EFFECT OF OBESITY AND INSULIN RESISTANCE ON DIABETIC CONTROL

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ABSTRACT

Diabetes Mellitus in obese and non-obese Indian individuals. **AIMS:** Effect of Obesity and insulin resistance on diabetic control. **SETTINGS AND DESIGN:** 50 each groups Diabetic individuals obese and non-obese. **METHODS AND MATERIAL:** On selected 50 each group diabetic patient and normal, following blood investigations has been performed - Plasma Glucose, Glycohemoglobin and Serum Insulin. **STATISTICAL ANALYSIS USED:** Individuals patient's results were analyzed and compared with the normal controls. **RESULTS AND CONCLUSION:** The changes in glycosylated haemoglobin are mainly proportional to the post lunch glucose level ($r = 0.773$) ($p < 0.01$) and not correlated to circulating insulin or the body mass index. However the levels were higher in obese diabetes (Type I and II both) than in non-obese. Mechanism of resistance in insulin receptor interactions due to obesity is well known. However, obesity does not seem to affect directly glycosylated haemoglobin. Under such circumstances, the reduction of weight for a diabetic person can improve sugar control by minimizing insulin resistance and thereby can improve glycosylated haemoglobin levels.

KEY WORDS

Diabetes Mellitus, plasma glucose, glycosylated haemoglobin, Obesity and insulin resistance

INTRODUCTION

The clinical, laboratory procedures includes determination of glycosylated Haemoglobin (HbA1c) and Insulin levels are significant means for detection in diagnosis, staging, monitoring and evaluation of response to therapy for control of the disease. Primary indicators are normal routine fasting and post prandial blood sugar levels. Standardized technique has been established for several decades. However, newer techniques have been also used in our study and different groups of biochemical investigations tried & reported to be useful (1, 2, 3).

HbA1c in whole blood originates principally from RBC and measurement of this fraction is valuable for the identifications of blood glucose status. Hence the present study was undertaken to determine the role of HbA1c and insulin levels in the different groups of Type I, Type II obese and non-obese diabetes and healthy normal individuals in particular. Therefore in the present plan of study attempts have been made to elucidate the functional attribution of these tests and relevant parameters for the early detection of diabetes

and to monitor the management of the disease.(4,5,6)

An abnormal growth of adipose tissue due to an enlargement of fat cell size (Hypertrophic Obesity) or increase in fat cell number (Hyperplastic Obesity) or a combination of both. A body mass index of 25 or more in males and females (5, 7, 8).

Primary goal of diabetic treatment is to achieve satisfactory control and to avoid long term complications. A number of various criteria are suggested for assessment of diabetic control. However, the diversity of treatment regimes and variability in diet makes the task difficult (9).

Glycosylated haemoglobin is one of the satisfactory tools for assessment of blood glucose control in diabetic patients. Presently ion exchange chromatography, affinity chromatography and high performance liquid chromatography are available methods for the estimation for HbA1c, the major glycated fraction (10, 11, 12). Number of commercially available kits give possible average sugar level depending on the regression analysis of their own methods.

Obesity and Insulin resistance are interdependent complications in diabetes. The glycosylation of haemoglobin is greatly affected by insulin resistance and thereby elevated sugar levels. The exact measure of circulating insulin indicate the degree of insulin resistance, the extent of obesity judged by body mass

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index (BMI) and the degree of control indicated by HbA1c can give valuable information of the corrective metabolism reported by different authors (13, 14, 15).

MATERIALS AND METHODS

The present study was planned for the group of 50 diabetic patient each of Type I and Type II with various treatment modes, attending the O.P.D. of Cumballa Hill Hospital and Purohit Hospital, Mumbai.

50 subjects from each group have been selected for this study are as follows.

- Controlled Type I Non Obese
- Uncontrolled Type I Non Obese
- Controlled Type II Non Obese
- Uncontrolled Type II Non Obese
- Controlled Type I Obese
- Uncontrolled Type I Obese
- Controlled Type II Obese
- Uncontrolled Type II Obese

Similarly 50 normal controls for each group have been examined for the same biochemical parameters.

The levels of fasting plasma glucose, post prandial glucose, HbA1c and insulin levels in Type I and Type II obese and non-obese diabetic patients were estimated on advanced automated analyser by the following principle based methods (16-18) :

- Plasma Glucose (GOD/POD) method
- Glycohemoglobin - Clonital method
- Serum Insulin - Clonital method.

Glucose is oxidised to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4 - aminoantipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of the colours formed is directly proportional to the amount of glucose present in the serum.

For **Glycosylated Haemoglobin(HbA1c)** is unaffected by diet, insulin or exercise on the day of testing and thus reflects the average glucose level over the last several weeks. Hence it reflects on the long-term metabolic control of glucose in individuals.

HbA1c was estimated using the Ion-Exchange resin method (Clonital). Whole blood is mixed with lysing reagent to prepare a hemolysate. This is then mixed with a weakly binding cation-exchange resin. The non-glycosylated haemoglobin binds to the resin leaving HbA1c free in the supernatant. The HbA1c percentage

is determined by measuring the absorbance of the HbA1c fraction and of the total Haemoglobin at 415 nm.

Insulin ELISA is a solid phase two - site enzyme immunoassay. It is based on the direct sandwich technique in which two monoclonal antibodies are directed against separated antigenic determinants on the insulin molecule. During incubation insulin in the sample reacts with peroxide - conjugated anti - insulin antibodies and anti - insulin antibodies bound to the micro titration well. A simple washing step removes unbound enzyme labelled antibody. The bound conjugate is detected by reaction with 3,3'.5,5'-tetramethylbenzidine. The reaction is stopped by adding acid to give a colorimetric end point that is read spectrophotometrically.

RESULTS AND DISCUSSIONS

50 healthy individuals properly scrutinized by the Physicians without any patho-physiological abnormalities.

They were considered to obtain base line data of glucose, glycosylated haemoglobin and insulin level. Patients suffering from carbohydrate intolerance were divided into two groups i.e. Type I diabetic and Type II diabetic in accordance with the WHO guidelines (1, 13, 19).

For the relevant multivariate and regression analysis to see the correlation study, SPSS (Pearsons) software package was used as per our main aim and objective analysis purpose.

The Type I diabetic patient were then further divided as per their body weight, height and Body Mass Index (BMI) and labelled as Type I Obese and Non-Obese patient.

Estimated values for fasting blood sugar, Post prandial blood sugar, glycosylated haemoglobin, fasting insulin and Post prandial insulin for Type I and Type II non-obese controlled and uncontrolled diabetes are presented in Figure 1 and 2.

Type I Non-Obese controlled diabetic patients have relatively almost the same values of Fasting and Post prandial blood sugar and glycosylated haemoglobin level than the normal individuals. However, their insulin (Fasting and Post prandial) i.e. (20.68 ± 6.46) and

Fig. 1. Blood sugar, insulin and glycosylated haemoglobin levels in different groups of Type I - non-Obese controlled and uncontrolled diabetic patients. Values are Mean $\pm$ SD. $P < 0.01$ as compared to normal controls (n = 50 in all the groups)

Fig. 2. Blood sugar, insulin and glycosylated haemoglobin levels in different groups of Type II - non-Obese controlled and uncontrolled diabetic patients. Values are Mean $\pm$ SD. $P < 0.01$ as compared to normal controls (n = 50 in all the groups)

(23.90 ± 5.24) level have 1.5 times more than normal (13.11 ± 5.36) and (17.12 ± 5.22), respectively.

Type I Non-Obese Uncontrolled diabetic patient showed nearly 2 times more the blood glucose level (Fasting and Post prandial) i.e. (152.03 ± 42.36) and

(226.10 ± 81.39) in comparison with normal individuals and their fasting insulin level shows no changes but their Post prandial insulin level (22.64 ± 14.42) as well as glycosylated haemoglobin (8.45 ± 2.46) are 1.5 times increased than the normal individuals.

Type II Non-Obese controlled diabetic patients fasting

blood sugar and glycosylated haemoglobin have no changes whereas the Post prandial blood sugar level slightly elevated with respect to the normal individuals. In the same sequence their fasting insulin (18.52 ± 6.18) as well as Post prandial insulin (20.02 ± 5.44) levels are 1.5 times more than the normal individuals.

Type II Non-Obese Uncontrolled diabetic patient showed their sugar status 2 times more than the normal individuals viz. FBS (154.87 ± 32.91) and PPBS (252.04 ± 38.50), HbA1c (11.04 ± 2.09) and Post prandial insulin (35.76 ± 6.64) levels, whereas their Fasting insulin (21.50 ± 7.80) level shows 1.5 times increase.

Estimated values for fasting blood sugar, Post prandial blood sugar, glycosylated haemoglobin, fasting insulin and Post prandial insulin for Type I and Type II obese controlled and uncontrolled diabetes are presented in Figure 3 and 4.

The Obese patient were examined and divided into controlled and uncontrolled diabetic depending on their glucose level. At the same time their insulin level and glycosylated haemoglobin levels were also estimated and these patients were grouped into Type I Obese controlled and Uncontrolled diabetic patient. Our findings are also presented in the form of histogram in 3 and 4 for Type I and Type II diabetes.

The data reveals that the fasting blood sugar and Post

prandial glucose level of obese controlled diabetic patients were found to be nearly same as that of the normal individuals (93.58 ± 7.91) and (122.44 ± 11.39).

Similarly in Type I Obese Uncontrolled diabetic patients fasting blood sugar (158.71 ± 31.10), HbA1c (15.56 ± 5.41) and fasting insulin (22.68 ± 10.66) were found to be increased by 1.5 times whereas the Post prandial blood sugar (249.65 ± 43.47) and Post prandial insulin (36.17 ± 8.85) level was more than 2 times with respect to normal individuals.

In Type II Obese controlled diabetic patients there is no increase in the sugar status, HbA1c and insulin levels. They were found to be similar as compared to the healthy normal.

Whereas Type II Obese Uncontrolled diabetic patient showed 2 times increase in the levels of fasting sugar (159.99 ± 32.09), Post prandial sugar (247.97 ± 36.38) and fasting insulin (23.32 ± 6.95), Post prandial insulin (35.87 ± 7.19) than the normal individuals while their glycosylated haemoglobin (16.69 ± 6.30) level is 4 fold increase in comparison to normal individuals. ($P < 0.01$).

SUMMARY AND CONCLUSIONS

Overall results represented in Figure 1 to 4 prominently supports the view that glycosylated haemoglobin can be a good indicative parameter for monitoring the

Fig. 3. Blood sugar, insulin and glycosylated haemoglobin levels in different groups of Type I - Obese controlled and uncontrolled diabetic patients. Values are Mean $\pm$ SD. $P < 0.01$ as compared to normal controls ($n = 50$ in all the groups)

Fig. 4. Blood sugar, insulin and glycosylated haemoglobin levels in different groups of Type I - Obese controlled and uncontrolled diabetic patients. Values are Mean $\pm$ SD. $P < 0.01$ as compared to normal controls (n = 50 in all the groups)

disease control irrespective of the Type I and Type II of diabetes and the body mass index, which is also reported by Bunn *et al.* (18).

The changes in glycosylated haemoglobin are mainly proportional to the post lunch glucose level ($r = 0.773$) ($p < 0.01$) and not correlated to circulating insulin or the body mass index. However, the levels were higher in obese diabetes (Type I and II both) than the non-obese (20, 21).

Mechanism of resistance in insulin receptor interactions due to obesity is well known however, obesity does not seem to affect glycosylated haemoglobin directly as reported by Bunn *et al.* (18, 21).

Under such circumstances, the reduction of weight for a diabetic person can improve sugar control by minimising insulin resistance and thereby can improve glycosylated haemoglobin levels (22).

Extension of present study in-patient receiving the oral drugs like Metformin hypoglycaemic agent promoting anaerobic respiration will be interacting model (23, 24).

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