



Patient awareness of extraintestinal manifestations of inflammatory bowel disease

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Received 26 August 2012; received in revised form 7 November 2012; accepted 24 November 2012

KEYWORDS

Crohn's disease;
Extraintestinal
manifestation;
Inflammatory bowel
disease;
Ulcerative colitis;
Venous thromboembolism

Abstract

Introduction: Patient awareness of extraintestinal manifestations of inflammatory bowel diseases is important in improving patient understanding of their disease and health outcomes. We aim to characterize patient awareness of extraintestinal complications related to their disease.

Methods: A cross-sectional survey was administered from July 2011 to May 2012. All adult (> 18 years) IBD patients attending gastroenterology clinics at a major tertiary teaching hospital (Mount Sinai Hospital, Toronto, ON, Canada) with a confirmed diagnosis of inflammatory bowel disease were invited to participate.

Results: A total of 299 patients participated: 177 Crohn's disease, 104 ulcerative colitis, and 18 IBD-unclassified. The vast majority of respondents obtained their information from their gastroenterologist (92%) and from the internet (78%). Most patients felt their inflammatory bowel disease knowledge was "very good" (34%) or "enough to get by" (54%). Most patients were aware of risk of colon cancer (75%), arthritis (77%), dermatological manifestations (49%), ocular inflammation (47%), and osteoporosis (53%). However, few patients were aware of venous thromboembolism (18%), nephrolithiasis (12%), or primary sclerosing cholangitis (20%). The majority of respondents were unsure of the signs and symptoms of venous thromboembolism, that the risk was increased during flares and hospitalizations, and that they require prophylaxis during an inflammatory bowel disease-related hospitalization.

Conclusion: Although the majority of respondents demonstrated awareness of most extraintestinal manifestations, few realized that venous thromboembolism was a life-threatening

Abbreviations: EIM, extraintestinal manifestation; IBD, inflammatory bowel disease; VTE, venous thromboembolism.

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systemic complication of inflammatory bowel disease. Greater knowledge of venous thromboembolism would enable patients to more promptly seek potentially life-saving intervention.

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1. Introduction

Inflammatory bowel diseases (IBD) comprising Crohn's disease (CD) and ulcerative colitis (UC) are associated with extraintestinal manifestations (EIM) and systemic complications. Up to 36% of IBD patients will experience extraintestinal manifestations in their lifetime.¹ These include dermatologic, ocular, and oral manifestations, arthritis, hepatobiliary disease, and nephrolithiasis. In addition, IBD patients are at increased risk for several systemic complications, including venous thromboembolism,² malignancy,³ metabolic bone disease,^{4,5} and reaction to live vaccines.^{6,7}

Prior studies have assessed patient awareness of the risks smoking has on IBD,^{8–10} patient perception of medication safety,¹¹ and general IBD knowledge.^{12–14} However, assessment of knowledge regarding specific extraintestinal manifestations and complications has not been reported.

Patient awareness of extraintestinal manifestations and systemic complications of IBD is an important aspect of management and may improve patient adherence with medications and follow-up.^{15–17} Optimal control of IBD disease activity often also achieves improvement in EIMs such as peripheral arthritis and this may serve as an additional incentive to continue medications during periods of remission. Moreover, patients should be aware of certain IBD-associated conditions that require urgent medical attention such as venous thromboembolism and uveitis. Recognition of these extraintestinal manifestations and systemic complications enables them to seek prompt medical attention and avert sequelae of delayed treatment.

In this cross-sectional study, we assessed IBD patients' awareness of complications related to their bowel disease, and where they obtain their information from, in order to identify gaps in patient education that may benefit from educational programs.

2. Methods

2.1. Study population

A cross-sectional survey consisting of a questionnaire to assess IBD patients' awareness of complications related to their disease was administered from July 2011 to May 2012. IBD patients attending the gastroenterology clinics at a major tertiary teaching hospital were invited to participate. All patients with a confirmed diagnosis of IBD (CD, UC, or IBD-unclassified) were eligible for inclusion. Patients were approached by study personnel and invited to complete the questionnaire.

2.2. Questionnaire

The questionnaire consisted of three sections. The first section included questions about where patients obtain their

information resources and support. The second section included a series of questions that queried patient awareness about extraintestinal complications of IBD (ocular inflammation, dermatological lesions, arthritis, osteoporosis, venous thromboembolism, colorectal cancer, and nephrolithiasis). To assess subjects' background propensity to respond in the affirmative, we included questions on conditions that were not associated with IBD (e.g., common cold, seasonal allergies, migraines, and fibromyalgia) to serve as negative controls. The third section included questions about patient demographics. A final question regarding personal experience with EIM, or knowledge of someone who had EIM was also asked. The questionnaire was reviewed by a small number of patients, by a social worker and nurse advocate who lead support groups for patients. The questions were revised to improve understandability and to also reduce anxiety that may have been induced by the survey.

2.3. Statistical analysis

Data were analyzed using (SPSS 20.0). The main statistical analysis involved using descriptive statistics to compare predictors of knowledge. Chi-square testing was used for categorical variables, and student's *t*-test or rank-sum for continuous variables. A *p*-value of less than 0.05 was considered significant.

2.4. Ethics

This study was approved by the Mount Sinai Hospital Research Ethics Board committee. All clinic patients gave their written informed consent at the time of completion of the questionnaire.

3. Results

The questionnaire was completed by 299 of the 336 (89% response rate) clinic patients who were invited to participate. The final survey question on personal history of EIM was added to the questionnaire after enrollment had begun and was completed by only 254 (85%) respondents. The mean age and age at diagnosis (\pm standard deviation [SD]) were 36.5 (\pm 13.4) years and 25.1 (\pm 11.8) years, respectively, with an equal male:female ratio. The distribution of IBD diagnosis was as follows: CD (59%), UC (35%), and IBD-unclassified (IBD-U, 6%). One-quarter of patients categorized themselves racially as non-White, and 13% were unemployed or on disability. More than a quarter achieved a post-university level of education (27%), while 55% and 18% achieved a university-level and high-school-level education, respectively. More than half of respondents (53%) reported a personal experience with EIMs (either personal history of EIM or history in family member or close friend). The prevalence of personal experience reported with specific EIMs was: arthritis

(39%), dermatological (18%), ocular (14%), osteoporosis (17%), nephrolithiasis (7%), primary sclerosing cholangitis (5%), and venous thromboembolism (6%).

3.1. Source of IBD education and information

Fig. 1 shows that the majority of patients obtained their IBD education from their gastroenterologists (92.0%) and the internet (78.3%). Family physicians (42.8%) and books (45.2%) were the next most frequently cited sources. Among those who stated that their gastroenterologist was their primary source of information, three-quarters reported that their gastroenterologist discussed EIM specifically with them. In contrast, only 34% of those who indicated their family physician as their primary source of IBD information reported receiving education on EIM. Most IBD patients felt their IBD knowledge was "very good" (34.0%) or "enough to get by" (54.4%).

3.2. Awareness of extraintestinal manifestations

Fig. 2 shows the proportion of patients that were aware of individual EIMs that were associated with IBD. About three-quarter were aware that colon cancer and arthritis were associated with IBD. Nearly half had knowledge of ocular and dermatological manifestations of IBD. In contrast, relatively fewer patients were aware that IBD could be complicated by venous thromboembolism (18.4%), nephrolithiasis (12.4%), and primary sclerosing cholangitis (20%). Awareness of these latter EIM's was only slightly higher than the prevalence of those who mistakenly believed that migraines, seasonal allergies, the common cold, and fibromyalgia were associated with IBD (Fig. 2).

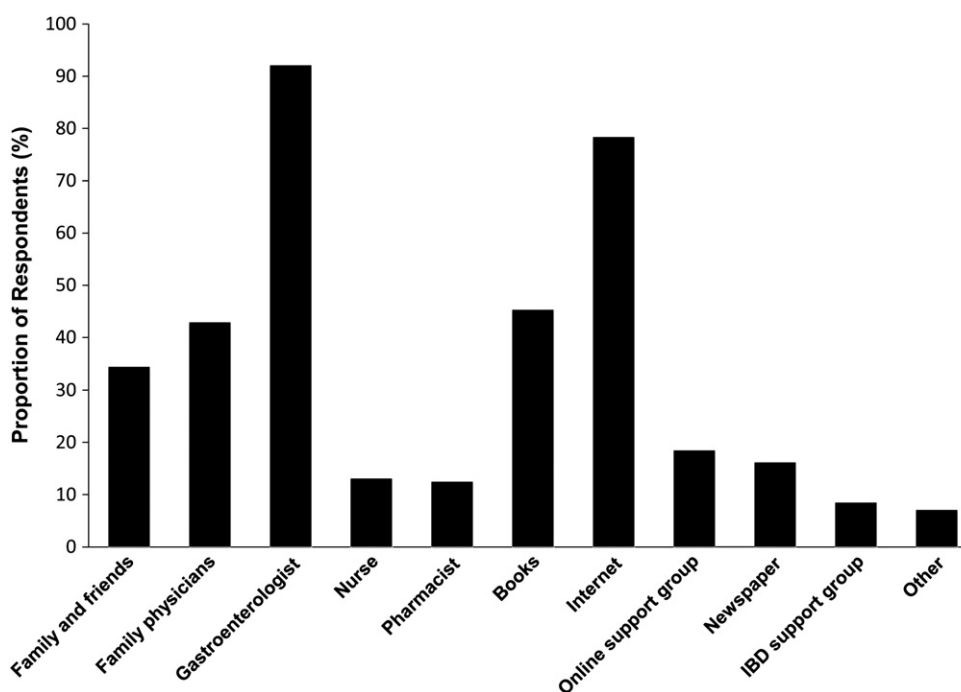


Figure 1 Patient sources of information for inflammatory bowel disease. Shown in the black bars represent the proportion of respondents who reported using a variety of sources for information related to their inflammatory bowel disease.

While nearly half identified ocular inflammation as a complication IBD, only 24% believed that it could potentially lead to blindness if untreated. A vast majority of individuals agreed that routine surveillance with colonoscopy was warranted for those with longstanding colitis (85%) and that use of steroids increased the risk of osteoporosis (81%). More than half agreed that treatment of IBD itself could improve symptoms from associated arthritis (58%) and that smoking in Crohn's disease could exacerbate the clinical course (54%). Less than half were aware that live vaccinations should be avoided by those who were on biologic agents or immunosuppressants for IBD (39%), while the majority was unsure (53%).

Certain factors were associated with increased awareness of associations of EIM with IBD, as shown in Table 1. Personal experience with any EIM was associated with increased awareness of joint inflammation, osteoporosis, eye complications, kidney stones, and skin lesions. Similarly, greater duration of IBD was associated with increased awareness of joint inflammation, osteoporosis, and kidney stones. Individuals with a higher education exhibited greater awareness of osteoporosis, eye complications, liver disease, and colon cancer as complications of IBD. Patients with CD had greater awareness of skin lesions (55.4% CD vs. 36.5% UC, $p=0.009$) and kidney stones (17.5% CD vs. 5.8% UC, $p=0.004$) as complications of IBD.

3.3. Knowledge of venous thromboembolism

The majority of respondents (66%) were unsure as to whether venous thromboembolism was associated with IBD (Table 2), while 55% were unsure whether they should receive DVT prophylaxis during hospitalizations for IBD flares. About half were aware that blood clots that develop in the legs could

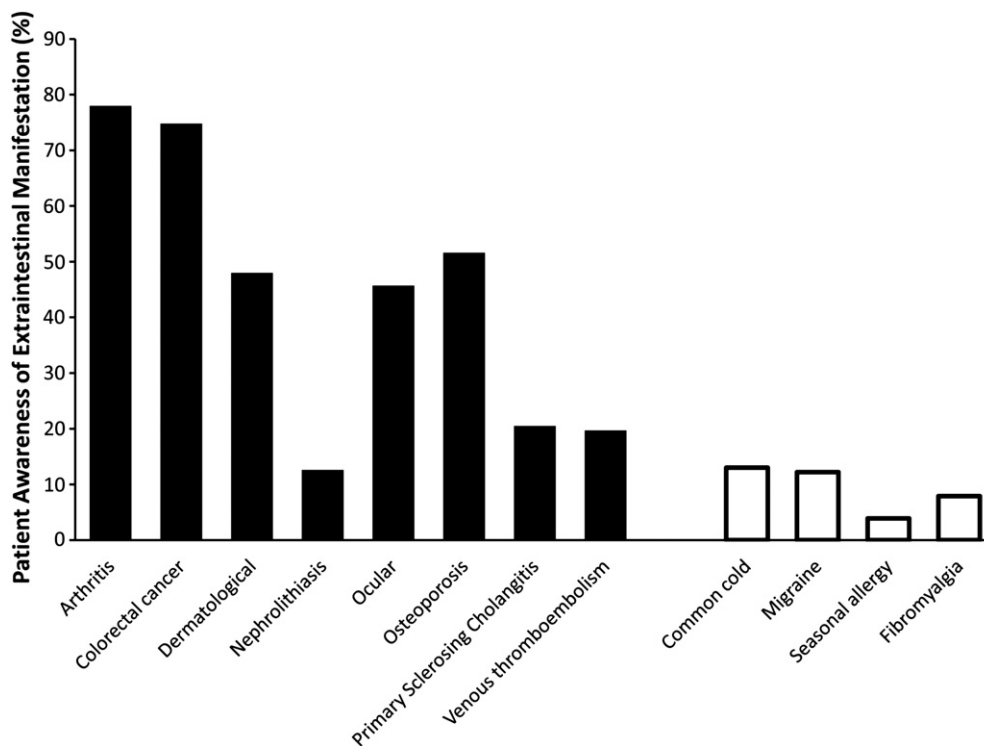


Figure 2 Patient awareness of extraintestinal manifestations of inflammatory bowel disease. The proportion of respondents who were aware of specific extraintestinal manifestations of IBD is shown in the black bars. Shown in the white bars are conditions which are not known to be associated with IBD and the proportion of patients who mistakenly reported that they were.

travel to the lungs. About half were not sure of the signs and symptoms of either deep venous thrombosis or pulmonary embolism, while about three-quarters were unsure whether having an IBD flare increased the risk of venous thrombosis and whether hospitalization for the flare was a factor.

4. Discussion

Awareness of inflammatory bowel disease (IBD) and complications has been shown to improve patient adherence with medications and follow up.^{15–17} Extraintestinal manifestations

and complications of IBD are among the worries and concerns of IBD patients.¹⁸ Our study illustrates that the majority of IBD patients are aware of certain extraintestinal manifestations and complications associated with IBD such as joint inflammation, osteoporosis, eye inflammation, and colon cancer. These are the more commonly known EIM that are found in popular patient information sources such as the Crohn's and Colitis Foundation of Canada website (www.ccfcc.ca) and the Crohn's and Colitis Foundation of America website (www.ccfca.org). The particularly high awareness of arthritis may also be due to its high prevalence in the IBD population. The extensive awareness of colon cancer was disproportionately high relative to its actual

Table 1 Factors associated with patient awareness of extraintestinal manifestations of inflammatory bowel disease.

	Disease duration (years)			Personal experience with any EIM		Educational attainment		
	<10	10 to 19	≥20	Yes	No	High school	College	Post-university
Arthritis	112 (69%)	68 (87%)	46 (87%)	122 (91%)	75 (63%)	35 (67%)	126 (77%)	65 (81%)
Osteoporosis	68 (42%)	47 (60%)	41 (77%)	81 (60%)	47 (39%)	18 (35%)	90 (55%)	49 (61%)
Ocular	71 (44%)	42 (54%)	22 (42%)	69 (52%)	44 (37%)	13 (25%)	78 (48%)	46 (58%)
Nephrolithiasis	14 (9%)	6 (8%)	16 (30%)	22 (16%)	9 (8%)	7 (14%)	21 (13%)	9 (11%)
Dermatological	79 (49%)	42 (54%)	22 (42%)	78 (58%)	43 (36%)	20 (39%)	84 (51%)	41 (51%)
Liver (PSC)	29 (18%)	15 (19%)	14 (26%)	31 (23%)	20 (17%)	6 (12%)	31 (19%)	23 (29%)
Venous thromboembolism	32 (20%)	12 (15%)	10 (19%)	28 (21%)	22 (18%)	6 (12%)	32 (20%)	17 (21%)
Colon cancer	122 (75%)	60 (77%)	39 (74%)	98 (73%)	91 (76%)	30 (58%)	130 (79%)	63 (79%)

* $p < 0.05$.

Table 2 Patient perceptions of venous thromboembolism in inflammatory bowel disease.

	Disagree	Unsure	Agree
Blood clots can be a complication of having IBD	39 (13%)	196 (66%)	61 (21%)
Blood clots in the leg can travel to the lungs	14 (5%)	130 (44%)	153 (52%)
People who are hospitalized for an IBD flare require medicines to prevent blood clots during their hospital stay	44 (15%)	164 (55%)	89 (30%)
IBD patients are not at increased risk of blood clots during a flare if they do not require hospitalization	42 (14%)	221 (74%)	35 (12%)
Younger people (<40 years) with IBD do not have increased risk of blood clots	45 (25%)	236 (80%)	16 (5%)
Symptoms of a blood clot in the legs include leg swelling (usually one side more than the other), deep aching pain, or redness.	7 (2%)	156 (53%)	132 (45%)
Having an active flare of IBD increases the risk of blood clots	15 (5%)	225 (76%)	57 (19%)
Sudden onset of shortness of breath and sharp chest pain with breathing can be symptoms of a clot developing in the lungs	7 (2%)	165 (56%)	124 (42%)

incidence, reflecting that it is highly emphasized in physician discussions with patients and in patient education materials.

Our survey also revealed that certain extraintestinal manifestations such as venous thromboembolism, PSC, and nephrolithiasis may be relatively underemphasized in patient education. Patient awareness of VTE may have important implications for associated morbidity and mortality. Numerous observational studies have demonstrated an increased risk of VTE among IBD patients compared to the general population.^{2,19–23} Moreover, disease activity appears to be major driving force for the increased risk of VTE. An individual's risk of VTE during an ambulatory IBD flare is nearly 9-fold higher than during remission, and nearly three-quarters of VTE events occur in IBD patients in the outpatient setting. In our survey, only 12% were aware that they were at increased risk of VTE in the ambulatory setting, and less than half were confident about recognizing the signs and symptoms of deep venous thrombosis and pulmonary embolism. Thus, IBD patients need to be counseled on how to recognize VTE in the outpatient setting in order to seek prompt medical attention and avoid the sequelae of delayed diagnosis and anticoagulation. The absolute risk of VTE during an IBD exacerbation is more than 3-fold higher during hospitalization compared to the ambulatory setting. Several societal guidelines advocate VTE prophylaxis in individuals hospitalized for IBD.^{24–28} Yet, only about half of medical patients with appropriate indication receive VTE prophylaxis actually receive it.²⁹ In our survey, less than a third of respondents perceived a need for VTE prophylaxis during hospitalization for an IBD flare. Given the suboptimal rates of VTE prophylaxis among medical patients, educating IBD patients on the need for VTE prophylaxis during hospitalizations would empower them to assure that they receive this potentially life-saving measure. A future study could assess whether improving patient knowledge of this complication improves the rate of VTE prophylaxis during hospitalization.

Uveitis is another IBD-associated condition that can lead to significant morbidity if not urgently treated. Though the majority of respondents in our survey were aware of ocular extraintestinal manifestations, less than a quarter were aware that untreated uveitis could potentially lead to blindness. Thus, there should be educational directives which focus on educating patients to recognize the symptoms of uveitis and the need to quickly undergo medical evaluation.

Our survey also revealed that less than half of respondents were aware that live vaccines should be avoided during treatment with biologics and immunosuppressants. As a corollary, individuals with IBD patients should be educated that they should be up-to-date with their vaccinations as soon as they are diagnosed in case they should eventually require immunosuppressive therapy. If necessary, live vaccines (measles, mumps, rubella, varicella, zoster, nasal influenza, oral polio, and yellow fever) should be given at least a month prior to initiation of immunosuppressant and biologic drugs. On the other hand, it should be reinforced to IBD patients on immunosuppressants that inactivated vaccines are safe and that they should receive recommended vaccinations against influenza, pneumococcus, hepatitis A and B, human papillomavirus, and meningococcus vaccines.⁷ An interventional vaccination program could be one way to ensure that IBD patients receive necessary vaccinations in time.

One of the main limitations of our study was potential referral bias. Because respondents attended an academic tertiary referral center, they may have had greater access to education on EIMS through direct physician interactions, patient education materials, or support groups. Discussions around EIMS of IBD in this tertiary center may differ from community physicians. Furthermore, patient knowledge of certain EIMS and gaps in knowledge of others may reflect physician perceptions of which EIMS are important and may have been specific to our center. We should also note that our study sample had a higher education level than is expected in the general population, and therefore may have better knowledge disease. Moreover, there may have been selection bias in that those patients with personal experience of extraintestinal manifestations of IBD may have been more likely participate, and since this was a self-administered questionnaire, patients may have overstated their knowledge of EIMS. Thus, the high rate of awareness of EIMS in our study population may not reflect that of the general IBD population. However, even in this group of respondents, we identified certain areas where there were gaps in knowledge, such as venous thromboembolism. In our study, we queried awareness of conditions not associated with IBD as negative controls. Consequently, we found that the background level of over-reporting awareness of EIM's was no greater than 13% in our study population. Certainly, a future direction of research would be to conduct a mail-out survey on EIM

awareness in a non-selected population of IBD patients. However, those studies are also hindered by selection bias, as it may be those with greater IBD knowledge or interest who choose to respond to the survey.

Our study has affirmed that most of our IBD patients are aware of EIMs that are either more prevalent or heavily emphasized (e.g., cancer). However, there are deficits in knowledge particularly of life-threatening systemic complications such as VTE. We acknowledge that there is little direct evidence in IBD that patient education improves health outcomes. However, at the very least, it may enable patients to have a greater participatory role in their healthcare and the patient–physician relationship. Our finding that more than 90% of IBD patients receive their IBD information from gastroenterologists provides an opportunity for educational interventions through physician counseling. However, given the time constraints on physician visits, nurse practitioners may also adapt to an important role in patient education. The internet was the second most cited source of information in our study and, in general, more than half of IBD patients access the internet for health-related information, and for IBD specific information.^{30–33} Though the internet can be an efficient venue through which to disseminate IBD-related information to patients, many websites may be marginal in quality and accuracy.^{34,35} Thus, patients should be directed to education websites and programs that are maintained by reputable advocacy groups such as the Crohn's and Colitis Foundation of America (CCFA) and the Crohn's and Colitis Foundation of Canada (CCFC). In Canada, IBD patients have frequent interactions with primary care physicians for their non-IBD related healthcare. Less than half in our survey perceived their family doctors as a source of IBD information. Because they are front-line physicians, it is even more important that they are aware of and recognize EIMs especially those such as venous thromboembolism and uveitis that require urgent referral. The next logical step would be to survey the educational needs of primary care providers with respect to EIMs.

Conflict of interest

There are no conflicts of interest.

Acknowledgments

Brenda O'Connor, Catherine Coulthard, Joanne Sulman provided input for the questionnaire. V.H. participated in the design of the study, administered the questionnaires, carried out the data analyses, and drafted the article. R.M. and R.T. administered the questionnaires and entered data. R.T. assisted with coordinating the study. G.N. conceived of the study, participated in the design and coordination, and edited the article. All authors read and approved the final article.

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