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Management of postoperative enterocutaneous fistulae in children: A decade experience in a single centre

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ABSTRACT

Background: Enterocutaneous fistula (ECF) in children poses a lot of management challenges due to sepsis, malnutrition, fluid and electrolyte deficits, which are frequent complications. Knowledge of prognostic factors of postoperative ECF is essential for therapeutic decision-making processes. This study examined the variables that relate to the outcomes of management of ECF in children. **Patients and Methods:** Consecutive children who were managed for postoperative ECF in our unit between 2000 and 2009 were evaluated. Data were analysed for clinical features, management and its outcome. **Results:** A total of 54 patients were managed for ECF. Majority of the fistulas were due to operation for infective causes, with typhoid intestinal perforation ranking the highest. Overall, spontaneous closure without operative intervention occurred in 29 (53.7%) patients. Twenty-one (38.9%) patients required restorative operations to close their fistulas, which was successful only in 12 (22.2%) patients. There was a strong correlation between high-output fistulas (jejunal location) and surgical closure (P<0.001). Hypoalbuminaemia and jejunal location profoundly resulted in non-spontaneous closure of ECF (P<0.001) and were associated with high morbidity (P<0.001). Thirteen (24.1%) patients died due to hypokalaemia, sepsis and hypoproteinaemia/hypoalbuminaemia. **Conclusions:** Majority of the ECF in children closed spontaneously following high-protein and high-carbohydrate nutrition. Hypoalbuminaemia and jejunal location were important prognostic variables resulting in non-spontaneous closure, while hypokalaemia, sepsis and hypoproteinaemia/hypoalbuminaemia were associated with high mortality in children with ECF.

Key words: Children, enterocutaneous fistulas, management, prognostic factors

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INTRODUCTION

The management of enterocutaneous fistula (ECF) is often associated with high morbidity and mortality rates, arising largely from the accompanying complications of sepsis, malnutrition, and electrolyte abnormalities.[1]

Fistulae may be either spontaneous or postoperative, and may involve diseased bowel or normal bowel. ECF may also be caused by trauma to the bowel or anastomotic breakdown. ECFs may be categorised by anatomical, physiological, or aetiologic criteria, all of which may influence the patient's clinical course and outcome, including the likelihood of spontaneous closure of the fistula.[2]

A number of variables afford the prediction of the possible outcome of an ECF fistula. Anatomical information of the fistula, with respect to its site and tract, is often the first data available that may allow the surgeon predict the natural history of the fistula and patient's ultimate need for surgical closure. Determination of the aetiologic factors involved in fistula formation also allows prediction of the clinical course of the patient and likelihood of spontaneous closure.

Spontaneous fistulae constitute 15–25% of all ECFs and are likely to occur as a complication of appendicitis, typhoid enteritis, perforated ulcer disease, cancer or radiation, as well as inflammatory bowel disease and diverticular disease (in the Western world).[3] Knowledge of prognostic factors related to specific outcomes in ECF is essential for therapeutic decision-making processes. Expert opinions regarding the principles of management of ECF are well documented in the adult population. In the paediatric age group, however, there is a dearth of studies reporting the most effective way of managing ECF. The few retrospective studies available concerning these patients are either incomplete or only describe small series of patients. Consequently, there is

no evidence-based recommendation on how children with ECF should be treated. This study examined the variables that relate to outcomes of management of ECF in children.

PATIENTS AND METHODS

This was a retrospective analysis of a database consisting of consecutive 54 children with ECF, treated in our unit between 2000 and 2009. Information was collated on a proforma from the nutrition team database and from patients' files and analysed for patient's age, sepsis, nutritional status (total protein/albumin), wound care, anatomy (small or large bowel), effluent output, management and its outcome.

Intestinal anastomotic leakages that developed within the first week after the primary surgical procedure and immediately corrected by re-laparotomy were excluded; however, when no re-laparotomy was performed and patients developed an ECF, such patients were included in the study. An ECF was considered closed when there was no more communication between the intestinal lumen and the abdominal wall. Recurrence was defined as a reconnection between the intestine and skin after the fistula had previously closed spontaneously or had been removed surgically.

Statistical analyses were performed with SPSS software (version 15; SPSS Inc., Chicago, IL, USA). Univariate analysis was performed using Pearson's chi-square test and Fisher's exact test, where appropriate. All independent variables with a two-tailed *P* value <0.10 were entered into a multiple logistic regression model. Two-tailed *P* values <0.05 were considered significant.

RESULTS

Of the 54 patients managed for ECFs, 36 (66.7%) were boys and 18 (33.3%) were girls (M:F = 2:1). Mean age was 6 years (range: 4–11 years). The fistulas occurred after a median of 5 days (range: 2–9 days) following the initial surgery. Thirty-eight (70.4%) patients were referred from private clinics and district hospitals, while the remaining 16 (29.6%) had their initial operations in our hospital. The median length of hospital stay was 42 days (range: 22–180 days) overall, but the median period of treatment was 90 days (range: 6–240 days). The patients' characteristics are as shown in Table 1.

Table 1: Characteristics of patients and postoperative enterocutaneous fistulas (*n* = 54)

Variable	Number	%
Gender		
Male	36	66.7
Female	18	33.3
Site of origin		
Jejunum	8	14.8
Ileum	42	77.8
Colon	4	7.4
Fistula output		
High (>7.15 ml/kg/24 hrs)	22	40.7
Low (<7.15 ml/kg/24 hrs)	32	59.3
Initial (causative) operation		
Urgent	42	77.8
Elective	12	22.2
Duration of fistula		
<120 days	36	66.7
>120 days	18	33.3
Fluid/electrolyte imbalance		
Present	10	18.5
Absent	44	81.5
Sepsis		
Present	22	59.3
Absent	32	40.7
Malnutrition*		
Present	30	74.1
Absent	24	25.9

*Weight loss, hypoproteinaemia (hypoalbuminaemia)

The initial operations that became complicated by fistula were bowel resection in 24 patients, primary closure of bowel perforations in 10, exploratory laparotomy and adhesiololysis in 8, and repair of healed omphalocoele (ventral hernia) in 5 other patients. These initial operations were urgent in 42 (77.8%) and elective in 12 (22.2%) cases.

The fistula was of high output in 32 (59.3%) patients and low output in 22 (40.7%) patients. The fistula was adjudged to be located on the ileum, based on its output in about two-thirds (32) of the patients. Forty patients were malnourished with hypoproteinaemia (and hypoalbuminaemia); majority of the malnutrition occurred within the first 3 weeks of developing the fistula. Fluid, urea and electrolyte derangement was present in 44 (81.8%) cases. The median level of blood urea nitrogen (BUN), serum sodium, potassium and chloride was 6.6 mmol/l (2.4–7.1 mmol/l), 138 mmol/l (124–154 mmol/l), 2.7 mmol/l (2.2–5.6.mmol/l) and 94 mmol/l (84–111 mmol/l), respectively.

Fifteen of the patients had intra-abdominal abscess collection at presentation. Ultrasound-guided drainage of the abscesses was attempted in 10 patients and was successful in 6, none of whom required further intervention. In the remaining nine patients, the procedure was technically impossible because of faecal peritonitis, presence of multiple abscesses, dense

adhesions and multi-loculated abscess, necessitating open drainage via re-laparotomy.

Typhoid intestinal perforation and complicated appendicitis were the main initial pathologies requiring surgery in 25 and 12 patients, respectively [Table 2]. Other initial pathologies included penetrating abdominal injuries caused by stab wound and gunshot resulting in jejunal perforation in three patients each, arrow injury to the abdomen that caused multiple jejunal and ileal perforations, and intestinal obstructions. The resultant fistulas were mainly of moderate to low output.

Initial and supportive treatment was directed at control of sepsis, correction of fluid and electrolyte derangements and nutritional support by the enteral route (occasionally via a nasogastric tube), using high-energy and protein diet fortified with multivitamins.

Table 2: Initial pathologies or operations that caused enterocutaneous fistulas in patients

Initial pathologies	Number
Typhoid perforation	25
Complicated appendicitis	12
Small bowel obstruction	5
Hirschsprung's disease	3
Stab wound	3
Gunshot injury	3
Omphalocoele	2
Injury from fall from height	1
Initial operation	
Small bowel resection	24
Exploratory laparotomy and adhesiololysis	8
Colostomy closure	3
Primary closure of typhoid bowel perforations	5
Healed omphalocoele (ventral) hernia repair	5
Primary closure of penetrating bowel perforations	5
Hemicolectomy and small bowel resection	4

Table 3: Outcomes of management of postoperative enterocutaneous fistula in 54 children

Site of fistula	Number of deaths no. (%)		
	Postoperative	Non-operative	Total number of deaths no. (%)
Jejunum	4 (7.4)	1 (1.9)	5 (9.3)
Ileum	5 (9.3)	3 (5.5)	8 (14.8)
Colon	0	0	0
Total	9 (16.7)	4 (7.4)	13 (24.1)

Fistula closure occurred in 41 (75.9%) patients. Spontaneous closure occurred in 29 (53.7%) patients, while surgical intervention successfully achieved closure in 12 (22.2%) patients [Table 3]. Successful surgical closure was performed after a mean period of 11 days (range: 7–24 days) for fistulas in the jejunum and 128 days (range: 120–182 days) for those on ileum, from the occurrence of the fistula. On the other hand, the mean time between fistula development and spontaneous closure was 72 days (range: 42–120 days) for ileum and 42 days (range: 21–64 days) for colon [Table 4].

Overall fistula-related mortality rate was 24.1% (13 patients); the deaths were due to severe sepsis (4), electrolyte derangement (4), or a combination of sepsis and malnutrition (5). Nine (16.7%) patients died at varying intervals in the postoperative period.

Spontaneous closure predominantly occurred in patients with serum albumin >25 g/dl (P=0.001) [Table 5]. On the other hand, jejunal location, fluid and electrolyte derangement and sepsis negatively impacted on spontaneous closure. Multiple logistic regression analysis showed that low output and normal-high levels of serum albumin were independent predictors for spontaneous closure. Surgical closure was negatively associated with high output (P=0.002) and jejunal location (P=0.001) [Table 6].

There was a strong positive relation between sepsis (P<0.003), electrolyte derangement (P<0.001), hypoalbuminaemia <25 g/dl (P<0.003), high output >7.15 ml/kg/24 hrs (P<0.001), jejunal location (P<0.004) and mortality [Table 7].

DISCUSSION

Factors contributing to the development of postoperative ECFs may be classified generally as patient-specific or technique-specific.[4] Specific risk factors for patients include operation for malignancies and inflammatory conditions, malnutrition, infection or sepsis, and

Table 4: Duration before spontaneous or operative closure of postoperative enterocutaneous fistula in 54 children

Site of origin	Number	Diagnosis – spontaneous closure (days)*	Number	Diagnosis – operative treatment (days)+
Jejunum	1	62 (55–114)	5	11 (7–24)
Ileum	24	72 (42–120)	7	128 (120–182)
Colon	4	42 (21–64)	0	

*Four patients died before completing spontaneous closure and were not included, +Nine patients died after attempted surgical closure and were not included

Table 5: Factors influencing spontaneous closure in postoperative enterocutaneous fistula in 54 children

Variable with spontaneous closure/total	Number of patients (%)	Univariate analysis *P* value	OR (95% CI)	Multivariate analysis *P* value
Jejunal fistula				
Yes	1/11 (9.1)	0.001	0.203 (0.131–0.538)	0.008
No	31/43 (72.1)			
High output				
Yes	18/22 (81.8)	0.051	0.330 (0.232–0.603)	0.014
No	15/32 (46.9)			
Fluid and electrolytic imbalance				
Yes	4/10 (40.0)	0.013	0.212 (0.119–0.742)	0.574
No	29/44 (65.9)			
Sepsis				
Yes	16/22 (72.7)	0.053	0.491 (0.233–0.621)	0.013
No	17/32 (53.1)			
Serum albumin > 2.5 g/dl				
Yes	28/30 (93.3)	0.001	0.259 (0.187–0.759)	0.005
No	5/24 (20.8)			

OR = Odds ratio (spontaneous vs. non-spontaneous closure), CI = Confidence interval

Table 6: Factors influencing need for surgery in 54 children with postoperative fistula (univariate and multivariate analysis)

Factor who underwent surgical treatment/total no. (%)	Number of patients	Univariate analysis *P* value	OR (95% CI)	Multivariate analysis *P* value
High output				
Yes	11/22 (50.0)	0.002	0.263 (0.113–0.826)	0.008
No	3/32 (9.4)			
Jejunal fistula				
Yes	9/11 (81.8)	0.001	0.114 (0.101–0.472)	0.002
No	10/43 (23.3)			

OR = Odds ratio (surgical treatment vs. non-surgical treatment)

Table 7: Factors associated with mortality in postoperative enterocutaneous fistula in 54 children (univariate and multivariate analysis)

Variable patients/total	Number of dead (%)	Univariate analysis *P* value	OR (95% CI)	Multivariate analysis *P* value
Serum albumin < 25 g/dl				
Yes	10/30 (33.3)	0.003	0.289 (0.118–0.413)	0.006
No	3/24 (12.5)			
Fluid and electrolytic imbalance				
Yes	5/10 (50.0)	0.001	0.216 (0.103–0.582)	0.008
No	8/44 (18.9)			
High output				
Yes	9/22 (40.9)	0.001	0.204 (0.117–0.631)	0.005
No	4/32 (11.8)			
Jejunal fistula				
Yes	5/11 (45.5)	0.004	0.315 (0.258–0.761)	0.041
No	8/43 (18.6)			
Sepsis				
Yes	8/22 (36.4)	0.003	0.340 (0.243–0.517)	0.016
No	5/32 (15.6)			

OR = Odds ratio (mortality vs. survival)

operations in an emergency setting with concomitant hypotension, anaemia, hypothermia, or poor oxygen delivery.[5,6]

Infective or inflammatory bowel conditions (typhoid perforation and complicated appendicitis) were the main pathologies whose management ultimately resulted in ECF in this study. Faecal fistula (FF) often results from these pathologies due to the presence of a negative nitrogen balance and improper healing of anastomotic line, with significant mortality up to 67%.[5,7-9] Following typhoid intestinal perforation repair, postoperative intestinal fistula is a frequent complication among those who survive the septicaemic phase of the perforation, with attendant severe morbidity and mortality.[10-15] In our patients, bowel anastomosis, adhensiolysis and closure of perforation accounted for 42 (77.8%) of the procedures that resulted in a fistula.

Majority of our patients (70.4%) in this report were outside referrals, with most of the surgeries that led to the fistula performed in peripheral hospitals. This is in consonance with the report by Kriwanek and Roka in which 63% of their patients (175) were outside referrals.[16] The high rate of fistula complicated surgeries arising from the peripheral hospitals may be related to lack of skills and poor techniques in performing intestinal related operations.

The overall goal of fistula management is to promote fistula closure. Quantification of fistula output allows more accurate management of the patient and may also provide prognostic information regarding mortality and likelihood of eventual surgical therapy. The fistula was of high output in 32 (59.3%) patients and low output in 22 (40.7%) patients. High-output fistula (>500 ml/day), typical of those located above the ligament of Treitz, those resulting from complete disruption of intestinal continuity (end fistula), and those with wide (>2 cm) and epithelialised tract is less likely to close spontaneously.[17] Moderate-output (200–500 ml/day) or low-output (<200 ml/day) fistulas are more likely to undergo spontaneous closure than those with high output.[17,18] Communication with an adjacent abscess cavity, presence of foreign bodies, a distal bowel obstruction, malignancy or irradiation, and debilitating conditions (e.g. tuberculosis, fungal infection, etc.) are the other factors precluding spontaneous fistula closure.[19]

The site of a fistula is closely linked with its physiology. Multiple logistic regression analysis confirmed low output independent predictors for spontaneous closure. Jejunal site was found to be the most opposed to spontaneous closure in this study as the fistulas are usually of high output by nature, with a greater fluid/electrolyte loss and the erosive capacity of the effluent on the skin. Early and aggressive fluid and electrolyte correction followed by surgical closure suffices for this group of patients in whom surgical closure was five times more successful than spontaneous closure and profound negative influences were found on spontaneous closure and mortality.

There is a strong association between fistula output and mortality. The external loss of intestinal fluids rich in electrolytes, minerals, and protein contributes to the physiologic complications of electrolyte imbalance and malnutrition in patients with ECFs. Postoperative ileus, loss of bowel integrity and absorptive surface area, and the external loss of protein-rich enteric contents – all contribute to the resultant malnutrition and fluid and electrolyte abnormalities.[20] Identifying the source of the fistula will allow a rough estimate of the composition of the fluid lost. In complex situations, analysis of fistula-output electrolyte composition may aid in maintaining normal levels of important electrolytes, including sodium, magnesium, potassium, phosphate, bicarbonate, and calcium.

The triad of complications of sepsis, malnutrition, and electrolyte and fluid abnormalities has a negative impact on the spontaneous closure of fistula.[21] Septic patients are extremely hypercatabolic and unable to achieve positive nitrogen balance, and loss of 2% of body protein stores per day occurs in adults despite the administration of parenteral nutrition. Efflux of bowel contents outside the lumen may lead to localised abscess, soft tissue infection, generalised peritonitis, or frank sepsis. Fifteen of our patients who had intra-abdominal abscess collection at presentation were drained to prevent this hypercatabolic state of sepsis. Minimal access drainage in the form of ultrasound-guided drainage of the abscesses was employed to minimise the metabolic response to surgery and was successful with no further intervention in 6 out of 10 patients. Most recent series suggest that sepsis, with its concomitant malnutrition, is the leading cause of death in patients with ECFs.

Our overall fistula-related mortality rate was 24.1% (13 patients) and was due to severe sepsis, and electrolyte derangement with or malnutrition. These patients with postoperative intestinal fistula in this study presented with severe malnutrition with electrolyte derangement

and sepsis. Malnutrition occurred as an early event (within the first 3 weeks) of developing the fistula. This suggests that nutritional therapy should receive early and timely attention considering that the average period that elapsed before spontaneous closure was over 7 weeks.

High-calorie and protein diet fortified with multivitamins given orally or via nasogastric tube was the mode of nutritional support given to our patients. This was accompanied by aggressive correction of deranged fluid and electrolyte and control of sepsis, since they remain principal causes of death and, above all, their presence may render established malnutrition difficult to correct. Provision of total parenteral nutrition has been associated with an increased rate of spontaneous closure of fistulas in several series. In patients requiring surgical closure of their fistulas, any improvement in the nutritional status will aid in maintaining bowel continuity by promoting wound healing, enhancing the immune system, and preserving lean cell mass.[3] Nutritional status remains an important predictor of mortality in patients with ECFs.

We observed a better survival rate among patients with serum albumin >35 g/dl and a correlation between hypoalbuminaemia and mortality. In other studies, serum albumin level lower than 35g/dl has likewise been associated with a mortality rate as high as 42%.[22] Similarly, serum transferrin level is a predictor of both mortality and the rate of spontaneous closure of ECFs, whereas retinol-binding protein and thyroxin-binding prealbumin predicted only mortality,[23,24] but interestingly, in this group of patients, serum albumin predicted neither mortality nor spontaneous closure.

Overall, spontaneous closure without operative intervention occurred in 29 (53.7%) patients. Initial and supportive treatment was directed at control of sepsis, correction of fluid and electrolyte derangements and nutritional support. Although FF may require surgical interventions, re-operation or the use of techniques such as exteriorisation of bowel and parenteral nutrition, emergency resuscitation to ensure normovolaemia and optimised oxygen delivery in anaemic patients should receive priority.[25] Further interventions should focus on control of infection, improvement of nutrition and performing meticulous procedures with sound surgical practice. Preoperatively, nutritional assessment, particularly in patients with a recent 10–15% weight loss, albumin of less than 3.0 g/dl, or low transferrin or total lymphocyte levels (although this is less well proven), who are at increased risk for poor healing and possible anastomotic dehiscence, is also important.

We like to conclude that ECF frequently complicates abdominal surgery for infective causes in children. Although caring for ECF patients can be quite tasking, it may be worthwhile because most ECFs tend to close spontaneously without surgical intervention in children. Sepsis, malnutrition, and fluid-electrolyte deficits are the most important sequelae to which patients with postoperative ECF are exposed, which if not properly managed, are often associated with a high mortality rate. Hypoalbuminaemia, sepsis and hypokalaemia are important prognostic variables in children with ECF. A careful patient selection allows a rational therapeutic approach in the management of ECF in children and ensures a favourable outcome.

Consequently, a secure abdominal wall closure that prevents underlying bowel injuries, avoidance of tension, ensuring adequate blood supply and haemostasis, using non-distended, non-diseased bowel for anastomosis, and proper repair of inadvertent enterotomies or serosal injuries should always be given adequate attention during surgical interventions.[19,25]

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