

Egyptian Perspectives in Tailoring Treatment Regimens for Patients With Inflammatory Bowel Disease: Step-Up Vs. Top-Down Approaches Survey

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Abstract

The prevalence of Inflammatory bowel disease has been rising worldwide causing significant health and economic burden. Treatment strategies in patients with IBD involve multiple pharmacological and surgical interventions and are based on disease severity, location of lesions, response to medications and co-morbidities.

The conventional treatment strategy for patients with IBD, namely “step-up” approach, involves initial therapy with amino salicylates and corticosteroids, followed by immunomodulators such as azathioprine and 6-mercaptopurine, then escalation to biological therapies as infliximab.

This step-up approach progresses through a therapeutic pyramid, considering medications at the top being more potent but posing more risk for adverse events or considered expensive.

The alternative treatment approach, referred to as “top-down” approach, involves the use of more potent drugs early in patient care to control disease progression and improve outcomes. Patients with active Crohn's disease benefit more from top-down approach than step-up approach.

Aim:

To evaluate the knowledge and compliance of physicians involved in management of patients with inflammatory bowel disease with the concept of “step-up vs. top-down” approaches in management of those patients. And, how they base their decisions when tailoring treatment regimens for their patients.

Methodology:

A self-administered questionnaire, designed according to European and US guidelines, using ten direct questions aiming at assessing Egyptian physicians who deal with patients with inflammatory bowel disease for their knowledge, background, site of practice, medication availability as well as the number of patients with inflammatory bowel disease they encounter. Also, the factors that control how they base their choice of treatment.

Results:

Two hundred and ten questionnaires were received out of the 300 distributed by email. Most of respondents work in University Hospitals. Approximately, 41% respondents reported that they encounter less than 5 patients every month. Around 29% of respondents noted that they have more than two biological therapies in their health care facility and 26% have only 2 types.

Majority of respondents (84%) were familiar with the concept of step-up vs. step-down approaches.

More than 50% of participants mentioned that they never start with biological therapy in moderate disease.

Around 60% of respondents believe that biological therapy should be given only to patients who failed conventional therapy with steroids with/without immune modulators, with severe complications or extraintestinal manifestations. Eighteen percent noted that it depends on the availability.

Conclusion:

Step up and Top-down approaches are well known to most physicians who deal with inflammatory bowel disease patients. Yet not everyone complies with those concepts. The most important causes for this are the old concepts of preserving biological therapy for patients who failed conventional therapy regardless of disease severity or complications. Also, availability and cost play a very important role in physicians' choice.

Introduction

The prevalence of Inflammatory bowel disease (IBD) has been rising worldwide causing significant health and economic burden. The most important types of IBD are Crohn's disease CD and ulcerative colitis UC.¹⁻³ Treatment strategies in patients with IBD involve multiple pharmacological and surgical interventions and are based on disease severity, location of lesions, response to medications and co-morbidities.² These treatment approaches aim at inducing and maintaining remission in patients with active disease, while avoiding long-term complications and improving their quality of life.^{2,4}

The conventional treatment strategy for patients with IBD, namely "step-up" approach, involves initial therapy with amino salicylates and corticosteroids, followed by immunomodulators such as azathioprine and 6-mercaptopurine, then escalation to biological therapies as infliximab.^{2,5} This step-up approach progresses through a therapeutic pyramid, considering medications at the top being more potent but posing more risk for adverse events or considered expensive.⁶ this approach requires failure of corticosteroids and azathioprine before considering biologic therapy.⁷

The alternative treatment approach, referred to as "top-down" approach, involves the use of more potent drugs early in patient care to control disease progression and improve outcomes. Biological treatments (e.g., infliximab, adalimumab, and vedolizumab, etc.), immunosuppressants (e.g., azathioprine, 6-mercaptopurine and methotrexate) or the combination of both treatments are administered immediately to induce early remission in patients with moderate to severe disease.^{2,6,7} Patients with active Crohn's disease benefit more from top-down approach than step-up approach.⁷ Most commonly, using infliximab combined with azathioprine is effective for achieving and maintaining steroid-free remission at an early stage of Crohn's disease. Unlike Crohn's disease, research on using top-down approach in Ulcerative Colitis remains inconclusive.^{4,7,8}

The heterogeneity of IBD pathology and presentation requires a personalized approach for each patient. Literature shows that there is considerable practice variability among physicians treating patients with IBD.^{9,10} This limit developing generalized treatment guidelines for IBD.^{9,10}

Patients And Methods

In this study, we surveyed 210 internal medicine physicians between 2nd September 2021 and 27th September 2021. They included 173 specialized gastroenterologists and the other 37 were nonspecialized gastroenterologists yet they were entitled to manage cases of IBD at their centers. We assessed the frequencies and reasons for using step-up versus top-down approaches as well as and the use of different biological agents for IBD treatment in their clinical practice.

A questionnaire was developed using ten direct questions aiming at assessing the tested population for their background, site of practice as well as the number of patients with inflammatory bowel disease they encounter.

Then those who took the survey were asked if they were familiar with the concept of step-up and top-down approaches. Also, the availability of biological therapies at their facilities and the reason why they choose to switch to biologics.

Results

Out of 210 Internal Medicine physicians who took the survey, 173 (82%) were gastroenterologists. Most of respondents (60%) work in University Hospitals, the rest are distributed between private clinics, teaching institutes, private hospitals, public hospitals, and military or police hospitals (Fig. 1).

Approximately, 41% respondents reported that they encounter less than 5 patients every month. Around 28% reported that they encounter between 5 and 10 patients monthly, 20% encounter between 10 and 30 patients, and only 7% encounter more than 30 patients every month.

One hundred and seventy-seven participants were familiar with the tested concept, and they represented 84.29% of the tested population.

Only 181 responded to the question whether they use the step-up or the top-down approaches. Out of those 147-participant mentioned that they use they step-up rather than the top-down approach and they represented 81.22%.

Around 29% of respondents reported that they have more than two biological therapies in their health care facility, 26% have 2 types and 18% have only one type, while 27% reported that biological therapies are not available in their health care facilities (Table 1).

Majority of respondents (84%) were familiar with the concept of step-up vs. step-down approach in treatment of IBD while 16% were unaware of the concept. Around 81% of respondents usually use the step-up approach, while 19% usually use the top-down approach in their practice.

More than 50% of participants mentioned that they never start with biological therapy in moderate disease. While 37.14% mentioned that they tailored their decision for each individual case, only 5%

reported that they sometimes start with biological therapy in patients with mild or moderate disease (Fig. 2).

Around 60% of respondents believe that biological therapy should be given only to patients who failed conventional therapy with steroids with/without immune modulators, with severe complications or extraintestinal manifestations. (Fig. 3).

When participants were asked about the causes for prescribing biological therapy, about 40% noted that failure of conventional therapy was the main reason followed by the clinical condition of the patient in about 34%. About 22% reported that it depends on the financial status of the patient. 18% noted that it depends on the availability (Table 2).

Table 1
Availability of Biological therapy

Do you have biological therapies available at your healthcare facility?		
Answer Choices	Responses	
Yes, more than 2 types available	29.05%	61
Yes, 2 types available	26.19%	55
yes, only one type available	18.10%	38
Not available	26.67%	56

Table 2
Factors affecting prescribing biological therapy:

Prescribing biological therapy in your facility depends on:		
Answer Choices	Responses	
Financial status of the patient	21.90%	46
Availability	17.62%	37
patient desire	2.86%	6
Clinical condition	34.76%	73
Failure of conventional therapy (Steroids+/- Immune-modulators)	40.95%	86
Other (please specify)	5.24%	11
	Answered	210

Discussion

Inflammatory bowel disease (IBD) is a group of disorders that cause chronic inflammation in the intestines. Management plans are tailored mostly according to patient factors. Although sometimes other factors play important role like availability and cost.

On one side the step-up approach, which refers to a sequential treatment strategy that often begins with a less potent, potentially less toxic treatment strategy, such as aminosalicylates, antibiotics, or budesonide, with escalation to the highly effective but potentially more toxic treatment strategies, such as prednisone, immunomodulators, and biological therapy, in patients who failed each line of therapy. In this strategy, one would avoid overtreatment and unnecessary exposure to the risk of developing adverse events.

On the other side, Top-down therapy has been proposed as an alternative idea starting with more potent drugs and deescalating according to the patient's response. It is agreed that the top-down approach can be very valuable in cases of Crohn's disease and may be in severe cases of ulcerative colitis⁶.

When we asked practitioners; the majority of respondents (84%) were familiar with the concept of step-up vs. step-down approaches which reflects the practitioners' good theoretical knowledge of the step-up and top-down approaches, practice guidelines and the recent advances made in the treatment of IBD in Egypt.

We further asked practitioners to specify the frequency of which they encounter IBD in their practice. Approximately, 41% of respondents reported that they encounter less than 5 patients every month. This can be explained by the prevalence of inflammatory bowel disease that is still rather low in Egypt despite the rising curve of newly diagnosed cases. but such low frequency of IBD encounters affects practitioners' familiarity with the disease, the overall comprehensive outlook on IBD, and the knowledge of the recent advances in IBD diagnosis and management.

In our study, more than 50% of participants mentioned that they never start with biological therapy in moderate disease. It is important to consider these results and the factors that might've led to such statistics. Limitations to the top-down approach include various factors like the clinical heterogeneity of early- and late-onset disease which makes IBD one of the diseases of which's treatment variables are difficult to control. The lack of familiarity with the biological therapy as well as immune modulators in regard to their safety and efficacy. Subsequently, this prevents practitioners from getting an overall comprehensive lookout on the efficacy of the top-down approach and thus explains the results at hand.

Furthermore, the created potential risks of over-treating patients with milder diseases are significant when using an aggressive first-line treatment for all patients. Also, creating a financial burden or limited availability are factors to be considered. All these factors combined have led practitioners to be hesitant to initiate biologic therapy.

Moreover, in our study, we found that around 60% of respondents believe that biological treatment should be given to patients who failed conventional treatment with steroids with/without immune modulators, with severe complications or extraintestinal manifestations, such results can be explained given that the primary costs related to hospitalization and surgery are reduced when patients are given anti-TNF

therapy. Furthermore, many studies have proposed that there are fewer adverse events with biological therapy in those cases than with corticosteroids. So, using an aggressive regimen for treating cases was conditioned to the for mentioned factors.

At present, practitioners in Egypt have held off on a top-down approach in milder, non-progressive cases and proceeded with a less aggressive approach such as step-up therapy and use the top-down approach when a more aggressive attempt at disease modification is warranted.

We believe that physicians who deal with IBD cases should be more familiar and comfortable when it comes to prescribing biological therapy. It's not necessarily associated with more risks or a higher cost as previously thought, as early control of the disease can spare the patient complications and in return extra cost.

Declarations

- **Ethics approval and consent to participate:**

All experimental protocols were approved by Cairo University ethical committee.

Informed consent was obtained from all subjects and/or their legal guardian(s).

- **Consent for publication:**

Not applicable

- **Availability of data and materials:**

All data generated or analyzed during this study are included in its supplementary information files.

- **Competing interests:**

Not applicable

- **Funding:**

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- **Authors' contributions:**

- Mohamed Negm: Came up with the idea, designed the survey and revised manuscript.
- Ahmed Cordie: distributed the survey, reviewed the results, and revised manuscript.
- Rawan ElGamal: wrote the introduction and results.
- Ranin Shawky: wrote the discussion and reviewed manuscript.
- Mario Rizk: revised references and tabulated all the data.

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Not applicable

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Figures

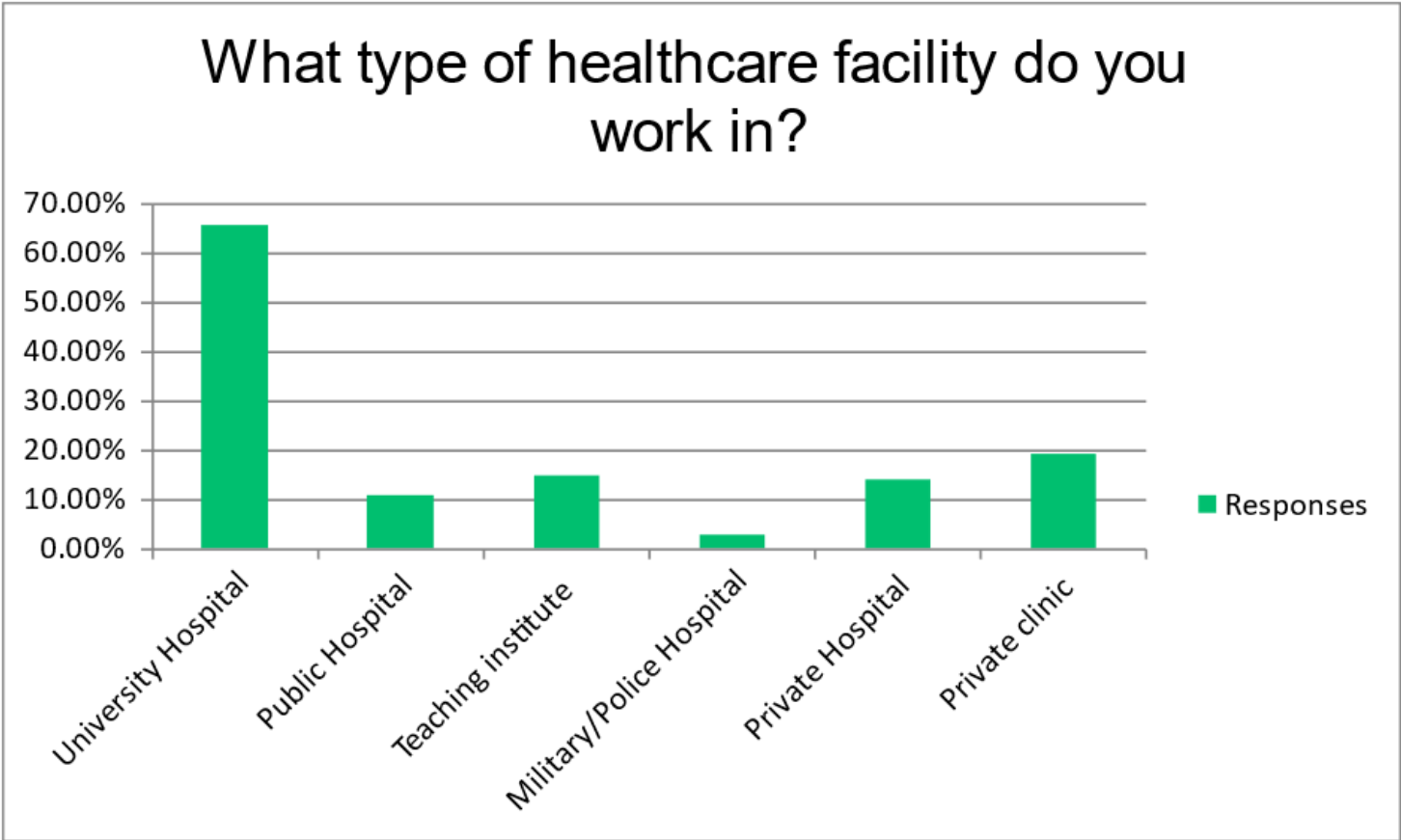


Figure 1

Type of healthcare facilities dealing with IBD patients:

Do you sometimes start with biological therapy in patients with moderate disease?

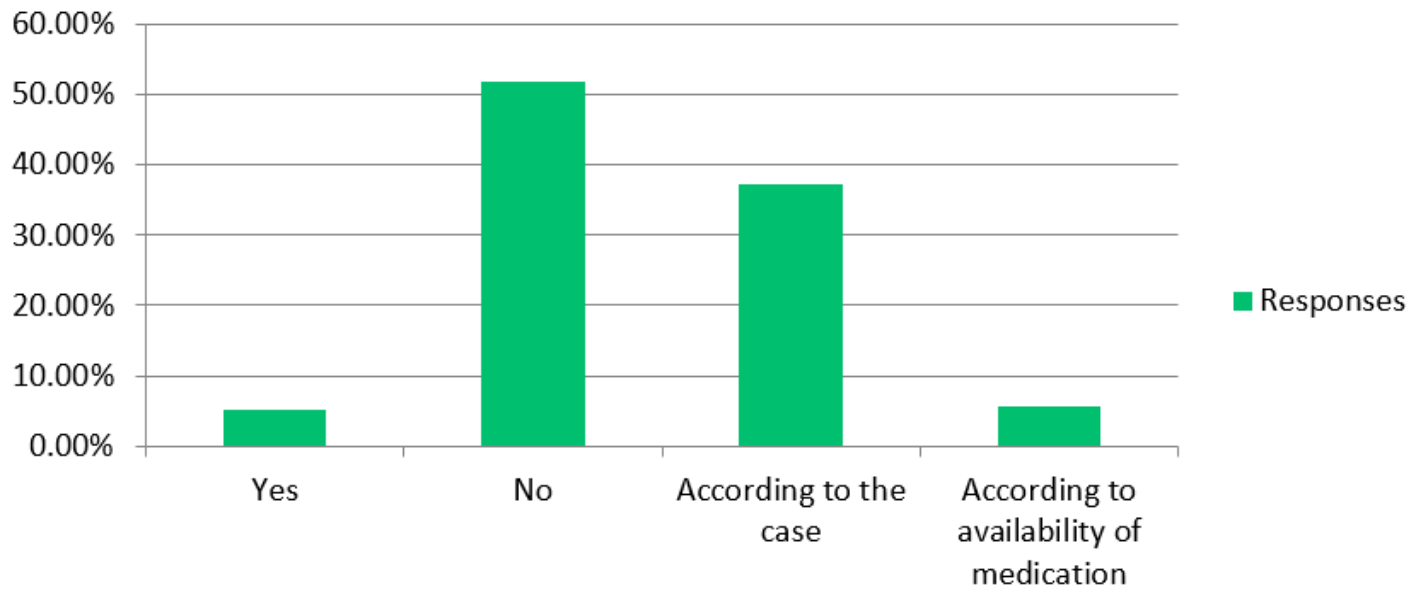


Figure 2

Starting biological therapy in moderate disease:

Do you think that biological therapy is only for patients who failed conventional therapy with steroids with/without immune-modulators, with severe complications or extraintestinal manifestations?

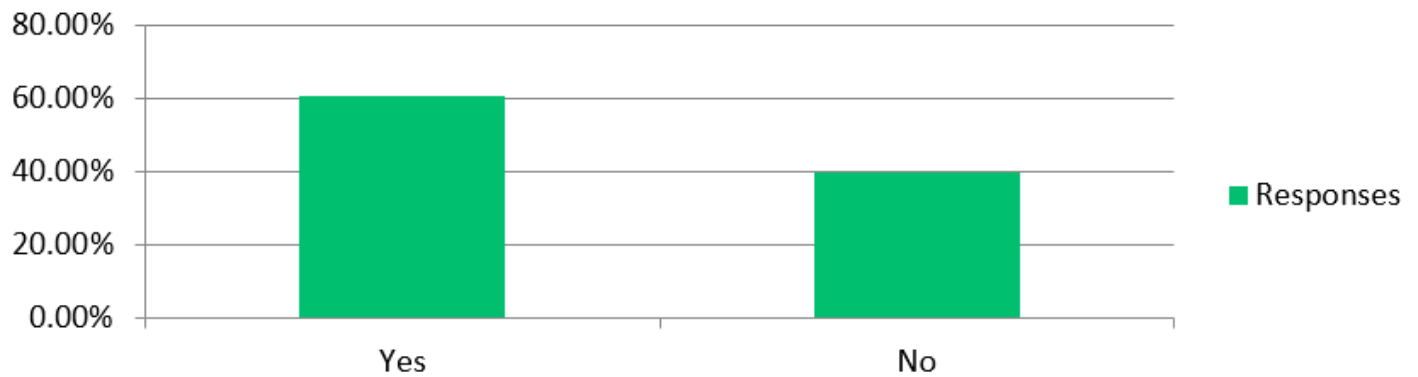


Figure 3

preservation of biological therapy for cases who failed conventional therapy:

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Inflammatoryboweldiseasestepupindividualanswersforeachphysician.xlsx](#)
- [Inflammatoryboweldiseasestepupvs.stepdownapproachesgraphsandanswerpercentages.xlsx](#)