

AN EXAMPLE OF WHAT MACEDONIAN POPULATION KNOWS ABOUT FOOD ALLERGIES AND FOOD INTOLERANCE

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Abstract

A food allergy is a widespread disease, an exaggerated immune system response mostly to a food proteins, mediated by Ig E antibodies, followed by a certain clinical picture ranging from a mild to life threatening symptoms. Eight foods cause 90% of allergies: milk, egg, peanuts, tree nuts, fish, shell fish, wheat and soy. However, any food can cause an allergic reaction. Food intolerance is an adverse reaction to food that does not involve the immune system.

A pilot study to detect what Macedonians know about food allergies and intolerance. A Questionnaire composed of 12 questions was put on Faculty of Technology and Technical Sciences website and answers of 130 persons from different regions of Macedonia were collected. The participants were categorized by sex and age (from 18 to 29; 30 - 39; and over 40). The results obtained by arithmetical mean and expressed in percentage were analyzed.

63% of them know what kind of food can often cause an allergy, 60% know about the symptoms, 73% know that allergy can be fatal, 66% does not know how to prevent the symptoms, 69% think that food allergy does not disappear throughout the life, 87% do read the declaration of the food product they are buying, 79% think that the food products are not properly labeled for allergic substances, 53% do not know the intolerance symptoms and 70% do not know how to protect themselves from food intolerance.

Macedonians are quite well informed about food allergies, their symptoms and fatal outcome, but are less informed about its prevention as well as about food intolerance. There should be more sufficient labeling of all allergic substances on the food products in Macedonia. A wider population should be included in the survey to confirm these findings.

Key words: Food, Allergy, Allergens, Intolerance.

1. Introduction

Food allergies (FA) are worldwide spread immune based disease, becoming a growing public health concern in developed as well as developing countries now days. Recent findings of this disorder, a subject of interest of numerous researchers, ranging from fundamental research about FA pathogenesis mechanisms in animal models and genetic predisposition, to clinical trials and epidemiological surveys studies are briefly presented. Furthermore, we did find poor literary data suggesting what the population of other countries including ours, know about FA and food intolerance, whether they are having a general information about the nature of this occasionally life threatening disorder, or for the differences between FA and food intolerance, the symptoms, the treatment and the proper labeling of allergic substances since each of us can potentially develop food allergy in certain period of life. That's why we conducted a pilot study with online questionnaire, to find out what Macedonians do know about FA and food intolerance which is presented in the second part of the paper. The results obtained suggest further initiatives that Macedonian health sector and society should consider.



The basic characteristic of physiologically balanced immune system is self-non self-discrimination i.e. our immune system recognizes the foreign substances within the frame of our Human Leukocyte Antigens (HLA). However in food allergy, an inadequate immune response to otherwise harmless food occurs. Once the immune system decides that a particular food is harmful, it creates most often specific Immunoglobulin (Ig) E antibodies to fight it. In general, FA can be caused by IgE and non IgE induced mechanisms.

The IgE-mediated reactions are usually divided into immediate onset reactions (immediate in time) and immediate plus late-phase (in which the immediate onset symptoms are followed by prolonged or on-going symptoms). IgE food allergic reactions also known as immediate type hypersensitivity or type I reaction that involves a wide range of molecular events starting from primary exposure of food allergens, processing of allergens by antigen presenting cells, induction of transcription factors, cytokines and chemokines production, priming IgE on mast cells or basophils, to signaling events followed by secondary exposure of allergens, degranulation and release of mediators like: leukotrienes, histamines, prostaglandins, β -hexosaminidase and ultimately anaphylaxis [1].

The gastrointestinal tract (GIT) processes ingested food for absorption. It neutralizes foreign antigens and blocks them from entering into the circulation. Enzymes from: salivary, gastric, pancreatic and intestinal secretions, combined with: mastication, gastric acid, and peristalsis, reduce ingested substances to small sugars, peptides and fats. Non-specific (mucin coat) and specific (secretory IgA) mechanisms 'hold up' and/ or block potentially harmful antigenic substances from penetrating the intestinal barrier. Many of the immunological and mechanical barriers involved in this process are immature at birth, leaving the infant at risk. Large amounts of immunologically intact food proteins penetrate the gut barrier in children and adults and enter into the circulation, but clinical tolerance prevents pathologic reactions. A failure to develop tolerance or a breakdown in tolerance results in excessive production of food-specific IgE antibodies. Mast cells line the GIT from the lips to the rectum. Food antigens are most rapidly absorbed from the small intestine, colon and rectum and more slowly from the esophagus and stomach. When food allergens penetrate mucosal barriers and reach specific IgE antibodies bound to mast cells, mediators such as histamine, leukotrienes and prostaglandins are released inducing an immediate hypersensitivity reaction manifested by vasodilatation, smooth muscle contraction and other alterations in normal physiology [2].

IgE mediated food related disorders can appear in form of: akin manifestations (acute urticaria, angioedema and eczema); GIT affection (lip, tongue and palatal pru-

ritus and swelling, laryngeal edema, nausea, abdominal cramping, vomiting and diarrhea, oral allergy syndrome and infantile colic); and respiratory reactions (allergic rhinoconjuctivitis, anaphylaxis, food-associated and exercise-induced anaphylaxis) [3]. Anaphylaxis is the most serious life threatening manifestation of FA. Every food allergy reaction has the possibility of developing potentially fatal anaphylactic reaction. This can occur within minutes of exposure to an allergen. In addition to gastrointestinal symptoms, individuals may experience: urticaria, angioedema, asthma, rhinitis, conjunctivitis, hypotension, shock and cardiac arrhythmias, caused by the massive release of mediators from mast cells and basophiles. Food-associated, exercise-induced anaphylaxis occurs when exercise takes place 2 - 4 hours after ingestion of a food to which the individual is allergic. Food or exercise alone will not cause this reaction. Risk factors for food-induced anaphylaxis include asthma and previous allergic reactions to the causative food [4].

Although FA are most often caused by specific (s) IgE-mediated reactions to food, relevant to reactions likely mediated by immunologic but non-IgE-induced mechanisms should be considered as well. Although pathogenesis of non IgE mediated FA (NFA) is still not well understood, recent studies indicate widely variable clinical manifestations of NFA. In parallel to our better appreciation of clinical features of NFA, complex regulatory mechanisms of gut immune homeostasis have become known with progress in our understanding of the gut mucosal immune system. In addition, a role of gut commensal flora on the gut immune system has also become better understood along with the effects of dietary components [5]. Subtle changes in interactions between environmental factors (microbiota, dietary components, etc.) and the gut immune responses can affect gut immune homeostasis, which can result in undesired adverse reactions to food proteins [6].

Non-IgE-mediated food allergic disorders (some appear to be T-cell-mediated), have been manifested in form of: gastrointestinal affection (dietary protein enterocolitis syndrome, dietary protein proctitis, dietary protein enteropathy and Celiac disease, exacerbation of eosinophilic gastrointestinal disorders-eosinophilic gastritis, eosinophilic enteritis, eosinophilic colitis, and eosinophilic gastroenteritis); cutaneous disorders (food-induced allergic contact dermatitis-dermatitis herpetiformis); and respiratory disorders (food induced pulmonary haemosiderosis-Heiner's Syndrome). In these conditions, sensitization to food protein cannot be demonstrated based on sIgE. The diagnosis of non-IgE-mediated FA is based on signs and symptoms occurring reproducibly on exposure to food, resolution of those signs and symptoms with specific food avoidance, and, most often, histologic evidence of an immunologically mediated process, such as eosinophilic inflammation of the GIT [7].



Foods or food components that elicit reproducible adverse reactions but do not have established or likely immunologic mechanisms, are not considered as food allergens. Instead, these non-immunologic adverse reactions are termed as food intolerances and should be referred to as non-allergic food hypersensitivity [8].

Non-immune mediated reactions or food intolerances include: metabolic, pharmacologic, toxic, and undefined mechanisms. For example, an individual may be allergic to cow's milk (henceforth referred to as milk) due to an immunologic response to milk protein, or alternatively, that individual may be intolerant to milk due to an inability to digest the sugar lactose. In the former situation, milk protein is considered an allergen because it triggers an adverse immunologic reaction. Inability to digest lactose leads to excess fluid production in the GI tract, resulting in abdominal pain and diarrhea. This condition is termed lactose intolerance, and lactose is not an allergen because the response is not immune based. Everyday consumed food also includes numerous substances which may cause non-allergic hypersensitive reactions in some individuals. These reactions may be caused by high histamine content of certain food or by nonspecific histamine release (e.g.: tuna, mackerel, strawberry, and citrus). Most adverse reactions to food additives, such as artificial colors (for example, FD&C yellow 5 [tartrazine]), and various preservatives (for example, sulfites), have no defined immunologic mechanisms [9].

The best current treatment for food intolerance is to either avoid certain foods or eat them less often and in smaller amounts, as well as taking supplements that may help digestion. Some people find that if they stay off the specific food for a while, they have no reaction when eating it again - this is known as tolerance. Maintaining tolerance is often a question of knowing how long to abstain, and how much of it to eat when it is being reintroduced. As each person reacts differently, the only way to determine this is by trial-and-error. In some cases, these reactions may mimic reactions typical of an immunologic response. It is therefore important to keep these food components or mechanisms in mind when evaluating adverse food reactions.

The most important products that may cause allergic reaction in sensitized subjects include: cow milk, egg, soy, fish, shellfish, wheat, peanut, and tree nut despite the fact that every food can induce FA. The natural course of food allergy is of special importance since its frequency is higher in children than in adults [10, 11]. The outcome of food allergy in childhood is variable. Although childhood allergies to milk [12], egg [13], wheat [14], and soy [15] generally resolve in childhood, they appear to be resolving more slowly than in previous decades, with many children still allergic beyond age of 5 years. Allergies to: peanuts, tree nuts, fish, or shellfish [16] are generally lifelong allergies,

but some longstanding strategies of FA are changing in the light of new research studies. Namely, clinical practice guidelines from the United States in 2000 [17], recommended the exclusion of allergenic foods from the diets of infants at high risk for allergy, and from the diets of their mothers during pregnancy and lactation. Studies in which food allergens have been eliminated from the diet have consistently failed to show that elimination from the diet prevented the development of IgE-mediated food allergy [18]. In 2008, recommendations for the avoidance of allergens were withdrawn. However, recent studies led by Professor Gideon Lack [19, 20] give a proof that early introduction of peanut may offer protection from the development of peanut allergies (PA). Early consumption was effective not only in high-risk infants who show no sensitivity to peanuts early on, but it was also effective in infants who already demonstrated peanut sensitivity. Learning Early about Peanut Allergy, (LEAP) study team recommended that as soon as infants develop the first signs of eczema or egg allergy in the first months of life, they should receive skin testing to peanut and then eat peanut products either at home if the test is negative, or first under clinical supervision if the test is positive. Infants without such symptoms should be fed with peanut products from four months of life. The early introduction of peanuts significantly decreased the frequency of the development of PA among children at high risk for this allergy, and modulated immune responses to peanuts, which suggest that these findings should prompt a change in food allergy guidelines.

Scientists are trying to give an answer to the question why FA appears in certain percentage of population and the number of affected is permanently increasing. They are suggesting hereditary, genetic, and molecular risk factors such as: family history, parental or sibling allergy history [21, 22], genetic predisposition and genetic polymorphisms. Recent study [23] suggests that the HLA-DR and -DQ gene region probably possess significant genetic risk for peanut allergy as it accounted for about 20 percent of peanut allergy in the study population. Not everyone with these mutations, however, develops peanut allergy, and researchers wondered why. One possible reason, they determined, was that epigenetic changes may also play a role. Epigenetic changes, in which a methyl group attaches itself to the DNA, alter the expression of a gene without altering its underlying code. The levels of DNA methylation regulate whether people with genetic susceptibility to the peanut allergy actually developed it.

Brown *et al.*, [24] have confirmed that loss-of-function mutations within filaggrin showed a significant association with PA in patients with PA This association was closely replicated in the Canadian study. Importantly, the association of filaggrin mutation with PA was highly significant.



In context of gender, boys appear to be at higher risk than girls [25], and perhaps women more than men [8, 26] suggesting genetic or endocrinologic influences. Ethnicity (black children were more likely to be sensitized to multiple foods compared with white children) [27], have been considered as a risk factor for developing FA as well.

Potentially rectifiable risk factors include: vitamin D insufficiency, unhealthful dietary fat, obesity, increased hygiene, and the timing of exposure to foods. Furthermore, may be differences in macronutrient and micronutrient dietary content can explain the increase in allergies. Modern hygienic or dietary practices may play a role by disturbing the body's natural bacterial composition. While complex and largely undetermined factors such as genetics greatly affect whether individuals develop food allergies and how they manifest, the identification of a bacteria-induced barrier-protective response represents a new paradigm for preventing sensitization to food. Environmental stimuli such as: antibiotic overuse, high fat diets, caesarean birth, removal of common pathogens and even formula feeding have affected the microbiota with which we've co-evolved and might contribute to the increasing susceptibility to FA according to recent study in mice [5]. These investigators suggest that presence of Clostridia, a common class of gut bacteria, protects against food allergies. By inducing immune responses that prevent food allergens from entering the bloodstream, Clostridia minimize allergen exposure and prevent sensitization, a key step in the development of food allergies. To identify this protective mechanism, researchers studied cellular and molecular immune responses to bacteria in the gut. Genetic analysis revealed that Clostridia caused innate immune cells to produce high levels of interleukin-22 (IL-22), a signaling molecule known to decrease the permeability of the intestinal lining. However, these findings should be applied at a population level, and the cause-and-effect relationship in individuals requires further study. Results such as these are exciting, as they suggest potential future treatments with probiotic therapy that may be able to be applied to humans with FA.

There are numerous epidemiologic studies which emphasize the prevalence of FA. US statistics estimated a number of 9 million, or 4% of adults with FA, nearly 6 million or 8% of children do have FA with young children as affected the most. Food allergy prevalence in the USA has increased 55% in the last five years. Anaphylaxis is estimated to cause about 2,500 emergency room visits annually and its believed to be responsible for up to 125 deaths each year. Peanut and tree nuts account for 92% of severe and fatal reactions [10]. The prevalence of food allergy in the French general population is estimated to 3.5%, being more frequent among children; in Macedonian population it is estimated to 4.2%, which means over 80,000 subjects in

Republic of Macedonia experienced an adverse reaction to food, or 5.0% of FA were experienced by children and 3.3% by adults; in Berlin general population the prevalence of FA is estimated to 3.6%; while 5% prevalence of FA in children and 2% in adults is found in the UK and Scandinavian countries [8]. Anaphylaxis due to food allergy is estimated to cause about 200 deaths each year in the West European countries.

It should be noted that most of the studies about the epidemiology of FA documenting the prevalence of: peanut, milk, and egg allergies are mostly limited to US and Western countries. The knowledge about FA in the developing world is limited and relies mainly on case series. Furthermore there are methodological explanations for the differences in prevalence observed in different studies. Double-blind, placebo-controlled food challenges, which represent the gold standard, are only used in a minority of studies. Consequently, other studies use questionnaires (mainly unvalidated), IgE positivity, or skin prick test (SPT) response positivity as markers of FA [28]. Although there are methodological limitations, there is strong impression of an international increase in allergy and food allergy [9, 29].

Today, we have more optimistic information and knowledge about the pathogenesis, diagnosis, prevention and treatment of FA thanks to numerous genetic and environmental risk factors that have been identified. Route of sensitization, allergen characterization, and immune response provide insights for diagnosis and treatment. Improved understanding of food allergy from the study of animal models together with human studies is likely to contribute to the development of novel strategies to prevent and treat food allergy [30]. Combination of environmental and genetic risks factors can open pathways into improved prevention of FA in future. There is a wide spectrum of disease caused by food allergy related to different immune mechanisms and the target organs affected.

Diagnosis depends on combining knowledge of pathophysiology and epidemiology with the patient's history and test results. It is clearly possible to have sensitization without clinical reactivity and vice versa. Component - resolved diagnosis is more often applied in clinical practice. The medical history is the key, noninvasive tests are supportive and possibly diagnostic, and the oral food challenge (OFC) is the most definitive test because identification of food-specific IgE by means of testing indicates sensitization but is not, in isolation, diagnostic. Sometimes, even after performing skin prick and blood tests, an allergist is unable to arrive at a definitive diagnosis. In this case, the patient may be asked to undergo an oral food challenge (OFC), a highly accurate diagnostic test for food allergy [31].

Management currently requires attention to allergen avoidance and emergency treatment, and numerous resources are available to patients and physicians to promote education and counseling to improve safety and guality of life. Recommendations about the prevention of food allergy and atopic disease through diet have changed radically, with rescinding of many recommendations about extensive and prolonged allergen avoidance. Numerous therapies have reached clinical trials, with some showing promise to dramatically alter treatment. With deeper insights into genetics and the microbiome, incorporation of bioinformatics, and numerous approaches to treatment in preclinical and clinical studies, we are poised to witness a revolution in our approach to food allergy over the next several years.

A pilot study was conducted in order to find out what Macedonian population knows about: food allergy, the symptoms of this disorder, the occasional severity and fatal outcome, treatment, the difference between FA and food intolerance, the symptoms and treatment of food intolerance, the difference between these two disorders, and their opinion about labeling of Macedonian products which can consist some allergic substances. The results obtained allow us to propose certain initiatives that Macedonian health sector and society should be aware of.

2. Materials and Methods

A questionnaire composed of 12 questions was put on Faculty's of Technology and Technical Sciences in Veles, Macedonia, website and answers of 130 persons from different regions of Macedonia were collected. The participants were categorized by sex and age (from 18 to 29; 30 - 39; and over 40). The results obtained were analyzed by arithmetical mean and expressed in percentage.

3. Results and Discussion

The answers were given mostly by younger people, a bigger group (70%) were 18 to 29 of age; 17% were 30 to 39 years of age; and 13% were up to 40 years old (91 v. 22 v.17 individuals respectively). The results are shown in Figure 1.



igure1. Percentage of participants include according to age

The peak incidence of deaths from anaphylaxis associated with nut allergy occurs in teenagers and young adults. During adolescence, the management of food allergy shifts from being the responsibility of parents to that of the young person. This is a group who therefore need special attention in the clinic. Teenagers are a particularly high-risk group, with the peak incidence of deaths from anaphylaxis associated with nut allergy occurring in the 15 - 24 year age group that we should be aware of [32].

In our study women participated more compared to men (60% v. 40% i.e. 78 v. 52 individuals respectively) (Figure 2).

In early childhood boys appear to be at higher risk than girls [25], but in adulthood women are dominant gender prone to FA [8, 26] which should be emphasized when organizing educational courses.

Answers to the question what respondents know about which food can induce allergy are shown on Figure 3.

To the question whether individuals know which food can induce allergy the most, higher percentage of 63% (82 individuals) gave positive answer, compared to 37% (48 individuals) who did not know which kind of food can induce FA the most. Since FA can occur any period of life it is recommendable the population to know that eight foods cause 90% of allergies: milk, egg, peanuts, tree nuts, fish, shell fish, wheat and soy [12 - 16].

Figure 4 shows whether individuals recognize the symptoms of FA.



Figure 2. Percentage of participants categorized by gender



Figure 3. Do you know which food can induce allergy?



Figure 4. Are you familiar with the symptoms occurring after certain food consumption?



60% (78 individuals) are familiar with the symptoms, while 40% (52 individuals) do not know which is spectrum of symptoms occurring during FA attack. Early recognition of symptoms can provide better treatment at the emergency centers or clinics and eventual better outcome. The study of Monk *et al.*, [32] on how do teenagers manage their food allergies, suggests that teenagers felt it would be helpful for their peers to be educated about food allergy. If a wider population knows the symptoms of FA that strategy might help individuals with already known FA to avoid trigger foods and enable them to access help more readily if they suffer a reaction, or well informed individual about FA symptomatology can recognize it and give a support to someone who develops FA for the first time.

Figure 5 displays results on question whether food allergy can be life threatening.

In the atmosphere where we are faced with the fact that the prevalence of food allergies and associated anaphylaxis appears to be on the rise [10] it is concealing that a higher number of participants in this pilot study were aware of the fact that FA can be fatal. 73% (95 participants) were familiar with this observation, compared to 27% (45 participants) who are not common with the fatal outcome of FA.

Despite the fact that recent fundamental, experimental and clinical studies give a brighter insight to the pathogenesis of FA pawing a way to more than symptomatic treatment of FA, [3, 23, 24, and 31] most applied preventive method is avoidance of potentially allergic food, although there are scientist who strongly believe in the theory of applying small doses of food allergens starting early in life of the allergic child [19, 20]. It is very interesting to see the results on question what respondents know about the prevention and therapy of the food allergies (Figure 6).

34% (44 participants) in our study have information about the prevention and therapy of FA. However, a higher percentage of participants did not know anything about prevention and treatment of FA. It suggests that those participants were never faced with the severity of this disorder, or the symptoms manifested were rather mild.

On the question does food allergy disappear during life time less respondents 31% (40 participants) think that FA can disappear during the lifetime (Figure 7).

Much higher percentage (69%) or 90 participants do not share this opinion. Literary data suggest that allergies to: milk egg, wheat and soy generally resolve in childhood [12 - 15], while allergies to: peanuts, tree nuts, fish, or shellfish [16] are generally lifelong allergies. Patients at risk of anaphylaxis should carry a self-injectable adrenaline device - an autoinjector (SIA) at all times and, along with family, friends and teachers, need to be educated in when and how to administer it [33].

Figure 8 shows how much the respondents are paying attention on food declarations.



Figure 5. Do you think that food allergy can be life threatening?



Figure 6. Do you know about the prevention and therapy of the food allergies?



Figure 7. Does food allergy disappear during life time?



Figure 8. Do you pay attention to the food product declaration while buying?

Properly labeled food products are significant tool in FA prevention. Even small traces of allergic substances in the food product can cause a variety of allergic clinical manifestations. 87% (113 participants) have stated that they pay attention to the food declaration while buying it, so the culture of accepting and reading information about food content are quite high in Macedonia, compared to less percentage (13%) or 17 of those who do not read the declaration at all. It seems that the Government campaign "Eat healthy food" and knowledge for the content of the food product have a positive impact on the customers while buying food products.

In one study [32], interviews revealed that the majority of teenagers only checked the labels of new foods or when they felt unsure. As the reason for their their last reaction, a third cited in the questionnaire, is not checking the ingredients. More than three-quarters ate foods labeled with 'may contain' labels. More than half admitted trying food that might contain an allergen. A few said that they initially try a small amount of such a food and then wait to see what happens. In general, responses did not relate to whether or not participants had previously experienced an anaphylactic reaction. It suggests more consistent allergy warnings. The majority of interviewes also acknowledged difficulties when eating restaurant or take-away food.

Answers on the question of adequate notification of the allergic substances on the food products labels are shown in Figure 9.

27 participants (21%) were satisfied with it, compared to 103 participants (79%) who found the labeling of allergic substances unsatisfactory and unclear. Previous studies have highlighted the difficulty in allergen avoidance including insufficient education and guidance, unclear ingredient information on food products (which is compatible with our findings in this study) and the lack of knowledge among food establishment personnel [34].

Taking into consideration that FA and food intolerance are two basically different conditions, the first one defined as hypersensitivity being a result of altered immunological response, and the latter one as a consequence of non-immunologic adverse reactions, a difference between these conditions should be made. That is necessary since the approach to treatment is different. Level of respondents' distinction between food allergy and food intolerance is given in Figure 10.

A high percentage (71%) of participants or 92 of them were not able to make a difference, compared to lower percentage (29%) or 38 participants who have information that FA and food intolerance are different disorders (Figure 10).

In similar context was the question whether participants do recognize the symptoms of food intolerance, which are often gastrointestinal (Figure 11).

47% (61 participants) were familiar with the symptoms despite the previous result of not making difference between FA and food intolerance (Figure 10). May be it is the result of their opinion that FA and food intolerance are the synonyms of the same disorder.

We got expected results to the question whether participants in this pilot study know the preventive measures that should be taken to recuperate out from food intolerance as well as about the therapeutic approach to this disorder (Figure 12).

The most of the participants did not know the difference between FA and food intolerance and the symptoms following food intolerance, 70% (91 participants) were not familiar with the information of adequate prevention and therapy, compared to 30% (39 participants) who did.



Figure 9. Are allergic substances clearly notified on the food products label?



Figure 10. Are food allergy and food intolerance the same condition?



is prevented and treated?

The findings from this study has identified that wider population in Republic of Macedonia is not well informed about food allergies and food intolerances as two different entities, the first one being allergic or immune based hypersensitivity and the latter non-allergic food hypersensitivity, since the therapeutic approaches are different. It strongly suggests much more intensive efforts should be undertaken involving of our educational, medical, public health and media capacities in delivering information about managing food allergy which comprises from: avoidance of trigger foods, preparation for recognition and management of reactions to persons who suffer from food allergy and food intolerance, as well to young people and adults who never experienced it in order to recognize this condition if it ever happens to them, as well as to support someone who might suffer from these symptoms.

Previous research has demonstrated that patients with food allergy and parents of children with food allergy often do not carry their adrenaline as recommended and are poorly equipped to deal with reactions [35]. Training courses should be organized for teachers at elementary and high schools, and faculties in Republic of Macedonia. Workshops using video clips showing an allergic reaction could be used to emphasize the potential seriousness of foodallergy and practicing with a real SIA device on a piece of fruit might increase the use of these devices. Children who are suffering from severe forms of food allergy should carry their adrenalin as recommended and be better equipped to deal with these reactions. A video clips also proves to be useful way of educating patients' peers [32]. A randomized-controlled study, training for teachers and whole class asthma workshops for 7 - 9 year olds resulted in all pupils having a better understanding of asthma, with the pupils with asthma needing less medication and having an improved self-esteem and quality of life [36]. A similar intervention in the 12 - 15 year age group has been shown to be equally beneficial in other randomized-controlled study [37].

A person prone to food allergy or food intolerance experiences a real nightmare when dinning away from home because they must rely on food service staff to provide them with accurate information about ingredients so that they can make an informed decision about what to order. Incorrect or incomplete information puts these individuals at risk for an allergic reaction. Even a mild reaction will bring their dining experience to an abrupt end; a serious reaction may require transport to the hospital in an ambulance. The Centers for Disease Control and Prevention estimates that food allergies account for approximately 300,000 ambulatory care visits in the U.S. for children under the age of 18 years [38]. Education, cooperation, and teamwork are the keys to safely serving a guest who has food allergies. All food service staff - including: restaurant managers, servers, and kitchen staff - must become familiar with the issues surrounding food allergies and the proper way to answer guests' questions. Further, they must know what to do if an allergic reaction occurs. Surveys of members of the Food Allergy & Anaphylaxis Network (FAAN), a national nonprofit organization, indicate that an individual's restricted diet influences the shopping and dining out habits of the entire family and many of their close friends [39]. When these families find a product or restaurant that they like and trust, they become loyal customers and encourage others to patronize these manufacturers and establishments. So although food allergies affect as many as 12 million Americans, the impact on restaurant patronage is much greater.

Guidelines should be developed in Republic of Macedonia primarily for traditional style restaurants but also may be useful for operators of quick-service restaurants analogue to the comprehensive program for training staff to safely prepare and serve food to guests who have food allergies being developed by FAAN [39]. This guide provides general information about food allergies. Targeted sections contain specific information for: managers, front-of-the-house staff, and back-of-the-house staff and strategies to help them successfully fulfilling their role in ensuring a safe dining experience for guests with food allergies. Managing food allergies in a food service establishment requires a partnership between the guest and the restaurant staff. Working together, allergic reactions will be prevented. However, the food service facility should make sure that it complies with all local and state requirements of Republic of Macedonia relating to the safe handling of food and other consumable items, in addition to following safe food-handling procedures to prevent food contamination.

Finally, Macedonian Agency for Food and Veterinary have introduced the latest European Union product labeling criteria through changes in the current Law on food safety in 2015. In detailed, precise and specific information, products have their: origin, nutritional value, net weight variations and, most of all, possible allergens, labeled in bold or colored letters. The both, producers selling on EU or domestic market have the same labeling obligation as well as catering facilities. Trainings for food operators were organized. Despite this, the unsatisfactory labeling of allergic substances on the food products indicated by the participants of this pilot study, suggests that Macedonian Government intervention to deliver uniform, non-defensive, labeling practices should be continuously monitored by the Agency of Food and Veterinary of Republic of Macedonia.

4. Conclusions

- Macedonians are quite well informed about what food allergies are, the symptoms and fatal outcome, but are less familiar with its prevention as well as about food intolerance, its prevention and therapy and the difference between these two disorders.

- Unsufficient labeling of all allergic substances on the food products in Macedonia was notified.

- The results obtained suggest further initiatives that Macedonian Health Sector and society should consider such as: education of our population through training courses organized for teachers at elementary and high schools, faculties, restaurants about managing food allergies using video clips; organizing workshops for practicing with self-injected adrenalin for children suffering severe forms of food allergy delivered by health professionals of the clinics; developing guidelines for traditional style restaurants and operators of quick-service restaurants for training their management team and other staff to safely prepare and serve



food to guests who have food allergies; and improving the monitoring of allergic substances labels on the food products. Finally, a wider population should be included in the survey to confirm these findings.

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