Metabolic Control and Growth of Diabetic Children Diagnosed to be Celiac Disease and under Gluten Free Diet

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Abstract:

Back ground: Since untreated celiac disease may be associated with long-term health risk, so screening and early treatment seem to be justified.

Objectives: To find out the benefit of screening and treatment of celiac disease in diabetic children.

Patients & methods: Three hundred and fifty unselected diabetic children were screened for celiac disease by rapid immuno-chromographic assay for IgA antibodies to tissue transglutaminase and IgA, IgG antibodies to antigliadin, and those who had positive results on both tests or to positive tissue Transglutaminase antibodies.Duodenal biopsies were done through endoscope of the duodenum.Blood samples were taken for HbA1c level at diagnosis and during treatment with.gluten free diet (GFD) Height and weight were measured at diagnosis and after one year of treatment with gluten free diet (GFD),and assesed by the number of the SD below the mean on the growth centile chart of Tanner and Whitehouse.

Results: Thirty-eight out of 350 (10.9%) diabetic children had +ve tissue transglutaminase (tTG) antibodies and 36 out of 350(10.3%) diabetic children their histopathology suggests celiac disease.

There was no significant difference between the means of standard deviation below the mean for height and weight at diagnosis and after one year of treatment with GFD, so as no significant difference between the HbA1c at diagnosis and during treatment with GFD.

Conclusion: The short term observation follow up data to patients with type 1 DM diagnosed to have celiac disease and after one year of treatment with GFD did not demonstrate a positive influence on the growth and metabolic control of diabetes.

Key words : diabetes mellitus type 1,celiac disease,screening, tissue transglutaminase antibodies.

Introduction:-

In screening studies for ceilac disease (CD), IgA antibodies to endomysium on tissue transglutaminase have been found in 1-6.4% of unselected patients with type 1 DM [1,2,3,4,5,6,7], this is 2-10 times higher than in normal population [8], The occurrence of both diseases may be explained by similar genetic background associated with HLA Q2 or 8 and similar trigger mechanism for autoimmune process, more than 90% of CD patients and about 60-70% of diabetes carry the HLA heterodimer DQA1 O501- DQB10201 [8,9].

Although it is well established that patients with untreated CD that is clinically diagnosed cases may develop complications like lymphoma [10] and autoimmune disease [11], their development depends on time of exposure to gluten [12], but the natural history of silent CD is currently unclear [9] and controversy exist as to whether there is a need for screening of diabetic patients to detected silent CD and whether there is a beneficial role for GFD in those asymptomatic patients, GFD represents an additional burden on patients with type 1 DM, for it is not palatable and more expensive[9].

The aim of this study is to have a short observational follow up data on patients with silent CD and type 1 DM.

Patients & methods: -

A prospective study was done on 40 patients with type 1 DM and silent CD which were diagnosed by +ve tissue transglutaminase antibodies (+tTG) and + ve duodenal biopsy, the patients were followed at National Diabetic Center of Al-Mustasiryia University for the period between 1st June 2001- 1st June 2002.

Collecting data including age, sex, duration of the disease, presence of one or more of gastrointestinal manifestations, loss of appetite, dyspepsia, flatulence, abdominal distention, abdominal pain, chronic diarrhea, constipation, presence of hypoglycemia manifestations, and of severe hypoglycemia, like seizures, coma, presence of hyperglycemia and ketoacidosis.

The Height and Weight were assessed by standard percentile chart for height and weight for sex of Tanner and whitehouse at diagnosis of celiac disease and under treatment with GFD,and interpretated by the number of the SD below the mean . The HbA1c was measured at diagnosis and under treatment with GFD. The control of HbA1c of National diabetes Center (NDC) 6-6.5 % .
Value $\leq$ 0.05 was considered as significant.

Results: -

On screening 350 unselected diabetic children and adolescents, fourty diabetic children found to have silent celiac disease, table (1) shows 38/40(95%) were +ve for tTG antibodies and 34/40 (85%) were +ve for antigliadin antibodies and 36/40 (90%) their histopathological changes of the small intestine suggests presence of celiac disease.

Table (1): The distribution of the patients having serological and biopsy results.

	Antigliadin		Transglutaminase		Biopsy			
	positive	negative	positive	negative	positive	negative	Positive Serological tests	+ve Serological Tests & +v ebiopsy
No.	34	6	38	2	36	4	32	29
%	85	15	95	5	90	10	80	72.5

The mean age of unselected diabetic children who found to have silent CD was 11.6 ±3, while their mean age of the diagnosis of their diabetes was 4.8 ±3.2, Table (2) shows that most of the patients with type 1 DM and silent CD were of age above 11 years, the males were predominant at all age groups especially the young age groups.

In considering the duration of the diabetes and onset of CD, it was found that the highest with the duration is of 3-5 years (37.5%), then the duration of 0-2 years (35%) but the lesser 27.5% is when the duration is above 5 yrs as shown in table (3).

Table (2): Distribution of the patients according to the age and sex.

Age group	Male		Female		Male: Female ratio
	NO.	**%**	**NO.**	**%**	
2 – 6 years	4	10	-	-	4 : 0
7 – 11 years	9	22.5	3	7.5	3 : 1
> 11 years	16	40	8	20	2 : 1
Total	29	72 .5	11	27.5	2 : 6

Mean of age =11.85 ± 3.

Table (3): Distribution of the patients according to the duration of disease.

Duration	NO.	%
0 – 2 years	14	35
3 – 5 years	15	37.5
>5 years	11	27.5
Total	40	100

This table shows that CD can appear at any time in patients with DM even within duration of 0 – 2 years.

Table (4) and (5) shows the clinical impact of celiac disease of hypoglycemia, hyperglycemia and GIT manifestations and its relation to the age of the patient and duration of the disease, It was found that they were more evident at age above 11 years and when duration of less than 5 years, but they were of no significant difference.

In considering the height and weight at diagnosis and after one year of treatment with GFD, it was found no significant differences between the means of SDs below the mean for both height and weight as shown in table (6) which does also show no significant differences between HbA1c at diagnosis and during treatment with GFD.

Table (4): Relation of the presence of the clinical manifestation with age of the patients

Age group	GIT manifestation		**Hypoglycemia**		**Hyperglycemia**	
	NO.	**%**	**NO.**	**%**	**NO.**	**%**
2 – 6 years	3	7.5	4	10	4	10
7 – 11 years	9	22.5	8	20	11	27.5
>11 years	20	50	23	57	24	60
Total	32	80	35	87	39	97.5

($p>0.05$).

Table (5): Number and percentage of patients having a relation of clinical manifestation and duration of disease.

	GIT manifestation		**Hypoglycemia**		**Hyperglycemia**	
	NO.	**%**	**NO.**	**%**	**NO.**	**%**
<5 years	20	50	21	52	24	60
>5 years	11	27	10	25	11	27

($p>0.05$).

Table (6): Relation of hieght and weight Centile and Hb A1c before and after treatment of celiac disease.

	Ht. Centile Mean ± SD	**Wt. Centile Mean ± SD**	**Hb A1c Mean ± SD**
Before	-1.2±0.41	-1.18±0.38	11.57± 2.22
After	-1.18±0.38	-1.20±0.41	11.51± 2.02
P Value	>0.05	>0.05	>0.05

The mean of CD below the mean for height and weight of all diabetic children=(-1.43±1.77,-1.2±1.77)respectively.

Table (7) and (8) show the relationship of the increment in height and weight per year before and after treatment with GFD and its relation to the age of patients and duration of the disease, there were no significant difference, so as there was no significant difference between the decrement in HbA1c of the patient before diagnosis of celiac disease and during treatment with GFD in relation of the age and duration of the disease.

Table (7): Relation of the mean of the increment of Ht. and Wt, and decrement in Hb A1c according to the age groups.

Age group(years)	Ht	Wt	HbA1c
2-6	6.25±1.171	3.75±2.36	.55±0.77
7-11	4.63±1.52	4.50±2.01	3.33±0.56
>11	5.58±1.35	5.67±1.96	-0.22±0.85
P Value	>0.05	>0.05	<0.05

Table (8): Relation of the mean of the increment in Ht. and Wt. and decrement in Hb A1c according to the duration of disease.

Duration	Ht.	Wt.	HbA1c
< 5 years	5.74±2.42	4.78±1.95	-7.60±0.72
> 5 years	5.55±5.54	5.77±5.77	-5.46±0.98
P Value	>0.05	>0.05	<0.05

Discussion: -

The prevalence of +ve tissue trasnglutaminase (TGA) is (38/350) 10.9%, while the prevalence of celiac disease proved by biopsy, is (29/350) 8.3%, which is higher than that reported from Austria, Italy, France, UK, USA, Germany, Australia [1,2,3,4,5,6,7] but less than that reported from Algeria [4].

The higher percentage of + ve tTGA comparing to antigliadin antibodies 95% as 85% respectively, this is similar to that reported by Luis Sorell [13].

The mean age of unselected diabetic children who found to have silent CD was 11.6 ±3, while their mean age of the diagnosis of their diabetes was 4.8 ±3.2,This is similar to that reported by EuroDiab Ace study group who show variations and treats in including of childhood diabetes toward younger age [14].

The males were the predominant at all age groups especially the younger age group who are more likely to get the infection that trigger the diabetes, the development of celiac disease depends on time of exposure to gluten, but the boys are more likely to go out doors and to buy gluten containing food like biscuit and sandwich.

Concerning the diagnosis of celiac disease, it can appear at any time from the development of diabetes though maximum of 2-5 years(15)and it has been reported that seroconversion observed up to 8 years after manifestation of the disease [16], and because it has appeared within the first 2 years of the diagnosis of DM, this means screening has to be done yearly or every 2 years at least one year after the development of diabetes.

The clinical impact of CD on patients with diabetes, the hypoglycemia manifestation present in 70% of cases and 30% of the hypoglycemic attacks were severe as coma or seizures which is similar to that reported by Mohn [17], but they

were not reported by Kaukinea, Lorini, Smith and Sank konen [18,19,20,21].The presence of one of GIT manifestations in 80%, hyperglycemia manifestations present in 80% and DKA in 30% of them, but no similar study to compare.

The height increment had no significant difference between that at diagnosis and after one year of treatment with GFD, this is similar to Kaukinen [18]. Although the growth of diabetic children with CD is reduced in comparison to the nondiabetic children similar to Lorini study [19] ,but the height is not that different from the control in Westman, Acerin, Mohan and Sauk konen [3,17,21, 22].

The weight increases slowly, but no significant difference between that at diagnosis and after one year of treatment with GFD,this is similar to Mohan and Kaukinen [17,18] but Acerin, Sauk konen and Westman had significant increase in weight in their study[3,21,22],the differences in the results might be explained on the differences in the metabolic control.

Glycosylated Hb is much higher than the control 6-6.5% and this study shows decrement after treatment with GFD but of no significance, Lorini.and Sauk konen demonsrated an increase in HbA1c [19.21],our result shows an increase in HbA1c, only when corelating the HbA1c to the duration of the disease. The explanation for such difference,is that their children had a better diabetic control at onset of CD than poorer control of our diabetic children at onset of CD,but the metabolic control seems better when the duration of the disease is less than 5 years. While the metabolic control is not different from the control (all diabetic children) as was reported by Acerini, NotT Mohan, Smith, Kankinen [3,11,17,20,18].Kaukinen concluded no effect of GFD on metabolic control of DM in patients with DM and CD[18].

Although the GFD was not palatable and more expensive, the strict compliance could only be achieved in 80% similar to NotT [11] but less than Acerini and Mohan who reported 100%[3,17].

Conclusion: -

The metabolic control and growth of children with type 1 DM and silent CD did not improve after treatment with GFD; further studies are needed to see their compliance to GFD, their seroconversion and long-term health.

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