Role of glutathione-S transferase P_1 genetic variants in the etiopathogeneses of type 2 diabetes mellitus and its effect on glycemic control parameters

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Introduction: Diabetes Mellitus is a group of metabolic diseases characterized by chronic hyperglycemia. Type 2 diabetes is the most common form and comprises of 90% of people with diabetes around the world, it characterized by insulin resistance or relative insulin deficiency.

Glutathione-S-transferases (GSTs) are key enzymes of phase II related to the metabolism of numerous genotoxic compounds. Glutathione-S-transferases M1 (GSTM1) and T1 (GSTT1), the important subtypes of GSTs enzymes, are reportedly involved in detoxification of reactive oxygen species, which are considered to play a key role in the occurrence of various endocrine-related cancers(Amer et al., 2012). Another member of the glutathione-S-transferase (GST) family, *GSTP1*, which is located at 11q13, has a role in the detoxification of electrophilic compounds by glutathione conjugation . It has been found that two genetic polymorphisms in exon 5 and exon 6, lead to amino acid substitutions(Bid et al., 2010). However, only the transition in exon 5 was linked to activity of enzymes since this is located within the region coding for the enzyme's active site. The genetic change in exon 5 at the site -313, results in polymorphism at codon 105, where an adenosine-to-guanidine ($A > G$) transition causes an Ile-to-Val substitution.

Several investigators have determined the clinical or genetic factors associated with T2DM with interests to detoxification agents.

Patients and methods: In the present study, a total of 67 type2 Libyan diabetes patients were recruited from the Benghazi center for diagnosis and treatment of diabetes, 26 apparently healthy age and sex-matched individuals were selected from the high institute of medical professions' Benghazi to serve as controls(Booth et al.,

2006). Clinical information and medical history were obtained through patients' interview.

Venous blood samples were drawn from all the participants after at least 10 hours fasting, and analyzed for blood glucose, HbA1c, total cholesterol, triacylglycerol, and HDL-c using an auto analyzer with enzymatic techniques. LDL cholesterol was calculated according to Friedewald equation.

The data were analyzed using SPSS version 18, *P* values < 0.05 were considered to be statistically significant.

DNA is extracted from whole blood samples by using QIAamp DNA Blood Mini Kit(250), then amplified the desired gene with the specific primers using PCR thermal cycler TC 5000 and digested the PCR products with restriction enzyme ALW26I overnight. To detect the *GSTP*1Ile105Val genotype loading digested products on 2.5%agarose gel electrophoresis(Del Prato et al., 2002).

Results: In the present study, diabetic patients had significantly higher fasting blood glucose, HbA1c, total cholesterol, triacylglycerol, and LDL-c, and lower HDL-c than control patients group.

Healthy controls were carrying more G allele(val) than the type 2 diabetes mellitus as illustrated after running of digested PCR products on agarose gel (91bp+85bp) and in analysis by high resolution melting(HRM-RTPCR).

Conclusion: In the present study, *GSTP1*Ile105Val may not play role in the etiopathogeneses of diabetes mellitus and on glycemic control parameters.

References:

AMER, M. A., GHATTAS, M. H., ABO-ELMATTY, D. M. & ABOU-EL-ELA, S. H. 2012. Clinical research: Evaluation of glutathione S-transferase P1 genetic variants affecting type-2 diabetes susceptibility and glycemic control. *Archives of Medical Science,* 8**,** 631.

BID, H., KONWAR, R., SAXENA, M., CHAUDHARI, P., AGRAWAL, C. & BANERJEE, M. 2010. Association of glutathione S-transferase (GSTM1, T1 and P1) gene polymorphisms with type 2 diabetes mellitus in north Indian population. *Journal of postgraduate medicine,* 56**,** 176.

BOOTH, G. L., KAPRAL, M. K., FUNG, K. & TU, J. V. 2006. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *The Lancet,* 368**,** 29-36.

DEL PRATO, S., MARCHETTI, P. & BONADONNA, R. C. 2002. Phasic insulin release and metabolic regulation in type 2 diabetes. *Diabetes,* 51**,** S109-S116.