University of Alberta

DIETARY INTAKE IN CHILDREN AND ADOLESCENT
WITH CELIAC DISEASE ON GLUTEN FREE DIET

By

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Abstract

Celiac disease (CD), a gastrointestinal disorder caused by immunological reaction to gluten, can only be treated by a gluten-free diet (GFD). The purpose of this study was to assess the diet of children with CD. Twenty-five children with CD on GFD and twenty-three children with chronic gastrointestinal disorders were evaluated using 24-hour recalls and a food frequency questionnaire. Protein intake was significantly higher among CD patients. None of the CD patients met the recommended intake for vitamin D. The intake of calcium, folate and fiber was below the recommendations in most CD patients. However, the intake of vitamin D and calcium improved after supplementation. Most met vitamin B_{12} requirement, and 50% met the iron requirement. The intake of saturated fat was high in 50% of the CD patients, while the intake of total sugar was within the recommended limit. These findings have implications for dietary counseling for pediatric CD patients

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Graduate Student Role

This student participated in data collection (n=20 subjects), data entry and some analysis related to statistics and dietary analysis, and wrote the thesis under the supervision of Dr Diana Mager PhD RD.

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List of Abbreviations

24-hr recall: 24-hour Recall

25(OH)D: 25 Hydroxycholecalciferol-Vitamin D

AGA: Antigliadin Antibodies

AHS: Alberta Health Services

AI: Adequate Intake

AMDR: Acceptable Macronutrient Distribution

ATTG: Antitransglutaminase Antibody

BMC: Bone mineral content

BMI: Body Mass Index

BMI-z: Body Mass Index z-score

CD: Celiac Disease

CDC: Centre for Disease Control

DRI: Dietary Reference Intakes

EER: Estimated Energy Requirement

EMA: Antiendomysial Antibody

FFQ: Food Frequency Questionnaire

GERD: Gastroesophageal Reflux Disease

GFD: Gluten Free Diet

GFP: Gluten Free Products

GI: Gastrointestinal

HLA: Human Leukocyte Antigen

Ht-z: Height-for-age z-score

IgA: immunoglobulin A

IPSAS: Interactive Portion Size Assessment System

LCMS: Liquid chromatography–mass spectrometry

RDA: Recommended Dietary Allowance

SP: Spine

WB: Whole body

Wt.-z: Weight-for-age z-score

Chapter 1: Review of literature

1.1 Introduction

Celiac disease (CD) is a chronic disorder in the small intestine caused by an immunological reaction to gluten, a protein that is found in wheat, barley, rye, and spelt products (Siddiqui & Osayande, 2011). It occurs in genetically susceptible people with HLA (human leukocyte antigen) classes HLA-DQ2 and HLA-DQ8 (Fasano, 2005). In addition, CD is associated with other genetic and autoimmune disorders such as Down's Syndrome, Williams Syndrome, Turner Syndrome, IgA deficiency, Type 1 diabetes, and Sjogren's syndrome (Fasano, 2005).

A diet containing gluten, a water-soluble protein, is responsible for the immune response that leads to intestinal damage in CD. Found in wheat, rye, and barley, gluten is the important contributing environmental factor for celiac disease (Lionetti & Catassi, 2011; Ludvigsson et al., 2012). The genetic factors contributing to celiac disease are associated with HLA (human leukocyte antigen) classes HLA-DQ2 and HLA-DQ8 (Lionetti & Catassi, 2011). Most patients with celiac disease are HLA-DQ2 positive, and some are HLA-DQ8 positive (Lionetti & Catassi, 2011).

1.2 History of CD

Dr. Samuel Gee provided the first description of celiac disease in a lecture in 1887. He described childhood celiac disease symptoms such as abdominal distention and muscle wasting (Newton, 2012). He said that the cure for this disease should be diet (Newton, 2012). In 1924, Sidney Haas introduced a banana diet to treat the disease (Auricchio & Troncone, 1996). However, the relationship between gluten found in food and celiac disease was not clear until World War II, when Dr. Dicke noted that the clinical symptoms of celiac disease improved when patients ate lower amounts of cereals (Auricchio & Troncone, 1996). After the war, Dicke worked with a Dutch biochemist, J.H van de Kamer, and they found that the steatorrhea observed in celiac patients was a result of consuming wheat and rye flour (Auricchio & Troncone, 1996).

1.3 Pathogenesis of Celiac Disease

Celiac disease pathogenesis involves both environmental and genetic factors. An environmental factor is gliadin, which is one of the components of gluten, a protein found in wheat products. Genetic factors include HLA-DQ2 and HLA-DQ8, the genotypes found in individuals at high risk for celiac disease (Newton & Singer, 2012). HLA-DQ2 is more common than HLA-DQ8 (Lionetti & Catassi, 2011). Celiac disease occurs in the lamnia propria of the intestinal

mucosa as shown in (**Figure 1-1)** (Lionetti & Catassi, 2011). This mechanism starts when gliadin enters into the lamina propria of the intestinal mucosa, triggering an autoimmune response. After that, transglutaminase changes gliaden into a negatively charged protein. This increases the gliadin molecules' ability to bind to HLA-DQ8 or HLA-DQ2 receptors (Lionetti & Catassi, 2011). Once the gliadin binds to HLA-DQ8 or HLA-DQ2, the CD4+T cells become active. Activated CD4+T cells prompt metalloproteases, which then result in damage to the intestinal villi and resulting atrophy. In addition, these CD4+T cells activate B cells, which produce antibodies that bind to gluten and transglutaminase and damage the epithelia damage. The villous atrophy represented in the celiac mucosa is a result of activating the intraepithelial lymphocytes (natural killer) by CD4+T cells (Lionetti & Catassi, 2011).

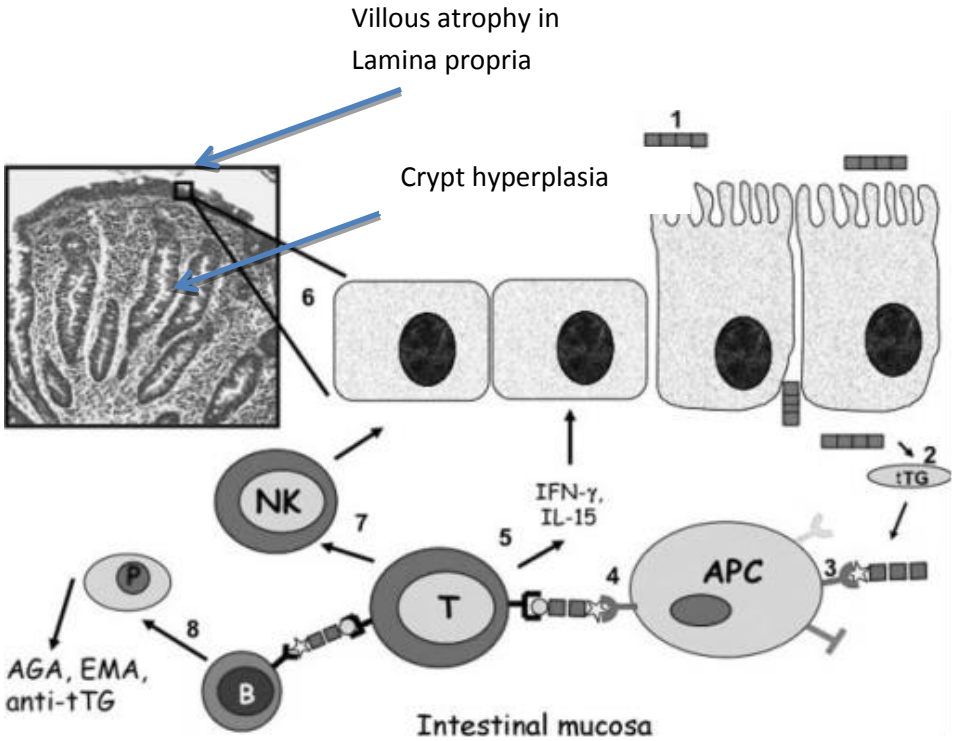


Figure 1-1: Underlying Disease Pathogenesis of CD: Importance of the Lamina Propria in the Intestinal Mucosa. Adapted from (Lionetti & Catassi, 2011)

The mucosal inflammation found in the celiac intestine develops from totally normal intestinal mucosa (**Figure 1-2**). Intraepithelial lymphocytosis appears as a first sign of the inflammation. The last stage of the inflammation appears with villous atrophy (Lindfors et al., 2011). In addition, the damaged celiac mucosa is characterized by flattening mucosa and a loss of villi (Siddiqui & Osayande, 2011).

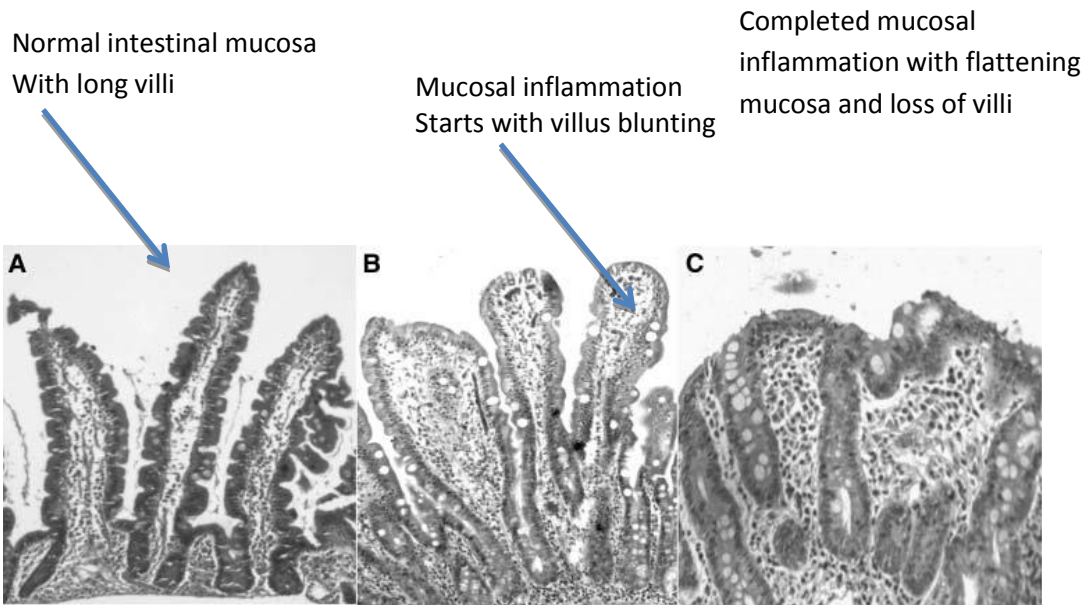


Figure 1-2: Shows that the mucosal Inflammation Found in the Celiac Intestine Develops from Totally Normal Intestinal Mucosa (A) Shows the Normal Mucosa. In (B) the Mucosal Inflammation Starts with Developing Crypt Hyperplasia. Finally, (C) Shows the Completed Mucosal Inflammation with Villous Atrophy. Adapted from (Lindfors et al., 2011).

1.4 Symptoms of CD

There are many signs and symptoms of celiac disease, including typical and atypical symptoms as shown in **Table 1-1**. However, celiac disease has been found in patients without any symptoms, not even GI symptoms (Mager et al., 2012, Turner et al 2009; Fasano, 2005). This asymptomatic celiac disease can develop as silent or latent celiac disease.

Silent celiac disease describes the condition of patients who do not show any apparent symptoms. However, these patients have positive serology and damaged mucosa (Lionetti & Catassi, 2011). Furthermore, these patients may have a family history of celiac disease, genetic disorders, or autoimmune disease, such as Type 1 diabetes (Lionetti & Catassi, 2011).

Latent celiac disease is characterized by normal intestinal mucosa and positive serology (positive anti-tTG antibody and positive EMA) (Lionetti & Catassi, 2011). However, intestinal damage will develop later, along with the typical symptoms (Fasano, 2005; Ludvigsson et al., 2012).

Table 1-1: The Symptoms of CD in Pediatric Population (Fasano, 2005;Lionetti & Catass, 2011)

Typical CD (classical symptoms and signs)	**Atypical CD (non-classical symptoms and signs)**
Abdominal distention	Anemia
Recurrent abdominal pain	Nausea
Chronic diarrhea	Vomiting
Impaired growth	Constipation
Weight loss	Puberty delay
Muscle wasting	Poor bone health
Reduced appetite	Short stature
	Dental enamel defects
	Dermatitis herpetiformis
	Infertility
	Recurrent stomatitis
	Arthritis

1.5 Prevalence of CD

Celiac disease is very common and affects approximately 1% of the world's population (Mahadov & Green, 2011). Surprisingly, current studies show that non-western populations have a similar prevalence of celiac disease as western populations (Asamoah, von Coelln, Savitt, & Lee, 2011). **Table 1-2** shows the prevalence of celiac disease among different countries. The highest prevalence of celiac disease has been found among the Saharawi population (Catassi et al., 1999).

The prevalence of celiac disease increases to 20% among patients who have relatives who have been diagnosed with celiac disease (Siddiqui & Osayande, 2011). It also increases among patients with other diseases such as Type 1 diabetes mellitus, osteoporosis, and anemia (Siddiqui & Osayande, 2011). In patients who have Type 1 diabetes mellitus, the prevalence increases to 3%–6% (Siddiqui & Osayande, 2011). It increases to 3% among patients who suffer from osteoporosis and to 10%–15% among patients diagnosed with anemia (Siddiqui & Osayande, 2011). Moreover, the incidence of celiac disease in females is greater than the incidence of the disease in males, with a ratio of 3.33:1. **Table 1-2** shows the prevalence of celiac disease around the world.

Table 1-2: Prevalence of CD among Different Countries (Lionetti & Catassi, 2011; Newton & Singer, 2012; Rubio-Tapia et al., 2012)

Country	**Prevalence of CD**
USA	0.71%
Britain	0.99%
Hungary	1.81%
Finland	2%
Italy	1.2%
Germany	0.3%
Egypt	0.53%
Libya	0.75%
Iran	0.88%
Turkey	0.6%
India	0.7%
Saharawi population living in Algeria	5.6%

1.6 Diagnosis of CD

A CD diagnosis should include serological, genetic, clinical, and histological factors (Villanacci et al., 2011). These factors should be evaluated while the patient is still consuming food that contains gluten because a gluten-free diet changes the results (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011). For example, eating a gluten-free diet will result in improvements in the intestinal villli, so when the patient undergoes an intestinal biopsy, it will not be possible to determine whether the patient actually has CD. Therefore, it is important for the patient to have the biopsy while still on a gluten-containing diet.

The diagnosis of celiac disease should be considered for patients in high risk groups, as shown in **Table 1-3**, regardless of symptoms.

Table 1-3: The Risk Groups of Patients Who Should Seek a diagnosis of CD (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011)

Patients with Strongly Suspected CD	**Patients with Moderately Suspected CD**	**Patients with First Degree Relative of CD**
This includes patients with typical symptoms, such as chronic malabsorption, repeated diarrhea, abdominal pain, abdominal distention, weight loss, muscle wasting, and dermatitis herpetiformis	This includes patients with atypical symptoms, such as vomiting, constipation, and dyspepsia; patients with extraintestinal symptoms such as ulcers, hyposomia, hypertransaminasemia, osteoporosis, osteopenia, tooth abnormalities, anemia, recurrent miscarriage, and infertility; patients with associated diseases, such as Type 1 diabetes mellitus, Down's syndrome, William's syndrome, IgA deficiency, and Turner's syndrome	Patients who have one relative or more with CD

1.6.1 Serum Antibody Markers

Many antibodies are used to screen for CD. These include

A) IgA Class Antitransglutaminase Antibody (tTG)

The IgA-TTG test with ELISA (enzyme-linked immunosorbent assays) is a first-line screening test (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011) and has the greatest sensitivity (98%) and specificity (90%) for diagnosing CD (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011). Moreover, the IgA-TTG test is less expensive than IgA class antiendomysial antibody (EMA) test (Ludvigsson et al., 2012). However, depending on the activity of the enzyme and the quality of the antigen TTG, the results of the ELISA assay may differ (Lindfors, Koskinen, & Kaukinen, 2011). For this reason, this test can yield false results (Lindfors, Koskinen, & Kaukinen, 2011). The false results yielded because of immunoglobulin A (IgA) deficiency and/or consuming food that is low in gluten content (Chow et al., 2012).

B) IgA Class Antiendomysial Antibody (EMA)

This test is less sensitive than the IgA-TTG test (90%) (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011). However, with an accuracy rate approaching 100%, the IgA-EMA has the highest specificity for celiac disease (Lindfors, Koskinen, & Kaukinen, 2011). Its drawbacks are that it is expensive, labor-

intensive, and subjective; that is, it needs to be done by experienced personnel (Lindfors, Koskinen, & Kaukinen, 2011).

C) IgA class antigliadin antibodies (AGA)

The level of sensitivity and specificity is lower than that of the tTGA and the EMA tests. It is not useful for adults and children over two years old (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011) However, it is the most sensitive test for children under two years old because it has a higher sensitivity than other tests for the first antibodies that appear in a child's life (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011).

1.6.2 Genetic Testing for CD

The human leukocyte antigens (HLA) DQ2 and DQ8 are the genetic factors associated with celiac disease (Lindfors, Koskinen, & Kaukinen, 2011). A genetic test that is positive for one or both of these antigens of the disease (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011). This test is not a diagnostic test, but can be used to exclude the possibility of celiac disease. These cases can include testing for a genetic predisposition in first-degree families, and when the histological test conflicts with the serological test. (Villanacci, Ceppa, Tavani, Vindigni, & Volta, 2011).

1.6.3 Small-bowel Mucosal Biopsy

A small-bowel mucosal biopsy is the gold standard for diagnosing celiac disease (Lindfors, Koskinen, & Kaukinen, 2011). This technique is used after screening for CD with serum antibody tests discussed in section 1.0 (Lindfors, Koskinen, & Kaukinen, 2011). When the celiac antibodies appear during a gluten-containing diet and disappear after a gluten-free diet, the bowel mucosal biopsy is performed to support the diagnosis (Lindfors, Koskinen, & Kaukinen, 2011). The small-bowel mucosal biopsy is the standard diagnostic test that is done both with positive antibodies or even if negative and suspicion high because of symptoms. (Lindfors, Koskinen, & Kaukinen, 2011). A review by Siddiqui and Osayande, 2011, suggested taking multiple specimens at the time of the biopsy. In a person with celiac disease, a small-bowel mucosal biopsy test shows intestinal damage with flattened mucosa and loss of villi. However, the intestine can recover if the person consumes a gluten-free diet for one year (Siddiqui & Osayande, 2011).

1.7 Treatment of CD

A gluten-free diet (GFD) is the only treatment for celiac disease (Siddiqui & Osayande, 2011). Consuming as little as 10-30 mg of gluten per day is considered to be toxic and causes intestinal damage (Siddiqui & Osayande, 2011). Grains containing gluten, such as wheat, barley, rye, and spelt, should be avoided (Lionetti & Catassi, 2011). **Table 1-4** shows the foods that are allowed on a GFD,

those that are not allowed, and the ingredients which should be checked to ensure they are gluten free, according to the Canadian Celiac Association.

Following a gluten-free diet for two weeks can improve clinical symptoms (Siddiqui & Osayande, 2011). However, many individuals with CD may take more time (months or years) to have complete resolution of gastrointestinal symptoms and/or malabsorption of nutrients (Lionetti & Catassi, 2011). Moreover, long-term treatment of celiac disease (one to two years) can improve the histological and serological signs (Lionetti & Catassi, 2011). However, following a GFD is difficult, especially in some places such as North America, Australasia, and Europe, because foods containing gluten are commonly consumed by individuals in these regions (Lionetti & Catassi, 2011). Moreover, a gluten-free diet is expensive, not easy to sustain, and not always available (Lionetti & Catassi, 2011).

Table 1-4: Shows the Foods that are Allowed, those that are not Allowed, and the Ingredients which Should be Checked to Ensure they are GF

Foods allowed	Food not allowed	Foods should be allowed only if labelled gluten-free
Basic food (unprocessed) products of: Vegetables/ Fruit Meat/ poultry/seafood Oils Dairy Beans/legumes Rice Honey Sugar Grains and baking products Baking soda Bean flour Buckwheat Chick pea flour/ corn flour Cornmeal/cornstarch Cream of tartar Flax Gelatin Green pea flour Gums Legumes Malto dextrin Mustard flour Potato flour/ potato starch Soya flour/ soya starch Spices Sweet potato Tapioca flour/tapioca starch Tofu/vanilla White vinegar	Food contains wheat, rye, or barley such as: Wheat bran/ wheat flour Wheat starch Oats [1] Atta Barley Beer Breading and bread stuffing Communion wafers Couscous Croutons Durum Graham flour Kamut Malt, malt extract, malt syrup and malt flavouring Malt vinegar Malted milk Modified wheat starch Rye bread and flour Seitan Semolina Spelt Triticale	Cheese Sauces Flavoured yogurt Rice and corn cereals Buckwheat pasta Seasoned or flavoured rice mixes Crackers/crackers Nuts or seeds Processed meat products: deli or luncheon meats, hot dogs Meat substitutes (e.g., vegetarian burgers, sausages) Dates French fried Canned soups Salad Dressings Cooking Spray Cake Potato chips Nuts and soy nuts. Flavoured teas or flavoured coffee Baking Powder Specialty mustards, mustard flour and curry paste

[1] In Canada, 88% of oat products are contaminated with gluten-containing grains (Koerner et al., 2011)/ Sources: Canadian Celiac Association http://www.celiac.ca/index.php/about-celiac-disease/ and Arnone and Fitzsimons, 2012.

1.8 Gluten-free Labelling

Labelling gluten-free products helps celiac patients to know which food products contain gluten, as well as saving them time when choosing food (Arnone & Fitzsimons, 2012). Labelling regulations differ from one country to another. According to the Canadian Celiac Association, by August 4, 2012, all products sold in Canada were to be labelled as containing gluten if the product's gluten level was greater than 10 ppm. In addition, food manufacturers were to identify sources of gluten, such as rye, wheat, and barley, if they were found in the product. Food manufacturers were advised to seek to avoid any cross-contamination (Diaz-Amigo & Popping, 2012). In addition, Health Canada Food Allergen Labelling (2012) indicated that the new labelling regulations required more details about the product ingredients. For example, more details concerning the constituent ingredients of margarines, flours, and seasonings were required, when previously this was not the case.

1.9 Cost of Gluten-free Products

Gluten-free products are more expensive than regular products, which affects compliance with a gluten-free diet. Researchers from the University of Dalhousie compared the prices of 56 gluten-free products with their equivalent gluten-containing products, and found that gluten-free products are 242% more expensive (Stevens & Rashid, 2008). Gluten-free soups and sauces were the most expensive, and cost 455% times more than their gluten-containing counterparts;

gluten-free meat products were the least expensive, and cost only 32% more (Stevens & Rashid, 2008). The high prices of these gluten-free products limit their availability, and leads to non-compliance with a gluten-free diet (Stevens & Rashid, 2008). Another study, conducted in the US, showed that the prices of the gluten-free products were greater than the comparable products by 240% (Lee et al., 2007). In this study, the prices of gluten free snacks, such as pretzels, cookies, and crackers, were significantly higher than those for the regular snacks. This study showed that the prices of gluten-free products in health food stores were 123% higher than the prices of the same products in regular stores (Lee et al., 2007). The author of this study concluded that these high prices may influence a celiac patient's diet compliance (Lee et al., 2007). Another recent study showed that gluten-free products were more costly than comparable products by 76-518% (Singh & Whelan, 2011). The same study found limited availability of gluten-free products, with an average of between 8.2 and 20 gluten-free products per store (Singh & Whelan, 2011). The highest availability of the gluten-free products was found in regular supermarkets, with a rate of 18/20 (90%), while the lowest availability was found in the corner shops, with rate of 1.8/20 (9%) (Singh & Whelan, 2011). Additionally, GFP may not reflect the typical foods consumed by individuals in some ethnic groups and limited availability of gluten free foods

may make it difficult to find foods within the diet; all of which may affect compliance to the GFD (Jeffrey et al., 2004).

To compensate for the high cost of gluten-free products, some countries are offering financial support to celiac patients (Garcia-Manzanares & Lucendo, 2011). For example, in some European countries, the financial assistance received by celiac patients ranges from 20-200 Euros per month (Garcia-Manzanares & Lucendo, 2011). In Canada, celiac patients receive financial assistance, in the form of a taxation rebate. According to the Canada Revenue Agency, the Government of Canada rebates an incremental cost, which is the difference between the prices of gluten-free products and their gluten-containing counterparts.

1.10 Nutritional Deficiency at Time of Diagnosis

Damage to the intestines of patients with celiac disease leads to many potential nutritional deficiencies, which often appear at the time of diagnosis. These include a suboptimal status of such nutrients as folic acid, iron, vitamin B12, Vitamin D, and calcium (Malterre, 2009; Bansal et al., 2011; Dickey, 2002; Stoian et al., 2011). We will review the studies that examined a serum nutritional status and nutritional intake in children and adults with celiac disease at the time of diagnosis.

1.10.1 Iron Deficiency

Iron deficiency is one of the most common symptoms of celiac disease discovered in adults and children at the time of diagnosis. It is usually the result of damage to the proximal intestine where iron is absorbed (Malterre, 2009; Bansal et al., 2011). A study conducted on 400 adults with celiac disease showed that 19% of females and 33% of males had iron deficiency anemia (Harper et al., 2007). A recent Indian study conducted on 83 celiac children between the ages of two and fourteen indicated that 98% had iron deficiency anemia at the time of diagnosis (Bansal et al., 2011). Another study looking at 168 Canadian celiac children between the ages of two and fifteen showed that 40% were anemic at the time of diagnosis (Rashid et al., 2005). A recent cross-sectional study which assessed the micronutrients status in patients with typical and atypical celiac disease between the ages of 1.6 and 75.4 showed that around 66% had an iron deficiency (Botero-Lopez et al., 2011). In addition, celiac disease has been found among people who have iron deficiency anemia (Cekin et al., 2012). A Turkish study of children with iron deficiency anemia showed that the prevalence of celiac disease among children who have iron deficiency anemia is 4.4% (Kalayci et al., 2005). In addition, a recent study found a prevalence of 7.14% of celiac patients among people with iron deficiency anemia (Cekin et al., 2012).

Celiac disease induced loss of appetite in children which leads to decrease the intake (Fasano, 2005; Lionetti & Catass, 2011). Iron deficiency found in children could be a result of a low intake of iron-rich food such as meat, meat products, brown bread, cereal, green leafy vegetables, rice flakes, and iron-fortified products (Kapur, 2003; Pynaert et al., 2005). A low iron intake has been found in children and adolescents. A Belgian study of adolescents between the ages of 13 and 18 showed that iron intake was below the recommended dietary allowance in 38.5% of females and 99.5% of males (Pyneart et al., 2005). Another study assessed the iron intake in children between the ages of 4 and 18, and found that the iron intake in girls was less than the intake in boys. The iron intake of 44% of the girls was less than the Lower Reference Nutrient Intake (Thane et al., 2003). A recent study examining the nutrition intake in early-diagnosed celiac adults (between 18-71 years old) found that the iron intake in 85% was below the recommended daily amounts (6mg/d) (Shepherd & Gibson, 2012).

1.10.1.1 Dietary Requirements for Iron

The Recommended Dietary Allowance (RDA) for iron is currently set at 7-10 mg/d for children under the age of 13, and for 8-15 mg/d for adolescents under age 18 years (**Table 1-5**).

Table 1-5: Recommended Daily Allowance for Iron in Children and Adolescents

Age (year)/Gender	RDA for Iron (mg/day)
1-3 y (Males, Females)	7
4-8 y (Males, Females)	10
9-13 y (Males, Females)	8
14-18 y (Males)	11
14-18 y (Females)	15

Source: Health Canada. 2009. http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-prod/monograph/mono_iron-fer-eng.php

1.10.1.2 Treatment of Iron Deficiency in Children and Adolescents with CD

Iron deficiency anemia in celiac disease can be treated with iron supplementation and/or by consuming a nutritionally complete GFD (Kapur et al, 2003). An Italian study showed that 77.8% and 94% of adults with celiac disease were successfully treated for iron deficiency anemia after following a GFD for six and twelve months respectively (Annibale et al., 2001). Iron supplements are recommended for patients who do not recover from iron deficiency after six months on a GFD (Malterre, 2009; Annibale et al., 2001). The recommendation for children with celiac disease who have iron deficiency anemia is to take iron

supplementation, in addition to consuming GF foods rich in iron (Kapur et al, 2003).

1.10.2 Folate Deficiency in CD

Folic acid deficiency has been found in people with celiac disease at the time of diagnosis. The deficiency is the result of an inflammation of the jejunum, where folic acid is absorbed (Garcia-Manzanares & Lucendo, 2011). A study of 156 adult celiac patients found 46% of the patients had a serum folic acid deficiency at the time of diagnosis (Dickey, 2002). Another study, conducted in the United States on 400 adult patients with celiac disease, showed that 10% of the males and 13% of the females had a serum folate deficiency at the time of diagnosis (Harper et al., 2007). A Finnish study on celiac adolescents and young adults between the ages of 16 and 25 found that 31% of the patients had a suboptimal status of blood folic acid at the time of diagnosis (Haapalahti et al., 2005). In addition, folic acid deficiency has been found to be positively associated with the severity of intestinal damage in children with celiac disease (Arikan et al., 2007). Suboptimal nutritional status could be a result of low intake of food rich in folate such as fruits, vegetables, cereal and dairy products (Baydoun et al., 2012). A recent study examining the nutrition intake in celiac adults (aged between 18-71 years old) at the time of diagnosis found that the folate intake in 85% was below the recommended daily intake (320µg/d) (Shepherd & Gibson,

2012). Folate deficiency in celiac disease can be treated with folate supplementation and a GFD (Halfdanarson et al., 2007).

1.10.3 Vitamin D and Calcium Status in CD

Vitamin D and calcium have been found to be deficient, at the time of diagnosis, in children and adults with celiac disease. This deficiency can cause bone disorders (Malterre, 2009). Vitamin D is a fat soluble vitamin important in building bone density (Malterre, 2009). Patients with better vitamin D status have a lower incidence of cancer, autoimmune disease, and hypertension (Engelsen, 2012). Moreover, the absorption of calcium, which is one of the bone-building nutrients, depends on the role that vitamin D plays in changing the gene expression of cells (Malterre, 2009). Calcium plays a significant role in enhancing bone development and achieving greatest peak bone mass (Hendrie et al., 2011). 25-hydroxy-vitamin-D (25(OH) D) is the indicator of vitamin D status in the body (Lerner et al., 2011). Health Canada (2012) indicates that a level of 25(OH) D <30 nmol/L is considered deficient, and is associated with bone health problems such as rickets and osteomalacia. Conversely, a level of 25(OH) D 50-75 nmol/L is deemed adequate. At serum amount of vitamin (D >125 nmol/L), "there may be reason for concern," according to Health Canada (2012).

Suboptimal vitamin D and calcium status has been shown to be highly prevalent in children and adolescents in Canada (Stoian et al., 2011). The major

risk factors for this is are related to poor dietary intake of vitamin D and poor sunlight exposure (Holick et al., 2011; Mager et al., 2012). The prevalence of healthy children living in Alberta who have vitamin D deficiency (25(OH) D3 ≤25 nmol/L) is 2%, and the prevalence of children who have inadequate vitamin D (25(OH) D3 between 25-75 nmol/L) is 37.4% (Stoian et al., 2011). The prevalence of healthy Canadian toddlers who have insufficient vitamin D status is 30% to 80% (Maguire et al., 2011). In the US, 40% of healthy children and toddlers have suboptimal vitamin D status (Gordon et al., 2008). A Canadian study found that 2.9/100,000 Canadian children have rickets (Ward, 2007).

In patients with untreated celiac disease, the prevalence of vitamin D and calcium deficiency at the time of diagnosis is higher than that found in healthy people, due to malabsorption and the inflammation of the small intestine, leading to poor bone health (Malterre, 2009). Many studies have shown that celiac patients have poor bone health at the time of diagnosis. A recent study found that 68% of adults with untreated celiac disease have low bone mineral density (Chakravarthi et al., 2012). A Canadian studied showed that vitamin D levels are insufficient for bone health in 60% of children with celiac disease (Mager et al 2012). Another Canadian study found that children with celiac disease suffered from poor bone health at time of diagnosis as well as after one year on a gluten free diet (Mager et al., 2012). In another study of children aged between 1.5 and

15 years, researchers compared levels of vitamin D and calcium in children with untreated celiac disease to those in healthy children, and they found that 25(OH) D3 and calcium levels in the celiac children were less than the levels found in healthy children. Also, ten of the celiac patients were osteopenic (Zanchi et al., 2008). A study comparing bone mineral content (BMC) in children with untreated celiac disease and control children also found that the children with celiac disease had poor bone health at the time of the diagnosis (Jatla et al., 2009). They found that spine (SP) and whole body (WB) bone mineral content (BMC) were lower in children with untreated celiac disease than in the control children (Jatla et al., 2009). Moreover, the risk of fracture is more common among adult celiac patients comparing with controls (Sánchez et al., 2011). However, there is no evidence that children with CD a have higher risk of fracture during childhood than children without CD (Ludvigsson et al., 2007)

Vitamin D and calcium deficiency found in children can be a result of low calcium and vitamin D intake (Holick et al., 2011). The Foods rich in vitamin D are salmon, herring, sardines, tuna, egg yolk, olive oil, fortified dairy products, and fortified juices (Holick et al., 2011). The dietary sources of calcium are dairy products such as cheese, yogurt, and milk (Hendie et al., 2011). The main source of vitamin D and calcium in Canadian children is milk (Gates et al., 2012), which is fortified by 100 IU/cup (Holick et al., 2011). Children who consume less than

200 IU/day could have a vitamin D deficiency (Stoian et al., 2011). Canada's Food Guide recommends that people over two years old consume two cups (500ml) of milk or fortified beverages every day. However, a recent study showed that the average milk intake in Canada is 0-1.5 cup/day, and the prevalence of children who consume milk as recommended by the Food Guide is only 32.5% (Hayek et al., 2010). Another study, of 156 Canadian children between the ages of eight and eleven, showed that the mean intake of milk was 1.3 cup/day, the mean intake of vitamin D and calcium from food was only 5.6 mcg/day and 908 mg/day respectively, and the mean intake of vitamin D from supplements and food together was 6.6 mcg/day (Mark et al., 2011). A recent Canadian study of 457 children from First Nations populations showed that 72.6-84.7% had an intake of milk and alternatives below the Canada Food Guide recommendations, and that the intake of calcium and vitamin D was less than the RDA by 86.2% and 96.4% respectively (Gates et al., 2012). A recent study examining the nutrition intake in newly diagnosed celiac adults (aged between 18-71 years old) found that the calcium intake in 64% was below recommended daily intake (840mg/d) (Shepherd & Gibson, 2012). Another Canadian study found that the calcium intake in 64% of newly diagnosed celiac children was below The Estimated Average Requirement (800 mg/d) (Mager et al., 2012)

1.10.3.1 Requirements for Vitamin D and Calcium

To maintain bone health, the RDA recommended by Health Canada for vitamin D is 600 IU/day, while for calcium it is 700-1300 mg/day for children and adolescents between the ages of three and eighteen. The upper intake of vitamin D, as Health Canada indicates, is 2400-4000 IU/day, while for calcium it is 2500-3000 mg/day. To avoid any adverse effects, Health Canada recommends that the intake of vitamin D and calcium should not exceed the upper intake. **Table 1-6** shows the RDA and the upper intake (UI) of vitamin D and calcium in children and adolescents, as stipulated by Health Canada (2012).

Table 1-6 shows the Recommended Dietary Allowance (RDA) and the Upper Intake (UI) of vitamin D and calcium in children and adolescents, as stipulated by Health Canada (2012)

Age group (year)	**Calcium (mg)**		**Vitamin D (IU)**	
	RDA[1] per day	**UI[2] per day**	**RDA[1] per day**	**UI[2] per day**
1-3 years	700	2500	600	2500
4-8 years	1000	2500	600	3000
9-18 years	1300	3000	600	4000
19-50 years	1000	2500	600	4000

[1] Recommended dietary allowance
[2] Upper Intake
Source: Health Canada 2012 http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php

A lack of exposure to the sun can be another reason for vitamin D deficiency found in celiac patients at the time of diagnosis, as the ultraviolet radiation exposure is important for the synthesis of vitamin D (Engelsen, 2010). A Canadian study found that the number of the hours of sunlight exposure did not differ significantly before and after one year of consuming a gluten free diet, which can contribute to poor bone health in children with celiac disease (Mager et al.,2012). Poor bone health in Canada, especially in northern Alberta, is a result of low ultraviolet radiation exposure, which can lead to a decrease in the synthesis of vitamin D (Hollis, 2005). The prevalence of Canadians who have insufficient vitamin D during the winter or spring is 97% (Schwalfenberg, 2007). A Canadian study found that 2.9/100,000 Canadian children have rickets, with the highest prevalence among children living in northern Canada (Ward et al., 2007). However, vitamin D deficiency in celiac patients has been seen even in sunny countries (Lerner et al., 2012). For example, a recent study showed that in Spain, 54.5% of adults with celiac disease have suboptimal vitamin D status (Lerner et al., 2012).

1.10.3.2 Treatment of Vitamin D and Calcium Deficiency

Vitamin D and calcium deficiency can be normalized in celiac disease sufferers by following a gluten-free diet and taking vitamin D and calcium

supplements (Duerksen et al., 2012). A recent study found that two years of a GFD and vitamin D and calcium supplements improved bone mineral density in hips by 60% and in the spine by 81% (Duerksen et al., 2012). Another study, conducted on Turkish children between the ages of two and sixteen, found that the levels of serum calcium and 25(OH)D3 were lower in children with untreated celiac disease, compared with patients who had been treated with a gluten-free diet for one year (Kavak et al., 2003). The same study found that bone mineral content (BMC) was significantly higher in patients who were being treated with a gluten-free diet (Kavak et al., 2003). However, a recent study showed that even after one year on a gluten-free diet, 25% of children and adolescents with celiac disease had suboptimal vitamin D status that coincided with suboptimal intake of vitamin D (Mager et al., 2012)

To prevent rickets in children, it is recommended that they consume 400 IU/day through supplements or diet (Ward, 2007). However, taking 400 IU of vitamin D3 supplements has been found to be inadequate to treat vitamin D deficiency in children with celiac disease (Dueksen et al., 2012). A recent study suggested that to normalize vitamin D levels, celiac children should take a weekly dose of vitamin D2 supplements of 50,000 IU for eight weeks (Dueksen et al., 2012). A supplement of 600-800 mg/day of calcium for children and 800-1200 mg/day for adults has been found to be sufficient to prevent bone loss (von Tirpitz

& Reinshagen, 2003). Another study showed that taking 1000 mg of calcium supplements with 400 IU of vitamin D3 improved hip bone density in adults who are at risk for fractures (Jackson et al., 2006).

1.10.4 Vitamin B_{12} Deficiency

Vitamin B_{12} deficiency is commonly found in celiac patients at the time of diagnosis. The causes of this deficiency are unknown, as vitamin B_{12} is absorbed in the terminal ileum which is not normally affected by celiac disease (Halfdanarson et al., 2007; Garcia-Manzanares & Lucendo, 2011). However, some studies suggest that vitamin B_{12} deficiency in celiac disease patients could be a result of bacterial overgrowth, reduced gastric acid, or an impaired small intestine (Halfdanarson et al., 2007).

Many studies have shown that celiac patients have a vitamin B_{12} deficiency at the time of diagnosis. A US study of 400 celiac adults showed that around 5% had serum vitamin B_{12} deficiency at diagnosis (Harper et al., 2007). Another study, conducted on 156 celiac patients older than 16 years of age indicated that 8% of the patients had a low serum vitamin B_{12} at the time of diagnosis (Dickey, 2002). A Turkish study, conducted on celiac children between the ages of one and sixteen found that vitamin B_{12} deficiency is positively associated with the total amount of villous atrophy in celiac patients (Arikan et al., 2007). However, vitamin B supplements can normalize B_{12} status even if

villous atrophy persists (Hadithi et al., 2009). Suboptimal vitamin B_{12} status can be a result of low intake of B_{12}-rich foods such as meat, eggs and milk (Baydoun et al., 2012).

1.10.5 Other Micronutrient Deficiencies

At the time of diagnosis, many micronutrient deficiencies such as copper, zinc, and magnesium have been found in celiac patients (Hogberg et al., 2009; Botero-Lopez et al., 2011; Rujner et al., 2004). For example, Hogberg et al. (2009) found that serum zinc levels in children with celiac disease were lower than the levels for children in the control group. A recent study assessed the nutritional status at diagnosis of 109 celiac patients between the ages of 1.6 and 75.4. Results showed that serum copper and serum zinc were deficient by 15% and 20%, respectively (Botero-Lopez et al., 2011). Another study compared the serum zinc status among individuals with celiac disease, Crohn's disease, and Wilson's disease, along with healthy individuals.

Celiac patients had a lower level of serum zinc at diagnosis than what was found in study subjects in the other groups (Ince et al., 2008). Another study, conducted on five females between the ages of 37 and 55, all of whom had recently been diagnosed with celiac disease, showed that four of them had a serum copper deficiency (Halfdanarson et al., 2009). Another study assessed the serum magnesium level in celiac children between the ages of five and eighteen,

and found that 21% of the children with celiac disease had a magnesium deficiency at the time of diagnosis (Rujner et al., 2004).

We will review the studies that assessed the nutritional status and nutritional intake in adults and children with celiac disease on GFD in the next section of this literature review.

1.11 Dietary Intake and Nutritional Status in Adults and Children with CD on GFD

A gluten-free diet is considered the only treatment for celiac disease (Siddiqui & Osayande, 2011). The diet has also been shown to be an effective treatment of a nutritional deficiency that appears at the time of diagnosis (Duerksen et al., 2012; Annibale et al., 2001). However, some studies have shown that celiac patients still suffer from the nutritional deficiency even after being treated with a gluten-free diet. There are many possible causes for such a deficiency/ deficiencies, malabsorption that is ongoing due to inadequate compliance with the GFD or suboptimal intake on a GFD. We will review the studies that have found a suboptimal intake in adults with celiac disease on a GFD in the next section of the literature review, as well as a limited number of studies that have found a suboptimal intake in children with celiac disease who were consuming GFDs.

Suboptimal intakes have been seen in adults with celiac disease who are on gluten-free diets. A British study assessed nutritional intake using a five-day food diary for 93 celiac patients between the ages of 21 and 79. All had been on a gluten-free diet for at least six months. One of the celiac patients was vegetarian and five of them excluded soya, egg and lactose from their diets. Compared with the northern region population in the UK, females with celiac disease in this study consumed more energy from all the macronutrients (protein, carbohydrate and fat) and more calcium and magnesium. However, these same women reported having a lower intake of fibre and a lower intake of some micronutrients including iron, zinc, magnesium, selenium, and folate. They had the same level of vitamin D intake as did the women in the UK Women Cohort Study (Wild et al., 2010). Men with celiac disease on a gluten-free diet in this study consumed more energy from fat and carbohydrates, compared with the data from the National Diet and Nutrition Survey (Wild et al., 2010). The researchers found that 47% of the energy consumed came from processed food and 17% of the energy intake comes from ready-to-eat meals (Wild et al., 2010). Kinsey, Burden, and Bannerman (2008), asked adult celiac patients mean age and (s.d.) were 58.6 (17) on gluten-free diets in the UK to keep a three-day food diary, and then assessed their daily intake. The results showed that protein consumption was higher in patients with celiac disease than in the control group. However, the consumption of fat, vitamin

D, and calcium was lower among celiac patients when compared with the control group (Kinsey et al., 2008). In addition, celiac patients on gluten-free diets reported having a poor vitamin status (Hallert et al., 2002). A Swedish study asked 30 celiac adults between the ages of 45 and 64 who had followed a gluten-free diet for at least eight years to keep a four-day food record (Hallert et al., 2002) and assessed their nutrient intake. The researchers found that the intake of vitamin B_{12} and folate in adults with celiac disease on gluten-free diets was less than the level in the control group. The intake of folate in both groups was below the Nordic Nutrition Recommendation (NNR) (300 µg) and the intake of B_{12} in both groups was above (NNR) (2 µg). However the intake of B_6 in celiac patients was similar the intake in the control group, and it was above (NNR) (1.5 mg) in both groups (Hallert et al., 2002). The same study found that compared to the control group, celiacs eat less fruit (Hallert et al., 2002) and more root vegetables and greens (Hallert et al., 2002). In addition, serum suboptimal vitamin B6 and folate status have been found in 20% and 37% of celiac patients respectively (Hallert et al., 2002). An American survey conducted to assess the nutrient intake of American adults with celiac disease who followed a gluten-free diet, and which used three-day food records, showed that most of the men and about half of the women surveyed met or exceeded the Recommended Intake of fibre (20-35g/d) (Thompson et al., 2005). It showed that iron intake had met or exceeded

the DRI (i.e., 8mg or 18 mg depending on the gender and age) in all of the men and around 44% of the women. The calcium intake had met or exceeded the DRI (1000mg or 1200mg depending on gender and age) in 63% of the men and 31% of the women (Thompson et al., 2005). The same study found that only 36% of celiac men and 4.6% of celiac women met the daily serving of grains recommended by the US food guide pyramid (i.e., 6 servings per day) (Thompson et al., 2005). The same study indicated that manyGF grains contain lower amounts of fiber comparing with gluten containing grains (Thompson et al., 2005).

Suboptimal food intake has been seen in children with celiac disease on gluten-free diets. A recent study of 54 children with celiac disease, between the ages of three and seventeen found that after one year on a gluten-free diet, 25% of children and adolescents with celiac disease had suboptimal serum vitamin D status that coincided with suboptimal intake of vitamin D. (Mager et al., 2012). Using five-day food records, a Swedish researcher assessed the dietary intake of 25 celiac children between the ages of seven and fourteen who followed a gluten-free diet (Ohlund et al., 2010). The results showed that the intake of fat, carbohydrates, and protein met the Nordic Nutrition Recommendation (NNR, 2004). However, the consumption of fibre and poly-unsaturated fatty acids was less than the Nordic Nutrition Recommendation (NNR, 2004). Moreover, the

consumption of saturated fatty acids and sucrose exceeded the Nordic Nutrition Recommendation (NNR, 2004). The study showed that the vitamin D intake of 68% of the children was below the average requirement (AR), and the intake of magnesium was less than the AR in 76% of the children with celiac disease. Additionally, the study showed that the intake of selenium was less than the AR in 56% of the children, and the intake of thiamin was below the AR in 28% of the children. Compared with controls on a normal diet, the children with celiac disease on a gluten-free diet in this study consumed less fibre and fewer micronutrients, such as vitamin D, riboflavin, magnesium, selenium, riboflavin, niacin, and thiamin. However, the intake of sucrose and saturated fatty acids was higher among children with celiac disease, as was the intake of iron and calcium (Ohlund et al., 2010). Another study, conducted in the Netherlands on celiac patients between the ages of 12 and 25 who were on a gluten–free diet found that the intake of iron and fibre was below the recommendations, while the intake of fat was greater than the Dutch recommendation (Hopman et al., 2006). A further study used a food-frequency questionnaire to assess the intake of magnesium in children with celiac disease, between the ages of five and eighteen who were on a gluten-free diet. Suboptimal intake of magnesium was found in 32% of treated patients and in 29% of untreated patients (Rujner et al., 2004). The same study found the intake of calcium in celiac patients was lower than the healthy controls

(Rujner et al., 2004). Serum magnesium deficiency was found in 19.6% of children with celiac disease on a gluten free diet (Rujner et al., 2004). A recent study assessing the intake of 18 children with CD and 18 healthy control children (median age, 7.6 years) found that the median energy intake in children with celiac disease is significantly higher than that among the healthy control group (Zuccotti et al., 2012). The researchers found the consumption of energy derived from fat and protein exceeded the recommendation (i.e., 9-12% for protein and 25-30% for fat) in both groups (Zuccotti et al., 2012). The intake of simple sugar exceeded the recommendation in both groups (<10%), and the intake of saturated fat was not significantly different in either group (Zuccotti et al., 2012).

Gluten-free products themselves have been found to have low levels of nutrients. A recent study conducted in Canada found that gluten free products have low levels of folate and iron comparing with gluten containing products (Kulai & Rashid et al., 2013). The GFD has been found to have high amounts of fat and sugar and low amounts of fiber, folate and iron (Saturni et al., 2010). This may be due to differences in micronutrient fortification (eg iron and folate) in gluten free products verses gluten free containing products. This may also result in higher levels of fat, sodium, simple sugar in GFP because of differences in food processing (Saturni et al., 2010; Thompson, 2000; Kulai & Rashid et al., 2013). For example, Thompson (2000) compared the amount of iron and folate in

gluten-free products with their gluten-containing counterparts, and found that approximately 81% of gluten-free cereal products have lower folate content, and 77% lower iron content. Thompson found that most of the gluten-free bread and pasta products are not fortified with either iron or folic acid (Thompson, 2000). Another Spanish study assessing the nutritional content of gluten-free bread found that many have lower protein and higher carbohydrate contents when compared to gluten-containing breads (Segura & Rosell, 2011).

1.12 Dietary Intake Assessment Methods

Dietary intake can be assessed by many methods, like direct observation, the Food Frequency Questionnaire (FFQ), the 24-hour recall, and the 3 to 7-day food intake record (Magarey et al., 2010; Henriquez-Sanchez et al., 2009; Ball et al., 2007). Doubly labeled water can be used to assess energy intake, and urinalyses can assess sodium intake (Burrows et al., 2010; Mann & Gerber, 2010). The most common methods to assess children's food intake are the FFQ, the 24-hour recall, and the 3- to 7-day food intake record (Magarey et al., 2010; Henriquez-Sanchez et al., 2009; Ball et al., 2007). Not every tool is ideal in all situations, as each tool has its strengths and weaknesses (Magarey et al., 2010; Henriquez-Sanchez et al., 2009). We will discuss these strengths and weaknesses, as well as the methods' validity in assessing children's dietary intake.

1.12.1 Food Frequency Questionnaire

The FFQ contains a list of food and beverages and a frequency section to report how often the participant consumed each food type during a time period, usually 1-12 months (Rockett et al., 2003). The participant indicates the item consumed and frequency of consumption, e.g., 1–2 per week, 1 per week, 2 per week, or 1 per day. The semi-quantitative FFQ lets participants choose food and pick from a list of portion sizes. For example, when participants choose milk, the corresponding portion size list includes standardized sizes, e.g., 1 cup. Participants indicate if they drank, for example, 1 cup, 1.5 cups, or 2 cups.

The FFQ's strengths are that it is relatively quick, easy, and inexpensive (Magarey et al., 2010; Molag et al., 2007). Additionally, the FFQ assesses specific nutrients such as Vitamin D and calcium intake in different food groups, and total diet through an extended period, usually 1-12 months (Magarey et al., 2010; Molag et al., 2007). It ranks individuals according to high, medium, and low nutrient intake (Magarey et al., 2010; Molag et al., 2007). It is more effective than other dietary assessment methods regarding usual diet in epidemiological studies (Henriquez-Sanchez et al., 2009; Magarey et al., 2010).

The FFQ's weaknesses are that portion sizes are difficult to estimate. Moreover, it relies on participants' memories and requires literacy and counting

(Henriquez-Sanchez et al., 2009; Magarey et al., 2010). Because children's cognitive ability is limited compared to adults', recalling food intake and portion sizes is more challenging (Faiedman et al., 2012). Caregivers should be asked to help children report food intake and portion sizes (Burrows et al., 2010; Andersen et al., 2011). However, some studies suggested that some parents do not know what their children eat in schools or daycares (Livingstons et al., 2004). Thus, including a day care provider in the assessment of the dietary intake is important. Portion size estimation, can improve with training and using portion size estimation aids like hold measures, picture booklet food photographs, and the computer-based Interactive Portion Size Assessment System (IPSAS) (Foster et al., 2009; Andersen et al., 2011; Small et al., 2012). Other FFQ limitations are that it must continually undergo redesigning to suit each target population in reflecting its cultural food items (Wakai, 2009). For example, Japanese researchers developed an FFQ with foods reflecting Japanese dietary habits (Wakai, 2009). The FFQ may result in over- or underestimation (Mulasi-Pokhriyal & Smith, 2012; Bertoli et al., 2005). For example, one FFQ overestimated children's calcium intake because it overestimated the portion size of milk and cheese (Vereecken et al., 2010). In addition, an FFQ was found to underestimate the percentage of energy from fat (Vereecken et al., 2010).

To assess the gluten intake in children 1-4 years old, an easy-to-use FFQ has been developed according to age-related food consumption (FQ-gluten4).

1.12.2 Twenty-Four Hour Recall

In the 24-hour recall dietary assessment method, a trained interviewer asks the participant about food and beverages consumed in the previous 24 hours, collecting data over 1 or more nonconsecutive days. A multiple pass technique provides details such as food type, brand names, and portion sizes. In the first pass, the interviewer asks the participant to list only the food and beverages consumed in the previous 24 hours. In the second pass, the interviewer requests more details about these food and beverages, such as brand names, preparation and cooking methods, and the name of the store or restaurant that provided the food (Bross et al., 2010). In the last pass, the participant estimates each food and beverage's portion size. Finally, the interviewer reviews the food list and details with the participant to make sure there are no missing items or mistakes.

The strengths of the 24-hour recall method are its low participant burden, detailed dietary information about 1 or more days, ability to be conducted over the phone, and no altered food choices the day before the interview. In addition, it is practical for assessing an individual or group's usual intake (Magarey et al., 2010; Arab et al., 2010).

The weaknesses of the 24-hour recall method are its reliance on memory, the participant's difficulty in estimating portion sizes, and its expense, as a trained interviewer must collect data (Magarey et al., 2010; Subar, 2007). Children's abilities to recall food intake and portion sizes are limited compared to adults' (Faiedman et al., 2012). Thus, caregivers/parents should help in diet recalls and portion size estimations that involve children (Andersen et al., 2011; Burrows et al., 2010). Portion size estimation, however, can improve with training and using portion size estimation aids listed above, including hold measures, picture booklet food photographs, and IPSAS (Foster et al., 2009; Andersen et al., 2011; Small et al., 2012). Another 24-hour recall limitation is that collecting one, 24-hour recall will not sufficiently represent an individual's typical dietary intake (i.e., it may not include seasonal variations) (Arab et al., 2010). Thus, 2 non-consecutive days of 24-hour recall should be used to assess a child's intake (Andersen et al., 2011). Taking the average of two consecutive days addresses the potential daily variations in food intake that occur.

Caregivers should help report their child's intake because reporting intake over a long time period (many days) will lower a child's burden for recall (Burrows et al., 2010). In addition, a 24-hour recall may result in over- or underestimation (Fisher et al., 2008; Rennie et al., 2006). For example, the 24-hour recall overestimated fat, fiber, sugar, iron, Vitamin D, and calcium because

food portion sizes were overestimated (Fisher et al., 2008). In addition, the 24-hour recall underestimated sodium by 50% (Leiba et al., 2005) and underreported energy intake (Rennie et al., 2006). In addition contrast to prospective diet records, 24 hour recalls do not require a high level of literacy in the interviewee. However, it requires the ability of the interviewer to have a high level of expertise regarding food portion size and types of foods consumed in a wide variety of populations (including in children) ; Thus, 24 hour recalls should be completed by a trained interviewer (Magarey et al., 2010).

1.12.3 Food Record (3-7 day food intake records)

In the food record dietary assessment method, the participant records all food and beverages consumed over several days, usually 3-7 (Bross et al., 2010). Most food records record serving sizes using portion size estimation aids (Bross et al., 2010).

The food record's strengths are its accuracy and exact, relative dietary information over an extended time, usually 3-7 days. Unlike the 24-hour recall, serving sizes are measured by portion size estimation aids including colored photographs, booklets, and household measures that can improve children's ability to assess portion size. In addition, unlike the 24-hour recall, a food record does not depend on memory (Bross et al., 2010; Magarey et al., 2010).

The food record's weaknesses are its expense and the counting and literacy necessary to complete it; the respondent burden is high because the participant must complete multiple records (Bross et al., 2010; Magarey et al., 2010; Rockett et al., 2003) and have a good ability to record food intake and measure food portion sizes. Thus, parents and caregivers should help report their children's intake to decrease the children's burden (Burrows et al., 2010). Some studies indicate that some parents do not know what their children eat in schools or daycares (Livingstons et al., 2004). This weakness can be overcome by including a daycare provider in the assessment of the dietary intake of the child. Moreover, participants can change food choices to make recording easier (Bross et al., 2010; Magarey et al., 2010; Rockett et al., 2003). The involvement of parents and caregivers in the assessment will help overcome another drawback of the food record: children's forgetting to record intakes (Bross et al., 2010; Burrows et al., 2010).

1.13 Validity of Dietary Assessment Methods

A tool's validity is its accuracy in assessing food intake (Burrows et al., 2010). To measure a tools' validity, each tool's data are compared with data from another reference tool (Burrows et al., 2010). For example, to measure the FFQ's validity, it was compared with the 24-hour recall method or food record, both of

which are considered reference methods. The correlation or comparing means presents the two tools' degree of agreement.

The validity of a dietary assessment method in a childhood population is affected by children's ability to estimate portion sizes, remember what foods they have eaten, and know different food types. Unless parents assist children (Livingstone et al., 2004), children's comparatively limited cognitive ability decreases the accuracy of recalling food intake and portion sizes (Faiedman et al., 2012). Children younger than 12 have a limited ability to recall intake (Livingstons et al., 2004). Recall skills improve rapidly from the 7-8 year age range (Livingstons et al., 2004). One study measured the ability of children ages 5-7 to recall their lunches; researchers found children's reporting accuracy ranged widely, from 0%-100% (Warren et al., 2003). The study suggested children can better recall familiar food (Warren et al., 2003). For example, the accuracy of recalling food brought from home was higher than the accuracy of recalling food the school provided (Warren et al., 2003). In addition, children were very good at recalling food they enjoyed, such as sweets (Warren et al., 2003). The percentage of accuracy for recalling sweets was 60% (Warren et al., 2003), though the recollection of leftovers was limited (Warren et al., 2003). This study's researchers suggested the reporter allow children to recall their intake without interruption. Afterward, the reporter can request food intake details, for example,

about main dishes, leftovers, and side dishes (Warren et al., 2003). As the time between consuming and recalling the food increases, recall accuracy decreases (Warren et al., 2003). To improve the accuracy of reporting children's intake, parents should be asked to help children report, especially children younger than 8 (Burrows et al., 2010). In addition, parents should assist children in reporting intake if the dietary assessment includes a long-time period (a week or more) (Burrows et al., 2010). Some studies suggested that some parents do not know what their children eat in schools or daycares (Livingstons et al., 2004). A recent Australian study found children 8-11 years old are more accurate about reporting their intake than their parents are (Burrows et al., 2012). The same study found mothers were less accurate than fathers in reporting a child's intake (Burrows et al., 2012).

The ability to estimate portion size and know different food types is limited in children (Livingstons et al., 2004). Children often do not pay attention to how much they eat (Livingstons et al., 2004). Adolescents 13-18 years old underestimated portion sizes of stable food (Korkalo et al., 2012). One study measured the ability of adolescents ages 13-18 to estimate portion size using food photographs. Only 20%-38% of adolescents estimated portion sizes accurately (Korkalo et al., 2012).

Portion size estimation aids like household measures and food photographs are considered effective in improving children and adolescents' accurate estimation of portion size (Livingstons et al., 2004). This portion size assessment tool can improve the accuracy of reporting portion size even in children 4-6 years old (Foster, 2008). Andersen et al. suggested using household measures and a picture booklet to help children assess intake portion sizes (Andersen et al., 2011). A recent study assessed how accurately Canadian youths 7-18 years old estimated portion sizes using measurement tools like household objects and modeling clay (Faiedman et al., 2012). The study found that using household objects — for example, a tennis ball is 0.5 cup, and an eraser, 1 teaspoon — improved portion size estimation up to 48%. Using modeling clay improved portion size estimation by 41% (Faiedman et al., 2012). The lowest accuracy of portion size estimation was found when using cups and spoons to assess children's portion sizes (Faiedman et al., 2012). Another study reported that 63.9% of youths 10-16 accurately assessed portion size using a line diagram; over- and underestimation were 18% and 18.1%, respectively (Thoradeniya et al., 2012). In addition, when combining two aids -- the line diagram and small photographs -- portion-size accuracy was a relatively high 68.3%. Overestimation was 11.8%, and underestimation was 19.9% (Thoradeniya et al., 2012). Another study found that when using food photographs and IPSAS, children's portion-size

estimation was as accurate as adults' (Foster et al., 2009). Using age-appropriate food photographs can improve the accuracy of children 4-11 years old estimating portion size: in such cases, underestimation is only 1% (Foster et al., 2006).

Some studies show that children may be more accurate at estimating portion sizes of the food they have been served than what they have consumed and leftovers (Foster, 2008). For example, youths 4-16 years old underestimated food served by only 2%, using the interactive portion size assessment system. Using photographs and food models, they overestimated their food served by 7% and 21% respectively (Foster, 2008). But the accuracy of reporting food consumed was lower. That's because using the interactive portion size assessment system the youths overestimated food consumed by 13%, and using photographs and food models, they overestimated by 18% and 46% respectively (Foster, 2008). Of the youths, 76% did not report leftovers (Foster, 2008).

The accuracy of reporting portion sizes increases by age (Foster, 2008). In addition, the time between consuming food and reporting portion size decreases as the accuracy of reporting portion size increases (Foster, 2008). Training could improve the accuracy of potion size estimation (Small et al., 2012). Last, caregivers should help children 4-6 years old assess portion size (Andersen et al., 2011).

1.12.1 Validity of FFQ

The FFQ is a valid tool for assessing children's calcium and Vitamin D intake. An adequate agreement has been reported between the reference method and the FFQ, with a correlation range of 0.8–0.4. **Table 1-7** summarizes the FFQ's validation studies that were used to assess children's Vitamin D and calcium intake. FFQ can overestimate some nutrients, due to portion size estimation errors (Vereecken et al., 2010). The estimation of calcium and Vitamin D intake is associated with the estimation of food and beverages (such as fortified milk) containing Vitamin D and calcium (Marshall et al., 2003; Vereecken et al., 2010). Thus, the underestimation of Vitamin D and calcium is the result of study subjects' underestimating their milk intake (Marshall et al., 2003). In addition, underestimating children's calcium intake results from underestimating their milk and cheese intake by 26% and 25%, respectively (Vereecken et al., 2010). But an FFQ's overestimation of calcium intake is comparable with the 24-hour recall (Moore et al., 2007). That overestimation results from either the long list of foods that make children feel they must choose more items than they consume or the 24-hour recall's underestimation of calcium intake (Moore et al., 2007). Moreover, the FFQ overestimated calcium intake compared with the food record by 48% (Bertoli et al., 2005).

The researchers attributed this overestimation to the long list of items in the FFQ or to children indicating foods high in calcium in the FFQ but not consuming the same food during the days they recorded intake during the 7-day recording period (Bertoli et al., 2005). The FFQ's reliability and validity was more accurate in children than in adolescents, and in younger children compared to older children (Bertoli et al., 2005; Harnack et al., 2006). Harnak et al. found that the FFQ's validity and reliability in assessing calcium intake was higher in children 11-12 years old compared with adolescents 13-14 years old, and higher in girls compared to boys (Harnack et al., 2006). The reason is calcium FFQ in that study more relative to younger children than older children and females than males (Harnack et al., 2006).

Table 1-7: Validation Studies of FFQ in Assessing Vitamin D and Calcium Intake in Children

Author/year	Sample Size: Population Demographics	Reference method for validation	Nutrients assessed in the study	Study conclusions
Bertoli et al., 2005	6–10 years and 16–20 years (n=37)	Seven-day weighted food record	Calcium	Adequate agreement between FFQ and food record, with correlation values of 0.5 for 6–10 years and 0.6 for 16–20 years, indicating that FFQ is a useful tool in assessing calcium and vitamin D in children.
Marshall et al., 2003	6–12 months and 3–5 years (n=240)	Four 24-hour recall	Calcium and vitamin D	Adequate correlation found between FFQ and 24-h recall. (6–12) months: calcium (0.64–0.67), vitamin D (0.6–0.8), 3–5 years: calcium 0.64–0.74, vitamin D 0.63–0.74)
Moore et al., 2007	9–12 years and 14–16 years (n=162)	One 24-hour recall	Calcium	FFQ is a useful tool for assessing calcium and vitamin D in children, with correlations between FFQ and reference method of 0.46 for 9–2 years and 0.43 for 14–16 years.
Harnack et al., 2006	11–14 years (n=248)	Three 24-hour recall	Calcium	The correlation between FFQ and 24-h recall was 0.43 for calcium. Thus, FFQ is considered an appropriate tool for assessing calcium intake in children.

Author/year	Sample Size: Population Demographics	Reference method for validation	Nutrients assessed in the study	Study conclusions
Taylor et al., 2009	12–18 years (n=107) females	Four-day food record (3 weekend days and 1 weekday)	Calcium and vitamin D	FFQ is a useful tool for assessing calcium and vitamin D in children, with the correlation values of 0.65 for calcium and 0.78 for vitamin D.
Vereecken et al., 2010	3–15 years (n=216)	Three-day food diary	Calcium	Overestimation of calcium because of overestimation of milk and cheese intake.

1.12.2 Validity of 24-hour Recall

The 24-hour recall method has been found to be an accurate tool for assessing macronutrients and micronutrients in children and adults (Holmes et al., 2008; Frankenfeld et al., 2012). However, some nutrient intake is overestimated, which could be a result of people overestimating portion sizes (Fisher et al., 2008). **Table 1-8** summarizes the validation studies of 24-hour recall in assessing vitamin D, calcium, iron, fat, fiber, and sugar in children and adults.

Table 1-8: Validation Studies of 24-hour Recall in Assessing Vitamin D, Calcium, Iron, Fat, Fiber, and Sugar in Children and Adults

Author/year	Age of the sample/ sample size (n)	Reference method for validation	Nutrients assessed in the study	Study conclusions
Holmes et al., 2008	2–17 years (n=124)	Four-day weighted food record	Fat, fiber, iron, and calcium	By comparing the means of the nutrients in the 24-h recall and reference methods, it was concluded that 24-h recall is the most useful tool for assessing food intake in children in low-income households.
Frankenfeld et al., 2012	18–62 years (n=93)	Four-day food record	Saturated fat, fiber, calcium, and iron	Adequate correlation between the 24-h recall and reference methods: 0.54 for saturated fat; 0.4 for fiber; 0.6 for calcium; and 0.3 for iron. Thus, 24-h recall is an appropriate tool for assessing dietary intake in adults.
Thakwalakwa et al., 2012	15 months old (n=169)	Single weighted food record	Fat and iron	Adequate agreement between 24-h recall and food record, with correlation values of 0.65 for fat and 0.8 for iron, indicating that 24-h recall is an appropriate tool for assessing these nutrients in young children.

Author/year	Age of the sample/ sample size (n)	Reference method for validation	Nutrients assessed in the study	Study conclusions
McNaughton et al., 2005	43 years (n=2265)	Five-day food record	Fat, fiber, iron, and calcium	Adequate agreement between the 24-h recall and food record with correlation values (women/men) of (0.56/0.45 for calcium; 0.51/0.48 for iron; 0.47/0.42 for fat; and 0.56/0.56 for fiber, indicating that 24-h recall is a useful tool for assessing these nutrients in adults.
Fisher et al., 2008	7–24 months old (n=157)	Three-day weighted food record	Fat, fiber, sugar, iron, vitamin D, and calcium	24- h recall overestimated the nutrients because of portion size assessment errors.

In conclusion, dietary intake can be assessed by many methods, including direct observation, the Food Frequency Questionnaire (FFQ), 24-hour recall, 3- to 7-day food intake record and doubly labeled water (Magarey et al., 2010; Henriquez-Sanchez et al., 2009; Ball et al., 2007; Burrows et al., 2010). Each tool has strengths and weaknesses in assessing food intake in children, as discussed previously. In addition, the dietary assessment has been more challenging in children than in adults, due children's limited ability to estimate portion sizes,

remember what they have eaten, and accurately name food types (Livingstone et al., 2004). Thus, to improve the accuracy of reporting children's intake, it is recommended that parents and caregivers help children report their intake (Burrows et al., 2010). In addition, portion size assessment tools and training have helped to improve the accuracy of reporting children's portion sizes (Foster, 2008; Small et al., 2012).

1.13 Conclusion

GFD is the only treatment for celiac disease (Duerksen et al., 2012; Annibale et al., 2001). It treats the damage that gluten can cause to the small intestine of individuals with the disease. Consuming a GFD improves the overall nutritional status in celiac children by reducing the potential for malabsorption of the nutrients that are important to childhood growth and development (Duerksen et al., 2012). However, some studies have shown that some adults with CD who consume a gluten free diet still suffer from suboptimal nutritional status for many reasons. Low intake of some nutrients such as iron, magnesium, folate, vitamin D, calcium and vitamin B_{12} can be one of these reasons (Wild et al., 2010; Kinsey et al., 2008). However, only a limited number of studies have examined the nutritional intake in children and adolescents with celiac disease who consume a gluten-free diet. Most of these studies have shown that children with CD on the GFD have suboptimal intake of iron, vitamin D, calcium, and fiber, and a high

intake of saturated fat and sugar compared to the dietary recommendations and/or control groups (Rujner et al., 200; Ohlund et al., 2010). Limited data are available regarding the nutritional adequacy of the GFD in children in Canada. The focus of this thesis is to assess dietary intakes of iron, calcium, vitamin D, fiber, saturated fat, folate, vitamin B_{12} and sugar in children and adolescents with celiac disease on a gluten free diet and to compare intakes of these nutrients with the intake of age-matched children and adolescents in a control group (children with other chronic gastrointestinal disorders). Comparison with recommended daily allowances for each of these nutrients was done to determine the nutritional adequacy of the GFD.

Chapter 2: Research Plan

2.1 Study Rationale

Celiac disease (CD) is a chronic autoimmune disorder in the small intestine caused by an immunological reaction to gluten, a protein that is found in wheat, barley, rye, and spelt products (Siddiqui & Osayande, 2011). This disease is very common and affects approximately 1% of the world's population (Mahadov& Green, 2011). Although diagnosed in adulthood, CD is most often diagnosed in early and late childhood. The cause of CD is an immunological reaction to dietary gluten (found in wheat, rye, barley etc.) in individuals who are HLA-DQ2/HLA-DQ8 carriers (Newton & Singer, 2012). A diet containing gluten, is responsible for the immune response that leads to intestinal damage. At time of diagnosis, the damage to the intestine of patients with CD causes a deficiency in some nutrients such as folic acid, iron, vitamin B_{12}, Vitamin D, and calcium due to malabsorption (Malterre, 2009; Bansal et al., 2011; Dickey, 2002; Stoian et al., 2011). This can place a child with celiac disease at increased risk for suboptimal nutritional status.

A gluten-free diet is the only treatment for CD. It has been shown to be an effective treatment for the underlying damage that gluten can cause to the small intestine (Duerksen et al., 2012; Annibale et al., 2001). This may resolve or

improve the overall nutritional status in children with Celiac Disease. However, some studies have shown that celiac patients still suffer from a nutritional deficiency even after being treated with a gluten-free diet. The cause of this appears to be multi-factorial, but low intakes of iron, folate, vitamin D, calcium and vitamin B_{12} have been shown to occur with a GFD (Wild et al., 2010; Kinsey et al., 2008). Thus, it is important to assess the nutritional intake in in children with celiac disease since children need sufficient nutrients to grow. However, only a limited number of studies have examined the nutritional intake in celiac children and adolescents who consume a gluten- free diet. Most of these studies have shown that children with CD on GFD consume lower amounts of iron vitamin D, calcium, and fiber compared to recommended amounts (Rujner et al., 200; Ohlund et al., 2010). However, the intake of sugar and saturated fat has been shown to be higher among children with CD on GFD compared to control groups (Ohlund et al., 2010). Additionally, suboptimal intake of vitamin B_{12} and folate has been found in adults with celiac disease on gluten-free (Hallert et al., 2002).

The purpose of this study is to assess the dietary intake of vitamin D, calcium, iron, fiber, sugar, folate, vitamin B_{12} and saturated fat in celiac children and adolescents on GFD because only a limited number of studies have examined these nutrients in these groups. The study will also compare their intake with the

intake of age-matched children and adolescents in a control group who attended the GI clinic.

2.2 Hypotheses & Objectives

Hypothesis 1: Children and adolescents with CD on gluten free diets (GFD) will have higher intakes of simple sugars/saturated fat than GI controls (control children who have other GI disorders (such as abdominal pain, functional constipation and gastroesophageal reflux) and lower intakes of calcium and vitamin D, iron, folate, fiber and vitamin B_{12} than controls.

Hypothesis 2: The intake of children with CD on GFD will not meet the Dietary Reference Intakes (RDI) of calcium and vitamin D, iron, folate, fiber and vitamin B_{12} and the intake of total sugar and saturated fat exceeded the recommendation.

Objective 1: To determine the level of vitamin D, calcium, saturated fat, folate, vitamin B_{12}, fiber and iron in children and adolescents with celiac disease on GFD and in age-matched control children and adolescents who attend the gastroenterology (GI) clinic, and compare them with Dietary Reference Intake (DRI).

Objective 2: To compare the level of vitamin D, calcium, saturated fat, fiber, folate, vitamin B_{12} and iron in children and adolescents with celiac disease on GFD with age-matched control children and adolescents who attend the GI clinic.

Chapter 3: Dietary Intake in Children and Adolescents with Celiac Disease on Gluten Free Diet

3.1 Introduction

Celiac disease (CD) is a chronic autoimmune disorder in the small intestine caused by an immunological reaction to gluten, a protein that is found in wheat, barley, rye, and spelt wheat products (Siddiqui & Osayande, 2011). The damage to the intestine causes malabsorption of many nutrients such as folic acid, iron, vitamin B_{12}, vitamin D, and calcium in adults and children with CD. (Malterre, 2009; Bansal et al., 2011; Dickey, 2002; Stoian et al., 2011). This malabsorption can lead to an increased risk for suboptimal nutritional status at time of diagnosis in CD (Malterre, 2009). The main treatment for CD is a gluten free diet (GFD) (Duerksen et al., 2012; Annibale et al., 2001). The consumption of the GFD by children with celiac disease can improve their overall nutritional status by reducing the potential for malabsorption of nutrients that are important to growth and development in childhood (Duerksen et al., 2012). While many individuals with CD may respond immediately to the GFD by significant reductions in gastrointestinal inflammation and malabsorption, others may take more time (>6 months) to have complete resolution of gastrointestinal symptoms and/or malabsorption of nutrients (Lionetti & Catassi, 2011). This may mean that it can take a substantial period of time for a child and/or adolescents with newly

diagnosed CD to recover from deficits in overall nutritional status even while on the GFD.

One main challenge for children on the GFD is access to affordable, available and nutritiously dense GF foods; all of which may influence the overall nutritional status of the child and adolescent with CD on the GFD. Suboptimal nutritional status has been found in some adults and children with CD even after consuming a gluten free diet (Wild et al., 2010; Kinsey et al., 2008). Low intake of some nutrients such as iron, magnesium, folate, vitamin D, vitamin K, calcium and vitamin B_{12} on the GFD may be one of the reasons that patients with CD on the GFD experience poor nutritional status. (Wild et al., 2010; Kinsey et al., 2008; Mager et al., 2012). Alternatively, a lack of adherence to the GFD by an individual with CD may result in sustained mucosal damage in the small intestine resulting in malabsorption of these nutrients and overall impaired nutritional status. In childhood, the number of studies that have examined nutritional intake in children and adolescent with celiac disease who consume a gluten- free diet is very limited. A few studies have found that children with CD on the GFD have suboptimal intake of some nutrients such as iron, vitamin D, calcium, fiber and high intakes of saturated fat and sugar comparing with control groups (healthy age-matched controls) and/or current nutritional recommendations for intake (Rujner et al., 200; Ohlund et al., 2010). In Canada, limited data are available

regarding the nutritional intake of Canadian children and adolescent with celiac disease on the GFD. Preliminary data suggest that the nutrient content of gluten free containing foods are higher in simple sugar, total fat, saturated fat and lower in nutrients such as folate , iron and some B vitamins (Saturni et al., 2010; Thompson, 2000; Kulai & Rashid et al., 2013, Mager et al 2012). Most of these differences are due to the fact that gluten free grain products are not fortified (folate) and/or enriched (iron) with nutrients to the same extent as gluten containing foods and that food processing has altered the nutrient content and density in these foods(fat, sodium and simple sugar content) when compared to gluten containing foods (Saturni et al., 2010; Thompson, 2000; Kulai & Rashid et al., 2013). Low iron intakes has been found in some studies in adults and children with CD (Wild et al.,2010; Ohlund et al., 2010), but whether this is due to reductions in intake of heme sources of iron or alterations in non-heme sources of iron in the diet is unclear. Gluten free products themselves have been found to have low levels of iron comparing with gluten containing products (particularly grains) (Thompson, 2000).

Other nutrients found to be at risk in adults and children with CD included B_{12}, vitamin D and calcium. In patients with untreated celiac disease, the prevalence of vitamin D and calcium deficiency at the time of diagnosis is higher than that which has been found in healthy people, due to malabsorption and the

inflammation of the small intestine, leading to poor bone health (Malterre, 2009). Additionally, low intake of vitamin D and calcium had been found both in the general population in Canada and in children and adults with CD; all suggestive that these nutrients are at risk in children on the GFD (Hayek et al., 2013, Mager et al 2012, Whiting et al 2012)); all indicating that vitamin D is a nutrient at risk in the child with CD. Low intake of vitamin B_{12} has been found in adult with CD on GFD (Hallert et al., 2002). CD is common among South Asian population comparing with other non-Europeans living in Europe (Butterworth et al., 2005). The prevalence of celiac disease among second-generation immigrants from South Asia in Sweden is 2% (Ludvigsson et al., 2011). Serum vitamin B_{12} deficiency is more common in South Asian population comparing with the general population in Canada because of the vegetarian diet (Gupta et al.; 2004). Finally, some studies have that shown that children with CD on the GFD have suboptimal intake of fiber and higher intake of saturated fat and sugar comparing with the recommendations and/or healthy children likely due to the higher fat and sugar and lower fiber content in the GFD (Rujner et al., 200; Ohlund et al., 2010, Saturni et al 2010). Taken all together this data suggests that children with CD are at risk for suboptimal nutritional intake.

The extent to which suboptimal nutrient intake is an issue in Canadian children with CD on the GFD is unknown, as currently few data are available

regarding dietary intake in children with CD in Canada. The study objective was to assess the dietary intake of iron, calcium, vitamin D, fiber, folate, vitamin B_{12} saturated fat and sugar in children and adolescent with celiac disease on a GFD and to determine if current intakes of these nutrients meet recommended levels of intake (DRI). The second objective was compare the intake of children with celiac disease on GFD with the intake of age matched control children and adolescent with other chronic gastrointestinal disorders. The hypothesis are that children and adolescent with CD on gluten free diet (GFD) will have higher intakes of simple sugars/saturated fat than GI controls (control children who have other GI disorder (such as abdominal pain, functional constipation and gastroesophageal reflux) and lower intakes of calcium and vitamin D, iron, folate, fiber and vitamin B_{12} than controls. The second hypothesis is that intakes of children with CD on GFD will not meet the DRI recommendations of calcium and vitamin D, iron, folate, fiber and vitamin B_{12}.

3.2 Methods

3.2.1 Patient Population and Study Design

This is a pilot, cross sectional study, that evaluated dietary intake in children and adolescent (aged three to eighteen years of age) with celiac disease and in children without CD (disease controls) who attend GI Clinics at the Stollery Children's Hospital, Edmonton Alberta. Children with CD were

recruited at time of routine clinic visit in the Celiac Clinic at Stollery Children's Hospital, Edmonton, Alberta. Control children who have other GI disorders (such as abdominal pain, functional constipation and gastroesophageal reflux) and who have had routine screening to rule out a diagnosis of CD in the GI Clinic at Stollery Children's Hospital, Edmonton, Alberta. **Table 3-1** summarizes the study inclusion/ and exclusion criteria.

Table 3-1: The Inclusion and Exclusion Criteria

Inclusion Criteria	**Exclusion Criteria**
1- The Cases: All children (3-18 years) clinically diagnosed with CD using biopsy as the diagnostic standard. **2- The Controls**: All children (3-18 years) referred to the GI clinic for other GI disorder (such as abdominal pain, constipation, gastroesophageal reflux and GERD) who have had screening blood work done to rule out a diagnosis of CD.	1-Children with additional medical and nutritional diagnosis known to influence overall dietary intake such as children who are undergoing dietary treatment for an underlying nutrition issue such as obesity and type 1 diabetes. 2-Children with other disease such as inflammatory bowel disease, CF and short bowel syndrome. 3-Children with wheat allergies or multiple food allergies such as peanut allergy and milk allergy. 4-Children with enteral or parenteral nutrition support.

A sample size of 40 participants in each group (CD/GI control) was determined to be sufficient to detect a 35% differences in dietary intake (calcium and vitamin D intake) between the two groups with an alpha of 0.05 and βof 0.8.

Only preliminary results for GI controls (n=23) and CD (cases; n=25) are presented within this current thesis chapter.

Ethics Approval was obtained from the Human Research Ethics Board at University of Alberta. Administrative and Operational Approval obtained from the Stollery Children's Hospital, Northern Clinical Trials Centre at AHS and Alberta Health Services (AHS), University of Alberta, Covenant Health. Informed consent/assent was obtained for all participant and/or their responsible caregivers prior to study enrollment (**Appendix B: Information /Assent/ Consent Forms**).

3.2.2 Anthropometric and Demographic Data

Anthropometric data were measured in both children with celiac disease and control children at time of routine clinic visits using validated methodologies. Weight was measured to the closest 0.1 kg by an upright scale (Sunbeam Products, Inc., Pelstar LLC, Alsip, IL, USA). Height was measured to the closest 0.1cm, using a wall-mounted stadiometer (Holtain Ltd, Crymych, Dyfed, UK) without shoes. These data were collected from the charts at time of recruitment.

Weight-for-age z-score (wt-z), Height-for-age z-score (ht-z), body mass index (BMI) and BMI z-score (BMI-z) were calculated by Epi Info 3.5.1 software™ (Atlanta, GA, USA) using Centre for Disease Control (CDC) growth standards (Delucchi et al., 2011). Additional data (age at time of diagnosis,

current age at time of assessment, gender, and presence of gastrointestinal symptoms and family history of celiac disease were reviewed in the patients with celiac disease only. Current age at time of visit, gender and the reason of visiting GI clinic were reviewed in control children. This information is collected as part of routine clinical care.

3.2.3 Dietary Intake Assessment

3.2.3.1 24 Hour Recall for Assessment of Macronutrient and Micronutrient Intake (Including Calcium and Vitamin D)

Dietary intake of calcium, vitamin D, saturated fat, iron, sugar and fiber, folate, vitamin B_{12} were assessed by validated 24-hour recalls (using the multi-pass technique) for two different days (one weekend and one weekday) in both children with celiac disease and control children (Holmes et al., 2008; Frankenfeld et al., 2012). The 24-h recalls were administered by trained graduate students and by undergraduate students for NUTR 400/401. In general, most of the parents/responsible caregivers shared in answering questions, particularly for those children under the age of 10 years of age. If responses between the child and parent differed in terms of food intake, particularly if during a time the parent was not present during a meal (such as in the daycare/school environments), then the child's answer was considered the most reliable as there is evidence that parents may be less aware of food consumption in these settings. (Livingstons et al., 2004).

A total of two 24 hour recalls per participant was part of the study protocol. The first 24-h recall was collected at time of visit in the clinic following subject enrollment and consent, and the second 24-h recall was collected by phone 1-2 weeks after the clinic visit. . Twenty-four hour recalls (using the multi-pass technique) were used to provide details like food type, brand names, and portion sizes (Bross et al., 2010). In the first pass, the participants were asked to list only the food and beverages consumed in the previous 24 hours. In the second pass, participants were asked to provide more details about these food and beverages, like brand names, preparation and cooking methods, and the name of the store or restaurant that provided the food (Bross et al., 2010). In the last pass, the participant estimates each food and beverage's portion size. The portion sizes were assessed using hands dimension.The landmarks of the hands were used to assess the portion sizes of the food. For example, a size of the fist = 1 cup serving of rice or cereal, palm of the hand= 3-ounce of chicken or beef and the size of a thumb = 1-ounce of cheese. Only 7 children with CD and 9 GI controls completed two days of 24-hour recall (one weekend and one weekday) and the rest of the participants (n=18 children with CD and n=14 GI controls) completed one day 24-hour recall. The children who completed the two days, completed one weekday (Monday-Friday) and one day weekend (Saturday or Sunday) and the children who completed one day, completed only weekday (Monday-Friday).

Finally, the serving sizes of the different food groups were evaluated based on Alberta Nutrition Guidelines for Children in different age group and gender (Downs et al., 2011). Nutritional intake obtained from the 24-hour recalls was analyzed using Food Processor ® (SQL 10.6 ESHA Research, Salem, OR, USA) (Mager et al., 2012). Calcium, vitamin D, saturated fat, iron and fiber, folate, vitamin B_{12} intake in the cases and the control were compared to the Dietary reference intakes (DRI) for age and gender (Otten et al., 2006).

Food sources of vitamin D and calcium in Figure 3-1 were classified according to the food frequency questionnaire (Taylor et al., 2010). Vitamin D and calcium food sources from 24-h recall (Figure 3-2 and Figure 3-3) were classified according to the four food groups (meat and alternatives, dairy products, vegetable and fruits and grains). Milk was considered as a separate category because it is the main source of vitamin D and calcium in Canada (Gates et al., 2012). Additional categories were added according to what children and adolescent commonly eat such as fast food (e.g. pizza, burger, French fries etc.) and sweets (e.g. cookies, candies, ice cream etc.). The main sources of iron, folate and vitamin B12 from 24-h recall (Figure 3-4, 3-5 and 3-6) were classified according to the four food groups (meat and alternatives, dairy products, vegetable and fruits and grains) and according to what kids commonly eat (e.g. fast food and sweets). The food sources of fiber, saturated fat and total sugar from

24-h recall (Figure3-7, 3-8 and 3-9) were classified according to the four food groups (meat and alternatives, dairy products, vegetable and fruits and grains) and according to what kids commonly eat (e.g. fast food and sweets). In the food sources of saturated fat, fats and oils (e.g. butter, margarine and oils) was considered as a separate category. In the food sources of total sugar, beverages (e.g. juices, tea and cola) were considered as a separate category.

3.2.3.2 Food Frequency for Assessment of Vitamin D and Calcium Intake

Vitamin D and calcium intake was also assessed using a validated food frequency questionnaire in both children with celiac disease and control children (Bertoli et al., 2005; Marshall et al., 2003). The assessment of vitamin supplementation (D, calcium and other micronutrients) was included in FFQ. The FFQ were administered by trained graduate students and undergraduate students for NUTR 400/401. Both the child/adolescents and their parents answered the questions. The participants were asked to choose the food they consumed from a list of food and beverages and the frequency of consumption (e.g., 1–2 per week, 1 per week, 2 per week, or 1 per day). Additionally, the children picked the portion size of that food consumed from a list of portion sizes. For example, when they choose milk, the corresponding portion size list includes standardized sizes (e.g., 1 cup, 1.5 cups, or 2 cups). The portion sizes were assessed using hands dimension.The landmarks of the hands were used to assess the portion sizes of the

food. For example, a size of the fist = 1 cup serving of rice or cereal, palm of the hand= 3-ounce of chicken or beef and the size of a thumb = 1-ounce of cheese. The FFQ used in this study is validated in assessing vitamin D and calcium in children and adolescents (Taylor et al., 2010).

3.2.4 Laboratory Variables

The following data were collected at time of the clinical visit from patient's clinical charts: results from routine clinical blood work included plasma concentrations of aTTG (antitransglutaminase antibody) and ferritin, phosphorus, calcium and 25 hydroxycholecalciferol (25(OH) D). All blood work was collected as a part of routine clinic assessment and the data collected from chart review at time of subject recruitment.

For purposes of this analysis, the serum 25(OH) D level above 75nmol/L was defined as optimal, serum 25(OH)D 50 –75nmol/L level was considered suboptimal and serum 25(OH)D level below 50nmol/L was considered deficient (Holick, 2007). Only blood work completed within 2-3 months of the clinic visit or at the time of the actual clinic visit was collected. All blood work was analyzed by Laboratory Services Alberta Health Services (AHS) following standardized protocols from the Core Laboratory (Synchron LX Systems Analyzer; Beckman Coulter, Fullerton, CA). Serum 25(OH) D was analyzed using LCMS (Liquid chromatography–mass spectrometry) following standardized protocols from the

Core Laboratory (Synchron LX Systems Analyzer; Beckman Coulter, Fullerton, CA).

3.2.5 Statistical Method

SPSS Statistics (version 19, SPSS Data Collection, Chicago, USA, 2010) was used in our study and ($p<0.05$) was considered statistically significant. Shapiro-Wilk test was used for testing the distribution of all outcome variables for normal distributions. To compare between children with CD and GI controls, independent T-test analysis was used for those variables demonstrating normal distributions. Mann-Whitney Test was used instead of T- test, for those variables demonstrated skewed distributions (not normally distributed). To assess the interrelationships between age (> and < 10 years), gender, age at diagnosis (CD), presence of GI symptomology (treated as a categorical variable) and duration of CD on macronutrient intake we performed a series of 2 x 2 ANOVA with and without interaction terms. When the interaction term was not significant ($P>0.05$), the terms were removed from the relevant study model. Where necessary the data were adjusted for potential confounders (such as age, gender). The Pearson correlation (r^2) was used to assess the interrelationship between anthropometric data/ macronutrients/ micronutrients and the duration of disease/ age of diagnosis

The F- test of homogeneity was used to test whether or not differences in the variability of individual nutrient intakes differed in children who had only one day of food intake assessment (24- h recall) versus the variability of nutrient intake as assessed by two different days of intake (24 –h recall). The F- test of homogeneity was done to assess the variability of data within-and-between groups. The Fisher-exact test was used to assess for differences in frequency of the number of patients who met/did not meet the DRI of the nutrients for age and gender. The data for 2 x 2 analysis was adjusted foe age and gender.

3.3 Results

3.3.1 Anthropometric and Demographic Data

Anthropometric and demographic data are presented in **Table 3-2**. The mean age of diagnosis above or equal to 10 years old was (11.0 ± 2.4) and the mean age of diagnosis of children below 10 years old was (4.8 ± 2.5) with (P=0.00). The number of females is significantly higher than the number of males (p=0.029); with females predominating the CD group. Weight (p=0.05) and weight-for-age-z score (p=0.046) was significantly higher in children in the GI group comparing with children with CD (p=0.05). When assessed for differences in age (> and < 10 years), children with CD above the age of 10 had a lower weight-for-age z scores than those children below 10 years of age ($p<0.05$). Additionally, BMI in GI control children are significantly higher than in children

with CD (p=0.007). No other significant differences in the other anthropometric data were found between children with CD and GI controls (p>0.05).

The interrelationship between Anthropometric data with age of CD diagnosis and duration of CD disease are presented in **Tables 3-4** and **3-5**. The mean duration of CD and the mean age at diagnosis were 2 ± 1.3 years and 8 ± 4.0 years, respectively. The effect of duration of the disease and Age (above and below 10 years of age) on anthropometric data are represented in (Appendix C **Table C-1).**

3.3.1.1 Interrelationships between Anthropometric Variables and GI Symptomology, Duration and Age at time of CD Diagnosis

Anthropometric and demographic Data for children with CD with-and-without GI symptoms are presented in **Table 3-3**. While all GI control patients had GI symptomology (major reason for referral), 11 GI children had abdominal pain, 5 had constipation, 2 had dysphagia, 2 had nausea and vomiting, 1had chronic diarrhea, 1 had epigastria and 1 had Gastroesophageal reflux disease (GERD), only 16 out of 23 children with CD had any GI symptoms at time of assessment. In the CD group, BMI-for-age z-score was significantly higher in children without GI symptoms comparing with children with GI symptoms (p=0.035) (**Table 3-3**). Weight, height and BMI were positively related to age at diagnosis (**Table 3-4**). In contrast, weight-z and height-z scores were significantly

lower in children with longer disease durations (P<0.05) (**Table 3-5**). This appeared to be the most apparent in children who were above 10 years of age (Appendix C **Table C-1**) where weight- z scores (-0.87 ± 1.3 vs. 0.37 ± 0.63) were all significantly lower than the weight-z scores for children with CD under the age of 10; particularly those with diagnosis with longer disease durations.

Table 3-2: Anthropometric and Demographic Data (Celiac and GI control)

Variables	**Celiac** [1,2] F=21/ M=4	**GI Control** [1] F=12/ M=11	**P<0.05** [4]	**P<0.05** [5]
Age (years)	10.3±4.0 (3.9-17.0)	11.9±-3.7 (5.5-17.9)	0.136	-
Height (cm)	139.5± 21.1 (109.1-181.7)	151.8± 24.1 (112.7-191.9)	-	0.083
Weight (kg)	34.1±13.2 (17.40-61.6)	47.8±21.42 (19.6-89.2)	-	0.050
BMI (kg/m^2)	16.8±2.1 (12.7-20.8)	19.6±4.2 (14.3-29.0)	0.007	-
Height-for-age z-score[3]	-0.06±1.47 (-2.17-2.90)	0.48±1.24 (-2.35-2.69)	0.185	-
Weight-for-age z-score[3]	-0.35±1.24 (-3.33-1.46)	0.41±1.29 (-2.08-3.13)	0.046	-
BMI-for-age z-score[3]	-0.33±1.07 (-2.88-1.31)	0.24±1.08 (-1.75-2.82)	0.075	-

[1] Values are shown as mean ± standard deviation (range)

[2] Only 24 children with CD have anthropometric data

[3] They were calculated by Epi Info 3.5.1 software (Atlanta, GA, USA) using Centre for Disease Control (CDC) growth standards (Delucchi et al., 2011).

[4] P value from T-test (P<0.05 considered significant)

[5] P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-3: Anthropometric and Demographic Data for Children with CD with GI Symptoms and Without GI Symptoms

Variables	Celiac with GI symptoms [1,2] **F**=14/ **M**=2	Celiac without GI symptoms[1,2] **F**=6/ **M**=2	P<0.05[4]	P<0.05[5]
Age (years)	10.8±4.1 (4.5-17.0)	10.017±3.6362 (5.3-15.3)	0.668	-
Height (cm)	139.1±22.6 (109.1-181.7)	140.2±19.2 (110.8-164.5)	0.903	-
Weight (kg)	32.9±13.7 (17.4-61.6)	36.4±12.6 (19.40-53.0)	0.566	-
BMI (kg/m^2)	16.3±1.9 (12.7-20.1)	17.9±2.2 (15.69-20.82)	0.082	-
Height-for-age z-score[3]	-0.30±1.63 (-2.00-3.00)	0.43±1.02 (-1.00-2.00)	0.257	-
Weight-for-age z-score[3]	-0.73±1.32 (-3.00-1.00)	0.41±0.59 (0.00-1.00)	-	0.098
BMI-for-age z-score[3]	-0.65±1.12 (-3.00-1.00)	0.30±0.62 (-1.00-1.00)	0.035	-

[1]Values are shown as mean ± standard deviation (range)

[2]Only 24 children with CD have GI symptomology data

[3]They were calculated by Epi Info 3.5.1 software (Atlanta, GA, USA) using Centre for Disease Control (CDC) growth standards (Delucchi et al., 2011).

[4]P value from T-test (P<0.05 considered significant)

[5]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-4: Interrelationship between Anthropometric Data and Age of Diagnosis

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Weight	Age at diagnosis	0.497	0.014
Height	Age at diagnosis	0.622	0.001
BMI	Age at diagnosis	0.425	0.038
Weight-for-age z-score	Age at diagnosis	-0.233	0.273
Height-for-age z-score	Age at diagnosis	-0.057	0.791
BMI-for-age z-score	Age at diagnosis	-0.396	0.056

[1]P<0.05 considered significant

Table 3-5: Interrelationship between Anthropometric Data and Duration of CD

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Weight	Duration of CD	0.223	0.294
Height	Duration of CD	-0.139	0.516
BMI	Duration of CD	0.088	0.683
Weight-for-age z-score	Duration of CD	-0.488	0.016
Height-for-age z-score	Duration of CD	-0.502	0.012
BMI-for-age z-score	Duration of CD	-0.222	0.297

[1]P<0.05 considered significant

3.3.2 Laboratory Data

Laboratory data are presented in **Table 3-6** for children with CD only. The laboratory data for serum 25(OH) D were available in (n=18) children with CD. 8 children out of 18 children had normal serum 25(OH) D (>75 nmol/L), 5 children had 25(OH) D (50-75 nmol/L) and 5 children had 25(OH) D below 50 nmol/L. ATTG level was normal in 12 out of 22 children with CD and the rest of them had high ATTG level (>7 U/mL). The laboratory data for ferritin were available in (n=22) children with CD, two of them had abnormal ferritin levels (less than 12 ug/L) and the rest (n=20) had normal ferritin levels.

Interrelationships between vitamin D, iron and duration of the disease and blood test are presented in (Appendix C **Table C-2)**. No significant interrelationship between ATTG level and vitamin D level were found when vitamin D and ATTG was treated as continuous or categorical variables ($p>0.05$). No significant different in ATTG level and 25(OH)D (nmol/L) level between the children above and below 10 years old with CD or between males and females were observed ($p>0.05$) . No significant different were found in ATTG level between celiac patient with GI and without GI symptomology.

Table 3-6: Laboratory Data in Children with CD

Variables n=18	Mean ± Standard Deviation (range)	Reference Range
25(OH)D (nmol/L)[2]	68.3±19.9 (34.0-101.0)	>75
Ferritin (ug/L)[1]	25.1±15.2(8.0-62.0)	12-300
ATTG (U/mL)[1]	10.6±10.4(1.0-45.0)	<7

[1]n=22
[2]n=18

3.3.3 Dietary Data

3.3.3.1 24-Hour Recall Data: Adjustments for Variations in Macronutrient Intake or Variability of the Data

Only 7 children with CD and 9 GI controls completed two days of 24-hour recall (one weekend and one weekday) and the rest of them (n=18 children with CD and n=14 GI controls) completed one day 24-hour recall. The children who completed the two days, completed one weekday (Monday-Friday) and one weekend (Saturday or Sunday) and the children who completed one 24 hr recall, completed only one weekday (Monday-Friday). There were no significant differences in the mean intake and/or variability (standard deviation) in the intake of energy, protein, carbohydrate, fat, vitamin D, calcium, vitamin B_{12}, iron, folate, fiber, saturated fat and total sugar. between weekend and weekdays for those children that completed a one day 24 hour recall (weekday) verses those that completed 24 hour recalls conducted on two different days (one weekend, one weekday) ($p>0.05$) (Appendix A, **Figure A-1, A-2, A-3**). Therefore, it was not

necessary to adjust any of the macro-and-micronutrient intake data for differences due to variations in assessment of intake of energy, protein, carbohydrate, fat, vitamin D, calcium, vitamin B_{12}, iron, folate, fiber, saturated fat and total sugar) between the children who had one 24 hour recall completed verses those that had two 24 hour recalls conducted. Although energy intake did not differ between groups, we also expressed nutrient intake on a per 1000 kcal basis (Appendix A, **Table A-9** and **Table A-10**). This data will be referred to in each individual section.

3.3.3.1. A Macronutrients Intake (Protein, Fat, Carbohydrate)

The macronutrient intake of the children with CD and GI controls is presented in **Tables 3-7 and 3-8**. Macronutrient intake in children with CD with GI symptoms and without GI symptoms is presented in **Table 3-9**. To assess the interrelationships between age (> and < 10 years), gender, age at diagnosis (CD), presence of GI symptomology and duration of CD on macronutrient intake we performed a series of 2 x 2 ANOVA. These are presented in (Appendix C **Table C-3, C-4, and C-5).** All of these analyses were performed in all the sections related to dietary intake. There were no age (> and < 10 years) or gender effects on macronutrients intake between groups ($p>0.05$). The only major difference observed in nutrient intake, was that children with CD had higher intakes of protein on an absolute per gm basis. Macronutrients intake in children with CD

with (ATTG>10.4) and (ATTG<10.4) is presented in (Appendix A, **Table A-7**). The intake of carbohydrate in celiac patient with (ATTG<10.4) (268.9 ± 68.1) is significantly higher than celiac with (ATTG>10.4) (175.6 ± 85.1) with (p=0.010).

3.3.3.1. B Macronutrient Intake Adjusted for Energy Intake (per 1000 kcal basis)

Macronutrients intake adjusted for energy (per 1000Kcal) is presented in Appendix A, **Table A-9**. After adjusted macronutrient intake on a per 1000 kcal basis, we observed that the GI control children consume a significantly higher amount of percentage of energy as carbohydrate (%) than children with CD (p=0.025). No significant different in macronutrients intake between children above and below 10 years old were found after data were expressed on a per 1000 kcal basis. In contrast, children with CD without GI symptomology consumed significantly higher intakes of carbohydrate (151.6 ± 12.2 g/d) comparing with celiac patients with GI symptomology (121.2 ± 32.4 g/d) (p=0.018). No significant relationship between the duration of the disease /age at diagnosis with macronutrients intake were observed.

Table 3-7: Proportion of children with Celiac Disease and GI Controls that met Recommended levels of Intake (DRI) for Macronutrients as Assessed by 24 hour Recall.

		Celiac M=4/F=21		GI Control M=12 /F=11		
Variables	**DRI**	**(n) met DRI**	**(n) not met DRI**	**(n) met DRI**	**(n) not met DRI**	**P<0.05[4]**
Energy (kcal)[1]	900-2600	24	1	19	4	0.180
Protein (g)[2]	13-52	25	0	21	2	0.224
Protein %[3]	5-30	25	0	23	0	-
Carbohydrate (g)[2]	130	23	2	20	3	0.292
Carbohydrate %[3]	45-65	18	7	20	3	0.292
Fat %[3]	25-40	18	7	16	7	1.00

DRI: Dietary Reference Intakes

[1]EER: Estimated Energy Requirement (Otten et al., 2006)

[2]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[3]AMDR: Acceptable Macronutrient Distribution Range (Otten et al., 2006)

[4]P<0.05 considered significant

Table 3-8: Macronutrient Intake in Children with CD and GI Controls as assessed by 24 hour Recall

Variables	Celiac [1] F=21/ M=4	GI Control[1] F=12/ M=11	DRI	P<0.05[5]	P<0.05[6]
Energy (kcal)[2]	1678±479 (822-2563)	1427±501 (696-2514)	900-2600	0.084	-
Protein (g)[3]	72.1±25.7 (22.5-151.4)	56.4±23.9 (20.0-122.4)	13-52	-	0.014
Protein %[4]	17.3±4.6 (11.0-28.1)	15.7±3.0 (9.2-21.8)	5-30	-	0.392
Carbohydrate (g)[3]	223.9±85.0 (55.8-379.9)	195.4±61.5 (90.5-305.4)	130	0.193	-
Carbohydrate %[4]	52.7±12.1 (20.3-74.9)	55.8±9.2 (37.2-70.8)	45-56	0.338	-
Fat (g)	56.6±20.3 (23.1-98.6)	49.2±28.9 (19.1-147.2)	-	0.307	-
Fat %[4]	31.0±9.3 (12.8-54.8)	30.1±8.5 (18.1-52.7)	25-40	0.740	-

[1]Values are shown as mean ± standard deviation (range)
DRI: Dietary Reference Intake.
[2]EER: Estimated Energy Requirement (Otten et al., 2006)
[3]RDA: Recommended Dietary Allowance (Otten et al., 2006)
[4]AMDR: Acceptable Macronutrient Distribution (Otten et al., 2006)
[5]p value from T-test (P<0.05 considered significant)
[6]P value of Mann Whitney test when the assumption of normality not met
(Food and Nutrition Board of Institute of Medicine of The Medicine Academes; 2005)
(P<0.05 considered significant)

Table 3-9: Macronutrient Intake in Children with CD with-and without GI symptomology

Variables	Celiac with GI symptoms [1,2] **F**=14/ **M**=2	Celiac without GI symptoms[1,2] **F**=6/ **M**=2	DRI	P<0.05[6]	P<0.05[7]
Energy (kcal)[3]	1691±495 (998-2563)	1662±511 (822-2346)	900-2600	0.896	-
Protein (g)[4]	76.6±27.4 (38.4-151.4)	62.6±22.3 (22.5-87.1)	13-52	-	0.159
Protein %[5]	18.5±5.0 (11.2-28.1)	14.8±2.6 (11.0-19.8)	5-30	-	0.076
Carbohydrate (g)[4]	210.1±91.5 (55.6-379.89)	250.6±74.7 (137.9-339.7)	130	0.292	-
Carbohydrate %[5]	48.5±13.0 (20.3-74.9)	60.6±4.9 (53.4-67.1)	45-56	0.018	-
Fat (g)[4]	61.7±19.8 (24.3-98.6)	48.3±20.0 (23.1-87.5)	-	0.133	-
Fat %[5]	33.9±10.0 (12.8-54.8)	26.0±5.0 (18.9-33.6)	25-40	0.047	-

[1]Values are shown as mean ± standard deviation (range)

[2]Only 24 children with CD have GI symptomology data

DRI: Dietary Reference Intake.

[3]EER: Estimated Energy Requirement (Otten et al., 2006)

[4]RDA: Recommended dietary allowance (Otten et al., 2006)

[5]AMDR: Acceptable Macronutrient Distribution (Otten et al., 2006)

[6]p value from T-test (P<0.05 considered significant)

[7]P value of Mann Whitney test when the assumption of normality was not met (P<0.05 considered significant)

Table 3-10: Interrelationships between Macronutrient Intake and Age of Diagnosis

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Protein	Age at diagnosis	0.288	0.162
Carbohydrate	Age at diagnosis	-0.019	0.929
Fat	Age at diagnosis	0.004	0.987

[1]P<0.05 considered significant

Table 3-11: Interrelationships between Macronutrient Intake and Duration of CD

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Protein	Duration of CD	0.164	0.433
Carbohydrate	Duration of CD	0.192	0.359
Fat	Duration of CD	0.052	0.805

[1]P<0.05 considered significant

3.3.3.2 Micronutrients, Saturated fat, Fiber and Total sugar intake

Micronutrients intake (iron, folate, B_{12}, calcium and vitamin D), saturated fat, fiber and total sugar are presented in **Table 3-12.** No significant different between children with CD and GI control in micronutrient (vitamin D, calcium, iron, folate, vitamin B_{12},), fiber, saturated fat and total sugar intake was observed. Micronutrient intake in children with CD with and without GI symptomology is presented in **Table 3-13**. A comprehensive analysis of the amount, comparison with the dietary reference intakes (DRI) and the major food sources consumed

within the diets of follows these tables for each nutrient. Each section contains an analysis of the important factors (presence of GI symptomology, age of the child, duration of CD, age at CD diagnosis), ATTG level and presence of micronutrient supplementation and the interrelationships this has on individual nutrient intake.

Table 3-12: Micronutrient Intake in Children with CD and GI Controls as Assessed by 24- hour Recall

Variables	Celiac [1] F=21/ M=4	GI Control[1] F=12/ M=11	DRI	P<0.05[6]	P<0.05[7]
Vitamin D (IU)[4]	214±168 (24-592)	147±104 (17-359)	600	-	0.288
Calcium (mg)[4]	927±479 (363-1865)	754±399 (150-1595)	700 - 1300	-	0.212
Iron (mg)[2]	10.7±4.2 (4.6-24.9)	11.9±3.6 (4.0-16.4)	7-15	-	0.489
Fiber (g)[3]	17.2±7.5 (5.9-33.8)	14.6±7.7 (5.9-41.4)	19-38	0.242	-
Saturated Fat (g)	20.9±8.4 (8.6-37.0)	18.0±10.9 (4.1-47.4)	-	0.299	-
Saturated Fat %[5]	11.41± 4.30 (6.54-26.7)	10.99±4.10 (2.20-18.8)	-	-	0.812
Vitamin B_{12} (µg)[2]	3.4±2.0 (1.2-8.4)	2.6±1.6 (0.4-5.3)	0.9-2.4	-	0.209
Folate (µg)[2]	153.0±99.0 (35.4-423.4)	212.1±108.1 (61.7-446.9)	150-400	-	0.054
Total Sugar (g)	77.5±38.2 (26.7-159.4)	67.3±35.2 (3.3-157.2)	-	0.342	-
Total Sugar %[5]	18.94±7.72 (5.0-32.8)	18.98± 7.89 (1.45-30.9)	-	0.991	-

[1]Values are shown as mean ± standard deviation (range)

DRI: Dietary Reference Intake.

[2]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[3]AI: Adequate Intake (Otten et al., 2006)

[4]RDA for calcium and vitamin D are from health Canada 2012 source: http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php

[5]Saturated fat recommendation (<10%) of total Energy and total sugar (<25%) of the total energy, Source: (Food and Nutrition Board of Institute of Medicine of The Medicine Academes; 2005)

[6]p value of T-test (P<0.05 considered significant)

[7]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-13: Micronutrient Intake in Children with CD with and without GI Symptomology based on 24 hour Recall

Variables	Celiac with GI symptoms [1,2] **F**=14/ **M**=2	Celiac without GI symptoms[1,2] **F**=6/ **M**=2	DRI	P<0.05[6]	P<0.05[7]
Vitamin D (IU)[4]	195±173 (24-592)	223±156 (55-422)	600	-	0.668
Calcium (mg)[4]	787±393 (368-1865)	1101±524 (363-1831)	700 - 1300	-	0.178
Iron (mg)[2]	10.4±4.6 (5.1-24.9)	11.4±3.7 (4.63-16.6)	7-15	-	0.178
Fiber (g)[3]	16.9±6.4 (5.9-32.8)	18.6±9.8 (6.0-33.8)	19-38	0.623	-
Saturated Fat (g)	22.4±8.1 (11.81-37.0)	18.6±9.1 (8.6-36.0)	-	0.298	-
Saturated Fat %5	12.4±4.9 (6.5-26.7)	9.7±2.1 (7.2-13.8)	-	-	0.159
Vitamin B_{12} (µg)[2]	3.2±1.9 (1.2-8.4)	3.3±1.4 (1.4-4.9)	0.9-2.4	-	0.624
Folate (µg)[2]	174.0±114.8 (35.4-423.4)	191.5±82.7 (60.34-315.3)	150-400	-	0.298
Total Sugar (g)	63.4±32.2 (26.7-115.5)	104.0±38.6 (53.5-159.4)	-	0.012	-
Total sugar %[5]	17.9±7.7 (1.5-30.9)	21.4 ±7.7 (4.5-32.8)	-	0.180	-

[1]Values are shown as mean ± standard deviation (range)

DRI: Dietary Reference Intake.

[2]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[3]AI: Adequate Intake (Otten et al., 2006)

[4]RDA for calcium and vitamin D are from health Canada 2012 source: http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php

[5]Saturated fat recommendation (<10%) of total Energy and total sugar (<25%) of the total energy, Source: (Food and Nutrition Board of Institute of Medicine of The Medicine Academes; 2005)

[6]p value of T-test (P<0.05 considered significant)

[7]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

3.3.3.2. A Vitamin D and Calcium Intake by Diet Only

Dietary intake of calcium and vitamin D was assessed using two different methods: FFQ and 24 hour recalls. The data for calcium and vitamin D intake without supplementation are shown in **Tables 3-12, 3-14**. None of the children with CD and GI control meet the RDA for vitamin D by diet alone; only 7 with CD and 4 GI control met the RDA for calcium by dietary intake only. **(Table 3-14).** Vitamin D and calcium intake by FFQ without supplementation in children with CD and GI controls is presented in **Table 3-15.** The Comparison between FFQ and 24-hour recall in vitamin D and calcium intake by diet only is presented in **Table 3-16**. FFQ values for estimation of calcium intake were significantly higher than the 24 hour dietary estimates ($p<0.05$) in the children with CD; primarily due to higher estimates of the frequency of intake of such dairy products as cheese. No differences in vitamin D intakes were noted between dietary intake methods of assessment using the two tools (FFQ and 24 hr recalls).

3.3.3.2. B Interrelationships between Demographic Factors and Vitamin D and Calcium

The effect of age (below and above 10 years old) and gender on vitamin D and calcium intake (by diet only) is presented in (Appendix C **Table C-6 and Table C-7).** There was no age (below and above 10 years old) effect on vitamin D and calcium intake. Females consumed a significantly higher amount of vitamin D than males. After adjusting the data for gender, there were no significant

differences in the vitamin D intake between children with CD and GI controls. The effect of age and duration of the disease on Vitamin D and Calcium Intake (by diet only) is presented in (Appendix C **Table C-8)**. Interrelationships between vitamin D and calcium intake (by diet only) and age of diagnosis are presented in **Table 3-17.** Interrelationships between vitamin D and calcium intake (by diet only) and duration of the disease are presented in **Table 3-18.** Females consumed a significantly higher amount of vitamin D than males. Vitamin D and calcium intake without supplementation in children with CD with (ATTG>10.4) and (ATTG<10.4) is presented in Appendix A **Table A-8**. There were no significant differences in vitamin D and calcium intake in children with CD with (ATTG>10.4) and (ATTG<10.4) ($p>0.05$).

3.3.3.2. C Vitamin D and Calcium Intake after Adjustment for Energy Intake

Vitamin D and calcium intake adjusted for energy (on a per 1000Kcal basis) is presented in (Appendix A, **Table A-10).** No significant different were noted between children with CD and GI control in vitamin D and calcium intake after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant different between children above and below 10 years old in vitamin D and calcium intake after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant different between celiac with GI symptomology and celiac without GI symptomology in vitamin D and calcium intake after adjusted for energy (per 1000Kcal) ($p>0.05$).

No significant interrelationship between vitamin D or calcium intake with duration of disease / age at diagnosis ($p>0.05$) after adjusted for energy (per 1000Kcal).

Table 3-14: Proportion of Children with CD and GI controls that met Recommended Levels of Intake (DRI) for Vitamin D and Calcium without Supplementation as Assessed by 24 hour Recall

		Celiac M=4/F=21		GI Control M=12 /F=11		
Variables	**DRI**	**(n) met DRI**	**(n) not met DRI**	**(n) met DRI**	**(n) not met DRI**	**P<0.05[2]**
Vitamin D (IU)[1] without supplementation	600	0	25	0	23	-
Calcium (mg)[1] without supplementation	700 - 1300	7	18	4	19	0.773

DRI: Dietary Reference Intakes
[1]RDA: Recommended Dietary Allowance (Otten et al., 2006)
[2]P<0.05 considered significant

Table 3-15: Vitamin D and Calcium intake by FFQ without Supplementation in Children with CD and GI Controls

Variables	Celiac[1] F=21/ M=4	GI Control[1] F=12/ M=11	P<0.05[2]	P<0.05[3]
Vitamin D without supplementation (IU)	218±139 (39-476)	196±188 (16-76)	-	0.242
Calcium without supplementation (mg)	1348±570 (668-2755)	992±713 (101-3056)	0.061	-

[1]Values are shown as mean ± standard deviation (range)

[2]p value of T-test (P<0.05 considered significant)

[3]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-16: Comparison between FFQ and 24-hour Recall in Vitamin D and Calcium Intake by Diet Only

Variables		FFQ[1]	24-hour recall[1]	P<0.05[2]
Vitamin D (IU)	Children with CD	218±139	213±168	0.691
	GI controls	196±188	147±103	0.606
Calcium (mg)	Children with CD	1348±570	927±479	0.004
	GI controls	992±713	754±398	0.307

[1]Values are shown as mean ± standard deviation (range)

[2]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-17: Interrelationships between Vitamin D and Calcium intake (without Supplementation) and Age of Diagnosis

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[2]
Vitamin D[1]	Age at diagnosis	0.126	0.548
Calcium[1]	Age at diagnosis	-0.143	0.494

[1]Vitamin D and Calcium without supplementation
[2]P<0.05 considered significant

Table 3-18: Interrelationships between vitamin D and Calcium Intake (without Supplementation) and Duration CD

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[2]
Vitamin D[1]	Duration of CD	-0.207	0.320
Calcium[1]	Duration of CD	-0.370	0.069

[1]Vitamin D and Calcium without supplementation
[2]P<0.05 considered significant

3.3.3.2. D Vitamin D and Calcium Intake (Diet and Supplementation)

Two sets of data were used to determine the effect of supplementation; the data from the 24 hour recall and the FFQ data.

A) Vitamin D and Calcium Intake Assessment by 24 hour Recall (Diet + Supplementation)

Table 3-19 summarizes vitamin D and calcium supplementation in children with CD and GI controls in this study. The proportion of children with CD and GI controls that met recommended levels of intake (DRI) for vitamin D and calcium with supplementation as assessed by 24 hour recall is presented in

Table 3-20. Table 3-21 presents the common multivitamin supplementation in children. The standard of clinical practice in the celiac clinic is to recommend 1000IU/day of vitamin D supplementation to all children at time of CD diagnosis. Only 4 children with CD had 1000IU or more of vitamin D supplementation. 17 children with CD were on vitamin supplementation (n=11 on multivitamins only (typically containing between 200-400 IU vitamin D/tablet), n=2 on multivitamin in addition to vitamin D supplementation, n=1 on multivitamin in addition to single preparations of calcium and vitamin D and n=3 on vitamin D supplementation only). Nine GI controls were on vitamin supplementation (n=8 on multivitamins only and n=1 on multivitamin in addition to calcium and vitamin D supplementation). Total vitamin D and calcium intake after supplementation is shown in **Table 3-22**. The total vitamin D intake after supplementation was 651 ± 573 IU in children with CD and 322 ± 267 IU in GI controls with (p=0.031). The total calcium intake after supplementation was 1036 ± 473 mg in children with CD and 840 ± 416 mg in GI controls. The dose of vitamin D supplementation taken by children with CD is significantly higher than GI controls (P=0.026). There were no significant different in calcium supplementation doses taken by children with CD and GI controls. There were significant differences in calcium intake with supplementation between 24-h recall and FFQ in children with CD (p=0.008) and GI control (p=0.000).

Table 3-19: Vitamin D and Calcium Supplementation in Children with CD and GI Controls with the Use of Supplements Only

Variables	Celiac[1] M=21 /F=4	GI Controls[1] M=12 /F=11	P<0.05[2]
Vitamin D supplements (IU)	438±522 (0-2000)	175±267 (0-1030)	0.026
Calcium supplements (mg)	109±251 (0-1200)	87±143 (0-600)	0.919

[1]Values are shown as mean ± standard deviation (range)

[2]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table 3-20: Proportion of Children with CD and GI controls that met Recommended Levels of Intake (DRI) for Vitamin D and Calcium with Supplementation as Assessed by 24 hour Recall with Supplementation (Diet + Supplementation)

		Celiac M=4/F=21		GI Control M=12 /F=11		
Variables	**DRI**	**(n) met DRI**	**(n) not met DRI**	**(n) met DRI**	**(n) not met DRI**	**P<0.05[2]**
Vitamin D (IU)[1] With supplementation	600	11	14	2	21	0.019
Calcium (mg)[1] with supplementation	700 - 1300	9	16	5	18	0.234

DRI: Dietary Reference Intakes

[1]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[2]P<0.05 considered significant

Table 3-21: The Common Multivitamin supplementation received by Children

Variable	Multivitamin A	Multivitamin B	Multivitamin C
Vitamin D (IU)	400	200	400
Calcium (mg)	0	0	180
Folate (µg)	200	100	100

Table 3-22: Total Vitamin D and Calcium Intake (24-hour Recall and Supplementation) in Children with CD and GI controls

Variable	Celiac[1] M=21 /F=4	GI Controls[1] M=12 /F=11	P<0.05[2]	P<0.05[3]
Total Vitamin D (IU) (24-h recall and vitamin D supplements)	651±573 (66-2391)	322±267 (37-1186)	-	0.031
Total Calcium (mg) (24-h recall and calcium supplements)	1036±473 (363-1981)	840±416 (359-41745)	0.137	-

[1]Values are shown as mean ± standard deviation (range)

[2]P value of T-test (P<0.05 considered significant)

[3]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

B) FFQ Data: Effect of Vitamin D and Calcium Supplementation on Total Vitamin D and Calcium (Diet + Supplementation)

Calcium and vitamin D intake by FFQ with supplementation are presented in **Table 3-23**. There were significant differences between the two groups in a total vitamin D after supplementation (p=0.041) and total calcium after supplementation (p=0.05). None of the patients met the RDA of vitamin D without supplementation in both groups in FFQ. After vitamin D

supplementation, 12 children with CD and 6 GI controls met RDA of vitamin D. The intake of calcium met RDA in 11 children with CD and 5 GI control children without supplementation. After supplementation, 13 children with CD and 6 GI children met RDA of calcium.

Table 3-23: Total Vitamin D and calcium intake by FFQ with Supplementation in Children with CD and GI controls

Variables	Celiac[1] F=21/ M=4	GI Control[1] F=12/ M=11	P<0.05[2]	P<0.05[3]
Vitamine D with supplementation	674±561 (63-2305)	371±298 (29-1090)	-	0.041
Calcium with supplementation	1457±593 (684-2905)	1078±708 (365-3206)	0.050	-

[1]Values are shown as mean ± standard deviation (range)

[2]P value of T-test

[3]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

3.3.3.2. E Major Food Sources of Vitamin D and Calcium in the Diets of the Children

A) FFQ Data

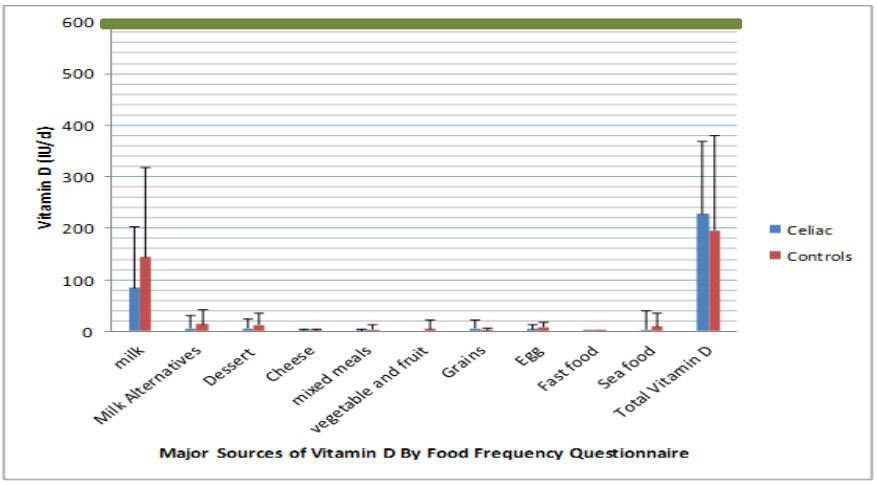
The different food sources of vitamin D and calcium from FFQ are presented in **Figure 3-1A** and **3-1B**. The major food sources of vitamin D in children with CD were milk (72%), dairy products (vitamin D fortified yogurt and butter Milk) (6%) and dessert (5%). The major food sources of calcium in children with CD were milk (37%), cheese (15%) and other dairy products (14%). The major food sources of vitamin D in GI controls were cow's milk (73%),

dairy products (vitamin D fortified yogurt and butter Milk) (7%) and dessert (6.6%). The major sources of calcium in GI controls were milk (46%) and cheese, dairy products and dessert with the same percent (10%) for each. In FFQ, The intake of vitamin D and calcium from cheese was significantly higher among children with CD comparing with GI controls with (p=0.016) and (p=0.005) respectively. No significant differences in vitamin D and calcium intake were found in the other food sources.

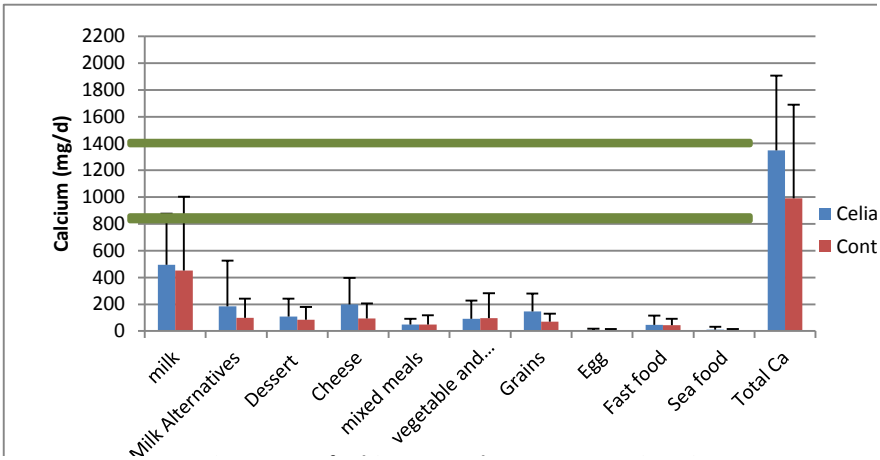
B) 24 HR Recall Data

The food sources of vitamin D from 24-h recall are presented in **Figure 3-3**. The main sources of vitamin D in children with CD were milk by 47% and other dairy products by 28% and the main sources of vitamin D in GI controls were milk by 66% and meat and alternatives by 12%. The food sources of calcium are presented in **Figure 3-2**. The main sources of calcium in children with CD were milk by 48% and dairy products by 27% and the main sources of calcium in GI controls were milk by 36% and other dairy products by 24%.No significant different in the sources of vitamin D and calcium between the two groups in 24-hour recall data.

3-1A



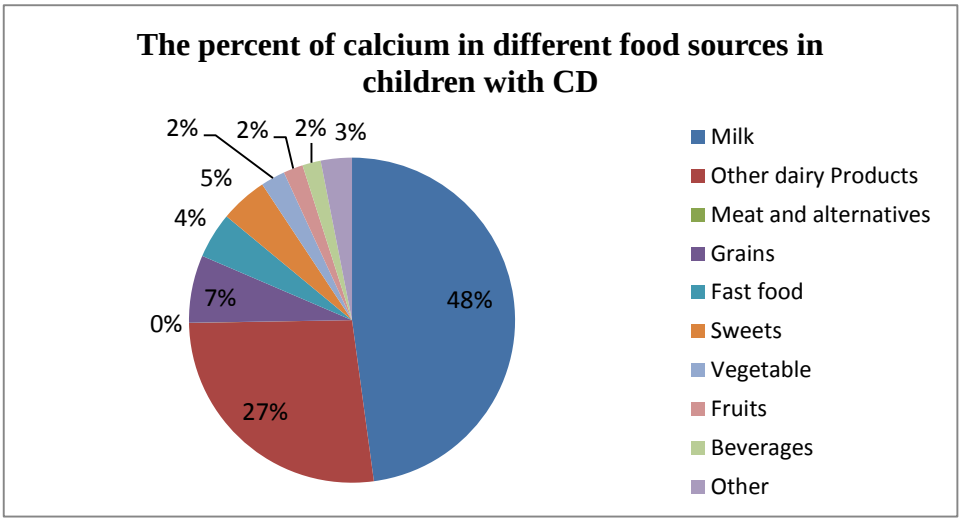
3-1B



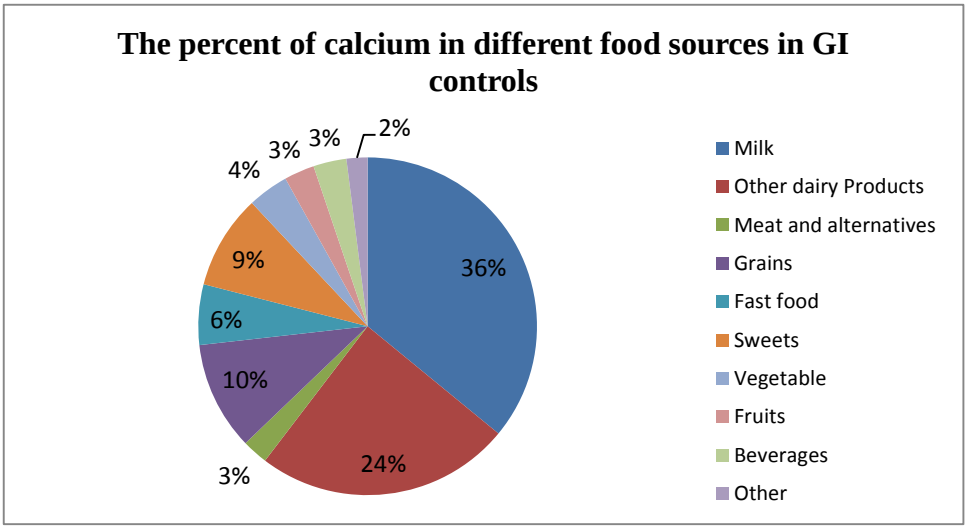
Milk: whole milk, low fat milk, skim milk, chocolate milk, Cream over coffee.
Milk alternatives: Butter Milk, Yogurt
Dessert: Ice-cream, Frozen yogurt, Pudding or custard, Cake, chocolate
Cheese: Mozzarella, Cottage cheese, Cheddar, Cream cheese
Mixed Meals: Macaroni cheese, Lasagna, Spaghetti with tomato sauce, Cream soup, cream sauce.
Grains: Bread, Waffles, Muffins, Pancake
Fast Food: Hamburger, Pizza
Sea-food: Oysters, Shrimp, Crab, crawfish, herring, Salmon, Sardines
Vegetable and Fruit: Broccoli, Greens, Calcium fortified Juice

Figure 3-1: Food Sources of Vitamin D (IU) (3-1A) and Calcium (mg) (3-1B) from the Diet only by FFQ. The green line presents the RDA of calcium and vitamin D

3-2 A



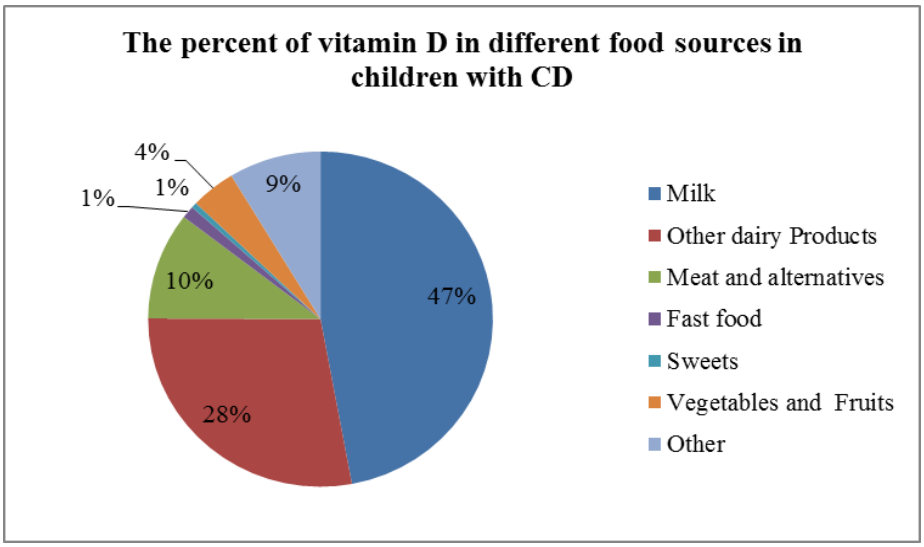
3-2 B



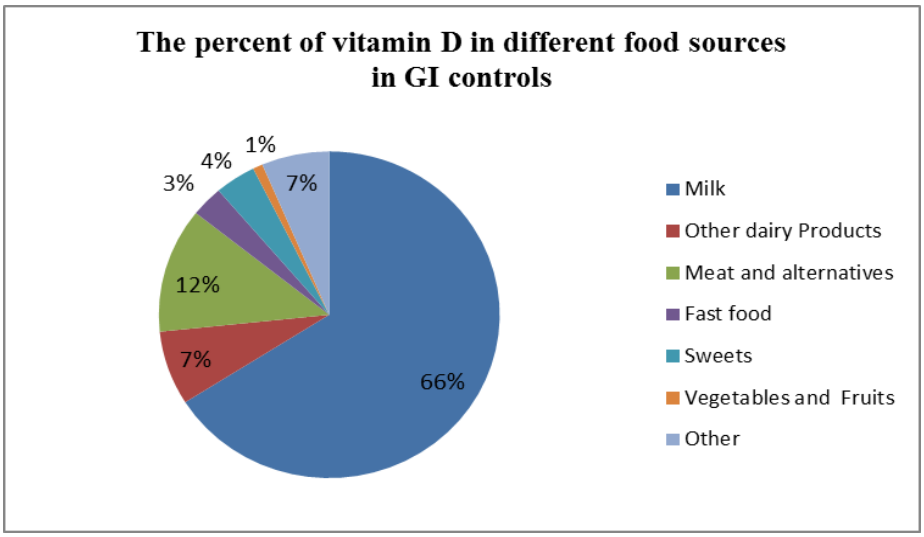
Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Other dairy products: Yogurt/Cheese/Sour cream
Fast food: Pizza/Burger/Hotdog/French fries/Chicken/ fingers
Sweets: Cookies/Candies/Ice cream/Pudding/Muffin/Cake/Honey/Jams/Table sugar/Syrup
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Vegetables: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic
Fruits: Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Beverages: Juices/tea/Cola/Hot chocolate
Other: Butter /Oil/dressing/Mayonnaise/Sauces/Canned soups / Ketchup/popcorn/Chips/Cracker

Figure 3-2: The Percent of Calcium in Different Food Sources from 24-hour Recall Data in Children with CD (3-2A) and in GI Controls (3-2B)

3-3A



3-3B



Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Other dairy products: Yogurt/Cheese/Sour cream
Fast food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Sweets: Cookies/Candies/ Ice cream/Pudding/Muffin/Waffles/Cake/Honey/Jams /Table sugar/Sweet sauces/Syrup
Vegetables and Fruits: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Other: Grains/Butter/Margarine/Oil/dressing/Mayonnaise/Sauces/Canned soups /Ketchup/Popcorn/Chips/Crackers/Juices/tea/Cola/Hot chocolate

Figure 3-3: The Percent of Vitamin D in Different Food Sources from 24-hour Recall Data in Children with CD (3-3A) and in GI Controls (3-3B)

3.3.3.2. F Iron, Folate and Vitamin B_{12} Intake

Iron, folate and vitamin B_{12} intake are presented in **Table 3-12**. No significant differences were found between children with CD and GI controls in iron, folate, vitamin B_{12} intake were found ($p>0.05$). The intake of iron, folate, vitamin B_{12} in celiac with and without GI symptomology is presented in **Table 3-13.** No significant differences in iron, folate and vitamin B_{12} intake were found between celiac patients with and without GI symptomology ($p>0.05$). The proportion of children with celiac disease and GI controls that met recommended levels of intake (DRI) for iron, vitamin B_{12} and Folate as assessed by 24 hour recall is presented in **Table 3-24.**

3.3.3.2. G Interrelationships between Demographic Factors and Intake of Iron, Folate and vitamin B_{12}

The effect of age (below and above 10 years old) and gender are presented in (Appendix C **Table C-9 Table C-10)**. There were no effect of age (below and above 10 years old) or gender on iron, folate and vitamin B_{12} intake. The effect of duration of disease and age (below and above 10 years old) on (iron, folate, vitamin B_{12}) intake is presented in (Appendix C **Table C-11)**. The interrelationships between (iron, folate, vitamin B_{12}) intake and age of diagnosis and duration of CD are presented in Table **3-25** and **Table 3-26**. No significant interrelationships between duration of the CD/age at diagnosis and iron, folate and

vitamin B_{12} intake ($p>0.05$). Iron, folate and vitamin B_{12} intake in children with CD with (ATTG>10.4) and (ATTG<10.4) is presented in Appendix A **Table A-8**. There were no significant differences in iron, folate and vitamin B_{12} intake in celiac patients with (ATTG>10.4) and celiac patients with (ATTG<10.4) ($p>0.05$).

3.3.3.2. H Intake of Iron, Folate and Vitamin B_{12} after Adjustment for Energy Intake

Iron, folate and vitamin B_{12} intake adjusted for energy (per 1000Kcal) is presented in Appendix A, **Table A-10**. After adjusted for energy (per 1000Kcal), the intake of iron in GI control (8.1 ± 2.5 mg) was significantly higher than children with CD (6.4 ± 1.8 mg) ($p=0.009$). Similarly, the intake of folate in GI controls after adjusted for energy (per 1000Kcal) (153.1 ± 70.6 µg) was significantly higher than the folate intake in children with CD (90.0 ± 47.6 µg) ($p=0.001$). No significant different in vitamin B_{12} intake between children with CD and GI controls after adjusted for energy (per 1000Kcal). No significant different between children above and below 10 years old in iron, vitamin B_{12}, and folate intake after adjusted for energy (per 1000Kcal) ($p>0.05$) were observed. No significant different between celiac with GI symptomology and celiac without GI symptomology in iron, vitamin B_{12}, and folate intake after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant interrelationship between iron, vitamin

B_{12}, and folate intake with duration of disease / age at diagnosis ($p>0.05$) after adjusted for energy (per 1000Kcal) were observed.

Table 3-24: Proportion of Children with Celiac Disease and GI Controls that met Recommended Levels of Intake (DRI) for Iron, Vitamin B_{12} and Folate as Assessed by 24 hour Recall

		Celiac M=4/F=21		GI Control M=12 /F=11		
Variables	**DRI**	**(n) met DRI**	**(n) not met DRI**	**(n) met DRI**	**(n) not met DRI**	**P<0.05[2]**
Iron (mg)[1]	7-15	13	12	14	9	0.573
Vitamin B_{12} (µg)[1]	0.9-2.4	24	1	15	8	0.009
Folate (µg)[1]	150-400	5	20	5	18	1.00

DRI: Dietary Reference Intakes

[1]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[2]p value from fisher exact test (P<0.05 considered significant)

Table 3-25: Interrelationships between (Iron, Folate, Vitamin B_{12}) Intake and Age of Diagnosis by Pearson Correlation (r^2)

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Iron	Age at diagnosis	0.173	0.408
Vitamin B_{12}	Age at diagnosis	0.072	0.731
Folate	Age at diagnosis	-0.169	0.419

[1]P<0.05 considered significant

Table 3-26: Interrelationships between (Iron, Folate, Vitamin B_{12}) Intake and Duration of CD by Pearson Correlation (r^2)

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Iron	Duration of CD	0.276	0.181
Vitamin B_{12}	Duration of CD	-0.180	0.390
Folate	Duration of CD	-0.010	0.963

[2]P<0.05 considered significant

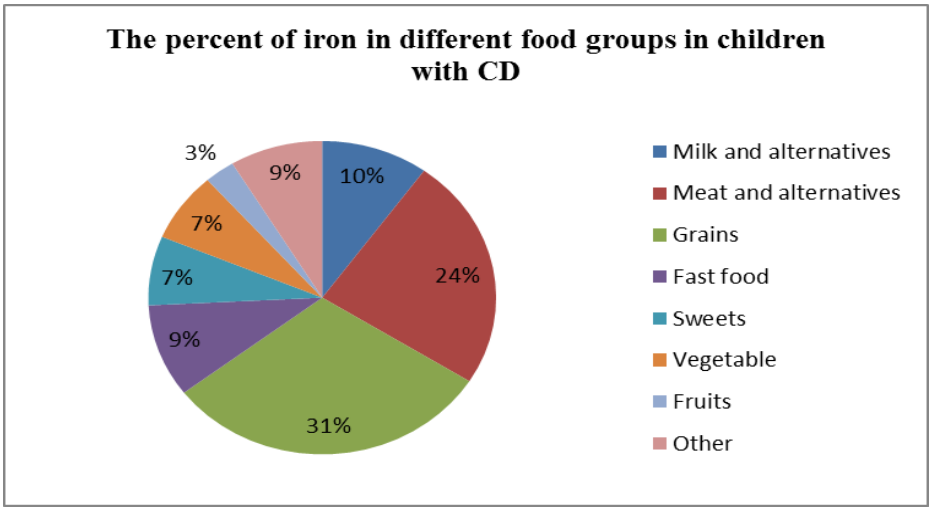
3.3.3.2. I Food Sources of (Iron, Folate, and Vitamin B_{12})

The food sources of iron are presented in **Figure 3-4**. The main sources of iron in children with CD were grains and meat by 31% and 24% respectively and the main sources of iron in GI controls were grains by 47% and fast food by 11%. The main sources of folate are presented in **Figure 3-5.** The main sources of folate in children with CD are meat and alternatives and grains by 28% and 23% respectively and the main sources of folate in GI controls are grains by 33% and vegetable and fruits by 22%. The food sources of vitamin B_{12} are presented in **Figure 3-6**. The main sources of vitamin B_{12} in children with CD were milk and

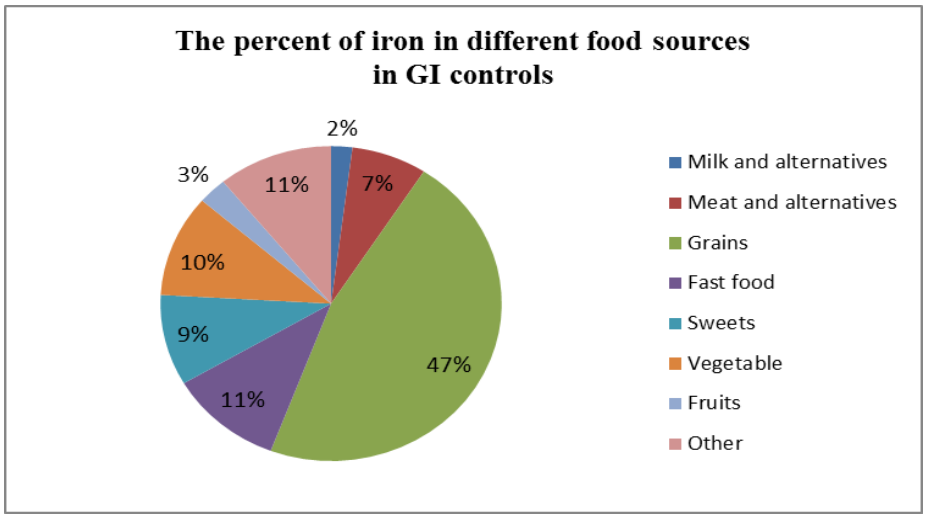
alternatives and meat and alternatives by 68% and 22% respectively. The main sources of vitamin B_{12} in GI controls were milk and alternatives and meat and alternatives by 51% and 20% respectively. For more information about the food sources of folate , vitamin B_{12} and iron see.

Folate found in gluten free grains and sweets (e.g. cookies, candies, pudding, muffin and cake) consumed by children with CD is significantly lower than folate found in gluten containing grains consumed by GI controls with ($p=0.003$) and ($p=0.000$) respectively. The amount of iron found in meat and alternatives consumed by children with CD is significantly higher than GI controls ($p=0.00$). No significant different in vitamin B_{12} food sources between GI control and children with CD. The comparison between GFP and gluten containing products folate content is represented in **(**Appendix A**, Table A-11).**

3-4 A



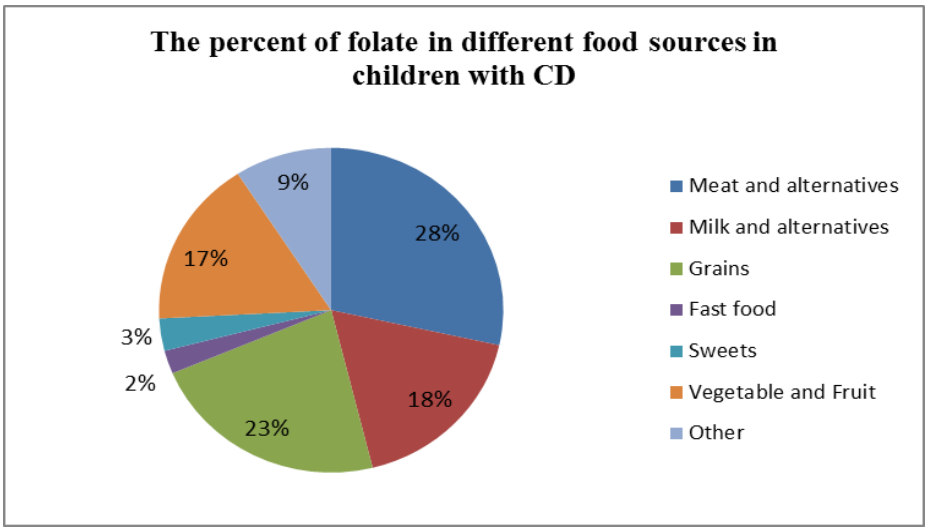
3-4 B



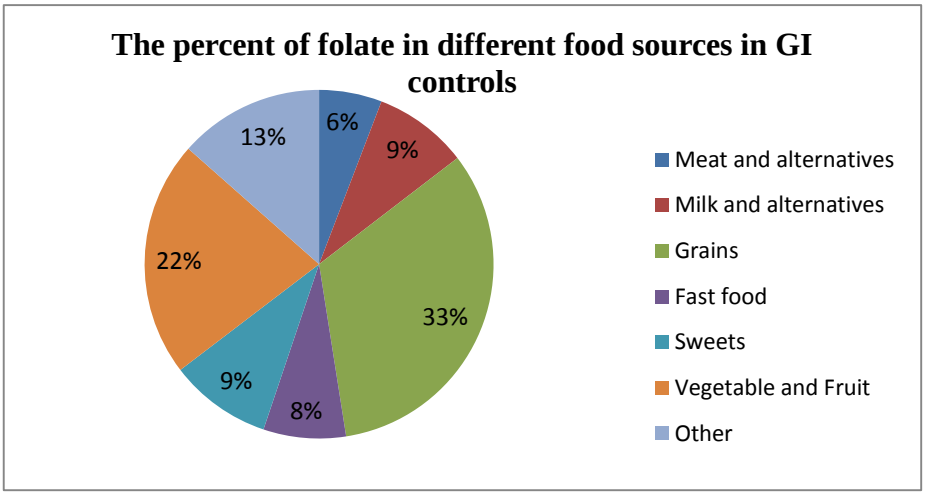
Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Milk and Alternatives: Milk/Yogurt/Cheese/Sour cream
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Sweets: Cookies/Candies/Ice cream/Pudding/Muffin/Waffles/Cake/Honey/Jams /Table sugar/Sweet sauces/Syrup
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Vegetables: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic
Fruits: Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Other: Butter/Margarine/Oil/dressing/Mayonnaise/Sauces/Canned soups/Ketchup Popcorn/Chips/Crackers/Juices/tea/Cola/Hot chocolate

Figure 3-4: The Percent of Iron in Different Food Sources from 24-hour Recall Data in Children with CD (3-4A) and in GI Control

3-5 A



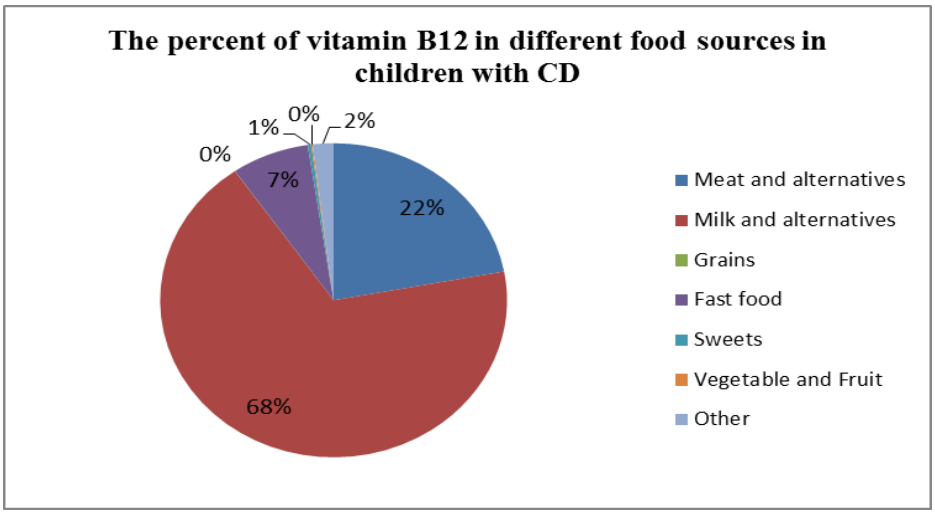
3-5 B



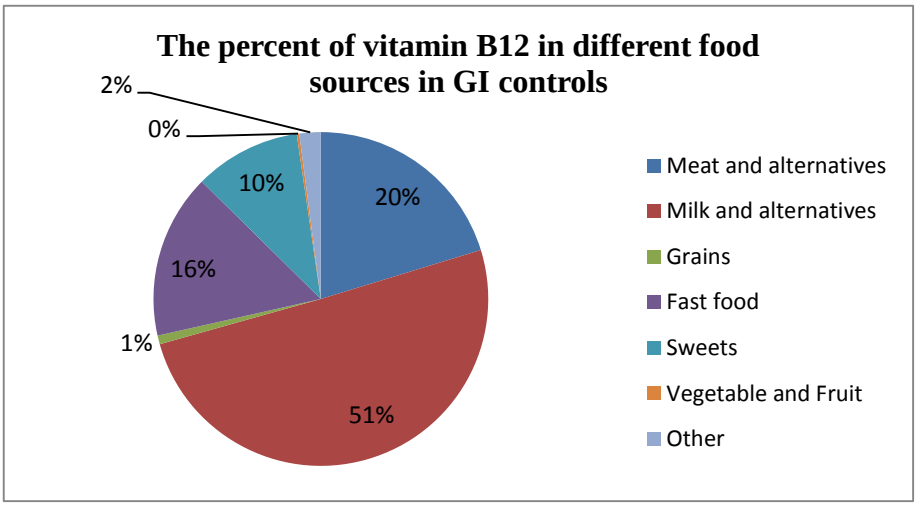
Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Milk and Alternatives: Milk/Yogurt/Cheese/Sour cream
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Vegetables and Fruits: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Sweets: Cookies/Candies/Ice cream/Pudding/Muffin/Cake/Honey/Jams/Table sugar/sweet sauces/syrup
Other: Tea/Cola/Hot chocolate/Juices/Popcorn/Chips/Crackers/Spices Butter/Margarine/Oil/dressing/Mayonnaise/Sauces/Canned soups

Figure 3-5: The Percent of Folate in Different Food Sources from 24-hour Recall Data in Children with CD (3-5 A) and in GI Controls (3-5)

3-6 A



3-6 B



Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Milk and Alternatives: Milk/Yogurt/Cheese/Sour cream
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Vegetables and Fruits: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Sweets: Cookies/Candies/ Ice cream/Pudding/Muffin/Waffles/Cake/Honey/Jams /table sugar/sweet sauces/syrup
Other: Tea/Cola/Hot chocolate/Juices/Popcorn/Chips/Crackers/Spices/Butter/Oil/Dressing

Figure 3-6: The Percent of Vitamin B_{12} in Different Food Sources from 24-hour Recall Data in Children with CD (3-6 A) and in GI Controls (3-6 B)

3.3.3.2. J. Fiber, Total sugar and Saturated Fat Intake

Fiber, saturated fat and total sugar intake are presented in **Table 3-12.** No significant different were found between children with CD and GI controls in fiber, saturated fat and total sugar intake ($p>0.05$). The proportion of children with Celiac Disease and GI controls that met recommended levels of intake (DRI) for fiber, saturated fat, total sugar as assessed by 24 hour recall is presented in **Table 3-27**.

3.3.3.2. K. Interrelationships between Demographic Factors and Fiber, Total Sugar and Saturated Fat Intake

Celiac children without GI symptomology consumed a significantly higher amount of total sugar comparing with celiac with GI symptomology ($p=0.012$). The effect of age (above and below 10 years of age) and gender on fiber, saturated fat and total sugar intake are presented in (Appendix C **Table C-12** and **Table C-13).** There were no gender or age (above and below 10 years of age) effect on fiber, saturated fat and total sugar intake. The effect of duration of celiac disease and age on (fiber, saturated fat and total sugar) intake is presented in (Appendix C **Table C-14).** The interrelationships between (fiber, saturated fat and total sugar) intake and age of diagnosis and duration of CD are presented in **Table 3-28** and **Table 3-29**. No significant interrelationship between duration of celiac

disease/age at diagnosis and (fiber, saturated fat and total sugar) intake were found with ($p>0.05$).

Fiber, saturated fat and total sugar intake in children with CD with (ATTG>10.4) and (ATTG<10.4) is presented in Appendix A, **Table A-8**. Fiber intake in celiac patients with (ATTG<10.4), (20.6 ± 7.9g) was significantly higher than fiber intake in celiac patients with (ATTG>10.4), (14.0 ± 4.7g) with ($p=0.038$). Similarity, total sugar intake in celiac patients with (ATTG<10.4), (96.1 ± 38.7g) was significantly higher than total sugar intake in celiac patients with (ATTG>10.4), (55.9 ± 27.7g) with ($p=0.015$). There were no significant differences in saturated fat intake in celiac patients with (ATTG>10.4) and celiac patients with (ATTG<10.4) ($p>0.05$).

3.3.3.2. L. Fiber, Saturated Fat and Total Sugar Intake after Adjustment for Energy Intake

Fiber, saturated fat and total sugar intake adjusted for energy (per 1000Kcal) is presented in Appendix A, **Table A-10**. No significant different in fiber, saturated fat and total sugar intake between children with CD and GI controls after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant different between children above and below 10 years old in iron, vitamin B_{12}, and folate intake after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant different between celiac with GI symptomology and celiac without GI

symptomology in Fiber, saturated fat and total sugar intake after adjusted for energy (per 1000Kcal) ($p>0.05$). No significant interrelationship between fiber, saturated fat and total sugar intake with duration of disease / age at diagnosis ($p>0.05$) after adjusted for energy (per 1000Kcal).

Table 3-27: Proportion of Children with Celiac Disease and GI Controls that met Recommended Levels of Intake (DRI) for Fiber, Saturated fat, Total Sugar as Assessed by 24 hour Recall

		Celiac M=4/F=21		GI Control M=12 /F=11		
Variables	**DRI**	**(n) met DRI**	**(n) not met DRI**	**(n) met DRI**	**(n) not met DRI**	**P<0.05[3]**
Fiber (g)[1]	19-38	4	21	1	22	0.350
Saturated fat%[2]	-	13	12	10	13	0.578
Total Sugar %[2]	-	20	5	13	5	1.000

DRI: Dietary Reference Intakes

[1]AI: Adequate Intake (Otten et al., 2006)

[2]Saturated fat recommendation (<10%) of total Energy and total sugar (<25%) of the total energy, Source:
(Food and Nutrition Board of Institute of Medicine of the Medicine Academes; 2005)

[3]P value from fisher exact test (P<0.05 considered significant)

Table 3-28: Interrelationships between (Fiber, Saturated fat and Total Sugar) Intake and Age of Diagnosis

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Fiber	Age at diagnosis	-0.005	0.982
Saturated fat	Age at diagnosis	0.076	0.717
Total sugar	Age at diagnosis	-0.215	0.302

[1]P<0.05 considered significant

Table 3-29: Interrelationships between (Fiber, Saturated fat and Total Sugar) Intake and Duration of CD

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model[1]
Fiber	Duration of CD	0.034	0.872
Saturated fat	Duration of CD	-0.194	0.353
Total sugar	Duration of CD	-0.070	0.739

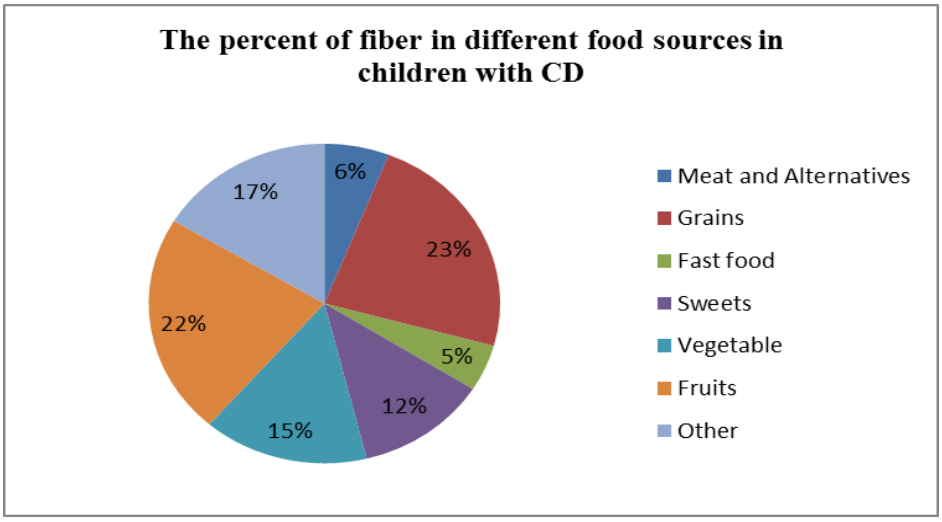
[1]P<0.05 considered significant

3.3.3.2. M. Food Sources of Fiber, Saturated fat and Total Sugar

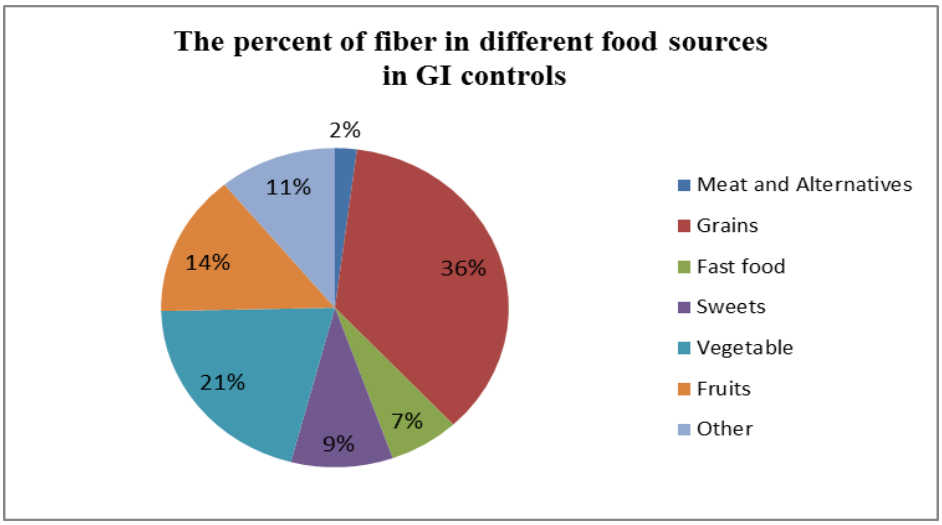
The food sources of fiber in children with CD and in GI control are presented in **Figure 3-7**. The main sources of fiber in children with CD were grains and fruit by 23% and 22% respectively and the main sources of fiber in GI controls were grains and vegetable by 36% and 21% respectively. The food sources of saturated fat are presented in **Figure 3-8**. The main sources of saturated fat in children with CD were meat and alternatives and milk and alternatives by 54% and 33% and the main sources of saturated fat in GI controls were milk and alternatives by 34% and (fast food, meat and alternatives and sweets) by 17% for

each one. The food sources of total sugar are presented in **Figure 3-9**. The main sources of sugar in children with CD were milk and alternatives and sweets (e.g. cookies and cake) by 27% and 24% and the main sources of sugar in GI controls were beverages and fruit by 30% and 18% respectively. Saturated fat content of milk and alternatives are significantly higher in children with CD comparing with GI control with (p=0.000). Comparison between GFP and gluten containing products in fiber content is presented in (Appendix A, **Table A-11**)

3-7A



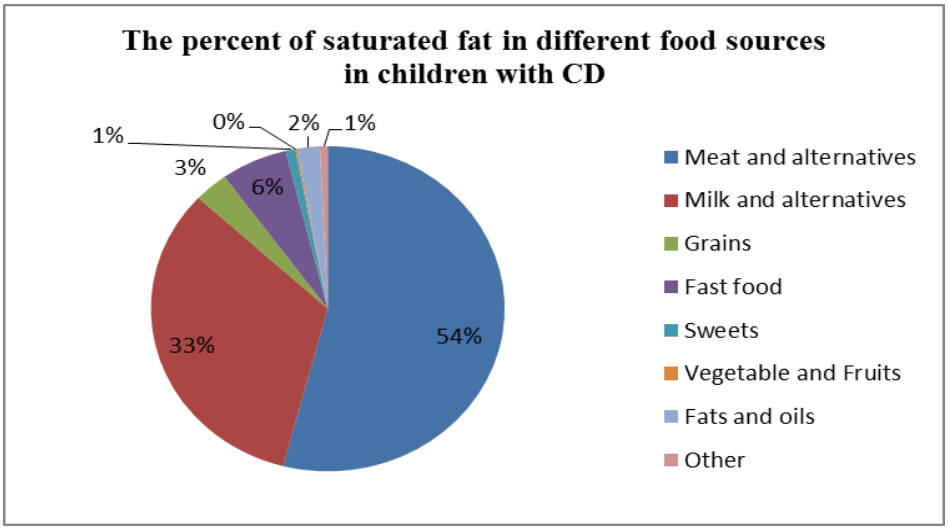
3-7B



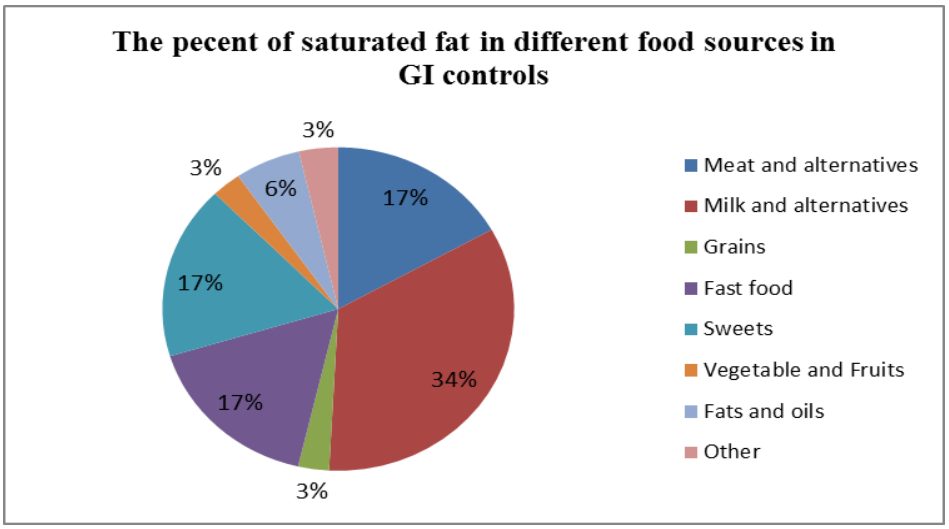
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Fruit: Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Vegetables: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic
Sweets: Cookies/Candies/Ice cream/Pudding/Muffin/Waffles/Cake/Honey/Jams /table sugar/sweet sauces/syrup/
Other: Milk/Yogurt/Cheese/Sour cream /Juices/tea/Cola/Hot chocolate/Butter/Margarine/Oil/dressing/Mayonnaise/Sauces/Canned soups /Ketchup/Popcorn/Chips/Crackers/

Figure 3-7: The Percent of Fiber in Different Food Sources from 24-hour Recall Data in Children with CD (3-7 A) and in GI Controls (3-7 B).

3-8 A



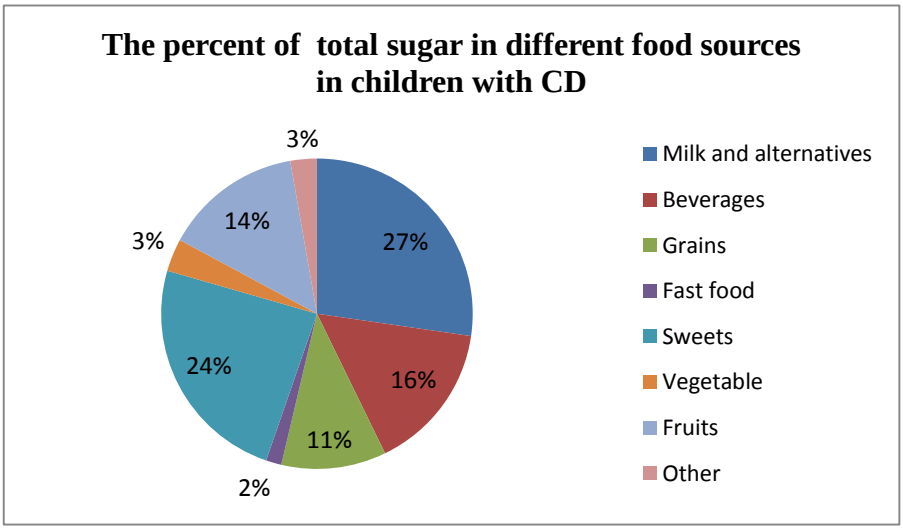
3-8 B



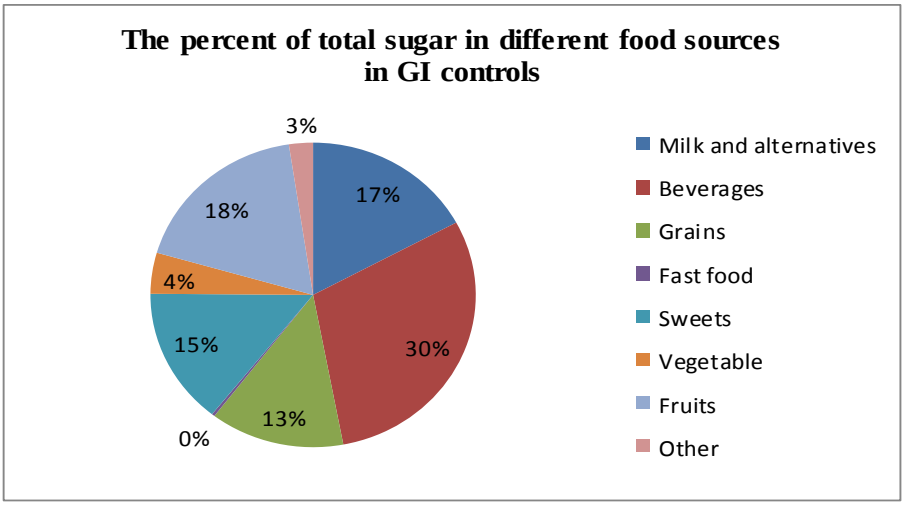
Meat and Alternatives: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nut
Milk and Alternatives: Milk/Yogurt/Cheese/Sour cream
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Vegetables and Fruits: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Sweets: Cookies/Candies/Ice cream/Pudding/Muffin/Waffles/Cake/Honey/Jams /Table sugar/Sweet sauces/Syrup
Fats and Oils: Butter/Margarine/Oil/dressing/Mayonnaise/Sauces/Canned soups
Other: Tea/Cola/Hot chocolate/Juices/Popcorn/Chips/Crackers/Spices

Figure 3-8: The Percent of Saturated Fat in Different Food Sources from 24-hour Recall Data in Children with CD (3-8 A) and in GI Controls (3-8)

3-9 A



3-9 B



Grains: Bread/Buns/Pasta/Rice/Breakfast cereal
Milk and Alternatives: Milk/Yogurt/Cheese/Sour cream
Fast Food: Pizza/Burger/Hotdog/French fries/Chicken fingers
Fruit: Apple/Orange/Strawberry/Grapes/Watermelon/Blueberry/Raspberry
Vegetables: Lettuce/Cucumber/Tomato/Potato/Carrot/Broccoli/Onion/Garlic
Beverages: Juices/tea/Cola/Hot chocolate
Sweets: Cookies/Candies/ Ice cream/Pudding/Muffin/Cake/Honey/Jams/Table sugar/ Sauces
Other: Chicken/Turkey/Egg/Beef/Pork/Seafood/Legumes/Nuts/Butter/Margarine/Oil/dressing/ Mayonnaise/Sauces/Canned soups /Ketchup/Popcorn/Chips/Crackers/Fast Food

Figure 3-9: The Percent of Total Sugar in Different Food Sources from 24-hour Recall Data in Children with CD (3-9A) and in GI Controls (3-9 B)

3.3.3.2 Nutrient Intake from Different Food Groups as Assessed from 24-hour Recall Data

To assess the quality of food intake in the children in the study, the 24 hour recall dietary data were analyzed for food group intake based upon Alberta Nutrition Guidelines for Children and Youth (Downs et al., 2011) in both groups. This analysis is presented from the 24-hour recall data in **Table 3-30**. No significant differences were found between children with CD and GI controls in the intake in the overall food groups. Only 5 children with CD and 6 GI children met the recommended number of serving of fruit and vegetables per day. 10 children with CD and 5 GI controls met the recommended number of serving of grains per day. Most of children with CD and GI controls (18 children with CD and 13 GI children) met the recommended number of serving of meat and alternatives per day. Only 9 children with CD and 6 GI children met the recommended number of serving of dairy products per day.

Table 3-30: Food Groups from 24-hour Recall in Children with CD and GI Control

Food Group	Celiac[1] F=21/ M=4	Control[1] F=12/ M=11	Recommended number of serving per day[2]	P<0.05[3]	P<0.05[4]
Vegetables and Fruit	3.8±2.2 (0.0-8.0)	3.9±2.3 (0.0-7.0)	5-8	0.878	-
Grains	4.8±2.5 (2.0-11.0)	4.33±1.6 (0.0-8.0)	4-7	-	0.803
Meat and Alternatives	1.9±1.2 (0.0-4.5)	2.0±0.9 (0.5-4.0)	1-3	-	0.567
Total Dairy Products	2.2±1.8 (0.0-6.5)	1.7±1.5 (0.0-5.5)	2-4	0.302	-
Milk Only	1.4±1.4 (0.0-5.0)	1.0±1.2 (0.0-5.0)	-	-	0.381

[1]Values are shown as mean ± standard deviation (range)

[2]Serving size based upon Alberta Nutrition Guidelines for Children and Youth (Downs et al., 2011).

[3]P value of T-test (P<0.05 considered significant)

[4]P value of Mann Whitney test when the assumption of normality dose not met (P<0.05 considered significan

3.4 Discussion

Consuming a gluten free diet (GFD) treats the damage that gluten can cause to the small intestine in individuals with CD (Duerksen et al., 2012). However, suboptimal nutritional status has been found in some adults with CD even after they consume a gluten free diet. This may because of low intakes of some nutrients such as iron, magnesium, folate, vitamin D, calcium and vitamin B_{12} on the GFD (Wild et al., 2010; Kinsey et al., 2008, Mager et al 2012). Iron, folate, vitamin D and calcium deficiency have been found at time of diagnosis of CD(Malterre, 2009; Bansal et al., 2011, Mager et al 2012) and in some patients, even those that appear compliant to the GFD, after many years on the GFD (Rujner et al., 200; Ohlund et al., 2010). This suggests that intake of these nutrients may be low in children and adults on the GFD.

The purpose of this study was to assess the dietary intake of vitamin D, calcium, iron, fiber, sugar, folate, vitamin B_{12} and saturated fat in children and adolescent with celiac disease on gluten free diet and to compare their intake with the intakes of age matched children and adolescent who attended the GI clinic. In addition, we compared current levels of intake of these nutrients to the dietary reference intakes (RDA or AI) for gender and age. We hypothesized that children and adolescent with CD on gluten free diet (GFD) will have higher intakes of simple sugars/saturated fat than GI controls (who have other GI disorder such as

abdominal pain, functional constipation and gastroesophageal reflux) and lower intakes of calcium and vitamin D, iron, folate, fiber and vitamin B12 than controls, The second hypothesis is that intakes of children with CD on GFD will not meet the DRI recommendations of calcium and vitamin D, iron, folate, fiber and vitamin B_{12} and the intake of saturated fat and total sugar exceeded the recommendation.

All children with CD did not meet the RDA of vitamin D (600IU/d) and most of the children with CD (19 out of 25) did not meet the RDA of calcium by diet only. This finding is not different from the general population in Canada. Around 25% of Canadian aged 6-79 years old fail to meet RDA of vitamin D by diet alone (Whiting et al., 2011). Another recent Canadian study found that most preschooler children aged 2-5 years old did not meet EAR of calcium by diet alone (Hayek et al., 2013). The intake of calcium was below EAR in 26% of the children aged 2-5 years old in Canada (Hayek et al., 2013). The same study found that the median intake of milk and dairy products were 1.7 and 2.5 serving /day respectively (Hayek et al., 2013). This finding is similar to what other researchers have observed in children with CD (Zucotti et al 2012, Ohlund et al 2010) and mirrors recent findings within our study group (Mager et al 2012). The intake of vitamin D and calcium without supplementation was less than the

recommendations in some studies in children with CD (Zuccotti et al., 2012; Ohlund et al., 2010; Hopman et al 2006).

The main sources of dietary vitamin D and calcium in all children in our study is milk (from both 24-hrecall and FFQ) which is the same main source found among Canadian children (Gates et al., 2012). The average milk serving in our study is 1.4 cup/day which can be translated to an approximate average intake of approximately 340 IU of vitamin D since every cup of milk is fortified with at least 100 IU of vitamin D in Canada (Holick et al., 2011). The low intake of milk has been found in the general population in Canada, particularly in adolescence. A recent study showed that the average milk intake in Canada is 0-1.5 cup/day (Hayek et al., 2010, Mark et al 2011). Interestingly, in our study there were no significant different observed between children with CD and GI controls in total vitamin D and calcium intake or in the main sources of vitamin D and calcium (milk) in the diet which suggests that low vitamin D intake is not just an issue in children with CD, but rather an issue for children with chronic gastrointestinal issues. This finding is contrast with other studies that found intake of vitamin D to be significantly lower among children with CD on GFD comparing with healthy controls (Zuccotti et al., 2012).

In fact most children only met their vitamin D requirements with the use of a vitamin D supplement; particularly in the children with CD where routine

clinical practice includes the prescription of a daily vitamin D supplement in the clinics at the Stollery Children's Hospital. In contrast, the children with chronic GI disorders were not consistently provided with the same advice and so did not meet their vitamin D needs on a consistent basis.

Fifty-two percent of children with celiac disease (13 out of 25) met the RDA of iron (7-15mg) and most them met the RDA of vitamin B_{12} (0.9-2.4µg) by diet alone. This was because most of children with CD met the Recommended number of servings of meat and alternatives per day which is one of the main sources of heme iron and vitamin B_{12} (Downs et al., 2011; Pynaert et al., 2005).This finding is consistent with another study conducted in Sweden that most children with CD on the GFD met the average requirement for iron through diet alone (Ohlund et al., 2010). In contrast, a recent Italian study found that the median intake of iron among children with CD on the GFD approximated current recommendations (9 mg/d), while median intakes of vitamin B_{12} were within recommended levels (Zuccotti et al., 2012). Another study found that the mean intake of iron less than the recommendation (13mg) (Hopman et al., 2006).

Most of the children with CD (21out of 25) did not meet the AI of fiber (19-38g/d). This finding is consistent with another study conducted in the Netherlands that found the mean intake of fiber in children with CD fell below recommended levels of intake (13mg/d) (Hopman et al., 2006). Fiber intake was

also below the recommendations (9.9g/d) among children with CD in another study (Ohlund et al., 2010). In our study, inadequate intakes of grains, vegetable and fruit which are the main sources of fiber, appears to be the reason of suboptimal intake of fiber. Interestingly, children in both groups consumed similar number of servings of grain products; and despite lower fiber contents in GF grains, maintained a similar intake of fiber as the GI controls that ate gluten containing grains. This finding is consistent with another study conducted in Italy which found no significant different in fiber intake between children with CD and healthy controls, although children in this study were able to meet their needs for fiber by their consumption of fruits and vegetables (Zuccotti et al., 2012).

Most of children with CD (20) (80%) did not meet the RDA of folate (150-400 µg/d). This percentage is higher than what have been found in general population. Twenty-two percent of men and thirty-five percent of women in Canada do not meet the recommendation of folate intake (Sharma et al., 2013). In our study, there were no significant differences observed between children with CD and GI controls in total folate intake. These findings are consistent with other studies which have found no significant different in folate intake between children with CD and healthy controls (Zuccotti et al., 2012). Suboptimal intake of folate in our study is likely due to the lower levels of folate found in GF grain products

(Baydoun et al., 2012, Thompson, 2000) (Appendix A, **Table A-19**). While most gluten containing flours in Canada are fortified with folate, there are currently no requirements for GF to have folate fortified in grains and therefore gluten free containing flours contain variable amounts of folate (Kulai & Rashid et al., 2013).

The intake of saturated fat and sugar exceeded the recommendation in 12 (48%) and 5 (20%) respectively of children with CD. In this study the average intake of saturated fatty acid and total sugar were 11.4 % and 19 % of total energy respectively in children with CD. This finding is close to the intake of the general population in Canada. The intake of saturated fat and total sugar in the general population in Canada are 12.5% and 20% of the total energy intake respectively (Mulder et al., 2013; Langlois & Garriguet et al., 2011). The percentage of children who exceeded the recommendation of saturated fat intake is higher in general population (81%) than what we have found in this study (48%) (Mulder et al., 2013). This finding is consisted with other study that found the mean intake of saturated fat exceeded the recommendation (<10% of the total energy) (Ohlund et al., 2010). The GFD has been found to have high amount of lipid and sugar comparing with Gluten containing products (Saturni et al., 2010; Thompson, 2000). In our study, there were no significant differences observed between children with CD and GI controls in the total saturated fat and total sugar intake. This finding is consistent with other study conducted in Italy which found no

significant different in saturated fat and simple sugar intake between children with CD and healthy controls (Zuccotti et al., 2012). In contrast, these findings are different from other studies. The intake of saturated fat was significantly lower in children with CD on GFD comparing with general population in Netherlands (Hopman et al., 2006). Other study found the intake of sucrose in children with CD is significantly higher than healthy controls (Ohlund et al., 2010).

In conclusion, no significant differences were found between children with CD and GI control in vitamin D, calcium, iron, folate, fiber, vitamin B_{12}, total sugar and saturated fat intakes. None of children with CD met RDA of vitamin D by diet only. Most of the children with CD did not meet RDA of calcium and folate and /or the AI of fiber. Most of children with CD met RDA of vitamin B_{12} and iron. 12 (48%) children with CD exceeded the 10% of the total energy from saturated fat and only 5 (20%) children with CD exceeded 25% of the total energy from total sugar. Following the GFD does not appear to influence the overall intake of children and adolescents with CD except for fiber, folate and total sugar.

Chapter 4: Conclusions and General Discussion

4.1 Study rationale and hypothesis

CD is a chronic autoimmune disorder of the small intestine caused by an immunological reaction to gluten, a protein that is found mainly in wheat, barley, rye, and spelt products (Siddiqui & Osayande, 2011). Consuming a GFD is the only treatment for CD, as it improves the overall nutritional status in celiac children by reducing the potential for malabsorption of nutrients that are important to childhood growth and development (Duerksen et al., 2012). However, some studies have shown that some adults with CD who consume a GFD still suffer from suboptimal nutritional status. Only a few studies have examined the nutritional intake in children and adolescents with CD on GFD. This study is the first Canadian study to assess the nutritional intake in children and adolescents with CD on GFD. The purpose of this study was to compare the dietary intake of vitamin D, calcium, iron, fiber, sugar, folate, vitamin B12 and saturated fat in children and adolescents with CD on a GFD with the intake in age-matched children and adolescents who attended the GI clinic for other GI disorders such as abdominal pain, functional constipation and gastroesophageal reflux and had been screened for CD. In addition, we compared the current levels of intake of these nutrients to the dietary reference intakes (RDA or AI) according to gender and age. We hypothesized that children and adolescents with CD on

GFD will have higher intake of simple sugars/saturated fat than GI controls and lower intake of calcium and vitamin D, iron, folate, fiber and vitamin B12 than controls. The second hypothesis was that the intake in children with CD on GFD will not meet the DRI recommendations for calcium, vitamin D, iron, folate, fiber and vitamin B12 and will exceed the daily recommendations for saturated fat and total sugar.

4.2 Summary of Main Study Findings

We found that the majority of children in this study did not meet the DRI for calcium, and vitamin D, including the controls. In fact with dietary counseling and supplementation the children with CD improved their vitamin D intake. Many children with CD did not meet the DRI for calcium, folate and fiber, also exceeded recommendations for saturated fat intake. However in contrast to our hypothesis, they did not exceed the DRI for total sugar and most met the vitamin B_{12} requirement, while half met the iron requirement. This has significant implications for the bone health and long term risk of chronic disease, such as cardiovascular risk for children with CD

In contrast to our hypothesis in this study, the intake of vitamin D, calcium, fiber, folate, vitamin B_{12}, saturated fat, iron and total sugar in the GI control group was similar to children with CD. In our study, the overall intake of three food groups (vegetable and fruits, grains, milk and alternatives) was low in

both children with CD and the GI controls when compared to recommended ranges. However, the intake of meat and alternatives was adequate in most of the children with CD and the GI controls.

4.3 Long term implications of suboptimal nutrient intake

Low vitamin D and calcium intake can cause bone disorders in children because vitamin D and calcium are important nutrients building bone density and enhancing bone development (Malterre, 2009; Hendrie et al., 2011). In the general population in Canada, suboptimal vitamin D and calcium status has been shown to be highly prevalent in children and adolescents because of poor dietary intake of vitamin D and poor sunlight exposure (Holick et al., 2011; Mager et al., 2012). In children with CD the low intake of vitamin D and calcium is of concern because the prevalence of vitamin D and calcium deficiency in CD patients is higher than that found in healthy people (Malterre, 2009). Many studies have shown that celiac patients have poor bone health at the time of diagnosis and even after following GFD (Chakravarthi et al., 2012; Jatla et al., 2009; Mager et al 2012).

Low iron intake leads to iron deficiency anemia. In children with CD the low intake of iron should be more concern because iron deficiency is one of the most common symptoms of celiac disease (Malterre, 2009; Bansal et al., 2011).

Many studies have found that the prevalence of iron deficiency anemia was high among CD patients (Harper et al., 2007; Bansal et al., 2011; Rashid et al., 2005; Botero-Lopez et al., 2011). Furthermore, celiac disease has been found among people who have iron deficiency anemia in many studies (Cekin et al., 2012; Kalayci et al., 2005). Folate has been found to be an important nutrient in cell synthesis and division, growth and preventing anemia (Monteagudo, et al; 2013). Thus, low folate intake is associated with anemia and impaired growth in childhood. Because CD is associated with impaired growth (Fasano, 2005;Lionetti & Catass, 2011), low folate intake in children with CD can make these symptoms even more complicated. Additionally, fiber intake has been used in treating constipation in children (Stewart & Schroeder; 2013). CD is presented with constipation in some patients as non classical symptoms (Fasano, 2005;Lionetti & Catass, 2011) and consuming insufficient amounts of fiber may make this symptom more complicated and harder to treat. High consumption of fat and sugar is associated with obesity and overweight in children and adolescent with CD (Valletta et al; 2010). Furthermore, the consumption of GFD (which has high amount of sugar and saturated fat) increases the risk of obesity in CD patients (Saturni et al., 2010; Thompson, 2000). Additionally, CD patients tend to compensate for low intake of gluten containing products by increasing the intake of fat (Valletta et al; 2010).

4.4 Factors influencing study findings

In this study we examined many factors that may influence the intake in children such as adherence to GFD, age, gender, and presence of GI symptomology in children with CD. The adherence to GFD only influenced the intake of total sugar, folate and fiber in children with CD. This may because GFD has been found to have high amounts of lipid and sugar and low amounts of fiber, folate and iron (Saturni et al., 2010; Thompson, 2000). This may also be due to the fact that gluten-free products are not fortified or enriched with important nutrients such as folate and iron to the same extent as gluten-containing foods; moreover, processing of gluten-free foods alters the content of nutrients such as fat, sodium and simple sugars (Saturni et al., 2010; Thompson, 2000; Kulai & Rashid et al., 2013).

The adherence to GFD in this study was examined by ATTG level test which is not 100% reliable. Thus, more research is needed to examine the adherence to GFD in children with CD using other methods such as direct questionnaire and more research is needed to evaluate the effect of the adherence on the nutrition intake in children with CD. Additionally, the age of the child did not influence intake: the intake of children above 10 years did not differ from the intake of children below 10 years of age. Although we did not find any differences in nutritional intake by age or gender, our ability to draw conclusions

about the influences of age and gender are limited by the smaller sample size in our cohort. More research is needed to evaluate the effect of age and gender of children with CD on their intake

In this study, the presence of GI symptoms at time of diagnosis did not influence the overall intake in children with CD except for total sugar intake. However, it is hard to draw conclusion about the effect of the GI symptomology because of the small sample size in our cohort. More research is needed to examine the effect of these symptomology on the intake in children with CD.

4.5 Clinical Implications for Dietary Therapy in Children with CD

The findings of this study indicate that children with CD have low intake of vitamin D, calcium, folate and fiber. Even though vitamin D supplementation is part of routine clinic practice, in this study, not all the children with CD took multivitamins and/or vitamin D. Only 11 children with CD on GFD in our study met the RDA for vitamin D. This indicated that some children with CD who took the supplementation did not take it regularly and/or took a lower dose than what recommended in the clinic (1000IU/day). Additionally, low intake of calcium was observed among children with CD even after supplementation. Thus, increasing the intake of milk (which is the main source of vitamin D and calcium) is recommended in addition to regular intake of vitamin D and calcium

supplementation and increasing the adherence to the supplementation recommendations is important.

Low intake of folate and fiber among children with CD was observed. Increasing the intake of food sources of folate and fiber, such as fruits, vegetables and folate fortified grainsis recommended. Moreover, folate supplementation could be routinely prescribed for children with CD. The amount of folate in pediatric multivitamin supplements ranges from 100 to 200mcg and this amount is sufficient to meet folate recommendation. More research is needed to assess the effect of folate supplementation on folate intake in children with CD.

CD patients consumed a significantly higher amount of protein (mostly from meat and alternatives) than controls to compensate for low intake of food containing gluten. The intake of protein is high in this population but it is not different from the intake in general population (Gagne et al., 2012). CD patients are not deficient in B_{12} because they increased protein intake from meat and alternatives which is main sources of vitamin B_{12}. However, the intake of saturated fat was high among children with CD which is associated with obesity (Valletta et al; 2010). Thus, children and adolescent and their care givers should be educated to, reduce saturated fat in their food by choosing the processed food that have lower amount of saturated fat.

Our results indicated that CD patients with GI symptomology consumed a significantly lower amount of carbohydrate comparing with CD patients without GI symptomology. This may indicated that celiac patients with GI symptomology tend to be more careful in avoiding grains containing gluten (have better adherence to GFD). Thus, the nutritional counseling should consider increasing the awareness of the importance of following a GFD especially with the CD patients who do not have GI symptomology.

4.6 Knowledge Translation

Although the children and adolescents with CD in this study have received a high quality of nutritional education and dietary follow up by a registered dietitian, they have low intakes of some nutrients such as vitamin D, calcium, folate and fiber. We expected that children with CD in the community (who don't attend the celiac clinic and don't have such strict dietary follow up) may have a worse nutritional intake and lower adherence to GFD. Thus, nutritional education should not only focus on following a GFD but also on increasing the intake of the four food groups especially the food sources of vitamin D, calcium and folate. Interestingly, our data shows that adherence to vitamin supplementation (particularly vitamin D) was less than 60%; a finding that is consistent in the literature regarding nutrient supplementation in adults (Bischoff-Ferrari, 2007). This result highlights the importance of increasing awareness to both the child and

family regarding the adherence to vitamin supplementation and regarding the overall nutritive value of the GFD. The role of the RD in nutrition counseling regarding both the gluten content and nutritional quality of the GFD is critically important in the overall care of the child with CD.

4.7 Study Limitations

Following a GFD is the only treatment for CD and can improve clinical and serological symptoms (Siddiqui & Osayande, 2011). In this study, the ATTG test was used to measure the adherence to GFD. However, this test can yield false results (Lindfors, Koskinen, & Kaukinen, 2011). Some studies have found an elevated ATTG level even after one year of consumption of a GFD (Mager et al., 2012). The accuracy of this test may influence the ability to determine adherence to GFD. The dietary intake was assessed using a validated 24-hour recall for two days (one weekend day and one week day). The average data for the two days were used to represent one day 24-h recall. However, only 7 children with CD and 9 GI controls completed two days of 24-hour recall (one weekend and one weekday). This result did not affect the results of our study because we did not find any significant differences in the mean intake and/or variability in the intake of protein, carbohydrate, fat, vitamin D, calcium, vitamin B_{12}, iron, folate, fiber, saturated fat and total sugar between the weekend and weekdays for those who had a one-day 24-hour recall (weekday) versus those who had 24-hour recalls

conducted on two different days (one weekend, one weekday). We could not differentiate between intake of natural sugar (e.g., from fruits) and added sugar (table sugar) because the program we used to analyze the dietary intake (food processor) does not provide details about the type of sugars consumed.

In this study, we did not evaluate the effects of the factors that may influence adherence to the GFD such as socioeconomic status, presence of gastrointestinal symptomology, and/or parental education. It has been found that gluten-free products are more expensive than their equivalent gluten-containing products in Canada and the prices may affect the adherence to the GFD (Stevens & Rashid, 2008). Moreover, socializing (e.g., eating with friends and dining out, travelling) may affect the adherence to GFD (Verrill et al., 2013). In this study we did not evaluated the effects of these factors on the adherence to GFD which considered one of the limitations. Moreover, the smaller sample size is a limitation of our study which may potentially be one of reasons that we did not find significant differences in the intake between the two groups (children with CD and GI controls). Additionally, in this study we did not assess the intake of vitamin K. Low intake of vitamin K was found in previous study and is important for overall bone health (Mager et al., 2012).

4. 8 Study Strengths

The dietary intake of children with CD was compared to the intake of the control group (GI controls). The control group in this study had been screened for CD at the clinic. One strength of our study is that we collected the brand names of the foods consumed, so the exact nutritional values of these foods were entered in our food processor program. This increases the accuracy of the nutritional assessment: the nutrition components of gluten-free products are not the same as those of gluten-containing products, because gluten-free products are not fortified with folate and enriched with iron to the same extent, and food processing alters the nutrient content (fat, sodium and simple sugars) (Saturni et al., 2010; Thompson, 2000; Kulai & Rashid et al., 2013). The other strength is that vitamin D and calcium were assessed using two methods instead of one (food frequency questionnaire and 24-h recall). Additionally, in this study, the main food sources of the nutrients (vitamin D, calcium, vitamin B_{12}, iron, fiber, saturated fat and total sugar) were assessed in the two groups (children with CD and GI controls), which was not the case in previous similar studies. All of these strengths increase the accuracy of assessing nutrition intake in children with CD.

4. 9 Future Research

Following a GFD is the only current treatment for CD that can improve clinical symptoms (Siddiqui & Osayande, 2011). However, there are some factors

that may affect the success of this treatment. This included adherence to the GFD adherence, parents' knowledge and attitude about both the GFD and nutrition in general, peer pressure, being aware (reading) of the nutritional contents of processed food, socializing (e.g., eating with friends and dining out) and travelling (Verrill et al., 2013). More studies are needed to evaluate the effect of these factors on adherence and nutritional intake on the GFD in children and adolescents with CD in Canada. It has been found that gluten-free products are more expensive than their equivalent gluten-containing products in Canada in only one study (Stevens & Rashid, 2008). Thus, more studies are needed to assess the effects of the prices of gluten-free products on availability and accessibility to these foods, and how that may affect adherence to GFD in children with CD. Moreover, a few studies have found that gluten-free products have lower nutritional quality than gluten-containing products. More studies are needed to assess the nutritional quality of GFD in Canada.

There is a need to study the role of imparting nutritional education to parents (or caregivers) in improving the dietary intake of children with CD. Moreover, our study indicated some significant differences in the intake between celiac patients with GI symptomology and celiac patients without symptomology. Thus, more researches needed to look more closely for adherence between symptom presentation groups. A special focus on the need for micronutrient

supplementation is needed as this population is already at high risk for pre-existing nutritional deficiencies. This is particularly important for the growing child with CD. Inclusion of a healthy control population (with no dietary restrictions and/or gastrointestinal issues) would be useful to indicate the differences in the intake between children with CD and children without CD. In summary, children and adolescents with both CD and chronic gastrointestinal issues such as functional constipation and gastroesophageal reflux disease have dietary intakes characterized by suboptimal vitamin D, calcium, fiber and folate intake. Consideration of micronutrient supplementation in this population is warranted as part of routine clinical care.

Appendix A: Tables (2 x 2 ANOVA Related to Anthropometric Data, ATTG Test and Adjustment for Energy (per 1000 Kcals)) and Figures

Table A-1: 2 x 2 ANOVA of Nutrients Intake with Groups (celiac/GI control) and Weight

Dependent Variable	**Independent Variables**	**P-value of The Model[1]**	**P-value of group (celiac/GI control)**	**P-value of weight[2]**
Protein	1) Groups (celiac/GI control) 2) Weight	0.031	0.016	0.098
Carbohydrate	1) Groups (celiac/GI control) 2) Weight	0.448	0.243	0.860
Fat	1) Groups (celiac/GI control) 2) Weight	0.378	0.207	0.382
Vitamin D	1) Groups (celiac/GI control) 2) Weight	0.305	0.133	0.217
Calcium	1) Groups (celiac/GI control) 2) Weight	0.926	0.738	0.507
Iron	1) Groups (celiac/GI control) 2) Weight	0.926	0.738	0.784
Fiber	1) Groups (celiac/GI control) 2) Weight	0.398	0.259	0.651
Saturated fat	1) Groups (celiac/GI control) 2) Weight	0.522	0.258	0.730

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of weight[2]
Vitamin B_{12}	1) Groups (celiac/GI control) 2) Weight	0.157	0.110	0.151
Folate	1) Groups (celiac/GI control) 2) Weight	0.108	0.047	0.836
Total sugar	1) Groups (celiac/GI control) 2) Weight	0.465	0.520	0.386

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant
[2]The main effect is weight

Table A-2: 2 x 2 ANOVA of Nutrients Intake with Groups (celiac/GI control) and Height

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of height[2]
Protein	1) Group (celiac/GI control) 2) Height	0.028	0.017	0.086
Carbohydrate	1) Group (celiac/GI control) 2) Height	0.160	0.123	0.151
Fat	1) Group (celiac/GI control) 2) Height	0.536	0.318	0.789
Vitamin D	1) Group (celiac/GI control) 2) Height	0.129	0.092	0.144

Dependent Variable	**Independent Variables**	**P-value of The Model[1]**	**P-value of group (celiac/GI control)**	**P-value of height[2]**
Calcium	1) Group (celiac/GI control) 2) Height	0.101	0.139	0.066
Iron	1) Group (celiac/GI control) 2) Height	0.318	0.970	0.139
Fiber	1) Group (celiac/GI control) 2) Height	0.435	0.201	0.867
Saturated fat	1) Group (celiac/GI control) 2) Height	0.443	0.231	0.506
Vitamin B_{12}	1) Group (celiac/GI control) 2) Height	0.051	0.084	0.038
Folate	1) Group (celiac/GI control) 2) Height	0.032	0.074	0.117
Total sugar	1) Group (celiac/GI control) 2) Height	0.565	0.326	0.544

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is height

Table A-3: 2 x 2 ANOVA Nutrients Intake with Groups (celiac/GI control) and BMI

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of BMI[2]
Protein	1) Group (celiac/GI control) 2) BMI	0.081	0.026	0.365
Carbohydrate	1) Group (celiac/GI control) 2) BMI	0.298	0.130	0.360
Fat	1) Group (celiac/GI control) 2) BMI	0.548	0.358	0.864
Vitamin D	1) Group (celiac/GI control) 2) BMI	0.376	0.184	0.873
Calcium	1) Group (celiac/GI control) 2) BMI	0.453	0.214	0.525
Iron	1) Group (celiac/GI control) 2) BMI	0.930	0.883	0.794
Fiber	1) Group (celiac/GI control) 2) BMI	0.438	0.264	0.900
Saturated fat	1) Group (celiac/GI control) 2) BMI	0.536	0.373	0.800
Vitamin B_{12}	1) Group (celiac/GI control) 2) BMI	0.336	0.145	0.455

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of BMI[2]
Folate	1) Group (celiac/GI control) 2) BMI	0.102	0.076	0.696
Total sugar	1) Group (celiac/GI control) 2) BMI	0.657	0.365	0.790

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is BMI

Table A-4: 2 x 2 ANOVA of Nutrients Intake with Groups (celiac/GI control) and Weight-for-age z-score

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of Weight-for-age z-score[2]
Protein	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.121	0.057	0.866
Carbohydrate	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.455	0.228	0.969
Fat	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.518	0.355	0.709

Dependent Variable	**Independent Variables**	**P-value of The Model[1]**	**P-value of group (celiac/GI control)**	**P-value of Weight-for-age z-score[2]**
Vitamin D	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.136	0.079	0.153
Calcium	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.122	0.083	0.117
Iron	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.604	0.584	0.337
Fiber	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.417	0.262	0.738
Saturated fat	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.504	0.362	0.666
Vitamin B_{12}	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.225	0.119	0.245
Folate	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.107	0.039	0.818
Total sugar	1) Groups (celiac/GI control) 2) Weight-for-age z-score	0.159	0.175	0.090

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is weight- for- age z-score

Table A-5: 2 x 2 ANOVA of Nutrients Intake with Groups (celiac/GI control) and Height-for-age z-score

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of Height-for-age z-score[2]
Protein	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.095	0.032	0.471
Carbohydrate	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.454	0.215	0.932
Fat	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.552	0.280	0.899
Vitamin D	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.037	0.066	0.032
Calcium	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.043	0.118	0.024
Iron	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.796	0.695	0.540
Fiber	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.415	0.237	0.727

Dependent Variable	**Independent Variables**	**P-value of The Model[1]**	**P-value of group (celiac/GI control)**	**P-value of Height-for-age z-score[2]**
Saturated fat	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.536	0.267	0.800
Vitamin B_{12}	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.083	0.101	0.068
Folate	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.078	0.056	0.407
Total sugar	1) Groups (celiac/GI control) 2) Height-for-age z-score	0.233	0.246	0.146

[1]$P<0.05$ is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is height-for-age z- score

Table A-6: 2 x 2 ANOVA of Nutrients Intake with Groups (celiac/GI control) and BMI-for-age z-score

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of BMI-for-age z-score[2]
Protein	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.108	0.064	0.614
Carbohydrate	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.453	0.219	0.926
Fat	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.529	0.337	0.751
Vitamin D	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.296	0.128	0.481
Calcium	1)Groups (celiac/GI control) 2) BMI-for-age z-score	0.346	0.193	0.333
Iron	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.642	0.615	0.371
Fiber	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.441	0.223	0.970

Dependent Variable	**Independent Variables**	**P-value of The Model[1]**	**P-value of group (celiac/GI control)**	**P-value of BMI-for-age z-score[2]**
Saturated fat	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.452	0.377	0.525
Vitamin B_{12}	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.170	0.568	0.378
Folate	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.071	0.024	0.353
Total sugar	1) Groups (celiac/GI control) 2) BMI-for-age z-score	0.191	0.201	0.113

[1]$P<0.05$ is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is BMI-for-age z- score

Table A-7: Macronutrients Intake in Children with CD with (ATTG>10.4) and (ATTG<10.4)

Variables	Celiac (ATTG>10.4) [1] n=9	Celiac (ATTG<10.4) [1] n=13	DRI	P<0.05[5]	P<0.05[6]
Energy (kcal)[2]	1452-375	1930-448	900-2600	0.016	-
Protein (g)[3]	65.9±21.0	81.5±26.2	13-52	-	0.242
Protein %[4]	18.3±5.3	17.1±4.4	5-30	-	0.333
Carbohydrate (g)3	175.6±85.1	268.9±68.1	130	0.010	-
Carbohydrate %[4]	47.5±17.5	55.9±7.4	45-56	0.132	-
Fat (g)	54.8±20.8	61.5±21.0	-	0.466	-
Fat %[4]	35.0±13.1	28.4±5.7	25-40	0.118	-

[1]Values are shown as mean ± standard deviation
DRI: Dietary Reference Intake.
[2]EER: Estimated Energy Requirement (Otten et al., 2006)
[3]RDA: Recommended Dietary Allowance (Otten et al., 2006)
[4]AMDR: Acceptable Macronutrient Distribution (Otten et al., 2006)
[5]p value from T-test (P<0.05 considered significant)
[6]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table A-8: Micronutrients and (Saturated fat, Total sugar and Fiber) Intake in Children with (ATTG>10.4) and (ATTG<10.4).

Variables	Celiac (ATTG>10.4) [1] n=9	Celiac (ATTG<10.4) [1] n=13	DRI	P<0.05[6]	P<0.05[7]
Vitamin D (IU)[4]	175±86	248±200	600	-	0.920
Calcium (mg)[4]	898±336	968±519	700 - 1300	-	0.973
Iron (mg)[2]	9.1±2.6	12.2±5.1	7-15	-	0.151
Fiber (g)[3]	14.0±4.7	20.6±7.9	19-38	0.038	-
Saturated Fat (g)	21.3±8.7	22.5±8.3	-	0.759	-
Saturated Fat %[5]	13.7±6.0	10.3±2.3	-	-	0.193
Vitamin B_{12} (µg)[2]	2.9±1.2	3.7±2.1	0.9-2.4	-	0.404
Folate (µg)[2]	118.7±84.6	173.5±105.6	150-400	-	0.151
Total Sugar (g)	55.9±27.7	96.1±38.7	-	0.015	-
Total sugar %[5]	16.3±8.7	20.8±7.5	-	0.214	-

[1]Values are shown as mean ± standard deviation (range)
DRI: Dietary Reference Intake.
[2]RDA: Recommended Dietary Allowance (Otten et al., 2006)
[3]AI: Adequate Intake (Otten et al., 2006)
[4]RDA for calcium and vitamin D are from health Canada 2012 source: http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php
[5]Saturated fat recommendation (<10%) of total Energy and total sugar (<25%) of the total energy, Source: (Food and Nutrition Board of Institute of Medicine of The Medicine Academes; 2005) [6]p value of T-test
[7]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table A-9: Macronutrients Intake Adjusted for Energy (per 1000Kcal)

Variables	Celiac [1] F=21/ M=4	GI Control[1] F=12/ M=11	DRI	P<0.05[5]	P<0.05[6]
Protein (g)[3]	43.7±11.4	39.3±7.5	13-52		0.392
Protein %[4]	11.3±4.9	12.3±4.8	5-30		0.556
Carbohydrate (g)[3]	131.9±30.2	139.4±22.9	130	0.338	-
Carbohydrate %[4]	33.9±13.7	44.5±17.9	45-56	0.025	-
Fat (g)	34.4±10.31	33.5±9.4	-	0.740	-
Fat %[4]	20.6±10.7	23.5±10.6	25-40	0.350	-

[1]Values are shown as mean ± standard deviation
DRI: Dietary Reference Intake.
[2]EER: Estimated Energy Requirement (Otten et al., 2006)
[3]RDA: Recommended Dietary Allowance (Otten et al., 2006)
[4]AMDR: Acceptable Macronutrient Distribution (Otten et al., 2006)
[5]p value from T-test (P<0.05 considered significant)
[6]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table A-10: Micronutrients and (Saturated fat, Total sugar and Fiber) Intake Adjusted for Energy (per 1000Kcal)

Variables	Celiac [1] F=21/ M=4	GI Control[1] F=12/ M=11	DRI	P<0.05[6]	P<0.05[7]
Vitamin D (IU)[4]	132±98	106.4±74.1	600	-	0.502
Calcium (mg)[4]	576±287	526.1±207.9	700 - 1300	-	0.749
Iron (mg)[2]	6.4±1.8	8.1±2.5	7-15	-	0.009
Fiber (g)[3]	10.2±3.2	10.6±5.1	19-38	0.723	-
Saturated Fat (g)	12.7±4.8	12.2±4.6	-	0.732	-
Saturated Fat %[5]	7.6±4.7	8.5±4.3	-	-	0.176
Vitamin B_{12} (µg)[2]	2.1±1.0	1.8±0.9	0.9-2.4	-	0.208
Folate (µg)[2]	90.0±47.6	153.1±70.6	150-400	0.001	
Total Sugar (g)	47.4±19.3	47.4±19.7	-	0.991	-
Total sugar %[5]	12.7±7.6	14.7±7.2	-	0.356	-

[1]Values are shown as mean ± standard deviation (range)

DRI: Dietary Reference Intake.

[2]RDA: Recommended Dietary Allowance (Otten et al., 2006)

[3]AI: Adequate Intake (Otten et al., 2006)

[4]RDA for calcium and vitamin D are from health Canada 2012 source: http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php

[5]Saturated fat recommendation (<10%) of total Energy and total sugar (<25%) of the total energy, Source: (Food and Nutrition Board of Institute of Medicine of The Medicine Academes; 2005)

[6]p value of T-test (P<0.05 considered significant)

[7]P value of Mann Whitney test when the assumption of normality not met (P<0.05 considered significant)

Table A-11: Comparison between GFP and Gluten containing products in Fiber and Folate content

Products	Serving Size	Gluten Free Products		Gluten Containing Products	
		Folate (µg)	Fiber	Folate (µg)	Fiber
Bread	1 slice	16	1	23	1.9
Pasta	1 cup	5.3	1.3	108	2.4
Cereal	1 cup	0-15	0.5	20	1.3

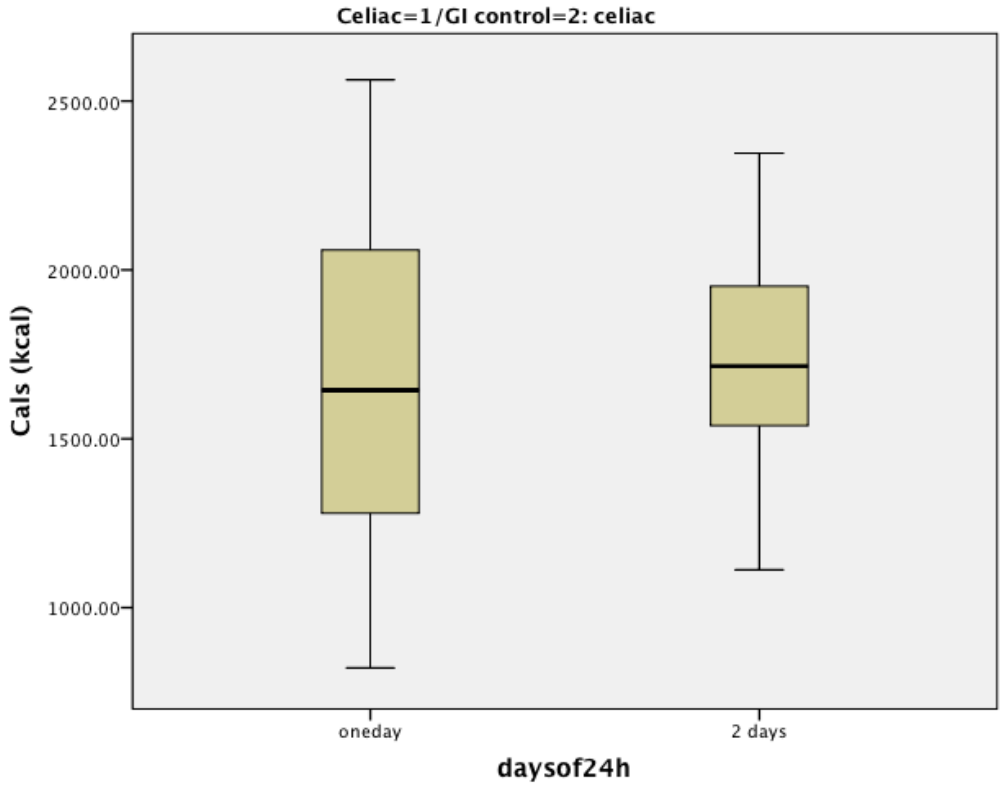


Figure A-1: The Test of Homogeneity of Variance between one day 24-h recall and two days 24-hour Recall in Children with CD

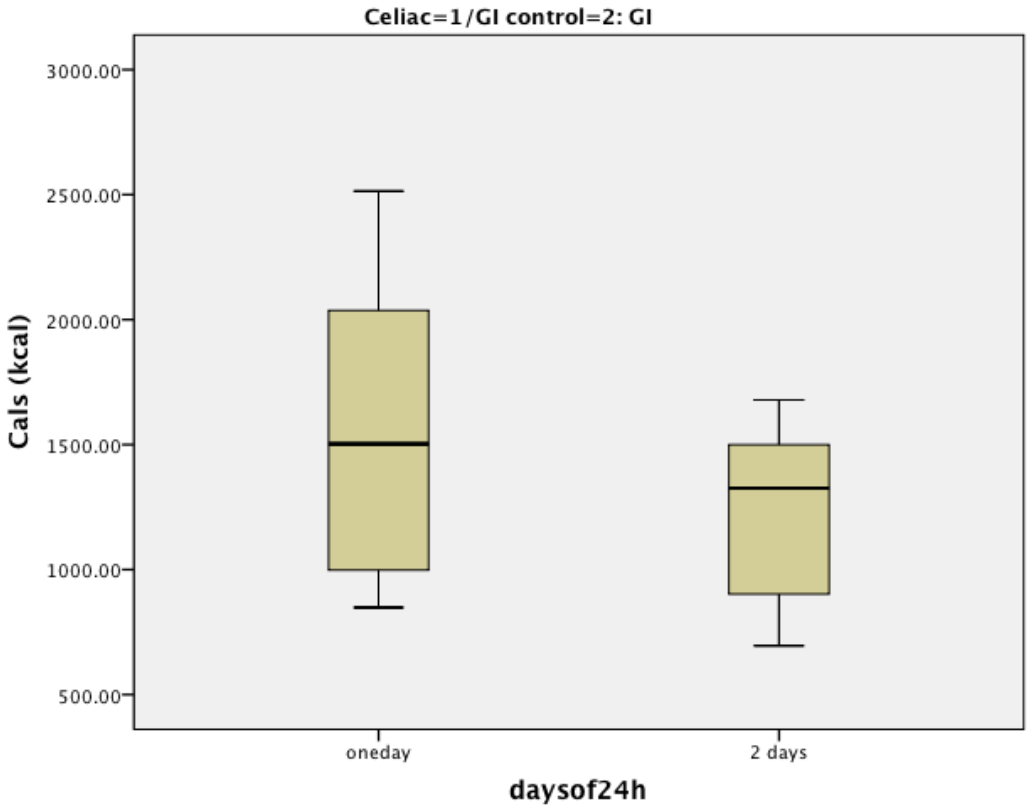


Figure A-2: The Test of Homogeneity of Variance between one day 24-h recall and two days 24-hour Recall in GI Control

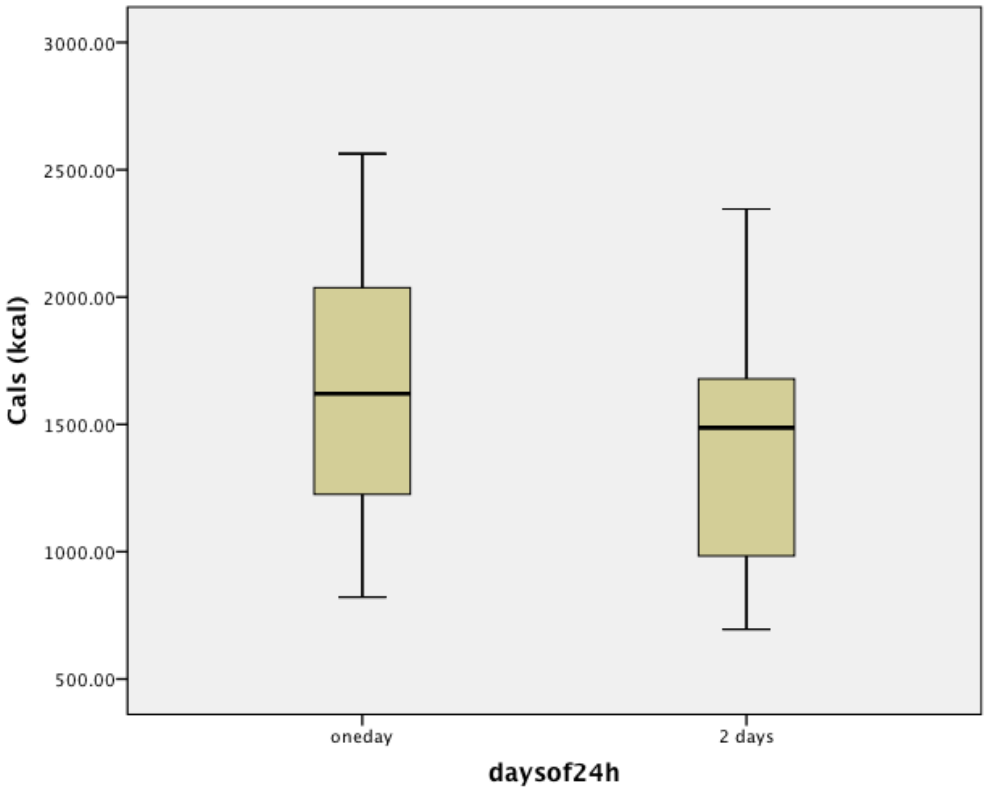


Figure A-3: The Test of Homogeneity of Variance between one day 24-h Recall and two days 24-hour Recall in Children with CD and GI control

Appendix B: Questionnaires and Forms

UNIVERSITY OF ALBERTA

Information Form (Children and Adolescents with Celiac Disease)

Title of Project: Does the gluten free diet meet the nutritional needs of children and adolescents with Celiac Disease?

Principal Investigators:
Justine Turner, MBBS FRACP PhD Telephone: 248-5420
Diana Mager, PhD RD Telephone: 492-7687

This letter is intended for the study subject. If you are signing on behalf of your child, the words 'you' and 'your' should be read as your child.

Purpose of the Study

Celiac disease is a common gastrointestinal illness which may be complicated by problems with absorbing vitamins and minerals. This that can cause problems with growth and overall nutritional status. The treatment for celiac disease is the gluten free diet (GFD). We would like you to participate in a research study that will help us understand if you are getting enough in your diet to grow and to find out what you feel about the gluten free diet. This information will help us understand whether or not children with celiac disease eating the gluten free diet are meeting their nutritional needs.

Procedure(s) of the study

1. Food Intake

We will ask you to tell us about what you are eating on the gluten free diet in clinic so we can understand what types of nutrients you get from the foods you eat. The way we will do this, is that we will ask you to tell us about what types of foods you eat every day. We will also ask you questions about how often you eat different types of foods and how much you eat. All of this information will help us understand how much nutrition you receive from the gluten free diet. The total amount of time this will take in clinic is about 30 minutes.

2. Quality of Life. We will also ask you to fill out a Quality of Life Questionnaire. You can fill this out in clinic or you can take this home and mail it back to us. We will give you a stamped self-addressed envelope to mail it back to us. Our research assistant will answer any questions you might have about this questionnaire. This questionnaire consists of 10 simple questions. This information will help us to understand how you feel about eating the gluten free diet.

3. Weight and Height
We would like to record down your weight and height and your age from your clinic visit. This information is important for us to collect so we can compare your daily intake of nutrients to the recommended levels of intake for your age.

4. Medical Record
We would also like to look at your medical records to find out about medications, relevant lab work (for example your blood work results related to diagnosis of celiac disease such as antibody levels for gluten) and results of other medical tests that were used to find out about your diagnosis of celiac disease. This will help us understand everything about you having celiac disease and how the gluten free diet is helping your gastrointestinal tract to feel better.

Benefits of this Study?
The benefit to you in this study is that we will be able to tell you if you are meeting all of your nutritional needs on the gluten free diet. Your participation in this study will help us learn more about the diets of children with celiac disease. There is very little information about this and we need to understand this so we can provide the best nutritional information about the gluten-free diet.

Risks
The additional tests in this study are the questionnaires that ask you about how you feel about the gluten free diet and about how often you eat certain foods. All of the *additional* tests used in this study are harmless.

Confidentiality: We will share the results about your diet with the dietitian in the clinic. This is important so they can give you advice about how to change your diet to make sure you meet all your nutrient needs. We will not share any other information in your personal health record with anyone. Any research data collected about you during this study will not identify you by name, only by your initials and a coded number. Your name will not be shared with anyone outside the research clinic and your name will not be in any reports published from this research.

The personal health information collected in this study may need to be checked by the Health Research Ethics Board (HREB) at the University of Alberta. This may be necessary so the HREB can make sure that the data collected in the study is accurate.

By signing the consent form you give permission for the collection, use and sharing of information from your medical records for purpose of this research. In the University of Alberta, study information is required to be kept for 5 years. Even if you withdraw from the study, the medical information which is obtained from you the research will not be destroyed. You have a right to check your health records and request changes if your personal information is incorrect.

Voluntary Participation:

You don't have to take part in this study at all or you can quit at any time. No-one will be upset with you if you decide that you don't want to do this or if you decide to stop part way through. You should tell your doctor or the other study investigators if you or your child does not want to participate in this study. This will not affect the care that you and your child will receive by anyone within the clinic or at the Stollery Children's Hospital. You can still continue to see the dietitian, nurse and doctor without participating in this study.

Do you have more questions?

You can ask your dietitian about anything you don't understand. You can also talk to Diana Mager or Justine Turner. Diana Mager's phone number is 492-7687. Justine Turner's telephone number is 248-5420. . If you have any problems or concerns about any part of this study please call the Research Ethics Office at 780-492-2615. This office has no connection with the study researchers.

Principal Investigator: Diana Mager, PhD RD Telephone: 780-492-7687
Principal Investigator: Dr. Justine Turner, MD Telephone: 780-248-5420

UNIVERSITY OF ALBERTA

Information Form (Healthy Children)

Title of Project: Does the gluten free diet meet the nutritional needs of children and adolescents with Celiac Disease?

Principal Investigators:
Justine Turner, MBBS FRACP PhD Telephone: 248-5420
Diana Mager, PhD RD Telephone: 492-7687

This letter is intended for the study subject. If you are signing on behalf of your child, the words 'you' and 'your' should be read as your child.

Purpose of the Study

Celiac disease is a common gastrointestinal illness which may be complicated by problems with absorbing vitamins and minerals. This that can cause problems with growth and overall nutritional status. The treatment for celiac disease is the gluten free diet (GFD). We would like you to participate in a research study that will help us understand if you are getting enough in your diet to grow and to find out what you feel about the gluten free diet. This information will help us understand whether or not children with celiac disease eating the gluten free diet are meeting their nutritional needs.

Procedure(s) of the study

1. Food Intake

We will ask you to tell us about what you are eating on the gluten free diet in clinic so we can understand what types of nutrients you get from the foods you eat. The way we will do this, is that we will ask you to tell us about what types of foods you eat every day. We will also ask you questions about how often you eat different types of foods and how much you eat. All of this information will help us understand how much nutrition you receive from the gluten free diet. The total amount of time this will take in clinic is about 30 minutes.

2) Weight and Height

We would like to record down your weight and height and your age from your clinic visit. This information is important for us to collect so we can

compare your daily intake of nutrients to the recommended levels of intake for your age.

3). Medical Record

We would also like to look at your medical records to find out about medications, relevant lab work (for example your blood work that was done in previously to make sure you don't have celiac disease). This is important as we are comparing the intakes of children without celiac disease to those children who are not on a gluten free diet. This will help us find out if children who eat a gluten free diet are meeting their nutritional needs.

Benefits of this Study?

Your participation in this study will help us learn more about the diets of children with celiac disease. It will also help us understand whether or not the gluten free diet is meeting all of your nutritional needs. There is very little information about this and we need to understand this so we can provide the best nutritional information about the gluten-free diet.

Risks

The additional tests in this study are the questionnaires that ask you about how you feel about the gluten free diet and about how often you eat certain foods. All of the *additional* tests used in this study are harmless.

Confidentiality: We will share the results about your diet with the dietitian in the clinic. This is important so they can give you advice about how to change your diet to make sure you meet all your nutrient needs. We will not share any other information in your personal health record with anyone. Any research data collected about you during this study will not identify you by name, only by your initials and a coded number. Your name will not be shared with anyone outside the research clinic and your name will not be in any reports published from this research.

The personal health information collected in this study may need to be checked by the Health Research Ethics Board (HREB) at the University of Alberta. This may be necessary so the HREB can make sure that the data collected in the study is accurate.

By signing the consent form you give permission for the collection, use and sharing of information from your medical records for purpose of this research. In the University of Alberta, study information is required to be kept for 5 years. Even if you withdraw from the study, the medical information which is obtained from you the research will not be destroyed. You have a right to check your health records and request changes if your personal information is incorrect.

Voluntary Participation:

You don't have to take part in this study at all or you can quit at any time. No-one will be upset with you if you decide that you don't want to do this or if you decide to stop part way through. You should tell your doctor or the other study investigators if you or your child does not want to participate in this study. This will not affect the care that you and your child will receive by anyone within the clinic or at the Stollery Children's Hospital. You can still continue to see the dietitian, nurse and doctor without participating in this study.

Do you have more questions?

You can ask your dietitian about anything you don't understand. You can also talk to Diana Mager or Justine Turner. Diana Mager's phone number is 492-7687. Justine Turner's telephone number is 248-5420. If you have any problems or concerns about any part of this study please call the Research Ethics Office at 780-492-2615. This office has no connection with the study researchers.

Principal Investigator: Diana Mager, PhD RD Telephone: 780-492-7687

Principal Investigator: Dr. Justine Turner, MD Telephone: 780-248-5420

PARENT CONSENT FORM

Title of Project: Does the gluten-free diet meet the nutritional needs of children and adolescents with Celiac Disease?

Principal Investigator(s):
Dr. Justine Turner MBBC FRACP PhD **Phone Number**: 780-248-5620
Diana Mager, PhD RD **Phone Number:** 780-492-7687

	Yes	No
Do you understand that your child has been asked to participate in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved for your child in taking?		
Part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to withdraw your child from the study at?		
Any time, without having to give a reason and without affecting		
Your child's future medical care?	☐	☐
Do you understand who will have access to your child's records?		
Including personally		
Identifiable health information?	☐	☐
Do you want the investigator(s) to inform your child's family doctor or pediatrician		
that your child is participating in this research study?	☐	☐

Doctor's name _____

Who explained this study to you?

_____

Child's Name _____

I agree for my child to take part in this study: YES ☐ NO ☐

Signature of Parent or Guardian _____ Date & Time

(Printed Name) _____

Signature of Parent or Guardian _____ Date & Time

(Printed Name) _____

Signature of Witness _____ Date & Time
Signature of Investigator or Designee _____ Date & Time _____

UNIVERSITY OF ALBERTA

Assent Form

Title of Project: Does a gluten free diet meet all the nutritional needs of children and adolescents with Celiac Disease.

Principal Investigators:
Diana Mager, PhD RD Telephone: 492-7687

Justine Turner, MBBS FRACP PhD Telephone: 248-5620

We would like you to participate in a research study that will help us understand whether or not children with Celiac Disease are getting enough nutrients on the gluten free diet.

What will you have to do?
If you and your parents agree that its okay to take part in this study we will ask you to:

1. We will also ask you some questions about what you eat every day on the. In total answering these questions might take 30-40 minutes of your time.
2. We will record down your weight, height and age from your clinic visit. We want to do this so we can compare what nutrients you get from your food to your requirements for these nutrients.
3. We will review your medical chart for your blood work to make sure you don't have celiac disease.

Will it help?
We do know that some children with celiac disease don't get enough vitamins and minerals for their age. We are not sure if a gluten free diet alone is enough to help them grow and we want to understand this. We want to compare the amount of vitamins and minerals you get on diet (on a typical diet) to the amount of vitamins and minerals that children with Celiac Disease get on their diet (gluten free diet). This is important so we know what nutritional advice we need to give to children with Celiac Disease.

Will it hurt?
None of the questions will hurt. You do not have to answer all the questions if you don't want to.

Can you quit?
You don't have to take part in the study at all, and you can quit at any time. No one will be mad at you if you decide you don't want to do this, or if you decide to stop part way through. You should tell the doctor or nurse that you want to quit.

Who will know**?**
No one except your parents and the doctor will know you're taking part in the study unless you want to tell them. Your name and your chart won't be seen by anyone except the doctors, research study employees and nurses during the study.

Your signature
We would like you to sign this form to show that you agree to take part. Your mom or dad will be asked to sign another form agreeing for you to take part in the study.

Do you have more questions?
You can ask your parent or guardian about anything you don't understand. You can also talk to Dr Turner or Dr. Mager. Dr Turner's phone number is 248-5620, Dr. Mager's phone number is 492-7687. If you have any problems or concerns about any part of this study please call the Human Research Ethics Board at 492-2615, This office has no connection with the study researchers.

I agree to take part in the study.

Signature of research participant:_____Date: _____

Signature of witness:_____Date: _____

Signature of investigator:_____ Date:_____

Version 2 November 10 2011

UNIVERSITY OF ALBERTA

Assent Form (Children with Celiac Disease)

Title of Project: Does a gluten free diet meet all the nutritional needs of children and adolescents with Celiac Disease.

Principal Investigators:
Diana Mager, PhD RD Telephone: 492-7687
Justine Turner, MBBS FRACP PhD Telephone: 248-5620

You have Celiac Disease. We would like you to participate in a research study that will help us understand whether or not you are getting enough nutrients in the foods that you eat.

What will you have to do?
If you and your parents agree that its okay to take part in this study we will:

1. Ask you about what you eat every day on the gluten free diet and how you feel about eating the gluten free diet. In total answering these questions might take 30-40 minutes of your time.
2. Record your weight, height and age from your clinic visit. We want to do this so we can compare what nutrients you get from your food to your requirements for these nutrients.
3. Review your medical chart for your blood work to see how the gluten free diet is helping your celiac disease.

Will it help?
We do know that some children with celiac disease don't get enough vitamins and minerals for their age. We are not sure if a gluten free diet alone is enough to help you grow and we want to understand this.

Will it hurt?
None of the questions will hurt. You do not have to answer all the questions if you don't want to.

Can you quit?
You don't have to take part in the study at all, and you can quit at any time. No one will be mad at you if you decide you don't want to do this, or if you decide to stop part way through. You should tell the doctor or nurse that you want to quit.

Who will know**?**
No one except your parents and the doctor will know you're taking part in the study unless you want to tell them. Your name and your chart won't be seen by anyone except the doctors, research study employees and nurses during the study.

Your signature
We would like you to sign this form to show that you agree to take part. Your mom or dad will be asked to sign another form agreeing for you to take part in the study.

Do you have more questions?
You can ask your parent or guardian about anything you don't understand. You can also talk to Dr Turner or Dr. Mager. Dr Turner's phone number is 248-5620, Dr. Mager's phone number is 492-7687. If you have any problems or concerns about any part of this study please call the Human Research Ethics Board at 492-2615, This office has no connection with the study researchers.

I agree to take part in the study.

Signature of research participant:_____Date: _____

Signature of witness:_____Date: _____

Signature of investigator:_____ Date:_____

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4-Hour recall
Participant ID #:
Interviewer Name:
Date:

Time, Location, Meal# or Snack#	Foods, Beverages, Condiments, Sauces, Spreads	Brand, Preparation Method	Portion Size

Instructions

The 24-hour recall will be conducted in four stages ("Multiple Pass Method").

Multiple Pass Method

1) Obtain a complete list of all foods and beverages consumed from the previous day, together with the time and place of consumption. Begin by asking about the first food and/or drink consumed in the morning. Avoid asking questions about specific meals (eg. breakfast, lunch, or supper). Rather, use neutral questions such as "*Tell me what you had to eat or drink after you woke up yesterday morning. What was the time? Did you eat that food at home? What did you have next and when was that?*" Proceed through the day, repeating these questions as necessary, and record each food or drink consumed. Prompting the subject about his or her activities during the previous day may help in recalling food intake.

2) Go over each of the responses, probing for more specific descriptions of all the foods and drinks consumed, including cooking methods and brand names. Information on the place and time of eating should also be recorded. Examples of prompts for specific food items are:

i) Meat: type of meat, description of cut, method of cooking, lean or lean + fat, sauces

ii) Poultry: type of poultry, parts or pieces eaten, method of cooking, white or dark meat, meat + skin or meat only, sauces

iii) Milk products: type of dairy product, brand name, percentage fat

iv) Bread/rolls: type of grain (eg. rye, whole wheat, etc.), homemade/store bought, size, toasted, condiments (eg. butter, jam, etc.)

v) Vegetables: fresh/frozen/canned, peeled/unpeeled, method of cooking, topping

vi) Beverages: volumetric or fluid ounces, size of can or bottle, sweetened/unsweetened, water

3) Obtain estimates of the amounts of all foods and beverages consumed. Record as volumes (eg. cups, tablespoons, millilitres) or as weights (eg. grams, pounds, ounces).

i) If the interview is in person, refer to the food models, measuring cups and spoons, plates, glasses, bowls, and serving sizes handout.

ii) If the interview is via phone ask the participant to take out a set of measuring cups and spoons, as well as the cup(s), bowl(s), glass (es) that they used the previous day. Send them a copy of the serving sizes handout in advance and ask them to refer to it during the conversation.

4) Review the recall with the subject to ensure that all items have been recorded correctly. A statement such as "*I will read back to you what I have recorded to make sure that I have not made any mistakes*" can be used. Finally, the subject should

be asked about the use of any vitamin and mineral supplements, protein or diet drinks, and any alcohol consumed. Inquire about foods/beverages consumed in the middle of the night. Check for missing condiments, food groups (eg. meat, milk products), and fluids.

Additional Notes:

* The same interviewer should do all four interviews of the same participant.
* Standardized household dishes and utensils and food models should be used as much as possible.
* If the recall is done by phone, ask the individual to set out some of their own dishes/utensils of known quantities.

Oct 13th 2011

Vitamin D and Calcium Intake Questionnaire

Name: Date:

If you eat any of the following foods write how much you would have in a serving, then check off how often

Food	Medium Serving	Patient's serving	Never or < once per a month	1-2 per month	2-3 per month	1 per week	2 per week	3-4 per week	5-6 per week	1 per day	> 1 per day
Cold cereal	*1 cup*										
Milk (whole, Low Fat, skim, choc, soy)	*8 oz (1 cup)*										
Milk over cereal	*4 oz (1/2 cup)*										
Milk, cream in coffee	*1 oz (2 tbsp)*										
Buttermilk, whole	*8 oz (1 cup)*										
Yogurt (fruited or flavored)	*1 cup 2containers*										
Yogurt (plain)	*1 cup 2containers*										
Ice cream or ice milk	*1/2cup*										
Frozen yogurt	*8 oz (1 cup)*										
Ice cream bar, fudge bar	*1 each*										
American or mozzarella	*1 oz*										

Food	Medium Serving	Patient's serving	Never or < once per a month	1-2 per month	2-3 per month	1 per week	2 per week	3-4 per week	5-6 per week	1 per day	> 1 per day
Cream Cheese	*1 oz*										
Macaroni and cheese, lasagna	*1 cup*										
Cheese pizza	*1/8 large*										
Cottage cheese	*1 cup*										
Cheese food or spread	*1 oz*										
Pudding or custard made with milk	*1/2 cup*										
Cream soup, chowders, cream sauces	*1 cup*										
Broccoli	*1/2 cup*										
Greens: mustard, turnip, collard, beet, spin.	*1/2 cup*										
Calcium Fortified Juice (orange, others)	*8 oz*										
Bread (white/wheat/pita)	*1 slice*										
Muffins	*1 medium*										
Biscuit, cornbread	*2" cube*										
Pancakes/waffles frozen	*4"*										
Pancakes/waffles-HM	*4"*										

Food	Medium Serving	Patient's serving	Never or < once per a month	1-2 per month	2-3 per month	1 per week	2 per week	3-4 per week	5-6 per week	1 per day	> 1 per day
Spaghetti w/tomato sauce	*1 cup*										
Eggs	*1 small each*										
Fast Food Hamburger	*1 each*										
Fast Food Cheeseburger	*1 each*										
Oysters, shrimp, crab, crawfish, herring	*3 oz*										
Canned Salmon w/Bones	*3.75oz can*										
Sardines	*3.75oz can*										
Cake	*3×3×2"*										
Almonds	*1/4 cup*										
Milk Chocolate	*1.6oz bar*										
Other food items (Ensure, Boost, Power bars, etc)											

	Brand Name	Serving	Serving/ day	Serving/ week
Multivitamins		1 Tablet		
Calcium Supplement		1 Tablet		
Vitamin D supplement		1 Tablet		

Measurement Conversions

1 cup = 8 ounces = 250 mL
1 ounce = 2 tbsp = 30 mL; 1 tbsp = 0.5 ounce = 15 mL
1 can of pop = 355mL = 1.5 cups
1 single container yogurt = 100g = about ½ cup

Appendix C: Tables (2X2 ANOVA Related to Age (below and above 10 years old), Duration of CD and Gender)

Table C-1: The effect of Duration of CD and Age (Above and below 10 years of age) on Anthropometric data

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of duration of the disease	P-value of age (below and above 10 years old)[2]
Weight	1) Duration of CD 2) Age (below and above 10 years old)	0.001	0.304	0.000
Height	1) Duration of CD 2) Age (below and above 10 years old)	0.000	0.299	0.000
BMI	1) Duration of CD 2) Age (below and above 10 years old)	0.195	0.596	0.074
Weight-for-age z-score	1) Duration of CD 2) Age (below and above 10 years old)	0.006	0.045	0.037
Height-for-age z-score	1) Duration of CD 2) Age (below and above 10 years old)	0.022	0.031	0.219
BMI-for-age z-score	1) Duration of CD 2) Age (below and above 10 years old)	0.053	0.628	0.030

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age above and below 10 years old

Table C-2: Interrelationships between Vitamin D, Calcium and Duration of CD and Blood Test

Dependent Variable	Independent Variables	Pearson Correlation (r^2)	P-value of The Model
Vitamin D(IU)	25(OH)D (nmol/L)	0.064	0.800
Iron (mg)	Ferritin (ug/L)	0.296	0.181
Duration of CD	ATTG (U/mL)	-0.267	0.733

Table C-3: Effect of Age (Above and below 10 years of age) on Macronutrient Intake in Children with CD and in GI controls

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of age (below and above 10 years old)[2]
Protein	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.047	0.024	0.067
Carbohydrate	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.421	0.164	0.288
Fat	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.704	0.301	0.543

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age above and below 10 years old

Table C-4: Effect of Gender on Macronutrient Intake in Children with CD and GI Controls

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of Gender (male and female)[2]
Protein	1) Groups (celiac/GI control) 2) Gender (male and female)	0.168	0.030	0.548
Carbohydrate	1) Groups (celiac/GI control) 2) Gender (male and female)	0.417	0.258	0.450
Fat	1) Groups (celiac/GI control) 2) Gender (male and female)	0.417	0.376	0.406

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is gender (male and female)

Table C-5: Effect of Age and Duration of CD on Macronutrient Intake in Children with CD

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of duration of the disease	P-value of age (below and above 10 years old)[2]
Protein	1) Duration of the disease 2) Age (below and above 10 years old)	0.320	0.625	0.200
Carbohydrate	1) Duration of the disease 2) Age (below and above 10 years old)	0.597	0.436	0.651
Fat	1) Duration of the disease 2) Age (below and above 10 years old)	0.846	0.903	0.605

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age (above and below 10 years old)

Table C-6: Effect of Age on Vitamin D and Calcium Intake (without Supplementation)

Dependent Variable	Independent Variables	P-value of The Model[2]	P-value of group (celiac/GI control)	P-value of age (below and above 10 years old)[3]
Vitamin D[1]	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.421	0.099	0.914
Calcium[1]	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.141	0.068	0.681

[1]Vitamin D and Calcium without supplementation

[2]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[3]The main effect is age above and below 10 years old

Table C-7: Effect of Gender on Vitamin D and Calcium Intake (without Supplementation)

Dependent Variable	Independent Variables	P-value of The Model[2]	P-value of group (celiac/GI control)	P-value of Gender (male and female)[3]
Vitamin D[1]	1) Groups (celiac/GI control) 2) Gender (male and female)	0.069	0.739	0.044
Calcium[1]	1) Groups (celiac/GI control) 2) Gender (male and female)	0.215	0.797	0.164

[1]Vitamin D and Calcium without supplementation

[2]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

3 main effect is gender (male and female)

Table C-8: Effect of Age and Duration of CD on Vitamin D and Calcium Intake (without supplementation)

Dependent Variable	Independent Variables	P-value of The Model	P-value of duration of the disease[2]	P-value of age (below and above 10 years old)[3]
Vitamin D[1]	1) Duration of CD 2) Age (below and above 10 years old)	0.617	0.348	0.966
Calcium[1]	1) Duration of CD 2) Age (below and above 10 years old)	0.158	0.107	0.502

[1] Vitamin D and Calcium without supplementation

[2] $P<0.05$ is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[3] The main effect is age (above and below 10 years old)

Table C-9: The Effect of Age (below and above 10 years old) on (Iron, Folate, vitamin B_{12}) Intake in Children with CD and Children with Chronic GI Diseases

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of age (below and above 10 years old)[2]
Iron	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.415	0.660	0.234
Vitamin B_{12}	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.194	0.060	0.472
Folate	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.091	0.153	0.141

[1]$P<0.05$ is considered significant, P value of the interaction was removed from the model because the interaction is not significant
[2]The main effect is age above and below 10 years old

Table C-10: The Effect of Gender on (Iron, Folate, vitamin B_{12}) Intake by in Children with CD and Children with Chronic GI Diseases

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of Gender (male and female)[2]
Iron	1) Groups (celiac/GI control) 2) Gender (male and female)	0.262	0.838	0.069
Vitamin B_{12}	1) Groups (celiac/GI control) 2) Gender (male and female)	0.133	0.720	0.077
Folate	1) Groups (celiac/GI control) 2) Gender (male and female)	0.086	0.012	0.245

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is gender (male and female)

Table C-11: The Effect of Duration of CD and Age on (Iron, Folate, vitamin B_{12}) Intake in Children with CD and Children with Chronic GI Diseases

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of duration of CD	P-value of age (below and above 10 years old)[2]
Iron	1) Duration of CD 2) Age (below and above 10 years old)	0.182	0.295	0.204
Vitamin B_{12}	1) Duration of CD 2) Age (below and above 10 years old)	0.654	0.458	0.723
Folate	1) Duration of CD 2) Age (below and above 10 years old)	0.914	0.891	0.677

[1]$P<0.05$ is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age (above and below 10 years old)

Table C-12: The Effect of Age (above and below 10 years of age) on (Fiber, Saturated Fat and Total Sugar) Intake in Children with CD and Children with Chronic GI Diseases

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of age (below and above 10 years old)[2]
Fiber	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old))	0.446	0.230	0.276
Saturated fat	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.699	0.296	0.549
Total sugar	1) Groups (celiac/GI control) 2) Ages (below and above 10 years old)	0.497	0.290	0.527

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age (above and below 10 years old)

Table C-13: The Effect of Gender on, Fiber, Saturated Fat and Total Sugar Intake in Children with CD and Children with Chronic GI Diseases

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of group (celiac/GI control)	P-value of Gender (male and female)[2]
Fiber	1) Groups (celiac/GI control) 2) Gender (male and female)	0.076	0.351	0.163
Saturated fat	1) Groups (celiac/GI control) 2) Gender (male and female)	0.337	0.369	0.341
Total sugar	1) Groups (celiac/GI control) 2) Gender (male and female)	0.625	0.754	0.617

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is gender (male and female)

Table C-14: The Effect of Duration of CD and Age on, Fiber, Saturated Fat and Total Sugar Intake

Dependent Variable	Independent Variables	P-value of The Model[1]	P-value of duration of CD	P-value of age (below and above 10 years old)[2]
Fiber	1) Duration of CD 2) Age (below and above 10 years old)	0.621	0.955	0.342
Saturated fat	1) Duration of CD 2) Age (below and above 10 years old)	0.487	0.288	0.443
Total sugar	1) Duration of CD 2) Age (below and above 10 years old)	0.521	0.935	0.280

[1]P<0.05 is considered significant, P value of the interaction was removed from the model because the interaction is not significant

[2]The main effect is age (above and below 10 years old)

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