Abstract

Diabetes mellitus is a combined metabolic disorder which includes hyperglycemia, dyslipidemia, stroke and several other complications. Oxidative stress is increased in diabetes and the overproduction of the ROS (reactive oxygen species) in diabetes is a direct consequence of persistent hyperglycemia for the production of inflammatory cytokines in renal cells, which are the factors responsible for diabetic complications i.e. diabetic nephropathy. The present study was undertaken to investigate the association of type 2 diabetic nephropathy due to persistent hyperglycemia induced oxidative stress producing inflammation. This study was conducted in four groups in participants of west india: control (148), Type2 diabetes (DM) (103), nephropathy with diabetes (DN) (102) and nephropathy without diabetes (NDN) (108). Oxidative stress markers such as malonidealdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD) and catalase were measured in all the groups. Cytokine genes polymorphism was analyzed using PCR-RFLP method. Expression level of inflammatory cytokines was analyzed by Real Time PCR. In silico analysis of inflammatory cytokine genes was carried out to explore different gene variants and its effect on protein structure.

MDA was significantly increased in patients group compared to control. GSH and SOD were significantly decreased in patients group compared to control. The results in this study suggest that IL-1α, IL 10, IL 6 and ACE polymorphism may be associated with progression of diabetic nephropathy in type 2 diabetic patients of west India and may be responsible in part for genetic susceptibility to the progression of diabetic nephropathy. Inflammatory mediators such as IL-1α, TNF-α, IL-4, IL-18 IL-10, IL-6, VEGF and ACE were found to be elevated in diseased group in comparison to control group. There was significant elevation in inflammatory mediators was found in DN group compared to DM group. In silico analysis revealed many inflammatory cytokine gene variants which needs to be validated. We also found many ns SNPs which are potential candidates for case-control study and have not been explored yet.

Findings of the present study suggest that inflammatory cytokine genes polymorphism may help to identify patients at high risk for susceptibility of diabetic nephropathy and it also denotes that inflammatory markers might have increased due to hyperglycemia induced oxidative stress.