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Editorial

Nephrology from a gender perspective☆

La nefrología desde una perspectiva de género

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Approaching medicine from a gender perspective is a relatively recent attempt to identify elements that perpetuate health inequalities between men and women, and considers an opportunity that the two gender may have different experiences and manifestations of the same disease.[1] Chronic kidney disease (CKD) shows differences between gender in prevalence and rate of progression, but also in treatment and outcomes, as shown by a recent analysis of DOPPS, which includes data from our country, Spain.[2] In the background of these differences are due to biological differences related to the gender and therefore they are not avoidable. But there are also factors related to sociocultural attributes of masculinity and femininity that can be modified to avoid gender inequality in CKD and can serve as areas for improvement. Nephrology, unlike other specialties, has largely ignored this approach, and not many studies investigate scientific evidence of this aspect.[3] However "the absence of evidence does not imply evidence of absence".[4,5] The objective of this editorial is to highlight some inequalities or biases in relation to gender in health care, the sex–gender interaction and its influence on kidney disease outcomes. Understanding these differences may help specialists in nephrology to better address the needs of their patients.

Differences between sex and gender inequalities in chronic kidney disease, progression and access to dialysis

CKD shows differences in prevalence according to gender (higher in women),[6] evolution (faster progression in men)[4,5] and prognosis (young women on dialysis increase their non-cardiovascular mortality and lose the survival advantage over men in general population).[2,7]

The greater prevalence of CKD in women[6] may be due to their longer life expectancy achieving the risk age of CKD, or to inaccuracy of the formulas that estimate the GFR that classify them in a degree of CKD more severe than the real.[8]

Surprisingly, despite this high prevalence of CKD in women worldwide, in an American study, women constituted the group with greatest risk of late initiation of dialysis, even later than ethnic minorities, the unemployed and patients

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without health insurance[9] and women presented high mortality in predialysis for this reason.[10] In the DOPPS study, women started renal replacement therapy (RRT) older and with lower GFR than men.[2] The Spanish registry[11] shows a higher incidence of men than women in RRT, although we do not have data on mortality separated by gender in this population.

Differences between countries points to a gender bias, with differences in decision-making between men and women – older women opt for conservative treatment rather than dialysis[12] – and in primary medical care fewer women than men are diagnosed of CKD, with less referral to nephrology and therefore there is not follow up on renal disease progression.[12]

Once the RRT is initiated, gender biases in health care are detected. We describe a lower possibility of initiating dialysis through arteriovenous fistula (AVF) in women. In Spain, 20.8% of women are dialyzed with a catheter, 67.7% with AVF and 11.5% with a prosthesis compared to 10.8%, 81.2% and 8% respectively in men.[2,13] This disparity is justified by the belief that AVF in women has a worse prognosis than in men,[14,15] this could influence the decision of place a catheter vs AVF. However the recently published *Spanish Clinical Guide about vascular access for hemodialysis* states that female sex is not a risk factor in the prognosis of vascular access.[16]

Another possible bias that needs to be addressed is the increased risk in women of not receiving optimal dialysis[17] because they need more dose of dialysis (KTV > 1.6)[18] and more dialysis time to improve survival.[17] Using the objective of KTV in men (KTV > 1.4) in all patients, men and women may favor inequality. It has been reported that women receive less time of dialysis (<12 h/week).[19]

The DOPPS study shows that the sex-gender interaction – more use of catheters and lower dose of dialysis in women – significantly influences the mortality of young women in dialysis, which could justify the loss of survival advantage of women with respect to the general population, despite not being differences in mortality between sexes,[2] and even presenting a better survival in women than men in RRT in the Spanish registry,[11] and these would be objectives to be considered to improve the results.[2]

Conversely, women are more likely to be diagnosed of anemia and to receive excess erythropoietin I,[20] because physiologically they have less hemoglobin than men and clinical guidelines usually consider a single cut-off point for anemia in both sexes.[21]

Gender inequalities in kidney transplantation: access to kidney transplantation, organ donation and evolution of the transplant

Women are less likely to receive a corpse transplant,[22] which is attributed to higher levels of preformed antibodies; however, women are living donors more frequently than men.[23] In Spain, in 2015, 64% of living donors were women and 62% of recipients were male.[24] These differences can not be attributed, as in other countries, to gender related psycho-socio-economic factors or the lack of social support networks.[25] Differences may be related to differences in gender behavior,[26] as well as biological factors – major incidence in men of diseases that require a transplant and a higher prevalence of arteriosclerosis – that may explain less inadequacy as donors.[27]

It is argued that differences related to gender also influence the results of transplantation: worse prognosis of male recipients attributed to worse adherence and less concern for the graft,[28] and some studies attribute a worse survival of the kidneys of donor women to the lower number of nephrons, more HLA antigenic response or greater susceptibility to nephrotoxic.[29]

In conclusion, the application of the gender perspective improves the scientific rigor and reproducibility of clinical trials, and may provide clues that could lead to new pharmacological targets and treatment strategies. Nephrology is not a leading discipline in this field. In this editorial we have highlighted aspects related to the prevalence, progression and treatment of women and men with CKD, which require further study. A gender perspective in clinical practice will help us to provide better and more personalized care to our patients.

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