Sultan Qaboos University Med J, August 2013, Vol. 13, Iss. 3, pp. 399-403, Epub. 25th Jun 13
Submitted 8th Jul 12
Revisions Req. 10th Sep & 25th Nov 12, 5th Mar & 7th May 13; Revisions Recd. 20th Oct 12, 21st Jan, 21st Apr & 27th May 13
Accepted 30th May 13

CLINICAL & BASIC RESEARCH

The Frequency of Type 2 Diabetes Mellitus among Diabetic Children in El Minia Governorate, Egypt

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معدل الاصابه بالنوع الثاني من مرض السكري بين أطفال مرضى السكري بمحافظة المنيا في مصر

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الملخص: **الهدف**: النوع الثاني من داء السكري (T2DM) في الأطفال والمراهقين أصبح مصدر قلق متزايد للصحة العامة في جميع أنحاء العالم. الهدف: تهدف هذه الدراسة إلى تقدير نسبة T2DM بين أطفال مرضى السكري في محافظة المنيا في مصر، و الكشف عن عوامل الخطر ذات الصلة. **الطريقة**: شملت الدراسه 210 من الأطفال المرضى بالسكري في محافظة المنيا الذين خضعوا للفحص البدني والفحوص المخبرية. ولأخذ تاريخهم الطبي الدقيق. **النتائج**: وجد T2DM في 28 مريضا (13.3%)، و كان حاضرا بشكل ملحوظ في 18 من الإناث (64.3%) حيث 20 (17.4%) منهم لديهم تاريخ عائلي إيجابي من DM. وكان مؤشر الخطوط المئوية لكتلة الجسم ومحيط الخصر في مرضى T2DM أعلى بكثير باعتبار العمر والجنس من مرضى T1DM. أيضا كانت مستويات الهيموجلوبين % A1c و الكولسترول و C–الببتيد أعلى بكثير في T2DM من مرضى T1DM. وأخيرا كان هناك ارتباطات إيجابية ضعيفة ذات دلالة إحصائية بين مستوى C–الببتيد و مؤشر كتلة الجسم ومحيط الخصر. **الخلاصة**: لم يعد مرض T2DM يصيب البالغين فقط ولكن يمكن أيضا أن يحدث في الأطفال والمراهقين. وتشير النتائج الى أن السمنة، والجنس الأنثوي ووجود تاريخ عائلي إيجابي من DM هي عوامل الخطر للإصابة ب T2DM. أيضا كان المرضى الذين يعانون من T2DM الأكثر فقدا للسيطرة على ارتفاع نسبة سكر الدم و الكولسترول من المصابين بأنواع مرض السكري الأخرى.

مفتاح الكلمات: مرض السكري؛ النوع الثاني؛ الأطفال؛ المراهقين؛ C–الببتيد؛ مؤشر كتلة الجسم؛ الهيموغلوبين A؛ المتسكّر؛ الكولسترول؛ مصر.

abstract: ***Objectives:*** Type 2 diabetes mellitus (T2DM) in children and adolescents is becoming an increasingly important public health concern throughout the world. This study aimed to estimate the frequency of T2DM among diabetic young people in El-Minia Governorate, Egypt, and to detect its risk factors. ***Methods***: A total of 210 diabetic patients under 18 years old in Minia Governorate were included in the study and underwent a thorough history-taking, a physical examination and laboratory investigations. ***Results***: T2DM was present in 28 patients (13.3%); it was significantly present in 18 females (64.3%) and 20 (71.4%) of them had a positive family history of DM. T2DM patients had significantly higher BMI and waist circumference centiles for age and sex than those with T1DM. Also, haemoglobin A1c %, serum C-peptide and cholesterol levels were significantly higher in T2DM than T1DM patients. Finally, there were weak significant positive correlations between C-peptide level and both BMI and waist circumference. ***Conclusion***: T2DM is no longer a disease of adults but can also occur in children and adolescents. The results suggested that obesity, female gender and a positive family history of DM are risk factors for T2DM. Also, patients with T2DM had poorer glycaemic control and hypercholesterolemia than those with other types of diabetes.

Keywords: Diabetes Mellitus, Type 2; Child; Adolescent; C-Peptide; Body Mass Index; Hemoglobin A, Glycosylated; Cholesterol; Egypt.

Advances in Knowledge

- *In this study, obesity, female gender and a positive family history of diabetes mellitus were risk factors for type 2 diabetes mellitus (T2DM).*
- *Also, patients with T2DM had poorer glycaemic control and hypercholesterolemia.*

Application to Patient Care

- *Clinicians need alerting to the possibility of non-type 1 diabetes occurring in childhood, and especially to considering the possibility of T2DM.*
- *T2DM is often associated with risk factors for cardiovascular disease that may already be present at the time of diagnosis. Therefore, prevention and treatment strategies need to be initiated, for example obesity management programmes for obese children, especially those with family history of diabetes.*

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- *Because of the relatively recent recognition of T2DM in the paediatric age group, many children with new onset T2DM may be misclassified as having T1DM.*
- *Conversely, as average weight increases in the population, overweight adolescents with autoimmune diabetes may be misdiagnosed as having T2DM.*

Diabetes mellitus (DM) is a group of metabolic diseases characterised by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.[1] There are two major types of diabetes, type 1 DM (T1DM) where there is autoimmune destruction of the pancreas that renders it incapable of making insulin. In type 2 DM (T2DM), patients can still produce insulin, but either not in a sufficient amount to meet their needs, or their body has become resistant to its effects with a compensatory increase in insulin production and release that can also end in beta cell damage.[2] Non-insulin-dependent DM (T2DM) in children and adolescents is becoming an important public health concern throughout the world.[3] Although T2DM is widely diagnosed in adults, its frequency has markedly increased in the paediatric age group over the past two decades. Depending on the population studies, T2DM now represents 8–45% of all new cases of diabetes reported among children and adolescents.[4]

Therefore, this study aimed to estimate the frequency of T2DM among diabetic children and adolescents in Minia Governorate, Egypt, and to detect its risk factors in this community.

Methods

This study was carried out in the period from January 2010 to December 2010. It included 210 patients on regular follow-up in the diabetes outpatient's clinic at Minia University Children Hospital, Minia Governate, Egypt. The subjects were 124 (59%) females and 86 (41%) males. Their ages ranged from 1 to 18 years, with a mean age of 11.3 ± 4.4 years.

The cases were classified into 2 groups according to their fasting serum C-peptide levels. Group I (T1DM) included those with a fasting C-peptide level of <0.2 ng/ml, and Group II (T2DM) those with a fasting C-peptide level of 0.2 to ≥3.5 ng/ml.[3–5] Written consent was obtained for each subject after approval of the study by the ethical committee of the Minia University Medical Faculty. All patients included in this study underwent a thorough history-taking and a complete physical examination including anthropometric measurements. Laboratory investigations included testing fasting C-peptide levels by the enzyme-linked immunosorbent assay (ELISA) technique (normal paediatric range 0.2–3.5 ng/ml),[5] haemoglobin A1(HbA1),[6] lipid profile (triglycerides [TG] with normal level up to 150 mg/dl[7] and serum cholesterol level with normal level up to 220 mg/dl in paediatric patients).[8] Both of the latter were assayed by using a fully automated clinical chemistry auto-analyser system Konelab 20i (Thermo Fisher Scientific Inc., Waltham, Massachusetts, USA).

The data were coded and verified prior to data entry. The Statistical Package for the Social Sciences (SPSS), Version 13 for Windows (IBM Corp., Chicago, Illinois, USA) was used for data entry and analysis. Descriptive statistics were calculated for qualitative data using the Chi-square test. For quantitative data, the student's t-test (for two groups) was used. The Z test was used to compare proportions and correlations; *P* values of less than 0.05 were considered to indicate statistical significance.[9]

Results

This study aimed to estimate the frequency of T2DM among diabetic children and adolescents in Minia Governate. The frequency of T2DM (Group II) was found to be 13.3% (28/210) while T1DM (Group I) represented 86.7% (182/210) of the study population. Table 1 shows that Group II subjects were significantly older, had a longer disease duration, and a positive family history of DM compared to Group I where $P < 0.05$. Moreover, there were significantly more females than males with T2DM (64.3% *versus* 58.2%). On the other hand, there was a non-significant difference between them as regarding the age of onset of the disease. As to the clinical findings, there was a significant difference in body mass index (BMI) percentile between Group I and Group II patients

Table 1: Comparison of type 1 and type 2 diabetes mellitus (T1DM and T2DM) patients' demographic and clinical data

Characteristic	Group		*P* value
	Group I (T1DM) n = 182	Group II (T2DM) n = 28	
Age (years) mean ± SD	11.01 ± 4.4	14.14 ± 2.4	0.0001*
Age of onset of disease (years) mean ± SD	7.6 ± 3.8	10.2 ± 2.4	0.4
Duration of disease (months) mean ± SD	39.7 ± 40.7	71.3 ± 42.01	0.0001*
Gender, n (%)			
Male	76 (41.8)	10 (35.7)	0.04*
Female	106 (58.2)	18 (64.3)	
Family history of DM, n (%)			
Positive	86 (47.3)	20 (71.4)	0.01
Negative	96 (52.7)	8 (28.6)	
BMI percentile			
<5	28 (15.4)	0 (0)	
5–25	86 (47.3)	8 (28.6)	
>25–75	60 (33)	20 (71.4)	0.002*
85–95	6 (3.3)	0 (0)	
>95	2 (1.1)	0 (0)	
Mean waist circumference (cm)			
mean ± SD	64.4 ± 8.78	74.78 ± 5.83	0.0001*

*SD = standard deviation; DM = diabetes mellitus; * = significant.*

with most patients in Group II (71.4%) having a BMI of 25–75% *versus* 33% in Group I where *P* <0.05. Moreover, patients in Group II had a highly significant higher waist circumference than those in Group I. The laboratory investigations revealed that HbA1c % and cholesterol levels were significantly higher in Group II subjects compared to Group I where *P* <0.05. On the other hand, there was insignificant difference between the two groups as regards TG [Table 2].

Concerning the different correlations, this study found that there were weak positive significant correlations between C-peptide levels (ng/ml) and BMI on centile (r = 0.24, *P* value at 0.0001 was significant).

Discussion

The prevalence of T2DM varies among different child and adolescent populations; it was first described in Pima Indian adolescents of Arizona, USA, in 1979.[10] Among Japanese school children, the prevalence of type 2 diabetes has increased in 20 years, from 2 to 76 per 100,000 individuals.[11] It was subsequently reported among various minority non-Caucasian ethnic groups, for example in the USA, Canada, Australia, New Zealand and among children from Japan, Hong Kong, Libya and Bangladesh,[12] as well as in Asian and Arab children in the UK.[13]

Table 2: Comparison of laboratory parameters of Groups I and II

Laboratory investigation	Group		*P* value
	Group I Mean ± SD	Group II Mean ± SD	
Mean serum C-peptide (ng/ml)	0.13 ± 0.04	4.2 ± 3.3	0.04*
Mean HbA1c (%)	7.4 ± 1.4	9.1 ± 0.8	0.0001*
Mean cholesterol (mg/dl)	167.2 ± 36.7	186.8 ± 47.4	0.01*
Mean triglycerides (mg/dl)	125.1 ± 182.2	144.5 ± 54.1	0.5

** = significant; HbA1c = haemoglobin A1c.*

As regards the results of the present study, the frequency of T2DM was 13.3% while T1DM was represented in 86.7% of patients. This result was in approximate agreement with the result of another Egyptian study which was performed by Elsamahy *et al.*, who demonstrated that 88.2% of children and adolescents included in their study had T1DM and only 11.8% had T2DM.[14] Another study, performed by Moussa *et al.* in Kuwait, revealed that T2DM was present in 11.5% of all school children in Kuwait.[15] Contrary to our results, Dabelea *et al.*[16] found that the majority of diabetics among the Navajo youth had T2DM (80.4%) although autoimmune T1DM was present in 19.6% of the studied cases, especially among younger children. However, the current study found that the Group II T2DM subjects were significantly older than those in Group I with T1DM [Table 1]. This might be due to pubertal insulin resistance, attributed to increased growth hormone secretion during puberty and not to sex hormone secretion.[17] This result was in agreement with the result obtained from the two studies done by Elsamahy *et al.*[14] and Moussa *et al.*[15] Also, our result is in agreement with

that of the study performed by Fagot-Campagna *et al*.[18] who found that the peak age of presentation of T2DM was around 13–14 years; this corresponds to late puberty, with females reaching this stage one year earlier than males.

Further, a highly significant difference was found between Group I and Group II as regards gender distribution; 64.3% of Group II were females whereas 58.2 % were males ($P = 0.04$). This result is in agreement with the results obtained by Kitagawa *et al*.[11] and Kadiki *et al*.[19] who concluded that female children and adolescents were more susceptible to the risk of developing T2DM. In contrast to our result, Moussa *et al*.[15] found that the prevalence of T2DM was higher in males than females. Further, most of our patients with T2DM (71.4% *versus* 47.3% of those with T1DM) had a positive family history of DM with a significant difference between them. This result was in agreement with studies by Haines *et al*.,[20] Elsamahy *et al*.,[14] Moussa *et al*.[15] and Mayer-Davis *et al*.[21] This could be explained by the fact that the patients' familial predisposition could be related to impaired insulin action as pre-pubertal healthy children; those with a family history of T2DM had a nearly 25% lower *in vivo* insulin sensitivity compared to cross-matched children without a family history of T2DM.[22]

Concerning anthropometric measurements, it was found that most of the patients in Group II (71.4%) had a BMI of >25–75% *versus* 33% of Group I with a significant difference between them. This could be explained by the hypothesis which postulated that obesity mediated insulin resistance.[23] Moreover, the patients in Group II had a significantly higher waist circumference than those in Group I. This result was in agreement with the result obtained by Dabelea *et al*.[16] and could be explained by the fact that the amount of visceral fat is directly correlated with insulinemia and negatively with insulin sensitivity.[18]

Concerning the laboratory investigations, mean C-peptide levels were significantly higher among Group II compared to Group I. Moreover, Group II had significantly higher levels of HbA1c % and cholesterol than Group I. This could be explained by the fact that poor glycaemic control among those with T2DM contributes substantially to a high lipid profile.[24,25] This result was in agreement with the results obtained by Dabelea *et al*.[16] and Mayer-Davis *et al*.[21] As regards the different correlations, there was a weak positive significant correlation between C-peptide levels and BMI on centile; this could be explained by the fact that obesity mediated insulin resistance with a subsequently elevated C-peptide level.[23]

This study has the limitation that autoantibody screening was not performed which might have supported the diagnosis of T2DM. Diabetes autoantibody testing should be considered for all paediatric patients with the clinical dignosis of T2DM because of the islet cell autoimmunity in otherwise 'typical' T2DM. However, this study may provide a basis for further and wider studies in Egypt and elsewhere to detect and evaluate T2DM in children.

Conclusion

T2DM is no longer solely a disease of adults but can also occur in children and adolescents. This study suggested that children and adolescents at risk for T2DM and metabolic syndromes included those of female gender, with obesity and having a positive family history of DM. Also, patients with T2DM had poorer glycaemic control and hypercholesterolemia.

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