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Obesity is associated with the upregulation of TLR4 protein but not associated with polymorphisms of TLR4D299G TLR4T399I

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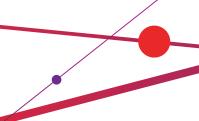
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Title: Obesity is associated with the upregulation of TLR4 protein but not associated with polymorphisms of TLR4D299G TLR4T399I.Background: Toll-like-receptor 4 (TLR4) is a pathogen-specific receptor. expressed in white blood cells, adipocytes, and other metabolic cells. Lipopolysaccharides (LPS) and free fatty acids (FFA) can act upon TLR4 and activate systematic inflammation that may lead to obesity and metabolic syndrome (MS). Aim: The aim of this research was to investigate the association of TLR4 polymorphisms of TLR4D299G TLR4T399I, with obesity and metabolic syndrome components in young adult female Arab subjects. Methodology: A prospective cross-sectional study was performed on female students from Qatar-University. The subjects were classified according to BMI classifications by WHO category into two groups: "obese; n=69" and "non-obese; n=136". Anthropometric measurements included weight (kg), height(m), waist circumference (WC) were assessed, and the body mass index (BMI) was calculated. Several biochemical assays were done to determine glucose and lipid profile. Plasma concentration of Interlukin-10 (IL-10) was measured using ELISA assay. Plasma concentration of IL-6, MCP-1, leptin, and insulin was measured using the multiplex Luminex assay. Also, fresh blood samples were used to measure TLR4 protein expression using flow cytometry assay.Results: TLR4D299G/T399I carriers had no significant association with obesity indicators; body mass index (BMI), body fat percentage (%BF), and waist circumference (WC). Haplotype analysis of TLR4 D299G/T399I showed that GT carriers of TLR4 D299G/T399I had a significant association with increased risk of insulin resistance with (odds ratio=4.73), 95% CI (1.19-18.90), (P-value=0.016). Increased level of leptin was associated with obesity phenotype by

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BMI, WC, and %BF. In addition, up-regulation of TLR4 protein increased significantly in obese subjects by 1.2 fold over the non-obese, with (P-value=0.006). Conclusions: TLR4 D299G/T399I polymorphism is associated with increased insulin resistance, a core component of metabolic syndromes but not with obesity. In addition, the up-regulation of TLR4 in obese subjects may be related to insulin resistance with increased leptin suggesting that increased free fatty acids may be a possible link to act as a ligand for TLR4.