GENDER GAP IN LIPID MANAGEMENT AMONGST DIABETES POPULATION: AN OBSERVATION

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ABSTRACT

Studies have consistently demonstrated that women with diabetes are more likely than men to have a LDL-C above treatment goals. However, this pattern of gender gap has not been observed in many studies for HgbA1c goal attainment. Although the reasons for this are not fully understood, intolerance to statin therapy in women due to differences in pharmacodynamics and pharmacokinetics may play a role as female sex and aging has been associated with statin-associated myopathy. The concept of gender gap is useful for identifying at-risk groups for prevention and treatment efforts.

Key Words: *Gender gap, diabetes, therapeutics, goal attainment*

Diabetes is a chronic disease with high incidence and prevalence.[1-3] It has a significant burden of illness due to complications and is costly to society.[1-3] An estimated 285 million people worldwide are affected by diabetes, and with a further 7 million people developing diabetes each year the number is expected to hit 438 million by 2030.[3] To reduce the burden of illness and complications due to diabetes clinicians set out to achieve predefined goals according to practice guidelines regarding blood glucose, lipid and blood pressure outcomes.[4-6] However, numerous studies demonstrate that a large proportion of patients with diabetes in the community do not achieve the predefined goals for optimal management of blood glucose, lipids and blood pressure.[7-9] Furthermore, there is a vast gender disparity regarding the epidemiology and burden of illness with diabetes among a patient population.[10] This pattern of morbidity and mortality is likely related to poorer glycemic and cardiovascular risk factor control.[11-13] Compared with men, women receive less aggressive diagnostic workups and therapy for cardiovascular disease.[14;15] Studies consistently demonstrate that women with diabetes are more likely than men to have a LDL-C above treatment goals.[13;16] This is an important quality issue because hyperlipidemia is a risk factor for cardiovascular disease, and women with diabetes have a considerably higher risk of cardiovascular related morbidity and mortality than men.[17;18] However, this pattern of gender gap has not been observed in many studies for HgbA1c goal attainment. In several reported studies, women had comparable or better outcomes than men for HgbA1c goal attainment. The discordant between LDL-C and HgbA1c therapeutic goal achievement can be observed in several studies from around the globe, despite different patient populations, different clinical practice guidelines and different time frames.[19-23]

An observational study on patients with diabetes from a managed care organization in the USA[19] reported that women, as compared to men, had decreased odds of reaching LDL-C goals (odds ratio 0.70, 95% CI 0.58–0.86), and statin use (odds ratio 0.69, 95% CI 0.58–0.81); however, women had 19% greater odds of reaching HgbA1c <7.0% (95% CI 1.02–1.41). Gender differences were evaluated with respect to quality of care for patients receiving primary care in the Veterans Affairs (VA) Health Care

System.[20] In an adjusted analysis, women, as compared with men, had better results for HbA1c <8.0% (odds ratio 1.05; 95% CI 1.03-1.07). In a cross-sectional study from Austria on patients with diabetes, women had significantly higher levels of LDL-C (P = 0.008), but not HgbA1c (P = NS).[21] In the latter study, whereas glycemic control was comparable between women and men, a more adverse cardiovascular risk factor profile was observed in female patients. This pattern has also been observed across races. An insured cohort of patients with diabetes in Michigan, USA[22] illustrated that LDL-C goal attainment amongst men was consistently and significantly better than amongst women regardless of race. However, in this cohort, women consistently had as good as or even better outcome than men for HgbA1c goals attainment in the total cohort, Caucasian subgroup and African American subgroup. More Caucasian men (78%) attained LDL-C less than 100 mg/dl in comparison to Caucasian women (69%) [p = 0.0001]. The same pattern of gender gap for LDL-C was observed amongst African Americans. However, there was no difference between men and women for HgbA1c goal attainment. The HgbA1c goal of less than 7.0% was achieved in 53% and 37% of men compared to 54% and 40% of women, for Caucasians and African Americans, respectively.

In an Italian multi-center study[23], in almost all the centers (233 out of 236), the proportion of men reaching the target for LDL-C was higher than that of women. On the other hand, for the attainment of the HbA1c, men were more likely than women to reach the target of 7.0% in 80% of the centers (190 out of 236 centers). The authors concluded that such a systematic gender difference in LDL-C goal attainment may imply the existence of pathophysiological differences between sexes. However, the results for HgbA1c could suggest the existence of a mixed effect of physiological mechanisms and attitudes.

A meta-analysis of randomized, controlled statin trials evaluating the gender specific incidence of cardiovascular events demonstrated statins reduced the overall risk of cardiovascular events in men and women, but women on statins did not have reductions in mortality and stroke like their male counterparts.[24]

A meta-analysis of studies on adherence to statins by men and women reported that women had 10% greater odds of non-adherence (odds ratio 1.10, 95% CI 1.07-1.13)[25]. Less than one third of the total gender difference in statin use has been attributed to individual-level variables such as demographics, economic status, physical health status, depression and lifestyle risk factors[26].

An analysis of variables that might influence compliance with anti-diabetic drug treatment assessed the effects of age, sex, educational background, duration of diabetes, dosage regimens of oral anti-diabetics, insulin therapy, level of patient independence, family support, co-morbidities, and sex and found none of these to be a determinant of compliance (odds ratio 1.92; 95% confidence interval: 0.60–6.12; p = 0.27).[27] In another study, HgbA1c reduction after treatment was compared between the elderly vs. non-elderly; males vs. females; overweight/obese vs. non-overweight/obese; and long-standing vs. newly diagnosed patients. While the results illustrated greater HgbA1c reduction amongst the non-elderly, non-overweight/obese and newly diagnosed patients as compared to the elderly, overweight/obese and long-standing diabetic patients; there was no difference between the sexes.[28]

The reasons for poorer lipid control among women with diabetes but not for HgbA1c are unclear; but, may be due, in part, to differences in treatment patterns.[13] The greater difficulty in reaching the targets may be related to the use of a lower aggressive approach (i.e., prescription of lower doses), poorer adherence of women to statins, or between sex physiopathological differences.[23] Examples of pathophysiological data on sex differences include differences in drug responses due to differences in pharmacodynamics and pharmacokinetics. For example, evidence supporting sex-based differences in statin metabolism implicates differences in body-fat content between men and women.[30] Females tend to have a higher percentage of body fat,

which affects volume of distribution of some drugs and can increase the half-life of a variety of medications, including the more lipophilic statins.[30] Furthermore, female sex and advanced age has been identified as predisposing factors for statin-associated myopathy among other factors.[31]

The concept of gender gap is useful for identifying at-risk groups for prevention and treatment efforts. Exploring gender differences is a driving force for ensuring that biomedical research is conducted on women and for raising awareness about the biological and physiological differences between men and women.[32] In the era of personalized medicine, greater attention to gender differences in drug disposition is crucial as a platform for therapeutics development and utilization.[33] This calls for further study to determine causes of possible gender disparities to tailor interventions for each risk factor to address the impact of gender differences.

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