Non-ketotic diabetes in Saudi Arabian youths: MODY or early onset of type 2 diabetes?

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Abstract

Background: Non-ketotic diabetes mellitus is commonly seen in young Saudi Arabian adults. This could be either early onset of typical type 2 diabetes, T2DM or maturity-onset diabetes of the young, MODY. Consanguinity is also prevalent and clouds the inheritance pattern of the disease. Distinction between the two on clinical grounds alone is not always possible. **Materials and Method:** Diabetic patients aged ≤ 25 years with family history of the disease who had maintained reasonable glycaemic control with diet and/or oral hypoglycaemic agents for at least two years were studied. Demographic data, presentation details and clinical course were analyzed for classification of patients as possible cases of MODY, using generally accepted criteria. **Results:** Twenty three patients with diabetes through three consecutive generations were identified as possible cases of MODY from a clinic population of about 200. However, they could also have been early onset cases of T2DM, and differentiation between the two could not be made with certainty without further tests. **Conclusion:** More studies including genetic testing would be needed to differentiate between early onset T2DM and MODY, according to the current WHO classification. Since most developing countries among which the increasing burden of DM lies cannot do this, there is a need to review the current classification of diabetes. (Int J Diabetes Metab 15:60-61, 2007)

Key words: *Diabetes classification, Type2 diabetes, MODY, consanguinity.*

Introduction

Maturity onset diabetes of the young, MODY, previously classified with type 2 diabetes, T2DM, is now part of type 3 diabetes according to the current World Health Organization (WHO) classification of diabetes.[1] Ketosis-resistance and non-insulin dependence which are key MODY features, are also typical of T2DM.[2] Such non-ketotic diabetes (NKDM) is common among youths in Eastern Saudi Arabia where consanguinity is common. Distinguishing clinically between MODY and T2DM can be difficult.

Methods and Results

Among 14-25-year old diabetic patients with reasonable control (glycated haemoglobin, HbA1c ≤ 8 %[3] on diet/oral hypoglycaemic agents (OHAs) for at least two years, data were obtained to classify them as possible MODY, using accepted criteria.[2] Overweight and obesity were defined as Body Mass Index, BMI of ≥ 25, and ≥ 30, respectively. Asymptomatic relatives were not tested. Patients' clinical profiles are summarized in table 1.

Nineteen males and 4 females from the special clinic population of 200, had positive family history of diabetes through three successive generations and satisfied most other clinical criteria for MODY. Consanguinity occurred in 70 % of cases while 50% had at least one diabetic sibling or cousin aged ≤ 25 years; 80 % had normal serum C-peptide concentration. Most patients were overweight or obese, and none had keto-acidosis even when the presenting plasma glucose concentration was ≥ 16.7mmol/l.

Table 1: Patients clinical profile

Characteristic	Prevalence (% of patients)
Obesity/overweight	60
Related parents	70
C-peptide	80 % normal values
Insulin need (2 years after diagnosis)	14
M/F ratio	19/4 = 5/1
Mean HBA1c <8% on diet/OHA	85%
Ketosis resistance	
Mean PPG (mmol/l)	21.3 (normal range 3.3-6.1)
Mean HCO3 (mmol/l)	24 (normal range 24-32)
DKA occurrence	0

DKA = Diabetic keto-acidosis
PPG= Presenting plasma glucose
HCO3= Serum bicarbonate

Discussion

Overweight/obesity prevalence among this group of diabetics was high at 60%, but similar to current Saudi Arabian trends.[4] Obesity is now increasing in prevalence world-wide;[5] it is traditionally more often associated with T2DM than with MODY, although significant obesity has been reported previously in MODY.[6] Thus its relevance to

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MODY diagnosis is now questionable.[7] Although equal sex distribution would be expected in an autosomal dominantly inherited condition like MODY, over 80 % of our patients were males. A female preponderance was found in a large Indian MODY population[6] and sporadic cases are also known to occur.[8] Diabetes onset at adolescence seems more common in Saudi males,[3] and Indians[9] whereas more females were found in small groups of young T2DM patients from both the UK and USA.[10, 11]

A high positive family history rate would be expected in heredity-associated diabetes like T2DM and MODY in Saudi Arabia where consanguinity is prevalent.[12] Thus, the family history which is usually a vital clue to dominant inheritance in MODY diagnosis, may be unhelpful in distinguishing clinically between them. Although several genes responsible for MODY have now been identified, we did not perform any genetic tests as these are currently research procedures.[13]

Early T2DM onset is associated with:

- 92% diabetes or glucose intolerance
- prevalence in both parents and 69 % in siblings aged 25-40yrs
- Insulin resistance
- Early requirement for insulin.[14]

Affection of only one parent in MODY and absence of insulin resistance are additional differences from T2DM.[7] Obesity predisposes to the latter but these characteristics were originally derived from populations without high consanguinity rates, and may not apply universally.

The pattern of the disease in our NKDM patients may be reflected similarly throughout the country. Testing asymptomatic relatives would verify this, as T2DM is frequently asymptomatic. The present study shows that diabetes classification can be challenging in young patients in developing countries where T1DM, T2DM and MODY are common. The first is usually recognizable by its clinical features. In doubtful cases, the patient is treated as T1DM to ensure that essential insulin is not denied. Accurate classification is nevertheless important because insulin supply may be limited and additionally, its inappropriate use in MODY patients may cause recurrent hypoglycaemia with consequent patient discouragement and poor compliance.

Most cases of the increasing prevalence of diabetes world-wide are expected to occur in developing countries.[15] Some of these countries have high consanguinity rates as well and most lack the resources for genetic testing. There is therefore a need for simplifying the current classification for universal application. MODY may be reclassified with T2DM and be grouped with its early onset, as they behave clinically alike. Both may then be called non-ketotic diabetes mellitus, NKDM, and MODY designated non-ketotic diabetes mellitus of the young, NKDY, with genetic testing used, where available, to distinguish between them.

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