Original article

# Effect of Gluten Free Diet Adherence on Growth Parameters of Children with Celiac Disease: A Follow Up of Patients in Al-Bieda Medical Center From 2005 to 2016

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#### ABSTRACT

Celiac disease (CD) is an autoimmune disease that develops in patients with a genetic predisposition, incurring a susceptibility to gluten-containing foods such as barley, wheat, and rye. The elimination of gluten from the diet is the main therapeutic approach and usually leads to clinical and laboratory improvement. This the study was designed to determine the role of dietary compliance and adherence effect of gluten free diet (GFD) among celiac disease patient. Thirty-six patients with Celiac disease (CD) who were confirmed by duodenal biopsy included in the study. The mean age of patients at diagnosis was 7.94. 69.2% of the patients aged  $\leq 6$  year were compliers, 56.5% of patients aged > 6years were compliers. 41.7% of GFD complaint patients were stunted. however, 30.4% of GFD non-compliant group were stunted as well. FTT was observed in 26% and 34.8% of the GFD complaint group and GFD non-compliant group respectively. complications found to be more common in GFD non complaint group (69.6%) in compare to the GFD complaint group (15.4%). the difference was statistically significant P-Value (0.000). we conclude that adherence to the GFD has a significant positive impact on health of children with CD, children with CD should be encouraged and regularly followed in terms of compliance with the GFD.

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#### INTRODUCTION

Celiac disease (CD) is an autoimmune enteropathy triggered by dietary gluten in genetically susceptible individuals1. Celiac disease (CD) occurs in about 1 in 100 patients in the Western world [1]. It is an immunemediated disease triggered by the exposure to gluten. While environmental factors are important, recent data highlights the importance of genetic factors [2,3]. The prevalence of CD-predisposing HLA haplotypes in the general population varies from one region to the other [4,5].

Patients with CD are at an increased risk of a number of disorders including lymphoma and autoimmunity [6,7]. Typically, patients with CD demonstrate small intestinal inflammation and villous atrophy [8-10]. The

disorder causes small intestinal mucosal inflammatory changes and altered architecture, often leading to impaired nutrient absorption, diarrhea and weight loss [11]. Several extra-intestinal changes may also occur, or represent the presenting clinical manifestation of underlying occult celiac disease. The treatment currently depends on consumption of a strict gluten-free diet so that mucosal healing can occur and complications are minimized. Adherence to a strict gluten-free diet is difficult, costly and compliance is difficult to monitor. But, a balanced gluten-free diet should be based on a combination of natural gluten-free foods and certified manufactured gluten-free foods [11]. Different factors may influence compliance, particularly age at diagnosis, and reported estimates of lack of compliance are highly variable [10].

For the current study, was undertaken to determine the role of dietary compliance and adherence effect of gluten free diet among celiac disease patients. Seroprevalence of CD in the population was considered as subjects having a positive anti-tissue transglutaminase (TTG) and confirmed by duodenal biopsy and villous atrophy.

## METHODS

#### Study design

We retrospectively enrolled patients who was diagnosed with CD during the period of 2005-2008 during. *Data collection* 

Data was collected from the medical records of 36 patients at outpatient pediatrics special gastroenterology clinics at Al-Biada Medical Center. The subjects were all detected and diagnosed during a survey done by Alarida et al 2011 [12] that aimed to determine the prevalence of CD in a large sample of the Libyan school population at their pre-school general health visit. Diagnosis was confirmed by small intestine biopsy. All patients were requested to start gluten free diet and asked to visit regularly for assessment and follow up. patients were seeking follow up care during the period from 2005 through 2016 was carefully scrutinized to obtain data. Secondary data on demographic characteristics, clinical picture, complication, management and outcomes was retrieved. The records file of all studied sample was reviewed for regular attendance, compliance to GFD and outcome assessment. The outcomes were measured in term of (a) Measurement growth parameters (b) Investigations including CBC, PBS, s. iron, s calcium determination.

#### Data analysis

Data was analyzed using the SSPS computer program. To find the significant difference between the observed variable studied, chi –square test, t test was used.

## RESULTS

Thirty-six patients with Celiac disease (CD) were confirmed by duodenal biopsy and villous atrophy were included in the study and all of them are classified as Modified Marsh classification 3B. Of the total cases, 27 patients (75%) were female and 9 patients (25%) were male (Figure 1).



## Figure 1. Sex distribution of studied patients

The mean age of patients at diagnosis was 7.94 (range 4–14) years, at the time of diagnosis, 22 (61.1%) patients were  $\leq 6$  years of age and 14 (38.9%) patients were > 6 years of age (Figure 2). In term of Compliance to the GFD among the studied patients 22 patients (61.1%) were complaint, while 14 (38.9%) had no compliance (Figure 3).



*Figure 2. Distribution of studied patients according to the age of diagnosis* 



## Figure 3. Distribution of studied patients according Compliance

In regard to age of diagnosis, children who was diagnosed at age  $\leq 6$  years found to be more compliant to the GFD than the children who was diagnosed > 6 years. (69.2% and 56.5% respectively). (Table1) & (Figure 4).

Table 1	Distribution of follow up patients according to GFD compliance

Age at Diagnosis	GFD compliance	GFD non-compliance	
< 6 Years	9 (69.2%)	4 ( 30.7 % )	
> 6 Years	13 (56.5%)	10 ( 43.4 % )	
Total = 36	22	14	

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Figure 4. Classification of patients regarding GFD compliance according to age.

Regarding the extent of adherence to gluten free diet effect on growth based on growth chart curves, stunting results were based on Z-score for height (less than 2SD below reference) and failure to thrive (FTT) based on Z-score for Weight (less than 2SD below reference). The results showed that (41.7%) of GFD complaint patients were stunted. However, (30.4%) of GFD non-compliant group were stunted as well. FTT was observed in (26%) and (34.8%) of the GFD compliant group and GFD non-compliant group respectively. Difference =  $\mu$  (GFD COMPLIANCE) -  $\mu$  (GFD NON-COMPLIANCE). Estimate difference: 0.590 was significance and 95% CI for difference: (-0.837; -0.344). DF = 38. T-Value = -4.84, P-Value = (0.000) (Table 2).

ltems	GFD compliance	GFD NON- compliance	T-Test	P value
Height				
< 2SD	41.70%	30.40%		
> 2SD	58.30%	69.65%		
			-4.84	0
Weight				
< 2SD		34.8		
> 2SD	74%	65.2		

Table 2. Adherence to gluten free diet effect on growth based on growth chart curves

Arising problems (complications) found to be more common in GFD non complaint group (69.6 %) in compare to the GFD complaint group (15.4 %). the difference was statistically significant P-Value (0.000) (Figure 5).



Figure 5. Arising problems for studied patients according to GFD compliance.

The complications were more frequently observed among the non GFD complaint group. The commonest complication observed was anemia. 75 % of GFD non-compliant group were anemic in compare to only 17% of GFD compliant. Hypocalcemia and FTT were observed in 34.8% and 26% respectively among GFD non-compliant group difference were statistically significant P-Value (0.007) & (0.005) for anemia and hypocalcemia respectively. Dermatitis was observed in (4.3 %) GFD non-compliant group (Figure 6).



Figure 6. Complication during follow up management

## DISCUSSION

CD is an autoimmune enteropathy that occurs in response to permanent susceptibility to gluten in individuals with a genetic predisposition. The only treatment of the disease is lifelong GFD [13,14]. Noncompliance to the GFD is a major problem and the greatest challenge that physicians face is predicting the compliance to the gluten-free diet in children. Noncompliance to GFD may occur due to factors like temptation and not liking the taste of gluten-free food and alternative food grains [15]. Complying with the GFD can be extremely challenging for children with celiac disease. In our study 61.1% of the children were found to be compliant to the GFD. This was in harmony with the rates of compliance as seen in various other studies. Strict dietary compliance was shown to vary from 45% to 81% in children by Hill et al. [10], 95% in a Canadian study on children <16 years of age by Rashid et al. [16], and 75% by Chauhan et al. in a study done on children 2–17 years of age, in north India in 2010 [15]. Whereas young children with celiac disease may adhere to a gluten-free diet because of parental influence, the situation remains complex in adolescents.

Children diagnosed at age  $\leq 6$  years were more compliant with GFD than children who was diagnosed at age > 6 years. Dietary compliance of patients who are diagnosed in the adolescence stage are worse than that of patients who are diagnosed in early childhood. Comba et al 2018 reported that the ages of patients that were non-compliant with gluten-free diet were higher than those of patients who were fully compliant with gluten-free diet. [17].

This low global level of adherence to a GFD in children with celiac disease is troubling given the known morbidity and mortality associated with long-term untreated celiac disease and the lack of any other effective treatment. Effective counseling about the diet is the single most important factor to ensure the required restriction in diet among these patients. In this study compliance with the GFD has been shown to result in the best positive effect on children's growth parameters. however, Compliance to a gluten-free diet has shown no significant difference between the two groups in terms of height z-scores.

While catch-up growth with gluten elimination is observed in children, several studies reported that anthropometric measurements are not correlated with dietary compliance [18]. Radlovic e t al. investigated the improvement in the weight, height among GFD complaint patients and GFD non complaint patient. They stated that there was improvement in the weight and height in both groups. However, the difference between the two groups was not statically significant [19]. Jadresin et al. reported that a significant difference existed in the weight z scores of compliant and non-compliant patients but observed no significant difference in the height z scores [18]. Comparably in this study a significant recovery was found in the weight z-scores of the patients in the GFD compliant groups in comparison to the non-compliant group. however, no significant difference was found in terms of height z-scores.

complications were found to be much higher in GFD non-compliant group (69.6 %) than GFD compliant group (15.4 %) and the observed difference was statistically significant.

Anemia was the most common complication observed in GFD non-compliant group during follow up. 75 % of patients in GFD non-compliant group found to be anemic which is significantly high compared to GFD compliant patients. According to previous studies the overall prevalence of anemia at the time of diagnosis of celiac disease has been estimated between 12% and 69% [20-24]. FTT was observed in (34.8%) in GFD non-compliant group compared to 26.1 % in GFD compliers group. These results are in accordance with Jadresin et al [18]. Anemia, short stature, reduced bone mineralization of the total body skeleton and hypocalcaemia has been shown to be a common complication of untreated CD. [26-30]

In our study hypocalcaemia was observed in (26%) in GFD non-compliance group. Nonetheless, calcium level was normal among the GFD compliers. This is in agreement with the recent studies performed on patients with CD in childhood [29,30,31,32]. Factor such as providing excellent education about the disease and a gluten-free diet will encourage optimal dietary compliance. Better strategies to ensure compliance in screening-detected children with celiac disease need to be developed, and education of health care professionals about the treatment of celiac disease and the FGD needs to be improved. It has been demonstrated that increased awareness and education about celiac disease as well as better availability of gluten-free foods helps to improve the child's and family's adjustment to this chronic disease [33,34]. Because physical symptoms usually resolve once a gluten-free diet is initiated, health professionals need to appreciate the emotional and psychosocial hurdles faced by children with celiac disease. Keys to improve compliance include the provision of on-going education and support to children with celiac disease and their families. The availability of gluten-free foods needs to increase, and legislation to identify hidden sources of gluten must be improved.

## CONCLUSION

In this study, we conclude that the adherence to the GFD has a significant positive effect on the growth parameters of the affected children especially weight. Compliers to the GFD have less complications compared to non-compliers.

## Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

## Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

#### REFERENCES

- 1. Lebwohl B, Ludvigsson JF, Green PH. Celiac disease and non-celiac gluten sensitivity. BMJ. 2015;351:h4347.
- 2. Liu E, Lee HS, Aronsson CA, et al. Risk of pediatric celiac disease according to HLA haplotype and country. N Engl J Med. 2014; 371:42–9.
- 3. Kuja-Halkola R, Lebwohl B, Halfvarson J, Wijmenga C, Magnusson PK, Ludvigsson JF. Heritability of non-HLA genetics in coeliac disease: a population-based study in 107 000 twins. Gut. 2016 Nov;65(11):1793-1798. doi: 10.1136/gutjnl-2016-311713.
- 4. Gujral N, Freeman HJ, Thomson AB. Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World J Gastroenterol 2012; 18:6036–6059.
- 5. Cummins AG, Roberts-Thomson IC. Prevalence of celiac disease in the Asia-Pacific region. J HJ. Detection of adult celiac disease with duodenal screening biopsies over a 30-year 2013.; 27: 405-408.
- 6. Elfstrom P, Sundstrom J, Ludvigsson JF. Systematic review with meta-analysis: associationsbetween coeliac disease and type 1 diabetes. Aliment Pharmacol Ther. 2014; 40:1123–32.
- 7. Ludvigsson JF, Leffler DA, Bai JC, Biagi F, Fasano A, Green PH, et al. The Oslo definitions for coeliac disease and related terms. Gut. 2013 Jan;62(1):43-52. doi: 10.1136/gutjnl-2011-301346.
- Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA; American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastroenterol. 2013 May;108(5):656-76; quiz 677. doi: 10.1038/ajg.2013.79.
- 9. Imrei M, Németh D, Szakács Z, Hegyi P, Kiss S, Alizadeh H, et al. Increased Prevalence of Celiac Disease in Patients with Cystic Fibrosis: A Systematic Review and Meta-Analysis. J Pers Med. 2021 Aug 28;11(9):859. doi: 10.3390/jpm11090859.
- Hill ID, Dirks MH, Liptak GS, Colletti RB, Fasano A, Guandalini S, Hoffenberg EJ, et al. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2005 Jan;40(1):1-19. doi: 10.1097/00005176-200501000-00001.
- 11. Perera DR, Weinstein WM, Rubin CE. Symposium on pathology of the gastrointestinal tract-Part II. Sm all intestinal biopsy. Hum Pathol 1975; 6: 157-217.
- 12. Alarida K, Harown J, Ahmaida A, Marinelli L, Venturini C, Kodermaz G, et al. Coeliac disease in Libyan children: a screening study based on the rapid determination of anti-transglutaminase antibodies. Dig Liver Dis. 2011 Sep;43(9):688-91. doi: 10.1016/j.dld.2011.01.002.
- 13. Guandalini. S. Celiac disease. In: Guandalini S, ed. Essential Pediatric Gastroenterology, Hepatology & Nutrition. New York: McGraw-Hill; 2005.P.221-30.
- 14. Moore J. K, West SR, Robins G. Advances in celiac disease. Curr Opin Gastroenterol 2011;27(2):112-8.
- 15. Chauhan JC, Kumar P, Dutta AK, Basu S, Kumar A. Assessment of dietary compliance to gluten free diet and psychosocial problems in Indian children with celiac disease. Indian J Pediatr. 2010 Jun;77(6):649-54. doi: 10.1007/s12098-010-0092-3. Epub 2010 Jun 8. PMID: 20532683.
- Rashid M, Cranney A, Zarkadas M, Graham ID, Switzer C, Case S, Molloy M, Warren RE, Burrows V, Butzner JD. Celiac disease: evaluation of the diagnosis and dietary compliance in Canadian children. Pediatrics. 2005 Dec;116(6):e754-9. doi: 10.1542/peds.2005-0904.
- 17. Comba A, Çaltepe G, Yüce Ö, Erena E, Kalaycı AG. Effects of age of diagnosis and dietary compliance on growth parameters of patients with celiac disease. Arch Argent Pediatr. 2018 Aug 1;116(4):248-255. English, Spanish. doi: 10.5546/aap.2018.eng.248. PMID: 30016020.
- 18. Jadresin O, Misak Z, Kolacek S, Sonicki Z, Zizić V. Compliance with gluten-free diet in children with coeliac disease. J Pediatr Gastroenterol Nutr. 2008 Sep;47(3):344-8. doi: 10.1097/MPG.0b013e31816f856b.
- 19. Radlović N, Mladenović M, Leković Z, Zivanović D, Brdar R, Radlović V, Ristić D, Pavlović M, Stojsić Z, Vuletić B, Djurdjević J, Gajić M. Effect of gluten-free diet on the growth and nutritional status of children with coeliac disease. Srp Arh Celok Lek. 2009 Nov-Dec;137(11-12):632-7. doi: 10.2298/sarh0912632r.

- 20. Bottaro G, Cataldo F, Rotolo N, Spina M, Corazza GR. The clinical pattern of subclinical/silent celiac disease: an analysis on 1026 consecutive cases. Am J Gastroenterol. 1999 Mar;94(3):691-6. doi: 10.1111/j.1572-0241.1999.00938.x.
- 21. Lo W, Sano K, Lebwohl B, Diamond B, Green PH. Changing presentation of adult celiac disease. Dig Dis Sci. 2003 Feb;48(2):395-8. doi: 10.1023/a:1021956200382.
- 22. Unsworth DJ, Lock FJ, Harvey RF. Iron-deficiency anaemia in premenopausal women. Lancet 1999;353:1100.
- 23. Kolho KL, Farkkila MA, Savilahti E. Undiagnosed coeliac disease is commonin Finnish adults. Scand J Gastroenterol 1998;33:1280–1283.
- 24. Hin H, Bird G, Fisher P, Mahy N, Jewell D. Coeliac disease in primary care: case finding study. BMJ. 1999 Jan 16;318(7177):164-7. doi: 10.1136/bmj.318.7177.164. Erratum in: BMJ 1999 Mar 27;318(7187):857.
- 25. Merendino RA, Di Pasquale G, Sturniolo GC, Ruello A, Albanese V, Minciullo PL, Di Mauro S, Gangemi S. Relationship between IL-18 and sICAM-1 serum levels in patients affected by coeliac disease: preliminary considerations. Immunol Lett. 2003 Feb 3;85(3):257-60. doi: 10.1016/s0165-2478(02)00243-2.
- 26. Caraceni MP, Molteni N, Bardella MT, Ortolani S, Nogara A, Bianchi PA. Bone and mineral metabolism in adult celiac disease. Am J Gastroenterol. 1988 Mar;83(3):274-7. PMID: 3257843.
- 27. Choudhary G, Gupta RK, Beniwal J. Bone Mineral Density in Celiac Disease. Indian J Pediatr. 2017 May;84(5):344-348. doi: 10.1007/s12098-016-2273-1.
- 28. Hoffmanová I, Anděl M. Osteoporóza a metabolické kostní změny u celiakie v dospělosti [Osteoporosis and bone alterations in celiac disease in adults]. Vnitr Lek. 2014 Jul-Aug;60(7-8):601-6.
- 29. Molteni N, Caraceni MP, Bardella MT, Ortolani S, Gandolini GG, Bianchi P. Bone mineral density in adult celiac patients and the effect of gluten-free diet from childhood. Am J Gastroenterol. 1990 Jan;85(1):51-3.
- 30. Mora S, Barera G, Ricotti A, Weber G, Bianchi C, Chiumello G. Reversal of low bone density with a gluten-free diet in children and adolescents with celiac disease. Am J Clin Nutr. 1998 Mar;67(3):477-81. doi: 10.1093/ajcn/67.3.477.
- 31. Mora S, Weber G, Barera G, Bellini A, Pasolini D, Prinster C, Bianchi C, Chiumello G. Effect of gluten-free diet on bone mineral content in growing patients with celiac disease. Am J Clin Nutr. 1993 Feb;57(2):224-8. doi: 10.1093/ajcn/57.2.224.
- 32. Barera G, Mora S, Brambilla P, Ricotti A, Menni L, Beccio S, Bianchi C. Body composition in children with celiac disease and the effects of a gluten-free diet: a prospective case-control study. Am J Clin Nutr. 2000 Jul;72(1):71-5. doi: 10.1093/ajcn/72.1.71.
- 33. Jackson PT, Glasgow JF, Thom R. Parents' understanding of coeliac disease and diet. Arch Dis Child. 1985;60:672– 674
- 34. Anson O, Weizman Z, Zeevi N. Celiac disease: parental knowledge and attitudes of dietary compliance. Pediatrics. 1990;85:98 –103.