Editorial comment to: Impact of Sexual Activity on Glycated Hemoglobin Levels in Patients with Type 2 Diabetes Mellitus after Penile Prosthesis Implantation

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The authors have addressed an important issue. Congratulation! Type 2 diabetes mellitus (DM) is a complex and multifactor metabolic disorder. One of the complications of type 2 DM is the sexual dysfunction, mainly in the form of erectile dysfunction in men. Hemoglobin A_{1C} (HbA_{1c}) is an invaluable tool for watching long-term glycemic control in patients with DM. In present retrospective study the authors aimed to determine the relationship between sexual activity and serum levels of HbA_{1c} with an inappropriate manner. As a result, the manuscript suffers from some important drawbacks. There are many confounding factors which can interfere with serum HbA_{1c} concentration measurements. Also, there are several situations in which the level of HbA_{1c} may not loyally reflect the actual values. Without adjusting for these confounding factors, the results might not be reliable.

Genetic variants (e.g. HbS trait, HbC trait), elevated fetal hemoglobin (HbF) and chemically altered derivatives of hemoglobin (e.g. carbamylated Hb) all can affect the accuracy of serum HbA_{1c} measurements. The impacts differ depending on the specific Hb variant or derivative and the method used for serum HbA_{1c} measurement. Any disorder or illness that reduces erythrocyte survival or shortens mean erythrocyte age will falsely lower serum HbA_{1c} test results irrespective of the laboratory method used.[1] HbA_{1c} results from patients with HbSS, HbCC, and HbSC must be interpreted with cautiousness given the pathological processes, including anemia, increased red blood cell turnover, and transfusion, that adversely affect serum HbA_{1c} levels. Other methods of measurement such as glycated serum protein or glycated albumin would be considered for these cases.

There are some systemic disorders such as certain forms of dyslipidemia, malignancies, and cirrhosis which can affect the serum HbA_{1c} concentrations. The iron deficiency anemia is a common condition which can lead to an increase in serum HbA_{1c} level by 1% to 1.5%.[2] In agreement with that observation, iron replacement therapy decreases both serum HbA_{1c} and fructosamine levels in individuals with or without DM.[3]

Also, any medical disorders or illnesses which are associated with changes in the relationship between mean glycemia and serum HbA_{1c} concentration, can alter serum HbA_{1c} levels too. The main disorders are those affecting red blood cells, comprising persistent fetal hemoglobin, hemoglobin S, C, or D, end stage renal disease, or diseases characterized by hemolysis or other conditions with decreased life span of red blood cells.[4]

The HbA_{1c} concentrations also have a quadratic association with sleep duration; namely, a shorter or longer sleep duration is associated with a higher level compared with a sleep duration of 6.5-7.4 h.[5]

Some of the factors that influence HbA1c and its measurement are as below:[1-4]

Increased HbA_{1c}: iron deficiency, vitamin B12 deficiency, decreased erythropoiesis, alcoholism, chronic renal failure, splenectomy, hyperbilirubinemia, carbamylated hemoglobin, large doses of aspirin, chronic opiate use, genetic heterozygous variants of hemoglobins S, C and E, medications, such as corticosteroids and antipsychotic agents, malaria, rheumatoid arthritis and increased serum triglyceride.

Decreased HbA_{1c}: administration of erythropoietin, iron and vitamin B12, reticulocytosis, chronic liver disease, small doses of aspirin, vitamin C and E, certain hemoglobinopathies, splenomegaly, medications such as antiretrovirals, ribavirin and dapsone, acute and chronic blood loss, hemolytic anemia, hereditary persistence of hemoglobin F, genetic heterozygous variants of hemoglobins S, C and E and malnutrition.

It has been demonstrated that older non-diabetic individuals have higher HbA_{1c} values than younger subjects, being approximately 0.4% higher at 70 years than at 40 years,[6] even after adjusting for confounding factors. Lower total fat intake is associated with lower HbA_{1c}. Saturated fat intake is positively associated with HbA_{1c}.[7] Finally, measurement method of HbA_{1c} is fundamental. Accurate and reliable methods to measure HbA_{1c} are necessary for optimal use. The most widely adopted system is that of the National Glycohemoglobin Standardization Program (NGSP).

None of the above mentioned confounding factors have been addressed in this study. Accounting for all of them is nearly impossible. But, it was very worthwhile if the study results have been put in multivariate regression analysis and adjusted for total energy intake, protein, alcohol use, age, family history of diabetes and physical activity. Therefore, I believe that the results of the present study should be interpreted with caution.

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Reply by Author

As principal co-authors of this paper, we welcome the opportunity to respond to the editorial comments on our article. In editorial comment, it was mentioned that there are some genetic variants, systemic illnesses and disorders, which can affect the serum Hemoglobin A_{1C} (HbA_{1c}) concentrations. Our study was performed retrospectively and analyzed medical records from computer files of patients that underwent penile prosthesis implantation.

We strongly agree with the comment and accept that serum HbA_{1c} concentrations could be effected by some situations. However, HbA_{1c} is the most commonly used test to examine long-term glycemic control in patients with diabetes mellitus. We also agree that adjusted results after getting information on diet and physical activity would make our study more powerful. As we pointed out in discussion section of our study, observational nature of our cohort, our findings must be interpreted within the context of the limitations applicable to observational, retrospective data. As mentioned in the editorial comment, it has been demonstrated that older non-diabetic individuals have higher HbA_{1c} values than younger subjects. In our study, we compared the HbA_{1c} results nearly 2 years (the mean time was 22.6 months) after the surgery of the same patients. We believe that this time period is insignificant and valid for every patients included in this study.