http://garmian.edu.krd https://doi.org/10.24271/garmian.167

Assessment of Anti–Gliadin (IgA & IgG), Thyroid Stimulating Hormon and Growth Hormon Level in Celiac Disease Patients in Erbil City – IRAQ

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Abstract

Celiac disease (CD) is an autoimmune human leukocyte antigen HLA–linked enteropathy that develop upon ingestion of gluten containing diet, with diarrhea, malabsorption and weight loss as a major presentation.

The disease is closely linked to a number of extra intestinal disorder especially endocrine diseases. This study aimed to assess level of thyroid stimulation hormone (TSH) and growth hormone (GH) level in patients with newly diagnosed (ND) CD and on gluten free diet (GFD)

A total of 26/50 newly diagnosed celiac disease patients and 20 on GFD diagnosed clinically and confirmed serologically using anti-gliadin IgA and IgG (IgA for diagnosis newly diagnosed and IgG for diagnosis of patients on GFD) were subjected to TSH and GH level assessment.

The anti-gliadin IgA and IgG were positive in 82% with celiac patients and 80% on GFD patients. Among children , 82.14% of newly diagnosed and 85.71% on GFD were IgA and IgG anti-gliadin seropositive, while in adults, 81.82% and 76.92 % of newly diagnosed and on GFD were IgA and IgG anti-gliadin seropositive respectively.

The results revealed elevated TSH level in sera of 80.77% and 30% of CD and on GFD patients respectively; meanwhile GH level was low in 73.07% and 10% of CD and GFD patients respectively. The frequency CD patients revealed TSH elevation and low GH in the same patient was 69.23 % and 10% in CD and on GFD patients respectively.

As a result, the present study delineated simultaneous occurrence and linkage between CD disease and subclinical hypothyroidism. Beside assessment of GH level in CD patients is necessary as marker for disorder of pituitary gland, possibly of autoimmune origin.

In newly diagnosed and patients on GFD patients, no significant correlation exists between anti-gliadin antibodies, TSH & GH level. Meanwhile significant correlation was found between TSH & GH in ND (r= - 0.568, P=0.002) & GFD (r= - 0.702, P= 0.001).

Keywords: celiac disease, anti-gliadin, thyroid stimulation hormone, growth hormone**.**

Introduction:

Celiac disease (CD) is animmune – mediated HLA linked enteropathy associated with an intolerance to gluten containing protein found in wheat, rye & barley grain (Freeman, 2016a).

Recently, the disease has been diagnosed without significant gastrointestinal symptoms in 2% of the serologically studied population & perhaps higher in patients referred for endoscopic screening biopsies (Alaeldini & Green, 2005).

CD is closely associated with autoimmune endocrine disorders, of these thyroid autoimmunity with increased occurrence of thyroid dysfunction (Butt *et al*., 2011). The linkage because of the shared HLA haplotype namely HLA-DQ2 and DQ8 (Freeman, 2016b). The association also might be related to common embryonic

origin because fetal thyroid gland is originated from the pharyngeal gut on the 17th day (Freeman, 2016a)

Children with CD history , short stature may be the only presenting clinical manifestation in the absence of the intestinal symptom (Meazza *et al*.,2014).

Involvement of growth hormone / Insulin growth factor-1 (GH/IGF-1) axis beside autoimmune disorders of pituitary gland & altered ghrelin secretion are among pathophysiological mechanism that the children might benefit from GH treatment (Fanciulli & Delitala, 2001).

Aim of study:

The study aimed to:

1 –Assessment of serum level of thyroid stimulation hormone (TSH) & growth hormone (GH) in both children & adult patients with newly diagnosed CD and on GFD using serologic tests namely anti-gliadin IgA and IgG.

2 – To find any correlation between TSH & GH level with serum level of IgA&IgG anti-gliadin antibodies

Materials and Methodes :

The study is cross-sectional & the patients enrolled were 50 (28 children & 22 adults)

newly diagnosed celiac disease & 20 patients on gluten free diet (GFD) comprised 7 children & 13 adults with average age between 5 – 50 years. The patients recruited were referred from different private pediatric clinic in Erbil /Kurdistan-Iraq; diagnosed on clinical ground as CD & confirmed serologically using serologic tests ; among these IgA & IgG anti-gliadin antibodies.

Out of the total 50 CD patients screened for subclinical thyropathy at the time of CD diagnosis

(exclusion criteria overt thyropathy was excluded) & with history of growth retardation (short stature), only 26 newly diagnosed CD were selected (20 children & 6 adults). The patients sera of both groups were subjected to TSH & GH level assessment. ELISA test was selected for the assessment of anti-gliadin IgA,IgG, TSH & GH serum levels.

The study was approved by the ethic committee at technical health college & verbal informed consent was obtained from each patients enrolled in this study.

SPSS program was used to detect any possible correlation between the parameters screened. Significant results was accepted at $P \leq 0.05$.

Kits	Company	Country
Anti-gliadin (IgA & IgG) by ELISA	Orgentic	Germany
TSH & GH by ELISA	Biocheck	USA

- Cut off value of anti-gliadin (IgA & IgG) up to 10 IU/ml.

Results :

The seropositivity rates of anti-gliadin- IgA and anti-gliadin- IgG for both adult and children included in this study were 82% and 80% in newly diagnosed celiac and patients on GFD respectively (Table 1). Among the adult patients , there were 81.82% and 76.92 % IgA and IgG anti-giliadin seropositivity in CD and patients on GFD respectively. On the other hand , in children, seropositvity rates of anti-gliadin IgA and IgG among CD and on GFD was 82.14% and 85.71% respectively (Table. 2) .

Table (1): Frequency of anti-gliadin IgA and IgG in newly diagnosed CD and patients on GFD

	No. seropositive	No. seronegative
anti-gliadin IgA (ND no=50)	41(82 %)	9 (18%)
anti-gliadin IgG (GFD no=20)	16(80%)	4 (20 %)

Table (2): Seropositvity rates of anti-gliadin IgA and IgG among CD and on GFD in adults and children

	Children/anti-gliadin serostatus		Adults / anti-gliadin serostatus	
	Seropositive	**Seronegative.**	**Seropositive**	**Seronegative.**
anti-gliadin IgA (ND)	23/28 (82.14%)	5/28 (17.86%)	18/22 (81.82%)	4/22 (18.18 %)
anti-gliadin IgG (GFD)	6/7 (85.71%)	1/7 (14.29%)	10/13 (76.92 %)	3/13 (23.08 %)

The level of TSH and GH were measured in newly diagnosed and patients on GFD (Table.3) . Elevated TSH levels were recorded in 80.77% newly diagnosed patients and 30% on GFD ,while the level of GH was low in 73.07% of newly diagnosed CD patients and 10% on GFD .

Table (3): Frequency of TSH and GH seropositivity in newly diagnosed CD and patients on GFD

	TSH level		GH level	
	Patients No. with elevated TSH (> 5 m.I.U.)	**Patients No. with normal TSH (0.5-5 m.I.U.)**	**Patients No. with low GH (< 1 ng/ml)**	**Patients No. with normal GH (1-10ng/ml)**
ND (No.= 26)	21 (80.7%)	5(19.3%)	19 (73.07%)	7 (26.92%)
GFD(No.= 20)	6 (30%)	14(70%)	2 (10%)	18 (90%)

The concentration of the two hormones were estimated in adults (Table. 4) .The results showed TSH elevation in 66.67% and 15.39% among newly diagnosed and patients on GFD respectively, whereas GH level was low in 66.67% newly diagnosed CD patients, meanwhile on GFD , the GH was normal among the total adult group screened (100%).

In children, 85% of newly diagnosed patients and 57.15% on GFD reveal elevated TSH level ,whereas the level of GH was low in 75% CD patients and 28.57% on GFD (Table. 5).

Table (4): Frequency of TSH and GH seropositivity in adults with newly diagnosed and patients on GFD

	TSH level		GH level	
	Patients No. with elevated TSH (> 5 m.I.U.)	**Patients No. with normal TSH (0.5-5 m.I.U.)**	**Patients No. with normal GH (1-10ng/ml)**	**Patients No. with low GH (< 1 ng/ml)**
ND (No.= 6)	4(66.67%)	2 (33.33%)	2 (3.33%)	4 (66.67%)
GFD(No.= 13)	2(15.39%)	11 (84.61%)	13 (100%)	0(0%)

Table (5): Frequency of TSH and GH seropositivity in children with ND and patients on GFD

	TSH level		GH level	
	Patients No. with elevated TSH (> 5 m.I.U.)	**Patients No. with normal TSH (0.5-5 m.I.U.)**	**Patients No. with low GH (< 1 ng/ml)**	**Patients No. with normal GH (1-10ng/ml)**
ND (No.= 20)	17(85%)	3 (15%)	15 (75%)	5 (25%)
GFD(No.= 7)	4(57.15%)	3 (42.85%)	2 (28.57%)	5 (71.43%)

Regarding hormonal average ranges ,TSH was elevated in 66.67% among newly diagnosed celiac patients at a range (5.1- 10m.I.U.) and in 66.66/ on GFD .Further in 14.29% & 16.67% TSH level was between (10.1 - 15 m.I.U.) in newly diagnosed and on GFD patients respectively. Meanwhile, 9.52% with CD revealed TSH level higher than 20m.I.U (Table, 6).

Table (6): Average TSH level in CD patients and on GFD.

	5.1-10 (m.I.U.)	**10.1-15 (m.I.U.)**	**15.1-20 (m.I.U.)**	**>20 (m.I.U.)**
ND patients no./ 21	14 (66.67%)	3 (14.29%)	2 (9.52%)	2 (9.52%)
GFD patients no./6	4 (66.66%)	1 (16.67%)	1(16.67%)	0 (0%)

The frequency of patients suffering from elevated TSH level and low GH level (for the same patient) were 69.23 % and 10 % among newly diagnosed and on GFD patients respectively. Meanwhile in 11.54% with CD and 20% on GFD, TSH level was elevated with normal GH level in the same patient respectively. In contrast, only 3.85% with CD & 0% on GFD, TSH level was normal with low GH level.

Table (7): Frequency of combined pictures of TSH and GH level in the same patient with CD and on GFD

	TSH↑ elevation and↓low GH level.	**TSH↑ elevation and normal GH level.**	**Normal TSH and low GH ↓ level**	**Normal TSH and GH level.**
ND (n=26)	18 (69.23 %)	3 (11.54%)	1(3.85%)	4 (15.38%)
GFD n=(20)	2 (10 %)	4 (20 %)	0 (0%)	14(70%)

According to data analysis there are no significant correlation exist between anti-gliad in level and the level of two hormones included in this study in CD and on GFD patients. Meanwhile, significant correlations were found between TSH and GH level in patients with newly diagnosed CD (r= - 0.568, p=0.002) and GFD patients (r= - 0.702, p=0.001).

Discussion:

In established cases of CD, the possibility exist for the presence of an occult endocrine disorder (Freeman, 2016a). The linkage between CD & other autoimmune disease like thyropathy reflect the presence of shared genetic trait like HLA-DQ2 & DQ8 independent of gluten exposure (Yanagawa *et al*.,1993 ; Kagnoff, 2005; Hadithi *et al*., 2007 & Collins *et al.*, 2012).

Celiac patients respond to gliadin peptide reflected by high prevalence of anti-gliadin antibody (Shor *et al*., 2012). In this study the frequency of anti-gliadin IgA & IgG in both children & adults on GFD was in the range of 85.71% - 76.92%; meanwhile in newly diagnosed patients the frequency was in the range of 82.14% - 81.82%, respectively (Table 2). Reif & Lerner, (2004) delineated sensitivity & specificity for IgA & IgG anti-gliadin antibodies of up to 91% & 94% for IgA & up to 88% & 92% for IgG.

The present study showed increased markers & occurrence of thyroid dysfunction reflected as elevated TSH in celiac patients ; with autoimmune origin might be the primary etiology.

Thus in this study, TSH was elevated in 80.7% & 30% in celiac patients & those on GFD (Table 3); with mild TSH elevation (5.1 – 10 m.I.U/ml.) constitute the predominant range (Table 6) .

Different studies reported different prevalence of subclinical hypothyroidism like 2.27% (Toscano *et al.,* 2000), 0.9 (Elfstron *et al.,*2008), 1.8 5% (Meloni *et al*., 2009), 10% (Butt *et al*., 2011) , 10.1% (Hakanan *et al*., 2001), 12.03% (Guidetti *et al*., 2001).

Butt *et al*., (2011) referred that celiac patients with mild serum TSH elevation, thyroid function should be more frequently tested because of increasing risk for developing overt thyrodism .

As thyroid dysfunction when diagnosed earlier eliminate the negative impact on growth in children with CD (Butt *et al*., 2011). This fact is clearly delineated in this study as 69.23% of newly diagnosed CD & 10% on GFD, TSH elevation was linked with low GH level (Table 7).

Different studies showed different impacts of GFD treatment on thyropathy (TSH) normalization or progression. In our study, in 80.7% , TSH was elevated in celiac patient, meanwhile on GFD, TSH was elevated in 30% (Table 3). Some studies refered for the protective role of GFD in celiac patients on normalization of TSH (Ventura *et al*.,1999 & Sategna-Guidetti *et al*., 2001) . In contrast, study of Mesto *et al*., (2012) revealed no impact of GFD after one year on progressive of autoimmune thyroiditis. Recently, a suggestion was made that CD & autoimmune thyroid disease improvement will not be changed with GFD (Kahaly & Schuppan,

2015) & need long term follow up in order to confirm or exclude such hypothesis merit.

The coexistence of other hormone defect like GH in celiac disease is a fact. Growth retardation is regarded as a characteristic symptom of CD; as growth failure might be the only clinical finding of CD, now becoming more & more frequent (Meazza, *et al*., 2014).

In this study GH level was low in 73.07% among celiac patients & in 10% on GFD(Table 3); with 69.23% in celiac patients & 10% on GFD, co-existence pictures of elevated TSH& low GH level exist (Table 7). This is supported by the presence of a significant negative correlation between TSH&GH level in both newly diagnosed celiac patient (r= -0.568, P= 0.02) & patients on GFD (r= -0.702, P= 0.001). Some refer that children on GFD who diagnosed earlier reveal higher increment gains in height compared with children diagnosed late (Patwari *et al*., 2005).

But lacking of clear catch –up growth in celiac patients on GFD after 1-2 years despite sero-negativity for EMA & anti-tTG; it is critical to evaluate GH secretion in response to at least two pharmacological stimuli (Meazza, *et al*., 2014). This is beside the fact that for optimal efficiency of GH on growth rate, need a normal thyroid secretion (Smyczynska *et al*., 2010). Recently thyroid hormone have been shown to regulate GH receptor (Bassett *et al*., 2006).

Hypothyroidism is almost always linked with growth failure, as thyroid hormone has a significant impact on GH secretion (Mytilinaios *et al*., 2017), particularly related to severity but not duration of hypothyroidism (Brauman *et al*., 1973 & Thomas *et al*., 2006) ; although Mytilinaios *et al*.(2017) refer that, the impacts of hypothyroidism on GH secretion are time dependent.

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