



RESEARCH ARTICLE

REVISED Patient knowledge of fecal calprotectin in inflammatory bowel disease (IBD): An observational study in Mexico [version 2; peer review: 2 approved]

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Abstract

Background: Fecal calprotectin (FC) can be a valuable tool to optimize health care for patients with inflammatory bowel disease (IBD). The objective of this observational study was to determine the level of knowledge of the FC test in Mexican patients with IBD.

Methods: A self-report questionnaire was distributed via Facebook to patients with IBD. The survey consisted of 15 questions in two categories: the first category assessed knowledge of IBD diagnosis, and the second category assessed knowledge of the FC test.

Results: In total, 460 patients with IBD participated, of which 83.9% (386) had ulcerative colitis (UC) and 16.0% (74) had Crohn's disease (CD). Regarding IBD diagnosis, 41.9% of participants stated that they did not know of a non-invasive test for fecal matter to identify

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1. **Javier P Gisbert** , Universidad Autónoma de Madrid, Madrid, Spain

inflammation of the colon. Regarding the FC test, 57.5% (UC) and 58.1% (CD) stated that they did not know about the test. Additionally, 65.8% (UC) and 51.3% (CD) of participants stated that they had never received the FC test and 82.6% (UC) and 77.0% (CD) recognized that the FC test was difficult to access in their medical practice. Furthermore, 66% (UC) and 52.7% (CD) of participants noted that their specialist doctor had never suggested the FC test to them, yet 89.1% (UC) and 87.8% (CD) stated that they would prefer FC analysis for their IBD follow-up assessments.

Conclusions: There is little knowledge of the FC biomarker among Mexican patients with IBD. This suggests the need for greater dissemination of its use and scope as a biomarker in IBD.

Keywords

Inflammatory bowel disease; Fecal calprotectin; Level of knowledge; Ulcerative colitis; Crohn's disease.

2. **Rupert W. Leong** , University of Sydney, Sydney, Australia

Any reports and responses or comments on the article can be found at the end of the article.

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The changes made were in the area of methods, highlighting the following: According to a previous study by Yamamoto *et al.*, 2015, the prevalence of IBD in Mexico is 150,000, and considering an expected prevalence difference and an acceptable error of 5 %, the sample size calculations were performed, this in order to clarify how the sample size calculation was performed. On the other hand, in the area of discussion, the reason why there were more cases of Ulcerative Colitis and why there was greater participation of women was added, adding that even in Mexico it is still a challenge to understand the real number of cases of IBD. The predominance of women, this imbalance may be due to environmental factors such as the use of oral contraceptives, psychosocial stress, dietary factors, among others. It was also added that the information on this Calprotectin test cannot be omitted, since national and international clinical guidelines for the diagnosis and treatment of IBD in the adult population recommend the use of the fecal calprotectin test in various clinical settings, including initial diagnosis, diagnosis of relapse, and response to treatment. And finally, internet access was added as a limitation, since it could have had an impact on the number of participants who answered the questionnaire. Everything added was justified with different bibliographic references.

Any further responses from the reviewers can be found at the end of the article

Abbreviations

IBD, Inflammatory bowel diseases; FC, Fecal Calprotectin; UC, Ulcerative Colitis; CD, Crohn's Disease.

Introduction

Inflammatory bowel disease (IBD) is defined as a group of chronic inflammatory disorders of unknown cause that affect the gastrointestinal tract and includes two diseases: Crohn's disease (CD) and Ulcerative Colitis (UC). These diseases are defined according to clinical, radiological, endoscopic, and histological criteria, and are characterized by chronic relapses, which present in outbreaks (active phases) and periods of remission (inactive phases)¹.

Currently, gastrointestinal endoscopy, histological examination of biopsies, and contrast imaging are mandatory techniques for the diagnosis and evaluation of IBD activity. Due to the complexity of the disease and the need for a multidisciplinary approach, diagnosing and treating the condition is a challenge for medical specialists. Patients generally take five to ten years to be diagnosed, which implies that treatments are applied late and therefore, the quality of life of patients with IBD is directly affected². Patients with IBD also worry about a timely diagnosis, as well as complications of the disease and secondary conditions^{3,4}.

Unfortunately, endoscopy is not easily accessible in many rural areas of the Mexican Republic and when performed are sometimes unnecessary, a problem compounded by the cost of the procedure. Recently, in different international institutions the use of biomarkers or biological markers has been routinely

applied. The most prominent biomarker used for IBD is fecal calprotectin (FC), which is a protein derived from neutrophils, released in the feces in response to inflammation of the intestinal mucosa. FC levels have been found to be associated with endoscopic severity, prediction of mucosal healing, and prediction of relapse; therefore, it is a useful biomarker for monitoring patient response to treatment^{5,6}. Additionally, a primary objective of the treatment of IBD is to improve the patient's health-related quality of life regardless of the type of therapy used. Patient knowledge of alternative methods for diagnosis and follow-up of IBD leads to increased well-being of the patients and to a reduction in overall healthcare costs⁷.

Despite the clinical utility of FC in IBD, the lack of dissemination and knowledge among patients could limit its acceptance and use as a clinical test. Currently in Mexico, there are no official statistics on the use of FC as a diagnostic marker and follow-up test for IBD. Consequently, the present study aims to assess knowledge regarding the use of FC as a diagnostic test among patients with IBD.

Methods**Study design**

This study used an observational cross-sectional design. Through the "Fundación Vivir con Crohn y CUCI A.C" (a non-profit foundation that offers information and support to people with IBD in Mexico), an electronic questionnaire was disseminated with questions aimed at assessing participant knowledge of FC and its use in IBD treatment. The questionnaire was developed by "Fundación Vivir con Crohn y CUCI A.C", gastroenterologists and health advocates of Hospital C.M.N. "20 de Noviembre", ISSSTE, in 2020. Two gastroenterologists in the group validated the 15 questions. A pilot test of the questionnaire was carried out with 5% of the population (23 people with IBD who attended the hospital), to ensure the validity of the questionnaire. The questionnaire was anonymous and voluntary, and consisted of 15 basic questions about the patient's social and demographic data, as well as questions related to knowledge of the FC test⁸. A link to the questionnaire was posted on the "Fundación Vivir con Crohn y CUCI A.C"'s Facebook site on the 3rd July 2020. The survey was hosted on [Google Forms](#).

Participants

Inclusion criteria were Mexican adults, aged 18 to 45 years old and diagnosed with inflammatory bowel disease. The sample size was calculated using the central limit theorem⁹ with a margin of error of 5% and a confidence interval of 95%. According to a previous study by Yamamoto *et al.*, 2015, the prevalence of IBD in Mexico is 150,000, and considering an expected prevalence difference and an acceptable error of 5%, the following calculations were made^{9,10}:

$$N = \left[\frac{Z_{\alpha/2}^2 [p[1-p]]}{d^2} \right]$$

N = Sample size calculation; $Z\alpha / 2$ = Z value of the alpha error with 95% confidence, assigning alpha = 0.05; P = expected population prevalence for the event under study (Yamamoto *et al.*, 2015); d = Difference between the expected population prevalence value and the acceptable error. Values: $Z\alpha / 2 = 1.96$; $p = 0.38$; $d = 0.30$.

$$N = \left[\frac{1.96^2 [0.38 [1 - 0.38]]}{0.30^2} \right] = 384$$

Which means that if you survey 384 people, the actual data you are looking for will be 95% of the time in the $\pm 5\%$ range relative to the data you see in the survey.

Data collection

A database was produced with Excel v19.0. The period of data collection was August to September 2020, where the following data were collected from each patient: 1) Type of IBD (UC and CD), 2) Sex of the patient, 3) Health System where they were treated, 4) Are you familiar with the non-invasive stool test to see if the intestine is inflamed? 5) Do you know of any test to determine if the disease is in the active phase? 6) Do you know of any test to determine if the disease is in the remission phase? 7) Do you consider that colonoscopy is necessary for the follow-up of IBD? 8) Do you know the FC test? 9) Have you ever had the FC test? 10) Does your medical unit have the FC test? 11) How accessible is it to perform the FC test in your medical unit? 12) How often does the specialist doctor suggest that you take the FC test? 13) Do you know approximately the cost of the FC test? 14) Do you think the price of the FC test is lower than the endoscopy study?, 15) For the follow-up of the disease would you prefer to perform Colonoscopy or the FC test?

Statistical analysis

Initially, a univariate analysis was carried out, where absolute and relative frequencies were used for qualitative variables and mean and standard deviation were used for quantitative variables. All tests were performed with Excel v19.0.

Ethical considerations

This study was based on the guidelines for clinical research established in the Declaration of Helsinki, in the Ministry of Health, and in the “Centro Médico Nacional, 20 de Noviembre, ISSSTE”. The Institutional Biosafety, Ethics and Research Committee, approved this study (number 033.2017). Written informed consent was obtained from each patient. As well as in the Biosafety, Ethics and Institutional Research Committees, patient information was deidentified and data were stored in a confidential registry of Hospital C.M.N. “20 de Noviembre”, ISSSTE.

Results

Population characteristics

In total, 460 patients with a diagnosis of IBD were obtained in 29 states of the Mexican Republic¹¹. The following states and cities of the Mexican Republic were the ones that

provided the information: Mexico City, Mexico City (131); State of Mexico, Toluca de Lerdo (68); Monterrey, Nuevo Leon (36); Guadalajara, Jalisco (32); Coahuila, Saltillo (20); Leon, Guanajuato (16); Sinaloa, Culiacán (16); Puebla, Puebla (15); Morelos, Cuernavaca (12); Veracruz, Xalapa (12); Baja California, Mexicali (11); Chihuahua, Chihuahua (11); Pachuca, Hidalgo (9); Querétaro, Querétaro (8); Ciudad Victoria, Tamaulipas (8); Hermosillo, Sonora (7); Durango, Durango (6); Chilpancingo, Guerrero (5); Nayarit, Tepic (5); Oaxaca, Oaxaca (5); Quintana Roo, Chetumal (5); San Luis Potosí, San Luis Potosí (5); Tlaxcala, Tlaxcala (5); Yucatán, Mérida (3); Aguascalientes, Aguascalientes (2); Campeche, Campeche (2); Michoacán, Morelia (2); Zacatecas, Zacatecas (2); Tabasco, Villahermosa (1) (Figure 1).

Table 1 shows the general characteristics of the study participants. Of the 460 patients who participated in the questionnaire, there was a greater number of patients with a diagnosis of ulcerative colitis (386; 83.9%) than Crohn’s disease (74, 16.0%), and a predominance of women (327, 71%) over men (133, 28.9%), as well as greater medical attention in the public health sector.

Participant knowledge of IBD tests

It was observed that more than 50% of participants were not aware of any non-invasive stool test (*i.e.* not endoscopy) to test whether the intestine is inflamed. Additionally, more than 50% stated that they did not know of any test to differentiate whether the disease is in the active or remission phase. Moreover, 90% of participants stated that colonoscopy was necessary for the follow-up of IBD (Table 2).

Participant knowledge of the fecal calprotectin test

It was observed that more than 50% of participants had no knowledge of the FC test and have never had it. Furthermore, 64% of participants did not know if their medical unit has the FC test and 83% consider the test hard to access in their medical unit. Additionally, more than 65% of the participants stated that they had never been offered the FC test. Despite this, almost 90% of patients said they would prefer to use the FC test to monitor their condition (Table 3).

Discussion

To ensure high quality care for patients with a chronic disease, it is important for the patient to have adequate information on their diagnosis, treatment and follow-up, and for the doctor to inform and discuss different options with the patient. Determining patient knowledge of their disease can help reduce costs in the health sector and at the same time improve the quality of life of patients. Assessing knowledge of fecal calprotectin (CF) in patients with IBD is, therefore, important to improve patient care for this chronic disease. This study is the first to our knowledge to evaluate this in Mexico.

Participants were recruited through the “Fundación Vivir con CU y Crohn SA”, and 460 patients with a diagnosis of IBD were surveyed, of which, 83.9% were diagnosed with UC and 16.0% with CD. The predominance of UC over CD is similar to that reported in other countries in Asia and Latin American

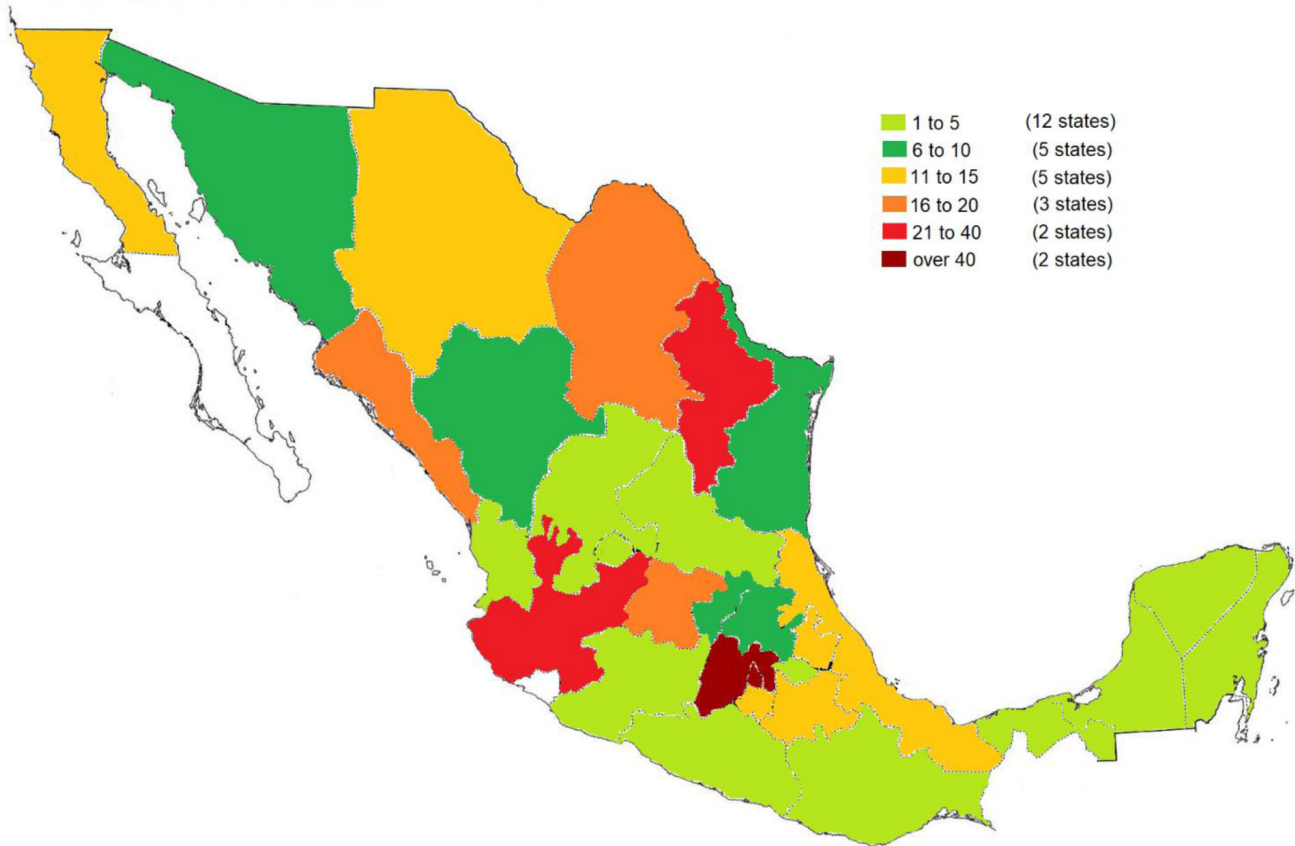


Figure 1. States of the Mexican Republic from which participants took part. The colours represent the number of participants recruited in each state. Mexico City and the State of Mexico (dark red) presented the greatest number of participants (over 40) with IBD. Monterrey and Guadalajara (red) presented 21 to 40 participants with IBD. The states of Coahuila, León and Sinaloa (orange) presented 16 to 20 participants with IBD. Puebla, Morelos, Veracruz, Baja California and Chihuahua (yellow) presented 11 to 15 participants with IBD. Pachuca, Querétaro, Ciudad Victoria, Hermosillo and Durango (dark green) presented 6 to 10 participants with IBD. Chilpancingo, Nayarit, Oaxaca, Quintana Roo, San Luis Potosí, Tlaxacala, Yucatán, Aguascalientes, Campeche, Michoacán, Zacatecas and Tabasco (light green) presented 1 to 5 participants with IBD.

Table 1. General characteristics of the study population.

	Ulcerative Colitis (UC)	Crohn's disease (CD)
Number of participants (%)	83.9 % (386)	16.0 % (74)
Sex W/M	273/113	54/20
Age	42.5±11.4	48.6±5.6
Healthcare system		
Private/Public	165/221	25/49

Data are presented as number (%), and median/±

countries, such as Colombia^{7,11}. Although the trend of IBD is similar to that of other countries, the lack of epidemiological data in Mexico remains a challenge to understand the real number of IBD cases. The predominance of women (327, 71%) over men (133, 28.9%), this imbalance may be due to environmental

factors such as the use of oral contraceptives, psychosocial stress, dietary factors, among others. On the other hand, it has been described that the use of social networks is more frequent in women than in men, so it can also be attributed that there is a greater number of women¹²⁻¹⁶.

Table 2. Participant knowledge of IBD tests.

	Ulcerative Colitis (UC) n= 386 (83.9 %)	Crohn's disease (CD) n= 74 (16 %)
Are you familiar with the non-invasive stool test to see if the intestine is inflamed?		
Yes	161 (41.7 %)	32 (43.2 %)
No	225 (58.2 %)	42 (56.7 %)
Do you know of any tests to know if it is in the active phase?		
Yes	142 (36.7 %)	32 (43.2 %)
No	244 (63.2 %)	42 (56.7 %)
Do you know of any test to know if it is in the remission phase?		
Yes	120 (31.0 %)	32 (43.2 %)
No	266 (68.9 %)	42 (56.7 %)
Do you consider that colonoscopy is necessary for the follow-up of IBD?		
Yes	352 (91.1 %)	67 (90.5 %)
No	34 (8.8 %)	7 (9.4 %)

Data are presented as number (%)

In the first category of questioning about the participants' knowledge of IBD tests, participants mostly reported to not know of any test for the state of the disease. This shows that the majority of participants were uninformed, which can lead to a deterioration in the quality of life¹⁷. When living with a chronic disease, it is essential to know about advances in medicine, to know the signs and symptoms, and how to better diagnose and monitor the disease to improve quality of life. The benefits of staying properly informed include awareness of useful tools and tests to diagnose and prevent the advancement of the disease^{11,18,19}.

More than 90% of the participants stated that colonoscopy is necessary for the follow-up of IBD. Colonoscopy can be used in the initial differential diagnosis, in the surveillance of carcinoma, and to evaluate abnormalities on imaging tests. However, undergoing a colonoscopy is invasive, expensive, and intolerable for some patients. In other studies, patients have claimed to have anxiety before and during the colonoscopy, given potential risks such as intestinal perforation. Colonoscopy has also been associated with several unfavorable outcomes, including missed diagnoses and avoidable repeat procedures^{20,21}. In addition, it is difficult to perform an endoscopic evaluation when there is injury to the intestinal mucosa, a frequent problem in IBD²²⁻²⁴.

In the second part of the questionnaire to identify the degree of knowledge of the CF test, more than 50% of the population in both groups answered that they had no knowledge of the FC test. They also said that the FC test had never been performed on them, and that their specialist doctor had never suggested performing the FC test. This highlights the scarcity of knowledge regarding this test in treating patients with IBD, and that

the doctor-patient relationship seems deficient. The doctor must inform the patient of their pathology, the procedures to follow, the treatment possibilities, eventual healing and, in general, must adhere to correct clinical practice to improve the information perceived by patients^{25,26}.

In addition, it must be clear that the only effective information is that provided by the health professional before the intervention or treatment in question. Adequate information should be provided sufficiently in advance and be honest and easy to understand, so that the patient can make an informed decision²⁷. That is why the dissemination of information to the patient, including the benefits and disadvantages of any potential procedure should be made known²⁸.

The study participants were questioned about the accessibility of the FC test in their medical unit. More than 70% stated that it was difficult to access this test, and in contrast, more than 50% of the population reported not knowing whether this test is available in their medical unit. The Mexican Consensus for the diagnosis and treatment of IBD suggests that the FC test is useful to evaluate the activity of IBD. The test's response to medical treatment correlates with mucosal scarring or endoscopic remission, and is a good predictor of relapse, so access should be easily available in any medical unit²⁹. Furthermore, expert guidelines suggest that disease activity should be reassessed every 3 to 6 months³⁰, therefore, it would be important for public and private medical units to have the FC test for regular cost-effective testing^{22,31}.

In questions about the cost of FC, more than 60% of participants stated that they did not know the cost of the test, and more than 60% believed that the price of FC is less than a

Table 3. Participant knowledge of the non-invasive Fecal Calprotectin test.

	Ulcerative Colitis (UC) n= 386 (83.9 %)	Crohn's disease (CD) n= 74 (16 %)
Are you familiar with the test called Fecal Calprotectin?		
Yes	164 (42.4 %)	31 (41.8 %)
No	222 (57.5 %)	43 (58.1 %)
Have you ever had a Fecal Calprotectin test?		
Yes	132 (34.1 %)	36 (48.6 %)
No	254 (65.8 %)	38 (51.3 %)
How often does the specialist doctor suggests performing the FC test?		
Every 3–4 months	35 (9.0 %)	6 (8.1 %)
Every 6 months	39 (10.1 %)	9 (12.1 %)
Once a year	27 (6.9 %)	8 (10.8 %)
One time only to prescribe another medicine	30 (7.7 %)	12 (16.2 %)
Never	255 (66.0 %)	39 (52.7 %)
Does your medical unit have the FC test?		
Yes	65 (16.8 %)	17 (22.9 %)
No	74 (19.1 %)	19 (25.6 %)
I don't know	247 (63.9 %)	38 (51.3 %)
How accessible is it to take the FC test in your medical unit?		
Hard	319 (82.6 %)	57 (77.0 %)
Easy	67 (17.3 %)	17 (22.9 %)
Do you know the approximate cost of the FC test?		
Yes	103 (26.6 %)	23 (31.0 %)
No	283 (73.3 %)	51 (68.9 %)
Do you think the price of the FC test is less than the endoscopy study?		
Yes	274 (70.9 %)	51 (68.9 %)
No	112 (29.01 %)	23 (31.0 %)
For the follow-up of the disease you prefer to perform:		
Colonoscopy	42 (10.8 %)	9 (12.1 %)
Fecal Calprotectin	344 (89.1 %)	65 (87.8 %)

Data are presented as number (%)

colonoscopy. On the contrary, a study carried out by Motaganahalli *et al.*, in 2019, suggests that the introduction of the FC test in the routine health care of IBD not only helps the patient, but is potentially cheaper than a colonoscopy³². The use of colonoscopies could be reduced by more than 80% if the FC test is used as the first approach³³. In addition, the use of the FC test over a colonoscopy would be more profitable, indirectly, for the patient, since colonoscopies cause loss of productivity and absence from work, require sedation and attendance at a medical care center^{34,35}.

Finally, the participants were questioned about which test they would prefer to carry out for an IBD follow-up appointment. More than 80% stated that they would prefer the FC

test. FC could not only be useful in the differentiation of patients with active IBD and those in remission, but it also correlates well with the degree of inflammatory activity evaluated by clinical indices such as endoscopy and histology, and predicts clinical relapse, as well as the mucosal healing and postoperative recurrence^{36,37}. Other authors have shown that FC levels are associated with the presence of histological alterations in endoscopic biopsies, being lower in the absence of anatomopathological inflammation^{38–40}. In different cohorts it has also been reported that the FC test is able to distinguish IBD from Irritable Bowel Syndrome^{41,42}. Therefore, the use of an alternative non-invasive biomarker such as FC that can accurately differentiate functional or organic diseases, detect inflammation of the intestinal mucosa, and monitor disease activity to

avoid invasive and costly testing could be highly useful^{43,44}. Likewise, this information cannot necessarily be omitted, since clinical guidelines such as that of European Crohn's and Colitis Organization [ECCO] the European Society of Gastrointestinal, Abdominal Radiology [ESGAR], British Society of Gastroenterology consensus guidelines and Mexican guidelines for the Diagnosis and Treatment of IBD in the Adult Population, recommend the use of the fecal calprotectin test in various clinical settings, including initial diagnosis, relapse diagnosis and response to treatment^{45–48}.

Assessing patient knowledge of non-invasive tests such as FC in patients with IBD may help to improve patient care as well as a reduction in medical costs during follow-up of the disease. This study suggests that knowledge of such tests can be improved with better communication with the medical personnel. The limitations of the study were that there was a much greater number of participants with ulcerative colitis than Crohn's disease, and the patients were only evaluated cross-sectionally. On the other hand, there is growing evidence suggesting that Facebook is a useful recruiting tool and therefore its use should be considered when implementing future health research. However, one of the important limitations of this study is Internet access.

In general, patients with chronic diseases should know about the tests that help to diagnose and monitor their disease. For IBD, assessing a biological biomarker, such as FC, is more specific than clinical indices, less expensive, more comfortable than endoscopic monitoring, and reduces the need for endoscopic examinations. Therefore, patients with IBD should be given the correct information on the use of FC which could be a valid alternative to evaluate the response to treatment and reduce the number of colonoscopies performed. To improve knowledge transfer to patients, we suggest improving accessibility to services, creating comprehensive care units, having medical specialists inform their patients about management of the disease, promoting medical research on the disease, and likewise, raising more awareness in society about IBD.

Conclusion

Using the application of a questionnaire, we evaluated the knowledge of patients with IBD about the diagnostic tests

that are required for the diagnosis and follow-up of the disease. There was a lack of awareness of the effective and low-cost Fecal Calprotectin test in the participants. In order for patients to make informed decisions regarding the management of their disease, doctors should provide adequate and timely information about the different options available.

Data availability

Underlying data

Harvard Dataverse: Patient knowledge of fecal calprotectin in inflammatory bowel disease (IBD): An observational study in Mexico. <https://doi.org/10.7910/DVN/AHPJOF>¹¹

This project contains the following underlying data:

- Database Maldonado et al.tab. (Excel spreadsheet of questionnaire responses)

Extended data

Harvard Dataverse: Patient knowledge of fecal calprotectin in inflammatory bowel disease (IBD): An observational study in Mexico. <https://doi.org/10.7910/DVN/NOOUQF>⁸

This project contains the following extended data:

- Questionnaire in English
- Questionnaire in Spanish

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

Consent

Written informed consent for publication of the participants' details was obtained from participants.

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Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 26 August 2022

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Rupert W. Leong 

Concord Clinical School, University of Sydney, Sydney, NSW, Australia

The article is relevant to local practice in the management of IBD patients. It is not generalisable based on the sample size and questionnaire design, but the main point of the study is to reflect on opportunities for treatment improvement in Mexico. Although there was a high proportion of UC versus CD it most likely reflects the local epidemiology, as previously documented in a review¹.

The lack of awareness of non-invasive testing is obviously multi-factorial. Awareness might not drive increased uptake due to the cost of testing faecal calprotectin, acceptability of testing, tissue processing, accuracy of results, timely reporting and use of the results by clinicians. All these are important factors before the test is widely endorsed and the effectiveness of real-world testing needs to be conducted locally. There is no doubt internationally that faecal calprotectin is an important target of treatment in IBD and in countries where colonoscopy is not widely-available the importance of faecal calprotectin is further accentuated.

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Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 12 February 2021

<https://doi.org/10.5256/f1000research.54322.r79014>

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Javier P Gisbert 

Departamento de Medicina, Universidad Autónoma de Madrid, Madrid, Spain

I think that the article is now ready to be indexed.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 06 January 2021

<https://doi.org/10.5256/f1000research.30540.r76438>

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Javier P Gisbert 

Departamento de Medicina, Universidad Autónoma de Madrid, Madrid, Spain

TITLE

OK.

ABSTRACT

OK.

INTRODUCTION

OK.

METHODS

It seems that the questionnaire had been previously used in another study (as a reference is provided for it). Was it previously validated? Please clarify this.

As the questionnaire was posted on Facebook site, there may be a bias for including only patients with internet access (which could be associated, for example, with younger age, higher educational status, etc.). This potential limitation should be discussed in the Discussion section.

In this respect, inclusion criteria were Mexican adults, aged 18 to 45 years old. Please justify this. This could induce another bias, as older patients could have lower internet access. Therefore, the results of the present study could have been biased to more favorable findings. This potential limitation should also be discussed in the Discussion section.

It is stated that the sample size was calculated using the central limit theorem with a margin of error of 5% and a confidence interval of 95%. However, more details should be provided, and the calculated sample size should be given.

Statistical analysis: It is stated that "Initially, a univariate analysis was carried out". This seems to imply that a multivariate analysis was also performed, but I cannot see any information regarding it.

RESULTS

Of the 460 patients who participated in the questionnaire, there was a much greater number of patients with a diagnosis of ulcerative colitis (386; 83.9%) than Crohn's disease (74, 16.0%). Even though the authors point out that "The predominance of UC over CD is similar to that reported in other countries in Asia and Latin American countries, such as Colombia", and they comment in the Discussion section that "The limitations of the study were that there was a much greater number of participants with ulcerative colitis than Crohn's disease", these explanations seem to be insufficient. Please try to explain better this possible bias.

The same is valid for the predominance of women (327, 71%) over men (133, 28.9%), please try to explain this misbalance.

DISCUSSION

It is repeatedly stated that: "The majority of participants were uninformed, which can lead to a deterioration in the quality of life". And that "They also said that the FC test had never been performed on them and that their specialist doctor had never suggested performing the FC test. This highlights the scarcity of knowledge regarding this test in treating patients with IBD, and that the doctor-patient relationship seems deficient". However, it should also be clarified that the lack of knowledge of the patient does not necessarily imply that the doctor has not informed the patient correctly, since it is possible that the determination of FC is simply not indicated in them. In other words, it is clear that FC is not always indicated in all patients, and for those patients, this information could be correctly omitted. Please clarify this in the Discussion section.

REFERENCES

OK.

TABLES

OK.

FIGURES

OK.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Inflammatory bowel disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 20 Jan 2021

Brenda Maldonado, ISSSTE, Félix Cuevas 540, Col del Valle Sur, Benito Juárez, Mexico

Dear Reviewer 1:

METHODS

Reviewer 1: It seems that the questionnaire had been previously used in another study (as a reference is provided for it). Was it previously validated? Please clarify this.

Answer: Thanks for the comment. The questionnaire was developed by "Fundación Vivir con Crohn y CUCI A.C"; gastroenterologists and health advocates of Hospital C.M.N. "20 de Noviembre", ISSSTE, in 2020. It is an original questionnaire, without prior use. Two gastroenterologists in the group validated the 15 questions. A pilot test of the questionnaire was carried out with 5% of the population (23 people with IBD who attended the hospital), to ensure the validity of the questionnaire.

Reviewer 1: As the questionnaire was posted on Facebook site, there may be a bias for

including only patients with internet access (which could be associated, for example, with younger age, higher educational status, etc.). This potential limitation should be discussed in the Discussion section.

Answer: Thank you for the suggestion. It will be added as a limitation in the discussion.

.....Although there is growing evidence to suggest that Facebook is a useful recruiting tool and therefore its use should be considered when implementing future health research. However, one of the important limitations of this study is Internet access....

Whitaker, C., Stevelink, S., & Fear, N. (2017). The Use of Facebook in Recruiting Participants for Health Research Purposes: A Systematic Review. Journal of medical Internet research, 19(8), e290. <https://doi.org/10.2196/jmir.7071>

Reviewer 1: In this respect, inclusion criteria were Mexican adults, aged 18 to 45 years old. Please justify this. This could induce another bias, as older patients could have lower internet access. Therefore, the results of the present study could have been biased to more favorable findings. This potential limitation should also be discussed in the Discussion section.

Answer: Thanks for the suggestion. The inclusion criterion based on the age of 18 to 45 years of age, was chosen because in previous studies it is presented primarily to people of productive age (Sairenji, T., Collins, K. L., & Evans, D. V. (2017). An Update on Inflammatory Bowel Disease. Primary care, 44(4), 673–692. <https://doi.org/10.1016/j.pop.2017.07.010>. Kamp, K., Dudley-Brown, S., Heitkemper, M., Wyatt, G., & Given, B. (2020). Symptoms among emerging adults with inflammatory bowel disease: a descriptive study. Research in nursing & health, 43(1), 48–55. <https://doi.org/10.1002/nur.21985>)

Reviewer 1: It is stated that the sample size was calculated using the central limit theorem with a margin of error of 5% and a confidence interval of 95%. However, more details should be provided, and the calculated sample size should be given.

Answer: According to a previous study by Yamamoto et al., 2015, the prevalence of IBD in Mexico is 150,000, and considering an expected prevalence difference and an acceptable error of 5%, the following calculations were made:

$N = Z_{\alpha/2} p_1 - pd^2$

N = Sample size calculation; $Z_{\alpha/2}$ = Z value of the alpha error with 95% confidence, assigning $\alpha = 0.05$; P = expected population prevalence for the event under study (Yamamoto et al., 2015); d = Difference between the expected population prevalence value and the acceptable error. Values: $Z_{\alpha/2} = 1.96$; $p = 0.38$; $d = 0.30$.

$N = 1.9620.381 - 0.380.302 = 384$

This means that if you survey 384 people, the actual data you are looking for will be 95% of the time in the $\pm 5\%$ range relative to the data you see in the survey.

Reviewer 1: Statistical analysis: It is stated that “Initially, a univariate analysis was carried out”. This seems to imply that a multivariate analysis was also performed, but I cannot see any information regarding it.

Answer: *Thank you for your comment. Only univariate analysis was performed*

RESULTS

Of the 460 patients who participated in the questionnaire, there was a much greater number of patients with a diagnosis of ulcerative colitis (386; 83.9%) than Crohn's disease (74, 16.0%). Even though the authors point out that "The predominance of UC over CD is similar to that reported in other countries in Asia and Latin American countries, such as Colombia", and they comment in the Discussion section that "The limitations of the study were that there was a much greater number of participants with ulcerative colitis than Crohn's disease", these explanations seem to be insufficient. Please try to explain better this possible bias.

Answer: *Thanks for the suggestion. We add the explanation*

"The limitations of the study were that there was a much greater number of participants with ulcerative colitis than Crohn's disease". Although the trend of IBD is similar to other countries, the lack of epidemiological data in Mexico is still a challenge to understand the true number of IBD cases.

Yamamoto-Furusho, J. K., Bosques-Padilla, F. J., Charúa-Guindic, L., Cortés-Espinosa, T., Miranda-Cordero, R. M., Saez, A., & Ledesma-Osorio, Y. (2020). Inflammatory bowel disease in Mexico: Epidemiology, burden of disease, and treatment trends. *Epidemiología, carga de la enfermedad y tendencias de tratamiento de la enfermedad inflamatoria intestinal en México. Revista de gastroenterología de México*, 85(3), 246–256.
<https://doi.org/10.1016/j.rgmx.2019.07.008>

The same is valid for the predominance of women (327, 71%) over men (133, 28.9%), please try to explain this misbalance.

Answer: *Thanks for the suggestion. We add the explanation*

The predominance of women (327, 71%) over men (133, 28.9%), this imbalance may be due to environmental factors such as the use of oral contraceptives, psychosocial stress, dietary factors, among others. On the other hand, it has been described that the use of social networks is more frequent in women than in men, so it can also be attributed that there is a greater number of women.

Grosberg, D., Grinvald, H., Reuveni, H., & Magnezi, R. (2016). Frequent Surfing on Social Health Networks is Associated With Increased Knowledge and Patient Health Activation. *Journal of medical Internet research*, 18(8), e212. <https://doi.org/10.2196/jmir.5832>
Algethmi, W., Baumann, C., Alnajjar, W., Sroji, A., Alsaahfi, M., Jawa, H., Qari, Y., Peyrin-Biroulet, L., Saadah, O. I., & Mosli, M. (2020). Environmental exposures and the risk of inflammatory bowel disease: a case-control study from Saudi Arabia. *European journal of gastroenterology & hepatology*, 32(3), 358–364.
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Ho, S. M., Lewis, J. D., Mayer, E. A., Plevy, S. E., Chuang, E., Rappaport, S. M., Croitoru, K., Korzenik, J. R., Krischer, J., Hyams, J. S., Judson, R., Kellis, M., Jerrett, M., Miller, G. W., Grant, M. L., Shtraizent, N., Honig, G., Hurtado-Lorenzo, A., & Wu, G. D. (2019). Challenges in IBD Research: Environmental Triggers. *Inflammatory bowel diseases*, 25(Suppl 2), S13–S23. <https://doi.org/10.1093/ibd/izz076>

DISCUSSION

It is repeatedly stated that: “The majority of participants were uninformed, which can lead to a deterioration in the quality of life”. And that “They also said that the FC test had never been performed on them and that their specialist doctor had never suggested performing the FC test. This highlights the scarcity of knowledge regarding this test in treating patients with IBD, and that the doctor-patient relationship seems deficient”. However, it should also be clarified that the lack of knowledge of the patient does not necessarily imply that the doctor has not informed the patient correctly, since it is possible that the determination of FC is simply not indicated in them. In other words, it is clear that FC is not always indicated in all patients, and for those patients, this information could be correctly omitted. Please clarify this in the Discussion section.

Answer: Thanks for the comment. We add the explanation.

This information cannot necessarily be omitted, since clinical guidelines such as that of European Crohn’s and Colitis Organization [ECCO] the European Society of Gastrointestinal, Abdominal Radiology [ESGAR], British Society of Gastroenterology consensus guidelines and Mexican guidelines for the Diagnosis and Treatment of IBD in the Adult Population, recommend the use of the fecal calprotectin test in various clinical settings, including initial diagnosis, relapse diagnosis and response to treatment.

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