Effect Of Raised Alanine Transaminase (ALT) Levels On Hba1c Response To SGLT2 Inhibitors In Type 2 Diabetes

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Introduction

- Sodium-glucose transport protein 2 inhibitors (SGLT2i), also called gliflozins, are a class of medications that inhibit reabsorption of glucose in the kidney and therefore lower blood sugar

- SGLT2 inhibitors are associated with weight loss, improved glycaemic controls improvement in heart failure outcomes , reduction in systolic blood pressure, and prevent progression of renal disease in type 2 diabetes. SGLT2 inhibitors also reduced alanine transaminase (ALT) level one of the most specific markers for NAFLD

- However, how raised ALT levels and hence NAFLD affects HbA1c response to SGLT2 inhibitors is not known

Study objective and Methods

- The objective of this study was to understand the effect of ALT on glycaemic response to SGLT2 inhibitors in patients with Type 2 diabetes
- Data for this study was obtained from a large nationwide audit of SGLT2 inhibitors (n=9,609) of patients with Type 2 Diabetes initiated on an SGLT2 inhibitor
- We used a gradient boosting machine learning algorithm (GBM) to identify if ALT is an important predictor of glycaemic response to SGLT2 inhibitors
- The results of the GBM model were confirmed using linear regression analysis where the absolute drop in HbA1c was modelled as a dependent variable with baseline ALT as independent variable adjusted for relevant covariates

Results

Demographics and audit characteristics (n=9,609)

Age(IQR)	59.1 (60-68)
Gender % females	40%
BMI median(IQR)	31.8 (28-36)
Baseline Weight median(IQR)	92(80-106)
Baseline HbA1c median(IQR)	8.8(7.9-10)
Baseline eGFR median(IQR)	89(74-90)
Baseline SBP median(IQR)	131(122-140)
Baseline Cholesterol median(IQR)	4.1(3.5-4.9)
% Metformin	7827 (81%)
% SU	2935 (30%)
% Insulin	1654 (17%)
% Gliptin	2238 (23%)
% ACE I/ARB	4225(43%)
% CCB	1878 (19%)
% Beta blocker	1190((12%)
% Statin	7411(77%)
% Aspirin	1966 (20%)

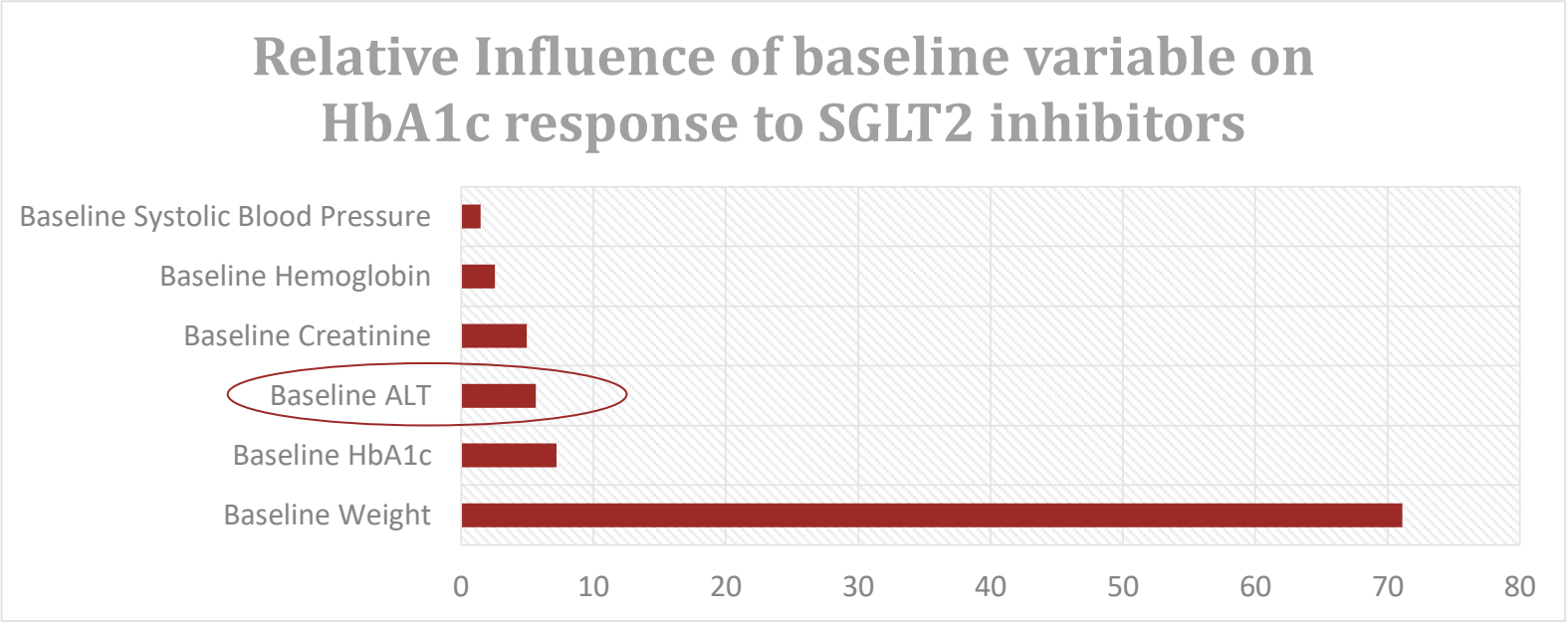
Results

- The study consisted of 9,609 patients initiated on Empagliflozin (n=5061) or Dapagliflozin (n=3711) or Canagliflozin (n=837)

- At the median 5.8 months follow-up period, the mean HbA1c drop was 0.81% and was similar in all three-drug classes

- The drop in HbA1c was 0.62%, 0.78% and 1.01% in 1st 2nd and 3rd quartiles of baseline ALT, respectively (P-Anova <0.0001)

Results: Gradient boosting model



The model accuracy was 0.73 (0.71-0.75) and area under the curve was 0.83

Results: Linear regression model

	Beta	SE	P-value
Baseline Age	0.007	0.001	<0.0001
Baseline HbA1c	0.465	0.006	<0.0001
Baseline ALT	0.007	0.001	<0.0001
Baseline eGFR	0.001	0.001	0.14
Gender	-0.012	0.023	0.59

Weight not included as correlated with baseline HbA1c

Conclusion

- Higher baseline ALT levels are associated with a more significant SGLT2 induced HbA1c drop

- SGLT2 inhibitors and are likely to be more effective in those with coexisting diabetes and NAFLD

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