5-1-2016

# CELIAC AND OTHER AUTOIMMUNE BOWEL DISEASES: IS GLUTEN INTOLERANCE OR URBANIZATION THE MAIN CULPRIT?

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# CELIAC AND OTHER AUTOIMMUNE BOWEL DISEASES: IS GLUTEN INTOLERANCE OR URBANIZATION THE MAIN CULPRIT?

by

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Presented to the Faculty of the Honors College of
The University of Texas at Arlington in Partial Fulfillment
of the Requirements
for the Degree of

HONORS BACHELOR OF SCIENCE IN BIOLOGY

THE UNIVERSITY OF TEXAS AT ARLINGTON

May 2016

ACKNOWLEDGMENTS

I would like to take this opportunity first and foremost to show my gratitude to my mentor, Dr. Wilk- Blaszcza, for giving me this opportunity to grow as a person and learn how to explore science from a research standpoint. From providing guidance when choosing a worthwhile research topic to completing the task in a timely and orderly manner, Dr. Wilk has been an incredible support and guide. She took me in and agreed to let me compile this research project in a short time, knowing it would be difficult for her and me, showed me how to work the different database systems and continuously kept me on track with deadlines. I have been able to learn such a vast range of facts, and this incredible chance to expand my knowledge base is credited foremost to Dr. Wilk.

Mrs. Bobbie Brown is the other person I would credit for the fact that this project was started and completed on time. From making time to calm me down during my hysterical breakdowns regarding deadlines to making sure she always stayed in touch with me and reminding about deadlines and research regulations, Mrs. Brown has been the best advisor an Honors student could ask for.

Last but not the least, I would like to show my appreciation towards those close to my heart: my peers at UTA, Mom, Roopal Rupani, Dad, Atul Rupani, my younger brother Sukan Rupani and my boyfriend Sachin Jayaram. The endless support and help these people have provided me both in my personal and academic life is limitless, and without these pillars, I would not be who I am today.

April 05, 2016

ABSTRACT

CELIAC AND OTHER AUTOIMMUNE BOWEL DISEASES:

IS GLUTEN INTOLERANCE OR URBANIZATION

THE MAIN CULPRIT?

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The University of Texas at Arlington, 2016

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Two and a half million Americans claim to be affected by an autoimmune disease called Celiac Disease (CD), with the majority of this group calling themselves what is called gluten-intolerant and following a gluten-free diet (GFD). The question I am addressing is, how could gluten, present in staple foods that have sustained society for thousands of years, suddenly become so threatening? The central hypothesis of my research is if not gluten, what other components in today's world is causing the immune system to attack the body, causing gastrointestinal problems. The statistical technique of surveying a random sample that represents a bigger population is used to analyze the effect of a gluten-free diet on CD and other autoimmune disease patients, and the results are presented in forms of tables and graphs to make statistical comparisons.

Studies that present gluten as a culprit in the flare up of CD and other autoimmune diseases, as well as those which have shown no effect of a GFD on patients with CD and other autoimmune diseases are used to discuss the theory. This study found that external factors causing a flare up in celiac patients is better supported than gluten causing or worsening this fatal disorder.

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# CHAPTER 1

# INTRODUCTION

The immune system is comprised of various genetic structures and processes within an organism that protects against diseases. To function in a proper manner, the immune system must detect a wide variety of agents, known as pathogens, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue. This differentiation is called self and non-self divisions of the immune system. To differentiate between the cells of the body and the cells of infectious pathogens that may act or look similar to these body cells, this discrimination within the immune system is very important (Wiley, 2012)

The GI tract, both intestines in particular, are a site of continuous immune response from the beginning of life due to variations in bacteria from various forms of food antigen, intestinal bacterial flora and pathogens from other sources. Being a port of entry into the body, this system is also susceptible to the pathogens from the outside environment. Most of the absorption of the food intake takes place in the gut, and this is possible because of the large surface area (400 m^2) covered with finger-like projections called villi protruding from the epithelial walls of the small intestine (MacDonald, 2003). Due to the large surface area and exposure to the outside environment, the gut bacteria (known as the intestinal flora) has to be alert at all times to avoid spread of infection. This group of microorganisms residing in the digestive tract is the largest and most complex community of organisms and is beneficial to the host by helping digest certain foods,

producing a few vitamins essential to the body such as K and B, protecting the intestinal mucosa and as discussed, and performing a barrier effect for the immune system. Many different factors affect this group, the biggest being human diet (Yolanda, 2010).

## 1.1 Autoimmune Diseases

When the immune system forgets to distinguish between the healthy human cells and the harmful pathogenic cells, and starts attacking host cells, autoimmune diseases occur. According to the American Autoimmune Related Diseases Association, over eight types of autoimmune disorders affect approximately fifty million Americans. Celiac sprue disease has been present in the population since the agricultural revolution (Guandalini, 2007) and is the third most common autoimmune disease that affects the predisposed population after rheumatoid arthritis and systemic lupus erythematosus (Roddick, 2015). It is a disorder primarily affecting the GI tract that presents with symptoms such as inflammation of the mucosal membrane of the intestine due to damage from the autoantibodies produced in response to gluten and other lipid or carbohydrate components (Brown, 2011), atrophy of intestinal villi, abdominal cramping and abdominal bloating. According to the National Institutes of Health professionals, there are five categories of celiac disease presentation, as shown in Figure 1(WGO, 2007).

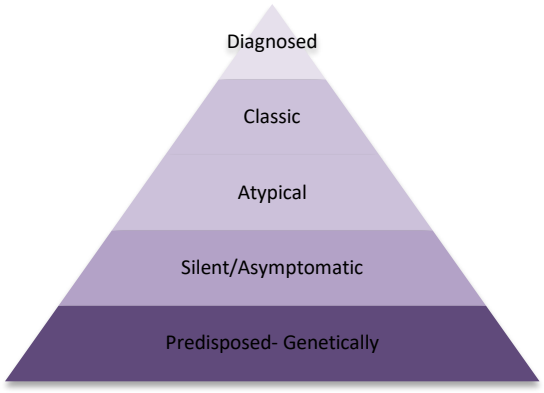


Figure 1.1: The Iceberg Model of CD

Celiac disease is hard to diagnose as it presents the same symptoms as Irritable Bowel Syndrome, commonly known as IBS (Mason 2016) and gluten sensitivity, an allergenic property of the body. IBS is a gastrointestinal condition that affects about one-fifth of the population and causes bloating and abdominal pain among other symptoms. Both IBS and CD disorders present mutual symptoms of abdominal pain, diarrhea, generalized weakness and unexpected weight loss. Because of these generalized symptoms, the population self-diagnoses often with celiac instead of seeking a proper check up by a medical physician and addressing the wide world of other possible immune disorders such as IBS or gluten sensitivity or even food allergies. These self-diagnosed patients adhere to what is commonly known as gluten-free diet that excludes grains such as wheat, barley, rye along with other foods such as breads, desserts containing gluten and even most beers. The main purpose behind avoiding these foods is avoiding the intake of gluten, a glycosylated complex protein that is found in grains such as wheat and rye. Two long chains of hydrophobic amino acid chains make up gluten, gliadins and glutenins. Gluten provides baked products their chewy texture and hence is an important baking ingredient (McGee, 2004). When gluten is consumed, the GALT or gut-associated

lymphoid tissue produces antibodies to attack the gliadin part of the gluten molecule, and in some cases attacks not just the gliadin, but tTG or transglutaminase enzyme, which is in charge of maintaining the smooth function of the microvilli of the gut as well, hence causing the abdominal symptoms.

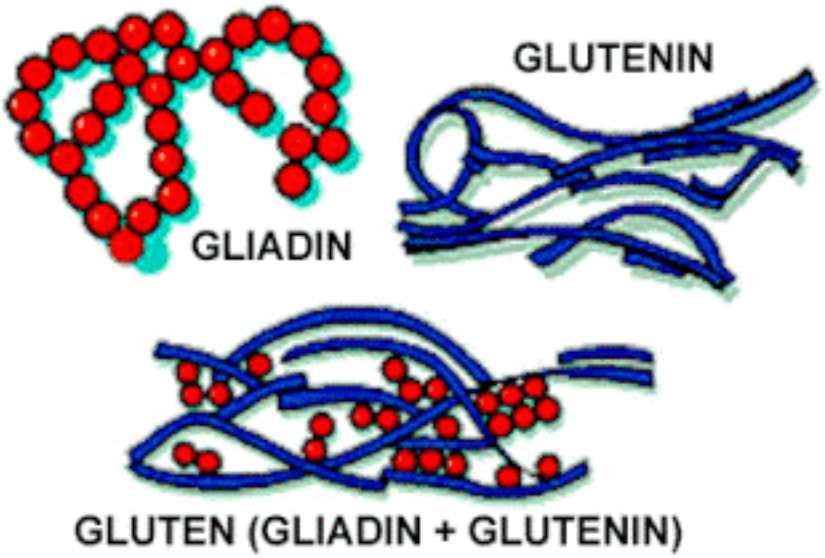


Figure 1.2: Components of Gluten – Gliadin and Glutenin

The purpose of this research is to understand whether the gluten content in these foods itself is the main problem causing digestive disorders in CD and other autoimmune disease patients or whether the revolutionized environment we live in that has altered the gluten, making it harmful to the population consuming it.

# CHAPTER 2

# METHODOLOGY

## 2.1 Statistical Technique Using Demographic Surveys

To execute this experimental research project, a biostatistical technique was implemented on a small sample size that was limited due to availability and time constraint of this research. Survey sampling is a statistical technique used in biological and various studies fields to quantify questions or symptoms or other aspects regarding a particular issue by gathering both background and current situation information. The purpose of choosing a small, randomized sample rather than conducting a population-wide census is to reduce the cost of the experiment as well as maintain a shorter timeline. The survey was pre-approved by the IRB at UTA and was classified as class/student project following the protocol under this clause.

In order to test the effect of gluten on the intestinal microbial and to see if these foods that contain gluten make celiac and other autoimmune diseases better or worse, a survey was conducted that included IBS patients, self-diagnosed celiac patients and clinically diagnosed patients with apparent abdominal symptoms over a period of four weeks with a questionnaire. This survey was prepared keeping in mind the common issues with IBS or celiac patients that frequently visit the ER at the Methodist Richardson Medical Center campus with symptoms such as chronic diarrhea, abdominal pain, nausea, vomiting and generalized weakness (Spiller et al 2005). The questionnaire was presented to 15 patients that I observed visiting the ER more than three times in the last six months with

the chief complaint listed as abdominal pain and associated symptoms of nausea/vomiting/diarrhea. The criterion to be eligible for the survey was to follow either a simple gluten-free diet or a strict gluten diet called a paleo diet that eliminates sugar and vegetable oils in addition to gluten and related components (Roess, 2015). The fifteen patients adhered to either of these diets prescribed by primary care physicians and showed adherence to these diets at their first and last day of the survey trial period through two scheduled visits with respective PCPs. The questionnaire, which was prepared with help of two co-workers and one mid-level provider, is presented in Appendix A. The questionnaire takes about 5-10 minutes to complete, is comprised of close-ended questions and was presented to sample members on the last day of the four-week trial period. Members of the sample group were given the option to stay anonymous to protect identity and medical records as stated per HIPPA, and the questionnaire was not conducted online due to limited time and resources regarding attaining approval from IRB and professional online survey tools.

## 2.2 Selection of Studies

Patients were picked by advertising in the neighborhood with a pamphlet to complete a survey for a school research project or asked during ER/hospital visits if they are willing to participate in a survey for a university project. Once subjects agreed, they were given the guidelines. Each patient had a visit scheduled with his or her primary care physician, and patients who did not have a PCP were appointed one at the time of discharge. Patients were prescribed the necessary diet and advised to adhere to it strictly for best results. From the fifteen patients entered into the survey sample group, two were eliminated at the end of the four-week period once surveys were returned as they confirmed to not

sticking to a strict GFD. Once the surveys were received, the data was entered into an Excel spreadsheet. Bar graphs, line graphs and comparative graphs are used to show the results of this study.

# CHAPTER 3

## RESULTS

Out of the 13 patients whose surveys were analyzed for data, 69.2% patients said they have experimented with a special diet one or more times in the past while 23.08% patients said they have not. 61.54% patients confirmed practicing GFD before, and 38.46% patients denied ever being on GFD before this trial period. 100% of the 13 respondents stated they followed the prescribed diet for four weeks prior to the survey. Patients stayed neutral when asked if GFD had a positive effect on their health, with 46.15% people saying yes while 53.85% people said denied any effect on their symptoms or health. 46.15% patients said there was a considerable weight difference after four weeks of GFD (lower or higher than baseline was not disclosed), and 38.46% patients said GFD made no difference to weight. 76.92% patients confirmed having intestinal problems while 23.08% denied having any severe abdominal problems, barring occasional discomfort. Out of these ten patients who had intestinal symptoms, four said an adherence to GFD for four weeks made a significant improvement in presentation of diarrhea or constipation. The other six reported no significant improvement in these symptoms. 84.62% patients report some form of abdominal pain or discomfort before the beginning of the GFD trial while 15.38% members denied abdominal symptoms. Of the 11 patients who reported having symptoms, five of them claimed to some relief from GFD while six of them confirmed minimal to no change in abdominal symptoms. 69.23% members of the sample group agreed to have been diagnosed with an autoimmune disorder in the past. Out of the nine patients who had been

diagnosed, seven of them stated a medical provider or family physician had diagnosed them while two of them confessed to self- diagnosis of a chronic autoimmune disease. At the end of the survey, on the 26$^{th}$ day, gluten was reintroduced into their diet and a week later, 30.78% patients reported return of some form of abdominal symptoms, degree of pain or discomfort not disclosed while 61.54% patients reported no return of abdominal symptoms through the six days of gluten re-intake. The numerical values of responses is depicted in Table 3.1.

Table 3.1: Numerical Values of the Responses Received on the Questionnaire Survey

| Questions | Yes | No | I do not wish to answer |
|---|---|---|---|
| 1. Have you ever followed a special diet before this period? | 9 | 3 | 1 |
| 2. If you have followed a GFD before, was it due to a self-diagnosed disorder? | 8 | 5 | - |
| 3. Did you adhere to the GFD prescribed to you by your PCP at your last visit? | 13 | - | - |
| 4. Was the overall effect of GFD on your health positive? | 6 | 7 | - |
| 5. Was there a weight difference between your first and last visit within these 4 weeks? | 6 | 5 | 2 |
| 6. Did you have frequent symptoms of intestinal transit (constipation or diarrhea) before the beginning of the 4-week survey period? | 10 | 3 | - |
| 7. If answered yes to above question, did you see an improvement after adhering to GFD? | 4 | 9 | - |
| 8. Did you have frequent episodes of abdominal pain, pressure or bloating before the beginning of the 4-week survey period? | 11 | 2 | - |
| 9. If answered yes to above question, did you see an improvement after adhering to GFD? | 5 | 8 | - |
| 10. Were you ever in the past, diagnosed with an Autoimmune disorder of the GI tract or a chronic inflammatory condition of the bowels? | 9 | 3 | 1 |
| 11. If yes, did you self diagnose or were you diagnosed by a PCP or medical provider and is included in your medical records? | 7 | 5 | 1 |
| 12. When gluten was re-introduced into your diet at the end of the $4^{th}$ week as gluten challenge trial, did your discomfort return? | 4 | 8 | 1 |

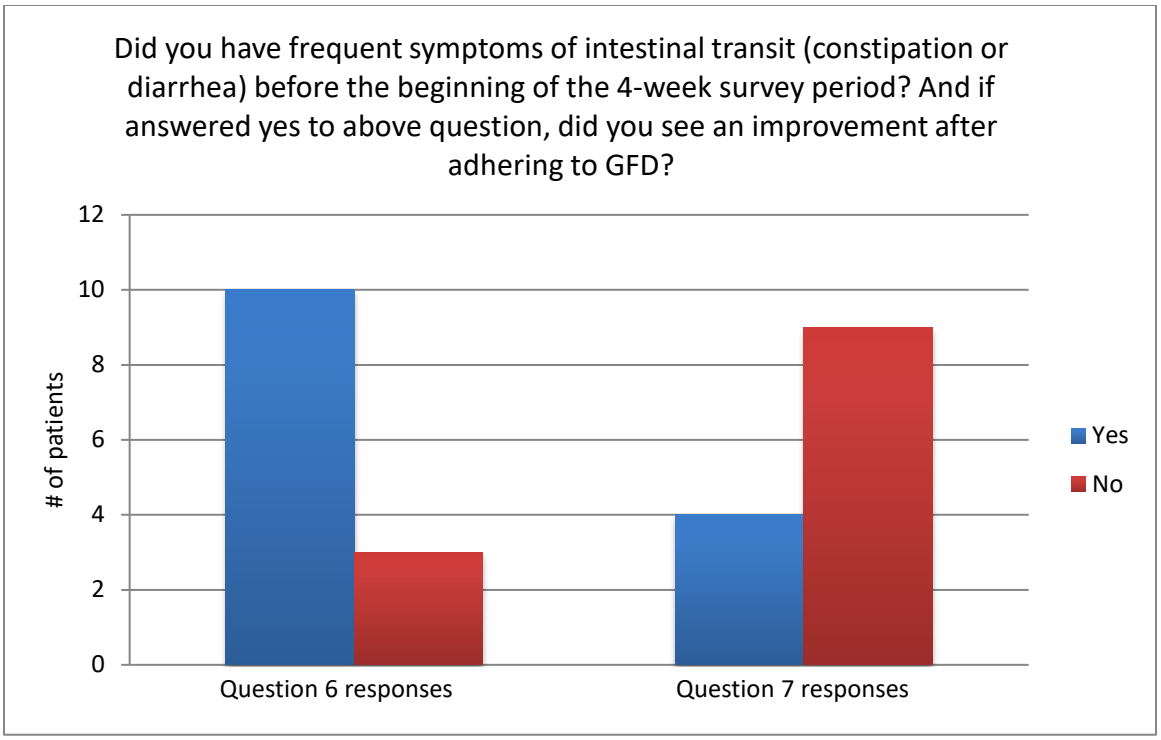


Figure 3.1: Numerical Values Comparisons of Patients Who Responded to Q6 and Q7

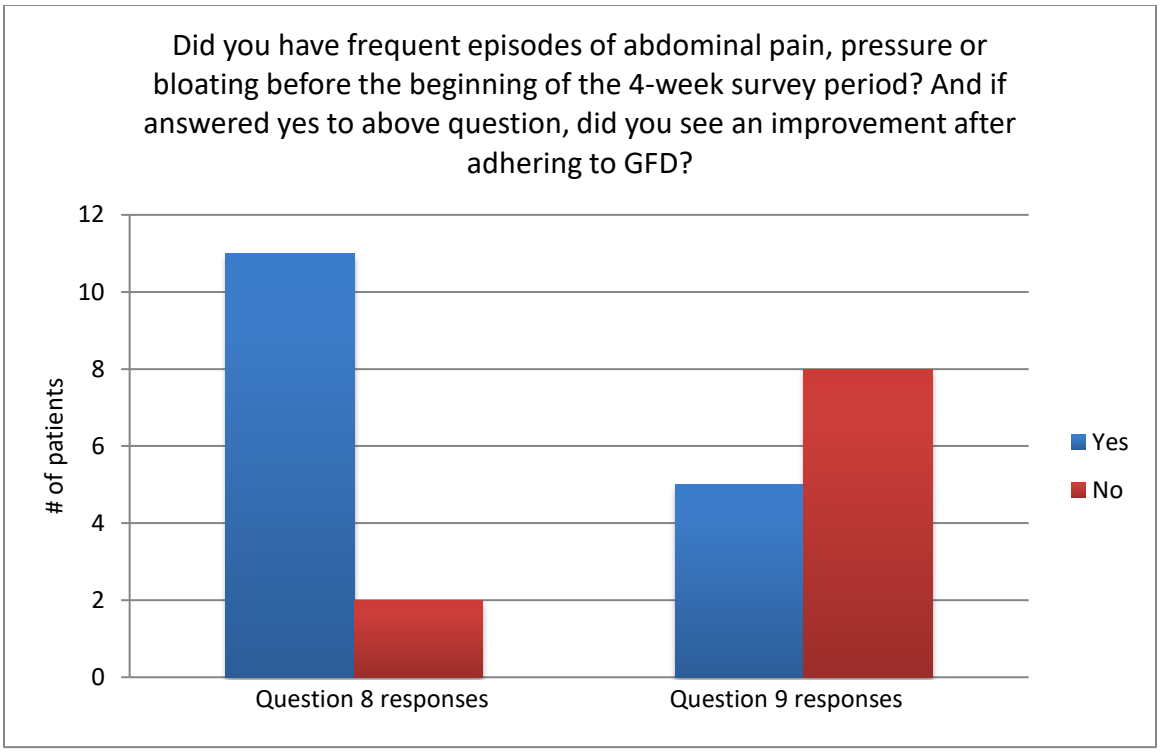


Figure 3.2: Numerical Values Comparisons of Patients Who Responded to Q8 and Q9

# CHAPTER 4

# DISCUSSION

Since the survey is based upon patient answers in regards to a diet requirement fulfilled at home, not necessarily under direct supervision, a certain amount of human error is expected. Furthermore, using a small sample group of 13 members limits the analysis of diagnosis and symptoms that may apply to an entire population. Since the members of the sample group are randomly picked, it provides some level of difference in cultural backgrounds, age and genetic inheritance. Since the survey was not conducted in a workplace or university solely, the level of education of the members cannot be generalized. Education level has an impact on answers to questions asked such as whether the patients self-diagnosed themselves using the Internet versus if they were responsible enough to be seen by a medical provider to be diagnosed.

The findings of the study conducted here that depict that GFD did not make a significance impact on autoimmune disorder symptoms in this sample group of patients corresponds with a similar study published in *Alimentary Pharmacology & Therapeutics* that was conducted on a larger scale of 465 patients and using medical techniques (Lanzini et al 2009) to showcase the condition of patients with autoimmune disorders before and during or after a GFD diet. The results are summarized in Tables 4.2 and 4.3 (Lanzini et al 2009).

Table 4.1: Summary of Results Presented in *Alimentary Pharmacology and Therapeutics* in 2009

| Characteristics | At diagnosis | During/After GFD |
|---|---|---|
| Mean BMI | 20.5 | 21.7 |
| Intestinal symptoms | 208 | 52 |
| Extra intestinal symptoms | 130 | 42 |
| CD Related Serology: | | |
| Negative | 0 | 405 |
| Positive | 465 | 60 |

Table 4.2: Summary of Results Presented in *Alimentary Pharmacology and Therapeutics* in 2009

| Characteristics | Responsive | Non-Responsive |
|---|---|---|
| Patients | 338 | 127 |
| Males | 90 | 19 |
| Females | 248 | 108 |
| Clinical Presentations: | | |
| Intestinal symptoms | 146 | 62 |
| Extra-intestinal symptoms | 96 | 34 |
| Serology on GFD | | |
| Negative | 297 | 97 |
| Positive | 35 | 26 |

Gluten is blamed for most, if not all, flare-ups of celiac and other autoimmune diseases. Wheat, the most common staple food grain that contains gluten around the world, is a hybrid grain produced from mixing different forms of grass that are cross-pollinated. Ancient wheat grains contained lower levels of protein, between 1-11% (McGee, 2004). Due to the lower level of chromosomal count in this grain historically, it also had lower levels of Gliadin, the main component of gluten blamed for gluten sensitivity. One reason why gluten was never considered a diet problem earlier is that the present wheat grain

contains about 13-16% protein therefore making it high in gluten content than older grains. Baking processes are made easier with a higher gluten content flour, but this may be the reason in the rise of gluten-related disorders (McGee 2004). Furthermore, ancient wheat grain, a 14-chromosome diploid grain called *einkorn* (Molberg et al, 2005), lacked a specific set of chromosomes that contained the components that stimulate T-cell gluten peptides and are precursors to gluten sensitivity and Celiac Disease (Molberg et al, 2005).

In a 2009 study, increasing concerns over the fertilizers used in today's agricultural practice are addressed as well as the impact they have on the growth and composition of the wheat plant (Grove et al, 2009). This research's findings are highly sought after as they explain how the wheat is being modified since its initial origin through not just selective breeding but also through environmental factors such as components used in agricultural products (Grove et al, 2009). Another environmental factor that affects the gluten content in grains such as wheat is the process of milling. Around the time that conventional milling began emerging in Asia and Europe, the United States began using an agent, azodicarbonamide, which is zinc peroxide, that aids in increasing the shelf life of wheat flour and whitens it for market value. This procedure is currently illegal in European countries, as it has proven health hazards such as digestive inflammatory disorders, carcinomas and pulmonary disorders (McGee, 2004). The Lacto fermentation process of wheat is another industrial process that highly determines the level of gluten in breads. A study conducted by researchers discovered that old-style breads were produced with lacto bacilli components had 12 parts of gluten per million in comparison to present-day bread that is produced with 75,000 parts per million (Rizzello et al, 2007). From this it can be

derived that the longer the fermentation process, the higher the gluten content (Rizzello et al, 2007).

From all the literature reviewed, it is evident that GFD patients adapt to this lifestyle based on a number of facts, some proven and some myths. But the effects of GFD are not always beneficial to the patient. A 2009-2010 survey conducted by NHANES reports that a significant decrease in levels of vitamin B and iron are seen in the blood serum iron and hemoglobin levels measured from patients on a GFD versus those who consume gluten on a daily basis without any restrictions (Nicollete et al, 2013).

The purpose of this research is to educate the group of people following a GFD about the probability that gluten might not even be the main cause of their abdominal problems, and that could be the environment could be the real culprit. If instead of following a GFD, better tools are used to cultivate a wheat crop that uses less harmful components in the fertilizers or alter the methods of increasing shelf life of the grains instead of using peroxide products in milling factories, patients suffering from CD, IBS and other autoimmune diseases could get the necessary nutrient content while still controlling the flare-ups of these diseases. Much research is needed in this field to investigate alternate theories about factors that may cause flare-ups of autoimmune disorders, and these factors should be tested through laboratory mediums and on larger sample groups to provide a better understanding of one of the most pressing issues in today's world.

# APPENDIX A

# QUESTIONNAIRE SURVEY

| Questions | Yes | No | I do not wish to answer |
|---|---|---|---|
| 1. Have you ever followed a special diet before this period? | | | |
| 2. If you have followed a GFD before, was it self-diagnosed? | | | |
| 3. Did you adhere to the GFD prescribed to you by your PCP at your last visit? | | | |
| 4. Was the overall effect of GFD on your health positive? | | | |
| 5. Was there a weight difference between your first and last visit within these 4 weeks? | | | |
| 6. Did you have frequent symptoms of intestinal transit (constipation or diarrhea) before the beginning of the 4-week survey period? | | | |
| 7. If answered yes to above question, did you see an improvement after adhering to GFD? | | | |
| 8. Did you have frequent episodes of abdominal pain, pressure or bloating before the beginning of the 4-week survey period? | | | |
| 9. If answered yes to above question, did you see an improvement after adhering to GFD? | | | |
| 10. Were you ever in the past, diagnosed with an Autoimmune disorder of the GI tract or a chronic inflammatory condition of the bowels? | | | |
| 11. If yes, did you self-diagnose or were you diagnosed by a PCP or medical provider and is included in your medical records? | | | |
| 12. When gluten was re-introduced into your diet at the end of the $4^{th}$ week as gluten challenge trial, did your discomfort return? | | | |

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## BIOGRAPHICAL INFORMATION

Miti was born in India and moved with her family to the United States in 2008, completed high school in Atlanta, Georgia, and then moved to Texas to pursue an Honors Bachelor degree in Biology at UT Arlington. Miti plans on continuing her education by attaining a Master's degree in Biology and one day teaching at a university. Miti has previously worked as a Resident Assistant at UT Arlington, as a tutor for Biology and currently at a medical center as an assistant to Emergency Department physicians. Later in life, Miti hopes to travel the world and maybe return to her home country to make a much-needed difference in education there.