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Assessment of Immunological Parameters of Gluten Sensitivity in Selected Skin Diseases

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Abstract: Background/objectives: Gluten-free diets have become very popular in recent years and unjustified exclusion of gluten happens extremely frequently. There are isolated reports which warn that symptoms of psoriasis, atopic dermatitis or chronic urticaria can be aggravated by the supply of gluten in the patient's diet. The aim of the study was (i) to assess the prevalence of antibodies typical for gluten-dependent enteropathy in patients with the above-mentioned skin diseases and in the comparison group; (ii) to assess the relationship between the declared diet in patients with selected dermatoses and the presence of antibodies typical for gluten-dependent enteropathy; (iii) to assess the occurrence of IgE specific to selected allergens, including wheat and rye flours, in the studied groups; (iv) to assess dietary behaviour in patients with selected skin diseases and in the comparison group. Methods: An interviewer-supervised auditory questionnaire was used to obtain information on the health status of the subjects. Their individual gluten intake was assessed by means of one of the retrospective dietary assessment methods. The method of consumption frequency was applied. Antibodies directed against smooth muscle endomysium, tissue transglutaminase and gliadin were detected in the patients and in the comparison group. The tests were performed using ready-made kits according to the manufacturer's recommended test instructions. In addition, blood allergy tests were performed in all the subjects in the study and control groups. Results: Based on the study, the diagnosis of visceral disease and gluten allergy was ruled out in all the subjects. However, significant differences were shown regarding the intake of certain foods. **Conclusions:** In patients with autoimmune diseases with associated gastrointestinal symptoms, a full diagnostic workup for gluten-dependent enteropathy and gluten intolerance is necessary. Patients who report gastrointestinal symptoms should not implement a gluten-free diet without appropriate diagnostics and consultation with their doctor.

Keywords: psoriasis; atopic dermatitis; chronic urticaria; coeliac disease; gluten

1. Introduction

A gluten-free diet is a diet excluding gluten: a complex of proteins, mainly gliadins and glutenins, which are contained in the germs of wheat grains as well as in other cereals, including those in the form of avenins in oats, secalins in rye, and hordeins in barley [1]. Several disorders associated with the consumption of foods that are sources of gluten have been described; these may be autoimmune or immunological disorders. Coeliac disease (CD), gluten/wheat allergy (WA) or non-celiac gluten sensitivity (NCGS) are the so-called gluten-dependent diseases known as gluten intolerance. The common and main treatment of these is a gluten-free diet. The symptomatology of these disorders may be similar. However, efforts should be made to differentiate them correctly as each has different complications and prognosis [2].

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According to ESPGHAN guidelines, individuals who are at risk of coeliac disease, even without symptoms suggestive of the disease, should be systematically screened for CD [3]. Given the gradual increase in the prevalence of atypical coeliac disease, it should be diagnosed not only in children with typical symptoms but also in adults, including the elderly [4].

According to the CD diagnostic guidelines, tests detecting 3 types of antibodies are therefore used: antibodies against tissue transglutaminase type 2 (anti-tTG2); antibodies against endomysial smooth muscle (EMA); antibodies against deamidated gliadin peptides (anti-DPG).

The scientific literature often concludes that the presence of one autoimmune disease is associated with an increased risk of another one, including CD [5].

Psoriasis is a chronic inflammatory skin disease [6]. Atopic dermatitis (AD) is also a chronic, recurrent condition [7], and urticaria is one of the most common allergic diseases [8]. These diseases greatly reduce the quality of life of patients, who often seek a solution to their health problem in their daily diet.

Given the need to confirm the presence of CD in order to implement a gluten-free diet, it seems appropriate to confirm the presence of IgAEmA, anti-tTG2 and anti-DPG antibodies in disease entities other than CD. This would deepen the knowledge of the pathogenesis of selected skin diseases and indicate the possibility of broadening therapeutic recommendations.

Taking into account the abovementioned assumptions, the aim of this study was to assess the prevalence of antibodies typical for gluten-dependent enteropathy (directed against tissue transglutaminase, smooth muscle endomysium and gliadin) in patients with psoriasis, chronic urticaria and AD and in a comparison group of healthy subjects. In addition, it was important to assess the association between the declared diet in the patients with the selected skin diseases and the presence of antibodies typical of gluten-dependent enteropathy. We also aimed at checking the prevalence of IgE specific to selected allergens, including wheat and rye flours, in the study groups. To assess the presence of antibodies fully, we had to check, through questionnaires, the dietary behaviour in the patients with the selected skin diseases and in the comparison group.

2. Materials and Methods

The study group consisted of 117 subjects including: 35 patients with psoriasis vulgaris (20 women and 15 men); 26 patients with AD (18 women and 8 men); and 21 patients with chronic nettle (18 women and 3 men). The comparison group consisted of 35 healthy subjects (25 women and 10 men).

The research itself and the questionnaires have been approved by the Ethics Committee of the Medical University of Lodz (RNN/42/13/KE). Informed consent was obtained from all subjects involved in the study.

An interviewer-supervised auditory questionnaire was used to obtain information on the health status of the subjects. The questionnaire was distributed among the patients during their 2019-2020 hospitalisation at the Department of Dermatology and Venereology of Medical University of Lodz, and among the comparison subjects who came to the outpatient clinic for routine dermoscopic examinations.

Their individual gluten intake was assessed by means of one of the retrospective dietary assessment methods. The method of consumption frequency was applied, and the research tool was the researchers' original questionnaire created on the basis of 'Division of Food Products Based on Their Gluten Content' proposed by the Polish Association of People with Coeliac Disease and on Gluten-Free Diets [9]. The respondents answered questions on how often they consumed the foods and dishes listed in the questionnaire.

Antibodies directed against smooth muscle endomysium, tissue transglutaminase and gliadin were detected in the patients and in the comparison group. The test material consisted of sera collected according to standard procedures. The tests were performed using ready-made kits according to the manufacturer's recommended test instructions. The concentration of the antibodies directed against smooth muscle endomysium was determined using a ready-to-use kit for in vitro

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testing of IgA autoantibodies against endomysium and gliadin in human serum [EUROPLUS Liver (Monkey)/Gliadin (GAF-3X)/Gut (Monkey) (IgA) (Euroimmun, Lübeck, Germany)]. The concentration of tissue transglutaminase antibodies was determined using ready-to-use in vitro tissue transglutaminase and gliadin (GAF-3X) autoantibody test kits in human serum or plasma [EUROLINE Profile Celiac IgA and EUROLINE Profile Celiac IgG] (Euroimmune, Lubeck, Germany).

In addition, blood allergy tests were performed in all the subjects in the study and control groups. An IgE inhalant allergy test and an IgE test for food allergies were performed by immunoblotting (Euroimmune, Lübeck, Germany).

Statistical analyses were carried out using the PQStat statistical package (version 1.8.2.238). The distribution of medical data scores and dichotomous survey responses were compared between the study groups using the chi^2 correlation test, with Fisher's exact test correction applied if the Cochran condition was not met. The distribution of individual food product consumption scores between the groups was compared using the Kruskal-Wallis test and the post-hoc Dunn's test with the Bonferroni correction. The cluster analysis was performed using the K-means and gradation methods, and the resulting clusters were contrasted with the groups in terms of diagnosis using the chi^2 correlation test. Statistical analyses were performed using the PQStat statistical package (version 1.8.2.230). A test probability of $p<0.05$ was considered significant, and a test probability of $p<0.01$ was considered highly significant.

3. Results

3.1. Clinical Characteristics of the Respondents

The majority of the respondents were female. However, there was no significant correlation between gender (Table 1) or age (Table 2) and diagnosis.

Table 1. Gender in the study groups.

Gender	Diagnosis							
	Control		AD		Psoriasis		Urticaria	
	N	%	N	%	N	%	N	%
Famale	25	71,43%	18	69,23%	20	57,14%	18	85,71%
Male	10	28,57%	8	30,77%	15	42,86%	3	14,29%
chi^2 correlation test	Chi^=5,16, df=3, p=0,1605							

Table 2. Age in the study groups.

Age	Diagnosis							
	Control		AD		Psoriasis		Urticaria	
	N	%	N	%	N	%	N	%
<18	1	2,86%	0	0%	3	8,57%	0	0%
18-30	6	17,14%	11	42,31%	7	20%	3	14,29%
31-40	6	17,14%	6	23,08%	11	31,43%	8	38,1%
41-50	13	37,14%	3	11,54%	2	5,71%	6	28,57%
>50	9	25,71%	6	23,08%	12	34,29%	4	19,05%
Fisher's exact test	p=0,1199							

A highly significant correlation was found between the study groups and the occurrence of gastrointestinal complaints (Table 3).

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Table 3. Gastrointestinal complaints in the surveyed groups (results with statistical significance are marked in red).

Do you suffer from digestive complaints?	Diagnosis							
	Control		AD		Psoriasis		Urticaria	
	N	%	N	%	N	%	N	%
No	35	100%	12	46,15%	23	65,71%	18	85,71%
Yes	0	0%	14	53,85%	12	34,29%	3	14,29%
chi^2 correlation test	Chi^=2625, df=3, p<0,0001							

3.2. Dietary Assessment

On the basis of the declared intake, it was shown that all the subjects consumed products which were sources of gluten on a daily basis. Statistically significant differences were noted regarding the frequency of consumption of some of the investigated food products.

The subjects with psoriasis declared the most frequent consumption of gluten-free bread. The patients with urticaria were significantly more likely to report using gluten-free flours. Patients with AD and psoriasis declared significantly less frequent consumption of gluten-free pasta compared to the control group. The control group declared significantly more frequent consumption of confectionery bread and cakes (Table 4).

Table 4. Results of cereal product consumption (results with statistical significance are marked in red).

Food Product	Diagnosis	Arithmetic Mean	Median	Standard Deviation	Minimum	Maximum	Lower Quartile	Upper Quartile	Kruskal-Wallis Test	Homogenous Groups	POST-HOC (Dunn Bonferroni)			
											Control	AD	Psoriasis	Urticaria
Bread with gluten	**Control**	**4,9**	**5,0**	**0,4**	**3,0**	**5,0**	**5,0**	**5,0**		a		1	1	1
	AD	4,8	5,0	1,0	0,0	5,0	5,0	5,0	**H=2,6320**	a	1		0,9327	1
	Psoriasis	4,7	5,0	0,8	2,0	5,0	5,0	5,0	**p=0,4519**	a	1	0,9327		1
	Urticaria	5,0	5,0	0,2	4,0	5,0	5,0	5,0		a	1	1	1	
Bread without gluten	Control	0,0	0,0	0,2	0,0	1,0	0,0	0,0		a		0,9183	0,0007	0,3383
	AD	0,2	0,0	0,5	0,0	2,0	0,0	0,0	H=15,2366	ab	0,9183		0,1943	1
	Psoriasis	0,8	0,0	1,2	0,0	5,0	0,0	1,0	p=0,0016	b	0,0007	0,1943		0,9008
	Urticaria	0,5	0,0	1,2	0,0	5,0	0,0	0,0		ab	0,3383	1	0,9008	
Flour with gluten	Control	2,5	3,0	1,1	0,0	4,0	2,0	3,0		a		1	1	1
	AD	2,4	2,0	1,4	0,0	5,0	1,0	3,8	H=2,2119	a	1		1	1
	Psoriasis	2,5	2,0	1,2	0,0	5,0	2,0	3,0	p=0,5296	a	1	1		1
	Urticaria	2,9	3,0	1,3	0,0	5,0	2,0	4,0		a	1	1	1	
Flour without gluten	Control	0,0	0,0	0,0	0,0	0,0	0,0	0,0		a		0,6175	0,5118	0,0006
	AD	0,2	0,0	0,5	0,0	2,0	0,0	0,0	H=15,0883	ab	0,6175		1	0,1608
	Psoriasis	0,2	0,0	0,6	0,0	2,0	0,0	0,0	p=0,0017	ab	0,5118	1		0,1002
	Urticaria	0,7	0,0	1,2	0,0	5,0	0,0	1,0		b	0,0006	0,1608	0,1002	
Flakes with gluten	Control	1,9	2,0	1,4	0,0	5,0	1,0	3,0		b		0,0336	0,2832	1
	AD	1,0	0,0	1,5	0,0	5,0	0,0	1,8	H=9,7805	a	0,0336		1	0,1711
	Psoriasis	1,4	1,0	1,8	0,0	5,0	0,0	2,5	p=0,0205	ab	0,2832	1		0,8849
	Urticaria	1,8	2,0	1,5	0,0	5,0	1,0	2,0		ab	1	0,1711	0,8849	
	Control	0,8	0,0	1,8	0,0	5,0	0,0	0,0	H=3,1238	a		1	1	1
	AD	0,3	0,0	0,7	0,0	2,0	0,0	0,0	p=0,3729	a	1		0,8968	1

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Flakes without gluten	Psoriasis	0,9	0,0	1,5	0,0	5,0	0,0	2,0		a	1	0,8968		1
	Urticaria	0,6	0,0	0,8	0,0	3,0	0,0	1,0		a	1	1	1	
Groats with gluten	Control	1,4	1,0	1,1	0,0	5,0	1,0	1,0		a		1	0,195	0,2318
	AD	1,5	1,0	0,8	0,0	3,0	1,0	2,0	H=6,1787	a	1		1	1
	Psoriasis	1,7	2,0	1,1	0,0	5,0	1,0	2,0	p=0,1032	a	0,195	1		1
	Urticaria	2,0	1,0	1,2	1,0	5,0	1,0	3,0		a	0,2318	1	1	
Groats without gluten	Control	0,9	1,0	0,8	0,0	2,0	0,0	2,0		a		0,5708	0,1917	0,7769
	AD	1,3	1,0	0,8	0,0	3,0	1,0	2,0	H=5,4126	a	0,5708		1	1
	Psoriasis	1,5	2,0	1,2	0,0	5,0	0,0	2,0	p=0,144	a	0,1917	1		1
	Urticaria	1,3	1,0	0,7	0,0	3,0	1,0	2,0		a	0,7769	1	1	
Pasta with gluten	Control	3,4	3,0	1,2	1,0	5,0	3,0	4,0		b		0,0001	0,0072	0,3421
	AD	2,0	2,0	0,8	0,0	3,0	2,0	2,8	H=21,3519	a	0,0001		0,9383	0,2146
	Psoriasis	2,5	2,0	1,0	1,0	5,0	2,0	3,0	p=0,0001	a	0,0072	0,9383		1
	Urticaria	2,8	2,0	1,0	1,0	5,0	2,0	4,0		ab	0,3421	0,2146	1	
Pasta without gluten	Control	0,1	0,0	0,2	0,0	1,0	0,0	0,0		a		0,6989	1	0,6777
	AD	0,3	0,0	0,6	0,0	2,0	0,0	0,0	H=3,6768	a	0,6989		1	1
	Psoriasis	0,1	0,0	0,4	0,0	2,0	0,0	0,0	p=0,2985	a	1	1		1
	Urticaria	0,5	0,0	1,3	0,0	5,0	0,0	0,0		a	0,6777	1	1	
Dumplings (Pierogi)	Control	1,3	1,0	0,7	0,0	3,0	1,0	2,0		a		0,7257	1	1
	AD	1,0	1,0	0,6	0,0	2,0	1,0	1,0	H=4,2366	a	0,7257		1	0,3367
	Psoriasis	1,1	1,0	0,6	0,0	2,0	1,0	1,5	p=0,237	a	1	1		1
	Urticaria	1,3	1,0	0,6	0,0	2,0	1,0	2,0		a	1	0,3367	1	
Dumplings (Pyzy)	Control	1,2	1,0	0,6	0,0	2,0	1,0	2,0		b		0,0177	<0,0001	0,1206
	AD	0,7	1,0	0,6	0,0	2,0	0,0	1,0	H=28,3973	a	0,0177		0,3325	1
	Psoriasis	0,3	0,0	0,5	0,0	1,0	0,0	1,0	p<0,0001	a	<0,0001	0,3325		0,1427
	Urticaria	0,8	1,0	0,7	0,0	2,0	0,0	1,0		ab	0,1206	1	0,1427	
Dumplings (Kopytka)	Control	1,2	1,0	0,5	0,0	2,0	1,0	2,0		b		0,6409	0,0001	1
	AD	1,0	1,0	0,7	0,0	2,0	0,3	1,0	H=20,6354	ab	0,6409		0,0813	1
	Psoriasis	0,5	1,0	0,6	0,0	2,0	0,0	1,0	p=0,0001	a	0,0001	0,0813		0,0278
	Urticaria	1,0	1,0	0,6	0,0	2,0	1,0	1,0		b	1	1	0,0278	
Pancakes	Control	1,3	1,0	0,7	0,0	3,0	1,0	2,0		a		1	1	1
	AD	1,2	1,0	0,7	0,0	3,0	1,0	2,0	H=1,9833	a	1		1	1
	Psoriasis	1,4	1,0	0,6	0,0	2,0	1,0	2,0	p=0,5759	a	1	1		1
	Urticaria	1,3	1,0	0,6	0,0	2,0	1,0	2,0		a	1	1	1	
Confectionery	Control	3,0	3,0	1,1	1,0	5,0	2,0	4,0		b		0,0092	0,0134	0,0333
	AD	1,8	2,0	1,3	0,0	5,0	1,0	3,0	H=14,5824	a	0,0092		1	1
	Psoriasis	2,0	2,0	1,3	0,0	5,0	1,0	3,0	p=0,0022	a	0,0134	1		1
	Urticaria	2,0	1,0	1,5	0,0	5,0	1,0	3,0		a	0,0333	1	1	
Cakes	Control	2,3	2,0	1,3	0,0	5,0	2,0	2,5		b		0,0262	0,0533	0,1048
	AD	1,4	1,0	1,0	0,0	4,0	1,0	2,0	H=11,17	a	0,0262		1	1
	Psoriasis	1,5	2,0	1,0	0,0	3,0	1,0	2,0	p=0,0108	ab	0,0533	1		1
	Urticaria	1,6	1,0	1,0	0,0	4,0	1,0	2,0		ab	0,1048	1	1	
Pizza	Control	1,0	1,0	0,2	0,0	2,0	1,0	1,0		a		0,1733	1	1
	AD	0,7	1,0	0,5	0,0	2,0	0,0	1,0	H=4,8097	a	0,1733		1	1
	Psoriasis	0,9	1,0	0,8	0,0	3,0	0,0	1,0	p=0,1863	a	1	1		1
	Urticaria	0,9	1,0	0,6	0,0	2,0	1,0	1,0		a	1	1	1	
Hamburger buns/hotdogs/sausage rolls	Control	1,1	1,0	1,2	0,0	4,0	0,5	1,0		b		0,8958	0,0076	0,4619
	AD	0,7	1,0	0,6	0,0	2,0	0,0	1,0	H=10,5797	ab	0,8958		0,7516	1
	Psoriasis	0,4	0,0	0,7	0,0	2,0	0,0	1,0	p=0,0142	a	0,0076	0,7516		1
	Urticaria	0,6	1,0	0,7	0,0	3,0	0,0	1,0		ab	0,4619	1	1	

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Significant differences were found in the frequency of consumption of milk and several dairy products among the subjects (Table 5). The patients with psoriasis declared that they drank milk less frequently. The respondents with urticaria were significantly more likely to report that they did not eat yellow cheese. The patients in the study groups were significantly more likely to eat natural curds compared to the control group. Consumption of flavoured yoghurts and processed cheese in the AD and psoriasis groups was lower than in the healthy subjects.

Table 5. Results of dairy product consumption (results with statistical significance are marked in red).

Food Product	Diagnosis	Arithmetic Mean	Median	Standard Deviation	Minimum	Maximum	Lower Quartile	Upper Quartile	Kruskal-Wallis Test	Homogenous Groups	POST-HOC (Dunn Bonferroni)			
											Control	AD	Psoriasis	Urticaria
Milk	Control	3,6	4,0	1,3	1,0	5,0	3,0	5,0	H=12,7773 p=0,0051	b		0,107	0,0032	0,7123
	AD	2,4	2,0	2,2	0,0	5,0	0,0	5,0		ab	0,107		1	1
	Psoriasis	2,1	2,0	1,6	0,0	5,0	0,5	3,0		a	0,0032	1		0,8996
	Urticaria	2,8	4,0	1,8	0,0	5,0	1,0	4,0		ab	0,7123	1	0,8996	
Kefir (kind of buttermilk)	Control	1,0	1,0	0,9	0,0	3,0	0,0	2,0	H=3,2058 p=0,361	a		1	1	1
	AD	1,0	0,0	1,3	0,0	5,0	0,0	2,0		a	1		0,5065	1
	Psoriasis	1,5	1,0	1,5	0,0	5,0	0,0	2,0		a	1	0,5065		1
	Urticaria	1,4	1,0	1,5	0,0	5,0	1,0	1,0		a	1	1	1	
Buttermilk	Control	1,0	1,0	0,8	0,0	2,0	0,0	2,0	H=1,8665 p=0,6006	a		1	1	1
	AD	1,0	0,0	1,5	0,0	5,0	0,0	1,8		a	1		1	1
	Psoriasis	0,9	1,0	1,2	0,0	5,0	0,0	1,5		a	1	1		1
	Urticaria	0,9	1,0	1,2	0,0	5,0	0,0	1,0		a	1	1	1	
Flavoured kefir	Control	0,3	0,0	0,5	0,0	2,0	0,0	0,5	H=0,2531 p=0,9686	a		1	1	1
	AD	0,4	0,0	1,1	0,0	5,0	0,0	0,0		a	1		1	1
	Psoriasis	0,3	0,0	0,6	0,0	2,0	0,0	0,0		a	1	1		1
	Urticaria	0,3	0,0	0,8	0,0	3,0	0,0	0,0		a	1	1	1	
Yoghurt	Control	1,3	1,0	0,9	0,0	3,0	1,0	2,0	H=0,8434 p=0,8391	a		1	1	1
	AD	1,5	1,5	1,3	0,0	5,0	0,0	2,0		a	1		1	1
	Psoriasis	1,5	1,0	1,5	0,0	5,0	0,0	2,0		a	1	1		1
	Urticaria	1,2	1,0	1,2	0,0	4,0	0,0	2,0		a	1	1	1	
Flavoured yoghurt	Control	2,0	2,0	1,0	0,0	4,0	1,0	3,0	H=17,8345 p=0,0005	b		0,0003	0,0197	0,1875
	AD	0,8	0,0	1,1	0,0	3,0	0,0	1,0		a	0,0003		1	0,7444
	Psoriasis	1,2	1,0	1,1	0,0	3,0	0,0	2,0		a	0,0197	1		1
	Urticaria	1,4	2,0	1,4	0,0	5,0	0,0	2,0		ab	0,1875	0,7444	1	
Cottage cheese (twaróg)	Control	1,5	1,0	0,7	1,0	3,0	1,0	2,0	H=15,9367 p=0,0012	a		1	0,2151	0,0011
	AD	1,6	2,0	1,6	0,0	5,0	0,0	2,0		a	1		0,9932	0,0147
	Psoriasis	1,9	2,0	1,1	0,0	5,0	1,5	3,0		ab	0,2151	0,9932		0,3289
	Urticaria	2,5	3,0	1,0	0,0	5,0	2,0	3,0		b	0,0011	0,0147	0,3289	
Cottage cheese (twarożki)	Control	0,4	0,0	0,6	0,0	2,0	0,0	1,0	H=18,4001 p=0,0004	a		0,3163	0,0041	0,0008
	AD	1,0	1,0	1,2	0,0	5,0	0,0	2,0		ab	0,3163		1	0,3564
	Psoriasis	1,3	2,0	1,2	0,0	3,0	0,0	2,0		b	0,0041	1		1
	Urticaria	1,7	2,0	1,4	0,0	5,0	0,0	3,0		b	0,0008	0,3564	1	
Yellow cheese	Control	2,3	2,0	1,3	0,0	5,0	2,0	3,0	H=7,0665 p=0,0698	a		1	1	0,055
	AD	2,2	2,0	1,8	0,0	5,0	0,3	3,0		a	1		1	0,3477

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	Psoriasis	2,1	2,0	1,5	0,0	5,0	1,0	3,0		a	1	1		0,3057
	Urticaria	1,3	1,0	1,4	0,0	5,0	0,0	2,0		a	0,055	0,3477	0,3057	
Cheese-based products	Control	0,1	0,0	0,2	0,0	1,0	0,0	0,0		a		1	1	1
	AD	0,3	0,0	1,1	0,0	5,0	0,0	0,0	H=2,4358	a	1		1	1
	Psoriasis	0,2	0,0	0,6	0,0	3,0	0,0	0,0	p=0,487	a	1	1		1
	Urticaria	0,0	0,0	0,2	0,0	1,0	0,0	0,0		a	1	1	1	
Processed cheese	Control	0,1	0,0	0,6	0,0	3,0	0,0	0,0		a		0,0217	0,0023	1
	AD	0,5	0,0	0,7	0,0	2,0	0,0	1,0	H=15,2738	b	0,0217		1	0,8422
	Psoriasis	0,7	0,0	1,0	0,0	4,0	0,0	1,0	p=0,0016	b	0,0023	1		0,3376
	Urticaria	0,2	0,0	0,4	0,0	1,0	0,0	0,0		ab	1	0,8422	0,3376	
Milk products containing cereals	Control	0,3	0,0	0,5	0,0	1,0	0,0	1,0		a		0,2827	1	1
	AD	0,1	0,0	0,3	0,0	1,0	0,0	0,0	H=4,0427	a	0,2827		1	1
	Psoriasis	0,3	0,0	0,7	0,0	2,0	0,0	0,0	p=0,2569	a	1	1		1
	Urticaria	0,3	0,0	0,6	0,0	2,0	0,0	0,0		a	1	1	1	

The majority of the subjects declared meat consumption, but the control group reported significantly more frequent consumption of meat and prepared meats. Significant differences were also found between the groups regarding the use of coatings which were sources of gluten. The use of such coatings was more frequent in the control group than in the psoriasis and urticaria groups (Table 6).

Table 6. Results of meat product consumption (results with statistical significance are marked in red).

Food Product	**Diagnosis**	**Arithmetic Mean**	**Median**	**Standard Deviation**	**Minimum**	**Maximum**	**Lower Quartile**	**Upper Quartile**	**Kruskal-Wallis Test**	Homogenous Groups	POST-HOC (Dunn Bonferroni) Control	AD	Psoriasis	Urticaria
Meat	**Control**	**4,7**	**5,0**	**0,6**	**3,0**	**5,0**	**5,0**	**5,0**	**H=46,9575 p<0,0001**	b		0,0006	<0,0001	<0,0001
	AD	3,3	3,0	1,3	0,0	5,0	3,0	5,0		a	0,0006		1	0,0903
	Psoriasis	3,0	3,0	1,5	0,0	5,0	2,0	4,0		a	<0,0001	1		0,4892
	Urticaria	2,3	2,0	1,1	0,0	4,0	2,0	3,0		a	<0,0001	0,0903	0,4892	
Fish	Control	1,2	1,0	0,6	0,0	3,0	1,0	1,5		a		0,8226	0,4334	1
	AD	1,6	1,5	1,1	0,0	5,0	1,0	2,0	H=3,7966	a	0,8226		1	1
	Psoriasis	1,6	2,0	1,1	0,0	5,0	1,0	2,0	p=0,2843	a	0,4334	1		1
	Urticaria	1,4	2,0	0,7	0,0	2,0	1,0	2,0		a	1	1	1	
Ready-made sliced meats	Control	4,7	5,0	0,6	3,0	5,0	5,0	5,0	H=29,4656 p<0,0001	b		0,0723	<0,0001	<0,0001
	AD	3,7	4,5	1,5	1,0	5,0	3,0	5,0		ab	0,0723		0,6319	0,1652
	Psoriasis	3,0	3,0	1,8	0,0	5,0	2,0	5,0		a	<0,0001	0,6319		1
	Urticaria	2,7	3,0	1,6	0,0	5,0	2,0	3,0		a	<0,0001	0,1652	1	
Offal products	Control	1,2	1,0	1,6	0,0	5,0	0,0	1,0		a		1	1	1
	AD	1,1	1,0	1,1	0,0	5,0	0,0	1,8	H=0,7377	a	1		1	1
	Psoriasis	1,1	1,0	0,9	0,0	3,0	0,0	2,0	p=0,8643	a	1	1		1
	Urticaria	1,0	1,0	1,0	0,0	3,0	0,0	2,0		a	1	1	1	
Delicatessen products	Control	1,5	1,0	1,3	0,0	5,0	1,0	1,0		a		0,0517	0,1937	0,0558
	AD	0,9	1,0	1,4	0,0	5,0	0,0	1,0	H=10,0727	a	0,0517		1	1
	Psoriasis	0,9	1,0	1,0	0,0	3,0	0,0	2,0		a	0,1937	1		1
	Urticaria	0,7	0,0	0,8	0,0	2,0	0,0	1,0	p=0,0180	a	0,0558	1	1	

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Coating with gluten flour	Control	2,7	3,0	1,0	1,0	5,0	2,0	3,0	H=16,3096 p=0,0010	b		0,4763	0,0027	0,0059
	AD	2,3	2,0	1,6	0,0	5,0	1,3	3,0		ab	0,4763		0,8247	0,7261
	Psoriasis	1,8	2,0	1,0	0,0	3,0	1,0	2,0		a	0,0027	0,8247		1
	Urticaria	1,7	2,0	1,1	0,0	3,0	1,0	2,0		a	0,0059	0,7261	1	
Coating with gluten-free flour	Control	0,3	0,0	0,5	0,0	1,0	0,0	1,0	H=3,3199 p=0,3449	a		1,3873	0,9049	0,3594
	AD	0,2	0,0	0,6	0,0	3,0	0,0	0,0		a	1,3873		0,5519	1,5624
	Psoriasis	0,3	0,0	0,6	0,0	2,0	0,0	0,0		a	0,9049	0,5519		1,1431
	Urticaria	0,6	0,0	1,1	0,0	4,0	0,0	1,0		a	0,3594	1,5624	1,1431	

No significant differences were found regarding the frequency of consumption of beer or the use of mustard, ketchup, ready-made sauces, seasoning mixes and stock cubes (Table 7).

Table 7. Results of consumption of condiments.

Food Product	**Diagnosis**	**Arithmetic Mean**	**Median**	**Standard Deviation**	**Minimum**	**Maximum**	**Lower Quartile**	**Upper Quartile**	**Kruskal-Wallis Test**	Homogenous Groups	POST-HOC (Dunn Bonferroni) Control	AD	Psoriasis	Urticaria
Mixtures of spices	**Control**	**1,2**	**1,0**	**1,3**	**0,0**	**5,0**	**0,0**	**2,0**	**H=4,9147 p=0,1782**	a		1	1	0,1924
	AD	1,8	1,5	1,8	0,0	5,0	0,0	3,0		a	1		1	1
	Psoriasis	1,6	1,0	1,6	0,0	5,0	0,0	3,0		a	1	1		1
	Urticaria	2,1	2,0	1,6	0,0	5,0	1,0	3,0		a	0,1924	1	1	
Mustard	Control	1,4	1,0	1,0	0,0	5,0	1,0	2,0	H=3,163 p=0,3672	a		1	1	1
	AD	1,3	1,0	1,1	0,0	4,0	1,0	2,0		a	1		0,9357	1
	Psoriasis	1,7	2,0	1,2	0,0	5,0	1,0	2,0		a	1	0,9357		0,8353
	Urticaria	1,4	1,0	1,3	0,0	5,0	1,0	2,0		a	1	1	0,8353	
Ketchup	Control	2,2	2,0	1,2	0,0	5,0	1,0	3,0	H=3,2578 p=0,3536	a		1	1	0,9957
	AD	1,8	2,0	1,4	0,0	5,0	1,0	2,8		a	1		1	1
	Psoriasis	2,3	2,0	1,7	0,0	5,0	1,0	3,5		a	1	1		1
	Urticaria	1,7	2,0	1,3	0,0	5,0	1,0	2,0		a	0,9957	1	1	
Ready-made sauces	Control	1,4	1,0	1,2	0,0	4,0	1,0	2,0	H=6,9643 p=0,073	a		0,1292	0,1735	0,7776
	AD	0,8	0,0	1,2	0,0	5,0	0,0	2,0		a	0,1292		1	1
	Psoriasis	0,8	1,0	1,0	0,0	3,0	0,0	1,5		a	0,1735	1		1
	Urticaria	1,0	1,0	1,1	0,0	4,0	0,0	1,0		a	0,7776	1	1	
Broth cubes	Control	1,5	1,0	1,5	0,0	5,0	0,0	2,0	H=7,0401 p=0,0706	a		1	1	1
	AD	1,1	1,0	1,2	0,0	4,0	0,0	2,0		a	1		0,1375	0,1751
	Psoriasis	1,7	2,0	1,0	0,0	4,0	1,0	2,5		a	1	0,1375		1
	Urticaria	2,0	2,0	1,5	0,0	5,0	1,0	3,0		a	1	0,1751	1	

Gradational analysis and cluster analysis were carried out. They mainly come in the form of a visual presentation of the results in graphs (Figure 1 and Figure 2). Due to the fact that there were many scales analysed and some had long names, they were coded in Table 8.

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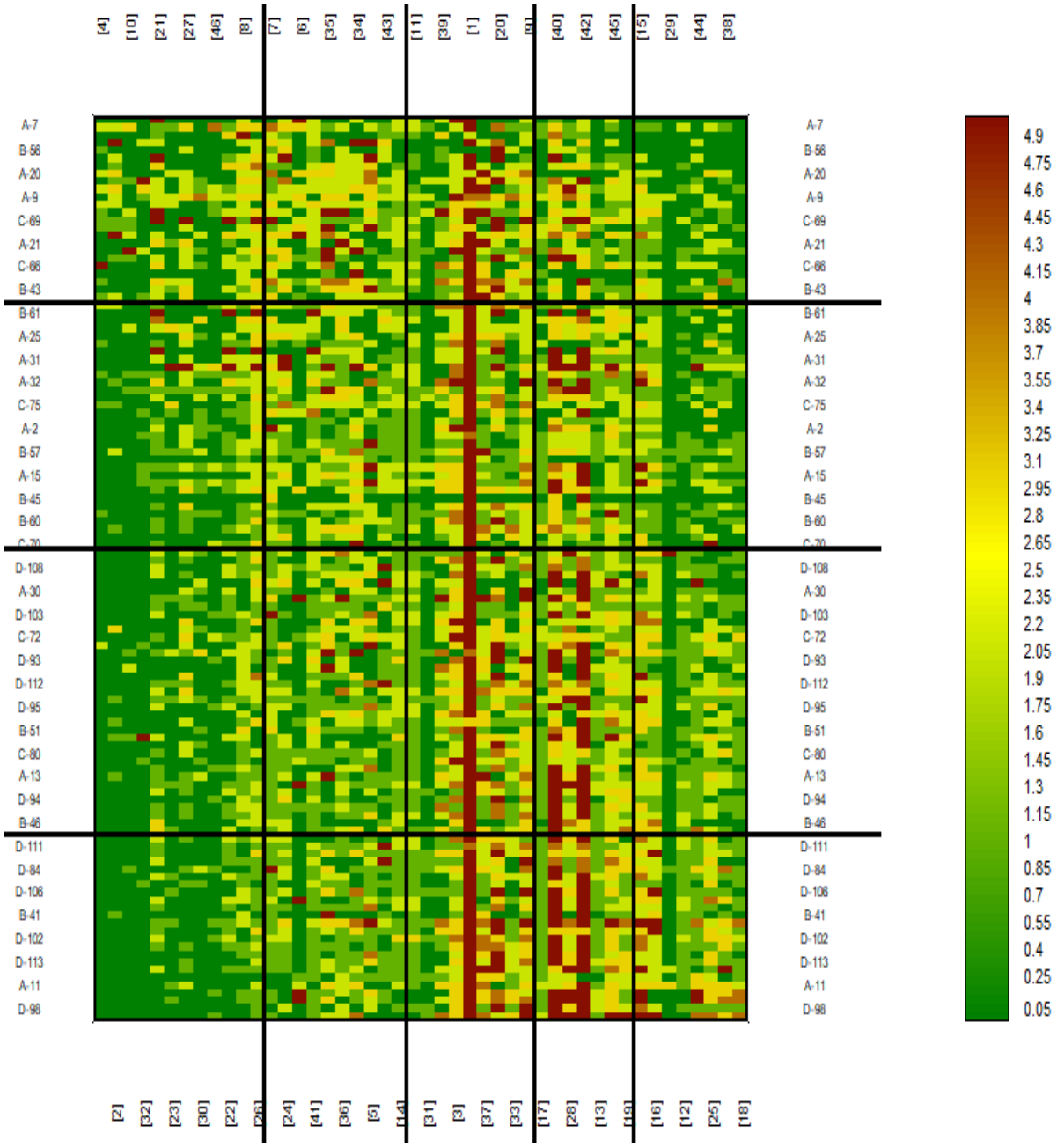

Figure 1. Distribution of results after gradational analysis with distinguished clusters.

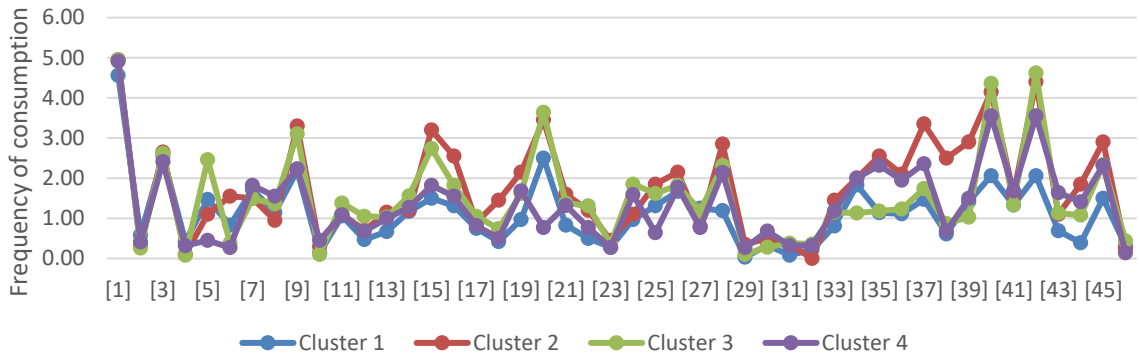

Figure 2. Consumption of food products in the four clusters of respondents determined by the K-means method.

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Table 8. Coded foods and study groups for the gradational and cluster analyses.

Food products	Study groups
1 - Bread with gluten	
2 - Bread without gluten	
3 - Flour with gluten	
4 - Flour without gluten	
5 - Flakes with gluten	
6 - Flakes without gluten	
7 - Groats with gluten	
8 - Groats without gluten	
9 - Pasta with gluten	
10 - Pasta without gluten	
11 - Dumplings	
12 - Dumplings	
13 - Dumplings	
14 - Pancakes	
15 - Confectionery	
16 - Cakes	
17 - Pizza	
18 - Hamburger buns/hotdogs/sausage rolls	
19 - Breadcrumbs	
20 - Milk	
21 - Kefir (kind of buttermilk)	
22 - Buttermilk	A - Psoriasis
23 - Flavoured kefir	B - AD
24 - Yoghurt	C - Urticaria
25 - Flavoured yoghurt	D - Control
26 - Cottage cheese	
27 - Cottage cheese	
28 - Yellow cheese	
29 - Cheese-based products	
30 - Processed cheese	
31 - Milk products containing cereals	
32 - Cereal coffee	
33 - Beer	
34 - Ready-made condiments	
35 - Mixtures of spices	
36 - Mustard	
37 - Ketchup	
38 - Ready-made sauces	
39 - Broth cubes	
40 - Meat	
41 - Fish	
42 - Ready-made sliced meats	
43 - Offal products	
44 - Cold foods (Delicatessen products)	
45 - Coating with gluten flour	
46 - Coating with gluten-free flour	

On the basis of the gradational analysis, 5 groups of products were distinguished (Table 9). These are clusters containing products consumed with similar frequency (correlated with each other). This means that if there are products in a cluster, they are consumed with similar frequency by the respondents.

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Table 9. Clusters of food products consumed with similar frequency.

Cluster 1	Cluster 2	Cluster 3	Cluster 4	Clusters 5
4 - Flour without gluten 2 - Bread without gluten 10 - Pasta without gluten 32 - Cereal coffee 21 - Kefir (kind of buttermilk) 23 - Flavoured kefir 30 - Processed cheese 27 - Cottage cheese (twarożki) 22 - Buttermilk 46 - Coating with gluten-free flour 26 - Cottage cheese (twarogi) 8 - Groats without gluten	7 - Groats with gluten 24 - Yoghurt 6 - Flakes without gluten 41 - Fish 34 - Ready-made condiments 35 - Mixtures of spices 36 - Mustard 5 - Flakes with gluten 43 - Offal products 14 - Pancakes	11 – Dumplings (pierogi) 31 - Milk products containing cereals 39 - Broth cubes 3 - Flour with gluten 1 - Bread with gluten 37 - Ketchup 20 – Milk 33 - Beer 9 - Pasta with gluten	17 - Pizza 40 - Meat 28 - Yellow cheese 42 - Ready-made sliced meats 13 – Dumplings (kopytka) 45 - Coating with gluten flour 19 -Breadcrumbs	15 - Confectionery 16 - Cakes 29 - Cheese-based products 12 - Dumplings (pyzy) 44 - Cold foods (Delicatessen products) 25 - Flavoured yoghurt 38 - Ready-made sauces 18 - Hamburger buns/hotdogs/sausage rolls

At the same time, 4 groups/clusters of respondents were distinguished:

1. The first one are those who consumed products from the first four groups relatively frequently and products from group 5 rarely.
2. The second one were those who consumed products from group 1 less frequently, still ate products from groups 2, 3 and 4, but still rarely ate products from group 5.
3. The third one are those who rarely consumed products from groups 1 and 2, but frequently consumed products from groups 3 and 4, and relatively more often ate products from group 5.
4. The fourth one are those who rarely ate products from groups 1 and 2 (especially rarely from group 1), often ate products from groups 3 and 4, and most often of all the clusters ate products from group 5.

In addition, a highly significant (Chi^2=62.45, df=9, p<0.0001) correlation was found between the clusters of patients determined in the gradational analysis and the diagnosis (Table 10).

Table 10. Correlation between clusters of patients determined in the gradational analysis and the diagnosis.

Diagnosis		GRAD clustering			
		1	2	3	4
Size	A - Psoriasis	13	15	5	2
	B - AD	4	9	10	3
	C - Urticaria	7	8	6	0
	D - Control	0	0	16	19
		1	2	3	4
verse %	A - Psoriasis	37,14%	42,86%	14,29%	5,71%
	B - AD	15,38%	34,62%	38,46%	11,54%
	C - Urticaria	33,33%	38,1%	28,57%	0%
	D - Control	0%	0%	45,71%	54,29%
		1	2	3	4

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column %	A - Psoriasis	54,17%	46,88%	13,51%	8,33%
	B - AD	16,67%	28,13%	27,03%	12,5%
	C - Urticaria	29,17%	25%	16,22%	0%
	D - Control	0%	0%	43,24%	79,17%

On the basis of the gradational analysis, it was found that the people with the skin diseases significantly less frequently eat the following highly processed products: confectionery, cakes, cheese-like products, dumplings, cold foods, flavoured yoghurts, ready-made sauces and hamburger, hot dog or casserole buns (fast food) (Table 11 and Figure 2).

Table 11. Consumption of food products in the four clusters of respondents determined by the K-means method (results with statistical significance are marked in red).

Produkt	Cluster 1		Cluster 2		Cluster 3		Cluster 4		ANOVA (p)
	X	sd	x	sd	X	sd	x	sd	
[1]	4,56	1,13	4,95	0,22	4,95	0,22	4,91	0,43	0,0499
[2]	0,58	1,18	0,30	1,13	0,26	0,55	0,41	0,80	0,4683
[3]	2,56	1,50	2,65	0,81	2,62	1,23	2,41	1,05	0,9157
[4]	0,42	0,69	0,10	0,31	0,08	0,35	0,32	1,13	0,1161
[5]	1,47	1,48	1,10	1,33	2,46	1,67	0,45	0,91	<0,0001
[6]	0,83	1,21	1,55	2,19	0,38	0,99	0,27	0,63	0,0044
[7]	1,72	1,19	1,50	1,36	1,49	1,00	1,82	0,73	0,5996
[8]	1,14	1,02	0,95	0,89	1,36	0,81	1,55	1,01	0,1545
[9]	2,19	0,98	3,30	0,98	3,10	1,27	2,23	0,81	0,0001
[10]	0,14	0,54	0,30	0,66	0,10	0,31	0,45	1,18	0,2079
[11]	1,06	0,58	1,10	0,64	1,38	0,59	1,09	0,61	0,0806
[12]	0,47	0,56	0,70	0,66	1,05	0,69	0,68	0,65	0,0018
[13]	0,67	0,59	1,15	0,59	1,03	0,71	1,00	0,62	0,0245
[14]	1,17	0,61	1,20	0,70	1,56	0,68	1,27	0,63	0,0466
[15]	1,50	1,11	3,20	1,28	2,74	1,33	1,82	1,10	<0,0001
[16]	1,31	0,86	2,55	1,54	1,82	0,94	1,55	1,14	0,0008
[17]	0,75	0,65	0,90	0,64	1,05	0,39	0,82	0,73	0,1627
[18]	0,42	0,50	1,45	1,43	0,74	0,68	0,50	0,67	0,0001
[19]	0,97	0,70	2,15	1,09	1,62	0,85	1,68	0,84	<0,0001
[20]	2,50	1,63	3,45	1,67	3,64	1,37	0,77	1,11	<0,0001
[21]	0,83	1,06	1,60	1,67	1,38	1,21	1,32	1,32	0,1262
[22]	0,50	0,77	1,20	1,54	1,31	1,20	0,77	0,97	0,012
[23]	0,28	0,70	0,45	0,69	0,36	0,90	0,27	0,70	0,8446
[24]	0,97	1,13	1,10	1,12	1,85	1,20	1,59	1,33	0,01
[25]	1,31	1,35	1,85	1,27	1,62	1,11	0,64	0,85	0,0047
[26]	1,67	1,17	2,15	1,27	1,82	1,12	1,77	1,15	0,524
[27]	1,25	1,16	0,80	1,01	1,18	1,37	0,77	0,92	0,3071
[28]	1,19	1,06	2,85	1,69	2,31	1,34	2,14	1,70	0,0002
[29]	0,03	0,17	0,35	0,81	0,10	0,38	0,27	1,08	0,213
[30]	0,33	0,48	0,50	0,95	0,28	0,76	0,68	0,89	0,203
[31]	0,08	0,28	0,35	0,59	0,38	0,67	0,32	0,57	0,0921
[32]	0,22	0,48	0,00	0,00	0,36	1,14	0,32	0,78	NA
[33]	0,81	0,98	1,45	1,10	1,15	0,87	1,18	1,18	0,1318
[34]	1,83	1,32	2,00	1,41	1,13	1,26	2,00	1,38	0,0259
[35]	1,14	1,27	2,55	1,57	1,18	1,35	2,32	1,81	0,0003
[36]	1,11	1,06	2,10	1,45	1,23	0,78	1,95	1,09	0,0009
[37]	1,47	1,44	3,35	1,14	1,74	1,07	2,36	1,33	<0,0001

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[38]	0,61	0,87	2,50	1,19	0,87	0,86	0,68	0,78	<0,0001
[39]	1,42	1,11	2,90	1,21	1,03	1,11	1,50	1,34	<0,0001
[40]	2,06	1,17	4,15	1,14	4,36	0,99	3,55	1,10	<0,0001
[41]	1,33	0,99	1,60	1,31	1,33	0,70	1,68	0,65	0,3695
[42]	2,06	1,60	4,40	0,88	4,62	0,78	3,55	1,22	<0,0001
[43]	0,69	0,89	1,10	0,64	1,13	1,51	1,64	1,09	0,028
[44]	0,39	0,73	1,85	1,63	1,08	0,81	1,41	1,22	<0,0001
[45]	1,50	1,25	2,90	1,17	2,33	1,08	2,32	0,95	0,0001
[46]	0,31	0,79	0,25	0,44	0,44	0,79	0,14	0,47	0,4182

A highly significant correlation was found between the clusters of patients determined by the K-means analysis and the diagnosis (Table 12). All the subjects in the patient groups surveyed declared:

- less frequent use of mustard, ketchup, ready-made sauces, seasoning mixes, stock cubes, bread crumbs;
- less frequent consumption of meat, ready-made cold cuts, offal products, cold foods and fish.

Table 12. Correlation between the patient clusters determined by the K-means analysis and the diagnosis.

Diagnosis		GRAD clustering			
		1	2	3	4
Size	A - Psoriasis	15	6	6	8
	B - AD	8	2	6	10
	C - Urticaria	13	2	4	2
	D - Control	0	10	23	2
		1	2	3	4
verse %	A - Psoriasis	42,86%	17,14%	17,14%	22,86%
	B - AD	30,77%	7,69%	23,08%	38,46%
	C - Urticaria	61,9%	9,52%	19,05%	9,52%
	D - Control	0%	28,57%	65,71%	5,71%
		1	2	3	4
column %	A - Psoriasis	41,67%	30%	15,38%	36,36%
	B - AD	22,22%	10%	15,38%	45,45%
	C - Urticaria	36,11%	10%	10,26%	9,09%
	D - Control	0%	50%	58,97%	9,09%

3.3. Laboratory Tests

Serum antibodies typical of gluten-dependent enteropathy, which include antibodies against tissue transglutaminase and against smooth muscle endomysium, and anti-gliadin antibodies were not found in the study and control groups.

Based on the allergy tests performed, there was no IgE-dependent allergy to wheat and rye flour in the study and control groups.

4. Discussion

Studies indicate that in Poland CD is diagnosed, on average, 7.3 years after the onset of the symptoms [10]. The ratio of diagnosed patients to undiagnosed patients varies from 1:2 to 1:20 depending on the country [11]. The disease can occur at any age, and currently the average age of diagnosis is around 45 years [12]. Some patients go undiagnosed for many years due to their atypical symptoms. These may include skin lesions [13].

Our study attempted to assess the prevalence of antibodies typical of gluten-dependent enteropathy in the patients with psoriasis, chronic urticaria and AD, and to diagnose the coexisting

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CD in the comparison group. In the study groups, a highly significant correlation was found between the occurrence of gastrointestinal complaints and the diagnosis of skin diseases in the study subjects. In order to interpret the serological result, it was necessary to assess the gluten intake in the patients' diet. If gluten exposure had been too short or a gluten-free diet had been used, the test result would not have been reliable [14].

Based on the declared frequency of consumption of selected foods, it was concluded that the respondents were not following a gluten-free diet at the time of the study. Their serum did not show the presence of antibodies typical of gluten-dependent enteropathy. The presence of CD could therefore be ruled out.

There are studies regarding patients with psoriasis that are consistent with our findings [15,16]. Nevertheless, certain findings which differ from ours have also been released, indicating a more frequent co-occurrence of psoriasis and CD, especially with the latent form [17,18].

The coexistence of CD and AD was not confirmed in our study group, which is consistent with the conclusion of Greco et al. [19]. However, there are reports in the scientific literature that contradict our findings [20,21], as well as those that confirm the influence of WA on the course of atopic eczema [22,23].

Some scientific literature data also indicate an increased incidence of chronic urticaria in patients diagnosed with CD [24,25]. A case of a woman with urticaria and WA has also been reported [26]. Still, our findings are consistent with the data obtained in an epidemiological study presented by Gabrielli et al. [27], who did not show an increased risk of CD in a population of adult patients with idiopathic chronic urticaria.

Taking into account the abovementioned studies and case reports indicating the co-occurrence of WA in patients with AD and chronic urticaria, additional allergy tests were performed in the study and control groups. No allergy to wheat and rye was found in any of the subjects.

The available research on the evaluation of eating habits among patients with psoriasis and AD confirm that patients make some dietary modifications to improve their skin condition. One of the most common changes made is gluten exclusion or restriction [28,29]. In our study group, it was noted that patients with AD, psoriasis and chronic urticaria used gluten-free products statistically more frequently than the comparison group, and less frequently consumed products that are or may be a source of gluten (including sliced meats, flavoured yoghurts) and highly processed foods. Nevertheless, in the study group, patients complained statistically more frequently about gastrointestinal symptoms so, after excluding CD and WA, this could suggest the presence of, for instance, NCGS. However, the diagnosis of this disease entity is very difficult mainly due to the lack of validated diagnostic criteria [30].

It is also worth noting that the scientific literature describes studies supporting the hypothesis that gluten and other wheat components may also cause irritable bowel syndrome (IBS) symptoms. The complaints described statistically more frequently by the patients involved in our study, such as abdominal pain, bloating, diarrhoea or constipation, could therefore be the result of this disorder [31]. Hill et al. [32] highlight that patients with IBS-like symptoms, in whom CD and WA have been ruled out, are defined as suffering from NCGS.

National Psoriasis Foundation recommendations advise against a gluten-free diet in patients, except for those with clinical or serological evidence of gluten sensitivity [33]. Also, guidelines for the management of AD do not recommend elimination diets in the absence of clinically significant food allergies [34]. The available data suggest that only patients with antibodies specific for gluten-dependent enteropathy or gluten intolerance may benefit from the use of a gluten-free diet. Such recommendations are confirmed by the study in question, in which no one was found to have CD or WA.

Despite many differences in the declared food intake between the study groups, it can be concluded that the patients did not follow gluten-free diets, which is important because an improperly balanced diet, once gluten cereal-based foods are excluded, may be associated with nutrient deficiencies. Traditional grains are rich sources of carbohydrates, dietary fibre, protein,

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minerals (zinc, selenium, iron) or B vitamins, while commonly available gluten-free products tend to be deficient in these and other components, so their deficiencies could exacerbate health problems [35].

5. Conclusions

In patients with autoimmune diseases who present with accompanying gastrointestinal symptoms, a comprehensive diagnostic evaluation for gluten-sensitive enteropathy and gluten intolerance is essential. It is important that individuals experiencing gastrointestinal complaints refrain from initiating a gluten-free diet without undergoing appropriate diagnostic procedures and consulting a physician. Patients with dermatologic conditions are more likely than the general population to independently alter their diet and restrict the intake of certain foods without adequate diagnostic confirmation of necessity. Therefore, further research involving large patient cohorts is required to definitively determine the relevance and therapeutic value of a gluten-free diet in inflammatory and autoimmune disorders in the absence of confirmed gluten-sensitive enteropathy. Additionally, providing education on evidence-based dietary recommendations to patients with skin diseases is strongly recommended.

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