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A systematic study on the glycosylated haemoglobin in diabetes associated hypertension in Chhattissgarh population

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ABSTRACT

In Chhattisgarh region of India, diabetes associated hypertension cases have not yet been systematically identified. An easy, cost effectiveness and less time consuming method has to be developed for the critically monitored diabetes associated complication cases. Hence the role of Glycosylated haemoglobin in diabetic with hypertension in Chhattishgarh was studied. 160 diabetic patients have participated in our study and it was completed the period of 2007-2009. The overall mean values have been determined for 20 diabetic patients in the period of two years including 20 control patients values were subjected for statistical analysis. The blood samples were collected from both male and female subjects belonging to different economic groups, different dwellings, and different professions. Estimation of various biochemical parameters were done in the samples collected. Efforts were made to establish a correlation between the above and glycosylated haemoglobin on the basis of the results obtained. The present study of the hypertension in diabetics leads to conclusion that a good glycemic control would be the useful tool to prevent the possibilities of development of diabetic complications. In conclusion, monitoring HbA1c level is an easy, cost effectiveness and less time consuming method for assessing diabetes as well as diabetes associated hypertension.

Key words: Hypertension, Diabetes mellitus, Glycosylated haemoglobin and HbA1c.

INTRODUCTION

Diabetes increases the risk of coronary events two-fold in men and four-fold in women, which is due to the frequency of associated cardiovascular risk factors, such as hypertension, dyslipidemia and clotting abnormalities. In observational studies, people with both diabetes and hypertension have approximately twice the risk of cardiovascular disorders as non-diabetic people with hypertension. Further, it has been investigated that hypertensive diabetic patients are at enhanced risk for retinopathy and neuropathy [1].

Hypertension is an extremely common co-morbid condition in diabetics, affecting 20-60 % of patients with diabetes. It has been well documented that hypertension substantially increases the risk of both macro-vascular and micro-vascular complications, including stroke, coronary artery disease, peripheral vascular disease, retinopathy, nephropathy and possibly neuropathy. Further, it has been well established that both type-1 and type-2 diabetes are associated with hypertension [2]. It has been defined by world health organization (WHO) guidelines that hypertension in general as a blood pressure exceeding 160/95 mm Hg and borderline hypertension as that lying below these limits [3]. Apart from other factors affecting the pathogenesis of hypertension, genetics plays a vital role, which has to be further explored [4. 5]. It has been suggested that dietary management with moderate sodium restriction has been effective in reducing blood pressure in individuals with hypertension. Moreover, it has been reported that each 10 mm Hg decrease in mean systolic blood pressure is associated with reductions in risk of 12 % for any complication related to diabetes 15 % for death related to diabetes, 11 % for myocardial infarction and 13 % for micro-vascular complications. Therefore, an easy, economic and less time consuming method has to be develpoed for regular monitoring of diabetes associated hypertension.

It has been well accepted that the Glycosylated haemoglobin (HbA1c) is used as the most reliable test for assessing chronic glycemia [6]. The HbA1c reflects overall blood glucose levels over a period of 2-3 months and further, used to monitor diabetic therapy. It has been recognized that the HbA1c as an essential adjunct to regular self-blood glucose measurement assisting in the achievement of the best possible glycemic control. The major use of the HbA1c assay is to assess changes in metabolic control that follow an alteration in treatment. Moreover, diabetes treatment is adjusted based on the HbA1c result, expressed as the percentage of haemoglobin that is glycated. The HbA1c does not require fasting blood sample and it is not affected by recent meals [7]. In our previous study, we have reported that the HbA1c level is a reliable parameter for assessing diabetes associated hyperlipidemia, nephropathy and neuropathy [8, 9, 10].

On this context, we have further extrapolated our research work to investigate the effect of the HbA1c level in diabetes associated hypertension in Chhattisgarh population.

MATERIALS AND METHODS

1.1. Subjects:

Subjects with both sex were belonging to different age groups (30 to 70 years), different economic groups (upper, middle and lower), different dwellings (urban, semi-urban, rural), different occupations (professionals, farmers, businessmen and students), from the patients of

Chhattisgarh population those who are suffering from the Type-2 Diabetes mellitus. Sample collection was normally carried out during the working hours i.e. in between 8.00 am to 5.30 pm. every day. A consent letter has been taken from all the subjects and the experiment is approved by Institution Ethics Review Board, Chhattisgarh Institute of Medical Science, Bilaspur, India.

Chemicals and Reagents:
All chemicals and reagents of Excellar quality of Roche diagnosis Ltd., (Germany and USA), Randox (UK), Bayer & Accurex (India) have been used for various chemical analyses and estimations.

Experimental Design:
The study was undertaken in 160 diabetic patients during 2009-10. The experiment was carried out in four different groups and was divided into control (CON), diabetes (DM), hypertension (HYT) and diabetes associated hypertension (DM+HYT) groups. The overall mean values have been determined for 20 diabetic patients in the period of two years including 20 control patients values were subjected for statistical analysis.

Sample Collection:
The blood samples were collected in the morning on fasting (8-12 hrs fasting after their dinner the previous night) and post-prandial (1.5 hrs. to 2 hrs after lunch). The same procedure was followed for each patient on his/her every visit. The Hb1Ac was estimated in EDTA anti-coagulated specimen, as it has to be done in the whole blood with preparation of haemolysate sample, while other parameters were estimated in serum or plasma samples. Special care was taken during sample collection from different patients to maintain and keep up time.

Biochemical estimation:
The fasting and post-prandial blood sugar levels were estimated by following end point colorimetric assay method [6] and the HbA1c was estimated by following Turbidometric inhibition Immuno assay method [11]. All the readings were taken by using Hitachi-912 fully automatic chemical analyzer.

Statistical analysis:
The results are expressed as Mean ± S.E.M. The statistical significance was determined by One-Way Analysis of Variance (ANOVA) followed by *Post-hoc* Student Newman Keuls test. $P < 0.05$ was considered to be statistically significant.

RESULTS AND DISCUSSION

Effect on fasting, post-prandial blood sugar and HbA1c levels:
The effect of fasting blood sugar level is illustrated in Fig-1 (A). Statistical analysis by One way ANOVA revealed that there was significant difference among groups [$F(3, 76) = 34.63$, $P<0.05$]. *Post hoc* analysis by Student Newmann keuls test revealed that diabetes (DM) and diabetes associated hypertension (DM+HYT) groups were significantly increased fasting blood sugar levels and no significant change in fasting blood sugar levels was observed in hypertension (HYT) group compared to control. Further, there was significant decrease in fasting blood sugar

level in HYT and was found to be no significant change in fasting blood sugar levels in DM+HYT compared to DM, indicating that hypertension alone has no role in the levels of fasting blood sugar level.

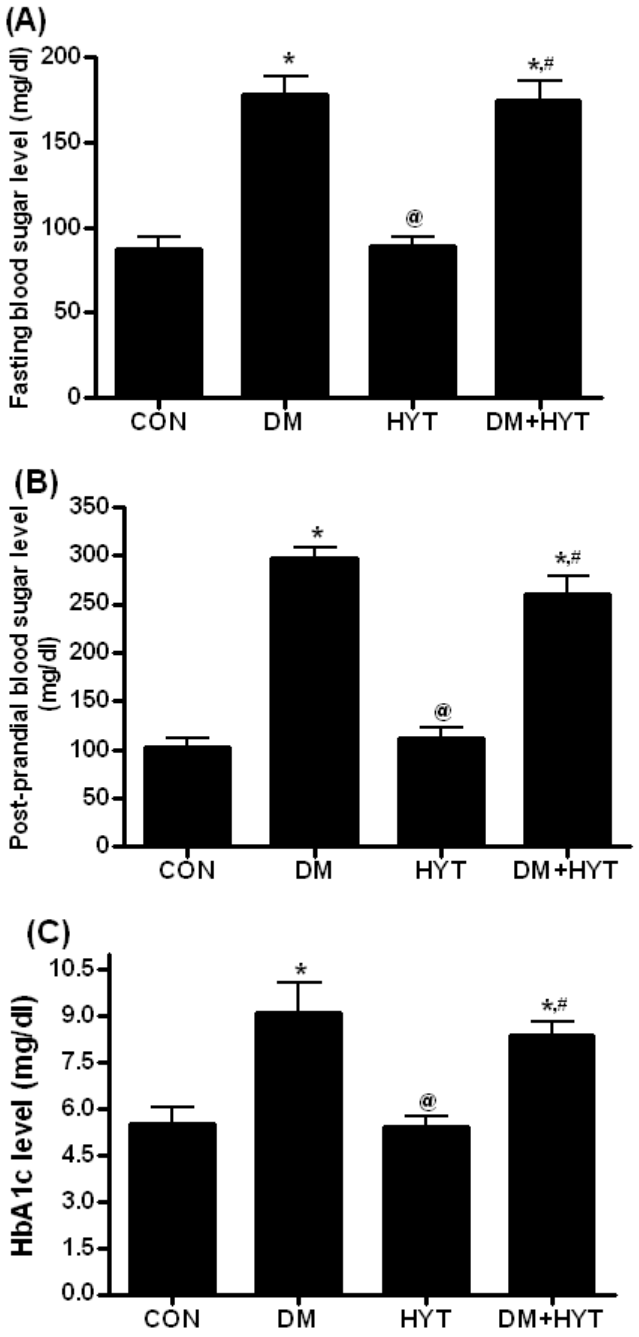

Fig. 1. The effect on level of fasting blood sugar (A), post-prandial blood sugar (B) and glycosylated haemoglobin (C) in control, diabetes (DM), hypertension (HYT) and diabetes associated hypertension (DM+HYT) are depicted

All values are Mean±SEM. $^{*}P<0.05$ compared to control, $^{@}P<0.05$ compared to DM and $^{\#}P<0.05$ compared to HYT [One-way ANOVA followed by Student Newmann keuls test].

Furthermore, DM+HYT showed significant increase in fasting blood sugar levels compared to HYT. The similar effect was observed in both post-prandial blood sugar [Fig-1 (B); $F(3, 76) = 63.12$, $P<0.05$] and HbA1c levels [Fig-1 (C); $F(3, 76) = 9.72$, $P<0.05$].

In the present investigation, diabetes associated hypertension (DM+HYT) showed significant elevated levels of HbA1c in blood. The present study gains critical importance as HbA1c is an important tool in clinical investigation and would guide in the pathogenesis of diabetes associated hypertension.

Hypertension is well documented risk factor for cerebrovascular and cardio-vascular diseases, especially in micro-albuminuria. The blood pressure is directly and continuously related to the risk of cardiovascular disease and stroke [12]. Hypertension is an extremely common feature and affects approximately 20-60% of diabetic persons. In most patients, the treatment should aim to normalize the blood pressure to <140/90 mm Hg. Treatment of hypertension begins with lifestyle management, including reduced dietary fat, lesser salt intake, and weight loss for obese patients and increased regular physical activity. If these measures are adapted, the blood pressure can be lowered up to 110/80 mmHg. In certain sub-groups of patients, the treatment modalities are of specific importance and should be constantly evaluated according to efficacy, cost effectiveness, safety and quality of life. It has been reported that hypertension develops microvascular disease in diabetic patients. Insulin resistance is closely associated with high blood pressure .There is some evidence that insulin is an endothelium dependent vasodilator, releasing nitric oxide from endothelium which relaxes vascular smooth muscle due to insensitivity to insulin action on the endothelium as well as on metabolic changes could contribute to the increased peripheral resistance that is the hallmark of hypertension in diabetes [13].

In the present study, we found that there was significant elevation in fasting, post-prandial and HbA1c levels in both diabetes and diabetes associated hypertension. The result was found to be similar with the previous published report [14-15]. The elevated blood sugar in diabetes mellitus perhaps due to insulin resistance, increased tissue inflammation, endothelial dysfunction, increased tissue rennin-angiotension aldosterone system and increased sympathetic nervous system. It has been assumed that diabetes is associated with cardiovascular risk factors, which may be present before the onset of hyperglycemia or develop after the diagnosis of diabetes. The metabolic syndrome is a cluster of various diseases such as hypertension, obesity, dyslipidemia and hyperglycemia, in which the insulin resistance and adiponectin/Leptin ratio plays key pathogenic role and it is supposed that this syndrome is a powerful determinant of diabetes and cardiovascular disease. Measurements of glycosylated hemoglobin remain the gold standard for the assessment of glycemic control in patients with diabetes mellitus. The HbA1c is the powerful predictor for development of diabetes associated hyperlipidemia, nephropathy, neuropathy irrespective of blood glucose measurement. Therefore, the HbA1c is the screening tool and the measurement is mandatory to assess diabetic complications in aforesaid groups. Therefore, the finding of the present study tells that in diabetic subject with HbA1c may create various clinical situations for the development of diabetes.

The long-term complications of diabetes have major consequences for individual and health care providers. The good glycemic control is more potent factor and is being assessed by the measurement of glycosylated hemoglobin. This assay plays central roles in diabetic

management, patients clinical guidance etc. It reduced the frequency of blood collection and thus reduced the time and cost compared to regular monitoring of blood glucose levels. The blood glucose was considered as a prime test for optimizing treatment of diabetes mellitus. However, the glycosylated hemoglobin (HbA1c) determination is the new better method to monitor the long term glucose control and it would prevent or delay the further diabetic complications. Diabetic patients those who are on an oral anti-hyperglycemic agent especially for insulin dependent diabetic patients should go for HbA1c test as recommended by American Diabetes Association.

CONCLUSION

In conclusion, monitoring HbA1c level is an easy, cost effectiveness and less time consuming method for assessing diabetes as well as diabetes associated hypertension.

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