### A STUDY ON RELATIONSHIP BETWEEN FASTING PLASMA GLUCOSE, COPPER AND CERULOPLASMIN LEVELS IN TYPE 2 DIABETES MELLITUS

Rangaswamy R<sup>1</sup>, Santosh R. G<sup>2</sup>

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ABSTRACT: INTRODUCTION: Diabetes mellitus (DM) is an endocrine disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion. Copper a transition metal is present in many tissues like liver, muscle etc., It can oxidize proteins and lipids which lead to increased production of free radical compounds. Ceruloplasmin an alpha 2 globulin is an acute phase copper containing plasma protein synthesized mainly by hepatic parenchymal cells, lymphocytes etc., Reactive oxygen species (ROS)/ free radicals production due to hyperglycemia in diabetes mellitus can directly or indirectly alter the integrity and physiological function of cells. Present study was undertaken to study the relationship between fasting plasma glucose (FPG), copper and ceruloplasmin in type 2 Diabetes mellitus. MATERIALS AND METHODOLOGY: The study group consisted of a total 100 subjects which included non-diabetic healthy control subjects (n = 50) and type 2 diabetic patients (n = 50). Fasting blood samples were collected and analysed for estimation of fasting plasma glucose, serum copper and ceruloplasmin. **RESULTS**: Results shows increase in levels of copper and FPG (P<0.001) and decrease in ceruloplasmin (P<0.001) in type 2 DM patients compared to healthy controls. **CONCLUSION:** Our study shows an increase in copper and FPG with decreased levels of ceruloplasmin which may be due to generation of ROS which leads to increased consumption of available antioxidants in the body.

**KEYWORDS:** Fasting plasma glucose (FPG), Copper, Ceruloplasmin, Type 2Diabetes Mellitus.

**INTRODUCTION:** Diabetes mellitus (DM) is an endocrine disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion.<sup>(1)</sup>. Reactive oxygen species (ROS)/free radicals production in hyperglycemia can directly or indirectly alter the integrity and physiological function of cells. ROS also act as a physiological mediator of many cellular responses including glucose dependent metabolic signal that contributes to glucose stimulated insulin secretion (GSIS) in  $\beta$ -cells.<sup>(2,3)</sup> Studies have shown involvement of transition metal ions like iron<sup>(4)</sup> and copper to cause oxidative stress. Plasma copper is transported mainly bound to ceruloplasmin (>95%) rest is bound to albumin, transcuprein and copper-amino acid complexes. Ceruloplasmin is an acute phase reactant, has ferro-O2-oxidoreductase activity directed towards ferrous ion stimulated lipid peroxidation and formation of hydroxyl radical in Fenton reaction.<sup>(5)</sup> Copper is toxic in its unbound form, causes redox imbalance due to its highly redox active nature, which leads to activation of stress sensitive intracellular signaling pathways through Haber-Weiss reaction.<sup>(6,7)</sup> The present study was undertaken to study the relationship between fasting plasma glucose (FPG) and copper with ceruloplasmin in type 2 DM patients

**MATERIALS AND METHODS:** The study group consisted of a total 100 subjects which included nondiabetic healthy control subjects (n=50) and diabetic patients (n=50). Informed consent was taken

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from all subjects involved in the study and study was approved by institutional ethics committee. Cases with any clinical evidence of retinopathy, nephropathy, neuropathy, coronary heart disease, hypertension, on antioxidant medication were excluded from the study. The controls were not on any medication or dietary restrictions. Fasting samples were collected under sterile measures and used for analysis of parameters. FPG was determined using modified glucose oxidase-peroxidase method.<sup>(8)</sup> Serum copper using BCDS,<sup>(9)</sup> ceruloplasmin using PPD.<sup>(10)</sup> Normal reference ranges of FPG is 70-110mg/dl, copper is 70-140 $\mu$ g/dl, and ceruloplasmin is 20-60mg/dl. Statistical analysis was done using SPSS version 17statistical software package and Unpaired 't' test. Results expressed as mean  $\pm$  SD. p- value<0.05 was considered as statistically significant.

Parameter	Controls	Cases	p-value
Fasting plasma glucose (mg/dl)	76.77 ±6.56	164.14±19.10	0.0001
Copper (µg/dl)	109.56±16.68	176.44±13.67	0.0001
Ceruloplasmin (mg/dl)	34.16±4.12	15.58±4.06	0.0001
Table 1: Comparison of various parameters between cases and controls			

\*P < 0.00-statistically significant

**RESULTS AND DISCUSSION:** Results shows increase in levels of copper and FPG (P<0.001) and decrease in ceruloplasmin (P<0.001) in type 2 DM compared to healthy controls. Copper a transition metal is present in many tissues like liver, muscle etc., It is involved in functioning of enzymes like ceruloplasmin, cytochrome oxidase, tyrosinase, superoxide dismutase, iron absorption process, HDL synthesis. It can oxidize proteins and lipids which lead to increased production of free radical compounds. Ceruloplasmin an alpha 2 globulin is an acute phase copper containing plasma protein synthesized mainly by hepatic parenchymal cells, lymphocytes etc., Hyperglycemia in diabetes mellitus may lead to increased oxidative stress thus leading to increase in transition metals like copper released from its storage site. Copper in its free form is a potent cytotoxic element because of its redox chemistry it readily participates in Fenton and Heiber-Weiss reactions to generate ROS which leads to increased consumption of available antioxidants in the body.

**CONCLUSION**: To conclude our study shows there is increased serum copper and fasting glucose with decreased ceruloplasmin levels in type 2 DM. Major limitation of the study is the sample size. Study with larger group may be required for further evaluation.

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### **AUTHORS:**

- 1. Rangaswamy R.
- 2. Santosh R. G.

### PARTICULARS OF CONTRIBUTORS:

- 1. Assistant Professor, Department of Biochemistry, Koppal Institute of Medical Sciences, Koppal, Karnataka.
- 2. Assistant Professor, Department of Medicine, Kannur Medical College, Kannur, Kerala.

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# NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rangaswamy R, Assistant Professor, Department of Biochemistry, Koppal Institute of Medical Sciences, Koppal, Karnataka. E-mail: rangaswamyr79@yahoo.com

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