Research Paper Biochemistry

O and N Linked Glycoproteins in Type –I Diabetes Mellitus with Insulin Secretion

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ABSTRACT

Aim: The aim of this study was to assess the ability of O and N linked glycoproteins in type-II Diabetes Mellitus with insulin resistance. Protein-bound carbohydrates are components of serum glycoproteins, the increase in protein-bound carbohydrate levels should be attributable to a quantitative change in serum glycoproteins Design/Methods: Type-II diabetic patients were selected on the basis of serum glucose and insulin levels. In this study, we demonstrated that O and N glycoproteins very helpful for type II diabetes Mellitus. Results: Pooled diabetic and normal sera, were analyzed for their concentrations of all major and several minor glycoproteins. The difference in concentrations between the diabetic and control pools was used to predict the increase in protein-bound hexose and fucose. Conclusions: We conclude that O and N linked glycoproteins has a definite role in the diagnosis of diabetes mellitus.

KEYWORDS : Insulin, Hexose, Fucose and Diabetes Mellitus

I. Introduction

Glycoprotein are important constituents of membranes and secretary proteins1, synthesis and secretion of glycoprotein in to circulation and the composition of sugar components are likely to be altered in pathological conditions2,3. Glycoproteins can be simply defined as proteins that have carbohydrate moiety covalently attached to their peptide portion.

The glycoprotein as a group have multiple and complex function it found in enzymes, hormones, blood substance and constituents of extracellular membranes. These are organic compounds, composed of both a protein and carbohydrate monosaccharide, usually hexosamine, fucose and sialic acid joined together covalently linked to polypeptide chain. The level of different types of serum glycoprotein are maintained within a narrow range in health but elevated in many pathological conditions4. This is due to altered glycosylation of secretary proteins.

Glycosyltransferases catalyze the transfer of a monosaccharide from specific sugar nucleotide donors onto particular position of a monosaccharide in a growing glycan chain in one or two possible anomeric linkages5,6.

O-GlcNAcylation is a specific type of glycosylation since O-GlcNAc residues are not elongated and do not form complex structur7e. This dynamic and inducible modification is more similar to phosphorylation than to classical glycosylation8.

II. Materials And Methods

IIa. Chemicals:

Insulin kits were purchased from immune Diagnostic kits, USA. All the other chemicals used were of analytical grade.

IIb. Experimental Design

Out of 100 patients were divided in to two groups. Group I – Normal subjects, Group-II – type II Diabetes Mellitus. Patients demographic data, including sex, age, and risk factors for cardiac events including high-risk age (men >45, women >55 years old), smoking history, medical history of hypertension, hyperlipidemia, diabetes, and a positive family history, drug history, presence of arrhythmia, laboratory data, ECG, and echocardiography findings, were recorded.

The study was conducted during the period of Feb 2015 to March 2016 in department of endocrinology, PGIMER and DR RAM MANOHAR LOHIA HOSPITALS, NEW DELHI. INDIA.

III. Statistical Analysis

Data were analyzed using the SPSS software package, version 17.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed using range, mean, SD, and median, whereas qualitative data were expressed as frequency and percentage. P value was assumed to be statistically significant at 0.05.

IV. ETHICAL CONCERN

Ethical clearance was obtained from the Ethical committee meeting conducted at PGIMER and DR RAM MANOHAR LOHIA HOSPITALS, NEW DELHI. INDIA.

V. Results

In Fasting Glucose concentration and insulin secretion in control and type –II diabetes mellitus

Table 1 shows the presentation according to concentration of fasting glucose and insulin secretion in control and type II diabetes mellitus patients. This table shows that fasting glucose($p<0.0001$) and insulin secretion($p<0.05$) were significantly increased in type II diabetes mellitus patients when compared with control subjects.

Particulars	Control	Type II Diabetes mellitus Patients	P value
In Fasting glucose (mg/dL)	91.3 ± 8.7	216.4 ± 19.4	<0.0001
Insulin Secretion (nmol/ m2/24hours)	68.4± 6.1	79.2± 8.3	<0.05

2. In Random Glucose concentration and insulin secretion in control and type –II diabetes mellitus

Table 2 shows that the concentration of Random glucose and insulin secretion in control and type II diabetes mellitus patients. This table shows that random glucose concentration ($P<0.0001$) were significantly increased in type II diabetes mellitus patients when compared with control subjects but the random insulin secretion concentration ($p<0.001$) were significantly decreased in type II diabetes mellitus patients when compared with normal subjects.

Particulars	Control	Type II Diabetes mellitus Patients	P value
In Random glucose (mg/dL)	103.7 ± 9.3	274.3 ± 27.1	<0.0001
Insulin Secretion (nmol/m2/24hours)	76.4± 7.5	29.1± 3.3	<0.001

3. In O and N linked Glycoproteins in control and type –II diabetes mellitus

Table 3 shows the presentation according to concentration of O and N linked glycoproteins in control and type II diabetes mellitus patients. This table shows that protein sialic acid , protein bound fucose, protein bound hexose and protein hexamine levels ($p<0.01$, $p<0.05$) were significantly increased in type II diabetes mellitus patients when compared with control subjects

Particulars	Control	Type II Diabetes mellitus Patients	P value
Protein sialic acid	1.6± 0.2	2.7± 0.3	<0.01
Protein bound Fucose	11.2± 1.3	17.7± 1.8	<0.01
Protein bound hexose	102.3± 10.1	115.6± 11.7	<0.05
Protein hexamine	1.4 ± 0.1	2.5± 0.2	<0.01

VI. Discussion

Type 2 diabetes is characterized by hyperglycemia caused by defects in insulin secretion (impaired -cell function) and insulin action (insulin resistance by the liver and muscle tissue) [9,10,11].

In a prospective study[12,13] of Pima Indians, a group at high risk for developing diabetes, body composition, insulin action, insulin secretion, and endogenous glucose output were measured over several years in subjects whose glucose tolerance went from normal to impaired to diabetic.

The elevation of protein-bound hexose observed in our pooled diabetic serum was quite adequately predicted from measured increases in serum glycoproteins. This observation, relating these two types of measure meant so closely, supports the conclusion that no disturbance of protein-bound hexose (galactose and mannose) occurs in the diabetic state. Studies of purified by Schmid's group also showed no change in protein-bound hexose, hexosamine, and sialic acid in this protein under conditions which markedly affected its synthesis rate[13,14]. The failure to observe a quantitative derangement in protein-bound hexose suggests that in diabetes mellitus no major disturbance of carbohydrate attachment to protein or of heterosaccharide unit size occurs in serum protein synthesis.

This is in contrast to the increase in protein-bound hexose (galactose and glucose) observed in basement membrane glycoprotein by Beisswenger and Spiro in diabetic glomeruli obtained from human kidneys. The serum glycoproteins are structurally different from basement membrane glycoprotein. The major carbohydrate linkage is to asparagine rather than hydroxyl lysine, serum glycoprotein heterosaccharide units average more than a dozen monosaccharides, while only two are attached to each hydroxyl lysine. Beisswenger and Spiro's data indicate an excessive oxidation of lysine to hydroxyl lysine rather than excess glycosylation, since the percentage of hydroxyl lysine sites glycosylated remains constant while hydroxyl lysine content is increased.

VII. Conclusion

We conclude that O and N linked glycoproteins has a definite role in the diagnosis of diabetes mellitus.

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