Gender-related diabetic nephropathy: Yes or no

Dear Editor,

The topic of gender in clinical studies and its importance is increasing day by day. Perhaps cardiovascular diseases and the role of female sex hormones are among the first cases where gender was seriously discussed. But today, the role of gender is much more serious and has established its role not only in the occurrence of diseases but also in the involved mechanisms. From the different efficacy of drugs in both sexes to the dependence of physiological systems such as renin–angiotensin system (RAS) on gender, scientific sources are increasing, and among them, diabetic nephropathy (DN) is not separate from this issue.

The association between DN and gender is one of the considerable subjects. There is a negative correlation between leucine and the risk of DN, however, in female diabetic patients with high levels of leucine, a lower risk of developing DN was observed.[1] Urinary thioredoxin has a positive correlation with estimated glomerular filtration rate in male diabetic patients but not in females, and it is a potential gender-related marker of renal damage in DN.[2] In noninsulin-dependent diabetic patients, DNA polymorphism M235T in the angiotensinogen gene is involved in the risk of DN in men, and such observation was not detected in women.[3] The dependence of the RAS on gender on the one hand, and the role of the RAS in causing the DN on the other hand, raises the question of the role of gender in the DN, so suggesting that a better understanding of the sex dimorphism on RAS may be helpful in the treatment process of diabetic kidney disease.[4] The transforming growth factor beta (TGF-ß) is upregulated by sex hormone, and TGF-β plays an important role in the regulation of extracellular matrix production in the diabetic kidney, whereas the urine level of TGF-β1 is high in diabetic patients.[5] The expression of TGF-β could be promoted by a high dose of glucose,[6] and the higher level of TGF-β was observed in male when compared with female.[7] Hence, the sex-related effect of TGF-ß, and its role in diabetic kidney disease was subjected to special attention.[8] On the contrary, in laboratory experimental research, no significant role of gender in DN progression was reported.[9] Angiotensin-converting enzyme (ACE) and ACE2 play a critical role in the RAS. These enzymes are gender and diabetes related, whereas both are involved in DN progression, so DN may be gender related.[10] It is explicitly stated in some sources that male sex is an important risk factor for DN,[11] and suggesting the implication of sex dimorphism in the development of DN in male.[12] From a hormonal point of view, it seems that testosterone promotes the occurrence and progression of DN, whereas estrogen has renoprotective effects,[13] and both need to be considered in clinics. Finally, although the role of gender as a risk factor in creating the mechanism and in the occurrence of DN is still not seriously considered in the clinic, it should not be neglected. In this direction, it is necessary to design and analyze more clinical studies to specify the exact role of gender in DN progression. First of all, it is necessary to design epidemiological studies for the prevalence and incidence of DN in any race to document the gender difference and related factors. If the gender difference in DN is found, the design of studies to find the exact mechanisms will help in the prevention and treatment of the disease.

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Conflicts of interest

There are no conflicts of interest.

Mehdi Nematbakhsh

Water and Electrolytes Research Center, and Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran

Address for correspondence:
Prof. Mehdi Nematbakhsh,
Water and Electrolytes Research Ceneter, and Department of Physiology, Isfahan University of Medical Sciences, Hezar Jerib Street, Isfahan, Iran.
E-mail: nematbakhsh@med.mui.ac.ir

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