all general hypertensive patients and all CKD patients with hypertension. So the possibility of selecting patients with severe co morbid cardiovascular diseases for echocardiography, remained as the selection bias. A bigger prospective study including all hypertensive patients and CKD/hypertensive patients is necessary for better evaluation of adequacy of BP control in general hypertensive patients and CKD patients with hypertension.

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