Prescription Pattern Analysis And Predictors of Hypertension Associated Metabolic Disorders In Population of Punjab

Praveen P Balgir[1], Jaspreet Kaur[2], Harsimran Kaur[3], Satbir Kaur[4], Rajesh Kumar Goel[5]
[1, 2]Dept of Biotechnology
[3,] 4Departement of Human Genetics,
[5]Department of Drug and Pharmaceutical Research
[1, 2, 3, 4, 5]Punjabi University, Patiala, Punjab, India-147002

Abstract-

Context

Hypertension (HT) is a major risk factor for heart attack and stroke. Cross-sectional studies have reported that the prevalence of metabolic dysfunctions in hypertensive patientsincreases with disease progression.

Aim

The present study was planned, with the objective of revealing predictors of metabolic disorders among chronic hypertensive Punjabi population. It is also help in identifying the most appropriate drugs combination regimen for the present population.

Settings and Design

A 3-year cross sectional retrospective study was planned, in which hypertensive patients from different districts of Punjab from 2013 to 2016 were enrolled who met the inclusion criteria.

Methods and Material

A total of 1400 hypertensive patients were selected. Adjusted relative risks associating each risk factor and incidence of hypertension by sex, after controlling for confounders such as age, body mass index (BMI), life style habits, other metabolic diseases, medication for hypertension, and change in medication were surveyed by filling the questionnaire with their informed consent.

Statistical analysis used: *Statistical Package for Social Sciences (SPSS) version16.*

Results

Among physiological risk factors age group, genders and family history was significantly associated with development of metabolic dysfunction. It was observed that out of a total of 1400 hypertensive patients, 490 (35%) patients were suffering from other metabolic disorders. While comparing drug regimen of patients, it was observed that 70.6% were onMono therapy and29.3 % were on two drug therapy. A significantly (p=0.009) higher number of patients on monotherapy were observed to develop other MD.

Conclusion

The alarming increase in the development of diabetes along with hypertension worldwide, should first prompt implementation of life style changes like intake of healthy diet, physical activity, moderation in alcohol consumption, smoking cessation and control blood glucose and lipid levels. The present study has thrown light on onset of a number of metabolic disorders associated with hypertensionvis-a-vis antihypertensive medication.

Keywords- Risk factors, Punjabi population, Hypertension, Anti- hypertensive drugs and Diabetes

I. INTRODUCTION

Hypertension (HT) is one of the major chronic diseases resulting in high morbidity and mortality all over amongst world populations. HT has become an important public health challenge now. The burden of hypertension varies remarkably throughout various regions of the world and is a serious public health problem in both developed and developing countries. World Health Organization (WHO, 2005) data indicate that by 2025 the global burden of hypertension will increase by 60% to be 1.56 billion individuals worldwide and higher in the developed nations[1].
HT is one of the most important risk factors for other metabolic disorders. Many of us are unaware of the presence of hypertension because hypertension does not show any

symptoms in early stage. Some simple screening test can helps to detect the presence of high blood pressure and it is purely treatable. Understanding the burden of hypertension, as a preventable disease, and underlying risk factors by organizing population screening is the first step towards planning any effective preventive programs, so that this disease can be cured at early stage. Prevention programs depend on the identification of potentially modifiable risk factors. For example, obesity, life style habits, and insulin resistance, all of which are identified as strong risk factors for HT along with other metabolic disorders[2].

HT and Type2 Diabetes are the 2 major chronic diseases frequently coexisting, with increased incidence with age. HT is about twice as common in patients withType2 Diabetes than in those without (8%)[3].The number of people with diabetes in India currently around 62 million, is expected to rise to 79.4 million by 2030[4,5]. HT substantially increases the risk of both macro vascular and micro vascular complications including stroke, coronary artery disease, peripheral vascular disease, retinopathy, nephropathy and neuropathy[6].

The progressive decline in glomerular function that is seen in diabetic patients with hypertension, especially those with albuminuria can be slowed with antihypertensive treatment. Appropriate use of anti-hypertensive agents can control Blood Pressure (BP) and reduce complications in patients with diabetes. Evidence also supports the need for using multiple anti-hypertensive agents rather than monotherapy to achieve target BP and greater reno protection[7].

Subsequently, the results of some epidemiological studies and clinical trials suggested a causal link between the hypertension and its risk factors. Various hypotheses have been put forward to explain the rising prevalence of hypertension in India. India, is a diverse nation, consist of various cultures. Many differences would be noted in the region-wise prevalence of hypertension, but research regarding the same is inadequate in Punjab. This inadequacy necessitates conduct of present study with the objective of assessing the prevalence and associated risk factors for developing metabolic dysfunction along with hypertension.

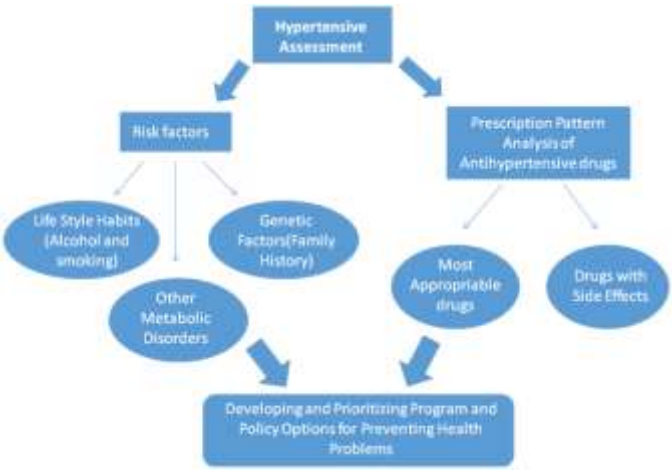

Figure 1: Overview of the study

II. SUBJECTS AND METHODS

Questionnaire

The following information was collected from each subject through a validated questionnaire: age, sex, weight, height, life-style habits like smoking and alcohol consumption, medication history, change in medication, family history and other metabolic diseases.This was an observational drug survey conducted in hypertensive subjects from various hospitals of different district of Punjab. It included patients from Abohar, Barnala, Chandigarh, Faridkot, Fazilka, Mohali, Mukstar, Patiala and Ropar. The total of 1400 (670 during 2013-14, 420 during 2014-15 and 310 during 2015-2016) hypertensive patients were screened.All patients in the study group were explained about the purpose of the study and the consent was obtained. The study was approved by institutional ethical committee (ICEC/4/2011).

Inclusion and exclusion criteria: Selection criteria for subjects:

Age: 30 - 70 Years,
Genders: Both

*Inclusion Criteria:*As per Indian hypertension guidelines -II: Hypertension in adults age 18 years and older is defined as systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood pressure (DBP) of 90 mm Hg or greater or any level of blood pressure in patients taking antihypertensive medication were included in our study.

Exclusion Criteria: Secondary forms of Hypertension isolated systolic HT, presence of a cardiac pacemaker, renal disease and pregnancy or lactation.

Definition of variables: HT was defined as SBP/DBP≥140/90 mmHg or if the patient was on medication for hypertension or had a positive self-reported history of hypertension[8]. Diabetes was defined as fasting blood sugar FBS >126 or non-fasting blood sugar≥200 or on any medications for diabetes mellitus[9]. Self-reported ischemic heart disease was taken as present if there was a self-reported history of myocardial infarction, percutaneous angioplasty or coronary artery bypasses surgery. BMI was calculated using the formula of weight(kg)/height(m^2) as data were collected for height and weight of the participants. The other variables like family history, metabolic disorders and life style habits (alcohol, smoking) were considered upon their voluntary disclosure. Individuals with either a parent or a sibling (brother or sister)having hypertension were considered to have a positive family history. A person was considered to be diabetic or suffering from any other metabolic disorder if he/she was already diagnosed case of diabetes and/or on treatment. Anyone smoking at least one cigarette per day for a minimum of the past six months was considered as smoker and others were classified as non-smokers. For alcohol intake subjects were categorized as alcoholic if they consume 30 ml of ethanol per day i.e. 720 ml of beer per day or 300 ml of wine.

Statistical Analysis: The physiological risk factors including age, sex, weight, height, life-style habits like smoking and alcohol consumption, medication history, change in medication, family history were analyzed in hypertensive subjects with MD and without MD.These statistical analyses were performed using GraphPad Prism version 7 and SPSS v 16.0 for windows. For all data analyses, p-value less than or equal to 0.05 was considered to be significant.

III. RESULTS

Total 1400 participants from the some districts of the Punjab were screened to identify the risk factors of hypertension in Punjabi population and to find the antihypertensive drugs prescription pattern followed by various physicians of Punjab. . The information regarding the history of presence of other metabolic disorders were also collected among hypertensives.

Table 1: District wise distribution of hypertensive study subjects from Punjab.

District	No. of surveyed patients
Ropar	50
Patiala	503
Abohar	50
Fazilka	50
Muktsar	160
Barnala	110
Faridkot	35
Mohali	212
Chandigarh	230
Total	1400

During the survey period of two years and seven months from August 2013 to 2016, 1400 hypertensive patients who met the inclusion criteria were selected.

The age group of the patients varies from 30-70 years (Table2). Only 26.07% of the total patients were below 40 years of age group, rest 74%was above 40 years. The age group with highest prevalence of hypertension was that of 40-49 years at 34.5%. When hypertensive patients from various age groups were compared as to prevalence of metabolic disorders amongst them, it was observed that across all age groups metabolic disorders werereported however here also 40-49 age group was observed to carry a higher burden of metabolic disorders as compared to other groups.

Table 2: Age wise comparison of the hypertensive study subjects

Age (in years)	Hypertensive n=1400 (%)	HT with MD n=490 (%)	HT without MD n=910 (%)	p-value (S/NS)	Odds ratio with 95% CI
30-39	365(26.07%)	98 (20%)	267 (29.3%)	(Reference)	
40-49	483(34.5%)	183 (37.3%)	300 (33.0%)	0.0008 (S)	1.6619 (1.2366 to 2.2336)
50-59	301 (21.5%)	103 (21.1%)	198 (21.8%)	0.04 (S)	1.4173 (1.0168 to 1.9755)
60 and above	251 (17.9%)	106 (21.6%)	145 (16.0%)	0.0001 (S)	1.9917 (1.4161 to 2.8012)

Gender wise distribution amongst patient population as to prevalence of metabolic disorders amongst them, revealed a statistically significant number of patients from both genders reporting suffering from metabolic disorders. Thus both sexes are equally prone to develop metabolic disorders.

Table 3:Gender wise distribution of the hypertensive study subjects

Gender	Hypertensive n=1400	HT with MD n=490	HT without MD n=910	p-value (S/NS)	Odds Ratio With 95% CI
Male	751 (53.6%)	272 (55.5%)	479 (52.6%)	0.0001 (S)	0.2828 (0.2330 to 0.3432)
Female	649 (46.3%)	218 (44.4%)	431 (47.3%)	0.0001 (S)	0.2541 (0.2059 to 0.3135)

Among male subjects habits of smoking and alcohol were also observed. Patients having drinking habits were found to be at higher risk of developing metabolic disorders (57%) as compared to non-drinkers (28.6%) with a significant p-value of <0.0001.This shows that consumption of alcohol also predisposes the males towards metabolic disorders, in other words we can say that it is an aggravating factor. 28% of males, who were not taking alcohol, also developed some metabolic disorders which may be attributed as response to some anti hypertensive drugs or other factors. The choice of medications may also affect one or more components of the metabolism of the individuals.However in present study the development of metabolic disorders in response to drugs did not show any significant difference amongst smoker and non-smoker hypertensive.

TTable 4: Prevalence of alcohol and smoking habits among hypertensive study subjects

Life-style habits	Hypertensive n=1400 (%)	HT with MD n=490 (%)	HT without MD n=910 (%)	p-value (S/NS)	Odds Ratio With 95% CI
Alcoholic	316 (22.6%)	180 (57%)	136 (43%)	<0.0001 (S)	3.3046 (2.5512 to 4.2804)
Non-Alcoholic	1084 (77.4%)	310 (28.6%)	774 (71.4%)		
Smoker	273 (19.5%)	82 (16.7%)	191 (21.1%)	0.06 (NS)	0.7566 (0.5685 to 1.0069
Non-smoker	1127 (80.5%)	408 (83.3%)	719 (79.0%)		

BMI comparison carried out among hypertensive patients revealed 32.0% (n= 448) of the subjects had a healthy BMI, rest 68.0% (952) subjects were overweight. Since BMI determines obesity which is a known risk factor in development of hypertension [10]. General obesity leads to various metabolic disorders also, a comparison of MD with respect to BMI among Hypertensive Patientsrevealed a statistically significant difference (p-value <0.0001), with higher MD rate amongst overweight Patients.

Table 5: BMI comparison of hypertensive study subjects

BMI	Hypertensive n=1400 (%)	HT with MD n=490 (%)	HT without MD n=910 (%)	p-value (S/NS)	Odds Ratio With 95% CI
BMI <24kg/m² (Desirable)	448 (32.0%)	72 (16.1%)	376 (83.9%)	<0.0001 (S)	0.1198 (0.0917 to 1.5665)
>25kg/m² (overweight)	952 (74.8%)	418 (43.9%)	534 (56.1%)		

Those who are taking antihypertensive drugs and also have family history of suffering from HT were observed to have significantly higher preponderance of patients ailing from other metabolic disorders. Among those who did not have a family history, majority 73% of patients did not suffer from any other MD.Since all antihypertensive drugs target proteins involved in the etiology of HT, the genetic variability in such proteins may result in variation in the pharmaco dynamic influences which get compounded in patients with family history[11], resulting in other metabolic disorders amongst such patients.

Table 6: Prevalence of family history of hypertension among study subjects

Family history	Hypertensive n=1400 (%)	HT with MD n=490 (%)	HT without MD n=910 (%)	p-value (S/NS)	Odds Ratio With 95% CI
Family History	378 (27.0%)	214 (56.6%)	164 (43.4%)	<0.0001 (S)	3.5270 (2.7582 to 4.5100)
No family history	1022 (73.0%)	276 (27%)	746 (73%)		

The patients who respond to hypertensive drugs as effective responders lead to lowering of blood pressure, however if the patients as a result of their genetic makeup show a variability in response to drugs they may develop other metabolic disorders[12]. To analyze the response of Patients from Punjab to the drugs being prescribed, the patients were grouped as per the drugs prescribed as shown in Table No.7. Among hypertensives 70.6% of patients were under monotherapy and rest 29.4% were on two-drug therapy. A major group of patients receiving monotherapy were using 37.8 % ACEIs (Enalapril, Ramipril, Meoxipril, Lisinopril) class followed by 28.2% ARBs (Telmisartan, Losartan, Olmesartan,), 23.7% BBs (Atenolol, Metoprolol), 6.2% CCBs (Amolodipine) and 4.2% were on diuretics (Furosemide, Torasmide) (Table No. 7). In combination therapy two drugs combinations,Consisted of ARBs + Diuretics (Telmisartan+Chlorthalidone) (46.2%) given to majority of patients followed by CCBs + BBs (Amolodipine+Atenolol) (33.6%) and CCBs+Diuertics(Amlodipine +Hydrochlorothiazide) (20.2%).

While comparing patients under monotherapy with two drug therapy, a significantly (p=0.009) higher number of patients on monotherapy were observed to develop other MD. Out of a total of 989 patients on monotherapy 376 (38%) were found to be suffering from other MD. On comparison among the different classes of monotherapy, highest % of Metabolic Disorder sufferers were found among the patients taking ARBs (52.7%) followed by BBs (46.5%) as compared to the overall 38% MD amongst all patients on montherapy .In case of ACEIs, CCB and Diuretics users, a statistically significant lower prevalence of MD was observed as to the overall 38% MD in monotherapy.

No significant difference was found amongst patients on the two drug therapy when various drug combination were compared for the propensity to develop MD, to overall 27% MD frequencies amongst such patients.

Table 7: Prevalence of commonly used antihypertensive agents among Hypertensive subjects

Drug Therapy	Drugs prescribed	Hypertensives	HT patients with MD	HT patients without MD	p-value (N/NS)	Odds ratio 95%CI
	1.Ace Inhibitors (ACEIs)	373 (37.8)%	98 (26.3%)	275 (73.7%)	0.0001 (S)	0.5810 0.4462 to 0.7565
	2.Angiotensin II Receptor Blockers (ARBs)	279 (28.2)%	147 (52.7%)	132 (47.3%)	<0.0001 (S)	1.8156 1.3890 to 2.3731
	3. Beta-blockers (BBs)	234 (23.7)%	109 (46.5%)	125 (53.4%)	0.02 (S)	1.4216 1.0688 to 1.8945
	4.Calcium channel blockers (CCBs)	61 (6.2)%	13 (21.3%)	48 (78.7%)	0.01 (S)	0.4415 0.2361 to 0.8258
	5.Diuretics	42 (4.2)%	9 (21.4%)	33 (78.6%)	0.03 (S)	0.4446 0.2104 to 0.9396
Total		989*	376* (38%)	613 (62%)		
Two Drug combinatio n	1.CCB + BBs	138 33.6%	41 (29.7%)	97 (70.3%)	0.65 (NS)	1.1012 0.7205 to 1.6830
	2.ARBs + Diuretics	190 46.2%	54 (28.4%)	136 (71.6%)	0.86 (NS)	1.0344 0.7059 to 1.15159
	3.CCBs+Diuretics	83 20.2 %	19 (22.9%)	64 (77.1%)	0.36 (NS)	0.7734 0.4437 to 1.3483
Total		411*	114* (27.7%)	297 (72.3%)		

*p-value= 0.009

Amongst all 1400 hypertensive patients 490 (35%)were observed to be suffering from metabolic disorders . The remaining 65% patients were hypertensive but had no other metabolic disorder. Out of 490 patients with metabolic disorder 270 were diabetic, 80 suffered high lipid profile, 56 were found to suffer from hyper/hypothyroidism, 49 were having kidney problems and 35 had suffered MI. Out of total 279 ARBs users, 147 (52.6%) developed MD. Out of these 147, 98 (66%) developed diabetes. Similarly a total of 234 BBs users, 109 (46.5)% developed MD. Out of which 47 (43.1%) developed diabetes. In case of 373 ACEIs users, 98 developed MD and out of which 27 (27.5%) were diabetic. Hence a comparison between these three classes was carried out in order to predict the relative risk for the development of new onset diabetes amongst the hypertensive patients under monotherapy (Table No.8).

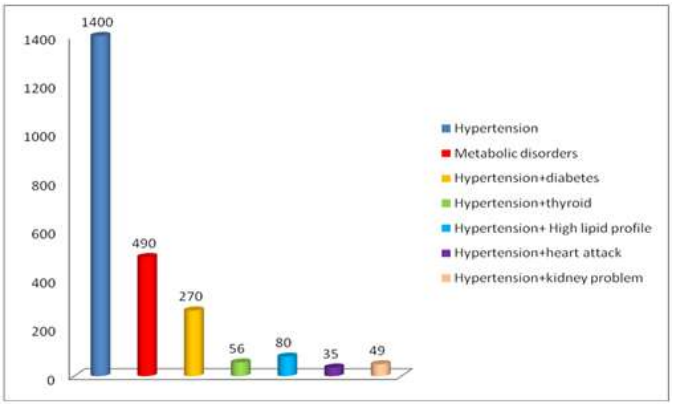

Figure 2: Distribution of Metabolic disorders among hypertensive subjects

It was observed that maximum numbers of hypertensive pateints were having diabetes as MD; as compared to other complications. Thus, drug pattern of the patients who developed diabetes after taking antihypertensive medication for the treatment of hypertension were studied. Out of 270 patients, 202 patients were taken into consideration who on developing hypertension were put on antihypertensive drugs after which they developed new onset diabetes.

From the antihypertensive prescription pattern it was found that among the 202 HT patients with diabetes, 172 (85.1%) wereon monotherapy and 14.9% were on two drug therapy.In case of mono-therapy most commonly prescribed drugs were ARBs (56.9%) followed by BBs (27.3%) and Ace Inhibitors (15.7%). Since two drug therapies did not show statistically significant effect as to development of MD (Table No7), further analysis was carried out on 172 (85.1%) patients using monotherapy. When the patients on monotherapy were compared (Table No.8) as to development of new onset diabetes both ARB and BB antihypertensive drug users showed more statistically significant preponderance as compared to ACE Inhibitor users.

Table 8: Distribution of anti-hypertensive drugs amongst hypertensive patients with diabetes

Metabolic Disorders	Drug Therapy	Drugs prescribed	Patients (%)	p-value (S/NS)	Odds Value (95 % CI)	Relative Risk (RR)
Diabetes	Mono-therapy	ARB	98 (56.9%)	ARB Vs BB 0.0003 (S)	2.085 (1.402 to 3.125)	1.691 (1.261 to 2.287)
		BBs	47 (27.3%)	BB Vs. ACE 0.04 (S)	1.741 (1.049 to 2.934)	1.582 (1.033 to 2.438)
		ACEIs	27 (15.7%)	ACE VsARB <0.0001 (S)	0.275 (0.168 to 0.438)	0.3738 (0.253 to 0.544)
		Total	172			

While comparing the relative risk among the diabetic patients,it was observed the value of RR was greater than 1(significant value) in ARBs and BBs and less than 1 in ACEIs.

IV. DISCUSSION

Many other studies also show the prevalence of metabolic disorders along with Hypertension [13,14,15]. Among physiological risk factors studied in present study, age group, both genders, high BMI, alcohol intake, family history showed a significant association of hypertensive patients developing other MD, the only exception with non-significant association was smoking. In the present study, highest number of other MD were found in the age group 40-49 years (37.3%) with p=0.0008 and Odds Ratio 1.6619 (1.2366 to 2.2336). Since in middle-age (40-49 years) individuals encounter intense pressure related to their professional, economic and social life, such stress which constitutes the main factor for developing many chronic diseases [16] may explain the high incidence of HT in this age group.

Hypertension is also associated with higher BMI, consistent with a number of other studies[17,18] wherein being overweight and obese is known to stimulate sympathetic nervous system activity, the changes in plasma insulin and leptin which also accompany weight gain, can lead to elevated BP levels. Present study also observed a significant association of hypertension and other MD with a significant p<0.0001, amongst patients with high BMI.

Several possible mechanisms have been proposed such as an imbalance of the central nervous system, impairment of the baroreceptors, enhanced sympathetic activity, and stimulation of the renin-angiotensin-aldosterone system to be major contributors of the alcohol-induced hypertension[19]. In present study distribution of life style variables amongst Punjabi population revealed that 22.5 % of the hypertensives in this population reported regular intake of alcohol and 19.5 % were smokers. In present study alcohol intake is observed to bean independent risk factor in the development of MD amongst hypertensive patients with statistical significance of p<0.0001 and odds ratio of 3.3046 (2.5512 to 4.2804).

Family History of hypertension was associated with the prevalence of obesity, central obesity and metabolic syndrome [20]. Present study also repudiates the prevalence of family history of hypertension showing a significant association (<0.0001) with risk of developing the other MDs.

It was observed that out of a total of 1400 hypertensive patients, 490 (35.3%) patients were suffering from other metabolic disorders. It was observed that a majority of 270 (55.1%) of the hypertensives with MD suffered from Diabetes. Out of these 68 pateints were already suffering from diabetes and developed HT later on. 202 pateints first developed hypertension and after they started antihypertensive medicationdeveloped diabetes. An analysis of such patients (202) was undertaken, as to influence of first line of drugs prescribed and development of Type 2 Diabetes amongst them.

Amongst the Punjabi Population the SPCs (Single Pill combinations) most commonly prescribed is the ARBs with Diuretics. The ARB telmisartan in combination with hydrochlorthiazide is most common ingredients, as proven in clinical trials to have better BP regulation on 24 hour basis, as compared to ACEI. Both ARBs as well as ACEIs show reno protective effect and regulate BP via their inhibitory activity to RAS pathway[21]. It makes these RAS blockers attractive for treating patients suffering from diabetes as well as non-diabetic nephropathy[8,22].

These drugs also score over CCB monotherapy which may lead to oedema and renal hyper filteration[23]. CCBs in combination with BBs formed the second preferred combination prescribed by physicians in Punjab.

The prevalence of coexistent hypertension and diabetes varies across different ethnic, racial, and social groups. Importantly, hypertension in patients with type 2 diabetes causes a significant increase in the risk of vascular complications in such population, and together both conditions predispose to chronic kidney diseases[24]. The overlap between hypertension and diabetes substantially increases the risk of cerebro-vascular disease and retinopathy. Diabetes mellitus is an independent risk factor for coronary artery disease, and the risk is markedly increased when hypertension is present. Type 2 diabetes mellitus was almost 2.5 times as likely to develop in subjects with hypertension as compared to subjects with normal blood pressure[25].

In present study, on comparing the HT patients with/without MD, we found that patients who were taking two drug combination therapies, were responding well towards their anti-hypertensive therapy, as the incidence of MD was found to be significantly lower at 27.7 % in combination therapies as compared to 38% in monotherapy.

Majority of HTpatients with diabetes (n=202) were on montherapy (n=172). They were found to be using ARBs (n=98), BBs (n=47) and ACEIs (n=27).ACE inhibitor users

were found (Table No.8) to have lowest relative risk (RR=0.37, 95% CI 0.25 to 0.54) of developing MD as compared with other two classes i.e ARBs and BBs (RR=1.69, 95% CI 1.26 to 2.28 and RR=1.58 95% CI 1.03 to 2.43 respectively) in HT patients with diabetes.

These results are compatible with previous studies in other populations [8,26] where ACEIs are a better therapeutic option in the treatment of hypertension as compared to ARB and BBs.

Further perusal of meta analysis using data from thirty-five randomized controlled trials (56,444 participants, ranging in number from 32 to 11,140) that included reports of 11 comparisons of ACEIs with placebo/no treatment, 12 comparisons of ACEIs with active treatment, 10 comparisons of ARBs with placebo and three comparisons of ARBs with active Treatment. Study quality was generally good: 60% of studies had a Jadad score greater than 3 and 17 studies scored 5 (the maximum possible). Half of the studies met the allocation concealment criteria (details not reported for the other studies).Compared with control (placebo or active treatment), ACEIs were associated with a statistically significant reduction in all-cause mortality (RR 0.87, 95% CI 0.78 to 0.98; 20 studies; I^2=26%), cardiovascular deaths (RR 0.83, 95% CI 0.70 to 0.99; 13 studies; I^2=40%) and major cardiovascular events (RR 0.86, 95% CI 0.77 to 0.95; 14 studies; I^2=59%). Results were similar when ACEIs were compared with placebo or active treatment [27].

In the current study, the relative risk for developing new onset diabetes was quite higher in the patients takingBBs. Similar finding were obtained in the Atherosclerosis Risk in Communities (ARIC) cohort study of 3804 patients with HTN, the BB group had a 28% higher risk of type 2 DM (T2DM) compared with the control group (RR=1.28, 95% CI 1.04 to 1.57)[28]. Another study, Losartan Intervention for Endpoint reduction in hypertension (LIFE), was a double-masked, randomized, parallel-group trial comparing losartan (ARB) and atenolol (BB) in patients with hypertension and LVH, which showed a 25% reduction in stroke, but not in MI, with losartan[29]. Similar results was found in another sudy, the relative risk for new-onset diabetes in participants taking a beta-blocker compared with those not taking, was 32% greater in older women and 20% greater in men. Their data was also consistent with previous reports in that neither ACEIs nor CCBs conferred a higher risk for new-onset diabetes. Further BB therapy resulted in decreased skeletal muscle perfusion causing adverse effects on lipid and glucose metabolism by increasing insulin resistance[30].

Deviations from JNC8 guidelines:

As per JNC8, the initial drugs of choice for hypertension include ACEIs, ARBs, thiazide and CCBs alone or in combo. In Punjab, 23.7% of all hypertensive patients were given beta blockers as drug of first choice drug. Out of these 46.5% were found to be suffering from other metabolic disorders, like diabetes, high lipid profile, heart attack, thyroid and renopathy. As per JNC8 patients with COPD, asthma, diabetes, and peripheral vascular disease may not be prescribed BBs. Traditional beta blockers such as atenolol, metoprolol and propanolol are the usual prescriptions in Punjab as stand alone or in combination with CCBs like amlodipine. These reduce blood pressure by reducing the cardiac output via negative chronotropic and ionotropic mechanisms.This reduced cardiac output leads to increased peripheral vasoconstriction a response by body to maintain blood pressure, followed by increased peripheral resistance a characteristic of chronic hypertension. This systemic vascular resistance lowers the blood supply to peripheral tissue like skeletal muscles with concomitant adverse effect on glucose and lipid metabolism, leading to an increase in risk of developing new onset diabetes[31].

Deviations from Indian hypertension guidelines-II (IHG-II)

According to IHG-II principles of drug treatment[32], low dose diuretics may be preferred initial therapy unless there are any compelling indications which was not observed as first choice in current study. As per IHG-II, CCBs and diuretics combination was under undesirable combinations, but it was given to 20.3 % patients in the current study.

Unfortunately, many epidemiologic studies of antihypertensive medications and the development of diabetes have been limited by their small numbers of subjects, lack of adequate comparison groups, short duration of follow-up, 16 suboptimal definitions of diabetes, or lack of information on important biologic characteristics (such as blood pressure) that may confound this relation. Present study also has same limitations of small number of subjects and short duration of follow-up.

V. CONCLUSION

The study reflects that the health risk transition in Punjab is likely to be at the middle stage. In our current study, all modifiable health-related factors including age, BMI, alcohol, and smokingbut excluding the non modifiable gender, were associated with hypertension prevalence. All the health related factors except smoking were found to be significantly associated with the development of other metabolic disorders (diabetes, kidney problems, high lipid profile, thyroid and

heart attacks) in the patients who were under antihypertensive treatment. The prescription patterns of antihypertensive drugs by physicians of Punjab reveal that 70.6% of patients were under monotherapy and rest 29.4% were on two-drug therapy. In case of hypertensive patients under mono-therapy, 38% were observed to suffer one metabolic disorder or the other as compared to 27.7 % in patients who were under two drug therapy. In case of monotherapies being prescribed by physicians a significant number of patients on BBs and ARBs developed from metabolic disorders, as compared to those on ACEIs, Diuretics and CCBs. In the current study, the highest relative risk for developing diabetes was seen in the patients taking BBs (RR=1.58 with 95% CI, 1.03 to 2.43)and ARBs RR=1.69 with 95% CI, 1.26 to 2.28). The association between hypertension and the development of diabetes should prompt research on shared risk factors and alert clinicians that such groups of individual who were prescribed BBs and ARBs need to monitor their glucose levels regularly for the detection of pre-diabetes and a changed drug regime accordingly.

Although some unique findings are emerging with some gene-treatment combinations but research in this area continues to be described by disparate results. Differences in study designs, variable methods for assessing pharmacologic treatments, diverse phenotypes and small sample sizes together with a short duration of follow-up may account for a large inconsistencies. Progress in this field will depend upon our ability to project large studies using high-fidelity phenotyping with various drugs and different ethnic groups.

VI. AUTHOR STATEMENTS

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Ethical approval

The study was approved by institutional ethical committee (ICEC/4/2011).

Competing interests

Authors declare no competing interests.

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