Acta Biomed 2018; Vol. 89, Supplement 9: 5-10 DOI: 10.23750/abm.v89i9-S.7871

Review

Growth changes after gluteen free diet in pediatric celiac patients: a literature-review

Alessia Ghiselli[1], Barbara Bizzarri[1], Federica Gaiani[1], Francesca Semeraro[1], Silvia Iuliano[1], Francesco Di Mario[1], Antonio Nouvenne[1], Stefano Kayali[1], Gian Luigi de' Angelis[1]

[1] Gastroenterology and Endoscopy Unit, Department of Medicine and Surgery, University of Parma, Parma, Italy

Summary. *Background:* Celiac disease is an auto-immune disorder characterized by clinical manifestations that appear in genetically predisposed subjects after gluten ingestion. In the last years, there has been a progressive change in clinical manifestations. Our aim was to evaluate the nutritional status of children with celiac disease at diagnosis and how the gluten-free diet (GFD) influences their growth. *Methods:* A search on PubMed/Medline was performed using "celiac disease", "body mass index" and "children" as key words. Medline, Scopus, PubMed publisher and Google Scholar were searched as well. We selected clinical studies describing the nutritional status of patients before and after GFD using indicators like height, weight, BMI, skeletal age. We excluded papers referred to adult population or in which other diseases were related to celiac disease. Also literature-reviews were excluded. *Results:* From 1999 to 2018, 10 studies were found. Overall, 1383 patients in pediatric age were evaluated for their nutritional status at diagnosis of celiac disease and after a variable period from 1 to 17 years of GFD. Indicators considered were height, weight, BMI and skeletal age. *Conclusions:* the nutritional status of celiac patients at diagnosis is variable including an increasing number of overweight and obese. GFD has a beneficial impact on growth changes determining a correction of BMI distribution towards a Gaussian shape. (www.actabiomedica.it)

Key words: celiac disease, BMI, growth, gluten free diet

Introduction

Celiac disease (CD), also known as gluten-sensitive enteropathy, is a life-long condition that affects the small intestine in genetically susceptible individuals (1). It is a multifactorial disease that arises from a complex interaction between genetic heritage, immunological and environmental factors. The genes involved are the major histocompatibility complex type II and, in particular, the HLA-DQ2 and HLA-DQ8 haplotypes. It's characterized by subtotal villous atrophy of the small intestine, intra-epithelial lymphocytosis and crypt hyperplasia, and is associated with a variable gluten-related presentation. (2). Young children often present with "classic" symptoms including diarrhea, abdominal distention, and growth retardation. Vomiting, abdominal pain and constipation are atypical manifestations, more common in older children and teenagers (1). Celiac disease can also present with extra-intestinal conditions such as arthritis, neurological diseases, and anemia (1).

The presentation of CD has changed over time (1). The prevalence of the classical presentation of CD has decreased in the last decades, while the prevalence of non-classical presentations has increased. Growth failure in terms of length (or height) or weight may be the earliest sign of the disease (2) but many reports show that CD can be associated with normal weight but also with overweight and obesity (3, 4). Variations in the nutritional status may be seen at diagnosis (5), which in pediatric age can be evaluated using indicators such as height, weight, BMI, skeletal age.

The quantification and the definition of BMI in children vary widely overworld, therefore it is difficult to compare papers from different countries. Anyway, the ideal definition, based on percentage of body fat, is impracticable for epidemiological use (6). Body mass index (BMI, weight/height^2) is widely used in adult populations, with a cut-off point of 30 kg/m^2 is recognized as a definition of adult obesity (6). BMI in childhood changes substantially with age and sex especially during the pubertal growth spurt (Figure 1). Therefore the BMI in pediatric age should be used not as an absolute value but as a relative value, with the support of centile curves. Clearly, a cut-off point related to age is needed to define pediatric obesity. In the United States, the 85th and 95th centiles of BMI for age and sex, have been recommended as cut off points to identify overweight and obesity (6).

It is now well established that many patients with celiac disease have a high or normal body mass index (BMI) at diagnosis. Some studies show that BMI increases on a gluten-free diet (GFD), especially in those who adhere closely to the diet while other studies show contradictory results (7). Few studies examining BMI and other growth parameters have been performed in children, with inconclusive findings (8).

The aim of this paper was to review the available literature on nutritional status of children with celiac disease at diagnosis, focusing on the influence of gluten-free diet (GFD) on growth, through the use of specific indicators.

Methods

In order to evaluate the nutritional status of children affected by CD at diagnosis, its evolution after gluten-free diet and the parameters that can be used to evaluate growth changes, we performed a literature search of PubMed database using Mesh terms "celiac disease", "body mass index" and "children". Medline, Scopus, PubMed publisher and Google Scholar were searched as well. The entire databases were considered, without restrictions of time. We included only full text papers selected with two filters "humans" and "language". Only papers in English were included.

Exclusion criteria were:

- papers referred to children affected by CD with other comorbidities such as arthritis, diabetes and thyroiditis.
- papers referred to adult population
- studies in which nutritional status of CD at diagnosis was compared with health children and not with the same group after GFD
- literature-review articles

Each article was tabulated in chronological order from the oldest to the most recent as follows: author and year of the study, number of patients, demographic data, period of follow up, growth indicators at diagnosis (BMI, skeletal age), growth indicators after gluten-free diet (BMI, skeletal age) (Table 1). Further parameters to evaluate nutritional status such as biochemical tests were not considered.

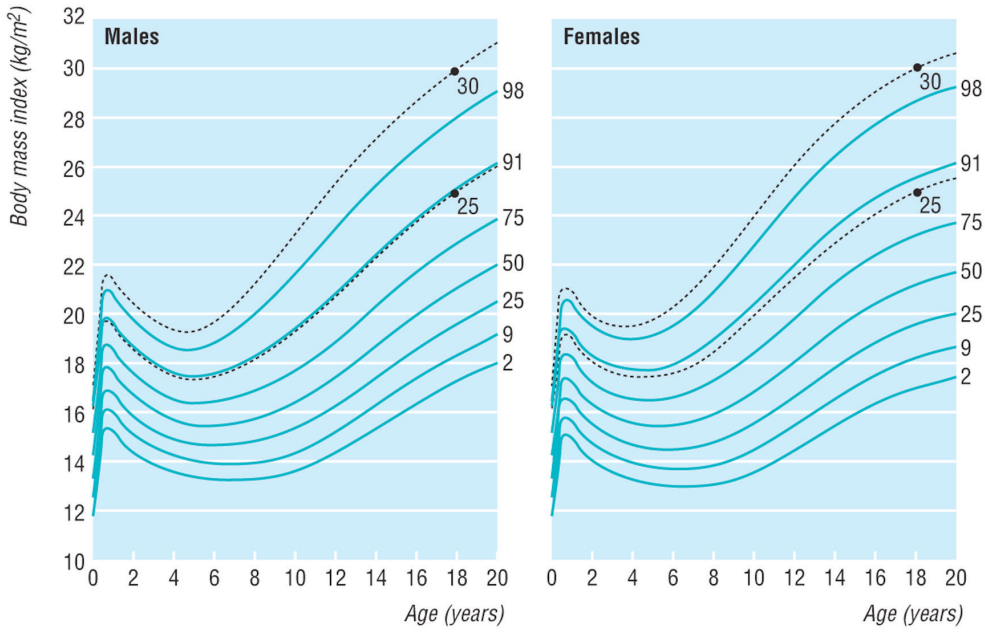
The publications were manually screened and reviewed to identify reports, and data were extracted from the papers according to the predetermined criteria. Two investigators independently reviewed and extracted data from the papers according to the predetermined criteria.

Results

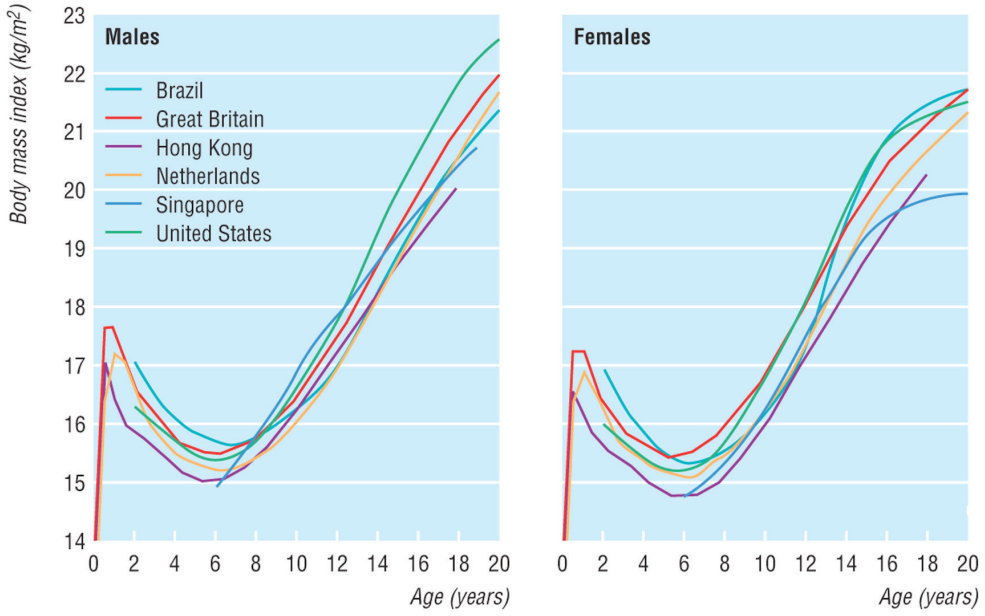
After a first research, 147 abstracts were found. Among them, 127 full text papers were analyzed. Finally, applying the filters "humans" and "language" and including only English papers, 105 papers were obtained. After manual screening according to established criteria, we selected 10 retrospective articles, published from 1999 to 2018.

The numerosity of the cohorts among papers varied widely, from a case reports study with 1 patient (9) up to the paper including the highest number of patients, with 445 subjects (10). Overall 1383 patient in pediatric age (from 1 to 17 years old) were evaluated for their nutritional status at diagnosis of celiac disease and after a variable period from 1 to 17 years of GFD.

Only in one study (11) skeletal age was used as growth indicator together with other parameters such as height and weight. In five papers (2, 9, 12-14), centile curves of BMI were considered as principal indicator for evaluation of growth changes after GFD. In the other four studies (8, 10, 15, 16) only weight was



Centiles for body mass index for British males and females. Centile curves are spaced two thirds of z score apart. Also shown are body mass index values of 25 and 30 kg/m² at age 18, with extra centile curves drawn through them



Median body mass index by age and sex in six nationally representative datasets

Figure 1.

Table 1. Papers included in the literature review

Author, year	N° patients	Demographic data	Period of follow up	Growth indicators at diagnosis (BMI, skeletal age)	Growth indicators after gluten-free diet (BMI, skeletal age)
Gemme G. 1999	26 (11 M, 15 F)	<3 years	15,3 years	Tendency to short stature, underweight and retarded skeletal age	Skeletal retardation, slightly below average height
Patwari AK, 2005	50	2-10 years	1-4 years	Short stature, underweight.	Normalisation of body mass, incomplete recovery in height
Oso O, 2006	1	14 years	3 years	BMI 37,2 Kg/m2	BMI 42,7 Kg/m2
Telega G, 2008	143 (93 F, 50 M)	1-17 years	17 years	11,2% overweight (BMI >90%)	-
Van Dommelen, 2008	134	<2,5 years	-	BMI decrement in patients with clinical manifestations	-
Valletta E., 2010	149	Children (median age 6,2 years)	1 year	5% malnutrition 23% underweight 11% overweight 3% obese	- - 21% overweight 4 % obese
Venkatasubramani N. 2010	143	childhood	1 year	7 pz BMI >95%	4 pz decreased 2 pz increased 1 pz not available
Reilly NR 2011	142	13 months-19 years	3 years	75% normal 13% overweight 6% obese	13% of normal became overweihgt 75% of overwheigt decreased BMI
Brambilla P, 2013	150	2-16 years	4 years	16% underweight 12% overweight or obese	8% underweight minimal increase of overweight
Capriati T., 2016	445	children	-	7,8 % overweight or obese	9,8 % overweight or obese

considered with the consequent identification of five categories: malnutrition, underweight, normal-weight, overweight and obese.

Discussion

Celiac disease is one of the most common chronic diseases in childhood (7). Children may present with the classical manifestations of disease characterized by chronic diarrhea, failure to thrive and abdominal distention or with non-classical features including gastrointestinal symptoms as well as extra-intestinal manifestations (3). Because of the damage to the small intestinal mucosa, it can be expected to result in malabsorption of nutrients leading to poor weight gain, weight loss and undernutrition. However, a few recent reports have identified an increasing number of adults, adolescents and children who are overweight, or even obese, at the time of initial diagnosis of CD (3). This concept has been well described by Dickey et al in 2006 (17) who reviewed a database of 371 celiac

patients showing how only few patients were underweight while a large part was overweight/obese.

In adult population affected by celiac disease it is easier to examine the relationship between the disease and nutritional status because BMI is a standardized and recognized parameter for the evaluation of corporeal mass. Cheng et al in 2010 (18) and Ukkola et al in 2012 (19) investigated BMI before and after GFD in celiac patients. Both concluded that GFD has a beneficial impact on BMI, underweight patients gain weight and overweight/obese patients lose weight.

In pediatric age, the relationship between nutritional status in CD before and after GFD is more difficult to evaluate because of the relative value of BMI and the necessity to use centile curves. Gemme et al in 1999 (11) was the only author to use skeletal age in addition to height, weight and BMI, and he concluded that after a period of GFD patients didn't catch up completely in height and skeletal age. Patwari et al in 2005 (15) used as anthropometric parameters only weight and height expressed as Z scores relative to National Center for Health Statistics standards. In this study 50 patients were analyzed and showed short stature and underweight before diet; after GFD they achieved a normalization of body mass but an incomplete recovery in height. The only case report study of Oso et al in 2006 (9) reported the case of a 14-y-old boy with celiac disease with a BMI at presentation of 37.2 kg/m^2 (>99.9th centile) that increased to 42.7 kg/m^2 despite dietary support confirming that obesity in childhood doesn't exclude the diagnosis of CD. Telega et al in 2008 (12) confirmed the presence of overweight in celiac patients at diagnosis. The same results can be observed in a study by van Dommelen et al in 2008 (2) in which she concluded that BMI is a better predictor for nutritional status than weight and much better than length or height. Valletta et al in 2010 (16) observed, in a population of 149 children after 1 year of gluten-free diet, a doubling of overweight while obese remain unchanged. Similar results were obtained from Brambilla et al in 2013 (8) where after 4 years of follow up he observed a halving of underweight and a minimal increase of overweight, and from Venkatasubramani et al in 2010 where, in a case study with 5% of obese (BMI > 95%), two-thirds decreased after GFD while one-third increased. Capriati et al in 2016 (10) presented an increase of both overweight and obese patients after GFD. BMI was used for this evaluation as a measure of nutritional status according to Italian growth charts of Cacciari. Instead Reilly et al in 2011 (14) after 3 years of observation, showed substantially a decrease of BMI in overweight. Overall considering all growth indicators, with limits due to demographic data, it can be concluded that GFD improves nutritional status of CD with a reduction of underweight and obese but also with a minimal increase of overweight. This determines a modification of BMI distribution towards a bell shape which better represents the distribution of biological variables.

Conclusions

Celiac disease is now considered a common chronic disease in childhood and no more a rare condition. Children more frequently present with atypical symptoms than with classical features and variations in nutrition may be seen at diagnosis. Many indicators can be used to evaluate the influence of GFD on growth even if BMI seems to be the best predictor. Overall GFD has a beneficial impact on growth changes determining a correction of BMI distribution towards a Gaussian shape. A careful follow-up of nutritional status after the diagnosis of CD is necessary, as new morbidities could also emerge in children strictly compliant with GFD, especially in overweight and obese.

References

1. Diamanti A, Capriati T, Basso MS, Panetta F, Di Ciommo Laurora VM, Bellucci F, et al. Celiac disease and overweight in children: an update. Nutrients 2014; 6(1): 207-20.
2. van Dommelen P, Grote FK, Oostdijk W, Keizer-Schrama SM, Boersma B, Damen GM, et al. Screening rules for growth to detect celiac disease: a case-control simulation study. BMC pediatrics 2008; 8: 35.
3. Shahraki T, Shahraki M, Hill ID. Frequency of overweight/obesity among a group of children with celiac disease in Iran. Przeglad gastroenterologiczny 2018; 13(2): 127-31.
4. Nenna R, Mosca A, Mennini M, Papa RE, Petrarca L, Mercurio R, et al. Coeliac disease screening among a large cohort of overweight/obese children. Journal of pediatric gastroenterology and nutrition 2015; 60(3): 405-7.

5. Aurangzeb B, Leach ST, Lemberg DA, Day AS. Nutritional status of children with coeliac disease. Acta paediatrica (Oslo, Norway : 1992) 2010; 99(7): 1020-5.
6. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ (Clinical research ed) 2000; 320(7244): 1240-3.
7. van der Pals M, Myleus A, Norstrom F, Hammarroth S, Hogberg L, Rosen A, et al. Body mass index is not a reliable tool in predicting celiac disease in children. BMC pediatrics 2014; 14: 165.
8. Brambilla P, Picca M, Dilillo D, Meneghin F, Cravidi C, Tischer MC, et al. Changes of body mass index in celiac children on a gluten-free diet. Nutrition, metabolism, and cardiovascular diseases : NMCD 2013; 23(3): 177-82.
9. Oso O, Fraser NC. A boy with coeliac disease and obesity. Acta paediatrica (Oslo, Norway : 1992) 2006; 95(5): 618-9.
10. Capriati T, Francavilla R, Ferretti F, Castellaneta S, Ancinelli M, Diamanti A. The overweight: a rare presentation of celiac disease. European journal of clinical nutrition 2016; 70(2) :282-4.
11. Gemme G, Vignolo M, Naselli A, Garzia P. Linear growth and skeletal maturation in subjects with treated celiac disease. Journal of pediatric gastroenterology and nutrition 1999; 29(3): 339-42.
12. Telega G, Bennet TR, Werlin S. Emerging new clinical patterns in the presentation of celiac disease. Archives of pediatrics & adolescent medicine 2008; 162(2): 164-8.
13. Venkatasubramani N, Telega G, Werlin SL. Obesity in pediatric celiac disease. Journal of pediatric gastroenterology and nutrition 2010; 51(3): 295-7.
14. Reilly NR, Aguilar K, Hassid BG, Cheng J, Defelice AR, Kazlow P, et al. Celiac disease in normal-weight and overweight children: clinical features and growth outcomes following a gluten-free diet. Journal of pediatric gastroenterology and nutrition 2011; 53(5): 528-31.
15. Patwari AK, Kapur G, Satyanarayana L, Anand VK, Jain A, Gangil A, et al. Catch-up growth in children with late-diagnosed coeliac disease. The British journal of nutrition 2005; 94(3): 437-42.
16. Valletta E, Fornaro M, Cipolli M, Conte S, Bissolo F, Danchielli C. Celiac disease and obesity: need for nutritional follow-up after diagnosis. European journal of clinical nutrition 2010; 64(11): 1371-2.
17. Dickey W, Kearney N. Overweight in celiac disease: prevalence, clinical characteristics, and effect of a gluten-free diet. The American journal of gastroenterology 2006; 101(10): 2356-9.
18. Cheng J, Brar PS, Lee AR, Green PH. Body mass index in celiac disease: beneficial effect of a gluten-free diet. Journal of clinical gastroenterology 2010; 44(4): 267-71.
19. Ukkola A, Maki M, Kurppa K, Collin P, Huhtala H, Kekkonen L, et al. Changes in body mass index on a gluten-free diet in coeliac disease: a nationwide study. Eur J Intern Med 2012; 23(4): 384-8.

Correspondence:
Alessia Ghiselli,
Gastroenterology and Endoscopy Unit,
Department of Medicine and Surgery, University of Parma,
Via Gramsci 14 - 43100 Parma, Italy
Tel. 0039 3394985339
Fax 0521/702989
E-mail: alessia.ghiselli@gmail.com