Celiac Disease and Dermatitis Herpetiformis

National survey indicates delays in diagnosis

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SUMMARY

A national survey of 1937 members of the Canadian Celiac Association was conducted by mail questionnaire in June 1989 to study problems in diagnosing and managing celiac disease (CD) and dermatitis herpetiformis. Although 82% of the 1294 respondents were biopsied, 14% were diagnosed by their dramatic response to the gluten-free diet. Fifteen percent of biopsy-proven respondents saw five or more doctors before CD was diagnosed. Mean delays in diagnosis ranged from 5.8 (±10.9) years for those with nausea or vomiting to 13.9 (±14.5) years for those with headache or migraine.

RÉSUMÉ

En juin 1989, un questionnaire postal a permis de mener une enquête nationale auprès de 1937 membres de l'Association cœliaque canadienne afin d'étudier les problèmes diagnostiques et thérapeutiques reliés à la maladie cœliaque et à la dermatite herpétiforme. Malgré la biopsie effectuée chez 82% des 1294 répondants, 14% ont vu leur diagnostic confirmé par leur réponse remarquable suite à une diète sans gluten. Quinze pourcent des répondants dont le diagnostic avait été prouvé par biopsie avaient vu au moins cinq médecins avant d'en arriver au diagnostic. Les délais diagnostiques moyens ont varié de 5.8 à 10.9 ans pour les patients qui présentaient des nausées et des vomissements et de 13.9 à 14.5 ans pour les patients présentant des céphalées ou des migraines.

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THE CLINICAL EFFECTS OF CELIAC disease (CD) vary widely but typically include diarrhea, weight loss, and malabsorption of nutrients. Some persons with the disease also have other seemingly unrelated conditions, such as edema, tetany, fatigue, and irritability.[1,2] Other conditions, such as dermatitis herpetiformis, lactose intolerance, and aphthous ulcerations, often accompany CD.[3] Thus, celiac patients may present to almost any hospital department, and diagnosis may be delayed or missed unless clinicians are aware of CD's many manifestations.

Changes in the clinical features of the disease over time have been noted,[4] and some have suggested that CD is underdiagnosed.[5] Even after diagnosis, the treatment of CD and dermatitis herpetiformis (DH), requiring lifelong adherence to the gluten-free diet – although seemingly simple – is a source of concern to many.[6] In 1960, a study found that 81% of patients remained undiagnosed for 5 years after the onset of their symptoms.[7] A more recent study suggested[8] that the delay has been markedly reduced, but other researchers[9] found a mean delay of 10.6 ±11 years before diagnosis. Thus, although the problem of delay in diagnosis has been identified, little progress has been made toward its solution.

To determine the problems facing its members, the Canadian Celiac Association decided to conduct a national survey by mail questionnaire. The main objectives were to determine:

- the length and nature of the diagnostic process;
- the occurrence of CD, or symptoms suggesting CD, in family members;
- the response of celiac patients to diet;
- the nature of advice received; and
- the problems of dietary compliance.

This report presents the results of the diagnostic aspects of the first objective. Data on the dietary aspects have been reported elsewhere.[10]

METHOD

A comprehensive questionnaire was developed by a survey committee comprised of representatives from the Medical and Nutrition Advisory Boards and members of the Canadian Celiac Association. The questionnaire consisted

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Table 1. **Duration of symptoms experienced by biopsy-proven respondents before diagnosis of celiac disease**

SYMPTOM	DELAYS IN DIAGNOSIS					NO. OF RESPONDENTS
	MEDIAN (YEARS)	MEAN (YEARS)	SD (YEARS)	RANGE		
				MINIMUM (MONTHS)	MAXIMUM (YEARS)	
Diarrhea	1.9	6.6	11.7	1	75	774
Abdominal pain	2.0	8.0	12.4	1	65	583
Gas or belching	2.5	8.4	13.0	1	74	629
Fatigue or lethargy	2.0	7.9	12.6	1	79	688
Bloating	2.0	7.9	12.4	1	79	770
Nausea or vomiting	1.0	5.8	10.9	1	65	334
Lack of appetite	1.0	6.2	12.7	1	70	330
Skin rash (DH)	4.0	10.3	13.0	1	57	155
Headache or migraine	10.0	13.9	14.5	1	62	204

of 43 questions, about half of which were medical. It was pre-tested on subjects of varying age and background for readability and ease of completion. Most questions required specific answers rather than being open-ended.

The questionnaire was mailed in June 1989 to 1937 members of the Association across Canada who had CD or DH. For persons younger than 18 years, we requested that the questionnaire be filled out by a parent or guardian. Strict confidentiality was maintained.

Cross-tabulations for biopsy-proven and non-biopsy-proven respondents were examined for all variables. Most data are given for biopsy-proven respondents.

RESULTS

Of 1937 questionnaires distributed, 1294 (67%) were returned and analyzed. Of the respondents, 93% reported that they had CD and 7% DH. Of those claiming to have CD, 82% were biopsy-proven. Female respondents comprised 74% of the total, and the female to male ratio was 2.82:1.

The reasons for diagnosis of CD given by those respondents who had no biopsy proof of CD were diagnosis before biopsy procedure was available (6%), dramatic response to the gluten-free diet (14%), self-diagnosis (3%), CD "confirmed" by doctor (11%), and DH (2%).

Respondents were asked whether they had experienced any of nine separate symptoms before they were "officially" diagnosed as having CD, and for how long they believed they had had these symptoms. Mean delays for biopsy-proven respondents varied from 5.8 ±10.9 years for those reporting nausea or vomiting to 13.9 ±14.5 years for those reporting headache or migraine. Most median delays were 1 to 3 years (*Table 1*). The proportion of biopsy-proven respondents experiencing symptoms was generally similar for male and female patients, but the number experiencing more than 5 years' delay was somewhat higher for female respondents for some symptoms (*Table 2*).

When asked how many doctors they had consulted about their problem, 25% of 960 biopsy-proven respondents said one doctor, 29% two doctors, 17% three doctors, 12% four doctors, 6% five doctors, 6% six to 10 doctors, and 3% more than 10 doctors.

When respondents were asked what other diagnoses were given for their condition before they were diagnosed with CD, they identified a variety of conditions (*Table 3*). Virus, influenza, and bacterial infection were most often reported.

Table 2. **Proportion of male and female biopsy-proven respondents experiencing delays in diagnosis of celiac disease**

	ALL BIOPSY-PROVEN RESPONDENTS				MORE THAN 5 YEARS' DELAY			
	MALE		FEMALE		MALE		FEMALE	
SYMPTOMS	N	(%)	N	(%)	N	(%)	N	(%)
Diarrhea	207	(83)	567	(72)	58	(23)	184	(23)
Abdominal pain	133	(82)	450	(82)	45	(28)	178	(33)
Gas or belching	151	(84)	478	(85)	57	(32)	189	(34)
Fatigue or lethargy	158	(83)	530	(85)	45	(24)	208	(33)
Bloating	142	(83)	500	(84)	50	(29)	190	(32)
Nausea or vomiting	57	(72)	275	(86)	15	(19)	76	(24)
Lack of appetite	65	(76)	265	(83)	9	(11)	67	(21)
Skin rash (DH)	57	(75)	98	(81)	21	(28)	54	(45)
Headache or migraine	31	(79)	173	(78)	14	(36)	115	(52)

DISCUSSION

The response to this survey compares favourably with that reported elsewhere.[11] The female to male ratio of 2.82:1 reflects the membership of the Canadian Celiac Association rather than the true ratio for CD in the Canadian population. A preponderance of female patients has also been reported in other surveys.[12]

Although 82% of respondents had biopsies, it is a matter of concern that 14% of respondents' diagnoses were based on a dramatic response to the gluten-free diet and 11% were "confirmed" by doctors by some other means. As has been recently reemphasized,[13] no sure diagnosis of celiac disease can be made without identifying the characteristic histological picture of the duodenal-jejunal mucosa. This point needs to be more widely recognized.

Less delay in diagnosis was encountered with nausea or vomiting and lack of appetite than with the other symptoms. Particularly long delays were reported with headache and migraine symptoms, suggesting that it was difficult to relate headache or migraine symptoms to CD. The ranges in delays indicated that some individuals had had the symptoms all their lives. With lack of appetite, skin rash, and headache and migraine symptoms, the proportion of female respondents reporting delays of more than 5 years tended to be greater than that of male respondents. The reason for this is unclear but may be related to menstrual and related disorders. The fact that 21% to 52% of biopsy-proven female respondents and 11% to 36% of biopsy-proven male respondents with these conditions have had diagnosis delayed for more than 5 years is a matter of real concern. It seems that, in spite of advances in modern diagnostic techniques, little progress has been made in hastening the diagnosis of CD.

When asked to indicate which conditions were diagnosed before CD diagnosis, respondents rated anemia, stress, nervous condition, and irritable bowel most frequently. Much more attention must be given, particularly to the finding of anemia, to a possible early indicator of CD. Considerable confusion of CD with irritable bowel syndrome appeared to have occurred in both the biopsy-proven and non–biopsy-proven groups.

Because so many doctors were consulted before CD was diagnosed, it was

obvious that many doctors did not understand the disease. In this regard, many respondents expressed deep concerns about the problems they had encountered in being properly and promptly diagnosed. They considered it quite unacceptable to have to see so many doctors to be diagnosed properly and to be given such a variety of diagnoses. There was a feeling among respondents that many doctors were not informed about the disease or were unaware of the need for a biopsy; that they did not know that adults were subject to CD as well as children; and that they were unaware that treatment of CD and DH requires strict adherence to the gluten-free diet.

Delay in diagnosing CD has resulted in long periods of ill health for many respondents. Little emphasis seems to have been placed on this aspect of the disease. Numerous screening methods have been proposed.[14-17] As Guandalini et al[13] have suggested, it may be time for a change in diagnosis. The diagnostic accuracy of estimating antigliadin antibodies is quite high. New patients with CD lack IgG antigliadin antibodies, and few patients who have IgA antigliadin antibodies do not have CD. The absence of IgG antigliadin antibodies and the presence of IgA antigliadin antibodies together are a reliable indication of CD. Much greater emphasis must be placed on developing appropriate screening methods.

CONCLUSION

Serious delays still exist in the diagnosis of CD. There is an urgent need to make physicians more aware of the symptoms of CD and to investigate and apply procedures that will hasten and simplify diagnosis. ■

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Table 3. **Diagnoses of diseases made before celiac disease was diagnosed**

DIAGNOSIS	RESPONDENTS (%) BIOPSY-PROVEN (N = 686)	RESPONDENTS (%) NOT BIOPSY-PROVEN (N = 145)
Anemia	47	30
Stress	45	39
Nervous condition	41	39
Irritable bowel	34	43
Stomach ulcer	23	14
Food allergy	19	32
Colitis	13	23
Menstrual problems	13	17
Edema	9	8
Gallstones	9	10
Diverticulitis	6	9
Dermatitis herpetiformis	4	5
Other	36	39

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