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EFFECT OF COMORBIDITIES ON TARGET BLOOD PRESSURE AND TREATMENT INTENSIFICATION IN HYPERTENSIVE PATIENTS

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ABSTRACT

Background: Hypertensive patients with comorbidity are at risk of poor outcomes; however, there is little information known about the association of comorbidity with outcomes i.e., blood pressure control, treatment intensification and medication adherence. Our aim is to investigate their association with hypertensive patients. **Methods and Results:** A retro-prospective observational study was conducted on 231 hypertensive patients for six months in Warangal. They were assigned as groups i.e., Only HTN (63), HTN with DM (56), HTN with CVA (58) and HTN with CHD (54).Recommended BP control levels were≤140/90mmHg in general and ≤150/90mmHg in >60yr HTN without any comorbid. The overall BP control rate was 53.67%.HTN with CVA had higher odds of uncontrolled BP (OR 7.38, 95% CI: 3.26 to 16.72, P<0.001) and higher odds of medication non-adherence (OR 2.48, 95% CI: 1.17 to 5.23, P=0.017). HTN with CVA or CHD increased the chance of treatment intensification by 5 fold (P=0.0001/0.0003 respectively).

INTRODUCTION:

Hypertension is a common disorder with an estimated prevalence of 22% to 27% worldwide, and it is an important risk factor for cardiovascular disease (CVD) such as stroke and myocardial infarction[1]. Patients with hypertension are primarily treated in general practice, making it the most frequent reason for consultations with general practitioners (GPs)[2]. Many studies of hypertensive patients rarely based on primary care populations. The importance of treating patients with hypertension to target blood pressure (BP) levels applies to patients with and without co morbidities. As an example, patients with CVD have associate degree increased risk of recurrent stroke or infarct if their BP is on top of suggested levels. Low BP diminishes tissue perfusion and high BP with its co morbidities is steadily harming to body. So, a target of BP control ought to be such that, it should not be too low or too high to harm the body organs and function within a physiological range [3]. Only a few studies exist on the prevalence of hypertension and rates of BP control among patients with CVD; these studies are mainly based on small selected populations or are not situated in primary

care populations. Recent studies in India shown that hypertension is emerging as a major health problem and is directly responsible for 57% of all death due to stroke and 24% of all death due to coronary heart disease. Although 69% of people with hypertension are aware that they have the disease, among them only 54% receive treatment and only 27.4% achieve adequate blood pressure control [2]. The BP control rates are generally based on patients with and without co morbidities. Furthermore, patients with a chronic disease like hypertension often have 1 or more additional chronic co morbidity, and when patients have 2 or more co morbidities, the treatment of each of the co morbidities is generally poorer, which further affects a patient's chance of achieving BP control. To our knowledge, it has not been investigated how additional co morbidities are associated with BP control when patients already have diabetes and/or CVD. In this article, we aimed to analyze the association of co morbidities with BP control in a large cohort of hypertensive patients from primary care. The main objective of the study was to analyze the association of comorbidities with blood pressure control in a group of hypertensive patients and to assess treatment intensification (defined as dose increase, start or addition of drugs) due to effect of comorbidities in hypertensive patients.

METHODOLOGY

Present study was a retro-prospective observational study conducted between December, 2014 and September, 2015 in out-patient department of Multispecialty hospital, Hanamkonda, Warangal, Telangana state which involved collecting, analyzing data and determining the association between different parameters collected. Study population with age in between 25 years to 80 years diagnosed with hypertension and/or with any mentioned co morbidity (i.e. DM, CVA or CHD) was taken by convenient sampling method. Persons with diabetic complications, chronic kidney disease and receiving maximal treatment in whom further intensification by the general physician is not indicated (i.e., ≥3 antihypertensive drug classes on maximal maintenance dose) were excluded from the study.

Study materials

All the relevant and necessary data was collected by interviewing patients or patient care takers, patient case sheets and prescriptions. The data collected includes demographics (age and sex), past medical and medication history (hypertension and any comorbidity), social history, blood pressure, treatment chart and adherence score (Hill-Bone scale)[4]. The above information collected was documented in the designed data collection form.

Study procedure:

The participants were included in the study according to inclusion criteria and then they were assigned to 4 major groups' i.e.

- **Group A**: Only HTN
- **Group B**: HTN with DM
- **Group C**: HTN with CVA and
- **Group D**: HTN with CHD

Patients Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured with a sphygmomanometer, placed on the right arm of a seated patients who had rested in the sitting position for 5min before the measurement. Three blood pressure measurements were registered during 6 month period and the mean of these measurements were used in the study. Treated hypertensives were defined as patients receiving antihypertensive treatment irrespective of their current BP level. According to JNC 8, each group treated hypertensives were divided into controlled and uncontrolled blood pressure groups[5].

In group A (HTN), controlled hypertension patients were defined as those with age <60yrs, SBP ≤ 140 mm Hg, DBP ≤90 mm Hg and those with age >60yrs, SBP ≤150 mm Hg and DBP ≤90 mm Hg. In group B (HTN with DM), group C (HTN with CVA) and group D (HTN with CHD), controlled

hypertension patients were defined as those with SBP ≤ 140 mm Hg and DBP ≤90 mm Hg. Treatment chart data was collected from all patient groups and assessed changes in treatment during every follow-up visit and used to analyze treatment intensification. Treatment intensification is defined as any dose increase and/or addition or start of new drugs[6]. Compliance to medication regimen was assessed by using Hill-Bone scale questionnaire. Questions were developed for this study to assess knowledge about hypertension treatment and compliance. The questions in the Medication Adherence Scale used in this study was developed using the Hill-Bone Adherence to Blood Pressure Therapy Scale. A total of seven questions relevant to the local setting were selected. In completing the questionnaires, patients were required to choose their response from a set of possible answers. Every question during this Medication Adherence Scale had a four-point Likert-type response format. Every response carried a score: none of the time = four, some time = three, most time = two, and every time = one. The overall scores were additional for every patient. The overall score for every patient might vary from seven (minimum) and twenty eight (maximum). Lower scores (<25) would mirror poorer adherence to medication medical care. A score of 26-28 were outlined as adherence[3]. The primary outcome measure is optimal BP control and to analyze association of comorbidities in relation to BP control. The key secondary outcome is to evaluate the relationship between comorbidity and treatment intensification.

RESULTS

The present study reviewed 282 patients, among them 231 patients were enrolled in the study according to inclusion criteria. Out of 231 patients included, most of them were male 133 (57.57%) followed by female 98 (42.42%). According to collected demographic data, the overall mean age was found 57.80 ± 10.58 yrs. The 231 patients were distributed according to their diagnosis into 4 groups i.e., group A (only hypertension without any comorbidity), group B (hypertension with diabetes), group C (hypertension with cerebro vascular accident) and group D (hypertension with coronary heart disease).

Table 3 shows that the association between comorbidities and blood pressure control was statistically significant. Group C (HTN+CVA) patients had higher odds of uncontrolled BP (OR 7.38, 95% CI: 1.95 to 9.47, p<0.001) compared with group A (only HTN) patients. The same statistically significant tendencies were seen for Group B (HTN+DM) patients with OR for uncontrolled BP at 4.03 (95% CI: 1.95 to 9.47, p=0.003) and group D (HTN+CHD) patients with OR for uncontrolled BP at 2.59 (95% CI: 1.16 to 5.79, p=0.019) when compared with group A (only HTN) patients. Table 4 shows that during the follow-up period, 32.46% underwent treatment intensification. Among included study population, 25.54% of patients had a start of new drug, 1.29% had addition of new drug and 5.62% had a dose increase.

Table 5 shows that the association between comorbidities and treatment intensification was statistically significant with group C and group D patients. Group C (HTN+CVA) patients had increased chances of treatment intensification (OR 5.58, 95% CI: 2.31 to 13.45) when compared with group A (only HTN) patients. Group D (HTN+CHD) patients with OR for treatment intensification at 5.17 (95% CI: 2.13 to 12.53) was significant whereas group B (HTN+DM) patients with OR for treatment intensification at 1.90 (95% CI: 0.75 to 4.82) was not significant when compared with Group A (only HTN) patients.

Table 9 shows that the association between comorbidities and medication adherence was statistically significant only with group C. Group C (HTN+CVA) patients

had higher odds of medication non-adherence (OR 2.48, 95% CI: 1.17 to 5.23) compared with group A (only HTN) patients. Group B (HTN+DM) and group D (HTN+CHD) patients with OR for medication non-adherence at 1.41 (95% CI: 0.66 to 2.98) and 0.614 (95% CI: 0.26 to 1.41) respectively were non-significant when compared with Group A (only HTN) patients.

DISCUSSION

In our study, the average number of antihypertensive medication was found to be 1.59 per patient and the most commonly prescribed antihypertensive medications were Angiotensin Receptor Blockers (ARB's) followed by beta blockers. The overall blood pressure control rate was 53.67% which was almost inconsistent with the study done by Naliya R Bulatova *et al*. where the average number of antihypertensive medication was 2.38 per prescription and the blood pressure control rate was 44%. This slight difference with previous studies may be due to JNC 8 BP goal recommendations followed in our study and Naliya R Bulatova study followed JNC 7 recommendations. Although our study showed higher BP control than previous study, their control rates are still inadequate, because their risk of comorbidities increases with BP above recommended level [7].

Blood pressure control rates for patients among all groups i.e., only HTN, HTN+DM, HTN+CVA and HTN+CHD were found to be 77.77%, 44.82%, 33.33% and 57.4% respectively. We found that hypertension patients with DM or CVA have a much lower degree of BP control than the hypertensive patients without any comorbidity which is consistent with the study done by Maja S. Paulsen *et al*. in which patients with diabetes (50%) have much lower degree of BP control than the general population of patients with hypertension and HTN+CHD patients (58.7%) have higher BP control than HTN+DM patients [2].

Our study also showed that co-morbidity is an important aspect to consider because uncontrolled BP odds ratio ranged from 2.59 (HTN+CHD) to 7.38 (HTN+CVA), which is suggestive that hypertensive patients with CVA need great attention in controlling BP. One of the most important finding of our study is an investigation of treatment intensification among hypertensive patients. Over 6 months follow-up, the hypertensive patients received less than expected intensification (67.53%) of either their medication class or dose despite having opportunities for intensification and documentation of elevated BP. Stacie L. Daugherty et al. similarly found that a suboptimal medication regimen was common, accounting for 58% of hypertensive patients [8]. Treatment intensification was significantly seen in hypertensive patients with CVA or CHD comorbidities. Potential reasons for less than expected treatment intensification may include competing demands of comorbid conditions and may be blood pressure levels felt to be close enough to control levels. Failure to intensify therapy may also be related to a lack of evidence to support the efficacy of adding additional agents to those already on 1 or more antihypertensive class[8]. The benefit of blood pressure reduction with antihypertensive drug treatment has become increasingly evident, with decrease in both all cause mortality and coronary artery disease as shown by multiple clinical trials and epidemiological studies[9]. In our study, adherence regard in taking antihypertensive was 63.20% (according to Hill-Bone Adherence scale) which is consistent with the study done by Gloria N. Mafutha *et al*. in which compliance with regard to taking antihypertensive medication was 70%. In our study, we found that medication adherence was significantly associated with hypertensive patients with CVA comorbidity.

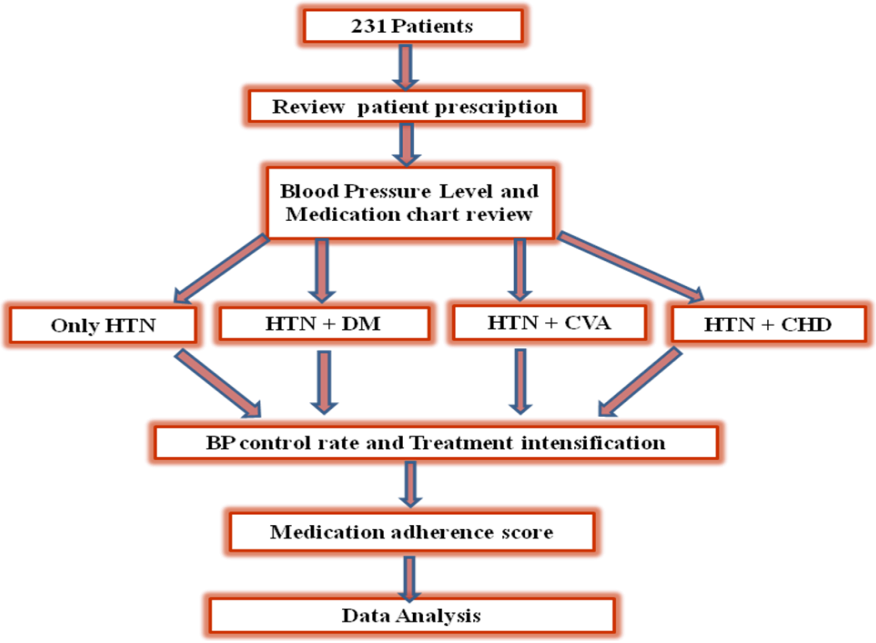

Fig 1: Methodology flow chart

Table 1: Proportion of patients along with mean and standard deviation of age among each group

Group	ICD Code	Number of patients (N %)	Age (in yrs)	
			Mean ± SD	P Value
Group A (HTN)	I10	63 (27.27)	56.76 ± 9.78	-
Group B (HTN + DM)	I15.2	58 (25.10)	57.79 ± 10.49	0.57
Group C (HTN + CVA)	I67.4	56 (24.24)	56.62 ± 11.95	0.94
Group D (HTN + CHD)	I11.0	54 (23.37)	60.5 ± 9.94	0.04

Table 2: Antihypertensive drug distribution among included study population

Group	1 Drug (n %)	2 Drugs (n%)	3 Drugs (n%)	4 Drugs (n%)
Group A (HTN)	33 (52.38%)	23 (36.50%)	7 (11.11%)	0 (00.00%)
Group B (HTN + DM)	26 (44.82%)	28 (48.27%)	3 (05.17%)	1 (01.72%)
Group C (HTN + CVA)	34 (60.71%)	20 (35.71%)	2 (03.57%)	0 (0.00%)
Group D (HTN + CHD)	23 (42.59%)	25 (46.29%)	5 (09.25%)	1 (01.85%)
TOTAL (N%)	116 (50.21%)	96 (41.55%)	17 (07.35%)	2 (0.86%)

Table 3: Effect of co morbidity on target BP

Group	Uncontrol	Control	Odds ratio (95% CI)	P Value
Group A (HTN)	14	49	-	-
Group B (HTN + DM)	32	26	4.03 (1.95 to 9.47	0.003
Group C (HTN + CVA)	38	18	7.38 (3.26 to 16.72)	<0.001
Group D (HTN + CHD)	23	31	2.59 (1.16 to 5.79)	0.019

Fig 2: Blood pressure control among different groups

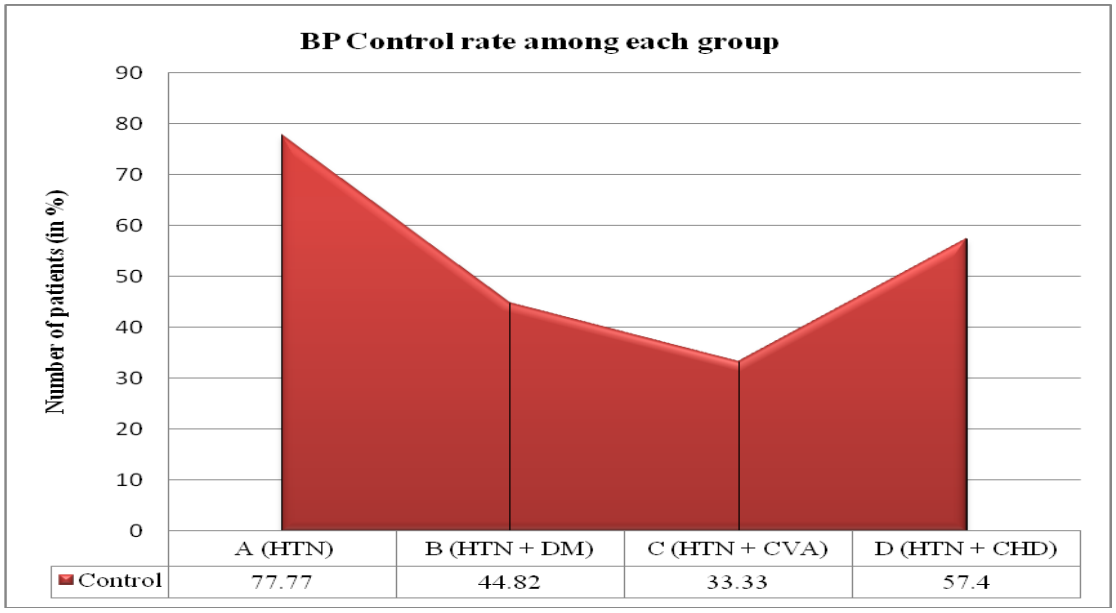

Fig 2 shows that patients in group A (HTN) had higher control rate 77.77% followed by group D (HTN+CHD) having control rate of 57.40% then Group B having 44.82% and least control rate was found in group C (HTN+CVA) 33.33%.

Table 4: Antihypertensive treatment pattern among study population

Total	Continue same treatment (CST)	Treatment intensification		
		Dose increase	CST+ New drug	New drug
No. of patients (N %)	156 (67.53)	13 (5.62)	3 (1.29)	59 (25.54)

Table 5: Effect of co morbidity on treatment intensification

Group	Treatment intensified	Treatment non-intensified	Odds ratio (95% CI)	P Value
Group A (HTN)	9	54	-	-
Group B (HTN + DM)	14	44	1.90 (0.75 to 4.82)	0.17 (NS)
Group C (HTN + CVA)	27	29	5.58 (2.31 to 13.45)	0.0001
Group D (HTN + CHD)	25	29	5.17 (2.13 to 12.53)	0.0003

Figure 3: Medication adherence among each group

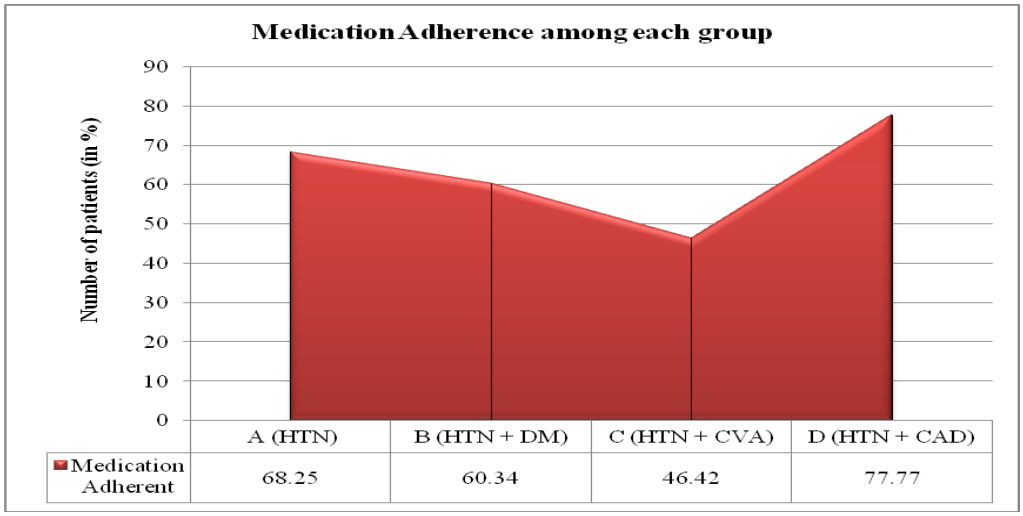

Table 6: Effect of co morbidities on medication adherence

Group	Medication non-adherent	Medication adherent	Odds ratio (95% CI)	P Value
Group A (HTN)	20	43	-	-
Group B (HTN + DM)	23	35	1.413 (0.66-2.98)	0.36 (NS)
Group C (HTN + CVA)	30	26	2.48 (1.17-5.23)	0.017
Group D (HTN + CHD)	12	42	0.614 (0.26-1.41)	0.25 (NS)

This indicates that treatment intensification, but not treatment adherence was significantly associated with DM or CHD comorbidities whereas, treatment intensification and medication adherence both were significantly associated with CVA co morbidity.

CONCLUSION

The most common comorbidity in hypertensive patients was DM followed by CVA then CHD. The rate of blood pressure control for hypertensive patients was low; approximately 1 in 2 patients with hypertension met blood pressure targets suggesting that the patients may either not treated aggressively enough or not adhered to medication. BP control rates differ within comorbidities of hypertension. Higher BP control rate was found in only hypertensive patients without any comorbidities and BP control rate was poorer among hypertensive patients with CVA. Our study findings suggest hypertensive patients with CVA need a greatest attention in controlling BP. The study also identifies that all comorbid conditions in hypertensive patients decrease the BP control rate. The association between co morbidities and treatment intensification was statistically significant in all our included groups. Most visits of patients with an elevated BP were not associated with subsequent treatment intensification. Good adherence was observed in overall study patients. The association between comorbidities and medication adherence was significant statistically only in patients with hypertension and CVA. Hypertensive patients with CVA appear to have least average medication adherence unlike other

comorbid hypertensive population. To achieve good adherence, patient education is required for patients with hypertension and CVA. Less treatment intensification and poor adherence rate were found to negatively affect the blood pressure control. Treatment intensification, but not the medication adherence was significantly associated with DM or CHD comorbidities whereas, treatment intensification and medication adherence both were significantly associated with CVA co morbidity in hypertensive patients.

LIMITATIONS OF THE STUDY

The limitation of the present study is small sample size. The study used co morbidity as documented in the medical records. The study included the start of new medication as a clear action competing with care but was not able to incorporate the effect of other interventions, such as discussion of life style issues.

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