

Enterocutaneous fistula :A Surgical challenge .Study at a tertiary care hospital



Medical Science

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ABSTRACT

Background: Enterocutaneous fistulae pose a therapeutic challenge to general surgeons all over the world and contribute significantly to high morbidity and mortality. The aim of this study was to describe our experience in the management of enterocutaneous fistulas, outlining the causes, fistula characteristics, treatment outcome and prognostic factors for fistula closure and mortality in our local setting.

Methods: A prospective study of patients with enterocutaneous fistulae was conducted at JSS Hospital, Mysore between December 2013 and November 2015. After informed written consent for the study and HIV testing, all patients who met the inclusion criteria were consecutively enrolled into the study. Data were collected using a pre-tested, coded questionnaire and analyzed using SPSS software version 11.5.

Results: Ninety two patients were seen during the study. There were 54 males (58.7%) and 38 (41.3%) females (M: F ratio = 1.4:1). Post-operative complication was the commonest cause of enterocutaneous fistulae in 91.3% of cases. The majority of patients (63.0%) had high output fistulae and the jejuo-ileum was commonly affected (60.9%). The complication rate was 34.8% and sepsis was the most common complication. Sixteen patients (17.4%) had HIV infection. Fistula closure was successfully achieved in 64 patients (69.6%). Of these, 42 patients (65.6%) had spontaneous closure and 22 patients (34.4%) underwent surgical closure. Mortality rate was 30.4%. Using multivariate logistic regression, the cause of fistula, fistula output, presence of complications and institutional origin of the patient were found to be significant predictors of spontaneous closure (p -value < 0.001), where as surgical closure was significantly associated with presence of complications and pre-morbid illness (p -value < 0.001). Fistula output, institutional origin of the patient, presence of complications and premorbid illness, HIV positivity and CD4 count were significant predictors of mortality.

Conclusion: Enterocutaneous fistulae pose a therapeutic challenge at JSS and contribute significantly to high morbidity and mortality. A multidisciplinary approach focusing on fluid resuscitation, nutritional supplementation, electrolyte replenishment, control of sepsis, containment of effluent, skin integrity and surgery at appropriate time is necessary to lessen morbidity and mortality with a higher fistula closure rate. The high rate of postoperative enterocutaneous fistulae resulting from anastomotic breakdown in patients referred from peripheral hospitals calls for urgent surgical skill training course in this region. The high rate of HIV infection in these patients needs further studies.

Introduction

Enterocutaneous fistulas, defined as abnormal communications between epithelial lining of the bowel and skin, are among the most challenging conditions managed by general surgeons^{[1],[2]}. Morbidity and mortality associated with enterocutaneous fistulae are still considerable, primarily due to inadequate nutrition, sepsis, fluid and electrolyte disturbance and skin digestion and the current treatment even if successful, may require prolonged hospitalization or repeated operations^{[1],[2],[3]}.

The etiological pattern of enterocutaneous fistula in the developed countries is reported to be different from that in the developing countries. While the most common causes of enterocutaneous fistula in the developed countries are inflammatory bowel diseases and diverticular diseases, the main cause in the developing countries is due to iatrogenic postoperative complications of abdominal surgery^{[1],[3],[5]}.

Understanding the etiological factors involved in fistula formation and determination of fistula characteristics is essential in planning for prevention strategies to minimize its occurrence and also allows prediction of the course of the patient and likelihood of spontaneous closure. Identification of factors that influence the likelihood of fistula closure and death is of greater value for the surgeon when making decision^[6].

This study was conducted to describe our experience in the management of enterocutaneous fistula and to compare this with what is happening in other parts of the world. The study outlined the etiological spectrum, fistula characteristics, treatment outcome and prognostic factors for fistula closure and mortality in our setting.

Patients and Methods

This was a prospective study of patients with enterocutaneous fistula admitted to the general surgical wards of JSS Medical col-

lege over a 2-year period between December 2013 and November 2015. During this study, patients with enterocutaneous fistula either occurred at JSS or admitted to JSS after being referred from peripheral hospitals were (depending on the age of the patient) admitted to the general or pediatric surgical wards.

On admission, these patients were aggressively resuscitated with fluid and electrolytes in the first 48 hours. Concurrent with fluid resuscitation, appropriate antibiotics (commonly parenteral ceftriaxone, metranidazole and gentamicin) were often prescribed. A colostomy bag was applied to the fistula opening to protect the skin from effluent and to give accurate measurement of the daily fistula output. Enteral feeding was commonly given for nutritional support. Facilities for total parenteral nutrition (TPN) are not usually available at our centre and therefore no patient in our study used TPN. Fluid and electrolyte imbalances were assessed by measurement of serum electrolytes and creatinine and this was done to all patients. Fistulogram and barium studies were occasionally performed to define the anatomical location of the fistula. The anatomical location of the fistula was also confirmed at surgery. Abdominal ultrasound was performed to localize abdominal collections. Patients were first treated conservatively for a minimum of four weeks to allow spontaneous closure. Surgical closure was only considered when spontaneous closure failed or when the patient developed complications.

In this study, all patients with enterocutaneous fistula were screened for inclusion criteria. Those who met the inclusion criteria were, after informed consent for the study and for HIV testing, consecutively enrolled in the study. The approval to carry out the study was sought from relevant authorities.

A pre-tested, coded questionnaire was used to collect data. Data entered in the questionnaire were: demographic data, premorbid illness, institutional origin of the patient, cause of the fistula, the time-interval between the causative event and appearance of the

fistula, fistula output, anatomical location of the fistula, type of nutritional support, HIV status and presence of complications; outcome variables included: spontaneous closure, surgical closure and mortality. Fistula output was recorded as high output when the fistula effluent was 500mL/24 hours or more and low output when the fistula output was less than 500mL/24 hours; Spontaneous closure was recorded when the fistula closed after conservative treatment alone. Surgical closure was recorded either as an ancillary surgical procedure (abscess drainage, enterostomy etc) or as definitive fistula closure (resection and anastomosis). Mortality was recorded if it occurred during the same hospitalization in which the fistula was treated. Data was analyzed using SPSS computer software version 11.5. In the univariate analysis, Chi-square test was used for categorical variables and t-test for continuous variables, to identify which of the independent (predictor) variables were the significant predictors of the outcome (spontaneous closure, surgical closure and mortality). Multivariate logistic regression analysis was used to determine predictor variables that are associated with outcome. A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 92 patients were studied. Fifty four (58.7%) patients were males and thirty eight (41.3%) females (M: F ratio = 1.4:1). Their ages ranged from 6 to 76 years (median 26 years) with the highest age incidence in the 21-30 years age group [Figure - 1].

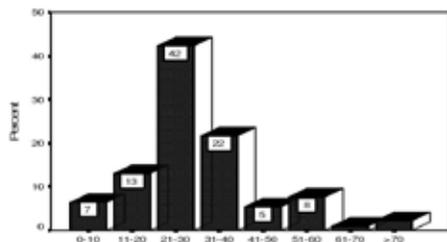


Figure 1: Age group distribution

Fourteen patients (15.2%) had pre-morbid illness such as diabetes mellitus in 6 patients, heart disease in 2 patients, tuberculosis in 2 patients, and renal disease, a huge goiter, obstructive jaundice and chronic chest infections in one patient each respectively.

Surgical complication was the most common cause of enterocutaneous fistula accounting for 84 patients (91.3%). Of these, 71 patients (84.5%) were referred from peripheral hospitals as a result of postoperative complications of abdominal surgery. Only in 13 patients (15.5%), enterocutaneous fistulae occurred at JSS. Of these, enterocutaneous fistulae resulted from complications of abdominal surgery performed by junior doctors (resident in surgery, medical officers and interns) in 9 patients (69.2%). Consultants /specialists contributed to enterocutaneous fistulae in the remaining 4 patients (30.8%). Anastomotic breakdown was the most common reason for fistulae resulting from postoperative complications in 65 patients (70.7%). Non-surgical causes of enterocutaneous fistulae occurred in eight patients (8.7%) mainly due to penetrating abdominal trauma in 3 patients, blunt abdominal trauma in 2 patients and inflammatory, neoplastic and strangulated Richter's inguinal hernia in one patient each respectively. One patient who had penetrating abdominal trauma had also multiple injuries. The time-interval between the causative event and appearance of the fistula varied from 1 to 82 days (median of 6 days).

Fifty eight patients (63.0%) had high output fistulae and the remaining 34 patients (37.0%) had low output fistulae. The mean fistula output for the high output and low output fistulae were 634 mL/ 24 hours and 358 mL/ 24 hours respectively. In this study, the jejunum-ileum was the most common part of the bowel affected and occurred in 45 patients (48.9%). This was followed

by the colon in 33 patients (35.9%). The duodenum was involved in 2 patients (2.2%), one patient due to gunshot penetrating abdominal trauma and the other patient was due to missed injury at first laparotomy. Cholecysto-enterocutaneous fistula occurred in one patient (1.0%) as a result of neglected cholelithiasis. The anatomical location of the fistula could not be established by any studies in 11 patients (11.9%) who had spontaneous fistula closure and those who died respectively (i.e. 28 patients died giving a mortality rate of 30.4%).

Significant intra abdominal collection was detected by abdominal ultrasound in 19 patients (20.7%) and all, except one patient who had burst abdomen, were treated successfully with laparotomy and drainage of pus.

All patients in this study received enteral feeding. No patient had total parenteral nutritional support. Complications mainly sepsis occurred in 32 patients (34.8%). In this study, 16 patients (17.4%) were HIV positive with CD4 count ranging from 50 to 675 cells/ml (median 245 cells/ml). The mortality rates was 75% and 21.1% for HIV positive and HIV negative patients respectively and it was significant. The mortality rates among patients with CD 4 count < 200 cells/mL and CD 4 count ≥200 cells/mL was 81.8% and 60.0% respectively. This was also significant. There was no significant association between HIV infected patients with CD 4 count < 200 cells/mL and either spontaneous or surgical fistula closure (*p*-value > 0.05).

Fistula closure was successfully achieved in 64 patients (69.6%). Of these, 42 patients (65.6%) had spontaneous closure and the remaining 22 patients (34.4%) underwent surgical closure. The time interval between the occurrence of the fistula and spontaneous closure ranged from 30-90 days (mean 52 days). Of the patients who underwent surgical closure, 10 patients (45.5%) required a second procedure for the final closure. These included; laparotomy and drainage of pus in 2 patients (20%), laparotomy and exteriorization of the fistula in 4 patients (40%) and laparotomy and enterostomy (ileostomy/ colostomy) in 4 patients (40%). The mean time interval between the second procedure and the final fistula closure was 34 days (range 30-50 days).

In this study, 28 patients (30.4%) died of complications related to sepsis, poor nutritional support, premorbid conditions and HIV infections. The prognostic factors for spontaneous closure, surgical closure and mortality in the univariate analysis are shown in [Table - 1]. Multivariate regression analysis is presented in [Table - 2], [Table - 3] and [Table - 4].

Table 1. Univariate analysis for spontaneous closure, surgical closure and mortality
 NB: "ns" stand for statistically non-significant

Independent variable	Spontaneous closure %	<i>p</i> -value	Surgical closure %	<i>p</i> -value	Mortality %	<i>p</i> -value
Age (years)						
< 50	46.3		23.2		38.5	
≥50	40.0	0.213	26.0	"ns"	28.0	"ns"
Gender						
Male	53.7		22.2		24.1	
Female	34.2	0.045	26.3	"ns"	39.5	"ns"
Premorbid illness						
Present	14.3		35.7		50.0	
Absent	51.3	0.321	21.8	"ns"	26.5	"ns"
Institutional origin						
BMC	66.7		26.8		6.8	
Not-BMC	41.6	0.032	23.4	"ns"	25.6	"ns"
Cause						
Surgical	47.6		22.6		29.8	
Non-surgical	25.0	0.021	27.5	"ns"	27.5	"ns"
Fistula output						
High output	32.8		29.3		37.9	
Low output	67.6	0.024	14.8	"ns"	17.6	"ns"
Anatomical location						
Duodenum	50.0		0.0		50.0	
Jejunum-Ileum	33.3		26.7		40.0	
Colon	51.5		33.3		18.2	
Biliary	0.0		100.0		0.0	
Not established	81.8	<0.05	0.0	"ns"	27.2	"ns"
Complications						
Present	13.6		9.1		77.3	
Absent	35.7	0.011	26.6	"ns"	15.7	0.001
HIV status						
Positive	12.5		12.5		75.0	
Negative	65.8	0.043	13.1	"ns"	21.1	"ns"
CD4 count (cells/ml)						
< 200	9.1		9.1		81.8	
≥ 200	26.0	0.023	26.0	"ns"	60.0	"ns"

Table 2. Multivariate logistics regression analysis for spontaneous closure

Independent (predictor) variable	Odds ratio	95% C.I.	p-value
Cause of fistula	3.6	1.3-97.1	“ns”
Fistula output	12.1	4.3-24.6	“ns”
Institutional origin of the patient	2.82	0.9-8.3	“ns”
Presence of complications	14.3	5.6-38.7	0.001

Table 3. Multivariate logistics regression analysis for surgical closure

Independent (predictor) variable	Odds ratio	95% C.I.	p-value
Presence of complications	15.4	5.9-37.2	0.001
Presence of pre-morbid illness	2.45	1.9- 10.7	“ns”

Table 4. Multivariate logistics regression analysis for mortality

Independent (predictor) variable	Odds ratio	95% C.I.	p-value
Institutional origin of the patient	2.13	1.0-4.6	“ns”
Fistula output	11.5	4.2-25.2	“ns”
Presence of pre-morbid conditions	10.2	5.3 -25.4	“ns”
Presence of complications	8.5	1.2-176.4	0.001
HIV positivity	4.1	1.9-9.3	0.001
CD4 count	11.0	4.7-26.6	0.000

Discussion

Since its first description, enterocutaneous fistulae still contribute significantly to high morbidity and mortality worldwide and pose therapeutic challenges to general surgeons despite improvement in its management [7]. This study was conducted to describe our own experience in the management of this devastating disease in our environment. The majority of our patients was youth in their most productive years and showed a male preponderance. However, the age and gender in this study were not significantly related to the chance of fistula closure or mortality. Similar findings have been reported from other studies [6],[8]. We could not establish the reason for the young age and male predominance.

In this study, postoperative enterocutaneous fistulae secondary to anastomotic breakdown were the most common preventable cause of enterocutaneous fistulae and the majority of patients were referred from peripheral hospitals. Similar admission trend was also noted in other studies [7],[9]. This observation reflects poor surgical technique in bowel anastomosis and lack of surgical skill training among doctors in the peripheral hospitals. This finding calls for urgent surgical skill training course among doctors in this region.

In our study, the institutional origin of the patient was a significant predictor of spontaneous fistula closure and mortality (p-value <0.001). Spontaneous closure was achieved in 66.7% of the patients operated upon primarily in our hospital and in only 41.6% of referred patients. Mortality rate was 35.0% and 6.8% for referred patients and patients operated upon primarily at JSS respectively (p-value <0.001). This is in agreement with other studies which reported similar findings [8],[10]. The reason for this observation may be due to the fact that JSS been a tertiary and referral hospital, the majority of patients referred to this hospital are in poor general condition, and on admission, most patients are malnourished and septic and have severe skin lesions with fluid and electrolyte imbalances, and organ dysfunction, so the chance of spontaneous closure and survival among referred patients is unlikely compared with patients operated upon primarily at JSS. These findings stress the importance of prompt

general and nutritional care when enterocutaneous fistula is diagnosed to avoid deterioration of the patient's condition.

Our study demonstrated high rates of high output fistulae compared with low output enterocutaneous fistulae. This is in contrast with one study which reported high rate of low output fistula [11]. High rates of high output fistulae in our study may be attributable to the fact that the jejunum-ileum which is the more proximal part of the digestive tract was commonly affected. As a general rule, the more proximal in the digestive tract, the greater the fistula output will be.

Accurate measurements of fistula output, although often difficult to obtain secondary to poor fitting ostomy appliances or nursing issues, can be helpful in predicting outcome. In our study, fistula output was found to be a significantly independent predictor of spontaneous closure and mortality (p-value <0.001). Spontaneous fistula closure was greater in low-output fistulas than in high-output fistulas. This was in agreement with findings of studies done elsewhere [12],[13],[14]. High output enterocutaneous fistulas are more likely to be associated with malnutrition, sepsis, fluid and electrolyte disturbances, lower incidence of spontaneous closure and mortality.

Although the anatomical location of the fistula was associated with both fistula closure and mortality in univariate analysis, the association was not statistically significant in multivariate logistic regression analysis.

The provision of nutritional support with either enteral or parenteral feeding is a key component of management in patients with enterocutaneous fistula and can also be used to predict outcome. These patients are often malnourished due to the lack of food intake, the hypercatabolism of sepsis, and the loss of protein-rich enteral content. Parenteral nutrition has long been recognized to be an integral part of the management of enterocutaneous fistulas [7],[11],[13]. However, in limited-resource countries like ours, parenteral nutrition may not be accessible. Parenteral feeding was not used in our patients due to its inaccessibility. Although the type of nutritional support was associated with both

fistula closure and mortality in some studies ^{[6],[8]}, this variable was not assessed in our study due to logistic problem.

The proportion of patients with complications in the present study is comparable with other studies ^{[5],[6],[8]}. The presence of complications was found to be significantly associated with both fistula closure (spontaneous and surgical) and mortality (p -value < 0.001). Mortality rate was 77.3% and 15.3% in patients with complications and those without complications respectively. Similar finding was also observed in other studies ^{[5],[15],[16]}. The reason for the high mortality rate associated with complications in our study is due to the fact that sepsis which contributes significantly to high mortality in these patients was the most cause of complications accounting for 72.7% of all cases with complications.

The prevalence of HIV infection in our patients (17.4%) was found to be higher than in general population (5.7%). Further studies are needed to explain this observation. Our study also demonstrated high mortality rates among HIV positive patients with low CD 4 count (< 200 cells/mL). We could not find any study in the literature outlining the impact of HIV positivity and CD 4 count on the outcome of patients with enterocutaneous fistula. The reason for the high mortality rate in HIV infected patients with low CD 4 count (< 200 cells/mL) is due to the fact that HIV infection causes low immunity predisposing these patients to sepsis which is the commonest cause of death in these patients.

The rate of spontaneous closure has been reported in literature to vary from 23% to 80% ^{[12],[17],[18]}. The rate of spontaneous closure in our study was higher than in other studies ^{[1],[3],[8],[11]}. In our study, the majority of patients had a spontaneous fistula closure after an average of 50 days. Reber et al ^[15] reported higher rates of spontaneous closure in fistula resulted from surgical causes than in fistulae resulted from non-surgical causes. They concluded that the likelihood of spontaneous closure is higher in fistula resulting from surgical causes and with no complications. The high rate of fistula from surgical causes reflected the high rate of spontaneous closure in our study.

The timing of definitive surgical closure of the fistula is a controversial subject. Most studies advocate delayed surgical closure for at least 3 months after the fistula has arisen to allow for fistula maturation, resolution of inflammation within the peritoneal cavity, optimization of the patient's nutritional state and for residual sepsis to resolve ^{[5],[7],[11]}. Premature attempts at operative closure with inflamed, erythematous or necrotic tissue increases the risk of peritoneal contamination, the formation of dense adhesions and recurrent fistula formation. This teaching has been challenged by a recent study which advocated an aggressive early surgical closure in which surgical intervention was done after a maximum period of 14 days of conservative treatment with judicious use of octreotide, nutritional support, stoma care and control of sepsis ^[1]. Our own experience generally tries to wait at least 8-12 weeks from the time of occurrence of the fistula. This is because most of our patients come from peripheral hospitals and require some weeks of preparation for nutritional parameters to improve so that operation can be carried out.

The overall mortality rate of enterocutaneous fistulae has been reported in literature to vary from 6.45% to 48% ^{[1],[3],[6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17]}. The high mortality rate in our study can be explained as follows; first, the majority of patients referred to JSS are in poor general condition, and on admission, most of them are malnourished and septic and have severe skin lesions with fluid and electrolyte imbalances, and organ dysfunction, so the chance of survival is unlikely. Second, the majority of our patients had high output fistulae predisposing them to fluid and electrolyte imbalances, sepsis, malnutrition, lower incidence of

spontaneous closure and mortality. Third, the presence of pre-morbid illness and high rate of septic complications contributed significantly to high mortality rate in these patients. Fourth, the high rate of HIV infection in these patients was also a predictor of mortality.

Lack of parenteral nutrition, failure to assess nutritional status of the study population and small sample size were the major limitations in this study. However, despite the above limitations, this study has clearly demonstrated that enterocutaneous fistulae are a major problem in our setting and are associated with considerable morbidity and mortality primarily due to inadequate nutrition, sepsis, fluid and electrolyte disturbance and skin digestion, and present a considerable challenge in their management. The study has also demonstrated HIV seroprevalence and its effect on the outcome of these patients.

Conclusion

Enterocutaneous fistulae present a therapeutic challenge at BMC and contribute significantly to high morbidity and mortality. The majority of fistulae are due to postoperative complication of abdominal surgeries performed in the peripheral hospitals. The likelihood of spontaneous fistula closure is higher for fistulas with surgical causes, low output, and with no complications. Surgical closure is more likely to be indicated in patients with pre-morbid illness and complications. Mortality is higher in HIV infected patients with low CD4 count, high-output fistulas and patients with pre-morbid illness and complications. HIV seroprevalence is higher in patients with enterocutaneous fistulae than in general population.

Recommendations

A multidisciplinary approach focusing on fluid resuscitation, nutritional supplementation, electrolyte replenishment, control of sepsis, containment of effluent, skin integrity and surgery at appropriate time is necessary to avoid morbidity and mortality associated with this complication. The high rate of preventable postoperative enterocutaneous fistulae resulting from anastomotic breakdown in patients referred from peripheral hospitals is unacceptable and calls for urgent surgical skill training course in this region. Further studies are needed to explain the higher rate of HIV infection in these patients.

Early referral to well equipped hospitals or Tertiary hospitals is highly recommended.

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