HbA1c and the severity of acute pancreatitis: a prospective cohort study in the UK Biobank

Alex Ainger,[1] Bhaskar Kumar,[1, 2] Stephen Lam[1, 2]

[1]Norwich Medical School, University of East Anglia, Norwich, United Kingdom

[2]Norfolk and Norwich University Hospital NHS Trust, Norwich, United Kingdom.

Introduction

- In a previous meta-analysis, we discovered a significant association between elevated HbA1c levels and a higher risk of severe acute pancreatitis (AP) **(OR = 2.14, 95% CI 1.32-3.48).**
- To further investigate this relationship, we conducted a new study using the UK Biobank – a dataset comprising clinical information from over half a million participants in England, Wales, and Scotland [1].

Aims

1. To determine the association between HbA1c and AP severity
2. To determine the association between HbA1c and the development of local pancreatic complications
3. To identify associations between HbA1C and systemic complications including mortality

Methods

Identification: Cases of AP were identified using ICD-10 and ICD-9 codes.

Severity Stratification: Defined by the development of complications within 30 days of diagnosis, or any significant procedures related to their diagnosis were performed, identified through OPCS codes.

Analyses:

- Patients were divided into three groups based on HbA1c levels and severe the incidence of cases, local/systemic complications, and mortality rates were examined
- Statistical significance was assessed using the Cochran-Armitage test and multivariable logistic regression for patients with and without diabetes.

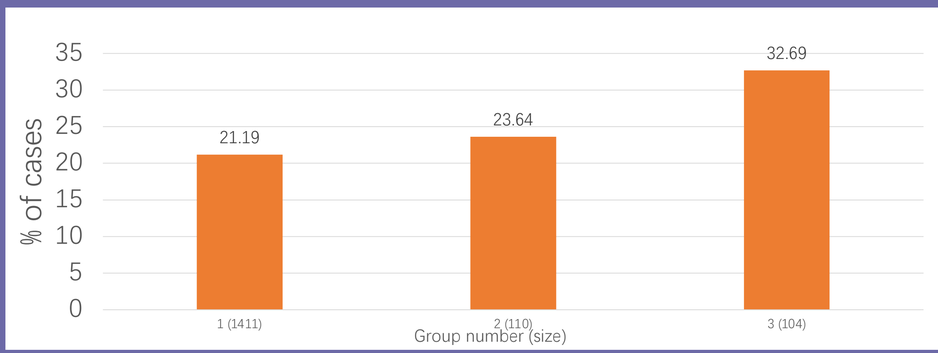
References

1. About our data. UK Biobank; 2022 [cited 2023Jul13]. Available from: https://www.ukbiobank.ac.uk/enable-your-research/about-our-data
2. Nagy A, Juhász MF, Görbe A, Váradi A, Izbéki F, Vincze Á, et al. Glucose levels show independent and dose-dependent association with worsening acute pancreatitis outcomes: Post-hoc analysis of a prospective, international cohort of 2250 acute pancreatitis cases. Pancreatology. 2021Oct;21(7):1237–46.
3. Han F, Shi X, Pan J, Wu K, Zhu Q, Yuan C, et al. Elevated serum HbA1c level, rather than previous history of diabetes, predicts the disease severity and clinical outcomes of acute pancreatitis. BMJ Open Diabetes Research & Care. 2023;11(1). doi:10.1136/bmjdrc-2022-003070

Results

A significant increasing trend in AP cases was observed with rising HbA1c levels (p=0.0126).

Figure 1: Plot of SAP cases amongst each HbA1c group



However, after accounting for variables like age and comorbid diseases, HbA1c did not influence the severity of AP (adjusted OR 1.02, p=0.656), local complications (adjusted OR 0.94, p=0.545), or systemic complications (adjusted OR 1.00, p=0.991).

Table 1: Regression analysis for SAP

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
HbA1c (mmolL) per 5 unit increase	1.10 (1.03 – 1.17)	**0.006**	1.02 (0.93 – 1.11)	0.656
Age (years) per 5 year increase	1.20 (1.11–1.30)	**<0.0001**	1.14 (1.05 – 1.24)	**0.002**
Sex	1.42 (1.12–1.80)	**0.003**	1.25 (0.98 – 1.61)	0.076
BMI	1.00 (0.98–1.02)	0.924	0.99 (0.97 – 1.02)	0.646
Current smoker	1.28 (0.92–1.77)	0.143	1.18 (0.82 – 1.70)	0.372
Alcohol dependent	1.73 (1.03–2.92)	**0.039**	1.51 (0.86 – 2.66)	0.149
COPD	2.03 (1.46–2.83)	**<0.0001**	1.41 (0.97 – 2.03)	0.068
Diabetes	1.63 (1.23–2.18)	**0.001**	1.26 (0.87 – 1.84)	0.225
CKD	2.28 (1.63–3.20)	**<0.0001**	1.62 (1.12 – 2.34)	**0.010**
CVA	1.87 (1.20–2.91)	**0.006**	1.21 (0.75 – 1.95)	0.426
MI	1.81 (1.27–2.59)	**0.001**	1.11 (0.71 – 1.73)	0.656
CHF	3.10 (2.12–4.54)	**<0.0001**	2.17 (1.40 – 3.37)	**0.001**
PVD	1.64 (1.16–2.30)	**0.005**	0.92 (0.60 – 1.41)	0.709

A 5 mmol .l-1 increase in HbA1c did raise mortality odds in non-diabetic patients (adjusted OR 1.47, p=0.030), suggesting its potential as a prognostic indicator for this group. Congestive heart failure and chronic kidney disease consistently elevated odds of a worse prognosis in AP cases.

Table 2: Regression analysis for mortality in patients without diabetes

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
HbA1c (mmol.l^{-1}) per 5 unit increase	1.62 (1.18 – 2.23)	**0.003**	1.47 (1.04 – 2.09)	**0.030**
Age (years) per 5 year increase	1.44 (1.20 – 1.73)	**<0.0001**	1.37 (1.12 – 1.67)	**0.002**
Sex	1.28 (0.78 – 2.10)	0.321	1.13 (0.66 – 1.93)	0.659
BMI	1.02 (0.98 – 1.07)	0.297	1.03 (0.98 – 1.08)	0.303
Current smoker	1.83 (1.01 – 3.32)	0.047	2.30 (1.16 – 4.57)	0.017
Alcohol dependent	1.19 (0.36 – 3.94)	0.771	1.15 (0.32 – 4.17)	0.827
COPD	1.90 (0.97 – 3.73)	0.061	0.99 (0.46 – 2.11)	0.973
CKD	3.34 (1.82 – 6.15)	**<0.0001**	1.98 (1.00 – 3.92)	0.048
CVA	0.55 (0.13 – 2.31)	0.416	0.27 (0.06 – 1.23)	0.091
MI	2.73 (1.44 – 5.17)	**0.002**	1.50 (0.66 – 3.41)	0.338
CHF	5.15 (2.71 – 9.79)	**<0.0001**	4.02 (1.84 – 8.80)	**<0.0001**
PVD	1.64 (0.82 – 3.29)	0.166	0.58 (0.24 – 1.42)	0.230

Discussion

- Regression analyses highlighted the fact that a myriad of factors affect AP outcomes
- Comparison with existing literature reveals a mosaic of sometimes conflicting evidence on HbA1c's relationship with AP[2][3]
- CKD and CHF emerged as pivotal conditions influencing AP severity and outcomes, even surpassing the impact of diabetes.

Strengths/limitations

✓ Pioneering study exploring the impact of HbA1C on AP

✓ Made strong efforts to reduce the effects of confounding

✓ To date is the largest study assessing the relationship

✗ The UK Biobank lacks AP severity measures, necessitating our independent assessment and introducing the risk of misclassification.

✗ The study depends on the accuracy of reporting by Biobank clinicians, thus specific complications may have been missed if not actively sought for.

Conclusions

- High HbA1c levels may be more aptly viewed as an indicator of poor overall health
- Elevated HbA1c remains potentially useful in identifying patients without diabetes who are at a heightened risk of AP mortality
- A comprehensive international cohort study with rigorous diagnostic protocols for local complications and proactive measures to include participants with higher HbA1c values should be performed to definitively assess the relationship.