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Original Article

Glycemic and non-glycemic targets in younger and older North Indian subjects with type 2 diabetes in a Tertiary care hospital: A 10 year's retrospective data analysis

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ABSTRACT

Background: Although optimizing glycemic and non-glycemic targets reduced micro- and macro-vascular complications in type 2 diabetes, multiple barriers hinder turning evidence into practice. Mounting evidence suggests that those with onset of disease in early or mid-adult life, compared with those with onset at an older age, may have a more severe disease course and worse glycemic control.
Aims & objective: We tested the hypothesis that those diagnosed at younger age would have worse glycemic control, even after adjustment for duration of diabetes, higher BMI and other known risk factors for worse glycemic control.
Materials & methods: A cross-sectional analysis of 560 type 2 diabetic subjects from North Indian populace in the year 1999–2012 who reported to endocrine clinic was performed. Sixty patients did not report in the successive year and final data analyses were done in 500 patients attending clinic regularly over a period of 10 years for evaluation of glycemic and non-glycemic targets. They were followed up at 3 monthly intervals with all patients undergoing anthropometric measurement (BMI (weight in kg/height in m^2), diet and lifestyle advice by a diabetic educator and consultation by endocrinologist. Fasting and postprandial plasma glucose, A1c (3 monthly), besides evaluation of SMBG that was performed in 50% of these patients regularly. Fasting lipids, S. creatinine and microalbuminuria were assessed annually and blood pressure recoding was done at each visit. The treatment was modified as per the investigation reports. We classified age at diabetes diagnosis as younger (<60 years) vs older (≥60 years). The primary outcome of interest was HbA1c ≥9%. Secondary outcomes were HbA1c ≥8% to <9% and HbA1c ≥7% to <8%.
Results: After adjustment for sex, duration of diabetes, hyperglycemic medications, BMI, co-morbid conditions, age <60 years at diagnosis remains significantly associated with greater odds of HbA1c ≥9% [OR 0.95(0.84–1.07)], HbA1c ≥8% to <9% [OR 1.04(0.93–1.15)] and HbA1c ≥7% to <8% [OR 1.05(0.85–1.17)] for female sex. Seventy two (72.7%) of patients <60 years achieved BP <140/90 mmHg ($p < 0.001$) as compared to 62.3% of patients ≥60 years who achieved BP <150/90 mmHg ($p < 0.001$) and LDL-cholesterol <100 mg/dl in 33.7% patients and 39.1% respectively ($p < 0.002$).
Conclusion: Younger age (<60 years) at type 2 diabetes diagnosis is significantly associated with worse subsequent glycemic control and lipid control, as younger patients at diagnosis have fewer competing co-morbidities and complications. As patient-centeredness is a priority in type 2 diabetes care, safe, aggressive and individualized treatment could benefit this higher-risk group.

1. Introduction

Diabetes is defined by its association with hyperglycemia-specific micro-vascular complications; however; it also imparts a two-to-four fold risk of cardiovascular disease (CVD). Although microvascular complication leads to significant morbidity and premature mortality, by far the greatest cause of death in people with type 2 diabetes is CVD. Glycemic management in type 2 diabetes has become increasingly complex and, to some extent, controversial, with a widening array of pharmalogical agents now available [1–5], concerns about their potential adverse effects and new uncertainties regarding the benefit of intensive glycemic control on microvascular complications [6–9]. Many clinicians are therefore, perplexed to the optimal strategies for their patients.

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Identifying subgroups at high risk of poor outcomes is an important goal, which may facilitate population management for diabetes. There is a need to identify different 'phenotypes' of type 2 diabetes that may need and benefit from more intensive interventions. As a consequence, the American Diabetes Associations (ADA) and the European Association for the study of diabetes (EASD) convented a joint task force to examine the evidence and developed recommendations for anti-hyperglycemic therapy in non-pregnant adults with type 2 diabetes [10]. The implementations of these guidelines will require clinicians to integrate current evidence with other constraints and imperatives in the context of patients-specific factors.

The available evidence suggests that those with onset of type 2 diabetes in early or mid-adult life, compared with those with onset at an older age (65 or other), may have a more severe disease course, with increased risk of microvascular complications and worse glycemic control [11–14]. These differences in the degree of dysglycemia may be due to the known risk factors such as longer duration of diabetes, BMI, quality of care, they may also reflect more significant insulin deficiency particularly in the context of Indian sub-continent where the disease is diagnosed at much younger ages. In this study, we tested the hypothesis that those diagnosed at younger age would have worse glycemic control, even after adjustment for duration of diabetes, BMI and other known risk factors for worse glycemic control.

2. Methods

2.1. Subjects

We conducted a cross-sectional analysis of 560 type 2 diabetic subjects from North Indian population who reported to endocrine clinic in the year 1999–2012. Type 2 diabetes was defined according to the expert committee on the diagnosis and classification of diabetes [15]. To minimize inclusion of type 1 diabetes patients, we excluded patients who were diagnose before the age of 30 and started on insulin around the time of diagnosis. We did not include participants with biochemical but not self-reported diabetes because age at diagnosis could not be determined in these cases. The endocrine clinic of Rajiv Gandhi Centre for Diabetes & Endocrinology (RGCDE), Faculty of Medicine of J. N. Medical College Hospital, Aligarh Muslim University, Aligarh, India is a tertiary care hospital. Sixty patients enrolled in the year 1999–2000 did not report in the successive and final analysis were done in 500 patients of type 2 diabetes attending clinic regularly over a period of 10 years for evaluation of glycemic and non-glycemic targets. None of these patients were insured. They were paying the cost of investigation and purchasing medicine on their own, however, consultation charges were free to the patients, being a Central Government organization. They were followed up at 3-monthy intervals with all patients undergoing anthropometric measurements (BMI = weight in kg/height in m^2), diet and lifestyle advise by a diabetic educator and consultation by a qualified endocrinologist. Fasting and post-prandial plasma glucose, A1c % (3 monthly), besides evaluation of SMBG (in 50% of these patients regularly) were performed. Fasting lipids, serum creatinine and microalbumin were assessed annually. The treatment was modified as per the investigation report.

2.2. Measures

For this study, we classified age of diabetes diagnosis as younger (<60 years) vs older (≥60 years) based on patients self report. In exploratory analysis, we also treated age at diagnosis as a continuous variable.

2.3. Outcomes

We used HbA1c percentage as a measure of glycemic control. Our primary outcome of interest was whether the HbA1c value was >9.0%, which represents out-of-control hyperglycaemia for all patients [16]. In order to determine whether glycemic control was worse at other commonly used thresholds [16], we conducted secondary analyses using outcomes of HbA1c above or below 8.0% and 7.0%.

2.4. Clinical variables

We considered several clinical variables thought to be associated with worse glycemic control as covariates. BMI (weight in kg divided by height in m^2) was categorized as 'lean' (<18.5 kg/m^2), 'normal' (18.5–22.9 kg/m^2), 'overweight' (23.0–24.9 kg/m^2) and 'obese' (≥25 kg/m^2). Duration of diabetes was calculated from the patient's report of age at diabetes diagnosis subtracted from current age. Diabetes treatment was classified into categories of metformin only, sulfonylurea only, mixed oral medications or insulin plus oral medications.

2.5. Statistical analysis

In this retrospective cross sectional data analysis, we performed descriptive statistical on the samples, using χ^2 test to evaluate the differences in categorical values and t test for continuous variables. A multivariate logistic regression was then performed in order to determine the independent association of age at diagnosis with HbA1c ≥9% adjusting for demographic and clinical factors described. Age at the time of study was directly included because it is a function of age at diagnosis and duration of diagnosis. A secondary analysis was then conducted to determine if age at diagnosis was also associated with increased risk of having HbA1c ≥8% or HbA1c ≥7% as well as whether age at diagnosis as a continuous variable was associated with HbA1c ≥9% adjusting for the same factors as above.

We used Sigma Plot (version 13) and SPSS (version 17) for analysis to account for the complex multistage survey design. A p value of <0.05 χ^2 or F tests was taken to indicate statistical significance.

3. Results

There were 560 Type 2 diabetic subjects enrolled in the endocrine clinic in the year 1999–2000 and after exclusions, 500 participants remained in the study sample, who attended clinic regularly over a period of 10 years. Table 1, presents full characteristics of the study samples. Overall, 10.8%, 26.6%, and 43.6% of participants had an HbA1c ≥9.0%, ≥8.0% to <9.0%, and HbA1c ≥7.0% to <8.0% respectively. Patients who were younger at diagnosis (<60 years) were likely to have an HbA1c ≥9.0% (11.6% vs 8.7%, $p < 0.003$), HbA1c ≥8.0% to <9.0% (20.3% vs 16.6%, $p < 0.003$), HbA1c ≥7% to <8.0% (51.5% vs 23.9%, $p < 0.003$). HbA1c ≤7.0% was observed in 18.0% in patients younger than 60 years of age as compared to 21.7% in those above 60 years at the time of diagnosis ($p < 0.003$). Fig. 1 depicts comparisons at each glycemic control threshold. After adjustment for sex, duration of diabetes, hyperglycemic medications, BMI, co-morbid conditions, age <60years at diagnosis compared with older age remained significantly associated with greater odds of HbA1c ≥9.0% [OR 0.95 (0.84–1.07)]. In secondary analysis adjusted for the same covariates, younger, compared with older age at diagnosis was also associated with greater Odds of an HbA1c >7.0%[OR 2.0(1.22–3.29)], HbA1c > 8.0% [1.87(1.13–3.08)] and HbA1c > 9.0%