Original Research Article **Pediatrics**

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

ROLE OF HA1C IN EARLY DETECTIONS OF PREDIABETIC CHILDREN

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ABSTRACT

Diabetes mellitus is a chronic metabolic disease as a result of defect in secretion of insulin or defect in insulin action despite of normal secretion or defect in both secretion and action , diabetes mellitus associated with hyperglycemia and high blood glucose levels , type 1 diabetes mellitus result from mainly immune mediatedor non-immune mediated due to chronic pancreatitis with destruction of β cells of pancreas responsible for its productions , glycosylated hemoglobin is an index of long period of diabetes without control or delayed discover of patients, the diabetic patients need continues care and educated fore self-managements. An early detection of diabetes mellitus among high-risk groups (relative to diabetic children and obese children) by HA1c. Prediabetic occurs because of the interaction between genetic and environmental factors. Our study was performed over 80 children following the Endocrine clinic of the Pediatric Department, of Zagazig general and Healthy Insurance Hospitals in Sharika Egypt, group 1 were 60 children of elevated risk for diabetes (relatives to diabetic children as siblings) 28 males and 32 females their age from 2y to 18y and another group 2 which were 20 children with obesity 8 males and 12 females their age from 3y to 18y, they underwent to full history, clinical examination, detailed measurements (anthropometric), full investigations with estimation of glycosylated hemoglobin (HbA1c) and genetic counseling of the family. As shown of glycosylated hemoglobin no significantly difference were found among our groups of study, at the start of study HA1c Normal range (**<5.7**) found in 57 (95%) in group 1 and in 16 (80%) in group 2, Prediabetic range (5.7-6.4) at the start were 2 siblings (3.3%) in group 1 and 2 obese children (10%) then also non-significant after 3 months follow up HA1c% were Prediabetic range (5.7-6.4) after 3 months were (1.7%) in 1 patient of group 1 and were (5%) in 1 obese patient of group 2 and Prediabetic range (5.7-6.4) after 6 months returned normal in group 1 and I obese female (5%) in group 2, The HbA1c test is an early detector of diabetes mellitus among high-risk groups. Prediabetes occurs because of the interaction between genetic and environmental factors. Controlling the environmental factors by proper family counseling can delay and even inhibit the emergence of diabetes.

KEYWORDS: *Diabetes mellitus, family counseling, HbA1c, obesity, high-risk Prediabetic.*

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Received on: 21-09-2017
Revised and Accepted on: 27-10-2017
DOI: http://dx.doi.org/10.22376/ijpbs.2017.8.4.b526-531

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease as a result of defect in secretion of insulin or defect in insulin action despite of normal secretion or defect in both secretion and action , diabetes mellitus associated with hyperglycemia and high blood glucose levels , type 1 diabetes mellitus result from mainly immune mediated or non-immune mediated due to chronic pancreatitis with destruction of β cells of pancreas responsible for its productions , glycosylated hemoglobin is an index of long period of diabetes without control or delayed discover of patients, the diabetic patients need continues care and educated foe self-managements[1]. Diabetes mellitus especially Type 1 which is most common metabolic endocrinal diseases affecting children with high effect on physical and emotional statues for a child development. Majority of patients more than (92%) of type 1 D.M. are the result of multifactorial causes[1, 2].The use overweight child instead of obese child is good term. Obesity is defined as excessive increasing body fat the child health and interfereswith child activities, it is difficult to estimate direct the body fat, but we can depend on body mass index to diagnose obesity which became more prevalent with its hazards on children and population[1]. Obesity of childhood affects all organs of the body leading to serious complications and effects in the form of hypertension, dyslipidemia, resistance to insulin and finally diabetes mellitus. patients with diabetes of type 2 mainly due to insulin resistance and deficiency[2,3] , obesity and its effect of insulin deficiency and resistance leads to inflammation of β cells of pancreas with its destruction of them [4]. The presence of antibodies against antigen of islet cells preceding the onset of appearance of diabetes clinically in cases of Prediabetic patients by several months, they should be informed about the increasing risk of consequences and serious effects of diabetes mellites[5]. The cases with normal level of HbA1c indicate normal and controlled blood glucose, that cases with normal level of HbA1c indicate normal and controlled blood glucose.on exposure of hemoglobin to high plasma glucose non-enzymatic pathway glycation glycosylated hemoglobin HA1c is formed [6]. On exposure of hemoglobin to high plasma glucose non enzymatic pathway glycation glycosylated hemoglobin HA1cis formed[6], that cases with normal level of HbA1c indicate normal and controlled blood glucose, the best diagnostic marker for high risk children is HbA1c which reflect normal and controlled blood glucose last 3 months[7].

Patients and methods

Our study was performed over 80 children following the Endocrine clinic of the Pediatric Department in Zagazig general and Healthy Insurance Hospitals in Sharika Egypt, group 1 were 60 children of elevated risk for diabetes (relatives to diabetic children as siblings) 28 males and 32 females their age from 2y to 18y and another group 2 which were 20 children with obesity 8 males and 12 females their age from 3y to 18y, they underwent to full history, detailed clinical examination, detailed measurements (anthropometric), full investigations with estimation of glycosylated hemoglobin (HbA1c) and genetic counseling of the family**.** Informed consent was obtained from the children's parents or caregivers; the study was approved by the ethical committee of the faculty of medicine Zagazig University and the hospital's director

STATISTICAL ANALYSIS

Data was expressed as mean ± standard deviation (X ± SD) or percentage (%). The means of two groups were compared using student "t"-test. Data were carried out with the Statistical Package for Social Sciences (SPSS), version 10 software. P-value less than 0.05 were considered statistically significant for all comparison.

RESULTS

As shown of glycosylated hemoglobin no significantly difference were found among our groups of study, at the start of study HA1c Normal range (**<5.7**) found in 57 (95%) in group 1 and in 16 (80%) in group 2, Prediabetic range (5.7-6.4) at the start were 2 siblings (3.3%) in group 1 and 2 obese children (10%) then also non-significant after 3 months follow up HA1c% were Prediabetic range (5.7-6.4) after 3 months were (1.7%) in 1 patient of group 1 and were (5%) in 1 obese patient of group 2 and Prediabetic range (5.7-6.4) after 6 months returned normal in group 1 and I obese female (5%) in group 2. Majority of patients more than (92%) of type 1 D.M and less than 8% of children with type 2 DM

Table1
Studied patients All sharing children

Examinations	group 1	n.1 %	group 2	n.2 %	Total no.	%
Number of patients	60	75.0%	20	25%	80	100%
Gynoid obesity	17	28.3%	12	60%	29	36.25%
Android obesity	04	06.7%	08	40%	12	15.00%
Bronchial asthma	06	10.0%	03	15%	09	11.20%
hepatomegaly	09	15.0%	05	25%	14	17.50%
hypertension	00	00.0%	03	15%	03	03.70%
Acanthosis nigricans	00	00.0%	01	05%	01	01.25%
Striae	04	06.6%	08	40%	12	15.00%
hypothyroidism	15	25.0%	00	00%	15	18.75%

- -Our study recorded 41 (51.25%) children were obese out of them 29 (36.25%) were of gynoid pattern and 12 (15%) of them were of android pattern, 28.3% (17) of gynoid pattern and 6.7% (4) of android pattern among relatives to diabetics group and (12) 60% gynoid pattern and (8) 40% of android pattern among obese group
- -Chronic bronchial asthma found in 6 (10%) of relatives to diabetic patients group 1 and in 3 (40%) of obese children group 2.
- -Hepatic enlargement found in 9 (15%) of relatives to diabetic patients group 1 and in 5 (25%) of obese children group 2.
- -Hypertensions were found in 3 (15%) of obese children group 2.
- -Acanthosis nigricans found only in one patient (5%) of obese children group 2.
- -Striae were found in 4 (6.6%) of relatives to diabetic patients group 1 and 8 (40%) of obese children group 2.
- -Hypothyroidism were found 15 (25%) of relatives to diabetic patients group 1.

Table 2
Family history of studied patients

Family history of same disease		Group 1 60	N.1 % 100%	Group 2 20	N.2% 100%	ẍ	*P* value
Positive First degree	Sibling	60	100%	0	00		
	Father	05	8.3%	3	15%	0.42	0.54 NS
	mother	10	16.7%	1	5%		
Second degree		16	26.7%	7	35%		
Third degree		14	23.3%	4	20%		
Negative		00	00	7	35%		

The first-degree family history in group 1 (relatives to diabetic patients) was 8.3%paternal and was (16.7%) maternal but in group 2 (obese children) was (15%) paternal and (5%) maternal history.

Table 3
Glycosylated hemoglobin

HA1c (%)	Group 1	%	Group 2	%	Fisher exact test	*P* value
Normal range (**<5.7**) at the start	57	95	16	80	1.79	0.18 NS
Prediabetic (5.7-6.4) at the start	02	3.3	02	10	1.46	0.23 NS
Prediabetic (5.7-6.4) after 3 mo	01	1.7	01	05	1.06	0.29 NS
Prediabetic (5.7-6.4) after 6 mo	00	00	01	05	0.42	0.52 NS

**** (HA1c :glycosylated hemoglobin)***

As shown of glycosylated hemoglobin no significantly difference were found among our groups of study, at the start of study HA1cNormal range (<5.7) found in 57 (95%) in group 1 and in 16 (80%) in group 2, Prediabetic range (5.7-6.4) at the start were 2 siblings (3.3%) in group 1 and 2 obese children (10%) then also non-significant after 3 months follow up HA1c% were Prediabetic range (5.7-6.4) after 3 months were (1.7%) in 1 patient of group 1 and were (5%) in 1 obese patient of group 2 and Prediabetic range (5.7-6.4) after 6 months returned normal in group 1 and I obese female (5%) in group 2.

Table 4
Anthropometric measurements of both groups

Anthropometric measurements		group 1	group 2	*t'*-test	*P* value
Weight (Kg)	Range	5 - 80	18 – 66	*U = 2.82*	0.005 HS
	Mean±SD	35.12 ± 18.79	50.44 ± 14.92		
Height (cm)	Range	50 – 170	85 – 156	0.36	0.71
	Mean±SD	129.45 ± 27.74	130.94 ± 20.14		
Sitting Height Circumference.	Range	54 – 99	50 – 88	2.55	0.01 S
	Mean±SD	80.10 ± 11.42	70.76 ± 14.26		
Span (cm)	Range	54 – 162	90 – 152	0.28	0.81
	Mean±SD	130.12 ± 17.11	129.42 ± 19.98		
Head Circumference.	Range	36 – 59	52 – 59	3.40	< 0.001 HS
	Mean±SD	53.30± 4.90	56.20 ± 1.89		
Hip Circumference.	Range	32 – 80	50 – 86	2.10	0.04 S
	Mean±SD	65.93 ± 8.92	72.14 ± 10.60		
Waist	Range	36 – 74	52 – 80	1.10	0.29

Circumference	Mean±SD	60.08 ± 11.92	63.93 ± 07.39		
Waist-Hip Ratio	Range Mean±SD	0.72 – 0.98 0.88 ± 0.10	0.74 – 1.12 0.90 ± 0.10	0.45	0.66
Body Mass Index	Range Mean±SD	10.06 – 27.96 18.24 ± 4.66	19.82 – 32.32 27.16 ± 3.64	6.64	< 0.001 HS

Highly significant difference found in our study anthropometric measurements between relatives of diabetic patients (35.12 ± 18.79) and obese children (50.44 ± 14.92) *P* value = (0.005),also the head circumference showed highly significant difference between group 1 was(53.30± 4.90) and was (56.20 ± 1.89) in group 2 *P* value =(< 0.001), with significantly difference of hip measurements which was (65.93 ± 8.92) in group 1 and was (72.14 ± 10.60) in group 1 with *P* value= (0.04), with significantly difference of sitting height measurements which was (80.10 ± 11.42) in group 1 and was (70.76 ± 14.26) *P* value =(0.01) and body mass index BMI showed highly significant difference which was (18.24 ± 4.66) in group 1 and was (27.16 ± 3.64) *P* value =(< 0.001),but no significant in the other measurements.

Table 5
Prediabetic cases

All studied patients (80)		Relatives of diabetic patients (3/60)			Obese group (3/20)		
Personal history	Age (year)	9	12	11	9	11	12
	Sex	Female	Male	Female	Male	Female	Female
	Residence	Urban	Rural	Urban	Urban	Rural	Urban
	B. N.	1st	1st	1st	6th	4th	5th
Family history	Consanguinity	Negative	Negative	Negative	Positive	Positive	Positive
	Same disease	Negative	Negative	Negative	Negative	Negative	Positive
	A.D.	Negative	Negative	Moth.SLE	Negative	Negative	Negative
Cardio-vascular	Blood pressure	Normal	Normal	Normal	Normal	hypertnsion	Normal
Chronic respiratory diseases		Bronchial asthma	Bronchial asthma	Bronchial asthma	Negative	Bronchial asthma	Bronchial asthma
Genital examination Tannerscore	Male genitalia	-	Tanner111	-	Tanner111	-	-
	Breast	Tanner1	-	Tanner1111	-	Tanner111	Tanner1
	Pubic hair	Tanner111	Tanner111	Tanner111	Tanner111	Tanner111	Tanner11
Anthro-pometric measure-ments	Weight kg	38	39	39	56	62	49
	Height C.	138	147	152	149	142	139
	Head circ.cm	53	51	54	56	58	55
	Waist circ.cm	52	53	52	68	80	72
	Hip circ.cm	62	59	62	76	78	80
	BMI	20 (75^{th})	18.1(5^{th})	16.9(5^{th})	25 (>95th)	30.8(>95th)	25.4(>95th)
	Span cm	126	124	122	138	136	138
Acanthosis nigricans		Negative	Negative	Negative	Negative	Positive	Positive
Laboratory investigation	Hemoglobin	Normal	Anemia	Anemia	Anemia	Normal	Normal
	HA1c% at start	6.2	6.4	6.2	6.3	5.9	6.3
	HA1c% after 3 m	5.6	6.0	6.3	5.9	6.1	5.8
	HA1c% after 6 m	5.4	5.8	6.2	6.2	6.4	5.6

**** B.N.：Birth number, *A D：Autoimmune diseases, *H.C.：Height Circumference, *BMI：Body Mass Index***

- Chronic bronchial asthma found in 6 (10%) of relatives to diabetic patients group 1 and in 3 (40%) of obese children group 2.
- Hypertensions were found in 3 (15%) of obese children group 2.
- Acanthosis nigricans found only in one patient (5%) of obese children group 2.
- The first-degree family history in group 1 (relatives to diabetic patients) was 8.3%paternal and was (16.7%) maternal but in group 2 (obese children) was (15%) paternal and (5%) maternal history.
- Highly significant difference found in our study anthropometric measurements between relatives of diabetic patients (35.12 ± 18.79) and obese children (50.44 ± 14.92) *P* value = (0.005),also the head circumference showed highly significant difference between group 1 was(53.30± 4.90) and was (56.20 ± 1.89) in group 2 *P* value =(< 0.001), with significantly difference of hip measurements which was (65.93 ± 8.92) in group 1 and was (72.14 ± 10.60) in group 1 with *P* value= (0.04), with significantly difference of sitting height measurements which was (80.10 ± 11.42) in group 1 and was (70.76 ± 14.26) *P* value =(0.01) and body mass index BMI showed highly significant difference which was (18.24 ± 4.66) in group 1 and was (27.16 ± 3.64) *P* value =(< 0.001),but no significant in the other measurements.
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DISCUSSION

Diabetes mellitus is a chronic metabolic disease as a result of defect in secretion of insulin or defect in insulin action despite of normal secretion or defect in both secretion and action , diabetes mellitus associated with hyperglycemia and high blood glucose levels , type 1 diabetes mellitus result from mainly immune mediated or non-immune mediated due to chronic pancreatitis with destruction of β cells of pancreas responsible for its productions , glycosylated hemoglobin is an index of long period of diabetes without control or delayed discover of patients, the diabetic patients need continues care and educated foe self-managements[1]. Diabetes mellitus especially Type 1 which is most common metabolic endocrinal diseases affecting children with high effect on physical and emotional statues for a child development. Majority of patients more than (92%) of type 1 D.M. are the result of multifactorial causes as revealed by Wyaatt DT, et.al[1]. Husilam D. [2] prefers to use overweight child instead of obese child. Obesity is defined as excessive increasing body fat the child health and interfereswith child activities, it is difficult to estimate direct the body fat, but we can depend on body mass index to diagnose obesity which became more prevalent with its hazards on children and population that revealed with Wyaatt DT, et.al[1].The obese children are liable to be diabetic either type 1 or type 2 DM but not the diabetic children liable to be obese. Taubees G.[3] Revealed that obesity of childhood affect all organs of the body leading to serious complications and effects in the form of hypertension, dyslipidemia, resistance to insulin and finally diabetes mellitus. Patients with diabetes of type 2 mainly due to insulin resistance and deficiency as recorded by Husilam D. [(2)], obesity and its effect of insulin deficiency and resistance leads to inflammation of β cells of pancreas with its destruction of them Chiarelly F, et.al [4]. Marrae M, et.al [1] they revealed that presence of antibodies against antigen of islet cells preceding the onset of appearance of diabetes clinically in cases of prediabetic patients by several months, they should be informed about the increasing risk of consequences and serious effects of diabetes mellites. Carrouli MD,et.al [6] they denote that cases with normal level of HbA1c indicate normal and controlled blood glucose, that cases with normal level of HbA1c indicate normal and controlled blood glucose.On exposure of hemoglobin to high plasma glucose non-enzymatic pathway glycation glycosylated hemoglobin HA1c is formed Our study recorded 41 (51.25%) children were obese out of them 29 (36.25%) were of gynoid pattern and 12 (15%) of them were of android pattern, 28.3% (17) of gynoid pattern and 6.7% (4) of android pattern among relatives to diabetics group and (12) 60% gynoid pattern and (8) 40% of android pattern among obese group. Aveazum A, et.al[8] stated that there is a good relation between diabetes and android obesity with liver accumulation of fat and enlargement. In our study chronic bronchial asthma found in 6 (10%) of relatives to diabetic patients group 1 and in 3 (40%) of obese children group 2, that agree with results of Airiaghi **L.** [9] who demonstrated that there is a good relation between diabetes mellitus type1 and bronchial asthma[9]. In our study hepatic enlargement found in 9 (15%) of relatives to diabetic patients group 1 and in 5 (25%) of obese children group 2, that agree with results by Das MD, et.al [10]. Hypertensions were found in 3 (15%) of obese children group 2 that coincide with results by Zhoeu YF,et.a [11] whom revealed that hypertension was highly increased with obesity [11]. In our study Acanthosis nigricans found only in one patients (5%) of obese children group 2 that agree with results by Akciay A,et.al[(12)], they recorded that the most important predictors of resistance to insulin Acanthosis nigricans,that found high insulin level in obese children with Acanthosis nigricans[12]. In our study hypothyroidism were found in 15 (25%) of relatives to diabetic patients group 1 that agree with results recorded by Wuy p. [13]. Our study revealed that 100% positive family history recorded among group 1 which is same as results taken by Clearey A,et.al [14], and (55%) of obese children from group2 had positive family history same as that documented by Keally T, et.al[15]. Highly significant difference found in our study anthropometric measurements between relatives of diabetic patients (35.12 ± 18.79) and obese children (50.44 ± 14.92) *P* value = (0.005), also the head circumference showed highly significant difference between group 1 was(53.30± 4.90) and was (56.20 ± 1.89) in group 2 *P* value =(< 0.001), with significantly difference of hip measurements which was (65.93 ± 8.92) in group 1 and was (72.14 ± 10.60) in group 1 with *P* value= (0.04), with significantly difference of sitting height measurements which was (80.10 ± 11.42) in group 1 and was (70.76 ± 14.26) *P* value =(0.01) and body mass index BMI showed highly significant difference which was (18.24 ± 4.66) in group 1 and was (27.16 ± 3.64) *P* value =(< 0.001),but no significant in the other measurements as results taken by Chiavarolli V, et.al [16], Allired EN,et.al[17] and Chiarelly F, et.al [4]. Not agree with our study results.

Recommendations

The occurance of prediabetic mainly due to the effect of genetic and environmental factors which must be controlled by early investigation test via HbA1c and family counseling The HbA1c test is an early detector of diabetes mellitus among high-risk groups. Prediabetic occurs because of the interaction between genetic and environmental factors. Controlling the environmental factors by proper family counseling can delay and even inhibit the emergence of diabetes.The family and community should advice to prevent overweight and obesity during childhood period and their lifestyle (suitable useful diets, daily exercise and change their behavior), also the Prediabetic children should do family counseling as it is very important for their managements as recommended by MsFarlane S et.al [18].

CONCLUSIONS

The family and community should advice to prevent overweight and obesity during childhood period and their lifestyle (suitable useful diets, daily exercise and change their behavior), also the Prediabetic children should do family counseling as it is very important for their managements.

CONFLICT OF INTEREST

Conflict of interest declared none.

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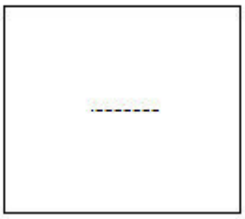

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We sincerely thank the above reviewers for peer reviewing the manuscript