# Acute phase reactant dynamics and incidence of microvascular dysfunctions in type 2 diabetes mellitus

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"n a manuscript published in October of 2011, Azenabor et al. reported that increased level of acute phase reactants such as  $\beta$ 2 microglobulin, fibrinogen, lipoprotein (a) and C-reactive protein (CRP) are associated with number of microvascular complications in type II diabetic subjects and suggested that they may play a role in pathogenesis of diabetic complications.<sup>1</sup> Several studies reported that elevated inflammatory markers are associated with diabetes mellitus.<sup>2,3</sup> CRP level is positively correlated with obesity and insulin resistance.4 Interestingly, antidiabetic and antihyperlipidemic agents can reduce inflammatory factors in diabetic patients.<sup>5</sup> Plasma inflammatory markers such as CRP and fibrinogen are higher even in patients with metabolic syndrome and it is demonstrated that the number of metabolic syndrome components are strongly correlated with serum level of inflammatory markers.6 Elevated inflammatory factors in diabetic subjects with complications compared to non-complicated patients have also been documented. The high sensitive CRP (hsCRP) level in diabetic patients with presence of diabetic retinopathy was higher than patients without diabetic retinopathy suggesting a link between inflammation and development of microvascular complications.7 However, it seems that effects of inflammatory markers on diabetic complications are more complicated and some points should be noted. First, there is a link between inflammation, antioxidants and

development of diabetic complications. It was shown that paraoxonase-1 (PON1) activity was decreased in diabetic patients and PON1/CRP ratio was also decreased in diabetic patients with retinopathy compared with those without retinopathy.7 Second, endothelial dysfunction markers should be considered as important factors in diabetic complications. Targher et al. indicated that serum von Willebrand factor, soluble intracellular adhesion molecule-1 (sI-CAM-1) and hsCRP were unchanged in type I diabetic patients without complications.8 They found that inflammatory markers and endothelial dysfunction markers were significantly elevated in diabetic patients with complications compared with those without complications. Third, some inflammatory markers are involved during angiogenesis processes. For example, CRP can modulate angiogenesis and may be involved in microvascular complications.9 Interleukin 6 also stimulates inflammatory cytokine production and involved in tumor angiogenesis.<sup>10</sup> Fourth, the magnitude of inflammatory markers elevation and presence of other risk factors should be considered. It is demonstrated that urinary albumin excretion higher than 12 mg/24h, hsCRP higher than 3 mg/kg and presence of hypertension are risk factors for development of microvascular complications in diabetic subjects.<sup>11</sup> Further research is needed to understand the role and mechanism of inflammation on insulin resistance and microvascular complications in diabetes.

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## **Conflict of Interests**

Authors have no conflict of interests.

### References

- 1. Azenabor A, Ogbera AO, Adejumo NE, Adejare AO. Acute phase reactant dynamics and incidence of microvascular dysfunctions in type 2 diabetes mellitus. J Res Med Sci 2011; 16(10): 1298-305.
- 2. Gomes MB, Piccirillo LJ, Nogueira VG, Matos HJ. Acute-phase proteins among patients with type 1 diabetes. Diabetes Metab 2003; 29(4 Pt 1): 405-11.
- 3. Nabipour I, Vahdat K, Jafari SM, Beigi S, Assadi M, Azizi F, et al. Elevated high sensitivity C-reactive protein is associated with type 2 diabetes mellitus: the Persian Gulf Healthy Heart Study. Endocr J 2008; 55(4): 717-22.
- 4. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA 1999; 282(22): 2131-5.
- 5. Dandona P. Effects of antidiabetic and antihyperlipidemic agents on C-reactive protein. Mayo Clin Proc 2008; 83(3): 333-42.
- 6. Kirilmaz B, Asgun F, Alioglu E, Ercan E, Tengiz I, Turk U, et al. High inflammatory activity related to the number of metabolic syndrome components. J Clin Hypertens (Greenwich ) 2010; 12(2): 136-44.
- 7. Nowak M, Wielkoszynski T, Marek B, Kos-Kudla B, Swietochowska E, Sieminska L, et al. Antioxidant potential, paraoxonase 1, ceruloplasmin activity and C-reactive protein concentration in diabetic retinopathy. Clin Exp Med 2010; 10(3): 185-92.
- 8. Targher G, Bertolini L, Zoppini G, Zenari L, Falezza G. Increased plasma markers of inflammation and endothelial dysfunction and their association with microvascular complications in Type 1 diabetic patients without clinically manifest macroangiopathy. Diabet Med 2005; 22(8): 999-1004.
- **9.** Turu MM, Slevin M, Matou S, West D, Rodriguez C, Luque A, et al. C-reactive protein exerts angiogenic effects on vascular endothelial cells and modulates associated signalling pathways and gene expression. BMC Cell Biol 2008; 9: 47.
- **10.** Coward J, Kulbe H, Chakravarty P, Leader D, Vassileva V, Leinster DA, et al. Interleukin-6 as a therapeutic target in human ovarian cancer. Clin Cancer Res 2011; 17(18): 6083-96.
- 11. Del Canizo Gomez FJ, Fernandez PC, Moreno R, I, de GP-J, Silveira RB, Gonzalez LT, et al. Microvascular complications and risk factors in patients with type 2 diabetes. Endocrinol Nutr 2011; 58(4): 163-8.