

Nutritional and Neurological Assessment in Adult Patients with Celiac Disease

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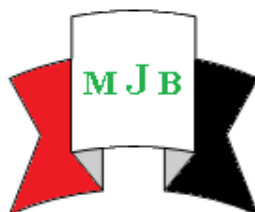
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Abstract

celiac disease is a chronic inflammatory, autoimmune disorder characterize by malabsorption of nutrient after ingestion of gluten, it is prevalence nearly 1% in many country, clinical manifestation either gastro intestinal manifestation such as diarrhea, abdominal pain, bloating, weight loss, constipation, or non-gastro intestinal manifestation such as anemia, neuropathy and unexplained infertility. The aim of this study is to assess the nutritional status and determine the diet satisfaction & burden of gluten-free diet therapy in celiac patients also to assess the autonomic and peripheral neuropathy in those patients.

This was Cross-sectional study conducted in gastroenterology and Hepatology Center at Marjan Medical City in Babylon province, Hilla city, from 15th February 2014 to 31 of May 2014. All patients included were proved celiac and on gluten-free diet. Data obtained included questionnaires, measurement which includes body mass index, nerve conductive study, blood pressure in response to standing position and hand grip and heart rate in deep breathing with laboratory investigation includes complete blood count, serum albumin, serological test of celiac disease.

The study included 70 patient, were 45 are female and 25 are male whose mean age was (30.67± 9.72) years old. of those 34.3% were underweight and 65.7% were not underweight (normal 51.4%, overweight 11.4%, obese 2.9%) , 18.6% of all included patient had family history of celiac disease, while the percentage of patients whose suffer from diarrhea, abdominal pain and problem in the feet (pain, numbness, tingling) were 60%, 64.3%, 37.1% respectively and 57.1% had anemia, 29.1% of married female had unfavorable outcome of pregnancy and 17.3% of married female and male had unexplained infertility. Regarding the neuropathy 34.3% had autonomic neuropathy and only 2.9% had peripheral neuropathy.

According to diet satisfaction and burden of gluten free diet there was statistical significant association between BMI and history to make menus, not being able to eat same foods as other family members, feeling satisfied after meals and feeling that the health condition is good.

In the finding of present study there are high percentage of underweight in contrast to overweight and obesity in patients with celiac disease with high prevalence of anemia mainly iron deficiency anemia and also shows high prevalence of autonomic neuropathy compare to peripheral neuropathy, the celiac disease may be the one cause of unexplained infertility and unfavorable outcome of pregnancy.

Regarding the diet satisfaction and burden of gluten free diet, most of the patients with underweight had no history to make menu and feeling not satisfied after meal and health condition is not good and most of celiac patient had burden of cooking gluten free diet.

Keywords: celiac disease, nutritional assessment, peripheral neuropathy, autonomic neuropathy

الخلاصة

خلفية البحث: -الداء الزلاقي هو التهاب المناعة الذاتية المزمن ويتميز بسوء الامتصاص للمواد الغذائية بعد تناول مواد غذائية حاوية على الكلوتين , نسبة انتشاره تقريبا ١% في العديد من البلدان, المظاهر السريرية هي اما مظاهر متعلقة بالجهاز الهضمي مثل الاسهال , الم البطن , الانتفاخ , فقدان الوزن , والامساك او مظاهر غير متعلقة بالجهاز الهضمي مثل فقر الدم , الاعتلال العصبي والعقم غير المفسر , العلاج الوحيد للداء الزلاقي هو اتباع نظام غذائي خالي من الكلوتين .

اهداف البحث: -تقييم الحالة التغذوية وتحديد الاكتفاء الغذائي وعبئ النظام الغذائي الخالي من الكلوتين وأيضا تقييم الاعتلال العصبي اللاإرادي والطرقي في نفس المرضى .

تصميم البحث:- دراسة مقطعية أجريت في مركز الجهاز الهضمي والكبد في مدينة مرجان الطبية , في محافظة بابل. مدينة الحلة ١٥ - ٢٠١٤ ولغاية ٣١- ٥- ٢٠١٤ وشملت جميع المرضى المثبتة اصابتهن بداء الزلاقي وهم على نظام غذائي خالي من الكلوتين . البيانات التي تم الحصول عليها شملت الاستبيانات , القياسات والتي تشمل مؤشر كتلة الوزن , دراسة التوصيل العصبي , ضغط الدم استجابة لوضع الوقوف وقبضة اليد ومعدل ضربات القلب في التنفس العميق والتحاليل المختبرية التي تشمل تعداد الدم الكامل , اليومين المصل واختبار المصلية أداء الزلاقي.

نتائج البحث: -الدراسة شملت ٧٠ مريض ٤٥ من الاناث و ٢٥ من الذكور الذين معدل أعمارهم ٣٠.٦٧ ± ٩.٧٢ سنة , منهم ٣٤.٣% يعانون نقص الوزن و ٦٥.٧% لا يعانون من نقص الوزن (وزن طبيعي ٥١.٤% , زيادة وزن ١١.٤% , سمنة ٢.٩%) . ١٨.٦% من جميع المرضى المشمولين لديهم تاريخ عائلي لمرض داء الزلاقي في حين نسبة المرضى الذين يعانون من الاسهال , ألم البطن ومشكلة في القمنين هي ٦٠% , ٦٤.٣% , ٣٧.١% على التوالي و ٥٧.١% لديهم فقر الدم , ٢٩.١% من النساء المتزوجات لديهم نتائج غير مؤاتية للحمل , ١٧.٣% من النساء والرجال المتزوجون لديهم عقم غير مفسر . فيما يخص الاعتلال العصبي ٣٤.٣% لديهم الاعتلال العصبي اللاإرادي فقط ٢.٩% لديهم الاعتلال العصبي الطرفي.

فيما يتعلق بالاكتفاء الغذائي وعبي النظام الغذائي الخالي من الكلوتين على المرضى المشاركين في الدراسة وجد ان هناك ترابط وثيق احصائيا بين مؤشر كتلة الوزن والتزام المريض بقائمة الطعام , عدم التمكن من تناول الأطعمة نفسها كغيرهم من افراد الاسرة , الشعور بالاكتفاء بعد الوجبة والشعور بان حالته الصحية جيدة.

الاستنتاجات:- وجود نسبة عالية من نقص الوزن مع نسبة عالية لفقر الدم وخاصة فقر الدم الناتج من نقص الحديد كما تظهر نسبة عالية للاعتلال العصبي اللاإرادي مقارنة بالاكتلال العصبي الطرفي. وقد يكون الداء الزلاقي أحد أسباب العقم غير المفسر والنتائج غير المؤاتية للحمل.

فيما يخص الاكتفاء الغذائي وعبي النظام الغذائي الخالي من الكلوتين , معظم المرضى المصابين بنقص الوزن ليس لديهم قائمة طعام والشعور بعدم الاكتفاء بعد تناول وجبة الطعام وان حالتهم الصحية ليست جيدة وان معظم مرضى داء الزلاقي لديهم عبي الطبخ للنظام الغذائي الخالي من الكلوتين.

مفاتيح الكلمات: الداء الزلاقي, تقييم التغذية, الاعتلال العصبي الارادي, الاعتلال العصبي الطرفي.

Introduction

Celiac disease (CD) is a chronic inflammatory and immune-mediated disease of the mucosa of the proximal small intestine due to irreversible gluten intolerance in genetically susceptible individuals [1, 2]. Wheat, rice and maize are the most widely consumed food grains in the world. Wheat is the most widely grown crop, Gluten is the main structural protein complex of wheat with equivalent toxic proteins found in other cereals, including rye and barley[3]. Gluten refers to a set of amino acid sequences found in the prolamine fraction of wheat, barley and rye, The characteristic finding on histopathology is a varying degree of villous atrophy and crypt hyperplasia, especially in the duodenum and jejunum, with inflammatory changes leading to malabsorption [1,2]. The prevalence of CD varies between 0.5%–1% in different parts of the world [4] in Iran the prevalence is 1:104 [5], in Turkey is 1:100 [6], while in United state is 1:105 [7], and in Tunisia is 1:709 [8]. CD also called gluten-sensitive enteropathy or non-tropical sprue [9], although it is classically a disease of infants ,and children it often presents in later, especially in the second and fifth, decades of life and, women are affected twice more than men [10,11].

There are two other condition that related to ingestion of gluten include wheat allergy (WA) and gluten sensitivity (GS) [3].

WA is the cross-linking of immunoglobulin (Ig)E by repeat sequences in gluten peptides (for example, serine-glutamine-glutamine-glutamine-(glutamine-) proline-proline-phenylalanine) that triggers the release of chemical mediators, such as histamine, from basophils and mast cells [3], while GS is gluten reactions in which neither allergic nor autoimmune mechanisms are involved. These individuals experience distress and develop an adverse reaction with gastrointestinal symptoms resemble those associated with CD when eating gluten-containing products and show improvement following GFD but it does not lead to damage in the small intestine [12, 13, 14, 15, 16].

The etiology of celiac disease is not clearly known. Many factors, such as environmental, genetic, and immunological factors are involved in the pathology of celiac disease. Gliadin, a part of gluten present in rye, wheat, and barley, is an environmental factor associated with celiac disease [9]. The immunologic component in the pathogenesis of celiac disease involves both innate and adaptive responses. The most important genes associated with susceptibility to celiac

disease are human leukocyte antigen HLA-DQ2 and HLA-DQ8 about 90% and 10% respectively [17], the gold stander for definitive diagnosis of CD is endoscopy with biopsy of the small intestine plus positive CD serology(18), these include Serum antibodies {anti-gliadin immunoglobulin A(IgA) antibody, IgA anti-endomysial antibody, and IgA antibodies to tissue transglutaminase (tTG) }are presentin celiac disease. Due to high specificity (90-95%) and high sensitivity (90%) [9,19].

The clinical manifestation of CD involves wide range of signs and symptoms the typical and most common Gastrointestinal manifestation due to celiac disease or secondary to vitamin deficiencies and nutrient malabsorption are diarrhea ,abdominal pain ,abdominal bloating ,weight loss ,anemia, while the atypical or extraintestinal manifestations are osteopenia, unexplained infertility, dermatitis herpetiformis , anemia, and neurologic complications [9, 20], other patients are asymptomatic and diagnosed by screening test for high risk group by serological investigation and histopathological studies. This type of disease is referred to as silent celiac disease. clinical manifestations of CD vary markedly with age of patients, duration and extent of disease and the presence of extra-intestinal manifestations [9, 20, 21].

Nutritional status assessed by measurement the body mass index and serum concentrations of folic acid , vitamin A, B₆, B₁₂, and D, zinc, haemoglobin (Hb) and ferritin should be done in celiac patient at the time of diagnosis and for follow up [22], almost all CD patient had at least one value below the lower limit of reference. Specifically, for vitamin A, 7.5% of patients showed deficient levels, for vitamin B₆ 14.5%, folic acid 20%, and vitamin B₁₂ 19%. Likewise, zinc deficiency was observed in 67% of the CD-patients, 46% had decreased iron storage , and 32% had anemia [22],CD is a common cause of various hematologic disorders, the most common of which is anemia and common

type of anemia is iron deficiency anemia (IDA) which may be the first manifestation of CD , The anemia of CD is usually due to malabsorption of micronutrients such as iron, folic acid, and vitamin B12 [23].

CD may initially present as one or more neurological signs and/or symptoms. On the other hand, it may be associated with or complicated by neurological manifestations. Neurological presentations are rare in children but as many as 36% of adult patients present with neurological changes [24]. With severe malnutrition after progression of celiac disease, different vitamin deficiencies may develop. Such problems can in turn overlap with neurological abnormalities including ataxia, epilepsy, peripheral neuropathy, autonomic neuropathy, dementia, and cognitive disorders [25, 26, 27].

The only treatment of CD patient is lifelong treatment with GFD [28], If the patient does not adhere to a GFD, both malabsorption and extraintestinal complications may develop [20]. Therefor early diagnosis and dietary treatment might slow down the progression of associated autoimmune diseases and other complication and help in resolving long-lasting health problems in coeliac disease[20].

Aim of this study is to assess the nutritional status and determine the diet satisfaction & burden of gluten-free diet therapy in celiac patient to assess the autonomic and peripheral neuropathy in those patients.

Material and Methods

This cross-sectional study was carried out at Gastroenterology and HepatologyCenter in Merjan Medical City in Babylon, Hilla City. included 70 patients (25 male and 45 female) , from 15th February 2014 to 31 of May 2014 were involved in this study.

Inclusion criteria: All patients included in our study are proved celiac disease by subjective symptom, positive serology and positive second part duodenal biopsy, and all patient on gluten free diet ,with average age between 18-60 years old.

exclusion criteria: We excluded all patient with diabetes ,chronic kidney disease , tuberculosis, alcoholic patients, also exclude any other cause of chronic diarrhea such as inflammatory bowel disease and all chronic disease that may interfere with the result of autonomic and peripheral neuropathy .

Study Instruments included:

1)Questionnaire

A- The socio-demographic characteristics that composed of age, sex, marital status, residence, occupational status and educational level.

B-The patient's medical history which composed of age of onset of disease, duration of disease, smoking status, family history of celiac disease, history of unexplained infertility, unfavourable outcome of pregnancy , presenting signs and symptoms and history of feet problem.

C-Questionnaire about gluten free diet which include:-

1- Asking about history of diet satisfaction for patients with celiac disease such as: feeling diet is delicious, feeling satisfaction after meal and able to enjoy meal.

2- Asking about burden of diet therapy such as: necessity to eat meal at regular hour, necessity to make menus, able to eat favorite foods, not being able to eat same food as other family members, economic burden of diet therapy and burden of cooking the gluten free diet.

3- Asking about perceived gluten free diet therapy such as: feeling that the health condition is good, feeling that the family bond has become closer and having learned to lead regular life.

2)Venous blood sample

5 milliliter (ml) of blood aspirated from included patients and sent to:

A-The complete blood count (CBC):

To measure the haemoglobin, white blood cell, neutrophils, red cell volume, the results of The blood sample will be processed by a machine which is Ruby Haematology Analyser (made in USA).

B- Serological test of celiac disease:

Which included immunoglobulins A and G level against tissue transglutaminase

antibodies and Antigliadin antibody. These tests always have been done by using a machine which is Chorus (made in Italy).

C-serum albumin:

This test done by using a machine, which is spectrophotometer (made in Germany).

3) Assessment of Cardiovascular Autonomic Neuropathy (CAN)

The assessment of the autonomic nervous system was achieved via the following testeswhich done by using machine patient monitor Philips (made in Germany) these test are:

A- Measurement of Heart Rate in Response to Deep Breathing for Assessment of the Parasympathetic Autonomic System

This test was performed by allowing the subject to sit quietly and breathe deeply at six breaths for one minute (five second in and five second out). The result obtain bythe difference between maximum heart rate during inspiration from the minimum heart rate during expiration during each breathing cycle. Normal>15, borderline 11-14, abnormal<10 [29].

B-Measurement of the Blood Pressure in Response to Standing Position for Assessment of the Sympathetic Autonomic System

The test was performed by measuring the subject's blood pressure while he was lying down quietly and again when he stands up. The postural fall in blood pressure is taken as the difference between the systolic blood pressure lying and the systolic blood pressure standing. Normal <10, borderline 11-29, abnormal >30 [30].

C-Measurement of the Blood Pressure in Response to Hand Grip for Assessment of the Sympathetic Autonomic System

It was performed by allowing the subject to do maximum voluntary contraction using a handgrip dynamometer. Handgrip was then maintained at 30% of that maximum for as long as possible up to five minutes. Blood pressure was measured three times before and at one-minute intervals during handgrip. The result was expressed as the difference between the highest diastolic blood pressure during handgrip exercise

and the mean of the three diastolic blood-pressures reading before handgrip began ,normal >16 ,borderline 11-15 ,abnormal <10 [31].

Diagnosis of autonomic neuropathy was made if two borderline test or one abnormal test.

4) Assessment of Peripheral Neuropathy by Nerve Conduction Study (NCS)

This test done by machines Nihon Kohden (made in Chapin) and Nicolet (made in Italy) for examination of lower limbs for detection of peripheral neuropathy by examined the sural nerve for sensory impairment while peroneal nerve and tibial nerve for motor impairment.

NCS involve the stimulation of the nerves with small surface electrical impulses over several points (usually limbs) Pairs of electrodes are used one to initiate the impulse and the other to record the response [32].

5) Nutritional Assessment :-

Anthropometric measurement

Which included measurement of weight (WT) , height (HT) and body mass index (BMI), which measured according to the formula of ($\text{Weight kg/Height m}^2$) in which the weight was measured in (kilogram) using the balanced scale for all subject (wearing light clothing) with an accepted error of 0.1 kg. Height was measured (in meter) using a fixed board measures to the nearest 0.5 cm with the patient standing without shoes, heels together and the head in the horizontal plane.

The BMI score included: - under wt ($\text{BMI} < 18.5 \text{ kg/ m}^2$) , normal wt ($\text{BMI} 18.5-24.9 \text{ kg/ m}^2$) ,over wt ($\text{BMI} 25-29.9 \text{ kg/ m}^2$) , obese ($\text{BMI} \geq 30 \text{ kg/ m}^2$).

Pilot study

Before starting to collect information, a pilot study was carried out for two weeks. The pilot study done in GIT center in Merjan Medical City for a period from 1st to 14th of February 2014 aimed to:

- Testing the reliability and validity of questionnaire form to reveal any modification needed.
- Estimate the time needed to collect the required data.

- To find out the potential difficulties.

The pilot sample was excluded from the study sample. The modifications were concentrated in the time allocated for filling the questionnaire.

Data Analysis: Statistical analysis was carried out using SPSS version 18

Results

The overall mean age of patients with celiac disease was (30.67 ± 9.72) years old. There was no significant mean difference for male (25.28 ± 10.03) years old and female (31.44 ± 9.57) years old, $t=0.891$, $df=68$, $p=0.376$. The overall mean weight of patients was (57.38 ± 13.52) kg, meanwhile, the mean height for patients was (179.38 ± 118.28) centimeter. The overall mean body mass index (BMI) for patients was (20.97 ± 4.03) kg/m^2 , (34.3%) of the patients were underweight and (65.7%) were not underweight [normal 36 (51.4%) and overweight 8 (11.4%) as well as obese 2 (2.9%)].

The Socio-Demographic Characteristics of Patients with Celiac Disease

(82.8%) of study population were age between 18-38 years old, (35.7%) were male and (64.3%) were female, the total patient who live in urban area were (47.1%), (61.4%) of them were married, there was significant association between BMI and marital status ($p \text{ value} = 0.014$) and not significant association with age groups, sex , residence , occupational status as well as educational level as show in table1.

The Medical History of Patients with Celiac Disease

The overall mean age of onset for patients with celiac disease was (22.56 ± 10.47) years old. the association of BMI with celiac patients' medical history, (66.7%) of underweight celiac patient had duration of disease less than one month's the total patient with positive family history are (18.6%), (4.3%) of patient were smoker, (29.1%) of included female were had history of unfavorable outcome of pregnancy (abortion , still birth , low birth weight) and (17.3%) of included male and

female had history of unexplained infertility all of them were female, there were significant associations between BMI with duration of disease $df=3$, p value= 0.027 and unexplained infertility $df=1$, p value= 0.027 as show in table 2.

The Medical Presentation of Patients with Celiac Disease

(79.2%) of study population with underweight present with diarrhea, (66.7%) of them were present with abdominal pain and bloating and (70.8%) present with problem in the feet (pain, numbness, tingling). there was significant association between BMI with diarrhea & problem in the feet presentation (p value = 0.018, 0.001) respectively but no significant association with abdominal pain and bloating as show in table 3.

Complete Blood Count and Serology for Patients with Celiac Disease

The overall mean HB of celiac patients was (11.24 ± 2.30) mg/dl. (83.3%) of study population with underweight present with anemia and (75%) of them had hypoalbuminemia, from the total patient only (14.3%) had leukopenia and (18.6%) had eosinophilia, the percentage of patient with positive anti tTg IgA are (55.7%), there were significant associations between BMI with HB, albumin as well as each of anti tTg IgA antibody and anti gliadin IgG antibody with no significant association with WBC count, eosinophil count, anti tTg IgG antibody and IgA for gliadin antibody as show in table 4.

The distribution of celiac patient by type of anemia shows 72% (29/40) of patient with anemia had hypochromic microcytic anemia and 25% (10/40) had macrocytic anemia while only 2.5% (1/40) had normochromic normocytic anemia.

The Burden of Diet Therapy for Patients with Celiac Disease

(60.9%) of not underweight patient eat meal at regular hours and (78.3%) of them had menus, (62.5%) of underweight patient not being able to eat favorite food, (25%) of them not being able to eat same food as other family member, and (80%) from all patient had burden of cooking, there were

significant association between BMI with Necessity to make menus and not being able to eat same food as other family member (p value = 0.001, 0.001) respectively as show in Table 5.

The Diet Satisfaction and Perceived GFD Therapy for Patients with Celiac Disease

(49.3%) of total study population feeling that diet are delicious, (83.3%) of patient with underweight feeling not satisfied after meal, while (89.1%) of study population with not underweight feeling that the health condition is good, from the total included patient (77.1%) Feeling that the family bond has become closer and (64.3%) had regular life. There was significant association between BMI with Feeling satisfied after meal and Feeling that health condition is good as show in table 6.

The Peripheral Neuropathy for Patients with Celiac Disease

The total percentage of peripheral neuropathy were (2.9%) from which (8.7%) of underweight with peripheral neuropathy. there was no significant association between BMI with Peripheral Neuropathy for celiac patients as show in table 7.

The Cardiovascular Autonomic Neuropathy (CAN) for Patients with Celiac Disease

(45.2%) of underweight patient had CAN while only (23.9%) of not underweight had CAN. There was significant association between BMI with cardiovascular autonomic neuropathy (p value = 0.011) as show in table 8.

Discussion

Celiac disease can cause malnutrition even if the patient was eating a healthy and balanced diet. That is because the CD affect the absorption of many of the nutrients in the foods this occurs due to effect of gluten on the villi of small intestine, which is the common site of nutrients absorption [33]. So the nutritional status of celiac patient should be assessed at the time of initial diagnosis and for follow up of the patient [22].

This study found that the total number of underweight are 24 (34.3%), were

normal weight 36 (51.4%), overweight 8 (11.4%) and obese 2 (2.9%) this result was comparable to other study that reported underweight are (17.3%), normal weight (60.7%), overweight (15.2%) and obese (6.8%) [34]. While other study reported that prevalence of underweight 22%, normal weight 49% and overweight and obese were 29% [22], the high prevalence of underweight may be attributed to insufficient nutritional intake on the other hand, increased fecal losses of nutrients as a result of malabsorption since malnutrition in CD occurs as a result of damage to the small intestinal mucosa which is the main site of nutrient absorption [35].

Distribution of sociodemographic characteristic in celiac patient

In our study shows the age group between 18-38 years constitute 58 (82.8%) of all CD patient from which 19(32.8%) were underweight and 39(67.2%) were not underweight (normal, overweight, obese) in contrast to the age between 39-59 years 12 (17.2%), from which 5(41.7%) were not underweight and 7(58%) were underweight and there was no significant association between age group & BMI. These results agree with the study done in Gastroenterology center in Basrah city, Iraq reported that the high prevalence of celiac disease were between 21-40 years which constitute 27/44(61.4%) [36], the explanation of this result may be related to the high prevalence of CD in second and fifth decade [9].

Resulted data of gender prevalence in this work revealed that male constitute 25 (35%), {8 (32%) are underweight and 17(37%) are not underweight}, while the female constitute 45 (64.3%), {16 (35.6%) are underweight and 29 (64.4%) are not underweight}, there was no significant association between gender & BMI. These results agreement with the study done in Gastroenterology center in Basrah city, Iraq reported sex prevalence were male (38.6%) and female (61.4%) [36]. other study done in Europe and the Middle East, all of which have a female predominance [37, 38]. The reason behind this female predominance is

unknown, but could be explained by the fact that the prevalence of immune mediated diseases in general is higher in female than in male [39].

Out of 70 patient 33 (47.1%) live in urban area 10 (41.7%) of them were underweight and 23 (50%) are not underweight while the total number of patient that live in rural area was 37 (52.9%) from which (14) underweight and (23) were not underweight with no significant association between residence & BMI.

Marital status has been another parameter in sociodemographic characteristic which has significant association with BMI (p value=0.014) as the total married patient constitute 43 (61.4%) , 10 of them are underweight and 33 are not underweight while the other group which include (single , widow and divorce) constitute 27 (38.5%) , (14) of them are underweight and (13) are not underweight .These results comparable to other study done in oxford university that reported the married celiac patients constitute 17/23 (73.9%), underweight while the other group which include (single, widow and divorce) constitute 6/23 (26.1%) [40].

The occupational status of celiac patient included in current study shows high percentage of non-employment (60%) while the self-employment (21.4%) and only (18.6%) were governmental-employment these results are differ from other results done in oxford which reported that non-employment are 1/23(4.3%), full time work 4/23(17.4%), part time work 6/23(26.1%) and the retired 12/23(52.2%) [40]. This finding explained the impact of disease on occupational status of the patient since most of our patient suffer from diarrhea, anemia, weakness which may be affect the job and make most of them were non-employment.

Also There was no significant association between level of education and BMI, the present study shows high percentage of patient were primary school education 28 (40%) while secondary school 12 (17.1%) , higher education constitute 21(30%) while the illiterate constitute 9

(12.9%). These results were compared with other results done in Columbia that reported grade school (0.6%), middle school (0.3%), high school (11%) and college (48%) while graduate school (40%) [41]. The correlation of CD and it is impact on the health and nutritional status of the patient and the level of intelligent, since (45.7%) of included patient developed sign and symptom of disease at age before 20 years this may be related to the escape from school .

Medical history of celiac patient:

The present study show that the percentage of age of onset of celiac disease is (45.7%) with less than 20 years , (50%) of them were underweight and (43.5%) were not underweight in contrast to (54.3%) the age of onset are after 20 years, there was no significant association between age of onset with BMI as shows in (table 2). This explained that celiac disease is not only occur in infancy and childhood but also can occurs at any age even if previously tested for celiac was negative [42].

31 (44.3%) of all participant had duration less than one month (ie. newly diagnosed), (66.7%) of them were underweight and (32.6%) were not underweight while those with duration more than twenty-four months constitute 18 (25.7%), from which 5 (20.8%) were underweight with 13 (28.3%) were not underweight. Duration of celiac disease had significant effect on BMI (p value =0.027), this explained that once patient start GFD his condition will be improve with increase weight, so when the duration more than 24 months the patient already start GFD meanwhile when patient newly diagnosed they not yet start GFD so the prevalence of underweight in them more than the prevalence of underweight in those had duration more than 24 months.

From the total patient included in current study only 13 (18.6%) had positive family history of celiac disease (25%) were underweight and 15.2% were not underweight in contrast to 57 (81.4%) had no family history, there was no significant association between family history with

BMI. This low percentage are disagree with other results done in Tampere, Finland reported that 62.4% (372/596) had positive family history and only 37.6 (224/596) with negative family history [27]. This difference may be contributed to the lack of family screening due to loss of population awareness.

Smoking status is another variable in our study which 3 (4.3%) of included patient was smoker, (2) are underweight and (1) is not underweight in contrast to 67 (95.7%) were not smoker, there was no significant association between smoking and BMI. These results comparable to other results reported 3/44 (6.8 %) were smoker compare to 41/44 (93.2 %) were not smoker [43]. This explained that cigarette smoking, or a factor closely linked to it, seems to exert a major protective effect against the development of symptomatic adult onset coeliac disease [43].

Out of 31 women (married , widow , divorce) only 9 (29%) women reported to had history of unfavorable outcome of pregnancy, compared to 22 (71%) had no such history. with no significant relationship between unfavorable outcome of pregnancy and BMI. other study done in Italy reported that more than 50% of women with untreated celiac disease experience miscarriages and unfavorable outcome of pregnancy but this result decrease after GFD [44]. This explain that malabsorption or malnutrition was not a consistent feature in women affected by coeliac disease who had an adverse outcome of pregnancy [45], while other hypothesis suggest that deficiency of zinc, folic acid and other micronutrient affect the outcome of pregnancy [46].

Approximately 17.8% (8/45) of patient (male and female) were founds to have unexplained infertility (failure of the couples to conceive after frequent unproductive coitus for more than one years without obvious cause), and all of them were female with no reported case with male infertility in contrast to 82.2% (37/45) with no history of unexplained infertility with significant effect of

unexplained infertility on BMI in celiac patient (p value = 0.027), (38.5%) of patient with unexplained infertility were underweight compared with (61.5%) of underweight reported no unexplained infertility, this result agree with the study done in united states reported that the prevalence of unexplained infertility in women with celiac disease is (27.1%) [47]. while other study reported male infertility is (0%) while female is (3.6%) [48]. This was suggested relationship between proper nutrition in females and the ability to conceive, Malnutrition affect the ability to conceive due to a negative energy balance and the decreased ability to maintain fat storage in afflicted females, Protein from food is efficiently and almost completely absorbed by the proximal part of the small intestine the mainly affects area in celiac disease, absorption of proteins can be compromised and decreased quantities are detected in the plasma [49], other suggestion are women with celiac disease are often deficient in micronutrients, such as fat soluble vitamin (A,D,E,K) as well as other nutrient such as iron which in turn affect the ovulatory function [50].

Medical Presentation of Patient with Celiac Disease:

The total percentage of included patient whose suffer from diarrhea were 42 (60%) and abdominal pain and bloating 45 (64.3%), this result are comparable to the study done in Basrah city, Iraq reported that the percentage of diarrhea and abdominal pain are 41/66 (62 %) and 38/66 (57.6%) respectively [36]. Other study conducted in Iran found that (32%) of Iranian celiac patient complaints from diarrhea and (33%) had abdominal pain while only (11%) had bloating and this study consider these three symptom are the common classical symptom in celiac disease of Iranian patient [51]. There was no significant association between abdominal pain and bloating with BMI while There was significant association between diarrhea and BMI (p value = 0.018), were (79.2%) of patient with diarrhea were underweight. This explained that diarrhea is the typical and

most common gastrointestinal manifestation due to celiac disease or secondary to vitamin deficiencies and nutrient malabsorption [20, 21].

Approximately 26 (37.1%) of our patient complain from problem in the feet which is either pain, numbness, or tingling in the feet these are the early symptom of neuropathy from which (70.8%) of patient were underweight compared to only (19.6%) of patient were not underweight so there was highly significant association between these problem and BMI that can be explain by that vitamin deficiency especially vitamin B complex and vitamin E which result from malabsorption may lead to these symptom [52].

Complete Blood Count (CBC), Albumin, and Serological Test in Celiac Patient:

Anemia is another parameter discuss in our study which is defined as HB below the normal reference level for the age and sex of the individual, in our study there are 40 (57.1%) of included patient had low level of HB these results was highly significant with BMI (p value =0.001), there was (83.3%) of underweight patient had anemia in contrast to (43.5%) of not underweight, this result of high percentage of anemia match with other study conducted in Al-Basrah city, Iraq reported that (77.3%) of celiac patient had anemia [36], while other study show (55%) of Iranian celiac patient are anemic [51]. some author focus on micronutrient deficiencies as the cause of anemia in individuals with celiac disease [53]. Other suggest that this hypothesis is inadequate, and that the etiology of anemia in celiac disease is multifactorial (ie. Anemia is not only occurs as a result of iron deficiency but also may be due to vitamin B12 and folic acid deficiency) [54], on the other hand low level of HB may be related to the dietary habits and low dietary intake of iron in the GFD.

Other components of CBC is WBC count we found that there has no meaningful association between WBC count and BMI, as 10 (14.3%) of study population had leukopenia in contrast to 60 (85.7%) with normal level of WBC, this result

comparable to the study done in America reported that leukopenia are uncommon in celiac patient and can be due to autoimmune mechanism or secondary to deficiency of folate, vitamin B12, or copper [55]. This result also can be explain by that eosinophil is one type of WBC also has no meaningful association with BMI.

The serum concentration of albumin was measured throughout this study and show the percentage of hypoalbuminemia in celiac patient was (35.7%) with highly significant association with BMI (p value =0.001) this result was comparable to the study done in Al-Kadhimiya Teaching Hospital in Baghdad, Iraq reported that there was significant decrease in albumin level in patient with celiac disease [56]. The explanation of this significant association is hypoalbuminemia can occur as a result of Malnutrition [57].

In our study we measure IgA as well as IgG antibody against antigliadin (AGA) and tissue transeglutaminase (tTg) because celiac patient at high risk of IgA deficiency than other population [58].

Serum level of tTg IgA or IgG antibody (Ab) are usually one of the first steps in the diagnosis CD and follow up of celiac patient on GFD since it decrease after starting GFD and increase after ingestion gluten [59]. The seroprevalance of anti tTg IgA Ab in our study are (55.7 %) and for anti tTg IgG Ab are (50%) there was significant association between anti tTg IgA Ab and BMI class (p value = 0.039) This was in agreement with the result obtained by Cindy Huany, *et al.* Who report woman found to have positive AGA and positive tTg IgG antibodies that are consistent with celiac disease [60]. Other study done in Al-Karbala, Iraq reported that the prevalence of tTg IgG and IgA in celiac patient are (6.83%) and (27.32 %) respectively [61], there was significant association between BMI class and serum level of tTg IgA Ab (p value = 0.039) and no significant association with serum level of tTg IgG Ab.

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diagnosis CD and follow up of celiac patient on GFD since it decrease after starting GFD and increase after ingestion gluten [59].

The concentration of anti- gliadin IgA and IgG were measured in the present study in the serum of patients with celiac disease show significant association between anti-gliadin IgA and BMI (p value = 0.041) while no significant association with anti-gliadin IgG .The seroprevalance of AGA IgG in current study are (21.4%) and for AGA IgA are (34.3%) this match the conducted in Al-Kadhimiya Teaching Hospital in Baghdad, Iraq reported highly significant increase of anti- gliadin IgA in celiac patient [56]. Other study done in Al-Karbala ,Iraq reported that the prevalence of AGA IgG and IgA in celiac patient are (32.91%) and (21.11%) respectively [61], there was significant association between BMI and serum level of AGA IgG and no significant association with serum level of AGA IgA, (p value = 0.041, 0.175) respectively.

Burden of Diet Therapy for Patients with Celiac Disease:

The overall number of celiac patients who eat their meal at regular hours are 44 (62%) , 16 (66.7%) of underweight patient reported history of eat meal at regular hours compare to 8 (33.3%) of them not reported such history with no significant association between eat meal at regular hours and BMI this mean that if a meal is skipped or delayed while patient on GFD , they are at no risk for developing of inadequate nutritional status.

There was great significant association between history to make menus and BMI (p value= 0.001), as that total of 42 (60%) of respondents had history to make menus compared with (40%) not reported such history and (25%) of underweight patient reported follow a menu and (75%) of them not follow a menu this may attribute to faulty knowledge about the GFD as it may be restrict whole favorite food item ,or it must buy the only highly expensive type of diet that make the underweight patient not follow a menu, also the lack of knowledge

about hidden gluten in the diet which may lead to eat some item that thought it is gluten free.

There was no significant association between BMI and able to eat favorite food, the 9 (37.5%) of respondents with underweight able to eat favorite food in contrast to 15 (62.5%) of respondents with underweight not being able to eat favorite food this explain that patient who not being able to eat favorite food may affect his nutritional status.

This study found no association between BMI and economic burden of GFD, the total included patients had economic burden of GFD are 29 (41.4%), as 11(45.8%) with underweight Compar to 18 (39.1%) with not underweight. Other study done in Columbia reported that 47.1 % (124/263) complained from cost of GFD [62]. This may attribute to even the high percentage of nonemployee in our study are 60% but the family may had high monthly income, lack of GFD derivative in the supermarket and lack of GFD list in the restaurant may also attribute to this result. Another parameter in burden of GFD is not being able to eat same food as other family members, which show highly significant association with BMI (p value=0.001), the total respondents 36 (50.7%) not being able to eat same food as other family members, 30 (65.2%) of respondents with not underweight not being able to eat same food as other family members, and only 6 (25%) of respondents with underweight, this mean the patient is not on strict GFD and any percentage of gluten in the diet may interfere with nutritional status of the celiac patient.

In this study, we also want to know other aspect of burden of CD regarding burden of cooking GFD. This study reported there was no association between BMI and history of burden of cooking the GFD, as (80%) of respondents with history of burden of cooking the GFD, compare to (20%) without such history this may be related to the lack GFD from the supermarket which make the patient for necessity to cook their GFD.

Diet Satisfaction and Perceived GFD Therapy for Patients with Celiac Disease:

There was no significant association between BMI and feeling that diet are delicious, as 13 (54.2%) of study population with underweight had not reported that diet are delicious with no difference in percentage about this feeling in not underweight patient.

Although eating healthy foods doesn't mean sacrificing taste, 20 (83.3%) of study population with underweight not satisfied after meals with significant association between BMI and feeling satisfied after meals (p value = 0.001), this may be related to the development of symptom of celiac disease like abdominal pain, bloating, and dyspepsia that make the patient can not satisfied after meals.

There was no significant association between BMI and able to enjoy after meal as the total included patient 38 (52.1%) were able to enjoy after meal, from which (60.9%) were not underweight this result may be related to appetite and dietary habits of those patient that make them enjoy with food item that GFD and increase in amount of these food item, that can affect the nutritional status.

The total patients in our study that feeling the health condition is not good after starting GFD were (32.9%), as (25%) with underweight had history of feeling the health condition is good compare with (75%) of them feeling that health condition is not good after start GFD, so there was significant association between BMI and feeling the health condition is good (p value = 0.001) many factor may be contributed to this persistence of symptom after GFD that attributed to (75%) of underweight reported as feeling that the health condition is not good due to they are not on strict GFD while some reported that irritable bowel syndrome (IBS) may be coexist with CD and responsible for persistence of symptom and make health condition not improved [63]. Another factor may contributed to the presences of small-intestinal bacterial overgrowth which

responsible for persistence of symptoms in celiac patient [64].

Family bond is another parameter to be discussed in our study. Meanwhile there were no significant association between BMI and feeling that the family bond has become closer, as the majority of the respondents in this study 54 (77.1%) reported closer family bond regardless underweight or not underweight. This may be due to ongoing threat of complication can be worrisome, depressing, and social relationships may be affected. Therefore, the great social support by the family, friends, doctor, dietitian, and other people living with celiac disease are one of important step in the treatment of CD [65].

About (64%) of celiac patient reported to learned to lead regular life this may be contributed to the nature of CD that require regular follow up and visit to the dietitian, the same item of food eat daily make the patient to had regular life. There was no significant association between BMI and learning to lead regular life, 10 (41.7%) of study population with underweight have not learned to lead a regular life, whereas 31(67.4%) of study population with not underweight have learned to lead a regular life.

The Distribution of Peripheral Neuropathy in Celiac Disease:

The total patients included for NCS are 68 were 2 patients refuse to include in our study due to their afraid from the procedure, it shows The prevalence of peripheral neuropathy in celiac patients included in our study is 2.9% (2/68), 2 (8.7%) patients with underweight had peripheral neuropathy in contrast to negative result in not underweight patients (normal, overweight, obese). There was no significant association between peripheral neuropathy & underweight patients. This results comparable to other study reported that (2.5%) of celiac patients are associated with peripheral neuropathy [66], but incomparable to other study that reported up to (50%) of celiac patients developed peripheral neuropathy [67]. The exact cause of polyneuropathy in CD is unknown. The

hypotheses include the action of antibodies on extra-intestinal tissue transglutaminas proteins [68, 69], pathogenic involvement of anti ganglioside antibodies [70].

The response to GFD in CD associated peripheral neuropathy has been inconsistent. Some authors reported symptom regression and resolution on GFD where as others reported no benefit from GFD [71].

The Distribution of Cardiovascular Autonomic Neuropathy for Patients with Celiac disease:

All patient were agree to assessed for CAN (take blood pressure in sitting &standing position, hand gripe maneuver and heart rate in deep breathing) we found that total patient had CAN represent 24 (34.3%) from which 13(54.2%) had CAN compare to 11 (23.9%) patient not underweight (normal, overweight, obese), there was significant association between underweight & CAN (p value=0.011), other study reported that 19% (5/27) had autonomic neuropathy [72], this higher results are incomparable to other study reported that (2.4%) of celiac patients are associated with autonomic neuropathy [73], this difference was thought due to number of factors first of all are late diagnosis & late presentation of patients in our city &lack of objective assessment of complains this explain that once nerve damage present it is not response to dietary treatment [74], also the neurotoxic effects of gliadin and deficiency of vitamin and minerals such as vitamin B complex, vitamin E and copper due to malabsorption are associated with neurological complication [52,75].

This difference in our study between peripheral neuropathy (assessed by NCS) and autonomic neuropathy (assessed by CAN) may be related to the use of NCS which is the initial diagnostic step. However, it is often normal in patients with an early neuropathy or a neuropathy that only involves the small fiber nerves [76, 77].

There is no reported work and reference in Iraqi electronic database for neurological complication in Iraqi celiac patient in

contrast to Iranian database which consider that neurological complication are the 3rd non gastrointestinal symptom [78].

Conclusions

In the finding of present study there are high percentage of underweight in contrast to overweight and obesity in patients with celiac disease with high prevalence of anemia mainly iron deficiency anemia and also shows high prevalence of autonomic neuropathy compare to peripheral neuropathy, the celiac disease may be the one cause of unexplained infertility and unfavorable outcome of pregnancy. Regarding the diet satisfaction and burden of gluten free diet, most of the patients with underweight had no history to make menu and feeling not satisfied after meal and health condition is not good and most of celiac patient had burden of cooking gluten free diet.

Recommendation

- 1- Infertile female particular those with unexplained infertility should be screen for CD.
- 2- Autonomic neuropathy should be consider in the regular follow up of celiac patient.
- 3- BMI should be included at the time of diagnosis and in the follow up of patient with celiac disease, as it is an indicator of clinical well-being.
- 4- Measurement of serum level of nutrient and mineral should be consider at the time of diagnosis and follow up of patient with celiac disease.
- 5- Educating the society regarding CD as a celiac group society, which helps in providing GFD in Market.
- 6- Increase in Iraqi medical awareness about atypical presentation of celiac disease and especially it is occurrence at adulthood.

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Table 1: The socio-demographic characteristic of celiac patients

Variable	BMI		Total	χ^2	df	P values
	Underweight No.(%)	Not underweight No.(%)				
Age Groups (years)						
18-38 years	19 (79.2)	39 (84.8)	58(82.8)	0.350 ^a	1	0.739
39-59 years	5 (20.8)	7 (15.2)	12(17.2)			
Gender						
Male	8 (33.3)	17 (37.0)	25(35.7)	0.090	1	0.764
Female	16 (66.7)	29 (63.0)	45(64.3)			
Residence						
Urban area	10 (41.7)	23 (50.0)	33 (47.1)	0.440	1	0.507
Rural area	14 (58.3)	23 (50.0)	37 (52.9)			
Marital Status						
Married	10 (41.7)	33 (71.7)	43(61.4)	6.020	1	0.014*
Single,widow,devorised	14 (58.3)	13 (28.3)	27(38.5)			
Occupational Status						
Gov. Employer	5 (20.8)	8 (17.4)	13(18.6)	0.525	2	0.796
Self-Employed	4 (16.7)	11 (23.9)	15(21.4)			
Non-Employed	15 (62.5)	27 (58.7)	42(60)			
Educational Level						
Illiterate	4 (16.7)	5 (10.9)	9 (12.9)	0.645	3	0.950
Primary School	9 (37.5)	19 (41.3)	28 (40.0)			
Secondary School	4 (16.7)	8 (17.4)	12 (17.1)			
Higher Education	7 (29.2)	14 (30.4)	21 (30.0)			

*p value ≤ 0.05 is significant

^aFisher Exact test

Table 2: The medical history of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight No (%)	Not Underweight No (%)	total			
Age of Onse(years)						
< 20 years	12 (50.0)	20 (43.5)	32(45.7)	0.270	1	0.603
≥ 20 years	12 (50.0)	26 (56.5)	38(54.3)			
Duration of Disease						
Less than month	16 (66.7)	15 (32.6)	31(44.3)	8.752 ^a	3	0.027*
1-12 months	3 (12.5)	11 (23.9)	14(20)			
13-24 months	0 (0.0)	7 (15.2)	7(10)			
> 25 months	5 (20.8)	13 (28.3)	18(25.7)			
Family History of Celiac Disease						
Yes	6 (25.0)	7 (15.2)	13 (18.6)	0.998	1	0.318
No	18 (75.0)	39 (84.8)	57 (81.4)			
Smoking						
Smokers	2 (8.3)	1 (2.2)	3(4.3)	1.459 ^a	1	0.269
Non-Smokers	22 (91.7)	45 (97.8)	67(95.7)			
Unfavourable Outcome of Pregnancy (female)						
Yes	5 (50)	4 (19.1)	9 (29.1)	3.101 ^a	1	0.220
No	5 (50)	17 (80.9)	22 (70.9)			
Unexplained Infertility (male&female)						
Present	5 (38.5)	3 (9.4)	8 (17.3)	7.200 ^a	1	0.027*
Absent	8 (61.5)	29 (90.6)	37 (82.2)			

*p value ≤ 0.05 is significant

^aFisher Exact test

Table 3: The medical presentation of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight No (%)	Not Underweight No (%)	total			
Diarrhoea						
Yes	19 (79.2)	23 (50.0)	42(60)	5.590	1	0.018*
No	5 (20.8)	23 (50.0)	28(40)			
Abdominal pain & Bloating						
Yes	16 (66.7)	29 (63.0)	45(64.3)	0.090	1	0.764
No	8 (33.3)	17 (37.0)	25(35.6)			
Problem in the feet(pain , numbness , tingling)						
Yes	17 (70.8)	9 (19.6)	26(37.1)	17.756	1	0.001*
No	7 (29.2)	37 (80.4)	44 (62.9)			

*p value ≤ 0.05 is significant

Table 4: The complete blood count, albumin and serology of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight No (%)	Not Underweight No (%)	total			
HB						
Anaemia	20 (83.3)	20 (43.5)	40(57.1)	10.229	1	0.001*
Normal HB	4 (16.7)	26 (56.5)	30(42.9)			
WBC						
Leukopenia	5 (20.8)	5 (10.9)	10(14.3)	1.279	1	0.258
Normal WBC	19 (79.2)	41 (89.1)	60(85.7)			
Eosinophil						
Eosinophilia	5 (20.8)	8 (17.4)	13(18.6)	0.124	1	0.725
Normal Eosinophil	19 (79.2)	38 (82.6)	57(81.4)			
Albumin						
Low Albumin	18 (75.0)	7 (15.2)	25(35.7)	24.551	1	0.001*
Normal level Albumin	6 (25.0)	39 (84.8)	45(64.3)			
Anti tTg IgG Antibody						
Normal < 12 U/ml	10 (41.7)	20 (43.5)	30(42.9)	0.592	2	0.744
Equivocal 12-18 U/ ml	1 (4.2)	4 (8.7)	5(7.1)			
High > 18 U/ml	13 (54.1)	22 (47.8)	35(50)			
Anti tTg IgA Antibody						
Normal < 12 U/ml	5 (20.8)	23 (50.0)	28(40)	5.962 ^a	2	0.039*
Equivocal 12-18 U/ ml	1 (4.2)	2 (4.3)	3(4.3)			
High > 18 U/ml	18 (75.0)	21 (45.7)	39(55.7)			
Anti gliadin IgG Antibody						
Normal < 12 U/ml	15 (62.5)	37 (80.4)	52(74.3)	5.901 ^a	2	0.041*
Equivocal 12-18 U/ ml	0 (0.0)	3 (6.5)	3(4.3)			
High > 18 U/ml	9 (37.5)	6 (13.1)	15(21.4)			
Anti gliadin IgA Antibody						
Normal < 12 U/ml	13 (54.2)	32 (69.6)	45(64.3)	2.966 ^a	2	0.175
Equivocal 12-18 U/ ml	1 (4.2)	0 (0.0)	1(1.4)			
High > 18 U/ml	10 (41.6)	14 (30.4)	24(34.3)			

*p value ≤ 0.05 is significant ,^aFisher Exact test

Normal hemoglobin(HB) =12-15, normal white blood cell (WBC) = 4000-11000

Normal eosinophil = 0.030-0.440 , normal albumin = 35-52,tTg;Tissue transglutaminases,

Ig; immunoglobulin

Table 5: The burden of diet therapy of celiac patients

Variable	BMI			χ^2	df	<i>P</i> values
	Underweight No (%)	Not Underweight No (%)	total			
Necessity to eat meal at regular hour						
Yes	16 (66.7)	28 (60.9)	44(62.9	0.227	1	0.634
No	8 (33.3)	18 (39.1)	26(37.1			
Necessity to make menu						
Yes	6 (25.0)	36 (78.3)	42(60.0	18.641	1	0.001*
No	18 (75.0)	10 (21.7)	28(40.0			
Able to eat favourite food						
Yes	9 (37.5)	28 (60.9)	37(56.4	3.457	1	0.063
No	15 (62.5)	18 (39.1)	33(43.6			
Economic burden of diet						
Yes	11 (45.8)	18 (39.1)	29(41.4	0.292	1	0.589
No	13 (54.2)	28 (60.9)	41(58.6			
Not being able to eat same food as other family member						
Yes	6 (25.0)	30(65.2)	36(50.7	10.212	1	0.001*
No	18 (75.0)	16(34.8)	34(49.3			
Burden of cooking the GFD						
Yes	21 (87.5)	35 (76.1)	56(80.0	1.284	1	0.257
No	3 (12.5)	11 (23.9)	14(20.0			

*p value ≤ 0.05 is significant

GFD; gluten free diet

Table 6: The diet satisfaction and perceived GFD therapy of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight	Not Underweight	total			
	No (%)	No (%)				
Diet satisfaction						
Feeling that diet are delicious					1	0.741
Yes	11 (45.8)	23 (50.0)	34(49.3	0.110		
No	13 (54.2)	23 (50.0)	36(50.3			
Feeling satisfied after meal						
Yes	4 (16.7)	34 (73.9)	38(52.1	20.827	1	0.001*
No	20 (83.3)	12 (26.1)	32(47.9			
Able to enjoy meal						
Yes	10 (41.7)	28 (60.9)	38(52.1	2.344	1	0.126
No	14 (58.3)	18 (39.1)	32(47.9			
Perceived GFD						
Feeling that health condition is good						
Yes	6 (25.0)	41 (89.1)	47(67.1	29.402	1	0.001*
No	18 (75.0)	5 (10.9)	23(32.9			
Feeling that the family bond has become closer						
Yes	19 (79.2)	35(76.1)	54(77.1	0.085 ^a	1	0.771
No	5 (20.8)	11 (23.9)	16(22.9			
Having learned to lead regular life						
Yes	14 (58.3)	31 (67.4)	45(64.3	0.564	1	0.453
No	10 (41.7)	15 (32.6)	25(35.7			

*p value ≤ 0.05 is significant

^aFisher Exact test

GFD ; gluten free diet

Table 7: The peripheral neuropathy of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight (%)	Not Underweight (%)	total			
Peripheral neuropathy						
Absent	21 (91.3)	45 (100.0)	66(97.1	a	1	0.111
Present	2 (8.7)	0 (0.0)	2(2.9)			

*p value ≤ 0.05 is significant

^a:Fisher Exact test

Table 8: The cardiovascular autonomic neuropathy of celiac patients

Variable	BMI			χ^2	df	P values
	Underweight (%)	Not Underweight (%)	total			
Cardiovascular Autonomic Neuropathy						
Present	13 (54.2)	11 (23.9)	24(34.3	6.407	1	0.011*
Absent	11 (45.8)	35 (76.1)	46(67.2			

*p value ≤ 0.05 is significant