

## Risk Assessment of developing type 2 diabetes mellitus in patient on antihypertensive medication

**Amarjeet Singh\***, Sudeep bhardwaj, Ashutosh aggarwal  
Department of Pharmacology,  
Seth G. L. Bihani S. D. College of Technical Education,  
Institute of Pharmaceutical Sciences & Drug Research  
\*amarjeetsingh024@gmail.com



### ABSTRACT

**Objective:** The purpose of this study was to examine the risk assessment of developing type 2 diabetes mellitus in patient on antihypertensive medication.

**Material & Method:** In the present study total 30 patient with essential hypertension of both sex with mean age (48.6±0.8313) were recruited as per the inclusion criteria. Patients were segregated on the behalf of therapy they were using. 22 patients were on Losartan+HCTZ therapy and 8 patients were on Atenolol therapy.

**Result:** After six month of antihypertensive therapy Atenolol group showing a significant difference in their blood glucose (0.0014) whereas in Losartan+HCTZ group significant difference was not observed (0.1542). Patients of Atenolol group when compared with patient of Losartan+HCTZ group a significant difference was observed in the serum cholesterol level (0.0290).

**Conclusion:** We found that the use of  $\beta$ -blocker was independently associated with increased risk of type 2 diabetes. So increase in blood glucose in the Atenolol group patient revealed a significant association between use of Atenolol therapy and metabolic dysfunction whereas in Losartan+HCTZ group significant increase in blood glucose was not observed and from these we can conclude therapy with Losartan+HCTZ therapy not associated with metabolic dysfunction.

**Keywords:** antihypertensive medication, diabetes mellitus, blood glucose

### INTRODUCTION

Hypertension (HTN) or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated<sup>[1]</sup>.

Hypertension is strongly associated with risk factors that impair glucose homeostasis and is often presented as a component of the metabolic syndrome. Indeed, hypertension is related with obesity, insulin resistance as well as diabetes mellitus<sup>[2,3]</sup>. As a result, hypertensive patients have a 2.5-fold higher risk of type 2 diabetes mellitus (T2DM) onset compared with normotensive subjects<sup>[4]</sup>. The

various classes of antihypertensive drugs have different effects on blood glucose metabolism. Indeed, antihypertensive agents, such as  $\beta$ -blockers and thiazide diuretics have been associated with negative effects on blood glucose in contrast to other classes, such as angiotensin receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACE-I). As a result, the treatment of hypertensive subjects should be carefully selected so as further deterioration in glucose homeostasis is minimized<sup>[5]</sup>.

**How to cite this article:** A Singh, S Bhardwaj, A Aggarwal; Risk Assessment of developing type 2 diabetes mellitus in patient on antihypertensive medication; PharmaTutor; 2015; 3(3); 41-48

The relation between the use of different classes of antihypertensive medications and the risk of incident type2 diabetes is unclear. Although thiazide diuretic or beta blocker use may increase the incidence of diabetes, prior studies have reported conflicting results<sup>[6]</sup>.

## MATERIAL AND METHOD

A prospective study was conducted in the population of Sri Ganganagar District of Rajasthan. This study was carried out after getting approval from the Institutional Ethics Committee of Seth G.L. Bihani S.D. College of Technical Education Institute of Pharmaceutical Sciences & Drug Research and written informed consent was obtained from all subject.

### Recruitment of Subjects:

Total 30 study subjects were recruited. 22 patient receiving Losartan + HCTZ as combination therapy and 8 patient receiving Atenolol as monotherapy.

### Selection criteria for subjects

#### Inclusion Criteria:

- Age: 30 Years - 59 Years,
- Genders: Both
- An average seated home DBP > 85 mmHg and home SBP < 180 mmHg. Subjects must also have an average seated (> 5 minutes) clinic DBP between 90 mmHg and 110 mmHg and SBP < 180 mmHg
- BMI : normal range < 18.5 >24.9 kg/m<sup>2</sup>
- Patient diagnosed with essential hypertension
- Drugs: Atenolol (as monotherapy) and Losartan plus Hydrochlorothiazide (as combination therapy)

#### Exclusion Criteria:

- Secondary hypertension
- Patients currently treated with three or more antihypertensive drugs, isolated systolic HTN other diseases requiring treatment with BP lowering medications
- Heart rate < 55 beats/min

- Known cardiovascular disease (including history of angina pectoris, heart failure presence of a cardiac pacemaker, history of myocardial infarction or revascularization procedure, or cerebrovascular disease, including stroke and TIA),
- Diabetes mellitus (Type 1 or 2)
- Primary renal disease
- Pregnancy or lactation
- Current treatment with NSAIDS, COX2-inhibitors, oral contraceptives or estrogen.

### Follow up of Patients

The subjects were followed up for 6 months for monitoring of blood glucose, lipid profile Total Cholesterol, HDL- Cholesterol, Triglycerides and anthropometric measurement. During the follow up period blood pressure was monitored on monthly basis. The examinations included interviews conducted at the subjects' homes.

Subjects were asked to fast for at least 12 hours before blood collection. Lipid profile measured two times first starting of study and second end of study. Fasting blood glucose level measured by glucometer on monthly basis. Blood pressure was measured with a mercury sphygmomanometer with subjects in the sitting position on monthly basis. Data on demographic variables (age, sex, smoking status, use of alcohol and family history of diabetes) were obtained by interview. Body-mass index (the weight in kilograms divided by the square of the height in meters) was calculated from anthropometric measurement taken at the base-line and end of study.

## RESULTS

In the present study total 30 patient with essential hypertension of both sex with mean age (48.6±0.8313) were recruited as per the inclusion criteria. The base line clinical characteristics like smoker, liquor, BMI, systolic BP, diastolic BP, Blood glucose, Lipid profile are shown in the table 1. From the above recruited total 30 hypertensive patient, 13 were found

alcoholic and 2 smoker. Patients were segregated on the behalf of therapy they were using. 22 patients were on Losartan + Hydrochlorothiazide therapy and 8 patients were on Atenolol therapy.

Comparison of Base line Clinical characteristics with clinical characteristics after six month of Losartan+HCTZ therapy are shown in table 2. Table 3 & table 4 are showing Clinical characteristics of male and female respectively for Losartan+HCTZ therapy.

Comparison of Base line Clinical characteristics with clinical characteristics after six month of Atenolol therapy are shown in table 5. Table 6 & 7 showing clinical characteristics of male & female respectively for Atenolol therapy.

#### Monitoring of blood glucose, BMI, Blood pressure

Patients were followed up for the six month for monitoring of blood glucose, Blood pressure, BMI. When BMI of recruited patient compared after six month of therapy no significant

difference was observed in both Atenolol and Losartan+HCTZ group respectively (0.9754) & (0.8961). After six month of antihypertensive therapy Atenolol group showing a significant difference in their blood glucose (0.0014) whereas in L+H group significant difference was not observed (0.1542). Table 8 & 9 are showing a comparison of BMI, Blood glucose, systolic BP, diastolic BP, lipid profile between Atenolol group and Losartan+HCTZ group after six month of therapy.

#### Monitoring of Lipid profile

Patients were followed up for the six month for monitoring of lipid profile. Patients of Atenolol group when compared with patient of Losartan+HCTZ group a significant difference was observed in the serum cholesterol level (0.0290). When TG, HDL, LDL, VLDL compared no significant difference was observed between Atenolol group and Losartan+HCTZ group shown in table 9.

Table No.1 Clinical characteristics of total patient at baseline

Characteristics	Total	Male	Female	p value
Number of subjects	30	25	5	
Age (year)	48.6±0.8313	48.04±0.8935	51.4±1.939	0.1344ns
Sex (% of male)	83.33			
Smoker %	6.66	8	0	0.0001
Liquor %	43.33	52	0	0.0001
BMI (kg/m <sup>2</sup> )	22.29±0.3098	22.378±0.3505	21.892±0.6644	0.5680ns
Blood pressure				
Systolic BP mmHG	130.53±1.020	130.24±1.074	132±3.16	0.5297ns
Diastolic BP mmHG	88.26±0.7907	88.16±0.9322	88.8±1.02	0.7687ns
Blood examination				
Glucose (mg/dl)	93.03±0.9878	92.44±1.124	96±1.378	0.1838ns
Total Cholesterol (mg/dl)	172.89±2.481	173.41±2.56	170.312±8.305	0.6491ns
HDL Cholesterol (mg/dl)	47.057±1.457	92.275±3.412	98.008±6.284	0.8667ns
Triglycerides (mg/dl)	93.231±3.016	47.17±1.577	46.496±4.209	0.4884ns
LDL	107.23±1.441	18.44±0.6815	19.596±1.257	0.3588ns
VLDL	18.63±0.6025	107.83±1.459	104.22±4.874	0.4853ns

Mean±SEM

ns non significant

\*\*\* significant

Table No. 2 Clinical characteristics of Losartan+HCTZ group at base line &amp; end of study

Characteristics	At base line	end of study	P value
Number of subject	22	22	
BMI (kg/m <sup>2</sup> )	22.18±0.4050	22.36±0.3397	0.8961 <sup>ns</sup>
Blood Pressure			
Systolic BP	129.81±1.22	127.81±0.9662	0.2061 <sup>ns</sup>
Diastolic BP	88.09±1.017	86.72±0.8275	0.3043 <sup>ns</sup>
Blood examination			
Blood glucose(mg/dl)	91.36±1.137	89.40±0.7227	0.1542 <sup>ns</sup>
Total cholesterol(mg/dl)	169.66±2.75	169.27±2.75	0.9213 <sup>ns</sup>
Triglyceride(mg/dl)	90.39±3.56	91.05±3.59	0.8962 <sup>ns</sup>
HDL cholesterol(mg/dl)	45.98±1.704	46.25±1.603	0.9087 <sup>ns</sup>
VLDL	18.065±0.7113	17.44±1.027	0.9039 <sup>ns</sup>
LDL	101.44±4.27	104.88±1.639	0.7269 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No. 3 Clinical characteristics of Losartan+HCTZ Male at base line &amp; end of study

Characteristics	Male (base line)	Male (end of study)	p value
Number of subject	19	19	
BMI(kg/m <sup>2</sup> )	22.44±0.4427	22.36±0.3397	0.9792 <sup>ns</sup>
Blood pressure			
Systolic BP	129.78±1.25	127.47±0.8765	0.1387 <sup>ns</sup>
Diastolic BP	88.21±1.176	86.63±0.8793	0.2895 <sup>ns</sup>
Blood examination			
Blood glucose (mg/dl)	90.63±1.19	89±0.6882	0.2431 <sup>ns</sup>
Total cholesterol (mg/dl)	171.59±2.926	171.20±2.914	0.9247 <sup>ns</sup>
Triglyceride (mg/dl)	90.28±4.055	91.14±4.068	0.8825 <sup>ns</sup>
HDL Cholesterol (mg/dl)	46.62±1.92	46.83±1.82	0.9368 <sup>ns</sup>
VLDL	18.04±0.8094	18.20±0.8118	0.8901 <sup>ns</sup>
LDL	106.97±1.653	106.17±1.648	0.7331 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No. 4 Clinical characteristics of Losartan+HCTZ Female at base line &amp; end of study

Characteristics	Female (base line)	Female(end of study)	p value
Number of subject	3	3	
BMI(kg/m <sup>2</sup> )	21.31±0.8313	21.72±0.7554	0.7336 <sup>ns</sup>

Blood Pressure			
Systolic BP mmHG	130±5.033	130±5.033	> 0.9999 <sup>ns</sup>
Diastolic BP mmHG	87.33±0.6667	87.33±2.906	> 0.9999 <sup>ns</sup>
Blood examination			
Blood glucose (mg/dl)	96±2.51	92±3.05	0.3694 <sup>ns</sup>
Total cholesterol (mg/dl)	157.42±3.025	157.07±3.78	0.9459 <sup>ns</sup>
Triglyceride (mg/dl)	91.06±6.35	90.51±7.15	0.9574 <sup>ns</sup>
HDL cholesterol (mg/dl)	41.93±1.434	42.56±0.6533	0.7069 <sup>ns</sup>
VLDL	18.20±1.268	18.09±1.431	0.9569 <sup>ns</sup>
LDL	97.28±3.102	96.406±3.011	0.8492 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No. 5 Clinical characteristics of Atenolol group at base line &amp; end of study

Characteristics	At base line	end of study	P value
Number of subject	8	8	
BMI(kg/m <sup>2</sup> )	22.30±0.4010	22.28±0.4951	0.9754 <sup>ns</sup>
Blood Pressure			
Systolic BP mmHG	132.5±1.76	130.5±1.296	0.3761
Diastolic BP mmHG	88.75±1.065	89.5±1.35	> 0.9999
Blood examination			
Blood glucose(mg/dl)	99.375±0.7545	99.87±1.469	0.0014 <sup>***</sup>
Total cholesterol(mg/dl)	181.79±4.19	181.35±4.27	0.9425 <sup>ns</sup>
Triglyceride(mg/dl)	101.04±4.968	100.58±4.791	0.9478 <sup>ns</sup>
HDL cholesterol(mg/dl)	50.02±2.708	50.16±2.41	0.9679 <sup>ns</sup>
VLDL	20.20±2.809	20.11±0.9584	0.9482 <sup>ns</sup>
LDL	111.58±2.55	111.07±2.55	0.8930 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No.6 Clinical characteristics of Atenolol Male at base line &amp; end of study

Characteristics	Male (base line)	Male (end of study)	P value
Number of subjects	6	6	
BMI(kg/m <sup>2</sup> )	22.155±0.4584	22.55±0.5198	0.5797 <sup>ns</sup>
Blood pressure			
Systolic BP	131.66±2.15	130.33±1.74	0.6410 <sup>ns</sup>
Diastolic BP	88±1.26	88.66±1.606	0.7510 <sup>ns</sup>
Blood examination			
Blood glucose (mg/dl)	98.16±0.7032	103.5±1.45	0.0080 <sup>***</sup>
Total Cholesterol (mg/dl)	179.18±4.975	178.54±5.043	0.9296 <sup>ns</sup>
Triglyceride (mg/dl)	98.57±5.917	98.06±5.68	0.9513 <sup>ns</sup>
HDL Cholesterol (mg/dl)	48.91±2.55	49.21±2.367	0.9330 <sup>ns</sup>

VLDL	19.71±1.18	19.60±1.136	0.9518 <sup>ns</sup>
LDL	110.565±3.076	109.72±3.18	0.8525 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No.7 Clinical characteristics of Atenolol Female at base line & end of study

Characteristics	Female(base line)	Female(end of study)	P value
Number of subjects	2	2	
BMI(kg/m <sup>2</sup> )	22.765±1.035	21.49±1.405	0.5424 <sup>ns</sup>
Blood pressure			
Systolic BP	135±3.0	131±1.0	0.3333 <sup>ns</sup>
Diastolic BP	91±1.0	92±2.0	0.6985 <sup>ns</sup>
Blood examination			
Blood glucose (mg/dl)	96±0.0	102±3.0	not analyzed
Total Cholesterol (mg/dl)	189.65±6.25	189.81±5.85	0.9864 <sup>ns</sup>
Triglyceride (mg/dl)	108.43±9.64	108.13±9.1	0.9840 <sup>ns</sup>
HDL Cholesterol (mg/dl)	53.345±9.635	53.04±8.26	0.9830 <sup>ns</sup>
VLDL	21.68±1.93	21.62±1.82	0.9840 <sup>ns</sup>
LDL	114.625±5.315	115.15±4.22	0.9449 <sup>ns</sup>

mean±SEM

\*\*\* significant value

ns non significant

Table No. 8 Clinical characteristics of Atenolol & Losartan+HCTZ group at baseline

Characteristics	Atenolol	Losartan+HCTZ	p value
Number of Subjects	8	22	
Age (year)	52.12±1.716	47.31±0.8069	0.0080 <sup>***</sup>
Sex (% of male)	75	86.36	
Smoker %	25	40.9	
Liquor %	50	0	
BMI (kg/m <sup>2</sup> )	22.30±0.4010	22.18±0.4050	0.9841 <sup>ns</sup>
<b>Blood pressure</b>			
Systolic BP mmHG	132.5±1.76	129.81±1.221	0.2519 <sup>ns</sup>
Diastolic BP mmHG	88.75±1.065	88.09±1.017	0.7193 <sup>ns</sup>
<b>Blood examination</b>			
Glucose (mg/dl)	99.375±0.7545	91.36±1.137	0.0032 <sup>***</sup>
Total Cholesterol (mg/dl)	181.79±4.19	169.66±2.75	0.0277 <sup>***</sup>
HDL Cholesterol (mg/dl)	50.02±2.708	45.98±1.704	0.2264 <sup>ns</sup>
Triglycerides (mg/dl)	101.04±4.968	90.39±3.56	0.1202 <sup>ns</sup>
LDL	111.58±2.553	101.44±4.27	0.0680 <sup>ns</sup>
VLDL	20.20±0.9930	18.065±0.7113	0.1183 <sup>ns</sup>

mean±SEM,

\*\*\* significant value ; ns non significant

Table No. 9 Clinical characteristics of Atenolol &amp; Losartan+HCTZ group at end of study

Characteristics	Atenolol	Losartan+HCTZ	P value
Number of Subjects	8	22	
BMI(Kg/m <sup>2</sup> )	22.28±0.4951	22.36±0.3397	0.9077 <sup>ns</sup>
Blood pressure			
Systolic BP mmHG	130.5±1.296	127.81±0.9662	0.1449 <sup>ns</sup>
Diastolic BP mmHG	89.5±1.35	86.72±0.8275	0.0933 <sup>ns</sup>
Blood examination			
Glucose (mg/dl)	99.87±1.469	89.40±0.7227	< 0.0001 <sup>***</sup>
Total Cholesterol (mg/dl)	181.35±4.272	169.27±2.755	0.0290 <sup>***</sup>
HDL Cholesterol (mg/dl)	50.16±2.41	46.25±1.603	0.2074 <sup>ns</sup>
Triglycerides (mg/dl)	100.58±4.791	91.05±3.594	0.1628 <sup>ns</sup>
LDL	111.07±2.553	104.88±1.639	0.0565 <sup>ns</sup>
VLDL	20.11±0.9584	17.44±1.027	0.1582 <sup>ns</sup>

Mean±SEM

\*\*\* significant value

ns non significant

Table No. 10 Group Analysis of clinical characteristics of all patients

Characteristics	Age group 30-39, 40-49, 50-59 (year)	Gender Male & Female	BMI 17.00-21.00 21.00-25.00
	p value	p value	p value
BMI(kg/m <sup>2</sup> )	0.4929 <sup>ns</sup>	0.2583 <sup>ns</sup>	<0.0001 <sup>***</sup>
Systolic BP mmHG	0.5091 <sup>ns</sup>	0.3096 <sup>ns</sup>	0.2152 <sup>ns</sup>
Diastolic BP mmHG	0.8626 <sup>ns</sup>	0.2962 <sup>ns</sup>	0.4236 <sup>ns</sup>
Blood glucose (mg/dl)	0.0354 <sup>ns</sup>	0.3145 <sup>ns</sup>	0.3862 <sup>ns</sup>
Total Cholesterol(mg/dl)	0.4139 <sup>ns</sup>	0.6831 <sup>ns</sup>	0.2517 <sup>ns</sup>
TG(mg/dl)	0.5511 <sup>ns</sup>	0.5624 <sup>ns</sup>	0.5295 <sup>ns</sup>
HDL cholesterol(mg/dl)	0.1513 <sup>ns</sup>	0.8626 <sup>ns</sup>	0.5026 <sup>ns</sup>
VLDL	0.5406 <sup>ns</sup>	0.5561 <sup>ns</sup>	0.5230 <sup>ns</sup>
LDL	0.6017 <sup>ns</sup>	0.4343 <sup>ns</sup>	0.0155 <sup>ns</sup>

## CONCLUSION

In the present study 30 patient with essential hypertension were recruited among these 25 were male and 5 were female. Average age of male patients was 48.04±0.8935 and average age of female was 51.4±1.939. There was no significance difference observed between average age of male and female (0.1344). 6.66% of the total recruited patient was found with smoking habit and 43.33% was found with

alcoholic habits. When BMI all the recruited patient compared a no significant difference was observed between male and female but some other study reported female with more BMI than males (7). The systolic BP and diastolic BP compared in all recruited patient no significant difference was observed between male and female. In all recruited hypertensive patient blood glucose was compared that blood glucose level slightly higher in female than male

but not a significant difference. Comparison of lipid profile Total cholesterol, TG, HDL, VLDL, LDL in all recruited patient no significant difference was found.

After six month no significant difference was observed in BMI in both Atenolol therapy and Losartan+HCTZ therapy group. After six month blood glucose was compared in both Atenolol therapy and Losartan+HCTZ therapy group there was significant difference observed in blood glucose level ( $< 0.0001$ ) which also reported by the Eric N Taylor et al 2006, Todd W. Gress et al 2000. Comparison of total cholesterol level shows significant difference between both Atenolol therapy and Losartan+HCTZ group (0.0290). No significant difference was observed in TG, HDL, VLDL and LDL in Atenolol therapy and Losartan+HCTZ group.

We found that the use of  $\beta$ -blocker was independently associated with increased risk of type 2 diabetes.

#### PREDICATORS OF HYPERTENSION

There was no significant effect observed among different age group, BMI group, and gender on blood pressure respectively

So increase in blood glucose in the Atenolol group patient revealed a significant association between use of Atenolol therapy and metabolic dysfunction whereas in Losartan+HCTZ group significant increase in blood glucose was not observed and from these we can conclude therapy with Losartan+HCTZ therapy not associated with metabolic dysfunction. These results are also showed by Yue Yang et al 2013 & Lindholm et al 2002.

#### ↓ REFERENCES

1. Paul A.James, Suzanne Oparil, Barry L. Carter MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler et al, "Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)", JAMA. doi:10.1001/jama.2013.284427
2. Lind L, Berne C, Lithell H. Prevalence of insulin resistance in essential hypertension. J Hypertens 1995; 13: 1457-1462 [PMID: 8866908]
3. Lender D, Arauz-Pacheco C, Adams-Huet B, Raskin P. Essential hypertension is associated with decreased insulin clearance and insulin resistance. Hypertension 1997; 29:111-114 [PMID: 9039089]
4. Todd W. Gress, Javier Nieto, Eyal Shahar et al, "Hypertension And Antihypertensive Therapy As Risk Factors For Type 2 Diabetes Mellitus", The New England J Of Medicine, 2000, 342, 908-917.
5. Christos V Rizos, Moses S Elisaf, "Antihypertensive drugs and glucose metabolism" World J Cardiol 2014 July 26; 6(7): 517-530 ISSN 1949-8462
6. Padwal R, Laupacis A: Antihypertensive therapy and incidence of type 2 diabetes: a systematic review. Diabetes Care 2004, 27:247–255.
7. Eric N Taylor, Frank B. Hu, Gary C. Curhan, "Antihypertensive medications and the risk of incident type 2 diabetes", cardiovascular and metabolic risk, Diabetes Care, May 2006, Volume 29, Number 5, 1065-1070