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*Editorial*

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# New Insight on Adipose Tissue Function in Advanced Renal Failure

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Adipose tissue has been considered simply as an exclusive fat storage organ for a long period. Later in the mid-1990s and after identification of leptin, a revolution occurred in understanding of white adipose tissue function. In fact, adipose tissue has been recognized as a dynamic endocrine organ, which could affect whole body homeostasis.[1] Thereafter, more than 50 secretory peptides, which are called "adipokines" or "adipocytokines", with diverse metabolic functions have been identified[2] and the biological role of adipose tissue became more sophisticated and interesting.

The adipokines may act through an autocrine, paracrine and endocrine manner. They are supposed to be involved in a wide range of physiologic to pathologic processes including dietary intake and appetite regulation, energy expenditure, insulin resistance, lipid metabolism, immunity, inflammation and acute-phase responses, vascular homeostasis, endothelial function, angiogenesis and so on.[2,3] Leptin, adiponectin, ghrelin, resistin, visfatin, vaspin, omentin, TNF-α, and IL-6 are among the most studied adipokines in health and disease. However, studies regarding the extensive biological and metabolic functions of adipokines are still ongoing.

Along with the recent advances in the field of obesity, adipose tissue and adipokines, a great interest has been emerged regarding their relationship with different pathophysiological conditions and their probable mechanism in metabolic disorders. Diabetes, metabolic syndrome, non-alcoholic fatty liver and cardiovascular diseases are among the common diseases, which have been studied. Moreover, pharmacological, nutritional and medical interventions have been done increasingly with the aim of altering the function of adipose tissue, and consequently the gene expression and circulating levels of adipokines in order to decline metabolic dysfunctions and improve the patients' outcomes. Investigating the role of adipose tissue and adipokines in renal insufficiencies especially in End Stage Renal Disease (ESRD) and patients under dialysis has been taken into consideration in recent years.

Adipokines could be destructive for kidney tissue due to the impairment of endothelial function, inducing oxidative stress and inflammation, and stimulating the sympathetic nervous system of kidneys.[4] It has been proposed that most adipokines act as proinflammatory factors. In contrast, few adipokines act as anti-inflammatory agents and could be protective against the metabolic complications.[5] Obesity could induce kidney disease through disrupting the balance between protective such as adiponectin and pathologic such as TNF-α adipokines.[4] The changes of the adipokines' levels such as leptin, adiponectin, visfatin, resistin, IL-6 and TNF-α could result in the reduction of Glomerular Filtration Rate (GFR) and increasing albuminuria, which are among the major pathophysiological mechanisms in CKD. Although the exact mechanism of adipokines' action is still unclear, they may play their role by affecting various types of cells in kidney nephrons.[6] Previous studies have shown that increased levels of leptin could lead to hypertrophy in glomerular mesangial cells that could activate fibrotic and inflammatory pathways, and also thickening of the basement membrane and consequently glomerulosclerosis.[6] Moreover, it has been demonstrated that hyperleptinemia could alter the metabolic function of proximal tubular cells and lead to tubular apoptosis.[7] These structural changes in the nephrons

could result in increased proteinuria, albuminuria and fibrotic pathways in tubular cells through altering the permeability of the cells.[6] Adiponectin, another major adipokine, is recognized essentially as a protective peptide.[6] It has been shown that in obesity, hypoadiponectinemia increases Reactive Oxygen Species (ROS) generation and thereby oxidative stress in podocytes, which could probably change the GFR.[6]

Regardless of the roles of adipocytokine in the pathophysiology of renal diseases, the gene expression and circulating levels of these peptides change significantly along with disease progression, particularly in ESRD and dialysis therapy.[6,8,9] Considering the multiple effects of adipocytokines, their alterations may have considerable biologic, metabolic, and clinical outcomes, which are not well studied in uremic conditions so far.[9,10] For example, the circulating levels of adiponectin increase in diabetic nephropathy and ESRD, which unexpectedly have been observed to be correlated with higher mortality[11-12] and complicate the role of adiponectin in kidney failure.

Moreover, with the identification of new adipokines including Zinc alpha-2 glycoprotein (ZAG), apelin, lipocalin, adiploin, etc. investigating their probable roles in different metabolic aspects of advanced kidney insufficiencies are of major importance. For instance, ZAG is an adipokine that has been proposed to play a role in various metabolic disorders including lipid metabolism,[13] insulin resistance,[14-15] energy hemostasis,[13,16-17] inflammation,[18,19] and determining body composition.[20,21] In addition, recent studies indicated that the circulating levels of ZAG are increased in hemodialysis.[22-23] However, there are not enough data regarding the effect of ZAG elevation on mentioned disorders in ESRD or patients under regular hemodialysis and the probable effects on patients' prognosis.

In summary, it seems that adipose tissue and its products could be considered as a novel field of study, which may play a major role in the metabolic alteration of advanced renal failure. The limited and mainly descriptive data indicate that further studies are required, more specifically with the aim of identifying the precise roles and mechanisms of adipose tissue and its products in uremic patients, and their probable impact on patients' outcome.

## CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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