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A medical and neuropsychiatric management survey in a Brazilian cohort of patients with inflammatory bowel disease (IBD)

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HIGHLIGHTS

- What is already known?
- The prevalence and spectrum of neuropsychiatric co-morbidities varies among different epidemiologic studies.
- What is new here?
- Patients self report a high percentage of neuropsychiatric diseases but tend to better recognize central rather than peripheral nervous system disorders.
- How can this study help patient care?
- This study may guide practioners to educate IBD patients about their neuropsychiatric co-morbidities.

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ABSTRACT – Inflammatory bowel disease (IBD) can be accompanied by several neurological disorders. Since 2004, we started a Brazilian cohort to assess neuropsychiatric complications in IBD patients. Changes in therapeutic strategy and differences in the prevalence and relevance of neuropsychiatric disorders have been reported in the literature. We conducted a short patient-reported survey about the medical management of IBD (with a special focus on neuropsychiatric management) and its complications. During the enrollment period (9/1/2021 to 8/31/2022), 279 patients with IBD answered the survey (128 patients with ulcerative colitis and 151 with Crohn's disease). This is the first medical management survey aimed to verify the level of perception of IBD patients about their neuropsychiatric conditions. We found a high prevalence of neurologic (59%), psychiatric (32%), and neuropsychiatric co-morbidities (69%). There is a marked discrepancy between the findings of neurological disorders reported in our studies over the first 10 years of the cohort in comparison with the current perception/knowledge among the patients registered in the present management survey. Patients tend to have a better understanding of central rather than peripheral nerve conditions.

Keywords – Inflammatory bowel disease; neuropyschiatric diseases; survey.

INTRODUCTION

The medical management of inflammatory bowel disease (IBD) has greatly evolved in recent years[1]. It has been repeatedly demonstrated that IBD may affect all corners of the body[1]. IBD may also be accompanied by several neurological disorders. In this regard, we have started since 2004 a Brazilian cohort study, named NEURODII, and designed to evaluate the neurological complications in IBD patients[2-4].

In Brazil, we witnessed a dramatic change in the availability of therapeutic strategies for the treatment of IBD since the start of the NEURODII study, but also have noticed epidemiological differences in the prevalence of several neurological disorders (unpublished results, papers in progress). Approximately one year after the start of the NEURODII cohort, infliximab and later adalimumab slowly started to be available in Brazil in our institution and since then additional immunobiological agents have been available for IBD management. Currently, there is no consensus about the overall prevalence and clinical relevance of each individual neurological comorbidity due to multiple methodological differences[2-4]. Peripheral neuropathy e.g. has been reported to be significantly increased in some studies but subsequently questioned by others[5]. In this study, we evaluated the patient-reported in our Brazilian cohort of IBD patients of the prevalence of several medical conditions, with special focus on neuropsychiatric disease.

METHODS

Study design

We conducted a short patient-reported survey about the medical management of IBD (with a special focus on neuropsychiatric management) and its complications in an outpatient clinic from the Hospital Universitário Walter Cantídio, Universidade Federal do Ceará, Fortaleza, Ceará, Brazil. We evaluated all consecutive patients from the cohort NEURODII with Crohn's disease (CD) or ulcerative colitis (UC) seen at the outpatient IBD Clinic from the Universidade Federal do Ceará from 9/1/2021 to 8/31/2022. The diagnosis of CD and UC was made by experienced gastroenterologists from our institution. Diagnosis was based on widely accepted diagnostic standards, combining clinical, endoscopic, radiological, and pathological criteria[2-4].

A questionnaire survey was filled out by each patient who signed an informed written consent form. It consisted of a 2-page survey with six questions and multiple sub items. The structured questionnaire contained space for collecting information related to the subtype of IBD (CD or UC) and the patient's demographic data (name, medical record number, telephone, gender, age). The main questions included: 1) Are you being currently followed-up by which medical specialties? 2) In addition to the gastroenterologist, have you been evaluated by any other medical specialist? If yes, which ones? 3) Have you ever been evaluated by a neurologist? Have you ever been evaluated by a psychiatrist? 4) What are your current medications? And which others have you ever used? 5) Please list the medical diagnosed made by any physician 6) Please circle the diseases that have already been diagnosed in you (out of a list of 53 psychiatric and neurological diseases cited in the literature as comorbidities of IBD).

Ethical aspects

This study was approved by the Institutional Review Board from the Universidade Federal do Ceará (CAAE 62248416.7.0000.5045). All patients signed a written informed consent before starting to answer the survey. None of the patients refused to participate in this study. However, two were excluded because they were under 18 years of age.

Statistical analysis

Descriptive statistics, chi-square testing, Mann–Whitney, analysis of variance followed by Student–Newman–Keuls test (for comparison of multiple groups) and *t* test were used to compare the differences among the patients with ulcerative colitis and Crohn's disease. Differences were considered significant if $P<0.05$.

RESULTS

During the enrollment period (9/1/2021 to

8/31/2022), 279 patients with IBD answered the survey (128 patients with UC and 151 with CD). Mean age was 42±16 years and there was a slight female predominance (56%). Among the 128 UC patients, mean age was 45±15 years and 87 (68%) were women. Mean age of the CD group was 39±15 years, 70 (46%) were women. TABLE 1 details the main demographic data and consultation characteristics. As can be seen in TABLE 1, in addition to gastroenterological follow-up, 11% (N=30) were followed by colorectal surgeons, 4.3% by rheumatologists and 3.6% by dermatologists.

Eighty-five patients reported follow-up by a neurologist at some point, 54 were CD patients (36%)* and 31 (24%)* were UC patients. Seventy % of the patients reported that they were being followed-up by only 1 medical specialty. The remainder 30% had follow-up with 2 to 7 medical specialties.

Among the most cited and specific drugs in use for the treatment of IBD, (except steroids and drugs with central nervous system effect), all others (azathioprine, inflixamab, adalimumab, sulfasalazine and mesalazine) showed a statistically significant difference in use between the CD and UC groups. Azathioprine, inflixamab and adalimumab were more commonly used by CD patients, while sulfasalazine and mesalazine were more consumed by individuals with UC.

TABLE 1. Demographic findings, follow-up details (number and list of medications employed in the treatment of IBD and its subtypes).

N	IBD 279	CD 151	UC 128
Age	42±16	39±15	45±15*
Male/female ratio	122/157	81/70	41/87
Colorectal surgery	30 (11%)	18 (12%)	12 (9.4%)
Orthopedics	2 (0.7%)	1 (0.7%)	1 (0.8%)
Rheumatology	12 (4.3%)	5 (3.3%)	7 (5.5%)
Ophthalmology	2 (0.7%)	2 (1.3%)	0 (0%)
Infectious diseases	0 (0%)	0 (0%)	0 (0%)
Dermatology	10 (3.6%)	**9 (6.0%)**	**1 (0.8%)***
Other specialties	49 (18%)	26 (17%)	23 (18%)
Consultation by neurologist	85 (30%)	**54 (36%)**	**31 (24%)***
Consultation by psychiatrist	56 (20%)	31 (21%)	25 (20%)
Monitoring by 1 specialty	194 (70%)	103 (68%)	91 (71%)
Monitoring by 2 specialties	63 (23%)	34 (23%)	29 (23%)
Monitoring by 3 specialties	16 (5.7%)	11 (7.3%)	5 (3.9%)
Monitoring by 4 specialties	3 (1.1%)	1 (0.7%)	2 (1.6%)
Monitoring by 5 specialties	2 (0.7%)	2 (1.3%)	0 (0%)
Monitoring by 6 specialties	0 (0%)	0 (0%)	0 (0%)
Monitoring by 7 specialties	1 (0.4%)	0 (0%)	1 (0.8%)
List of IBD therapies reported			
Azathioprine	124 (44%)	**89 (59%)**	**35 (27%)****
Inflixamab	40 (14%)	**32 (21%)**	**8 (6.2%)****
Adalimumab	30 (11%)	**27 (18%)**	**3 (2.3%)****
Sulfasalazine	22 (7.9%)	**7 (4.6%)**	**15 (12%)***
Mesalazine	133 (48%)	**35 (26%)**	**98 (77%)****
Prednisone	46 (16%)	25 (17%)	21 (16%)
Any Steroid	6 (2.2%)	3 (2%)	3 (2.3%)
CNS agents	47 (16.8%)	26 (17.2%)	21 (16.4%)

CD: Crohn's disease; CNS: Central Nervous System; IBD: inflammatory bowel disease; UC: ulcerative colitis. *P<0.05; **P<0.001.

TABLE 2 lists all the most prevalent psychiatric and neurological comorbidities reported by the IBD patients in our survey. As can be seen, there was no statistically significant difference between CD and UC patients (TABLE 2). In addition, the following neuropsychiatric conditions were not reported by any IBD patient: Cluster headache, Melkersson-Rosenthal syndrome, Pseudotumor cerebri, Optic neuritis, Multiple sclerosis, central nervous system (CNS) demyelinating disease, Neuromyelitis optica, Myelopathy, Insanity, Alzheimer's disease, fronto-temporal dementia, Pick's disease, Parkinson's disease, hereditary neurological disease, Amyotrophic lateral sclerosis, intracerebral hemorrhage, CNS vasculitis,

TABLE 2. Neurological and psychiatric comorbidities reported by patients with inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC).

N	IBD 279	CD 151	UC 128
Psychiatric comorbidities			
Schizophrenia	1 (0.3%)	1 (0.7%)	0 (0%)
Generalized anxiety disorder	13 (4.6%)	4 (2.6%)	9 (7.0%)
Anxiety	66 (23.6%)	31 (21%)	35 (27%)
Depression	45 (16.1%)	27 (18%)	18 (14%)
Bipolar disorder	6 (2.1%)	5 (3.3%)	1 (0.8%)
Alcoholism	3 (1.0%)	3 (2.0%)	0 (0.0%)
Drug addiction	3 (1.0%)	2 (1.3%)	1 (0.8%)
Any psychiatric comorbidity	89 (32%)	46 (30%)	43 (34%)
Neurological comorbidities			
Restless legs syndrome	4 (1.4%)	1 (0.7%)	3 (2.3%)
Fibromyalgia	12 (4.3%)	5 (3.3%)	7 (5.5%)
Headache#	132 (47%)	66 (44%)	66 (52%)
Migraine	41 (14.6%)	18 (12%)	23 (18%)
Tension headache	2 (0.7%)	1 (0.7%)	1 (0.8%)
Epilepsy	2 (0.7%)	1 (0.7%)	1 (0.8%)
Syncope&	21 (7.5%)	13 (8.6%)	8 (6.3%)
Chronic fatigue syndrome	4 (1.4%)	3 (2.0%)	1 (0.8%)
Trigeminal neuralgia	2 (0.7%)	2 (1.3%)	0 (0.0%)
Facial paralysis	7 (2.5%)	5 (3.3%)	2 (1.6%)
Hearing loss or hearing changes	15 (5.3%)	10 (6.6%)	5 (3.9%)
Cerebral venous thrombosis	1 (0.3%)	1 (0.7%)	0 (0.0%)
Stroke+	6 (2.2%)	6 (4.0%)	0 (0.0%)
Peripheral neuropathies	3 (1.0%)	1 (0.7%)	2 (1.6%)
Small fiber neuropathies	6 (2.1%)	4 (2.6%)	2 (1.6%)
Polyneuropathies	1 (0.3%)	0 (0.0%)	1 (0.8%)
Carpal tunnel syndrome	3 (1.0%)	2 (1.3%)	1 (0.8%)
Miopathy	1 (0.3%)	0 (0.0%)	1 (0.8%)
Myasthenia gravis	1 (0.3%)	1 (0.7%)	0 (0.0%)
Any neurological comorbidity	165 (59%)	83 (55%)	82 (64%)
Any neurological comorbidity except headache	64 (23%)	38 (25%)	26 (20%)
Any neuropsychiatric comorbidity	192 (69%)	95 (63%)	97 (76%)
Any neuropsychiatric comorbidity except headache	123 (44%)	65 (43%)	58 (45%)

*$P<0.05$. #Headache (The questionnaire contained two terms used in Portuguese, one popular and one medical term); &Syncope (The questionnaire contained four terms used in Portuguese, three popular and one medical term); +Stroke (The questionnaire contained three terms used in Portuguese, two popular and one medical term).

neuritis, Mononeuritis multiplex, autonomic neuropathy, inclusion body myositis, plexopathy, myositis, hereditary neuropathy, Guillain-Barré syndrome, Chronic inflammatory demyelinating polyneuropathy, polymyositis.

DISCUSSION

IBD as a chronic, fluctuating, multisystemic disease with a multitude of extraintestinal manifestations that can appear in any part of the body (associated or not with the intestinal activity)[1,6] demands a complex cascade of multiprofessional assistance.

Among the various approaches to follow-up, medical management surveys have been used to assess the patient's view of the various aspects of IBD[7]. They were used to evaluate quality of care received[7], as well as more specific approaches such as the importance of follow-up by different specialties[8], adequate educational and psychological support and the need for personalized treatment plans[9].

In the first 10 years of this cohort study – NEURODII – (2004–2014), all patients treated at our IBD outpatient clinic who agreed to participate in the study underwent neurological evaluation. However, after 2015, due to a significant increase in the total number of patients treated in our center, this assessment was switched to direct request from either a gastroenterologist or patient's spontaneous demand.

To our knowledge, this is the first medical management survey aimed to verify the level of perception of IBD patients about their neuropsychiatric conditions. The overall burden of neuropsychiatric disorders was very high, reaching a prevalence of 69% in this survey. Psychiatric disease by itself affected close to 30% of the patients (32%). As previously reported in the medical literature, headaches, especially migraine are common in patients with IBD[10]. Other common neurological disorders included facial palsy, epilepsy, syncope, hearing loss and a wide variety of peripheral neuropathies[4]. As can be observed in TABLES 1 and 2, there is a marked discrepancy between the findings of neurological disorders reported in our studies from this cohort over the first 10 years of the cohort in comparison with the current perception/knowledge among the patients registered in the present management survey. This is more evident for the peripheral nervous system disorders. Among 279 patients who answered the questionnaire, only 1.0% reported suffering from peripheral neuropathy, 2.1% reported small fiber neuropathy, 0.3% polyneuropathy and 1.0% answered that they had carpal tunnel syndrome. This contrasts with our previous prospective findings that reported a prevalence of large fiber neuropathy of 19.8% (24/121), prevalence of 12.4% (15/121) of small fiber neuropathy, and 5.8% (7/121) of carpal tunnel syndrome[4]. Overall, those discrepancies, may explain previous discrepancies of peripheral neuropathies observed among different centers[5].

CONCLUSION

In summary, this study highlights the importance of monitoring IBD patients by a multidisciplinary team for the diagnosis and management of extra-intestinal manifestations and especially neuropsychiatric disorders, which are often neglected or undiagnosed in these patients. Futher studies are necessary to evaluate whether newer therapies that significantly altered the IBD course also have impact on co-morbid neuropsychiatric diseases.

Authors' contribution

Leitão AMF and Gondim FAA carried out the design, data collection and interpretation, wrote the original manuscript, revised and approved the final version. Tabatinga Neto JL participated in the conception, data collection, review of the manuscript and approved the final version. Souza MHLP and Braga LLBC performed data analysis and interpretation, revised the manuscript and approved the final version.

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Leitão AMF, Tabatinga Neto JL, Souza MHLP, Braga LLBC, Gondim FAA. Uma pesquisa de manejo médico e neuropsiquiátrico em uma coorte brasileira de pacientes com doença inflamatória intestinal (DII). Arq gastroenterol. 2024;61:e23134.

RESUMO – A doença inflamatória intestinal (DII) pode ser acompanhada por vários distúrbios neurológicos. Desde 2004, iniciamos uma coorte brasileira para avaliar complicações neuropsiquiátricas em pacientes com DII. Mudanças na estratégia terapêutica e diferenças na prevalência e relevância dos transtornos neuropsiquiátricos têm sido relatadas na literatura. Realizamos uma breve pesquisa relatada pelos pacientes sobre o manejo médico da DII (com foco especial no manejo neuropsiquiátrico) e suas complicações. Durante o período de 01/09/2021 a 31/08/2022, 279 pacientes com DII responderam à pesquisa (128 pacientes com retocolite ulcerativa e 151 com doença de Crohn). Esta é a primeira pesquisa de gestão médica que visa verificar o nível de percepção dos pacientes com DII acerca de suas condições neuropsiquiátricas. Encontramos uma alta prevalência de comorbidades neurológicas (59%), psiquiátricas (32%) e neuropsiquiátricas (69%). Há uma discrepância marcante entre os achados de distúrbios neurológicos relatados em nossos estudos durante os primeiros 10 anos da coorte em comparação com a percepção/conhecimento atual entre os pacientes da presente pesquisa de manejo. Os pacientes tendem a ter uma melhor compreensão das condições que afetam o sistema nervoso central do que as que afetam o sistema nervoso periférico.

Palavras-chave – Doença inflamatória intestinal; doenças neuropsiquiátricas; enquete.

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