



CLINICAL STUDY OF FACTORS PREDICTING MORTALITY IN ENTEROCUTANEOUS FISTULAS

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ABSTRACT **Introduction:** Enterocutaneous fistulas pose a great challenge to General surgeons as well as Gastrosurgeons. About 75%–85% of enterocutaneous fistulas are iatrogenic in origin. Reported mortality rates range from 6%–33%. Knowing the factors contributing to mortality in ECF would help overcome the burden. **Materials and Methods:** This is a retrospective study of 42 enterocutaneous fistula patients treated at Department of General Surgery, Government General Hospital, Kakinada over a span of 4 years from June 2018- June 2022. **Results:** Out of 42 cases, 16 have expired. The most common primary etiology was malignancy and the highest association with mortality was noted with mesenteric ischemia. ECF from large bowel had higher mortality. Sepsis (p value = 0.02) was associated with higher mortality. High output fistulas had higher mortality. Hypoalbuminemia (p value = 0.02), associated Acute Kidney Injury (p value < 0.0001), those on TPN (p value = 0.02) and those surgically managed (p value = 0.0003) were significantly contributing to mortality. **Conclusion:** Despite many advances, enterocutaneous fistulas still contribute to a significant mortality rate. Control of sepsis, building the nutrition and correction of electrolyte abnormalities should be focused upon as they can improve the outcome in these patients.

KEYWORDS : Enterocutaneous fistula, ECF, mortality, outcome, predictive factors.

INTRODUCTION

Enterocutaneous fistulae (ECF) are defined as abnormal communications between the gastrointestinal tract and the skin and are often associated with intra-abdominal sepsis^[1]. Enterocutaneous fistulas are an important complication of gastrointestinal surgery. About 75%–85% of enterocutaneous fistulas are iatrogenic in origin which occur as postoperative complication while in 15%–25% of cases develop due to abdominal trauma or spontaneously due to malignancy, inflammatory bowel disease mainly Crohn's diseases, radiation enteritis, ischemia or infective conditions like diverticulitis and appendicitis^[2,3].

There are several ways in which ECF has been classified, including by output, etiology, and source^[1,4,5]. Most often, a high-output ECF is characterized as one with >500 mL/24 hours, low output <200 mL/24 hours, and a moderate output fistula between 200 and 500 mL/24 hours. Management of Enterocutaneous fistulas (ECF) is a complex and challenging problem commonly encountered by the general and specialized surgeon^[6]. Reported mortality rates range from 6%–33%, with the most common causes of death being attributable to malnutrition and sepsis^[7-10]. Closure rates without operative intervention in the era of advanced wound care and parenteral nutrition (PN) vary considerably in reports 19 to 92%^[11,12], with most studies demonstrating closure rates in the 20 to 30% range^[12-18]. With historical wound care measures, 90% of spontaneous closure occurred in the first month after sepsis resolution, with an additional 10% closing in the second month, and none closing spontaneously after 2 months^[17]. In view of huge burden and lack of proper knowledge in the field of ECF pose difficulties in the management of the patients.

MATERIALS AND METHODS:

This study is aimed at the outcome of enterocutaneous fistulas at a tertiary care hospital with respect to mortality. This study includes 42 enterocutaneous fistula patients treated at Department of General Surgery, Government General Hospital, Kakinada over a span of 4 years from June 2018 - June 2022. The data was collected retrospectively from the medical record room of Government General Hospital, Kakinada.

Fistulas following surgery both in-hospital and those referred from elsewhere were included in this study. The mean follow-up period was 6 months. Patients who are less than 18 years were excluded from this study. Spontaneous fistulas, traumatic fistulas and those occurring in pregnant women were excluded. Esophageal, biliary and pancreatic fistulas were excluded from the study. Elective surgical intervention was delayed till 12 weeks from the onset of fistula.

Patients who were included in the study were assessed by demographics, primary etiology, primary index surgery,

investigations, onset of fistula, site of fistulas, output (low output <500 ml, high output >500 ml), associated sepsis (TLC > 11,000 cells/cu.mm), nutritional status (anemia - Hb < 10g/dl, hypoalbuminemia - serum albumin < 2.5g/dl), Dyselectrolytemia (Serum Sodium < 135mEq/L or > 145mEq/L, Serum Potassium < 3.5mEq/L or > 5.5mEq/L, Serum Calcium < 9mg/dL or > 11mg/dL), associated comorbidities (Diabetes Mellitus, Hypertension, cardiac diseases), management, nutritional assistance (enteral nutrition/partial parenteral nutrition/ total parenteral nutrition) and mortality. All the above factors were individually evaluated and mortality rate was calculated for each factor. To assess factors significantly contributing to the mortality of patients, we compared patients with ECF who sustained mortality (group 1) with patients with ECF who survived (group 2).

Statistical analysis was done using chi-square test with 'p' value < 0.05 considered significant.

RESULTS:

A total of 832 emergency laparotomies and 1664 elective laparotomies were conducted in the Government General Hospital, Kakinada from June, 2018 – June, 2022. 42 cases of postoperative enterocutaneous fistulas were taken into the study of which 29(69%) developed following emergency laparotomies, 8(19%) following elective laparotomies and the remaining 5(1.2%) cases were postoperative cases referred from outside hospitals. Of the 42 cases, 21(50%) cases were >50 years. 29(69%) were males and 13(30.9%) were females. ECF with respect to site of origin was documented in Table 1. 12 out of 42(28.5%) had low output fistulas while the remaining 30(71.4%) are high output fistulas. With respect to etiology before index surgery, malignancy accounted to 14(33.3%) cases, 8(19%) were due to intestinal obstruction, 8(19%) following intestinal perforation, 5(11.9%) after appendicitis, 4(9.5%) due to complicated hernia, 2(4.7%) due to mesenteric ischemia and 1(2.3%) due to sigmoid volvulus. 19(45.2%) had occurrence of fistula within 1 week of index surgery and 23(54.7%) cases had fistulous onset after 1 week of surgery. 25(59.5%) cases had sepsis, hypoalbuminemia seen in 17(40.47%), anemia in 20(47.6%), dyselectrolytemia seen in 24(57.1%) cases. About 18(42.8%) cases had associated comorbidities. Enteral nutrition given in 15(35.7%), partial parenteral nutrition given in 19(45.2%) and total parenteral nutrition in 8(14.2%) cases. Enterocutaneous fistulas presenting after more than 1 week of index surgery 9 of 23 patients (39.1%) has increased mortality compared with fistulas in less than 1 week 7 of 19 patients(36.8%).

Out of the 42 patients, 16(38.1%) have expired due to fistula related causes. ECF from large bowel disease (40%) had highest mortality compared to small bowel (38.09%) and gastroduodenal disease. Out of the total fistulas, about 19 cases had fistulous onset within 1 week of

surgery, of which 7 have expired. The remaining 23 patients presented with enterocutaneous fistula after 1 week, of which 9 have expired. Enterocutaneous fistulas presenting after more than 1 week of index surgery (39.1%) has increased mortality compared with fistulas in less than 1 week (36.8%).

Table 1 : prevalence of entero cutaneous fistula based on site of origin

Site of fistula origin	Prevalence(%)
Gastroduodenal	6(14.2)
Small Bowel	21(50)
Large Bowel	15(35.7)

Based on the output, out of the total 42 cases, 12 cases had low output fistulas of <500ml/24 hours. 3(25%) out of the 12 low output cases have expired. Of the remaining 30 high output cases (>500ml/24 hours), 13(43.3%) cases have expired.

When comparing the mortality according to the site of fistula, out of the 42 enterocutaneous fistulas, 13 of them had fistula onset from the drain site, of which 4 (30.7%) have expired. 29 cases had fistula from the surgical incision site, of which 12 (41.3%) have expired.

Out of the 16 expired cases, sepsis contributed to the major cause of mortality accounting to 81.2% of the mortality, followed by hypoalbuminemia, anemia, age, dyselektrolytemia and comorbidities. All these factors were in turn evaluated in a reciprocal way in their contribution to mortality by dividing into 2 groups – The mortality group and the survival group and 'p' value was calculated using chi-square test and represented in Table 2

Table 2: Comparison between the mortality group and the survival group with various factors contributing to them. *mark indicates that the 'p' value is significant(<0.05)

Variables	Expired(n=16)	Survived(n=26)	P value
Age			
<50 years	6(37.5%)	15(57.6%)	0.2113
>50 years	10(62.5%)	11(42.3%)	0.2090
Gender –			
Males	12(75%)	17(65.3%)	0.5143
Females	4(25%)	9(34.6%)	0.5184
Site of origin			
Gastroduodenal	2(12.5%)	4(15.3%)	0.8032
Small bowel	8(50%)	13(50%)	1
Large Bowel	6(37.5%)	9(34.6%)	0.8507
Aetiology before surgery			
Malignancy	6(37.5%)	8(30.7%)	0.6537
Intestinal obstruction	5(31.2%)	3(11.5%)	0.1184
Intestinal perforation	2(12.5%)	6(23%)	0.4053
Complicated hernia	1(6.2%)	3(11.5%)	0.5737
Mesenteric ischemia	2(12.5%)	0(0%)	0.0680
Sigmoid volvulus	0(0%)	1(3.8%)	0.4356
Onset of fistulas			
<1 week	7(43.7%)	12(46.1%)	0.8808
>1 week	9(56.2%)	14(53.8%)	0.8808
Fistula Presentation			
Drain site	4(25%)	9(34.6%)	0.5184
Surgical Site	12(75%)	17(65.38%)	0.5143
Output of fistula			
Low	3(18.7%)	9(34.6%)	0.2736
High	13(81.2%)	17(65.3%)	0.2741
Biochemical parameters			
Anaemia – Hb <10g/dl	10(62.5%)	10(38.4%)	0.1335

TLC >11000 cells/cu.mm	13(81.2%)	12(46.1%)	0.0262*
Albumin <2.5g/dl	10(62.5%)	7(26.9%)	0.0241*
Dyselektrolytemia	11(68.7%)	13(50%)	0.2400
AKI	13(81.2%)	4(15.3%)	<0.0001*
Comorbidities affecting mortality	9(56.2%)	9(34.6%)	0.1747
Nutrition received			
Enteral Nutrition	1(6.25%)	6(23%)	0.1618
Partial Parenteral Nutrition	5(31.25%)	13(50%)	0.2387
Total Parenteral Nutrition	10(62.5%)	7(26.9%)	0.0241*
Management			
Conservatively managed	3(18.7%)	20(76.9%)	0.0003*
Surgically managed	13(81.2%)	6(23%)	0.0003*

19 cases were managed surgically, among them 13 (68.4%) have expired. 12 cases out 19 cases underwent resection and anastomosis, of which 10 (83.3%) have expired. 2 (33.3%) out of 6 patients died after creation of stoma. 1 (100%) patient who had repair of perforation expired. Re-fistula noted in 52.6% patients (10 out of 19); 9 following resection and anastomosis and 1 following stoma creation.

DISCUSSION:

Management of patient with enterocutaneous fistula still represents a major challenge and dilemma in general surgical practice^[19]. The main concern in the treatment of enterocutaneous fistula is to enhance the spontaneous closure^[20]. Although spontaneous closure occurs in some patients most of the cases need definite surgical intervention to excise the fistulous tract and to restore the continuity of intestine if the clinical and operative conditions permit^[20-22].

Most common type of enterocutaneous fistula, in our study was found to be small bowel origin(50%), which was found to be similar to other studies with a range of 44.2% to 81%^[6, 22,23,24,25,26]. Intestinal obstruction(55.5%) was found to be the most common etiological factor precipitating ECF in our study, as shown by Noori et al^[22], Martinez et al^[6], whereas inflammatory bowel disease was found to be the most common cause of ECF in Mawdsley et al^[24], Ortiz et al^[20] and Mc Intyre et al^[25]. Difference in the etiological factors causing ECF could be attributed to the varied study population. Mesenteric ischemia had 100% association with mortality.

We have taken into account the duration of fistula onset from the time of primary surgery and its relation to mortality which was not included in any of the other studies. 19 out of the 42 fistulas had occurred within the first week with 36.8% mortality and in the remaining 23 fistulas which presented after 1 week of index surgery had a mortality of 39.1%.

Out of the 42 enterocutaneous fistula cases, 12 were of low output with 25% mortality and in the remaining 30 high output fistulas with 43.3% mortality. The mortality in high output cases in the study conducted by Martinez et.al was about 23.07% when compared to the mortality in low output fistula cases which was about 15.6%^[6].

Mortality rates in various studies ranged from 3% to 30.9%^[6, 15, 22-26] whereas in our study it was found to be 38.1%. The most common cause of mortality in our study was sepsis similar to that of the other studies. Sepsis accounted to about 81.2 % of mortality in our study which was in accordance with that of Quinn et. al (86.2%)^[1], Martinez et. al (85.7%)^[6], Mawdsley et al(77%)^[24] and Campos et. al. (77.6%)^[15].

In our study, enterocutaneous fistulas arising from large bowel had highest mortality of 40% and the least were the gastroduodenal enterocutaneous fistulas accounting to 33.3% mortality. This was not correlating with the mortality in studies by Noori et. al^[22], Mawdsley et. al^[24] as it was found to be higher in small bowel enterocutaneous fistulas whereas in Altomare et. al^[23] reported mortality to be highest in pancreatic fistulas. This could be due to the increased proportion of malignancy cases in our study population.

With respect to nutritional support, mortality of those on enteric

nutrition was 14.2% and those on combined enteral and parenteral nutrition was 27.7% and 58.8% of those on total parenteral nutrition in our study. The mortality in regards to the nutritional support was not calculated in studies by Quinn et. al^[1], Martinez et. al^[6], Campos et. al^[15], Noori et. al^[22], Altomare et. al^[23], Mawdsley et. al^[24] and McIntyre et. al^[25].

Mortality in surgically managed patients was higher when compared to those who were managed conservatively in our study similar to the results in Noori et. al^[22]. Surgical management in ECF is a double edged sword, with some studies showing better healing rate as in Martinez et. al^[6] and Mawdsley et. al^[24]. The need for surgery in management of ECF should be tailored according to the patient's clinical condition and patient's ability to handle surgical stress. Surgery in the early phase of ECF should be focused on controlling sepsis and establishing nutrition. Matured and well-controlled fistulas which failed to heal spontaneously should be considered for surgery at 3-6 months.

The re-fistula rate in our study was found to be 52.6%, Martinez et. al^[6] estimated it to be 31%. High re-fistula rate can be because of missed enterotomies, poor wound healing and primary etiology. Prognosticating patients undergoing surgical management regarding re-fistula rate should be of utmost importance.

Factors such as sepsis, hypoalbuminemia, associated Acute Kidney Injury, those patients with TPN and those who have been surgically managed are found to be significantly contributing to the mortality in enterocutaneous fistulas in our study (Table-2). Quinn et. al^[1] attributed increasing age at presentation to higher mortality. Altomare et. al^[23] found sepsis, hypoalbuminemia, increased APACHE II score and high output of the fistulas to be significant factors contributing to mortality. Mawdsley et. al^[24] noted high output fistulas and increasing age of presentation to be significantly contributing to the mortality. Kushvinnoff et. al^[27] mentioned that systemic sepsis, serum transferrin, Retinol binding protein and Thyroxine binding pre-albumin as predictors of mortality. Measures at controlling sepsis, nutritional build-up and aggressive management of complications can alter the outcome of patients with ECF.

Limitations: Our study did not include other prognostic biomarkers of sepsis which gained value during the recent times like CRP, Serum Procalcitonin^[28] and serum transferrin^[27] due to unavailability of resources at our institution. Our study could not focus on other non-operative management strategies such as NPWT, Fibrin sealant, Fibrin plugs which gave promising results in some studies^[29,30,31,32]. This was mainly due to financial constraint of the patients attending our institute. Role of somatostatin analogues like Octreotide was not considered in our study. Our study did not assess the importance of radiological imaging pertaining to fistula length and anatomy, contributing in the management of ECF. Future studies can focus on these areas for better contribution to the literature in the management of ECF.

CONCLUSIONS

Despite many advances, enterocutaneous fistulas still contribute to a significant mortality rate. Control of sepsis, building the nutrition and correction of electrolyte abnormalities should be focused upon as they can improve the outcome in these patients.

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