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# Early and Correct Diagnosis of Celiac Disease in the Prevention of Growth Disorders and Child Development

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## ORIGINAL PAPER

### ABSTRACT

Coeliac, in ordinary people known as “flour allergy” and in medicine world known as gluten enteropathy which means enteric damage caused by gluten. Data about incidence of gluten enteropathy is different in different countries around the World and depend on is it or is it not the right diagnosis for enteric disorder. Sometimes, this disease is unrecognized because of unspecific clinical signs. This disease is happening in every moment of a lifetime, most common during the childhood when the children try to eat any food which contains gluten. Anyway, if children had no symptoms it doesn't mean that disease not exists, and that is because we have to do diagnostic tests to confirm gluten enteropathy. Gluten intolerance is chronic disease and demand use of the specific non gluten food during the lifetime. Early diagnosis is right way to prevent unregularly growth. Aim of this study was to show the influence of early diagnostic about growth. For each patient we had a permission of parents and we showed our original results for three month we investigated.

**Key words:** gluten enteropathy, age, complications, growth.

## 1. INTRODUCTION

Celiac disease, popularly known as the „allergy to wheat flour“ in medicine is marked by the term „gluten enteropathy“, or damage to the intestine caused by gluten. Celiac disease is essentially not a disease but a predisposition for the disease because only by intake of gluten causes the damages in the lining of the small intestine in people who are genetically predisposed.

Data on the prevalence of celiac disease among the population varies considerably in different countries. People who have had symptoms and which were based on biopsy diagnosed celiac disease the ratio ranged to 1:1000. However, the introduction of immunological methods such as antibody test (screening method), are changing drastically the knowledge about the number of patients. Today it is assumed that the average incidence in Europe is much larger and is about 1:200. Also with the introduction of these diagnostic methods became known that celiac disease occurs in several clinical forms and that this disease was previously diagnosed only at the moment when the clinical symptoms were fully developed (1).

At the Ninth International Congress of celiac disease in the U.S. in 2000 presented are new data on the prevalence of celiac disease: Italy 1:186 inhabitants, Sweden 1:180, Ireland

1:100, Finland 1:130, Hungary 1:85, United States 1:126, in Croatia, it is assumed that the ratio is 1:500. This disease is rare in African Americans, Chinese and Japanese population, it is more common in women and more widespread in adults. When it comes to Bosnia and Herzegovina, there are no reliable indicators of the prevalence of celiac disease because of the war and post-war conditions of life caused a mass migration of the population and wiped out their former records on the disease incidence. On the other hand official statistical researches in B&H on diseases, conditions and injuries did not list celiac disease as an entity, but it is included in a group of diseases (2).

In B&H there are probably thousands of people with celiac disease but it is believed that this disease is one of the most common chronic diseases in general.

Flour is comprised of starch, a small part of the proteins with the gluten component (3). Gluten is composed of gliadin, or those substances that do not tolerate people with celiac disease.

With usual diet daily intake is 10-30 grams of gliadin. The intake of 100 milligrams per day leads to intestinal mucosal damage while the intake of less than 10mg does not cause the same damage.

Because of the simplification is generally only speaks of



Figure 1. Vili intestinales - normal mucosa

gluten (or gliadin). The small intestine contains intestinal villi (*villi intestinales*). Intestinal villi are long from 0.3 to 1 mm (1 mm kv.–about 5 million).

Fringes are lined with epithelium (from enterocytes) which performs absorption of food. Enterocytes are short-lived (2-5 days) and are constantly updated. Severe inflammation leads to a gradual decrease of the villi and extension of the crypts.

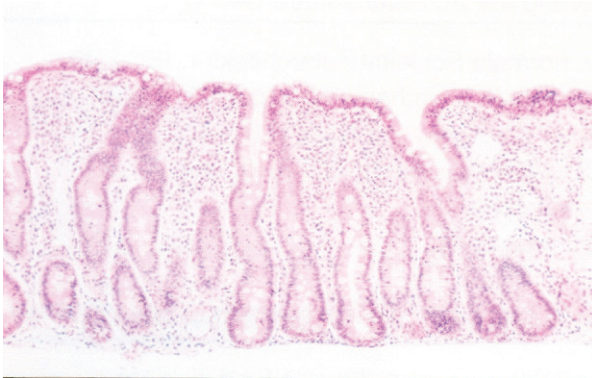


Figure 2. Crypt hyperplasia, Atrophia vili intestinales

Life span of enterocytes is reduced from two to five days at only six hours, which result in a complete or almost complete disappearance of villi (*Atrophia villorum subtotalis*), which leads to reduced capability to absorb nutrients from the food they need bodies.

Although it is easily visible villus atrophy, one of the characteristics of celiac disease, it can be observed in some other diseases. Therefore, it is inevitable to pay attention to other features of mucosa in untreated celiac disease: crypts were significantly prolonged (crypt hyperplasia), epithelial cells are lower and less layered than usual, the number of

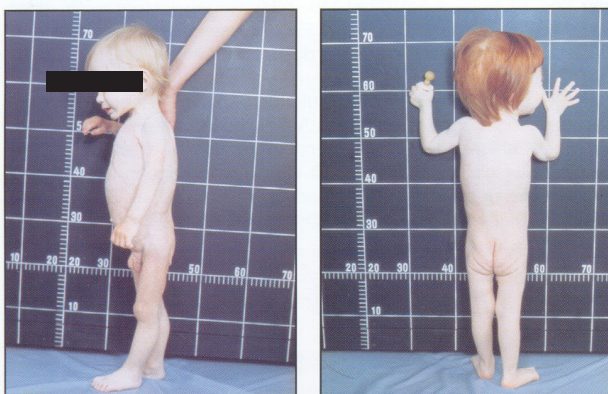


Figure 3. Growth slowing, anorexia

cells between the epithelial cells (intraepithelial lymphocytes–black arrow), increased number of lymphocytes, eosinophils and plasma cells in the mucosa and beneath the epithelium (light arrow).

All this suggests that for the diagnosis of celiac disease is not enough to state that the biopsy sample shows almost total or total villus atrophy!

Celiac disease in children usually starts by introducing flour food during infancy. The disease usually manifests in the second half of infancy.

The first symptoms occur 3-4 months after the introduction of foods that contain gluten.

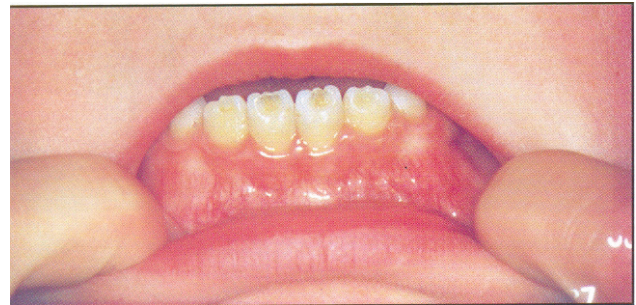


Figure 4. Damage of the thooth enamel



Figure 5. Clinical manifestation Coeliakia of older child (Patient No.1)

Regardless of when they occur, as celiac disease is always the same, just a different way in which it is manifested, all depending on the age.

Celiac disease in infants is usually manifested after a few weeks or months after the transition is made from breast milk to the other foods that contain gluten like wheat, rye, barley and oats.

The child, who had until then developed in accordance with their age, occurs growth slowing symptoms or just some of them: chronic diarrhea or constipation; bright and abundant stools, abdominal pain, and vomiting, bloated abdomen.

Anorexia due to lack of appetite, mood swings and changes in the skin. Damage to the tooth enamel is also one of the signs of this disease.

Classical (typical) form of celiac disease is manifested by diarrhea, weight loss, malabsorption and clinical vitamin deficiency.

There is a noticeable loss of villi in the mucosa of the small intestine, antibodies findings (IgA anti-gliadin [AGA],

IgA anti-endomysiac [AEA], IgA anti-tissue transglutaminase [TTG]) positive (5).

Already after a few weeks or months of strict gluten-free diet the symptoms disappear, improving the morphology of small bowel mucosa reverts even to its normal state.

Asymptomatic (silent) form of celiac disease is characterized by the positive histological findings (biopsy sample) and by positive antibody with slight or even no symptoms (6).

This situation is explained by the fact that is affected only one part (upper) of the small intestine, while the lower parts partially or fully compensate for disturbances.

In such forms is generally advisable to start with a gluten-free diet.

Latent celiac disease is manifested by normal histologic (biopsy) finding of small intestine and can still be found endomysiac antibodies—then we talk about so called latent celiac disease.

This phenomenon is usually recorded when previously there was damage to the small intestine in the form of celiac disease, and was later brought into the normal mucosa, or if you will in the future develop celiac disease (potential celiac disease).

First tests show that the complications in asymptomatic and latent forms of celiac disease may be the same as for the classical form of celiac disease.

Based on today's findings persons with potential celiac disease should not go on a gluten-free diet, but should regularly carry out tests for antibodies and possibly control biopsy after a few years or in the case of the onset of symptoms (7).

The diagnosis is made on the basis of laboratory findings, medical history, findings of the examination, immunological tests and biopsy of small bowel mucosa.

Biopsy and histopathological examination of the upper part of the small intestine is the main criterion for the diagnosis of gluten enteropathy, which needs to be done before the patient is put on a gluten-free diet.

There is no diagnosis of celiac disease without biopsy of small bowel mucosa and characteristic histological features of this disease.

Also on the basis of the test antibody without biopsy, may not be used for diagnosis of celiac disease (not recommended nor vice versa).

Simply, the diagnosis of celiac disease based on the findings of the BTC is based on three main criteria:

The histological findings of severe damage to the lining of the small intestine at the time when the child is on a normal diet;

Improved clinical state and findings of normal or slightly abnormal intestinal mucosa after exclusion of gluten from the diet (gluten-free diet) and

A clinical relapse or re-histological findings of severe or moderately severe damage to the intestinal mucosa within two years after re-taking foods with gluten.

If celiac disease is diagnosed in children younger than two years, these children are placed on a gluten-free diet 4 years or up to the age of six years of life.

If the child is older than two years it is a lifetime diet. The treatment for strict dieting gluten (wheat, rye, barley

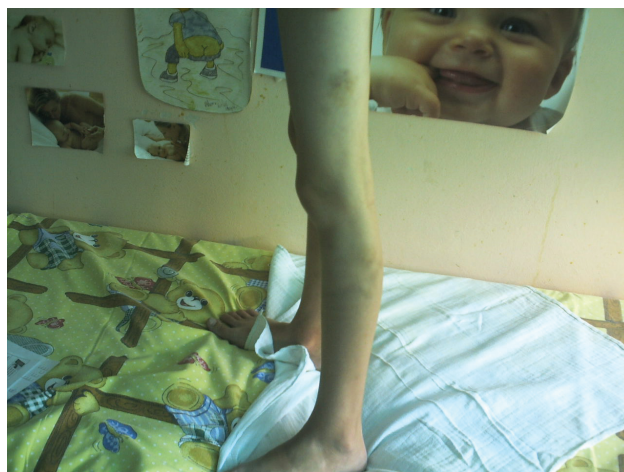


Figure 6. Clinical manifestation Coeliac disease of older child (signs of haemorrhagic diathesis, Patient No 1)

and oats) and it is the only possible treatment for patients.

This means that the child must be strict and complete, with a lifetime avoiding foods that contain gluten.

Re-exposure to foods containing gluten cause relapse and can lead to many complications, such as all types of tumors that develop in the small intestine.

Allowed are the rice, corn, soybeans, potatoes, all kinds of fruits and vegetables and all kinds of meat and fish. Today there are many types of ready-made gluten-free, and the packaging have crossed class of wheat.

Patients with celiac disease usually cannot tolerate milk and the intolerance of lactose in milk is the result of irritation of the intestinal villi in the lining of the inability to digest milk sugar. Fortunately, the gluten-free diet villi are recovering so that lactose intolerance is temporary.

If the disease is detected in time and left untreated, increases the risk of malignant diseases and the development of lymphoma, cancer of the small intestine, pharynx, esophagus and testicles.

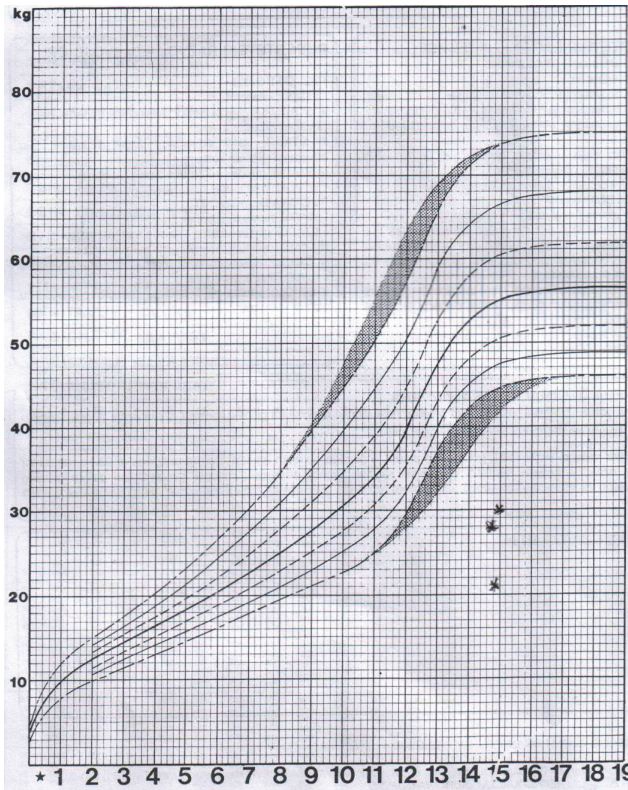
In women are frequent miscarriages, while the children of women who suffer from untreated celiac disease can be born with malformations.

Some even mentioned the emergence of mental disorders such as schizophrenia.

All of these are reasons enough to approach this disease



Figure 7. Child after 3 months gluten free diet (Patient No 1)



Graph 1. Findings on skeletal maturity (Patient No 1) very seriously and the more it begins to think especially in the adult population.

For adults there are atypical development, where alternate phase improvements with the stage of deterioration (e.g. only periodic diarrhea).

## 2. CASE REPORT/RESULTS

H.S. born on October 29th 1991, admitted on June 26th 2006 at the age 14 years and 8 months.

Indication for admission was delay in development compared to peers which is noticed by parents accompanied by occasional diarrhea at infant age, at 3 months, which is why was previously repeatedly hospitalized in the local health center. On admission girl child with body weight 21kg, height 131 cm, with signs of severe protein-energy malnutrition, with signs of liver failure, hemorrhagic diathesis (bruises on the skin) without any signs of puberty as seen in on the photo....

From the findings: SE 25/55, Er 3.36, Hb 65.5, Htc 0.22, D-xyl. Test: I, II, III, IV-pathological, ALT 206, AST 174, LDH 654, GGT, AF, CK, bilirubin, blood sugar, urea, urine, proteinogram, APTT, INR and Tr (made after TS DE) were within reference values. Bone maturity of 7 years and 10 months. Results are presented on Figure 1-13, Graph 1-3.

We did a biopsy of small intestine (BTC) after stabilization of the clinical condition of the child. PH findings were in favor of celiac disease.

The girl was placed on a gluten-free diet and we continue out-patient follow up.

Three months later, control examination: (12/09/2006) when it was found evident psychophysical recovery where in girl dominated a happy smile and overall satisfaction of the girl and their parents.

Physical parameters were significantly better as well as

the nutritional status. Since this was the quarterly review along with laboratory data valid finding to us was the body weight (BW) of girl who was then 27.7 kg or weight gain was 8kg and 700 grams while we planned to follow height in six months due to the expected physiological variations of growth.

Weight gain can be clearly seen in shown nomogram.

From the findings: ESR, CBC, proteinogram, bilirubin, AST, ALT, GGT, CK, AF, APTT, INR and urine within the reference values.

On the second control examination, six months later (12/25/2006) we find the physical parameters: BW 30 kg BH 137.5 cm, which really shows a positive response to a gluten-free diet and it's one of our parameters for clear diagnosis of celiac disease.

From the findings: ESR, CBC, proteinogram, bilirubin, AST, ALT, GGT, CK, AF, APTT, INR and urine within the reference values.

Chronological age was 15 years with an evident maturing as seen with the first signs of puberty and bone maturity, which was 10 years. Increment in physical parameters is shown in the following nomograms for weight and height.

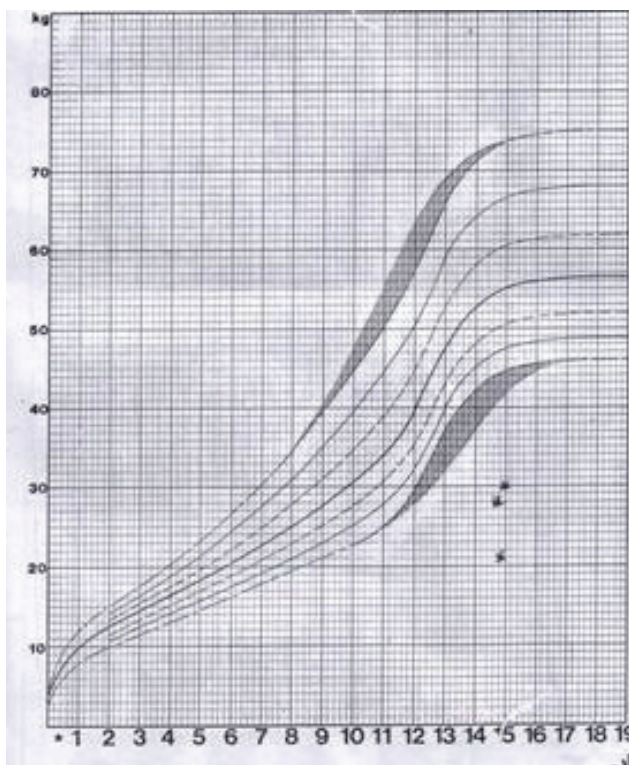
Clinically lighter case we had a year later. Girl B.Z born January 12th 2003, admitted February 16th 2007. Chronological age of 14 years. The body weight of 28 kg on admission and body height 143 cm, with no signs of puberty. Bone maturity 8yrs and 10 months.

From the findings: D xylose test-Aplaned curve. PH finding of the small intestine biopsy: present all the elements of gluten enteropathy.

At the control, 4 months after the introduction of gluten-



Figure 8. Child after 6 months gluten free diet (Patient No 1)



Graph 2. Weight gain on normogram (Patient No 2)

free diet values of physical parameters were BW: 41 kg and BH: 144.5 cm, corresponding to increase of 13 kg and 1.5cm. It was also found that maturation is reflected in the findings of skeletal maturity which then suited the age of 10 years.

On the second control examination 7 months after the introduction of gluten-free diet the girl has BW of 47 kg and BH of 151.5 cm, corresponding the increment of physical parameters in BW +19 kg and +8.5cm in BH.

It is also found that maturation is reflected in the skeletal maturity that matched the age of 11 years.

The classic clinical form of celiac disease at infant age is shown in child S.T.: which is diagnosed at age 18 months after birth.

Happiness and quality of health this boy is seen through his smile and the appearance, but also the previous image speaks of his clinical condition at the very beginning of the disease.



Figure 9. Clinical manifestation Coeliakia of older child (Patient No 2)

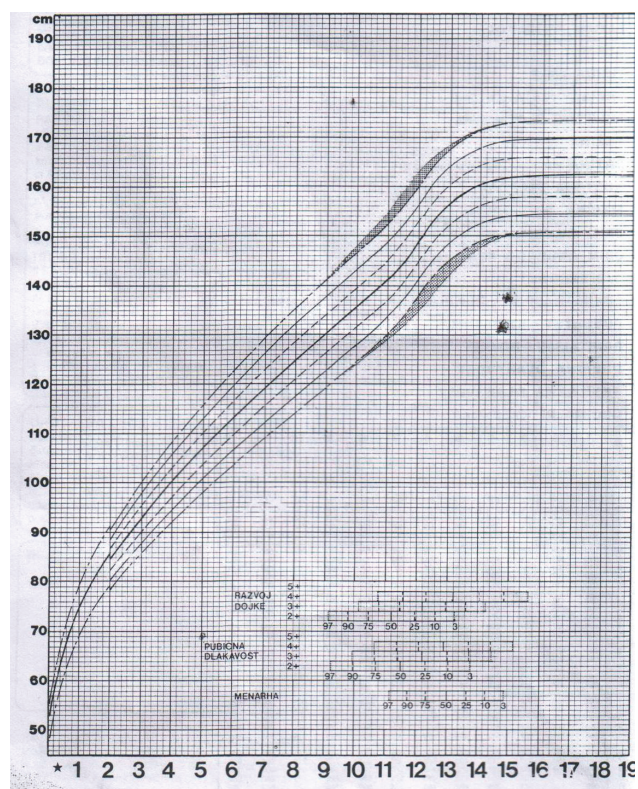
**This boy had long periods of stagnation in growth and development, mucosal lesions were of low intensity and its forecast for a healthy life in the future in any case is better.** It would be fortunate that the previous two cases taken this clinical course.

### 3. DISCUSSION

Celiac disease is more common than previously thought and new studies showed that the blood tests for antibodies as a noninvasive diagnostic procedure is of great help in detecting the disease.

Celiac disease occurs in people who are genetically predisposed to the illness. The disease can affect one of 99 children, according to a study published in the New England Journal of Medicine.

According to research by doctor Markk Maki, from the pediatric research center at the University of Tampere in Finland, children with the most severe form of the disease



Graph 3. Findings on skeletal maturity (Patient No 2)

may only have signs such as weight loss and anemia.

Also recently has been shown that there are more mild forms of the disease who have a variety of symptoms, which is not related to cancer. According to research by doctor Alessio Fasano, professor of pediatrics, medicine and physiology and director of the Center for Celiac Disease Research at the University of Maryland, undiagnosed celiac disease are associated with a number of diseases, including osteoporosis, chronic fatigue, anemia, miscarriages and changes in behavior. Because the symptoms are different, sometimes it is difficult to diagnose.

For the needs of this new study, Maki and his colleagues analyzed blood samples from 3654 students aged 7-16 years. Samples were collected during 1994as part of the study which investigated the risk for diabetes.



Figure 10. Clinical manifestation Coeliac disease of older child - after 3 months gluten free diet (Patient No 2)

It was found that 56 of these children have tested positive for the disease, however, until 2001 celiac disease was diagnosed in 10 children.

„Cure“ for celiac disease is a gluten-free diet, a protein responsible for celiac disease.

In the study by Green and Jarby in the section for histological analysis found that:

- The biggest problem in the diagnosis of celiac disease is an interpretation of a biopsy specimen pathological intestines;
- During a biopsy is needed and an adequate number of samples;
- Poorly oriented biopsies, such as if the crypt is tegmental cut will reduce the crypt: villa ratio.

For an adequate number of samples for biopsy International Council requires 4 biopsy samples: 2 from the distal duodenum and the 2 from proximal, but recent results are conflicting.

Orientation is defined as the location of the biopsy samples that exactly shows all bowel wall layers and this can be achieved with the use of milli-pore filters in which endoscopists biopsy samples placed in a straight line and accurately identify each sample in a separate space. Absence of symptoms does not mean that celiac disease is not present and is required to prevent complications as



Figure 11. Clinical manifestation Coeliac disease of older child after 6 months gluten free diet (Patient No 2)

soon as possible to confirm or exclude the same. Celiac disease can develop at any time in life and most often in young children who for the first time are met with food containing gluten. With early diagnosis of celiac disease not only we prevent disorders of growth and development, but also the risk of malignant diseases, the emergence of mental disorders, miscarriages and birth of children with congenital malformations. Gluten intolerance is a permanent condition, which requires that patients diagnosed with celiac disease throughout life must follow a gluten-free diet. Applying the above postulates for diagnosis of celiac disease with setting diagnosis or exclusion of this disease suspicion, we will successfully prevent timely disruptions in the growth and development of children and contribute to a positive quality of life.

#### 4. CONCLUSIONS

Celiac disease can develop at any time in life and most often in young children who for the first time met with food containing gluten.

Absence of symptoms does not mean that celiac disease is not present and is required to prevent complications as soon as possible to confirm or exclude the same. Gluten intolerance is a permanent condition, that is, patients diagnosed with celiac disease throughout life must follow a gluten-free diet. EARLY DIAGNOSIS OF DISEASE – prevention of irregular growth and development of the child.

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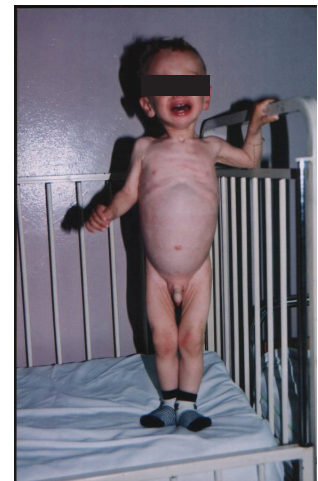


Figure 12. Clinical manifestation Coeliac disease on the beginning of the disease (Patient No 3)



Figure 13. Child after gluten free diet (Patient No 3)