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Estimated glucose disposal rate demographics and clinical characteristics of young adults with type 1 diabetes mellitus: A cross-sectional pilot study

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Abstract

Background: Estimated glucose disposal rate (eGDR) is a practical measure of Insulin Resistance (IR) which can be easily incorporated into clinical practice. We profiled eGDR in younger adults with type 1 diabetes mellitus (T1DM) by their demographic and clinical characteristics.

Methods: In this single centre study, medical records of TIDM were assessed and eGDR tertiles correlated with demographic and clinical variables.

Results: Of 175 T1DM individuals, 108 (61.7%) were males. Mean age (±SD) was 22.0 ± 1.6 years and median time from diagnosis 11.0 years (range 1–23). Individuals were predominantly Caucasian (81.7%), with 27.4% being overweight (BMI: 25–30 kg/m^2) and 13.7% obese (BMI > 30 kg/m^2). Mean total cholesterol (TC) levels were significantly lower in high and middle eGDR tertiles (4.4 ± 1 and 4.3 ± 0.8 mmol/l, respectively) compared with low eGDR tertile (4.8 ± 1, $p < 0.05$ for both). Triglyceride (TG) levels showed a similar trend at 1.1 ± 0.5 and 1.1 ± 0.5 mmol/l for high and middle eGDR tertile compared to low eGDR tertile (1.5 ± 1 mmol/l, $p < 0.05$ for both). Renal function was similar across eGDR tertiles and no difference in retinopathy was detected.

Conclusion: TC and TG are altered in individuals with T1DM and low eGDR, suggesting that this subgroup requires optimal lipid management to ameliorate their vascular risk.

Keywords

Type 1 diabetes, children, adolescents, estimated glucose disposal rate, insulin resistance

Introduction

In recent times, it has been noted that a phenotype of type 1 diabetes exists which displays both features of insulin deficiency (through and autoimmune process) and insulin resistance, through less well explained mechanisms. Termed 'double diabetes',[1] a number of factors have been described as potentially causative in the insulin resistance seen including genetic, lifestyle and the injection of exogenous insulin.[2] Importantly, insulin resistance has been shown to increase vascular endothelial dysfunction[3] and induce a cytokine-mediated inflammatory response[2] which in turn has been proposed to increase cardiovascular risk and other diabetes complications in this group.[4]

Within clinical practice, IR is broadly defined as daily insulin requirements exceeding one international unit (IU)/kg/day. Several tools and methods are currently available to quantify IR in T1DM patients, including insulin tolerance test, insulin sensitivity test and continuous infusion of glucose with model assessment.[5] However, the utilization of these tools for routine clinical practice is limited or difficult to implement in routine practice.[6] Among the available tools, the euglycemic hyperinsulinemic clamp method is considered the gold standard to quantify IR. However, this

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method is labour intensive and is not suited for the routine assessment of IR in clinic settings. Estimated glucose disposal rate (eGDR) has been proposed as a new practical measure of IR, given it reflects insulin resistance measured using clamp methods.[7]

An advantage of eGDR is the simplicity where it can be calculated using simple clinical factors including glycated haemoglobin (HbA1c) value, waist circumference (or BMI) and hypertension status, making this a pragmatic marker to analyze IR in clinic settings.[7] Moreover, eGDR has a prognostic significance as studies have shown that low eGDR is associated with an increased risk of vascular complications as well as mortality in T1DM.[8,9]

The objective of this pilot study was to gain an understanding of the eGDR values amongst those in a dedicated young adult T1DM clinic. Specifically, this study aimed to profile the demographic and clinical characteristics of our selected population by eGDR values.

Methods

This study was classified as a clinical audit and was exempt from Ethics approval.

Study setting and population

This is a cross-sectional retrospective study conducted on patients diagnosed with T1DM currently attending the young adult diabetes clinic at a large teaching hospital in the UK. Data were collected from electronic clinical records, with most recent clinic attendance being used for data collection.

Our inclusion criteria included a formal diagnosis of T1DM (clinical history and elevated random plasma glucose levels at presentation at >11.1 mmol/l) in association with ketonaemia and/or positive antibody tests for glutamic acid decarboxylase/islet cell antibodies. Exclusion criteria were as follows: individuals with a diagnosis of less than 1 year, younger than 18 or older than 40 years of age, patients who were currently pregnant, individuals with end stage renal failure requiring dialysis.

Study variables

We collected demographic variables including age, sex, ethnicity, and date of initial appointment to the endocrinology clinic. We identified clinical variables from the patient medical records including mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) over the last year, duration of TIDM, BMI, HbA1c, microalbuminuria, retinopathy and lipid profile (total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein (LDL), and triglycerides (TG).

We defined underweight as BMI of $<18\,kg/m^2$, normal weight as BMI between 18 and $24.9\,kg/m^2$, overweight as BMI of 25 to $29.9\,kg/m^2$ and obesity as a BMI of $30\,kg/m^2$ or greater. Normal weight was defined as individuals with a BMI between 18.0 and $24.9\,kg/m^2$.

HbA1c is expressed in mmol/mol as well as percentages. We defined the duration of diabetes greater than 10 years as 'long duration'.

We calculated eGDR with the following equation[8]:

$$eGDR_{BMI} = 19.02 - \left(0.22 \text{ x BMI } \left[kg/m^2\right]\right) - \left(3.26 \text{ x HTN}\right) - \left(0.61 \text{ x HbA1c } [\%]\right)$$

Statistical analysis

We used SPSS® software version 23 for Windows for all statistical analyses. We computed mean (standard deviation) for continuous variables and used frequency distribution for categorical variables. We conducted independent samples *t*-test assuming equal variances to examine the relationship between eGDR values among sex and duration of diabetes categories. We excluded variables such as SBP, DBP and BMI that are highly correlated with eGDR values. We categorized eGDR values in tertiles. To examine the relationship between eGDR values and continuous quantitative variables including age and lipid profile (total cholesterol, HDL, LDL, TG) we performed a one-way ANOVA test. Where the dependent variable was continuous, we conducted bivariate linear regression and for categorical variables, we performed a bivariate logistic regression.

Results

Among the 175 study participants, 108 (61.7%) were males and 67 were females (38.3%). Mean age was 22.0 years (SD ± 1.6). The median time from diagnosis of T1DM was 11.0 years (range 1–23 years). Study participants were predominantly Caucasian (81.7%), with 27.4% being overweight (BMI: 25–$29.9\,kg/m^2$) and 13.7% obese (BMI>$30\,kg/m^2$). Twenty-one participants had background retinopathy. Mean eGDR ±SD was 8.0 ± 1.6. We categorised eGDR values in tertiles including low eGDR<7.4, Middle eGDR = 7.4 to 8.9 and High eGDR > 8.9

The demographic and clinical characteristics of the study participants are displayed in Table 1.

There was a statistically significant difference between total cholesterol levels in the tertiles of eGDR as determined by one-way ANOVA (F (2155) =5.56, $p = 0.005$). A Tukey post hoc test with Bonferroni correction revealed that mean total cholesterol levels was lower in the high eGDR tertile (4.37 ± 0.95 mmol/l) and middle eGDR tertile (4.28 ± 0.75 mmol/l) than low eGDR tertile (4.83 ± 0.98; $p = 0.022$ and 0.007, respectively). There was no statistically significant difference in mean total

Table 1. Demographic, social and clinical characteristics ($n = 175$).

Characteristic	Mean (SD)/Proportion (n (%))				p-value[c]
	Total ($n = 175$)	eGDR < 7.34 ($n = 58$)	eGDR 7.34–8.92 ($n = 56$)	eGDR ⩾8.93 ($n = 61$)	
Age, years	22.0 (1.6)	21.9 (1.6)	22.2 (1.6)	22.0 (1.5)	0.546
Sex, male	108 (61.7%)	36 (62.1%)	36 (64.3%)	36 (59.0%)	0.840
Ethnicity					0.068
Caucasian	143 (81.7%)	45 (77.6%)	45(80.4%)	53 (86.9%)	
African/Caribbean	4 (2.3%)	1 (1.7%)	2 (3.6%)	1 (1.6%)	
South Asians	11 (6.3%)	3 (5.2%)	7 (12.5%)	1 (1.6%)	
Other	4 (2.3%)	1 (1.7%)	0	3 (4.9%)	
unknown	13 (7.4%)	8 (13.8%)	2 (3.6%)	3 (4.9%)	
Long standing diabetes >10 years	90 (51.7)	32 (55.2%)	35 (62.5%)	23 (38.3%)	0.027
BMI, kg/m^2	25.0 (5.2)	28.7 (6.0)	24.8 (3.1)[b]	21.5 (3.0)[b]	<0.001
BMI, groups					<0.001
Underweight (<18)	4 (2.3)	1 (1.7%)	0	3 (4.9%)	
Normal (18–24)	99 (56.6)	17 (29.3%)	29 (51.8%)	53 (86.9%)	
Overweight (25–29)	48 (27.4)	18 (31.0%)	25 (44.6%)	5 (8.2%)	
Obese (30 and above)	24 (13.7)	22 (37.9%)	2 (3.6%)	0	
HbA1c, mmol/mol	74.2 (23.1)	91.8 (27.7)	73.1 (12.0)[b]	60.1 (10.6)[b]	<0.001
eGDR (mg/kg min)	8.0 (1.6)	6.2 (1.0)	8.2 (0.4)[b]	9.6 (0.7)[b]	<0.001
eGFR, ml/min/1.73 m^2	89.8 (1.9)	89.8 (1.8)	89.5 (2.7)	89.9 (0.5)	0.548
Mean blood pressure, mmHg					
Systolic	126.5 (13.9)	128.8 (14.4)	127.5 (13.1)	123.5 (14.0)	0.097
Diastolic	72.9 (7.7)	74.1 (7.8)	72.8 (7.2)	71.8 (8.0)	0.249
Lipid profile[a]					
Total cholesterol, mmol/l	4.5 (0.9)	4.8 (1.0)	4.3 (0.8)[b]	4.4 (1.0)[b]	0.005
Triglycerides, mmol/l	1.6 (0.4)	1.5 (1.0)	1.1 (0.5)[b]	1.1 (0.5)[b]	0.004
HDL, mmol/l	1.2 (0.7)	1.4 (0.3)	1.6 (0.5)	1.6 (0.4)	0.066
LDL, mmol/l	2.4 (0.7)	2.6 (0.8)	2.3 (0.7)	2.3 (0.7)	0.063
Background retinopathy	21 (12.0)	5 (8.6%)	10 (17.9%)	6 (9.8%)	0.257

eGDR, estimated glucose disposal rate.
[a]Data was missing: 17 for total cholesterol, 22 for triglyceride, 32 for HDL and 34 for LDL.
[b]Post-hoc Bonferroni, $p < 0.05$ compared to low eGDR tertile.
[c]One-way ANOVA or Pearson Chi Square.

cholesterol levels between middle and high eGDR groups ($p = 0.878$). Results are displayed in Supplemental Table 1.

There was a statistically significant difference between triglyceride levels in the tertiles of eGDR as determined by one-way ANOVA (F (2,140) $= 5.86$, $p = 0.004$). A Tukey post hoc test with Bonferroni correction revealed that the triglyceride levels was statistically lower in the middle eGDR tertile (1.12 ± 0.48 mmol/l) and higher eGDR tertile (1.08 ± 0.48 mmol/l) compared to the low eGDR tertile (1.52 ± 0.99 mmol/l). Results are displayed in Supplemental Table 2. There was no statistically significant difference in the mean triglyceride levels between the middle and high eGDR tertile ($p = 0.937$). Data is displayed in Table 1.

Discussion

Mean eGDR for our study participants was 8.0 mg/kg min (1.6), and similar eGDR values have been reported in a cross-sectional study involving 61 T1DM patients in a largely similar age group.[10] However, the latter study showed an association of eGDR with microvascular complications while our work failed to demonstrate a similar relationship, despite the larger number of individuals analysed. However, nephropathy was assessed as eGFR and microalbuminuria data were not available to fully assess nephropathy.

The diabetes-specific mechanisms for obesity and insulin resistance in our cohort are not entirely clear and may be related to the use of higher insulin doses, having an anabolic effect. Unfortunately, full data on insulin dosing and schedules were not available for analysis and this remains an area for future research. Another possible mechanism is increased rate of hypoglycaemia, which may contribute to obesity in individuals with T1DM. Data surrounding the relationship between eGDR/obesity and hypoglycaemia are not currently available and future work should investigate this area, particularly with the increasing availability

of continuous glucose monitoring in individuals with T1DM.

TC and TG levels were higher in the low eGDR group compared to the high eGDR group. However, a cross-sectional study conducted in Spain (n = 115, median age 12.6 years (10.5–15.4), did not find a correlation between eGDR values and lipid levels.[11] One important consideration to make is how these results could implicate future clinical practice. The American Diabetes Association guideline for children and adolescents with diabetes recommends considering statin therapy if LDL levels are >4.1 mmol/l following appropriate dietary advice (>3.4 mmol/L in those at CV risk), with a treatment goal of <2.6 mmol/L.[12] Our data suggest, that in our young adult population, most participants would not meet criteria for treatment yet in those with eGDR 7.34 to 8.92 LDL, values are close to treatment target. Therefore, it can be argued that aggressive statin therapy may be indicated, particularly when duration of diabetes is >10 years, a concept supported by UK guidelines[13] Given that >50% of patients in the lower tertiles of eGDR had a longer diabetes duration (>10 years), careful consideration may be given to commencing statin therapy to target lower LDL levels in this population. However, it should be noted that there is a lack of randomised controlled trials in this group of individuals to conclusively support this approach. Treatment targets for triglycerides from the ADA suggest consideration of pharmacological treatment when values are >2.3 mmol/L, after optimisation of hyperglycaemia.[14] Although our data do not suggest that a high percentage of patients meet this criterion, the mean age of the lowest eGDR tertile was just 22 years with a mean triglyceride concentration of 1.6 mmol/L. Given the presence of insulin resistance at such a young age with the prospect of decades of living with T1DM, consideration may be given to treating more aggressively in those with low eGDR, although the lack of randomized controlled trials forces the decision making process to remain at the discretion of the health care professional and after careful assessment of the risks/benefits. Importantly, one must remember the fact that statin therapy is absolutely contraindicated in pregnancy and those looking to conceive and given the age demographics of our population, it is likely that this is not an appropriate management strategy in young female patients.

Our study did not show a sex-related difference in eGDR values consistent with a previous study conducted in T1DM patients under 18 years. Also, our study did not find any ethnicity-related differences in eGDR values, although the majority were Caucasians and given small sample size, concrete conclusions cannot be drawn. Moreover, previous studies focused on the major ethnic groups within the United States highlighted the relationship between eGDR with diabetic vascular complications. In a cross-sectional study conducted by Epstein et al. African Americans were found to have had significantly less insulin sensitivity than Caucasians or Hispanics.[15]

Our study has limitations. Given the cross-sectional study design, causality cannot be inferred, and the study findings can only suggest that eGDR is a potential marker for chronic diabetic complications in T1DM patients. Due to the small sample size, we did not conduct a multivariate logistic regression model to confirm associations with clinical variables examined in the bivariate analyses.

In conclusion, a novel finding of the study is a relationship between eGDR and macrovascular markers in a young population of T1DM. Individuals with low eGDR values had significantly higher total cholesterol and triglyceride levels, suggesting that this group will require more aggressive lipid management to prevent future macrovascular disease. Large-scale prospective studies are warranted to confirm the utility of eGDR in predicting macrovascular disease and as a clinical marker that assesses response to preventative management strategies.

Author contributions

RN, RA, SP conceived and designed the study. RN and NK analysed the data. RN drafted the manuscript with critical input from all authors.

Declaration of conflicting interests

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Data availability

All data collected and inputted into spreadsheet will be available from authors with written request and following agreement on the intended purpose of the request for secondary data analysis.

Supplemental material

Supplemental material for this article is available online.

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