

Variation in Inflammatory Bowel Disease Care among Saudi Pediatric Gastroenterologists

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ABSTRACT

Background/Aim: Although international guidelines in inflammatory bowel disease (IBD) management are currently available, variations in IBD care still exist. The aim of this study was to determine the extent of the variation in IBD care among Saudi pediatric gastroenterologists. **Materials and Methods:** A cross-sectional survey was conducted among all pediatric gastroenterologists who were members of the Saudi Society of Pediatric Gastroenterology, Hepatology, and Nutrition (SASPGHAN) from August 2015 to December 2015. The questionnaire included items on demographic characteristics and utilization of different diagnostic and therapeutic interventions in IBD care. **Results:** Of the 45 registered pediatric gastroenterologists surveyed, 37 (82%) returned the survey from 20 centers across the country; 75.7% were practicing in tertiary care centers. There was a considerable variation in the use of different diagnostic tests during the initial evaluation of the disease. Utilization of calprotectin assays, magnetic resonance imaging enterography, and bone densitometry seemed to vary the most between physicians practicing at tertiary and secondary care centers. There were statistically significant differences in the prescription of biological therapy between the two groups. **Conclusions:** We found a considerable variation in the use of different diagnostic and therapeutic interventions in the management of pediatric IBD patients. Such variations could lead to unintended differences in patient outcomes. Implementation of the available evidence-based guidelines may limit such variations and ultimately could improve the quality of IBD care provided.

Key Words: Children, inflammatory bowel disease, Saudi, variation of care

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The prevalence of inflammatory bowel disease (IBD) is increasing in the Kingdom of Saudi Arabia (KSA). El Mouzan *et al.* found that the overall incidence rate of IBD in Saudi children is 0.47 per 100,000 individuals, even though the rate is lower than that reported from western countries, it has gradually increased over time.^[1]

Though there are published international guidelines available from different organizations such as the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN), the European Society for Pediatric

Gastroenterology, Hepatology, and Nutrition (ESPGHAN), and the European Crohn's and Colitis Organization (ECCO) regarding IBD management, variations in IBD care among pediatric gastroenterologists still exist in daily practice.^[2-4]

Several factors could explain such variations, which include disease-related factors, availability of resources, geographic region, hospital volume, and the experience of the treating physicians. In addition, poor adherence to evidence-based guidelines by the physicians themselves has been described.^[3] Adherence to evidence-based guidelines has been shown to reduce the variation in care and improve patient outcomes.^[5]

Recognizing such variation and identifying the underlying reasons are important because of the potential impact

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on resource utilization, costs, and patient outcomes. Appropriately addressing these issues could help in uniformly providing high quality medical care for these patients.^[6,7]

This study aimed to determine the extent of variation in IBD care among Saudi pediatric gastroenterologists.

MATERIALS AND METHODS

We designed and conducted a cross-sectional survey in which we invited all pediatric gastroenterologists who were members of the Saudi Society of Pediatric Gastroenterology, Hepatology, and Nutrition (SASPGHAN) to participate in this study. An online link leading to the questionnaire was sent to all the members between August 2015 and December 2015. A reminder follow-up email was sent 2 weeks after the initial invitation. We only included the active practicing members of the SASPGHAN group at the time of the initial survey. Fellows under training were excluded from participation in the study.

We designed a questionnaire with three sections; the first section contained questions regarding the demographic data of the participating physician, including sex, practice setting (secondary versus tertiary), and years of experience. The second section assessed the variation in the utilization of different diagnostic tests during the initial evaluation of the disease. Finally, the third section focused on the variation in IBD management parameters.

The content of the survey was reviewed by 2 local content-expert pediatric gastroenterologists. We then carried out a pilot study among 5 senior pediatric gastroenterologists as a pre-test for the validation of the survey and to ensure its readability and comprehensiveness.

Analysis

Each variable was initially described using descriptive statistics. Where relevant, we used the χ^2 test (or its alternative the Fisher Exact test if any cell count was less than 5) for categorical variables to measure the differences between physicians. A *P* value of <0.05 was considered significant. Statistical Package for the Social Sciences (SPSS, version 21, Chicago, IL, USA) was used for statistical analysis of the data.

Ethical considerations

The study protocol was approved by the institutional research board (IRB) at the King Khalid University Hospital, King Saud University (KSU). The completion and return of the questionnaire were regarded as consent. All responses were anonymous.

RESULTS

Of the 45 pediatric gastroenterologists registered in the SASPGHAN membership directory at the beginning of the survey, 37 (82%) completed and returned the survey from 20 centers across the country. Overall, 51.4% of the respondents were practicing in the central province and 75.7% in tertiary care centers. The majority of the respondents were males (89%). Table 1 describes the baseline characteristics of the survey respondents.

We divided the participants into two groups, according to the setting of their practice to explore the effect of the center setting on the variation in the care provided; Group 1 included physicians practicing at secondary care centers, *n* = 9 (24.3%), and Group 2 consisted of physicians practicing at tertiary care centers, *n* = 28 (75.7%).

Variation in utilization of diagnostic tests at the initial evaluation of the disease

Figure 1 displays the variation between the pediatric gastroenterologists in the utilization of different diagnostic tests during the initial evaluation of the disease.

When participants were asked about the imaging tools used for evaluating small bowel disease, magnetic resonance imaging (MRI) enterography was reported to be utilized

Table 1: Baseline characteristics of the participating pediatric gastroenterologists, *n*=37

Characteristics	<i>n</i> (%)
Sex	
Male	33 (89.2)
Female	4 (10.8)
Practice setting	
Secondary	9 (24.3)
Tertiary	28 (75.7)
Years of practice	
1-5 years	11 (29.7)
6-10 years	15 (40.5)
More than 10 years	11 (29.7)
Geographic location	
Central province	19 (51.4)
Western province	9 (24.3)
Eastern province	4 (10.8)
Southern province	4 (10.8)
Northern province	1 (2.7)
Number of patients with IBD per center	
1-20	21 (56.8)
21-40	6 (16.2)
41-60	5 (13.5)
61-80	5 (13.5)

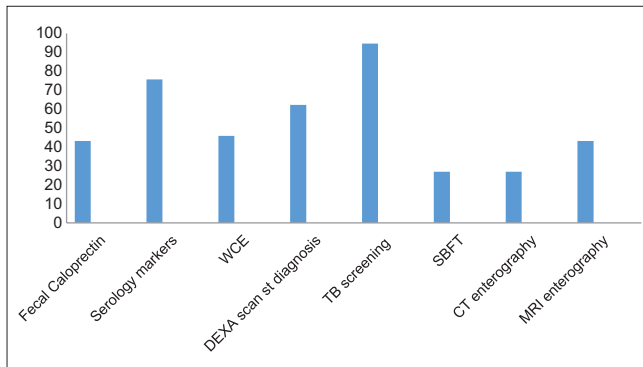


Figure 1: Variation in utilization of diagnostic tests at the initial evaluation of inflammatory bowel disease

by 16 (43.2%), while small bowel follow through (SBFT) and computed tomography (CT) enterography were each utilized by 10 (27%). Wireless capsule endoscopy (WCE) was utilized by 17 (45.9%) respondents at least once during their practice for disease assessment. Bone densitometry assessment using dual-energy X-ray absorptiometry (DEXA) scan was performed by 23 (62.2%) respondents during the initial evaluation of the disease.

We compared the utilization of these diagnostic tests between the two groups (physicians practicing at secondary care centers versus those practicing at tertiary care centers). We found a significant variation in the use of calprotectin assays, MRI enterography, and DEXA scans, which were utilized more frequently by the physicians practicing at the tertiary care centers compared to those practicing at the secondary care centers ($P = 0.005$, $P = 0.006$, $P = 0.001$, respectively), who tended to utilize computed tomography (CT) enterography more often to evaluate small bowel disease ($P = 0.041$). There were no statistically significant differences in the utilization of the other diagnostic tests. The physician's years of experience did not influence the utilization pattern between the two groups. Table 2 displays the results of the comparison of the different diagnostic tests utilized between the two groups.

Variations in the pattern of inflammatory bowel disease management

Most of the participants 34 (91.9%) reported that they currently do not have a protocol for IBD management at their respective centers; however, most of them reported that they followed the internationally published guidelines from the NASPGAN, the ESPGHAN, and/or the ECCO.

When participants were asked about the first-line choice of medications used for the induction of remission in patients with moderate-severe colitis, 22 (59.5%) reported that they prescribed combination therapy of aminosaliclates and steroid, 13 (35.1%) reported using steroid monotherapy, whereas only 2 (5.4%) reported using biological therapy. We

Table 2: Variation in the utilization of different diagnostic tests according to the practice setting of the participated pediatric gastroenterologist

Variable	Response n (%)	Care level			P
		Secondary (n=9)	Tertiary (n=28)	Total n (%)	
Serology	Yes	6 (66.7)	22 (78.6)	28 (75.7)	0.657
	No	3 (33.3)	6 (21.4)	9 (24.3)	
Calprotectin assay	Yes	0 (0)	16 (57.1)	16 (43.2)	0.005
	No	9 (100)	12 (42.9)	21 (56.8)	
TB screening tests	Yes	8 (88.9)	27 (96.4)	35 (94.6)	0.432
	No	1 (11.1)	1 (3.6)	2 (5.4)	
WCE	Yes	2 (22.2)	15 (53.6)	17 (45.9)	0.137
	No	7 (77.8)	13 (46.4)	20 (54.1)	
DEXA scan	Yes	1 (11.1)	22 (78.6)	23 (62.2)	0.001
	No	8 (88.9)	6 (21.4)	14 (37.8)	
SBFT	Yes	4 (55.6)	6 (21.4)	10 (27)	0.215
	No	5 (44.4)	22 (78.6)	27 (73)	
CT enterography	Yes	5 (55.6)	5 (17.9)	10 (27)	0.041
	No	4 (44.4)	23 (82.1)	27 (73)	
MRI enterography	Yes	0 (0)	17 (60.7)	17 (45.9)	0.006
	No	9 (100)	11 (39.3)	20 (54.1)	

WCE: Wireless capsule endoscopy; CT: Computed tomography; SBFT: Small bowel follow through; DEXA: Dual-energy X-ray absorptiometry

did not find any significant variation between the two groups in regards to prescription of medications.

When participants were asked about their first-line choice of medications used for maintenance therapy in patients with moderate-to-severe colitis, the majority (83.8%) reported using immune-modulator medications (IMMs) with or without aminosaliclates, 10.8% reported using aminosaliclates alone, whereas only 5.4% reported using biological monotherapy. There was no significant variation between the two groups with regards to their use of medications. In addition, we did not find any statistically significant difference according to the physicians' level of experience.

Thiopurines (azathioprine or mercaptopurine) were the first IMMs used by all the respondents. Fifteen (40.5%) reported starting thiopurines routinely 2–4 weeks after starting induction therapy, 13 (35.1%) reported starting thiopurines routinely at the beginning of the treatment (concomitantly with the induction therapy), and 9 (24.3%) reported that IMM usage was limited to patients with frequent flare ups who were on aminosaliclates or for patients who were steroid-refractory/dependent.

Assessment of thiopurine methyltransferase (TPMT) activity before the initiation of thiopurines was reported by only 10 (27%) of the respondents.

Exclusive enteral nutrition (EEN) for induction of remission in patients with luminal Crohn's disease (CD) was used by

23 (62.2%) respondents; however, only 7 (19%) reported regular use for their patients, while 14 (37.8%) reported that they never used EEN before.

Twenty-four (64.9%) of the respondents used biological therapy at least once in their practice; anti-tumor necrosis factor (anti-TNF), particularly infliximab, was their first choice. Among the biological therapy prescribers, 15/24 (62.5%) reported using combination therapy (anti-TNF with IMMs), whereas 9/24 (37.5%) reported using anti-TNF as a monotherapy. Almost 42% of respondents reported measuring anti-TNF trough levels and anti-drug antibody levels to monitor the medication effects; the remainder (58.3%) reported that they never measured anti-TNF trough level or anti-drug antibodies because of limited access to these tests.

Eighteen (48.6%) of the respondents reported stopping at least one of the immune-suppressant mediations (IMM or biological therapy) for patients with sustained remission. Of these, 8/18 (44.4%) reported stopping the medications within 2–3 years of achieving a full clinical and biochemical remission, 5/18 (27.8%) reported stopping therapy after 3 years, 2/18 (11.1%) reported stopping after 6–12 months of achieving full clinical and biochemical remission, whereas the 3 remaining (16.7%) respondents did not answer this question. Only 13.5% of the respondents reported having a local policy for transition of care of adolescents.

When we compared the two groups with regards to different parameters of IBD care, we found significant variation in regards to the prescription of biological therapy, which was indicated more often by the physicians practicing at tertiary care centers compared to those practicing at secondary care centers ($P = 0.042$). No other significant variations were

found between the two groups for any of the remaining measured parameters. Table 3 displays the pattern of variations in the different parameters of IBD care.

DISCUSSION

There is an increasing trend in the prevalence of IBD in the KSA, with an overall incidence rate of 0.47 per 100,000 individuals.^[1] This cross-sectional study was conducted to examine the variation in IBD care patterns among pediatric gastroenterologists. To our knowledge, this is the first study that addressed this question in this country. The high response rate (82%) of our sample likely reflects the real daily practice of pediatric gastroenterologists in the country.

The study showed that there is considerable variation in the IBD care provided by Saudi pediatric gastroenterologists, both in terms of utilizing different diagnostic tests for the initial evaluation of the disease and in some of the therapeutic interventions.

Utilization of calprotectin assays, MRI enterography, and bone densitometry seemed to vary the most between the physicians practicing at the tertiary care centers and those practicing at the secondary care centers. This most likely reflected the differences in hospital volumes and available resources between the secondary and tertiary care centers.

There was a considerable variation in the pattern of care provided for the different parameters of IBD management. The majority of the respondents (83.8%) reported prescribing thiopurines as their first choice for maintenance after induction of remission. The joint ECCO/ESPGHAN consensus guidelines recommend the use of thiopurines for maintenance

Table 3: The pattern of variations in different parameters of inflammatory bowel disease care

Variable	Response n (%)	Care level			P
		Secondary (n=9)	Tertiary (n=28)	Total n (%)	
Presence of local IBD protocol	Yes	2 (22.2)	1 (3.6)	3 (8.1)	0.141
	No	7 (77.8)	27 (96.4)	34 (91.9)	
Verification of immunization status before starting immunosuppressant drugs	Yes	5 (55.6)	19 (67.9)	24 (64.9)	0.691
	No	4 (44.4)	9 (32.1)	13 (35.1)	
Verification of TPMT levels before starting thiopurines	Yes	0 (0)	10 (35.7)	10 (27)	0.079
	No	9 (33.3)	18 (66.7)	27 (73)	
Use of nutritional therapy in induction of remission in patients with luminal CD	Yes	7 (77.8)	16 (57.1)	23 (62.2)	0.434
	No	2 (22.2)	12 (42.9)	14 (37.8)	
Prescription of biological therapy	Yes	3 (33.3)	21 (75)	24 (64.9)	0.042
	No	6 (66.7)	7 (25)	13 (35.1)	
Verification of anti-TNF trough level and anti-drug antibodies	Yes	0	10	10 (27)	0.079
	No	9	18	27 (73)	
Checking for mucosal healing	Yes	6 (66.7)	14 (50)	20 (54.1)	0.462
	No	3 (33.3)	14 (50)	17 (45.9)	
Stopping immunosuppressant medications for patients with sustained remission	Yes	4 (44.4)	14 (50)	18 (48.6)	1
	No	5 (55.6)	14 (50)	19 (51.4)	

IBD: Inflammatory bowel disease; TPMT: Thiopurine methyltransferase; CD: Crohn's disease

therapy after induction of remission for patients with ulcerative colitis (UC) and CD with moderate-severe activity.^[8,9]

The current joint consensus guidelines encourage TPMT genotyping and/or phenotyping (TPMT activity), if testing is available, to identify patients at risk of early profound myelosuppression.^[8,9] TPMT testing was practiced only by 27% of the respondents, all of whom were practicing at tertiary care centers; this, in fact, reflects the effect of the available resources on the care provided.

Anti-TNF agents are indicated for UC or CD patients with no response, loss of response, or intolerance to aminosalicylates and/or thiopurines maintenance therapy.^[8] Sixty-five percent of the respondents reported prescribing anti-TNF agents at least once during their practice as a maintenance therapy. Anti-TNF agents were prescribed more frequently by physicians practicing at tertiary care centers. This is not unexpected as these centers are larger and usually admit more severe cases. Almost 42% of the anti-TNF users reported measuring anti-TNF trough level and anti-drug antibody levels. The current guidelines concerning the recommendations for measuring anti-TNF trough level and anti-drug antibody levels are not clear.

Sixty-two percent of the respondents reported using combination therapy (anti-TNF and IMM), whereas 37.5% reported using anti-TNF alone as a monotherapy. It has been shown that combination therapy is associated with a lower rate of development of antibodies and loss of response;^[10] however, it may increase the risk of lymphoma, particularly hepatosplenic T-cell lymphoma in young males.^[11,12] Furthermore, more recent evidence has shown that combination therapy is not more effective than anti-TNF monotherapy in inducing or maintaining response or remission.^[13,14] The current ECCO/ESPGHAN consensus guidelines recommend treatment individualization based on benefit-risk stratification.^[9]

Mucosal healing is associated with improved outcomes in IBD patients;^[15] 54% of the respondents in the present study performed endoscopic evaluation to assess mucosal healing. However, there is no evidence available to suggest that endoscopic evaluation of mucosal healing is significantly superior to clinical judgment, according to the latest ECCO/ESPGHAN consensus guidelines.^[8]

In general, IMM and biological therapy should be continued for a prolonged period as long as they are effective; however, the question that always arises from the patients with IBD and their families is when these medications should be suspended. So far, answering this question remains a controversial issue.

Almost half of the respondents in the present study reported discontinuation of immune-suppressant medications (IMM or biological therapy) in patients with sustained remission. The timing of discontinuation varied between them; however, the majority reported withdrawal of these medications after 2–3 years of achieving sustained remission. It is important to keep in mind that 50% or more of the patients may relapse within 2 years of immune-suppressant discontinuation.^[16,17]

The current joint ECCO/ESPGHAN consensus guidelines for both UC and CD management recommend considering the discontinuation of immunosuppressant medications in patients with sustained remission for several years; however, not before growth and puberty is completed.^[8,9] Furthermore, the CD consensus guidelines clearly state “stopping all treatment is not advisable in children with CD except in a small minority of patients with very mild and limited disease on long period of remission.”^[9]

The exact timing of immunosuppressant discontinuation was discussed by a multidisciplinary European expert panel for adult patients with CD. The panel recommended that IMM monotherapy may be withdrawn after 4 years of clinical remission, whereas anti-TNF monotherapy can be withdrawn after 2 years of both clinical and endoscopic remission and after 4 years of clinical remission. In case of combination therapy, the panel recommended withdrawal of anti-TNF, while continuing the IMM after 2 years of clinical remission.^[18]

EEN has been proven to be effective in inducing remission in patients with luminal CD.^[19] The joint ECCO/ESPGHAN consensus guidelines recommend using EEN as the first-line therapy to induce remission in children with active luminal CD.^[9] In the present study, 63% used EEN for luminal CD at some stage, however, only 19% used it regularly for their patients. A survey of physician attitudes and practices of enteral nutrition in North America showed that 55% reported sparse use of EEN in children with CD and only 12% reported regular use.^[20] An Australian survey showed that 57% of the respondents felt that EEN was an appropriate therapy for CD; however, only 38% regularly used EEN for their patients.^[21] Almost 38% of the respondents in the present study reported that they never tried EEN as an induction therapy for luminal CD. They perceived compliance as the major barrier for increasing EEN usage in their practice. The patients' poor compliance to EEN is common and its effect on EEN utilization has been reported previously.^[20]

Optimization of immunizations is an important part of the preventive care of IBD patients.^[22] Almost 65% of the respondents in the present study reported checking immunization status before starting immunosuppressant

medications. In a recent survey, Lester *et al.* reported that 51% of the respondents in their survey verbally inquired regarding immunization status at diagnosis; 31% obtained records and 9% obtained serology.^[23]

The current immunization guidelines recommend vaccinating all IBD patients with inactivated vaccines, regardless of the immunosuppression status. However, administration of live vaccines (including the Rotaviral, MMR, Varicella, and intranasal influenza vaccines) is contraindicated in immunosuppressed patients because of concerns for possible vaccine-related adverse events.^[22,24]

IBD patients exhibit a higher risk for bone loss than the general population.^[25] Significant deficits in bone mineral density have been well-documented in children presenting with IBD; this was more obvious in patients with Crohn's disease.^[22,26,27]

The latest NASPGHAN clinical guidelines from 2011 strongly recommend obtaining a DEXA scan of the total body and the spine for children with IBD at presentation, or at any point if they have other risk factors such as suboptimal growth, puberty delay, prolonged use of steroids, and history of significant fractures.^[28] Sixty-two percent of the respondents in the present study reported that they requested DEXA scan for their patients at the initial evaluation. More awareness by clinicians is required to improve the practice of screening IBD patients at their initial presentation.

A smooth transition of the care of adolescents with IBD has been shown to be associated with better disease and development outcomes.^[29] In the present study, only 13.5% of the respondents reported having a local policy for the transition of care of adolescents. In a recent study, Gray *et al.* demonstrated similar findings whereby only 14% of the pediatric providers reported having a written transition protocol at their institution for IBD patients.^[30]

The joint ECCO/ESPGHAN consensus guidelines recommend, "Every adolescent should be included in transition programs that could be adapted according to the local organization of pediatric and adult facilities."^[8]

Our study is not without limitations. Although the sample size of the study is small, the response rate (82%) is sufficient enough to reflect the real-life practice of Saudi pediatric gastroenterologists. Half of the respondents are currently practicing in the central region of the country, which in fact represents the actual distribution of pediatric gastroenterologists in this country; however, this might limit the generalizability of our results to the whole country.

CONCLUSION

Our study indicates that there is considerable variability in the care provided for IBD patients among Saudi pediatric gastroenterologists. Such variations could lead to unintended differences in patient outcomes. Although the differences in available resources seem to be the primary source of the observed variations, further studies are still necessary to investigate other reasons for these differences and to determine their impact on patient outcomes. Pediatric gastroenterologists need to be aware of the available clinical guidelines and guarantee a greater adherence to them. Such awareness can be improved by organizing regular focused workshops and continuous medical education (SME) related seminars for practicing physicians to keep them updated. In addition, creation and implementation of local consensus guidelines can limit such variations in care and all these will ultimately improve the quality of care provided.

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Conflicts of interest

There are no conflicts of interest.

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