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Re: Association of Leptin With Mortality in Patients on Maintenance Hemodialysis: a Prospective Study

Dear Editor,

We Read with interest an article published by Bian and colleagues in the previous issue of the Iranian Journal of Kidney Diseases on leptin in dialysis patients.[1] Leptin, a protein produced by the *obese* gene is expressed, synthesized and secreted by white adipocytes. The exact pathophysiology of leptin is unclear. Metabolic effects of leptin include a wide range. It regulates adipose tissue mass and body weight by a feedback mechanism.[2-4]

In addition to the main known effects of leptin, recent studies have demonstrated that leptin has a wide variety of effects in different tissues.[5] These different functions develop through its action in peripheral tissues or in the central nervous system. Some other lines of evidence which consider the renal clearance as the main route for leptin metabolism propose that the calculated plasma half-life for leptin and molecular weight are as same as the other peptide hormones that are degraded by the proximal renal tubule. Moreover, recent studies showed that the leptin receptors are often expressed in the lung and the kidney.[6]

Leptin may act in relation to cardiovascular homeostasis. It indicates its potential role in cardiovascular system via p38 MAPK.[7] Leptin takes part in the regulation of sympathetic tone and arterial blood pressure.[8] Also, elevated circulating plasma leptin level revealed to be in association with chronic intravenous infusion of leptin.[9] Various mechanisms are suggested for leptin-induced atherosclerosis namely, endothelial dysfunction after great amounts of nitric oxide, induction of a pro-inflammatory state, abnormal lipid metabolism in the vessel wall, increased proliferation and migration of vascular smooth muscle cells, and increased platelet aggregation and abnormal haemostasis.[10,11]

Leptin is cleared by the kidney. As a result, the plasma leptin concentration rises in patients with end-stage renal disease. Leptin has an impact on the kidney through different mechanisms such as modulation of growth, induction of transforming growth factor-□, natriuresis, upregulation of

transforming growth factor-β, pro-inflammatory responses, oxidative stress, stimulation of glucose uptake, sympathetic nerve activation, and hypertension. Increased serum levels of leptin in obese individuals may lead to glomerulosclerosis.[12] Praga and colleagues reported that proteinuria and chronic kidney failure after unilateral nephrectomy are more frequently seen in obese patients.[13] Different and sometimes opposite results regarding the effect of leptin on cardiovascular and kidney diseases mortality and morbidity have been reported. It comprises protective and destructive effects.[14] To explain this issue, it can be noted that in cases where no associations were seen between leptin and mortality of obese patient with high body mass index, leptin resistance could be a vindicator.

Mortality in patients with chronic kidney disease is still a complicated and important dilemma. In addition to classical risk factors, some other factors such as malnutrition, inflammation exist which may slightly be able to explain the high mortality rate in these patients.[15] Scholze and coworkers reported the relationship between low serum leptin concentration and increased mortality in patients with end-stage renal disease on hemodialysis.[16] In the past two decades, cardiovascular diseases have been introduced as the most leading cause of death in hemodialysis patients. Combinations of traditional and novel risk factors are responsible for these events.

In vivo studies have shown a considerable correlation between leptin levels and hyperlipidemia, hypertension, chronic inflammation, and perturbed fibrinolysis. Díez and colleagues reported that leptin-body mass index ratio was not a powerful risk factor for mortality in hemodialysis patients.[17] An interpretation on this non-significant relationship could be the frequency of cardiovascular risk factors in ESRD patients. Physiological studies demonstrated that increased body mass index level correlate with decreased mortality in hemodialysis patients, and increased leptin serum levels leads to reduction of vascular capacity and consequently developing cardiovascular disorders.[18] Collectively, these findings suggest that leptin exerts different effects diverse populations, such as hemodialysis patients and healthy subjects.

Bian and colleagues conducted their study to investigate the relationship between leptin and mortality in a cohort study in patients with stable maintenance hemodialysis. Results of statistical tests and models demonstrated an association between these two variables. They mentioned that the low leptin level is an independent risk factor of all-cause mortality in stable maintenance hemodialysis patients, but leptin was not associated with cardiovascular mortality.[1] These findings and point of views are verifier and corroborant and in some cases in contrast with existing data in literature. According to these various and conflicting results, the need for confirmatory studies, especially meta-analysis studies would seem to be necessary and urgent.

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Re: Kidney Function and Metabolic Profile of Chronic Kidney Disease and Hemodialysis Patients During Ramadan Fasting

Dear Editor,

We Read with great interest the article by Al Wakeel about fasting effects on hemodialysis, published in the *Iranian Journal of Kidney Diseases*.[1] Ramadan is one of the months in Islamic calendar in which people have been given glade tidings to good and blessing. Muslims after the age of puberty abstain from eating and drinking from dawn until sunset during Ramadan. They have two meals per day, *Iftar* at sunset and *Sohor* before dawn and there is no limitation on any special food items during sunset until dawn. Dispensation from fasting is allowed during sickness, menstruation, pregnancy, breast feeding, and travel, and also for debilitated elderly people. The philosophy of fasting in the Islamic culture is to teach endurance and train patience and to feel for the sufferings of the deprived.[2] Since the Arabic calendar employs a lunar cycle, the Arabic year contains 354 days. So, Ramadan moves back eleven days every year and may be situated in any of the four seasons. Thus, fasting hours can be variable from 11 to 18 hours.

Theoretically, it seems that abstain from drinking may lead to acute kidney damage due to dehydration, especially in patients with salt-wasting nephropathy. The question is whether Ramadan with special type of fasting has any adverse effect on patients with mild to moderate kidney failure. Several studies have shown that fasting during Ramadan not only does not have any adverse effect on healthy people, but also can improve some clinical and biochemical parameters.[3,4] Recently, in a review article, Khedmat and coworkers evaluated a few investigations and concluded that fasting Ramadan did not induce abnormalities of urinary volume, osmolality, pH, solute and electrolyte excretion, serum urea and creatinine levels, or serum sodium and potassium balance in healthy people, and if any it was insignificant.[5] Fakhrzadeh and colleagues reported a significant improvement in weight and body mass index, fasting plasma glucose, and lipid profile in adults after fasting.[3] They also showed neither systolic nor diastolic blood pressure were worse during Ramadan fasting.[3]

Although Islam has exempted sick individuals from fasting, these people enjoy fasting according to their religious believe. They often ask their physician if they can fast during Ramadan. The impact of fasting on kidney conditions such as kidney transplant,[6-8] renal calculus formation,[9] and other disorders has attracted the attention of investigators. Argani and colleagues evaluated some biochemical and immunological parameters in 24 stable kidney transplant recipients and showed that Ramadan fasting was not harmful for these patients in a period of 12 hours fasting pattern.[6] We also studied serum creatinine before and after Ramadan