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ORIGINAL ARTICLE

STUDY OF GLYCOSYLATED HEMOGLOBIN LEVELS IN HYPERTENSIVE AND NORMOTENSIVE NON DIABETIC POPULATION

Anita Arya[1], Tripti Saxena[2], Kaustubh Mundada[3], Maya Malvi[4]

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ABSTRACT: INTRODUCTION: Hypertension and Diabetes Mellitus are among the most common chronic diseases in the world and major risk factors for Coronary Artery Disease, Stroke, Peripheral Vascular Disease, and Chronic Kidney Disease. Also both share same risk factors like central obesity, increasing age and sedentary lifestyle. Hypertension is known to predict diabetes. **OBJECTIVE:** The objective of the review was to determine the relationship between glycosylated hemoglobin and hypertension in non-diabetic subjects. **METHODS:** The study was done at the author's department of medicine for one year from January 2013 to December 2013. It was an observational cross-sectional study. The study group comprised of 100 hypertensive subjects and 50 control subjects above 18 years. Blood pressure, Height, Weight was measured and Body Mass Index was calculated for all participants.HbA1c, urine for microalbuminuria, Lipid profile and renal functions tests were performed in all subjects. **RESULTS:** We found that the mean Hba1c in hypertensive group was 6.44±1.20 and in control group was 4.59±1.48 which was statistically significant (p<0.0001).Thus compared to 6% of controls, around 40% of hypertensive were found to have Hba1c in range of pre-diabetics (5.7-6-4) or diabetes (>6.4). Similarly 45% of hypertensive had microalbuminuria compared to 7% of control group. The mean±SD for albuminuria in study cases was 33.94±24.02 whereas that for control was 18.50±8.04 which was statistically significant (p value, 0-0001). **CONCLUSION:** Hypertension is associated with increased HbA1c levels. Whether this association is due to shared risk factors or is independent of obesity requires further study.

KEYWORDS: Hypertension, Diabetes Mellitus, Glycosylated Hemoglobin, Microalbuminuria.

INTRODUCTION: Hypertension is one of the world's major health problems and leading cause of death not only to the society but also to healthcare providers leading to considerable morbidity and mortality. It is the most common, readily identifiable and reversible risk factor for coronary artery disease, stroke, heart failure, renal failure, aortic dissection and peripheral arterial disease[1,2,3,4] According to The World health statistics 2012 report one in three adults worldwide has raised blood pressure.[5] High blood pressure currently causes two thirds of all stroke and half of cases of ischemic heart disease worldwide and is leading cause of premature death.[1,3,5]

Hypertension is often associated with additional cardiovascular risk factors. Diabetes Mellitus (DM) and Hypertension often occur as they share the same risk factors. Hypertension is known to predict diabetes. According to International Diabetes Federation, 387 million people are suffering from DM and this number is expected to rise to 592 million in 2035 (8% of global adult population). India is home to 2nd largest number of diabetics (66 million).

Glycosylated haemoglobin is a stable indicator of unstressed preceding 2-3 months average blood sugars levels and is a marker of chronic hyperglycaemia. It is standard measurement for diagnosis as well as monitoring glucose control in diabetic patients.[6,7,8]

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In this review we tried to find the association of hypertension with HbA1c in non-diabetic patients and brief review of literature.

MATERIALS AND METHODS: The study was done at the author's department of medicine for one year from January 2013 to December 2013.It was an observational cross-sectional study. The study group comprised of 100 hypertensive subjects and 50 normotensive subjects above 18 years. All patients with history of diabetes mellitus were excluded.

Detailed history was taken and through general and systemic examination was done. Weight was measured on electronic digital scale and height was measured with the help of flexible anthropometer and Body mass index was calculated as weight (kg) divided by squared height (metres).[9] Blood pressure was measured manually with a mercury sphygmomanometer. Three readings of blood pressure with gap of 2 minutes were measured in sitting position after rest for 5 minutes and the mean was taken. Hypertension was defined according to JNC 7 criteria as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or patient on antihypertensive medication irrespective of blood pressure.[10]

Lipid profile, renal function tests, urine microscopy and fasting blood glucose were done in all subjects. Quantitative measurement for microalbuminuria was done by TURBILYTE-MA which is a turbidemetry immunoassay for detection of albumin in urine based on principle of agglutination reaction. HbA1c was measured using the cation exchange resin method.

Statistical Analysis was done as desired and mean and Standard deviation was calculated in cases and control to characterize the study population stratified by age, sex, BMI, Hypertension, microalbuminuria, dyslipidemia and Hba1c.

RESULTS: Of the 100 hypertensive cases, 78 were males and 22 were females. Among the 50 controls 34(68%) were males and 16(32%) were females. The mean age of cases was 43.5±6.3 and of control was 40.1±5.6. The mean BMI for hypertensive cases was 28±4.3 and for control was 25±3.2 which was statistically significant ($p<0.0001$).

Among the cases 31 males and 9 females i.e. 40 % were found to have HbA1c more than 5.6. Of these 14 were frank diabetics (HbA1c>6.5) and 26 were pre-diabetic (HbA1c >5.6).Comparatively among the controls only5 males and 1 female had HbA1c above 5.6 i.e. 6%. The mean Hba1c in cases group was 6.44±1.20 and in control group was 4.59±1.48 which was statistically significant ($p<0.0001$).Thus compared to 6% of controls, around 40% of hypertensive were found to be diabetics or at risk for diabetes (pre diabetes). (Table 1 and 2).

45 hypertensives were found to have albumin in urine >30mg with 3 patients having frank albuminuria (>300mg). Comparatively only 7 (14%) subjects from control group had albumin in urine >30mg and none >300mg.The mean±SD for albuminuria in cases was 33.94±24.02 whereas that for control was 18.50±8.04 which was statistically significant (p value, 0-0001). (Table 1 and 3)
Similarly dyslipidemia was also significantly more present in hypertensives. Both mean HDL and mean triglyceride were higher in cases as compared to control group (p value <0.0001 Table 3). 55% of Hypertensive had LDL levels more than 150mg/dl compared to 4% of control. Similarly the mean HDL level for hypertensive cases was 35.36 ± 6.38 compared to 43.5±10.07 for control (Table 1).

DISCUSSION: In our study we found that almost 40% of hypertensive patients had HbA1c value in the range of diabetes and pre-diabetes. Comparatively only 6% of control subjects were found to be

diabetic. This association was also observed below the diagnostic threshold of diabetes. In addition microalbuminuria and dyslipidemia were also significantly present in hypertensives patients having higher HbA1c as compared to controls.

This association of hypertension and hyperglycaemia may reflect the presence of shared risk factor like central obesity, increasing age and sedentary lifestyle. Increased central or abdominal adiposity has been associated with hyperinsulimenia, insulin resistance and diabetes mellitus type 2. Abdominal obesity has been also associated with atherogenic lipid profile, microalbuminuria independent of hypertension and DM, increase peripheral vascular resistance and hypertension.

Diabetic mellitus is one of leading cause of end stage renal disease, non-traumatic lower extremity amputations and adult blindness. It also major risk factor for cardiovascular disorders and stroke. A recent estimate suggested that DM was the fifth leading cause of death worldwide.

Although few studies have examined the association of hypertension and hba1c, there are conflicting results. Though most studies have not found an association independent of known risk factors like obesity, increased Body Mass Index, Waist to Hip ratio, age,[11] some have concluded an increased association independent of these known risk factors.[12,13,14] One reason for these conflicting results may be due to confounding factors. For example the Framingham Heart Study which found a positive correlation but did not adjust for BMI or age.[15]

Another reason for conflicting results might be the method used for measuring hyperglycemias. Measuring fasting blood glucose or glucose tolerance test is practically inconvenient, have intraindividual variability and does not reflect long term glucose status.[16] In contrast Hba1c is a marker of glycemic status of previous8 to 12 weeks and better characterises glycemic status; is convenient to measure and thereby reduce operational errors.[6,7]

One explanation for hyperglycemia leading to hypertension is hyperglycemia causes high glucose flux across endothelial cell membrane resulting in increased oxidative stress which reduces the bioavailability of nitric oxide and contributes to endothelial cell dysfunction that may subsequently lead to systemic hypertension.[17,18] Also formation of advanced glycation end products may contribute to inflammation, oxidative stress and endothelial dysfunction interfering with both structural functional aspects of vascular relaxation.[19,20] In addition inflammatory processes have been implicated in formation of both hyperglycemia and hypertension. Also hyperglycemia leads to increased vascular resistance and stiffness.[21]

A major limitation of our study was small sample size and its cross-sectional nature. Cross-sectional data do not allow conclusions regarding cause and effect. What is needed is a large prospective study on the relationship of HbA1c at baseline and the incidence of subsequent systemic arterial hypertension with adjustment for abdominal obesity (BMI, Waist to Hip ratio) to find independent association.

CONCLUSION: Hypertension is associated with increased HbA1c levels. In our study we found that 40% of hypertensives had HbA1c more than 5.6. Of these 14 were frank diabetics (HbA1c>6.5) and 26 were pre-diabetic (HbA1c>5.6). This association was also observed below the diagnostic threshold of diabetes. Whether this association is due to shared risk factors or is independent of obesity requires further study.

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Sl. No.	Mean±SD	
	Cases	Control
1. Age	43.5±6.3	40.1±5.6
2. Body Mass Index	28 ±4.3	25±3.2
3. Total Cholesterol	212.91±54.6	137.85±29.1
4. Triglyceride	210.01±54.6	77.7±24.2
5. HDL	35.36±6.38	43.5±10.07
6. LDL	127.53±53.5	76.8±32.1
7. VLDL	127.53±22.0	15.54±4.85
8. Microalbuminuria	33.94±24.02	18.50±8.04
9. HbA1c	6.44±1.20	4.59±1.48

Table 1: Mean values of cases and control stratified by lipid profile, microalbuminuria, Hba1cand Body mass index

Sl. No.	Range(mg/dl)	Cases (No.)	Cases (%)	Control (No.)	Control (%)
1	4.0 – 5.6	60	61%	44	88%
2	5.7 – 6.4	26	26%	03	06%
3	6.5 – 8.0	12	12%	02	04%
4	>8.0	02	02%	01	02%
Total		**100**		**50**	

Table 2: Range wise comparison of HbA1c levels between Hypertensive Cases and Healthy Controls

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Sl. No.	Range(mg/dl)	Cases(No.)	Cases (%)	Control (No.)	Control (%)
1	<30	55	55%	43	86%
2	30 -300	42	42%	07	14%
3	>300	03	03%	00	00%
Total		**100**		**50**	

Table 3: Rangewise comparison of Microalbumin levels between Cases and Healthy Controls

AUTHORS:

1. Anita Arya
2. Tripti Saxena
3. Kaustubh Mundada
4. Maya Malvi

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Medicine, Hamidia Hospital, Gandhi Medical College, Bhopal.
2. Associate Professor and HOD, Department of Biochemistry, Gandhi Medical College, Bhopal.
3. 3rd Year Post Graduate Resident, Department of Medicine, Hamidia Hospital, Gandhi Medical College, Bhopal.
4. Student, Department of Biochemistry, Gandhi Medical College, Bhopal.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Kaustubh Mundada,
Room No. 78, F Block,
GMC Hostel,
Gandhi Medical College,
Bhopal-462001, Madhya Pradesh.
E-mail:kaustubh2013@gmail.com

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