Factors Iinfluencing Onset and Metabolic Control in Children and adolescents with type 1 Diabetes Mellitus

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Abstract:
Background: Good glycemic control is crucial in preventing long - term diabetic complications.
Objective: To determine the effect of a number of host & environmental factors on the onset and glycemic control of type 1 diabetes mellitus (DM1).
Patients & methods: A total of 240 children and adolescents with type 1 diabetes mellitus (102 boys and 138 girls), their age range was 1.5 – 18 years, attending the Iraqi Diabetic Center / Al-Mustansiriya Medical College / Baghdad, were included in this cross – sectional study over a nine - month period, between 2nd of February and 3rd of November 2005.They had diabetes durations ranging from 3 months to 16.5 years.
Clinical data (age of onset, duration of diabetes, body mass index [BMI] which was measured and divided according to their percentiles into 6 levels [A-F] , insulin regimen, family history of diabetes, seasonality of clinical onset, consanguinity, sequence of birth) and HbA1c level were recorded.
Results: Patients presented no gender difference (P>0.05), and prepubertal group has accounted for the highest percentage (53.8%), but Poor glycemic control was highly significant in the pubertal group (HbA1c 9.61 $\pm$ 2.19 %) [P<0.01). The overall HbA1c was 9.18 $\pm$ 2.07 and the majority of BMI was located between group B($\geq$75%) and group E ($\geq$10%).
We found better metabolic control in patients with duration of diabetes below 2 years ($p < 0.05$). Insulin regimen and BMI did not significantly affect HbA1c concentrations (P >0.05).
Fifty two percent of the cases had a family history of diabetes & close consanguinity was present in (57.1%) of patients families.
Conclusion: glycemic control was affected by age, duration but not by sex, family history, or insulin regimen & the onset was peaked during Summer months with higher prevalence among children born first.

Keywords: type 1 diabetes mellitus, HbA1c, family history

Introduction:

Type 1A diabetes (DM1) result from immunologic damage to the insulin - producing B cells of pancreatic islets, the immunologic damage requires a genetic predisposition and is probably affected by environmental factors [1, 2, 3] .

There are two possible sources of bias in the assessment of family history of diabetes : 1- a person with diabetes may be more likely to report a diabetic relative, and 2- relatives of individuals with diabetes may be more likely to be tested for diabetes [4].

Geographical and temporal variation in the incidence suggest that environmental factors, such as infections, dietary components or toxins, could precipitate the disease in susceptible individuals [5, 6].

There is a clear seasonal variation in the diagnosis of diabetes [7, 8] , and children diagnosed during high incidence peaks more often have a preceding, perhaps precipitating, infection [7] .

Body mass index in childhood changes substantially with age[9, 10] .

Glycosylated hemoglobin (HbA1c) should be measured every 3 months. Normal values vary among laboratories but are usually below 6.2% [1] .

The desired ranges vary according to age. These ranges are as follow :

12 years or older, less than 7.8%, 5 - 11 years less than 8.5%, under 5 years 7.5 - 9%, higher levels are allowed in younger children to reduce the risk of hypoglycemia [1]. Following the American and British Associations for insulin-dependent diabetes mellitus (IDDM), used a classification of “good ", "moderate", or "poor" control of illness: (a) good control [HbA1c < or =7%] ; (b) moderate control [7% < HbA1c < or =8%]; and (c) poor control (HbA1c >8%] [11] .

Aim of The Study:

To determine the effect of a number of host & environmental factors on the onset and glycemic control of type 1 diabetes mellitus (DM1) in children and adolescents.

Patients &Methods:

A total of 240 children and adolescents with type 1 diabetes mellitus (102 boys and 138 girls), attending the Iraqi Diabetic Center / Al-Mustansiriya Medical College / Baghdad, were included in this cross – sectional study over a nine - month period, between 2nd of February and 3rd of November 2005.

In practice, the total cases were grouped according

to their age as prepubertal group- which was divided into two groups (age < 6years); & (age 6 - 12 years) and pubertal group (age > 12 years).

The patients were divided into two subgroups according to diabetes duration: < or = 2 years (n=127) and > 2 years (n=113), i.e., outside the honeymoon period.

Clinical data regarding age of onset, duration of diabetes [date of diagnosis from first insulin injection] [7], insulin regimen, family history of diabetes, seasonality of clinical onset, consanguinity, sequence of birth and HbA1c level were recorded and statistically analyzed .

Body mass index (BMI) was calculated as (weight per height^2) when weight was in kilograms and height was in meters [10] , and (BMI) was divided according to their percentiles into 6 levels [A-F, A(≥85%), B(≥75%), C(≥50%), D(≥25%), E(≥10%), F(<10%)].

Control (Standards) for BMI have been developed, age 1-19 years, on the bases of 1971-1974 National Health and Nutritional Examination Survey. In the United States, the 85th and 95th centiles of body mass index for age and sex based on nationally representative survey have been recommended as cut off points to identify overweight and obesity [10, 12] . BMI less than 10th percentile was considered underweight [13] .

In our study HbA1c was determined in human whole blood by the VARIANT^{TM} hemoglobin A1c program using ion - exchange high - performance liquid chromatography (HPLC) [non- diabetic level <6%] [14]

,While in DM1 we had depend on the following, good control [HbA1c < or =7%] ; moderate control [7% < HbA1c < or =8%]; and poor control (HbA1c >8%].

All results were expressed in numbers and percentages, the statistical analysis was done using t-test and Chi-square and P-value <0.05 was considered as significant and below 0.01was considered highly significant.

Results:

Among the total number of (240) children and adolescents with type 1 diabetes mellitus (DM1), (102 boys [42.5%] and 138 girls [57.5%]), The total cases were grouped according to their age as prepubertal group- (53.8%), which was divided into two groups (age < 6years[12.5%]); & (age 6 - 12 years [41.3%]) and pubertal group (age > 12 years [46.3%]).

Table (1) shows that the duration of diabetes was ranging from 3 months to 16.5 years (3.5 ± 3.7), their age range was 1.5 – 18 years (11.3±4.2 years), the age of onset was 6 months – 17years (7.8 ± 4.0), the overall HbA1c was 9.18 ± 2.07 and BMI was (18.05 ± 3.68).

Increased (HbA1c) was highly significant in patients >12years compared with those under 12 years [<6 years & 6-12 years] (HbA1c 9.61 ± 2.19 % vs. 9.00 ± 1.81% and 8.75 ± 1.92% respectively p< 0.01). But according to the sex difference there was no variation (P>0.05) as shown in table (2).

Table 1: the age, age of onset, BMI, HbA1c, duration of diabetes in the study sample.

characteristics	Mean+SD (Range) Median
Age (years)	11.3±4.2 1.5-18.0 12.0
Age of onset (years)	7.8±4.0 0.5-17.0 8.0
BMI (kg/m^2)	18.05±3.68 8.86-33.91 17.36
HbA1C (%)	9.18±2.07 5.40-15.90 8.90
Duration (years)	3.50±3.70 3m-16.50 2.00

Table 2: the correlation between the age, sex and HbA1c in the study groups.

characteristics	(<6)	(6-12)	(>12)	P value
Sex female	17 (56.7%)	57 (57.6%)	64 (57.7%)	0.995
Male	13 (43.3%)	42 (42.4%)	47 (42.3%)	
HbA1c	9.00±1.81 (5.4-12.2)	8.75±1.92 (5.8-15.9)	9.61±2.19 (5.7-15.7)	0.009*

* Highly significant

In addition, we found discrepancy of metabolic control in patients with duration of diabetes below 2 years and those above 2 in children and adolescents (HbA1c ≤ 2years :8.91± 2.07 % vs. > 2years : 9.49 ± 2.04 % ($p < 0.05$).

According to the sex difference there were no significant variation in mean age, age of onset, BMI, HbA1c and duration of diabetes ($P>0.05$) as shown in table (3).

Table (4) shows that (52.1%) of patients had a family history of diabetes (7.9% for DM1, 35.4% for DM2 and 8.8% for those with DM1 & DM2) while (47.9%) had no family history, also shows that close consanguinity was present in (57.1%) of patients families. For seasonal variation, peaking was found during Summer months (47.9%), while (42.1%) during Winter and a higher incidence of onset among children born first (29.2%), while (22.1%) and (20%) for the second and third born children respectively.

Table 3: the distribution of age, age of onset, BMI, HbA1c, duration according to sex.

Characteristics	Females	Males	P value
	Mean±SD (Range) Median	Mean±SD (Range) Median	
Age (years)	11.4±4.2 (1.7-18.0) 11.5	11.3±4.2 (1.5-18.0) 12.0	0.907
Age of onset (years)	8.1±4.1 (0.5-17.0) 8.0	7.5±3.9 (.5-16.0) 7.0	0.296
BMI (kg/m^2)	18.29±3.96 (10.36-33.91) 17.15	17.73±3.24 (8.86-32.79) 17.39	0.242
HbA1C (%)	9.13±2.24 (5.40-15.90) 8.90	9.25±1.83 (5.80-13.80) 8.90	0.666
Duration (years)	3.29±3.53 (3m-16.50) 2.00	3.78±3.92 (3m-14.00) 2.00	0.315

Table 4: the distribution of family history, consanguinity, seasonality, sequence of birth in the study group.

Factors		No	%
Family History of DM	Yes	125	52.1
	DM1	19	7.9
	DM2	85	35.4
	DM1&DM2	21	8.8
	No	115	47.9
Consanguinity	Yes	137	57.1
	No	103	42.9
Season	Summer	115	47.9
	Winter	101	42.1
	Autumn	12	5.0
	Spring	12	5.0
Birth order	1^{st}	70	29.2
	2^{nd}	53	22.1
	3^{rd}	48	20.0
	4^{th}	22	9.2
	5^{th}	21	8.8
	6^{th}	11	4.6
	7^{th}–11^{th}	15	6.3

Table (5) shows that the onset of DM1 was peaking during summer months in all groups (46.7%, 48.5%, 54.1% for group <6, 6-12 and >12 respectively), also there was no gender variation in the seasonality of clinical onset (both males and females had peaking onset during Summer months, 48.6% for females and 47.1% for males).

Regarding metabolic control (HbA1c) was not affected weather there was positive family history of diabetes or not , also the age of onset, BMI, duration of diabetes and consanguinity were not influenced by family history of diabetes (P>0.05) as shown in table (6).

Table 5: the distribution of seasonality of clinical onset according to age and sex.

	Summer		Winter		Autumn		spring		P value
	No	%	No	%	No	%	No	%	
Age groups <6	14	46.7	12	40.0	2	6.7	2	6.7	0.328
6-12	48	48.5	41	41.4	7	7.1	3	3.0	
>12	60	54.1	41	36.9	3	2.7	7	6.3	
Sex Female	67	48.6	59	42.8	4	2.9	8	5.8	0.342
Male	48	47.1	42	41.2	8	7.8	4	3.9	

Table 6: the correlation of age of onset, BMI, HbA1c, consanguinity and duration with the family history.

Characteristics	Family history of DM		P value
	Yes	No	
	Mean±SD (Range)	Mean±SD (Range)	
Age of Onset (years)	7.46±3.96 (0.50-17.00)	8.25±4.09 (1.00-17.00)	0.131
BMI (kg/m^2)	17.92±3.89 (8.86-33.91)	18.21±3.44 (10.36-32.79)	0.543
HBA1C (%)	9.25±2.13 (5.70-15.90)	9.10±2.01 (5.40-14.40)	0.561
Duration (years)	3.70±3.71 (0.25-16.50)	3.37±3.61 (0.25-14.00)	0.487
Consanguinity Yes	59 (47.2%)	44 (38.3%)	0.162
No	66 (52.8%)	71 (61.7%)	

Table (7) shows, (65.4%) of patients were treated with two daily insulin injections of an individualized mixture of rapid- and intermediate - acting insulin, (12.9%) were treated with three daily injections, while the remaining both (10.8%) of patients were treated with either one or four daily injections, HbA1c concentrations were not significantly affected by insulin regimen (number of insulin injections), they were 9.1%, 8.69%, 10.2%, and 9.18% for those who received one injection/ day, 2/day, 3/day and 4 injections/day respectively (p > 0.05).

The majority of BMI percentiles were located between group B (≥75%) and group E (≥10%), while group F (<10%) was accounted for only (17.9%) and group A (≥85%) was accounted for (14.2%) as shown in table (8).

The HbA1c did not significantly affected by BMI percentiles their concentrations were 9.17±2.08%, 9.09±1.96% and 9.27±2.14% for overweight "A (≥85-)" , normal "B--E (<85-10)" and underweight "F (<10-)" groups respectively (P>0.05).

Table 7: the correlation between HbA1c and insulin regimen.

Insulin injections	No	%	HbA1C Mean± SD (Range)
1.00/day	26	10.8	9.10±2.91 (7.70-13.70)
2.00/day	157	65.4	8.69±3.19 (5.40-14.00)
3.00/day	31	12.9	10.20±3.296 (8.20-15.90)
4.00/day	26	10.8	9.18±2.94 (7.60-14.30)
Total	240	100	9.18±2.07 (5.40-15.90)

P=0.109

Table 8: the distribution of BMI percentiles in the study sample.

BMI percentile groups	No	%
A (≥85--)	34	14.2
B (≥75)	28	11.7
C (≥50)	56	23.3
D (≥25)	42	17.5
E (≥10)	37	15.4
F (<10--)	43	17.9

Discussion:

Results showed that DM1 in a group of 240 patients presented no gender preference and that the mean age, age of onset, duration, BMI and HbA1c similar in both genders, a finding is in agreement with others [14, 15, 16].

In our study, the overall BMI reflected good metabolic control, while HbA1c had a mean value of 9.18%, suggesting poor glycemic control these findings were similar to that reported by Zalloua,-P-A, et al.[16], also we found that glycemic control was worse in the pubertal group compared to the prepubertal groups, which is similar to that adopted by Fluck CE, et al., Scottish study group, Laffel LMB, et al., and Nordly,-S, et al.[15, 17, 18, 19] But in contrast to that reported by Dorchy H, et al., they found that HbA1c was not related to age, i.e., it was not poorer at adolescents [14]. In addition, we found better metabolic control in patients with duration of diabetes below 2 years in children and adolescents, a finding is similar to other studies [5, 14].

As well, sex, family history and insulin regimen did not influence Glycemic control as noted by others [14, 15, 19], in contrast to Scottish study group, who reported that HbA1c concentrations were significantly worse in those using 2 insulin injections per day, and in those with positive family history of diabetes [17].

In this study, (52%) of the cases had a family history of diabetes, this figure was higher than that reported by Frank DeStefans, et al., and Hagura R, et al.They found that only 21% and 16-33% of cases had a family history respectively [2, 20].

Furthermore, consanguinity was frequent in our patients families (57.1%) which was not different from those reported in the literature[16].

Also these findings were similar to that reported by Mengesha B, et al., they found that the overall findings of their study indicated that heredity has an important role in the genesis of DM in the Ethiopian diabetics [21].

We found that DM1 showed a higher prevalence

of onset among first born children and a decreased incidence as birth order increased, which was similar to that adopted by Zalloua,-P-A, et al. [16]. But in contrast to that reported by Rami B, et al., they found that children with diabetes were more likely to be second - or third - born children [22].

Finally, onset of DM1 showed seasonal variation, peaking during Summer months, which was in contrast to that reported by Zalloua,-P-A, et al., they found that peaking was during Winter months [16]. The seasonality of clinical onset was similar regardless the age and sex, which was differ from that adopted by Roche,-E-F, et al., they noted that females showed no seasonal difference in month of clinical onset, while this difference was observe only in males , they assume that females seems to be less susceptible than males to the environmental infections influences [23].

Conclusion and recommendation:

The glycemic control was worse in pubertal age group, and among those who had duration of diabetes longer than 2 years.

Sex, family history of diabetes and insulin regimen did not influence Glycemic control.

Also consanguinity and family history of diabetes were frequent among DM1 patient's families and the onset was peaked during summer months with higher prevalence among children born first.

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