Original Article

Enterocutaneous Fistulae: Etiology, Treatment, and Outcome – A Study from South India

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ABSTRACT

Background/Aim: Enterocutaneous fistula (ECF) is a difficult condition managed in the surgical wards and is associated with significant morbidity and mortality. Sepsis, malnutrition, and electrolyte abnormality is the classical triad of complications of ECF. Sepsis with malnutrition is the leading cause of death in cases of ECF. Although it is a common condition, no recent report in literature on the profile of patients with ECF has been documented from the southern part of India. **Materials and Methods:** All consecutive patients who developed or presented with ECF during the study period were included in the study. The etiology, anatomic distribution, fistula output, clinical course, complications, predictive factors for spontaneous closure, and outcomes for patients with ECF were studied. **Results:** A total of 41 patients were included in this prospective observational study, of which 34 were males and 7 were females. About 95% of ECF were postoperative. Ileum was found to be the most common site of ECF. Also, 49% of fistulas were high output and 51% were low output. Serum albumin levels correlated significantly with fistula healing and mortality. Surgical intervention was required in 41% of patients. **Conclusion:** Most of the ECF are encountered in the postoperative period. Serum albumin levels can predict fistula healing and mortality. Conservative management should be the first line of treatment. Mortality in patients with ECF continues to be significant and is commonly related to malnutrition and sepsis.

Key Words: Enterocutaneous fistula, high-output fistula, Octreotide, serum albumin

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Enterocutaneous fistula (ECF) may occur due to a disruption in the gastrointestinal tract either due to surgery or disease, or both. These are most commonly seen in the postoperative setting and are associated with significant morbidity and mortality. The difficulties encountered in their management are related to sepsis, malnutrition, fluid and electrolyte imbalances, and consequent metabolic disturbances.[1] Hence, favorable outcome in patients with ECF depends on control of sepsis, adequate nutritional support, maintenance of fluid-electrolyte balance, and skin protection.[2,3]

Earlier studies have reported mortality as high as 65% in patients with ECF. Advances in imaging, nutritional support, and availability of effective antibiotics have reduced this to around 20%.[4,5] This study was carried out to document our institutional experience with ECF and to determine the etiological factors, presentation, prognosis, and outcome in patients with ECF in this part of the country.

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MATERIALS AND METHODS

This descriptive study was conducted prospectively in the department of surgery, JIPMER, Pondicherry, between September 2006 and June 2008. All consecutive patients, who developed or presented with ECF during the study period were included in the study. Patients with esophageal, biliary, pancreatic, and perianal fistulas were excluded from this study. A diagnosis of ECF was made clinically on detection of intestinal or fecal effluent from the drain site or abdominal incision site. This study has received the approval of the Institute Ethics Committee and an informed written consent was taken from all enrolled patients.

All enrolled patients were managed as per the policy of the department. Parameters studied included patients demographic profile, serial hemoglobin levels repeated weekly; biochemical parameters including blood sugar, blood urea, serum electrolytes (sodium, potassium) repeated every third day; serum total proteins, serum albumin repeated weekly. Ultrasound (US) abdomen and contrast-enhanced computer tomography (CECT) were done as per need of individual patients. Contrast studies were not routinely performed and were limited to cases where the source of the fistula was unclear, such as in patients referred with inadequate details, or in postoperative cases with more than one anastomosis.

The description of fistula included cause, anatomical location, fistula output, complications, and outcome. Fistula output was quantified by direct measurement, in the presence of drain or by calculating number of dressing pads soaked per day. A fistula output of 500 mL/day was taken as the cutoff between high and low output fistulas. The choice of this method to quantify fistula output was mainly owing to the ease and cost of measurement and may have a higher error rate than a more objective measure using wound collection devices. Decision to conserve or to operate was taken by the consultant in charge of the patient.

To examine the statistical significance of association between attributes, Chi-square test and Fisher's exact test were used. The Statistical Package for Social Sciences (SPSS) software version 10.0 was used. A probability value of less than 5% ($P < 0.05$) was considered significant.

RESULTS

A total of 41 patients were included in the study, of which 34 were males (83%) and seven were females (17%) and the male:female ratio was 5.5:1. Most patients with ECF were aged 40-60 yrs (mean age, 41.23 ± 2.72). A total of 95% of the fistulas were seen in the postoperative setting. Of 41 patients, 2 had gastric fistula and were excluded from further analysis. Seven patients had colonic fistula and the remaining had small intestinal fistula; 14 ileal, 10 duodenal, and 8 jejunal. There were 20 patients (48.8%) with high-output fistula as compared to 21 patients (51.2%) with low output fistula. Duodenal and jejunal fistulae accounted for 70% of high-output fistulae. Colonic fistula were more likely to have a low output ($P = 0.04$) [Table 1]. Mortality was significantly higher in patients with high-output fistula ($P = 0.03$) [Table 2].

Malignancy and tuberculosis accounted for one case each. Anastomotic line disruption following resection of gangrene gut, and postoperative leak following omental patch closure for peptic perforation accounted for half of the cases. The remaining cases included patients with enteric perforation, pancreatic abscess, and disrupted anastomosis following ileostomy closure. There were no cases of Crohn's disease.

Table 1: Comparison of small bowel and large bowel fistulas between patients with high- and low-output fistulae (*n*=39)*

	Small bowel fistula (*N*)	Large bowel fistula (*N*)	*P*†
High output (*n*=20)	19	1	0.043
Low output (*n*=19)	13	6	

*Two patients had gastric fistulas, and hence excluded during comparison, †Fisher's exact test

Table 2: Comparison of mortality between patients with different parameters (*n*=35)*

	Healed (*N*)	Died (*N*)	*P*†
High output (*n*=16)	10	6	0.0318
Low output (*n*=19)	18	1	
Enteral treatment (*n* =29)	25	4	0.0792
Parenteral treatment (*n*=6)	3	3	
Octreotide used (*n*=10)	8	2	1.0000
Octreotide not used (*n*=25)	20	5	
Serum albumin >3.5 g/dl (*n*=3)	3	0	
Serum albumin 2.5-3.5 g/dl (*n*=20)	20	0	0.0001‡
Serum albumin <2.5 g/dl (*n*=12)	5	7	
Anemia present (*n*=18)	14	4	1.0000
Anemia absent (*n*=17)	14	3	
Serum electrolyte sodium (<135 mEq/l) (*n*=21)	18	3	0.400
Serum electrolyte sodium (≥135 mEq/l) (*n*=14)	10	4	
Body mass index (≥18 kg/m^2)§ (*n*=19)	17	2	0.611
Body mass index (<18 kg/m^2)§ (*n*=11)	9	2	

*Patients who were discharged at request were excluded from analysis; †Fishers exact test; ‡Chi-square test. ***0.1 was added to each cell for application of Chi-square test; §Only 30 patients were included for analysis

Skin excoriation, cellulitis, and intra-abdominal abscess were complications observed in the study. Skin excoriation was seen in 17 of 41 patients (41.5%) with fistula. Ileum was the source of fistula in 40% of the cases with skin excoriation. Of 20 patients (45%) with high-output fistula, 9 had this complication as compared to 8 of 21 patients (38%) with low-output fistula. The association between skin excoriation and fistula output was not statistically significant ($P = 0.75$). Cellulitis was seen in three patients (8.6%).

Of 41 patients (34%), 14 developed intra-abdominal abscess, for which percutaneous or open drainage was carried out.

Nine of 21 patients (43%) in the low-output fistula group had intra-abdominal abscess as a complication as compared to five of 20 patients (25%) in the high-output group. The association between intra-abdominal abscess and fistula output was not significant. It was also found that the association between intra-abdominal abscess and mortality was not significant ($P = 1$).

Total parenteral nutrition (TPN) was utilised only in six patients. Parenteral nutrition supplemented enteral nutrition in 4 patients, while 29 patients were managed exclusively on enteral nutrition (EN). In cases of proximal ECFs, a feeding jejunostomy was done where feasible for supplementation by EN. In the EN group, 25 of 29 fistulae (86.2%) healed, while only three fistulae (50%) healed in the parenteral nutrition group. Mortality was lesser in patients receiving EN (16%) as compared to those on TPN (50%). This was, however, not statistically significant.

The use of Octreotide was not standardized but limited to patients with high-output proximal fistulae. Patients received Octreotide subcutaneously at a dose of 100 μg every 8 hours. Eight of 10 patients (80%) who received Octreotide showed a reduction in fistula output as well as healing of fistula. Similarly, 20 of 25 patients (80%) who did not receive Octreotide injections showed healing of fistula. The association between the use of Octreotide and mortality was not significant [Table 3].

Anemia was defined as hemoglobin of less than 10 g %. Of the 35 patients, 18 (51%) had anemia and 17 (49%) were not anemic. There was no statistically significant association between anemia and healing of fistula [Table 2]. Serum albumin was greater than 3.5 g% in 3 patients (9%), serum albumin level 2.5-3.5 g% in 20 patients (57%), and less than 2.5 g% in 12 patients (34%). Fistula healing was 100% in patients with serum albumin more than 3.5 g% and 82% in patients with serum albumin 2.5-3.5 g %. Of the total 12 patients with serum albumin, <2.5 g% fistula healed in only five patients (41.5%). All patients who died (n=7) had a serum albumin level less than 2.5 g%, and this was statistically significant [Table 2] [Figure 1].

There were 19 patients with body mass index (BMI) of ≥18 kg/m^2. In this group, fistula healed in 17 patients (89.5%), whereas two patients (10.5%) died. Of 11 patients with BMI <18 kg/m^2 fistula healed in nine patients (81.8%), while two patients (18.2%) died. This difference in mortality was not statistically significant ($P = 0.611$) [Table 2]. There were 21 patients with serum sodium <135 mEq/L, of which fistula healed in 18 patients (85.5%), whereas three patients (14.5%) died. There were 14 patients with serum sodium ≥135 mEq/L. Fistula healed in 10 patients (71.5%), while four patients (29.5%) died. There was a difference between the two groups, though it was not statistically significant ($P = 0.4$) [Table 2].

Of the 41 patients included in the study, 24 patients (58.5%) were managed conservatively, whereas 17 patients (41.5%) required surgical intervention. Resection of the fistulous segment was carried out with procedures such as primary anastomosis, re-anastomosis, enterostomy and laparostomy with sump drainage. Among the surgically managed patients, three required multiple surgical interventions to close fistula.

Duration of hospital stay was in the range of 7-81 days (mean = 29.7 ± 2.7). Hospital stay was compared between high-output and low-output fistula patients. In the high-output fistula group, mean duration of hospital stay was 36.6 ± 4.5 days as compared to 23.9 ± 2.7 days in low-output fistula patients. This longer hospital stay in high-output fistula patients was statistically significant ($P = 0.01$) [Table 3]. In conservatively managed patients, mean duration of hospital stay was 26 ± 2.9 days as compared to 35.2 ± 5.1 days in operatively managed patients. Hospital stay in patients managed by surgical intervention was longer than conservatively managed patients.

DISCUSSION

In Western population, 75%-85% of patients develop ECF

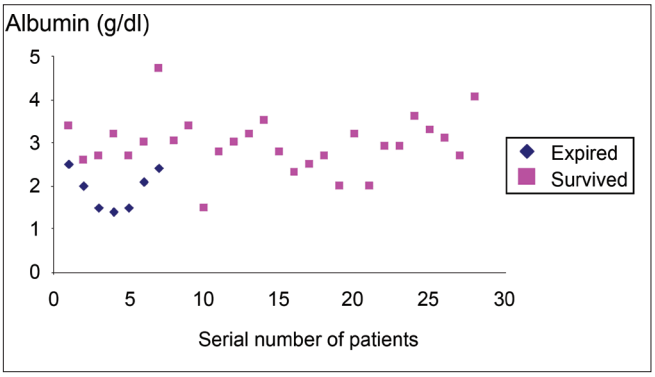

Figure 1: Serum albumin – predictive factor for spontaneous closure of fistula ($P < 0.001$)

Table 3: Number of hospital stay days in patients treated conservatively and operatively

Hospital stay (days)	No. treated conservatively *N* (%)	No. treated operatively *N* (%)
≤20	9 (43)	02 (14)
21-40	9 (43)	07 (50)
41-60	3 (14)	04 (29)
>60	0	01 (7)
Total	21	14
Mean ± SEM	26 ± 2.9 days	35.2 ± 5.1 days

as a complication following surgery of gastrointestinal tract. Spontaneous fistula accounted for the remaining 15%-25%. All cases, except one, in the present case series, developed an ECF following an operative procedure. In an earlier study carried out by Manisegaran *et al.*, from our institute in 1994, it was found that 88% of ECF occurred in the postoperative period.[6] The lesser incidence of inflammatory bowel diseases in this part of the world may account for this difference.

In the present study, 95% of the patients developed fistula postoperatively due to anastomotic leak. The common surgeries that were performed were intestinal resection with end-to-end anastomosis, or enterostomy closure following ileal perforation and gangrene gut. A similar finding was also reported by Reber *et al.* in their study.[7] It was found that ileum was the most frequent site for fistula formation, representing 36% of all fistulas. A similar distribution is reported in a study conducted by Roback *et al.*, in an analysis in 55 patients.[8]

Levy *et al.*, in their study on 335 patients, provided EN as the exclusive nutritional support in 85% of their patients. They concluded that conservative management is the treatment of choice in the initial period.[9] In the present study, 64.5% patients were started on oral feeds, 19.5% started on enteral feeds through feeding jejunostomy and 16% were started on TPN. While an association between the mode of nutrition and healing was not significant, this finding is a pointer to the fact that the majority of patients with ECF can be managed with EN. Reber *et al.* reported that the results of fistula management with both TPN and enteral feeds showed no significant difference in mortality rate and spontaneous closure rate.[7]

In the present study, duodenal and jejunal fistulae accounted for 70% of high-output fistulae. The mortality rate of high-output fistulae was 28.5%, whereas ileal and colonic fistulae with a low output accounted for 63% of patients with a mortality rate of 6% ($P = 0.03$). Patients with high-output fistulae have a higher incidence of fistula-associated complications such as electrolyte imbalance, sepsis, and skin excoriation, resulting in difficult management. The fistula closure rate is also lesser. Fazio *et al.* reported that mortality rate was 2-3 times higher in high-output patients as compared to low-output patients.[10] Narsos *et al.* also reported a mortality rate of 48% for jejunal fistulas and 18% for ileal fistulas in their study.[11]

In the present study, patients with ECF with a serum albumin of <2.5 g/dl had a higher mortality of 58.5%. Patients with serum albumin of >3.5 g/dl had no mortality; this was comparable to a study by Fazio *et al.*, who reported no mortality in patients with serum albumin >3.5 g/dl and a mortality rate of 42% in patients with serum albumin level <2.5 g/dl.[10] Serum albumin is definitely an important predictor for healing of fistula and mortality.

In a randomized control trial by Nabiola *et al.*, it was found that although the use of Octreotide did not help in healing of fistula, it reduces the fistula output by 70% in the first 48 hrs in patients with ECF.[12] In our study, 80% of the patients who received Octreotide showed a reduction in fistula output and healing time. However, there was no statistical difference noted between patients who received Octreotide and those who did not. In Hollender's series, the presence of intra-abdominal infection was observed in 63%, with a mortality rate of 82%. In the present study, intra-abdominal abscess was present in 38% of the patients and a mortality of 6%. Hollender's study was reported in the year 1983.[13] The advances in percutaneous drainage of abscesses and the availability of better antibiotics could be responsible for the huge difference in mortality reported.

In the present study, a BMI of less than 18 kg/m^2 was seen in 37% of patients. However, there was no statistically significant association between BMI and healing. This could be due to the fact that overall, patients attending this institute are small built and just exceed the BMI over 18 kg/m^2. Similarly, no significant association between anemia and healing of fistula could be found. This is in contradiction to the findings of some of the studies in literature.[14]

In the present study, 58.5% of the total patients were managed conservatively, whereas 41.5% of patients required surgical intervention. The common surgeries done in our patients are excision of segment of bowel containing fistula and end-to-end anastomosis, exteriorization of both ends, adhesiolysis and primary closure, and bilateral exclusion bypass of fistula. Rubelowsky *et al.* reported that reoperation and conservative management are complementary in patient treatment. Spontaneous closure rates have been estimated to be between 50% and 80%.[15] We agree with Lorenzo *et al.* and Tarazi *et al.*, in that the timing of operation and selection of the operative procedure depends on the type of fistula, response to conservative management, and the state of the patient.[16,17]

Review of literature over the last 25 years shows that the overall mortality rate for postoperative fistulas of the small intestine averages 30%. In the present study, the mortality rate in patients with small intestinal fistulas managed conservatively and with operation was 13% and 9%, respectively. In our series, 17% of the patients had colocutaneous fistulas, of which 95% of patients were managed conservatively, with no mortality. Of the 41 patients in the present study, fistula healed in 28 patients (68.5%), while seven patients (17%) died. Six patients were discharged at request. Among the remaining 35 patients, 22 (63%) were treated conservatively and 13 patients (37%) required surgical intervention. The mortality rate in patients treated conservatively was 18% and in those who required surgical intervention it was 23%. The overall mortality in the present study is 20% after excluding

Table 4: Mortality rates of enterocutaneous fistula

Authors	Year	No. cases treated	Mortality rate (%)
Manisekaran *et al.*[6]	1994	52	48
Haffejee *et al.*[18]	2004	494	13
Draus *et al.*[19]	2006	106	7
Martinez *et al.*[20]	2008	174	13
Visschers *et al.*[21]	2008	135	9.6
Present study	2008	35	20

patients who were discharged at request. Comparison of mortality in different studies is depicted in Table 4.

In conclusion, postoperative ECF is accounted as the most common cause of ECF. Most patients respond to conservative management; however, surgical intervention is required in a subset of patients when conservative methods for healing of fistulas fail. Nutritional status of the patient and fistula output are significant predictors of healing of ECF as well as mortality. Control of sepsis, management of fluid, and electrolyte imbalance, meticulous wound care, and nutrition support allow spontaneous fistula closure and low mortality.

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