Serum L-Fucose, Total Sialic Acid and Ceruloplasmin Levels in
Type II Diabetic Subjects of Somwarpet Taluk– A Preliminary
Study

Prathiroopa¹, Kavyashree SJ¹, Ashwitha KM¹, Suresh Babu TV¹,
*Manjula Shantaram²

Post Graduate Students¹, Professor and Guide²
Department of Post Graduate Studies & Research in Biochemistry
PG Center, Chikka Aluvara, Somwarpet Taluk, Kodagu District, Karnataka
*manjula59@gmail.com

Abstract: The present study was aimed at verifying whether serum L-fucose, total sialic acid (TSA) and ceruloplasmin can be used as prognostic indicators for type II diabetes mellitus, which will help in detecting complications of diabetes at an earlier stage. Thirty confirmed type II diabetic patients and 30 non-diabetic subjects were considered for the study. Serum L-fucose, total sialic acid and ceruloplasmin were estimated by Winzler’s methods and diamine oxidase methods respectively. Serum L-fucose and TSA were significantly increased in diabetes when compared to the non diabetic control, where as ceruloplasmin was apparently increased in diabetes. Serum L-fucose, total sialic acid and ceruloplasmin can be used as prognostic indicators for type II diabetes mellitus.

Keywords: Ceruloplasmin, L-Fucose, Serum, Total Sialic Acid, Type II Diabetes Mellitus

1. INTRODUCTION

Diabetes mellitus is a clinical condition characterized by hyperglycemia due to insufficient or inefficient insulin. As a consequence, the blood glucose level is elevated which spills over into urine in diabetes mellitus. The important feature of diabetes mellitus is that the body cells are starved of glucose despite its very high concentration around i.e. scarcity in plenty [1]. Type II diabetes mellitus is a worldwide chronic metabolic disease that is seriously harmful to human health.

Glycoconjugates play an important role as markers in diabetes mellitus. Glycoconjugates are biologically vital molecules with varied functions. They consist of oligosaccharides of changeable size and complexity, attached to a non-sugar moiety. Glycoconjugate structures are often very complex and have intricate biosynthetic pathways. Carbohydrate antigens are expressed on the cell surface as components of glycoproteins, glycosphingolipids and proteoglycans; these antigens constitute significantly to fundamental biological functions, such as cell differentiation, cell adhesion, cell-cell interactions, pathogen-host recognition, toxin- receptor interactions, cancer metastasis, immune responses and regulation of signaling pathways [2]. Several studies have revealed that glycoconjugates play key roles in infection and disease [3,4].

L-Fucose (6-deoxy-L-galactose) is a monosaccharide that is a common component of many N- and O-linked glycans and glycolipids produced by mammalian cells. Fucose is the fundamental sub-unit of the fucoidan polysaccharide. Alpha1→3 linked core fucose is a suspected carbohydrate antigen for Ig E-mediated allergy. Two structural features distinguish fucose from other six-carbon sugars present in mammals which include the lack of a hydroxyl group on the carbon at the 6-position (C-6) and the L-configuration. In fucosylated glycans, fucose can exist as a terminal modification or serve as an attachment point for adding other sugars. In human N-linked glycans, fucose is most commonly linked by α-1,6 to the reducing terminal beta-N-acetyl glucosamine. However, fucose at the non-reducing terminally linked α-1, 2 to galactose forms the H antigen, the substructure of the A and B blood group antigens. However, recently glycosyl transferase activities capable of adding sugars directly to fucose have been identified [5]. McMillan and Barbara have found elevation of glycoprotein fucose in diabetes mellitus [6]. Sawke and Sawke estimated role of serum fucose as a useful, diagnostic and prognostic marker when used singly or in combination in malignant diseases.
Sialic acid is the generic term for the N- or O-substituted derivatives of neuraminic acid, a monosaccharide with a nine-carbon backbone [10]. It is also the name for the most common member of this group, N-acetyl neuraminic acid (Neu5Ac or NANA). Sialic acids are found widely distributed in animal tissues and mostly in glycoproteins and gangliosides which occur at the end of sugar chains connected to the surface of cells. That is because it seems to have appeared late in evolution [11]. In humans, the brain has the highest sialic acid concentration where they have an important role in neural transmission and in ganglioside structure. Relationship between sialic acid and metabolic variables in Indian type II diabetic patients was proved [12]. Ghosh et al. have estimated the serum sialic acid in patients with type II diabetes mellitus in Sikkim [13]. Serum Sialic acid and microalbuminuria in non-insulin dependent diabetes mellitus was estimated [14]. Correlation of microalbumin and sialic acid with anthropometric variables in type 2 diabetic patients with and without nephropathy was checked [15]. Suchetha et al., investigated the status of sialic acid and total antioxidant levels in Indian type 2 diabetes mellitus patients in and around Mangalore [16].

Ceruloplasmin is an abundant glycoprotein in human plasma and is mainly produced in liver [17]. Ceruloplasmin contains six cupredoxin domains and has a high molecular weight of 134 kDa [18]. In addition to its role as a ferroxidase, ceruloplasmin exhibits several other catalytic activities. For example, ceruloplasmin was reported to have both NO-oxidase and glutathione peroxidase activities [19, 20]. Furthermore, ceruloplasmin is capable of oxidizing an extensive group of organic substrates that includes both xenobiotics such as organic amines and physiologically relevant substrates like biogenic amines [21, 22]. Cunningham et al. observed an elevated plasma ceruloplasmin in insulin-dependent diabetes mellitus: evidence for increased oxidative stress as a variable complication [23]. Elevated serum ceruloplasmin levels in subjects with metabolic syndrome: A population-based study was carried out by Kim [24]. Levels of ceruloplasmin, transferrin and lipid peroxidation in the serum of patients with type 2 diabetes mellitus were studied [25]. Shenoy et al. estimated the serum ceruloplasmin levels in the patients suffering from psoriasis [26]. Elevation of serum ceruloplasmin levels in brain tumours was observed by Manjula et al. [27].

The objective of the study was to assess the levels of serum L-fucose, total sialic acid and ceruloplasmin in the diabetic cases of Somwarpet taluk since there are fewer reports available on this aspect. Further, the study was aimed with a view that it would be of prognostic importance in diabetic subjects.

2. MATERIALS AND METHODS
2.1. Sample Collection
For this study, 30 individuals with type 2 diabetes of both the sexes, aged between 30-80 years were selected from Somwarpet taluk. Diabetic patients were diagnosed with the disease during the last three years in government hospitals of Kushalnagar and Somwarpet. At the same time, 30 healthy individuals were taken as controls. To convince the study subjects and clarify their doubts, questionnaires were made in the local language and distributed. Duly signed consent forms were collected, prior to drawing of blood.

Five ml of blood samples were collected by venipuncture at any time of the day. The blood was centrifuged and serum was separated and stored at -4°C for subsequent analysis of Glucose, L-Fucose, Total Sialic acid and Ceruloplasmin levels.

Diabetes was confirmed by estimating the serum glucose level by using GOD-POD kit. Serum L-fucose and total sialic acid were estimated by standard methods [28] and serum ceruloplasmin was determined by diamine oxidase method [29].

2.2. Statistical Analysis
The data was collected and statistically analyzed by comparing glucose, L-fucose, TSA and ceruloplasmin levels in confirmed type II diabetic subjects and non-diabetic subjects and results were expressed as mean ± standard deviation (SD). Student’s unpaired’t’ test was used to compare the levels in study groups.
3. RESULTS AND DISCUSSION

In this study, blood glucose mean value in control subjects (n=30) was found to be 90.90 ± 27.34 mg/dL while in diabetic patients (n=30) was 136.7 ± 38.0 mg/dL. Blood glucose was estimated by GOD-POD method using a readymade standard kit. There was a significant increase (P<0.001) in glucose levels in diabetic patients when compared to non-diabetic controls. This confirmed the diabetic status of the study subjects.

Serum L-fucose mean value in controls was 9.6 ± 3.9 mg/dL and in diabetics, 18.6 ± 10.4 mg/dL (Figure 1) which was increased significantly (P<0.001). In earlier studies, similar results were observed [6]. There was an increased content of serum glycoproteins in diabetic condition, this might possibly would have come from disruptions of membranes. Depleted glycoprotein in diabetic might be due to increased depolymerisation of glycoproteins and accelerated secretion of glycoproteins into the serum.

Levels of L-Fucose in Non-Diabetic and Diabetic Subjects

![L-Fucose levels](image1)

**Fig1.** Serum L-Fucose increases significantly (P-value<0.001) in confirmed diabetic subjects when compared to non-diabetic.

Mean serum total sialic acid level in non-diabetic controls was 52.1± 3.98 mg/dL while in diabetic patients it was found to be 73.08 ± 4.9 mg/dL (Figure 2). Increase in TSA was highly significant (P<0.001). There was a strong and independent association between elevated serum total sialic acid levels in Type II diabetic patients and in our prospective study. Elevated level of serum sialic acid is a risk factor for overall mortality in type II diabetic patients. Serum sialic acid is a marker of the acute-phase response [30, 31]. In acute-phase glycoproteins, sialic acid is a component of the oligosaccharide side chain. Due to the electronegative charge on exposed sites of glycation, sialic acid is involved in the capillary permeability, platelet aggregation and activity of enzymes, by antigenic activity and receptor function [32].

![Total Sialic Acid](image2)

**Fig2.** Serum Total Sialic Acid levels in diabetics and non diabetics in mg/dL. Serum Total sialic acid level was significantly increased in type 2 diabetic subjects when compared to Controls (P<0.001).
Type II diabetes mellitus is usually associated with increased total sialic acid possibly due to generalised endothelial dysfunction or macrovascular disease, either through loss of sialic acid containing glycoproteins from vascular cells into the bloodstream or through an acute phase response. Type II diabetes may be considered as acute phase disease because the serum levels of acute phase proteins have increased without tissue complications. Alternatively, or in addition, declining renal function may retard the excretion of acute phase proteins or sialic acid containing proteins, leading to high levels of total sialic acid [33].

The hypothesis that peroxidative tissue damage may be an important factor in the pathogenesis of complications of diabetes has recently received increasing support with the confirmation [34]. High glucose concentration enhanced the formation of superoxide (O2.-) radicals and H2O2 but decreased antioxidant enzymes such as, SOD, CAT, and GPx [35]. Oxygen free radicals react with biological substances; however the most susceptible ones are polyunsaturated fatty acids. Reactions with these cell membrane constituents lead to lipid peroxidation [36, 37].

In the present study, mean serum ceruloplasmin level in non-diabetic controls was 61.4± 37.3 mg/dL and in diabetics it was 79.4± 47.5 mg/dL (Figure 3). These values were statistically not significant even though there was an apparent increase in diabetic subjects. Studies by Kim and Daimon also showed the same results [24, 38]. High blood glucose level may cause an increase in serum ceruloplasmin in Type II diabetes, which could be associated with the development of vascular injury (diabetic complication) in type II diabetes. It has been suggested that ceruloplasmin may be an antioxidant enzyme because it inhibits the auto-oxidation of lipids of ox-brain homogenate [39]. However, the mechanism of the antioxidant effect of ceruloplasmin has not been clarified in complex system such as in vivo because the antioxidant effect of ceruloplasmin may depend on the ferroxidase activity, ascorbate oxidase activity, O2 scavenging activity, and GSH-dependent peroxidase activity [40].

**Estimation of serum Ceruloplasmin level**

![](image.png)

**Fig3. Serum Ceruloplasmin levels in diabetic and non diabetic subjects in mg/dL.** The increase in serum Ceruloplasmin level was not significant in type II diabetic patients (P= 0.056).

Increase of serum ceruloplasmin level during induced inflammatory conditions suggests the involvement of serum ceruloplasmin as one of the body’s inbuilt defensive mechanisms against noxious responses or inflammation [41]. Hence this may suggest that serum ceruloplasmin is increased to overcome the inflammation due to hyperglycemia in diabetes.

4. **CONCLUSION**

From this comparative study of serum L–fucose, total sialic acid and ceruloplasmin in diabetics and non diabetics, it can be concluded that serum L-fucose and total sialic acid levels were significantly increased in the diabetic subjects when compared with non-diabetic controls, where as serum ceruloplasmin level was apparently increased in diabetics. Thus, these three biomarkers can be used as prognostic indicators of type II diabetes mellitus.
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ACKNOWLEDGEMENT
Authors would like to express their gratitude to the Chief Medical Officers of Government Hospitals of Kushalnagar and Somwarpet and Ganesh Laboratory in Kushalnagar for their support in conducting this study.

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AUTHORS’ BIOGRAPHY

Ms. Prathiroopa, Currently Senior Research Fellow, Indian Institute of Horticulture Research, Bangalore. Secured Distinction in MSc, Biochemistry, Mangalore University in 2014.

Ms. Kavyashree SJ, Currently teaching in a Higher Secondary School at Shrangeri. Secured Distinction in MSc, Biochemistry, Mangalore University in 2014.

Ms. Ashwitha KM, Currently working at Ideal Diagnostic Laboratory at Kasaragod. Secured Distinction in MSc, Biochemistry, Mangalore University in 2014.

Mr. Suresh Babu TV, Currently pursuing for his PhD in the PG Dept. of Biochemistry, Mangalore University. Secured first class in MSc Biochemistry Mangalore University in 2014.

Dr. Manjula Shantaram, Professor and Co-ordinator of PG Dept. of Biochemistry, PG Centre, Chikka Aluvara, Kodagu District. She is a PhD guide in three Universities and guided seven PhD candidates and currently guiding seven more. Published a text book in Biochemistry and also 80 scientific research papers in national & international journals.