



A Retrospective Study of the Drug Prescribing Pattern in Crohn's Disease (CD) in a Tertiary Care Hospital

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ABSTRACT

Crohn's disease (CD) is a type of inflammatory bowel disease (IBD) which exhibits relapsing and remitting course. There are a few reports on its epidemiology but there is a paucity of studies on management of CD in India. The objective of the study was to analyze drug prescribing pattern in Crohn's disease (CD); to determine the efficacy of various treatment regimens with regard to improvement in patient's symptoms and its correlation with laboratory parameters like hemoglobin (Hb) level during follow up visit. A retrospective observational study was conducted at Kasturba Hospital, Manipal, from 1st Jan 2009 to 31st Dec 2010. All patients who were diagnosed to have CD based on clinical, endoscopic and histological evidence were included in the study. The case files of patients were retrieved from medical records section and data was collected according to the proforma. Statistical analysis was primarily descriptive. Comparisons between categorical variables were done using chi-square test. Paired t-test was used for comparison of hemoglobin levels. In our study, the total numbers of patients with Crohn's disease were 17. The peak incidence of disease was in the age group of 20-29 years and it was more common in males. The prescription rate of aminosaliclates, glucocorticoids and immunosuppressants were 70.6, 52.9 and 64.7% respectively. Mesalamine, prednisolone, and azathioprine were the commonly prescribed drugs. The most commonly prescribed treatment regimen was a combination of aminosaliclylate, steroid and an immunosuppressant (23.5%). A good correlation was seen between improvement in patient's symptoms and laboratory parameters like increase in hemoglobin level (83.3%) during follow up visit. The results of this study help us to know the different treatment strategies employed in the management of CD and their response.

Keywords: Crohn's disease, aminosaliclates, glucocorticoids, immunosuppressants, drug prescribing pattern.

INTRODUCTION

Crohn's disease (CD), an inflammatory bowel disease (IBD), is characterized by patchy transmural inflammation involving any segment of gastrointestinal tract. It exhibits relapsing and remitting course and there is a significant reduction in quality of life during exacerbations of the disease.^{1,2}

Crohn's disease was considered almost nonexistent till 1986, but since 15 years, it is being reported more frequently from different parts of India especially southern India.³ The peak age of onset is between 15 and 30 years. The male to female ratio is 1.1-1.8:1. The prevalence rate of CD is more in people with higher socioeconomic status and urban areas.⁴

The earlier studies reported from India showed a lower incidence of IBD and milder disease pattern. However, subsequent reports suggest increasing incidence and a more aggressive course of the disease. This is probably due to increasing awareness, western lifestyle, availability of better facilities for diagnosis, improvement in sanitation and hygiene.^{3,5}

According to the American College of Gastroenterology (ACG) 2009 guidelines, the primary goals of treatment of

CD are induction and maintenance of remission of symptoms to provide an improved quality of life, and minimize short- and long term toxicity and complications. Newer goals of therapy include the induction and maintenance of mucosal (and histologic) healing that are beginning to translate into changing the "natural history" of CD.⁶

At present, there is a paucity of studies on management of CD in India. Hence, the present study was undertaken to analyze the different treatment strategies being employed for Crohn's disease and their outcome in a tertiary care teaching hospital.

MATERIALS AND METHODS

A retrospective observational study was carried out at Kasturba Hospital, Manipal, a tertiary care teaching hospital from 1st Jan 2009 to 31st Dec 2010. The case record files of patients with a diagnosis of Crohn's disease were retrieved from medical records section after obtaining approval from University Ethics Committee (letter no. UEC/44/2010).

All the patients diagnosed to have CD based on clinical, endoscopic and histopathological evidence during the above period were included in the study. Patients with



infectious colitis and CD patients with malignancy were excluded.

We reviewed the prescriptions of above patients and the details were collected during that particular hospital stay. To evaluate the drug prescribing pattern, a specially designed proforma containing relevant details such as demographics (age, gender), clinical data (symptoms, laboratory findings), and drug data was used. Drug data includes drugs prescribed (generic/brand name) with their dose, route and frequency of administration.

We also collected follow up visit findings (symptom improvement, Hb level during follow up visit) within 3 months of first visit. The follow up time limit was restricted to first 3 months because the patients visiting during this period were generally compliant to prescribed pharmacotherapy. The efficacy of pharmacotherapy was recorded as per patient's response, relief or no relief of symptoms during follow up visit. The symptom relief was correlated with improvement in laboratory parameters like increase in hemoglobin (Hb) during follow up visit.

The data collected was presented as follows:

Age and gender distribution of the study sample, clinical features and laboratory findings, prescription rate of different classes of drugs used, prescription rate of different treatment regimens, follow up visits clinical and laboratory findings, correlation between relief of symptoms and change in hemoglobin levels, mean change in hemoglobin level after starting treatment and percentage of patients who underwent surgery.

Statistical analysis was primarily descriptive. Comparisons between categorical variables were done using chi-square test, with the level of significance set at $p < 0.05$. Paired *t*-test was used for comparison of hemoglobin levels before and after starting treatment. Statistical significance was considered when the *p* value was less than 0.05. SPSS 17 software package was used for all statistical calculations. The graphs were prepared using Microsoft Excel package.

RESULTS

We studied the case records of 100 patients who visited the hospital from 1st Jan 2009 to 31st Dec 2010 and were diagnosed as IBD based on clinical, endoscopic and histological findings. Among the 100 patients of IBD, 83 were ulcerative colitis (UC) and 17 were Crohn's disease (CD). Out of 17 patients of CD, 3 (17.6%) were new and 14 (82.4%) were old cases. Among them, 11 (64.7%) were male and 6 (35.3%) female. The male to female ratio was

1.83: 1. The mean age of the patients was 38.46 ± 14.25 years and peak incidence of disease was in the age group 20-29 years (Fig 1).

Abdominal pain (75%) was the most common presenting symptom followed by weight loss (64.7%), diarrhea (52.9%), bloody stools (30.8) and fever (29.4%) as shown in Fig 2. A few patients had extra-intestinal manifestations such as arthritis (5.9%) and oral ulcers (5.9%).

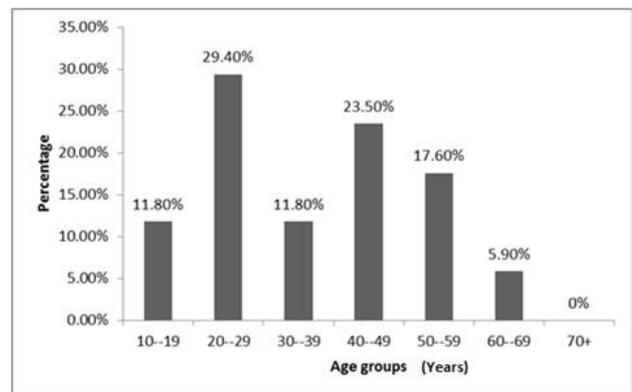


Figure 1: Age distribution of study sample for Crohn's disease

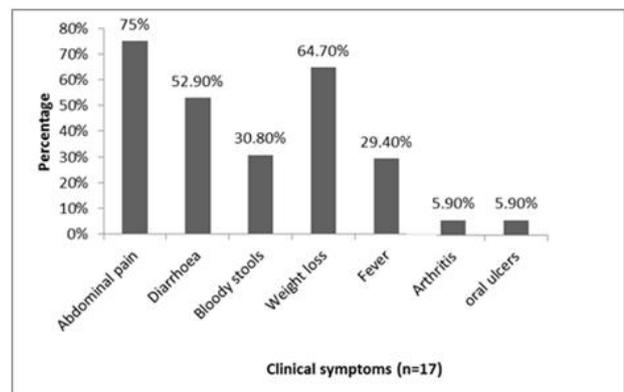


Figure 2: Clinical features of Crohn's disease

Anemia of varying degrees with hemoglobin level below 12 g% (Table 1) was seen in 13 patients (76.5%). The mean Hb level was 10.73 ± 2.19 g%. ESR values were available for 15 patients. Among them, 14 patients (93.3%) had raised ESR level during the first visit. The mean ESR level was 54.86 ± 31.91 mm/h. Hypoalbuminemia was seen in 61.5% patients during first visit.

Table 1: Hemoglobin levels

Hemoglobin level (g %)	No. of patients (n=17)
<8	2 (11.8%)
8-10	3 (17.6%)
10-12	8 (47.1%)
>12	4 (23.5%)

The different classes of drugs prescribed were aminosaliclates, glucocorticoids, and immunosuppressants; 12 patients (70.6%) were on aminosaliclates, 9 (52.9%) on glucocorticoids and 11 (64.7%) received immunosuppressants. The most commonly prescribed aminosaliclate was mesalamine (91.7%); sulfasalazine was prescribed for 1 patient (8.3%). Prednisolone was the commonly used glucocorticoid (88.9%), and budesonide was given only for 1 patient (11.1%). Azathioprine was the most commonly prescribed immunosuppressant (72.7%); methotrexate was given to 2 patients (18.2%) and 6-mercaptopurine (6-MP) was prescribed for 1 patient (9.1%) as shown in Table 2.

Of the 17 patients with Crohn’s disease, 3 (17.6%) were on aminosalicylate monotherapy; 3 (17.6%) on immunosuppressant monotherapy; 3 (17.6%) on combination of aminosalicylate + steroid; 2 (11.8%) on aminosalicylate + immunosuppressant; 2 (11.8%) on immunosuppressant + steroid; and 4 (23.5%) were started on triple drug combination of aminosalicylate + steroid + immunosuppressant. The commonly prescribed treatment regimen in our study group was a combination of aminosalicylate, glucocorticoid and an immunosuppressant (23.5%) as shown in Fig 3.

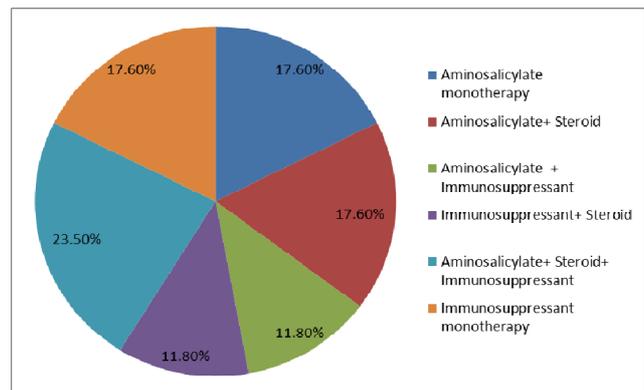


Figure 3: Prescription rate of different treatment regimens for Crohn’s disease

Table 2: Prescription rate of individual drugs

Drug class	Individual drug	Prescription rate	Dose range	Routes of administration
Aminosalicylate (n=12)	Mesalamine	11 (91.7%)	2.4-3.2 g/day	Oral, rectal
	Sulfasalazine	01 (8.3%)	3 g/day	
Glucocorticoids (n=09)	Prednisolone	08 (88.9%)	5-40 mg/day	Oral, rectal
	Budesonide	01 (11.1%)	9 mg/day	
Immunosuppressants (n=11)	Azathioprine	08 (72.7%)	25-100 mg/day	Oral, subcutaneous(Methotrexate)
	Methotrexate	02 (18.2%)	75 mg/day	
	6-Mercaptopurine	01 (9.1%)	12.5 mg/week	

Table 3: Correlation between relief of symptoms and change in hemoglobin levels

No. of patients with record of Hb levels during follow up visit	Symptom status	No. of patients with Hb levels increased from last visit	No. of patients with Hb levels decreased from last visit
CD (n=12)	Relief of symptoms (n=12)	10 (83.33%)	02 (16.67%)
	No relief (n=0)	0 (0.0%)	0 (0.0%)

Table 4: Mean change in hemoglobin level

No. of patients	Mean Hb before treatment (g%)	Mean Hb after treatment (g%)	Mean change in Hb (g%)	95% CI	p value
12	11.09 ± 2.04	11.88 ± 1.83	0.79 ± 0.30	0.13 - 1.45	0.023*

Statistical test: Paired t-test, * p< 0.05

Prescription rate of different adjunctive therapy was 41.2, 29.4, 11.7 and 5.9% for iron with vitamin supplements, proton pump inhibitors (PPIs), probiotics and antibiotics respectively.

Out of 17 patients, 13 came for follow up within 3 months of 1st visit. Among them, only 9 had active disease at initial visit. During the follow up visit, all 9 (100%) were relieved of their symptoms.

Out of 13 patients with CD who came for follow up, hemoglobin levels were available for 12 patients. All 12 patients showed relief of symptoms during follow up period (Table 3). Among those 12 patients, 10 (83.33%) showed an increase and 2 (16.67%) showed a decrease in their Hb level.

Mean Hb levels before and after treatment were 11.09 ± 2.04 g% and 11.88 ± 1.83 g% respectively (Table 4). The mean change in hemoglobin level after treatment was 0.79 ± 0.30 g%, which is statistically significant (Table 4).

Three (17.6%) out of 17 patients in CD underwent surgery because of failure of medical treatment.

DISCUSSION

This study evaluated the drug prescribing pattern and efficacy of treatment with regard to improvement of patient’s symptoms in 17 patients with Crohn’s disease in a tertiary care hospital in South India.

Our study showed the peak incidence of CD was in the age group 20-29 years. This was consistent with similar



studies done in South India.⁷ However our study failed to show the second peak of the disease in elderly between the age group of 60-70 years which was described in western studies.⁸ In our study, male predominance was seen, which is in concordance with other Indian studies.^{7,9} However, western studies have reported slight female predominance in Crohn's disease.⁸

Abdominal pain (75%) was the most common symptom in patients with CD. Earlier studies from India also showed similar findings.^{7, 10, 11} Abdominal pain is a major manifestation in CD since pain receptors in serosa are involved due to transmural involvement.

Anemia of varying degrees with hemoglobin level below 12 g% was seen in 76.5% of the patients; the mean Hb level (10.73 ± 2.19 g%) was higher than that reported by Kumar et al (8.9 ± 2 g%).¹² The percentage of patients with raised ESR was more (93.3%) when compared to that reported by Zacharias et al (65%).⁷ The mean ESR level of patients was 54.86 ± 31.91 mm/h which is almost similar to that reported by Kumar et al (57 ± 38 mm/hr).¹² A decrease in serum albumin levels was seen in 61.5% of the patients. Previous study by Zacharias et al also reported that hypoalbuminemia is the most frequent laboratory finding in Crohn's disease.⁷

In our study group, the prescription rate of different classes of drugs used were slightly different from that reported by Philip et al in Crohn's disease, which shows the prescription rate of 85, 57, and 15% for aminosalicylates, steroids and immunosuppressants respectively and 3 patients received infliximab therapy.¹⁰ None of the patients in our study group received any of the biologic agents. This may be on account of the ability of conventional drugs to treat many patients effectively particularly when used in combination. The other reasons could be the high cost of treatment and serious adverse effects with the use of biologic agents.

The different doses of aminosalicylates, glucocorticoids and immunosuppressants used in our study were as per ACG guidelines.⁶ The low prescription rate of sulfasalazine in spite of lower cost may be due to poor tolerability of the patients because of side effects produced by sulfapyridine moiety of sulfasalazine.

There was a good correlation seen between patients who got relief from their symptoms and showed an increase in their hemoglobin (Hb) levels during follow up when compared to their Hb levels taken at the time of 1st visit. About 83.33% of patients who experienced relief of symptoms, showed an increase in their hemoglobin levels during the follow up visit.

The percentage of patients who underwent surgery because of failure of medical treatment in our study was 17.6%. Earlier study by Kumar et al., reported a surgery rate of 20% which was slightly higher than our study results.¹²

CONCLUSION

In conclusion, aminosalicylates were the commonly prescribed drugs in our study. A combination of aminosalicylate, steroid and immunosuppressant was frequently used. Majority of the patients were relieved of their symptoms. There was a good correlation between improvement in symptoms and laboratory parameters, like increase in hemoglobin levels.

The limitations of our study were small sample size, lack of information on disease severity and restricting our follow up for only up to three months from the 1st visit. Crohn's disease is a condition which requires lifelong medication. Poor adherence to medication has been an important barrier for successful management of CD. Non-adherence has been associated with increased relapse rates, higher risk of colorectal cancer, poor quality of life, and significantly increased health care costs. Therefore, improving the adherence to medication is an important approach for better results in patients with Crohn's disease.

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