

# Effect of Early Corticosteroid Use in Inflammatory Bowel Disease with Clostridioides Difficile Infection: Systematic Review and Meta-analysis.

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**Background:** Inflammatory bowel disease (IBD) patients are highly susceptible to Clostridioides difficile infection (CDI) and are associated with increased length of hospital stay and colectomy rates. Early use of steroids in such patients has been debatable amongst physicians despite the presence of certain guidelines. This study aims to assess the effect of early steroid use in IBD patients managed for CDI, in terms of various secondary outcomes.

**Methods:** A comprehensive search of multiple electronic databases for published articles and abstracts was performed through Jan 2023. I2% statistics assessed heterogeneity and a leave-out meta-analysis was performed as required. Standard mean difference (SMD) with 95% CI was used for continuous variables.

**Results:** A total of 11 studies were included, comprising 8283 patients with IBD, of which 559 were diagnosed with CDI. 32.9% (n=184) were female, with mean age of 43.4±15.86 years, and mean IBD duration of 6.97±5.44 years. 63.12 % of the patients were on baseline antibiotics at the presentation time or 3 months before. The primary outcome was early corticosteroid (CS) use (within 48 hr) concurrent with antibiotics. The secondary outcomes were the recurrence rate, rate of progression to severe CDI, mortality at 1 year, and colectomy at 1 year. A further subgroup analysis was done based on sample size, and the pooled prevalence (PP) of CDI recurrence rate was found to be higher in patients with n>20 at 21% [9–36; I<sup>2</sup> 77%] as compared to the cohort (n<20) with p < 0.01. It was also higher than the PP of CDI recurrence in patients who remained only on antibiotics, calculated as 13% (95% CI: [5–23; I<sup>2</sup> 77%], p< 0.01. The PP of progression to severe CDI in patients with early CS use was 16% (11 - 23; I<sup>2</sup>=0%) in the subgroup of n>20, higher compared to patients on only antibiotics with PP of 14% (10 - 20; I<sup>2</sup>=0%). Other results are explained in Table 1 and Table 2.

**Conclusion:** Based on this study, worse clinical outcomes were reflected for patients who were started on steroids concurrently with antibiotics within 48 hrs. A small cohort size and a relative imbalance between antibiotic and concurrent early CS use could have resulted in some bias. Secondary outcomes could be influenced by existing IBD severity. Regardless, based on the above results, larger-scale studies are needed to establish stronger guidelines and determine when to initiate corticosteroid therapy in IBD patients safely.

Table 1: Baseline Antibiotic use only

IBD with CDI: Antibiotic use only	Pooled proportions (95% confidence interval; I <sup>2</sup> %); number of studies
CDI recurrence rate	13% (5 - 23; I <sup>2</sup> =77%); 6
Progression to severe CDI	14% (10 - 20; I <sup>2</sup> =0%); 4
Colectomy at 1 year	13% (3 - 28; I <sup>2</sup> = 81%); 4
Mortality at 1 year	1% (0 - 6; I <sup>2</sup> = 60%); 5

<b>IBD with CDI: Antibiotic AND CS use- primary outcome</b>	<b>Pooled proportions (95% confidence interval; I<sup>2</sup>%); number of studies</b>	<b>Pooled proportions (95% confidence interval; I<sup>2</sup>%); number of studies</b>	<b>P value</b>
<b>Subgroup analysis- Secondary outcomes</b>	<b>N &gt; 20</b>	<b>N &lt; 20</b>	
CDI recurrence rate	21% (9 - 36; I <sup>2</sup> =77% ) 1	17% (10 - 26; I <sup>2</sup> =0%); 4	< 0.01
Progression to severe CDI	16% (11 - 23; I <sup>2</sup> =0%); 2	10% (2 - 20; I <sup>2</sup> =0%); 2	
Colectomy at 1 year	16% (0 - 46; I <sup>2</sup> = 92%); 2	9% (0 - 51; I <sup>2</sup> = 86%); 2	< 0.01
Mortality at 1 yr	3% (0 - 17; I <sup>2</sup> = 84%); 2	0% (0 - 3; I <sup>2</sup> = 0%); 3	

Table 2: Early initiation (within 48 hr) of corticosteroids with antibiotics.