GMR
The Original

# STEP-UP AND TOP-DOWN APPROACHES IN THE TREATMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE

**Ajmal[1*], Shamama Hassan[2], Salman Ibrahim[3], Hinif Ullah[4], Farkhanda Bakht[5], Muhammad Bilal[6]**

[1-6]Paediatric Gastroenterology & Hepatology, Combined Military Hospital, Rawalpindi
[*]**Corresponding author:** Dr Ajmal, Email: drajmalkhan44&gmail.com

**ABSTRACT**
**Objective:** To compare the efficacy of step-up and top-down treatment approaches in paediatric inflammatory bowel disease.
**Study Design:** Randomised controlled trial.
**Duration and Place of Study:** Conducted from 29 October 2025 to 29 March 2026 at the Department of Paediatrics Combined Military Hospital, Rawalpindi.
**Methodology:** A total of 68 children aged 2 to 17 years with Crohn disease were included. Group A received step-up therapy and Group B received top-down therapy. Clinical remission was assessed after 4 weeks using paediatric Crohn disease activity index score less than 10. Data were analysed using IBM SPSS version 26. Chi-square test and Fisher exact test were applied and p-value less than 0.05 was considered significant.
**Results:** Mean age was 9.21 ± 4.48 years in Group A and 7.76 ± 3.46 years in Group B. Males were 20 (58.8%) in Group A and 19 (55.9%) in Group B. Overall efficacy was significantly higher in top-down group with 26 (76.5%) compared to 7 (20.6%) in step-up group ($p<0.001$). Treatment failure was 27 (79.4%) in Group A and 8 (23.5%) in Group B. Significant associations of efficacy were observed with age ($p=0.003$), gender ($p=0.001$), weight ($p=0.001$), residential status ($p=0.001$), socioeconomic status ($p=0.001$), and disease duration ($p<0.001$).
**Conclusion:** Top-down therapy show more effective results in achieving clinical remission in paediatric inflammatory bowel disease as compared to step-up therapy.

**KEYWORDS:** Crohn disease, Inflammatory bowel diseases, Paediatrics, Remission induction, Therapeutics

## INTRODUCTION

Pediatric inflammatory bowel disease is a chronic inflammation disorder of the gastrointestinal tract that mostly includes Crohn disease and ulcerative colitis that is becoming more commonly seen in children.[1] This condition generally has symptoms including abdominal pain, chronic diarrhea, rectal bleeding, weight loss, and growth deficiency.[2] Its exact cause is not yet fully known, but researchers have suggested that it arises due to a complex interplay between genetics, immune dysfunction, and environment factors.[3] When it occurs in children, the disorder is seen to be more severe in comparison to that occurring in adults, and complications of the disease include malnutrition, puberty problems, and arthralgia or other extraintestinal symptoms.[4]

Step-up Therapy in Pediatric IBD is considered a classic therapy approach, which relies on less powerful drugs at first and escalates to the use of better ones in case the patient's condition is not manageable.[5] Usually, remission therapy starts with aminosalicylates, nutrition, and steroids, which are later accompanied by the introduction of immunomodulators like azathioprine or methotrexate, depending on the severity of the condition.[6] Severe cases can involve the application of biologics, especially anti-TNF drugs, at a later stage of the treatment process. This therapy is considered relatively safe at the beginning of the procedure since it does not imply the immediate use of powerful drugs but might lead to some delays with proper treatment and ongoing inflammation.[7]

The use of the top-down approach represents a more assertive therapeutic option that utilizes strong interventions, including biological therapies, in order to rapidly manage the disease process especially in those patients who have high chances of developing severe disease features.[8] It is expected to help manage inflammation, ensure mucosal healing and avoid any potential complications. This can be through the early use of anti-TNFs in combination or not with immunomodulatory drugs. While this method is effective in ensuring better disease management and growth benefits in children, there are also challenges such as infection, increased costs and potential safety concerns with biologics.[9]

There appears to be an increase in cases of pediatric IBD with more aggressive course, but there are still inadequate protocols on step-up versus top-down approach to treat them. Most of the existing literature involves data gathered from adults and not children. Late start with treatments can lead to poor development among others while early aggressive management poses more risks at greater cost. Thus, there is a requirement for the study to find out the most appropriate way of treating these patients without endangering their health.

## METHODOLOGY

This randomised controlled trial was carried out in the Department of Pediatrics at Combined Military Hospital Rawalpindi over a period from 29th October 2025 to 29th March 2026. Approval for the study was taken from the institutional ethical review committee of the hospital before starting the data collection and all procedures was conducted according to ethical standards. The total sample size was 68 patients divided equally into two groups with 34 patients in each arm. Sample size was estimated by using WHO sample size calculator with 80% power, taking anticipated efficacy of 25% in step-up approach and 57% in top-down approach.[10]

Inclusion Criteria: Children of either gender aged 2 to 17 years who presented with Crohn's disease for duration less than 1 year and having Pediatric Crohn's Disease Activity Index score ≥10 was included. The disease was considered present when there was persistent abdominal pain with score >5 on visual analogue scale occurring at least 3 times per week, or chronic diarrhoea with ≥3 loose stools per day, or weight loss more than 5% of body weight for more than 4 weeks, along with endoscopic findings such as skip areas of inflammation, multiple small aphthous ulcers less than 5 mm, cobblestone appearance of mucosa or intestinal narrowing.

Exclusion Criteria: Patients having previous intestinal surgery, prior use of immunomodulators or biologic therapy, severe malnutrition, contraindication to corticosteroids or history of liver disease was excluded. Written informed consent was taken from parents or caregivers before enrolment of each child, and confidentiality of data was ensured.

Baseline information was recorded including age, gender, weight, duration of complaints, family history of IBD and residential status. After selection, patients were allocated into two groups by blocked randomisation. Group A included 34 patients managed with step-up approach, while Group B included 34 patients managed with top-down approach. In Group A, treatment was started with oral mesalamine at dose 50 mg/kg/day in two divided doses for 2 weeks. If adequate response was not achieved, indicated by score remaining above 10, therapy was escalated to oral prednisolone at 1 mg/kg/day with maximum 40 mg/day for 8 weeks followed by tapering. In case of persistent moderate to severe disease with score above 30, azathioprine at dose 2 mg/kg/day was added. In Group B, patients were given infliximab 5 mg/kg intravenously at weeks 0, 2 and 6, along with azathioprine 2 mg/kg/day from start. In severe cases, short course of oral prednisolone 1 mg/kg/day was used for temporary control of symptoms.

All patients were assessed clinically both at baseline and following 4 weeks of medication using the Pediatric Crohn's Disease Activity Index (PCDAI). The PCDAI involves assessing clinical manifestations, examination results, laboratory markers (hematocrit, erythrocyte sedimentation rate, and albumin), and growth. Clinical remission was determined by the attainment of PCDAI score below 10 within 4 weeks of medication.

Data was analysed using IBM SPSS Statistics 26. Categorical variables such as gender, socioeconomic status, family history of IBD, residential status and efficacy was presented as frequencies and percentages. Continuous variables including age, weight and duration of complaints was expressed as mean ± standard deviation. Comparison between two groups was done by Chi-square test or Fisher exact test where required. A p-value less than 0.05 was taken as statistically significant. Stratification was applied for variables including age, gender, weight, duration of symptoms and family history of IBD and post-stratification analysis was again done using same statistical tests.

## RESULTS

In the present study the mean age of patients in Group A was 9.21 ± 4.48 years, whilst in Group B it was 7.76 ± 3.46 years. The mean weight in Group A was 29.56 ± 10.05 kg compared to 27.41 ± 8.69 kg in Group B. The mean duration of disease at presentation were 15.15 ± 8.03 weeks in Group A and 14.94 ± 6.53 weeks in Group B. With regards to gender distribution, males were slightly predominant in both groups, accounting for 20 (58.8%) in Group A and 19 (55.9%) in Group B, whereas females comprised 14 (41.2%) and 15 (44.1%) respectively. In terms of residential status, the majority of patients in Group A were from urban areas 21 (61.8%), compared to 18 (52.9%) in Group B, whilst rural residents constituted 13 (38.2%) and 16 (47.1%) in the respective groups. Regarding socioeconomic status, the middle class were most represented in both groups with 16 (47.1%) in Group A and 15 (44.1%) in Group B, followed by low socioeconomic class with 13 (38.2%) and 14 (41.2%) respectively, and the high socioeconomic class formed the smallest proportion at 5 (14.7%) in both groups. A family history of IBD was reported in 6 (17.6%) patients in Group A and only 2 (5.9%) in Group B (Table-I).

**Table I: Patient Demographics in Both Groups**

**n=68**

| **Variables** | **Step-Up Approach (Group A) n=34** | **Top-Down Approach (Group B) n=34** |
|---|---|---|
| | Mean ± SD | Mean ± SD |
| Age (years) | 9.21 ± 4.48 | 7.76 ± 3.46 |
| Weight (kg) | 29.56 ± 10.05 | 27.41 ± 8.69 |
| Duration (weeks) | 15.15 ± 8.03 | 14.94 ± 6.53 |
| **Gender** | **n (%)** | **n (%)** |
| Male | 20 (58.8%) | 19 (55.9%) |

| | | |
|---|---|---|
| Female | 14 (41.2%) | 15 (44.1%) |
| **Residence** | | |
| Rural | 13 (38.2%) | 16 (47.1%) |
| Urban | 21 (61.8%) | 18 (52.9%) |
| **Socioeconomic Status** | | |
| Low | 13 (38.2%) | 14 (41.2%) |
| Middle | 16 (47.1%) | 15 (44.1%) |
| High | 5 (14.7%) | 5 (14.7%) |
| **Family History of IBD** | | |
| Yes | 6 (17.6%) | 2 (5.9%) |
| No | 28 (82.4%) | 32 (94.1%) |

With respect to overall treatment efficacy, a statistically significant difference was observed between the two groups ($p<0.001$). The Top-Down approach demonstrated considerably higher efficacy, with 26 (76.5%) patients achieving a positive response, in comparison to only 7 (20.6%) in the Step-Up group. Conversely, treatment failure was much more prevalent in Group A at 27 (79.4%) as opposed to 8 (23.5%) in Group B (Table-II).

**Table II: Comparison of Efficacy between the Two Groups**

**n=68**

| Efficacy | Step-Up Group (A) n=34 n (%) | Top-Down Group (B) n=34 n (%) | P value |
|---|---|---|---|
| Yes | 7 (20.6%) | 26 (76.5%) | <0.001 |
| No | 27 (79.4%) | 8 (23.5%) | |
| Total | 34 (100%) | 34 (100%) | |

Among patients aged ≤10 years, efficacy was achieved in 4 (22.2%) in Group A and 19 (73.1%) in Group B ($p=0.003$), whilst among those aged >10 years, the figures were 3 (18.8%) and 7 (87.5%) respectively ($p=0.002$). Regarding gender, efficacy among males were 4 (20.0%) in Group A and 15 (78.9%) in Group B ($p=0.001$), and among females 3 (21.4%) and 11 (73.3%) respectively ($p=0.009$). Among patients weighing >20 kg, efficacy was noted in 5 (20.0%) and 18 (69.2%) in Groups A and B respectively ($p=0.001$). In the middle socioeconomic group, 4 (25.0%) in Group A and 13 (86.7%) in Group B achieved efficacy ($p=0.001$), whilst the high socioeconomic class showed no significant difference ($p=0.524$). Among urban residents, efficacy was reported in 6 (28.6%) and 16 (88.9%) in Groups A and B respectively ($p=0.001$). Among patients without a family history of IBD, efficacy was 6 (21.4%) in Group A and 24 (75.0%) in Group B ($p<0.001$), whereas those with a positive family history showed no significant association ($p=0.107$). With regards to disease duration, among patients with duration >12 weeks, no efficacy was observed in Group A (0.0%) compared to 15 (65.2%) in Group B ($p<0.001$) (Table-III).

**Table III: Association of Efficacy with Demographic Variables**

| Demographic Variables | Group | Yes n (%) | No n (%) | P-value |
|---|---|---|---|---|
| **Age (years)** | | | | |
| ≤10 | A | 4 (22.2%) | 14 (77.8%) | 0.003* |
| | B | 19 (73.1%) | 7 (26.9%) | |
| >10 | A | 3 (18.8%) | 13 (81.3%) | 0.002† |
| | B | 7 (87.5%) | 1 (12.5%) | |
| **Gender** | | | | |
| Male | A | 4 (20.0%) | 16 (80.0%) | 0.001* |
| | B | 15 (78.9%) | 4 (21.1%) | |
| Female | A | 3 (21.4%) | 11 (78.6%) | 0.009† |
| | B | 11 (73.3%) | 4 (26.7%) | |
| **Weight (kg)** | | | | |
| ≤20 | A | 2 (22.2%) | 7 (77.8%) | 0.002† |
| | B | 8 (100.0%) | 0 (0.0%) | |
| >20 | A | 5 (20.0%) | 20 (80.0%) | 0.001* |
| | B | 18 (69.2%) | 8 (30.8%) | |
| **Socioeconomic Status** | | | | |
| Low | A | 1 (7.7%) | 12 (92.3%) | 0.004† |
| | B | 9 (64.3%) | 5 (35.7%) | |
| Middle | A | 4 (25.0%) | 12 (75.0%) | 0.001† |
| | B | 13 (86.7%) | 2 (13.3%) | |
| High | A | 2 (40.0%) | 3 (60.0%) | 0.524† |
| | B | 4 (80.0%) | 1 (20.0%) | |

| | | | | |
|---|---|---|---|---|
| **Residential Status** | | | | |
| Rural | A | 1 (7.7%) | 12 (92.3%) | 0.006† |
| | B | 10 (62.5%) | 6 (37.5%) | |
| Urban | A | 6 (28.6%) | 15 (71.4%) | 0.001* |
| | B | 16 (88.9%) | 2 (11.1%) | |
| **Family History of IBD** | | | | |
| Yes | A | 1 (16.7%) | 5 (83.3%) | 0.107† |
| | B | 2 (100.0%) | 0 (0.0%) | |
| No | A | 6 (21.4%) | 22 (78.6%) | <0.001* |
| | B | 24 (75.0%) | 8 (25.0%) | |
| **Duration (weeks)** | | | | |
| ≤12 | A | 7 (46.7%) | 8 (53.3%) | 0.007† |
| | B | 11 (100.0%) | 0 (0.0%) | |
| >12 | A | 0 (0.0%) | 19 (100.0%) | <0.001* |
| | B | 15 (65.2%) | 8 (34.8%) | |

†Fisher's Exact Test, *Chi-square Test

**DISCUSSION**

In the current investigation, the total efficacy rate for the top-down group was significantly greater, with 26 (76.5%) responding positively compared with just 7 (20.6%) in the step-up group ($p < 0.001$). This result is largely due to the top-down strategy, where the early use of biological agents like infliximab targeting tumor necrosis factor-alpha is employed to achieve more effective inhibition of the inflammatory cascade before irreparable damage occurs to the bowels. As for the variable age, there was significantly superior efficacy in both the ≤10-year-old ($p = 0.003$) and >10-year-old patient groups ($p = 0.002$). This is probably because the disease is more advanced or progresses faster among younger children; thus, early intervention with biological therapies can help manage the inflammation at an earlier stage.

The present study findings have demonstrated that top-down approach was significantly more effective than step-up approach in paediatric IBD, with 26 (76.5%) patients achieving efficacy in top-down group compared to only 7 (20.6%) in step-up group ($p<0.001$). This agrees with Tsui *et al.* [11] who also reported that early combined biological therapy improved remission and outcomes in Crohn's disease, although they noted that early biologics alone did not consistently outperformed step-up therapy. Similarly, Spencer *et al.* [12] reported markedly better outcomes with early therapy, where CHARM trial showed remission rates of 43% in patients with shorter disease duration, which is comparable to the superior efficacy observed with top-down approach in present study. Lee *et al.* [13] also reported that top-down use has increased considerably over time, with corticosteroid use being significantly lower in top-down group (32.5% vs 94.2%), further supporting the growing clinical preference for early aggressive therapy.

Regarding age-related findings, both younger and older patients showed significantly better efficacy with top-down approach ($p=0.003$ and $p=0.002$ respectively), which is supported by Shambayati *et al.* [14] who emphasised that paediatric IBD tends to be more aggressive with higher complication rates, thus warranting early effective intervention. Furthermore, Spencer *et al.* [12] reported in the paediatric RISK cohort that remission was achieved in 85.3% with early anti-TNF therapy versus 60.3% without ($p=0.0017$), which is broadly consistent with the present findings.

With regards to disease duration, patients with duration more than 12 weeks showed no efficacy in step-up group (0.0%) compared to 15 (65.2%) in top-down group ($p<0.001$), suggesting that delayed treatment allows progressive mucosal damage to occur. This is supported by Rogler *et al.* [15] who demonstrated that early aggressive treatment reduces hospitalisations and surgeries, and by Spencer *et al.* [12] where PRECiSE 2 trial showed 90% response in early treatment versus only 57% in late treatment, highlighting the critical importance of timely intervention.

Patients without family history of IBD showed significantly better response in top-down group 24 (75.0%) versus 6 (21.4%) in step-up group ($p<0.001$), whilst positive family history subgroup did not reached significance ($p=0.107$), likely due to very small sample size. Shambayati *et al.* [14] reported that approximately 20% of paediatric IBD patients has a family history, which is somewhat comparable to 17.6% observed in Group A of present study, though no specific efficacy comparison by family history was made in that study.

In contrast to present findings, Bradley *et al.* [16] emphasised predominance of step-up therapy in paediatric ulcerative colitis and reported limited rationale for top-down approach, particularly highlighting effectiveness of 5-ASA as first-line therapy. This difference may be because Bradley *et al.* [16] focused specifically on ulcerative colitis where mucosal disease may responds better to conventional therapy, whereas present study included broader paediatric IBD population where Crohn's disease with transmural inflammation may requires early aggressive biological therapy.[17,18]

There are a number of shortcomings associated with the current study that need to be acknowledged. Firstly, this study was conducted in a single centre and therefore might not be easily generalizable to the wider cohort of

pediatric IBD patients. The sample size used for the study was relatively small as it involved just 68 participants, which might have undermined the ability of the study to draw valid conclusions in relation to the analysis conducted among the sub-group with a positive family history.

## CONCLUSION

According to the results of the current study, the top-down method appears to be much more efficient in achieving clinical remission in pediatric inflammatory bowel disease than the step-up approach. This superiority of the top-down strategy was confirmed by all demographic subgroups of patients.

**Acknowledgment**

Author thankful to medical staff of department their hard work in keeping records and organizing patient data help a lot for this study completion.

**Conflict of Interest:**

Author state there is no any conflict of interest related to this study.

**REFERENCES**:

1. Al-Beltagi M, Saeed NK, Mani PKC, Bediwy AS, Elbeltagi R. Inflammatory bowel disease in paediatrics: navigating the old challenges and emerging frontiers. *World J Gastroenterol*. 2025;**31**(35):111934. DOI: https://doi.org/10.3748/wjg.v31.i35.111934
2. Pivac I, Jelicic Kadic A, Despot R, Zitko V, Tudor D, Runjic E, *et al.* Characteristics of the inflammatory bowel disease in children: a Croatian single-centre retrospective study. *Children (Basel)*. 2023;**10**(10):1677. DOI: https://doi.org/10.3390/children10101677
3. El-Matary W. Advances in nutritional management of pediatric inflammatory bowel disease. *Nutrients*. 2021;**13**(2):324. DOI: https://doi.org/10.3390/nu13020324
4. Gurler E, Gerenli N, Celtik C, Dursun F, Kirmizibekmez H. Pediatric inflammatory bowel diseases: effects of disease and treatment regimens on growth and puberty. *North Clin Istanb*. 2025;**12**(4):396-403. DOI: https://doi.org/10.14744/nci.2024.93342
5. Ashton JJ, Beattie RM. Inflammatory bowel disease: recent developments. *Arch Dis Child*. 2024;**109**(5):370-376. DOI: https://doi.org/10.1136/archdischild-2023-325668
6. Bhalla A, Shahi A, Maity M, Safa F, Srividya V, Clementina R, *et al.* Inflammatory bowel disease in children: current diagnosis and treatment strategies. *Cureus*. 2025;**17**(2):e78462. DOI: https://doi.org/10.7759/cureus.78462
7. Claßen M, de Laffolie J, Claßen M, Schnell A, Sohrabi K, Hoerning A, *et al.* Significant advantages for first line treatment with TNF-alpha inhibitors in pediatric patients with inflammatory bowel disease - data from the multicenter CEDATA-GPGE registry study. *Front Pediatr*. 2022;**10**:903677. DOI: https://doi.org/10.3389/fped.2022.903677
8. Hathagoda W, Rajindrajith S, Niriella MA. Challenges in the management of inflammatory bowel disease in children: a narrative review. *Clin Exp Gastroenterol*. 2025;**18**:259-275. DOI: https://doi.org/10.2147/CEG.S557464
9. Noor NM, Davies N, Tahir W, Bond S, Dowling F, Patel KV, *et al.* Anti-tumor necrosis factor treatment from diagnosis is more effective and less costly than conventional "step-up" care for patients with active Crohn's disease: a cost-effectiveness analysis from the PROFILE trial. *J Crohns Colitis*. 2025;**19**(9):jjaf150. DOI: https://doi.org/10.1093/ecco-jcc/jjaf150
10. De Caro G, Lugani P, Fornaroli F, Vincenzi F, Bizzarri B, Manfredi M, *et al.* The clinical and endoscopic efficacy of step-up and top-down therapy in pediatric Crohn's disease. *Am J Gastroenterol*. 2015;**110**(Suppl 1):S823
11. Tsui JJ, Huynh HQ. Is top-down therapy a more effective alternative to conventional step-up therapy for Crohn's disease? *Ann Gastroenterol*. 2018;**31**(3):1-12. DOI: https://doi.org/10.20524/aog.2018.0253
12. Spencer EA. Choosing the right therapy at the right time for paediatric IBD. 2023. DOI: https://doi.org/10.1016/S0889-8553(23)00057-2
13. Lee WJ, Todd A Lee, Gregory S Calip, Katie J Suda, Glen T Schumock. Top-down versus step-up prescribing strategies for TNF inhibitors in paediatric IBD. University of Illinois; 2013.
14. Shambayati M. Advances in paediatric inflammatory bowel disease. Integris Baptist Medical Centre; 2018.
15. Rogler G. Top-down or step-up treatment in Crohn's disease? *Dig Dis*. 2013;**31**:83-90. DOI: https://doi.org/10.1159/000347190
16. Bradley GM, Oliva-Hemker M. Paediatric ulcerative colitis: current treatment approaches including role of infliximab. *Biologics*. 2012;**6**:125-134. DOI: https://doi.org/10.2147/BTT.S31833
17. Cushing K, Higgins PDR. Management of crohn disease: a review. *JAMA*. 2021;**325**(1):69-80. DOI: https://doi.org/10.1001/jama.2020.18936
18. Garcia NM, Cohen NA, Rubin DT. Treat-to-target and sequencing therapies in crohn's disease. *United European Gastroenterol J*. 2022;**10**(10):1121-1128. DOI: https://doi.org/10.1002/ueg2.12336