**Abstract:**

Type 2 diabetes mellitus (T2DM) is highly prevalent amongst the adult population of Saudi Arabia. Due to the increasing number of available choices to control the associated hyperglycemia, lack of diabetic guidelines, and treating physicians have become increasingly uncertain of best management policy (1, 3). Strict glycemic control over time has long been reported to decrease microvascular complications associated with the disease (2, 3). In spite of the fact that insulin therapy is very effective in controlling all levels of hyperglycemia, as well as coexisting dyslipidemia (5), it was reported to increase frequency of severe hypoglycemic episode (6). In addition, use of insulin therapy was associated with increased risk of cardiovascular disease (CVD) directly (7), or indirectly due to weight gain following insulin therapy (8). Increased risk of CVD has also been associated with the presence of metabolic syndrome (9-10), as well as increased levels of C-reactive protein (CRP) (11, 12), and gamma glutamyl transferase (GGT) (13). The aim of our study is to understand the relationship between management, glycemic control, components of metabolic syndrome and serum levels of GGT and CRP.

**Methods:**

Patients diagnosed with type 2 diabetes mellitus, were randomly recruited from the diabetes out-patients clinics at King Abdulaziz University hospital and King Fahad Armed forces hospital (KFAFH) in Jeddah, Saudi Arabia, during the course of the first month of the 2nd of July, 2014. Ethical approval was obtained from the Committee on the Ethics of Human Research at the "Faculty of Medicine-King Abdulaziz University," and the Committee on the Ethics of Medical Research at KFAFH. Patients were asked to sign an informed consent form to participate. Exclusion criteria included: pregnancy, having any other severe chronic illness or diabetes comorbidities (i.e., stage renal disease, liver disease, recent myocardial infarction, etc). Blood pressure was measured following the recommendations of the American Heart Association Council (14), using a standard mercury sphygmomanometer attached to a cuff of appropriate size placed on the upper right arm, after 5 min of rest, while the subject was seated for 10 minutes were taken, and the mean of the two readings was calculated. Anthropometric measurements were taken for all. Height was measured barefoot to the nearest 0.5 cm using a standard stadiometer. Weight was measured to the nearest 0.5 kg while existing light clothing using a calibrated scale. Both measurements were used to calculate body mass index (BMI). Waist measurements was taken at the level of the umbilicus, and hip measurement at the maximal protrusion of the gluteal muscles, both to the nearest 0.5 cm. BMI was used to classify patients as being normal (18.5 < 25), overweight (25 ≥ 30), or obese (30 ≥ 39). In addition, a questionnaire comprising the demographic and management plan that the patient was following to control his/her diabetes was filled during face-to-face interview. Treatment plan was recorded as, lifestyle modification (i.e., diet and exercise), oral hypoglycemic agents (metformin, sulfonylurea, alpha glucoseinhibitor, thiazolidinedione, or DPP4 inhibitor), insulin, non-insulin injectable drugs (GLP-1 agonist), or any combination of them. Fasting blood sample was obtained for measurement of glucose, glycated haemoglobin (HbA1c) profile, high sensitive C-reactive protein (hs-CRP) and GGT. Serum glucose and lipids (cholesterol, triglycerides and high density lipoprotein (HDL) were assayed using automatic enzymatic methods (Dimension Vista Siemens Company). The homocysteine level was measured using laboratory methods (Dimension Vista Siemens Company). Gamma glutamyltransferase (GGT) level was measured using the Friedewald equation (14). Glycated haemoglobin (HbA1c) was performed using Dimension Vista 1500 Intelligent Lab (Siemens Company). HbA1c 5 ± 7 % was considered controlled and HbA1c >7% was considered uncontrolled, in accordance to the American Diabetes Association Guidelines (18). Hypertension was defined as a systolic blood pressure >140 mm Hg, and/or diastolic blood pressure >90 mm Hg or current use of antihypertensive medications (19). The consensus definition (20) was used to diagnose metabolic syndrome.

**Statistical Analysis:** Data was entered, coded, and analyzed using SPSS version 20. Descriptive statistics, such as mean, SD, and or median, were calculated for all measured parameters. Comparisons between two groups were performed using unpaired Student t test for normally distributed, and the Mann Whitney U test for non-normally distributed parameters. Differences between more than two means were tested using one way ANOVA. Chi squared tests were used for categorical variables. All p values that were <0.05 were deemed statistically significant.

**Discussion:**

Diabetes mellitus (DM) is associated with a myriad of micro- and macro-vascular complications. Hyperglycemia increased blood pressure, dyslipidaemia (components of metabolic syndrome), inflammation and oxidative stress are all characteristics of DM, and are implicated in the development of these complications (21-22). However, their control leads to decreased risk of both complications (23-24). Monitoring of glycemic control, lipid profile, and insulin profile are routinely carried out in diabetic patients, with treatment adjusted as need be to achieve target control. However, monitoring of oxidative stress biomarkers has not been commonly done.

In comparatively recent studies, C-reactive protein (CRP) was suggested; based on multiple prospective epidemiological and clinical outcome studies that demonstrated that increased CRP was associated with increased risk of CVD directly (7), or indirectly due to weight gain following insulin therapy (8). Increased risk of CVD has also been associated with the presence of metabolic syndrome (9, 10), as well as increased levels of C-reactive protein (CRP) (11, 12), and gamma glutamyl transferase (GGT) (13). The aim of our study is to understand the relationship between management, glycemic control, components of metabolic syndrome and serum levels of GGT and CRP.

**Results:**

A total of 153 subjects were recruited (78.4% males, 38.6% females). Serum samples were obtained in 152 (99.3%) patients. Serum levels of GGT and CRP were respectively measured; 58% of the patients had levels of GGT >35 U/L, and 55% of the patients had levels of CRP >3 mg/L. In addition, Mean age of males was found to be significantly higher than females (P=0.000). Males had significantly lower means of BMI, waist circumference and triglycerides. Females had significantly lower means of HbA1c (P<0.0001), and higher means of triglycerides (P=0.006) and GGT (P=0.04) were observed when comparing males to females (Table 1).

**Conclusion:**

Serum GGT and the CRP levels do not appear to be related to management regimen in T2DM Saudi patients. Poor glycemic control and hypertension are associated with higher mean GGT. Not surprisingly, serum hCRP correlates with waist circumference, however, GGT correlates positively with triglycerides, and negatively with HbA1c, known components of metabolic syndrome. Due to their value in independent risk predictors of vascular injury they should be included in routine monitoring of diabetic patients. Furtherstudies are needed to understand how these markers will ultimately lead to CVD prediction and how targeting these markers with conventional and contemporary measurements will lead to CVD risk reduction.