

**ORIGINAL ARTICLE****Colorectal Anastomosis Leak: Rate , Risk Factors and Outcome in a Tertiary Teaching Hospital, Addis Ababa Ethiopia, a Five Year Retrospective Study****Gutema Wako<sup>1</sup>, Henok Teshome<sup>2</sup>, Engida Abebe<sup>3</sup>****OPEN ACCESS**

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**ABSTRACT**

**BACKGROUND:** Anastomotic leakage is a morbid and potentially fatal complication of colorectal surgery. Determination of peri-operative risk factors for colorectal anastomosis leak helps to identify patients requiring increased postoperative surveillance.

**METHODS:** Institution based retrospective study was done to determine colorectal anastomosis leak rate and risk factors associated with it at a teaching hospital in Addis Ababa Ethiopia. Patients operated from January 2013 to December 2017 G.C were included. Univariate analysis followed by a multivariate logistic regression model was used to determine the influence of patient factors and operative events on postoperative anastomotic leakage.

**RESULTS:** Inclusion criteria were met by 221 patients. Mean age of patients was 46.44(SD=19.1) with range of 1 to 85 years. Male accounted to 166 (74.8%) of the patients. Anastomotic leakage occurred in 12 (5.2%) of the patients. Mean time to diagnosis was 9.55 days (95% CI, 7.2-11.8) after surgery. Univariate analyses showed high preoperative level of creatinine, ASA score III and IV, emergency operation, operative time more than three hours, and malignant diseases were associated with colorectal anastomosis leak. Multivariate logistic regression model failed to show an association. Colorectal anastomosis leak increased the inpatient mortality rate by 50%. Median length of hospitalization in colorectal anastomosis leak group was 27.5 days, versus 7 days in patients without leak.

**CONCLUSION:** Colorectal anastomosis leak remains common problem after colorectal surgery resulting significant post-operative mortality and morbidity.

**Key words:** Anastomosis, Anastomosis Leak, Risk factors

**INTRODUCTION**

Colorectal anastomosis is performed for several conditions of the colon; colorectal cancer, redundant sigmoid, trauma to the colon and rectum, colostomy reversal etc. When it occurs, anastomotic leakage (AL) after colorectal surgery is a dreadful complication leading to significant morbidity and mortality, not to mention longer hospital stay and significantly increased cost of care (1). Reported rates of

anastomotic leakage vary widely (2.6 % and 19%) depending on definition, site and type of anastomosis and the cohort under investigation. Mortality rates due to AL vary between 10 % and 20 % (2-6). Several studies have identified risk factors for AL; however, there is no universal agreement on which risk factors consistently feature (7-11).

Widely accepted definition of anastomosis leak (AL) is lacking. An attempt to address this was made in 2010 by the International Study Group of Rectal Cancer (ISREC), based on exhaustive synthesis of Current literature. ISREC defined AL as 'a communication between the intra- and extra-luminal compartments owing to a defect of the integrity of the intestinal wall at the anastomotic site. In addition, a pelvic abscess adjacent to an anastomosis, even if no communication with the bowel lumen could be demonstrated, was considered to have originated from a leak. Recommendation was made for a simple grading system, based on clinical management, as follows: Grade A, resulting in no change in management; Grade B, requiring active therapeutic intervention but manageable without re laparotomy; and Grade C, requiring relaparotomy (1,2).

Anastomotic defect causes leakage of colonic content into the abdominal and/or pelvic space leading to peritonitis, abscess formation and sepsis that can be fatal. The diagnostic methods commonly used when a leakage is suspected are CT scan, contrast enema, endoscopic examination, and reoperation. Anastomotic leakage typically becomes clinically apparent between the 5<sup>th</sup> and 8<sup>th</sup> postoperative day but many exceptions exist (5). Definition of clinically apparent anastomotic leakage is: 1) fecal fistula to skin or vagina 2) Fever more than 38 degree centigrade or septicemia 3) Radiological or Endoscopic signs of anastomotic leakage 4) Intra-peritoneal abscess or peritonitis in the presence of an anastomotic leak. Local data showing incidence of anastomotic leakage and its impact on clinical outcome is not available. As colorectal surgery is among the common surgeries practiced in our hospital the AL is expected to be there. To the best of our knowledge there is no study done in Ethiopia on burden and risk factors for AL. The benefits of

identifying patients at high risk of anastomotic leakage provide the opportunity for better informed preoperative patient counseling and the potential for treatments to be tailoring. The objective of this study was to determine the rate, risk factors and outcome of clinically significant anastomotic leak after colorectal surgery.

## MATERIALS AND METHODS

A retrospective study was performed at St. Paul's Hospital Millennium Medical College, in Addis Ababa, Ethiopia, from January to August 2018. St. Paul's Hospital Millennium Medical College is a teaching hospital for both undergraduate and postgraduate studies with 110 surgical beds. All patients who had colorectal anastomosis from January 2013 to December 2017 GC were included in the study. Patients operated elsewhere and referred to SPHMMC, who had protective stoma, missed or incomplete charts were excluded from the study.

The operation theater log book was used to identify patients and individual patients medical records were reviewed to extract data. Data on patients' socio- demographic characteristics, clinical/lab parameters including co-morbidities, smoking habits, ASA score, hematocrit level, serum Albumin level, history of previous abdominal surgery, preoperative chemo radiation, intra-operative blood transfusion, indication for operation, urgency of operation, type of procedure, duration of operation, Anastomotic leak, surgical site infection, wound dehiscence, ECF, re laparotomy were collected by trained surgical residents in a pretested data collection format. Data collection was supervised and quality of data checked every day.

The data was analyzed using SPSS version 23. Univariate analysis followed by a multivariate logistic regression model was used to determine the influence of patient factors and operative events on postoperative anastomotic leakage. Statistical test chi square at 0.05 level of significance was used. A written ethical clearance letter was given from SPHMMC's institutional review board. Data acquired was used only for the study and patients' information used in the research was kept confidential.

As this is a retrospective study, all the limitations of such type of study should be expected. Some of the patients lacked properly registered data and complete investigations. The non-response rate of the study was 17%.

Anastomotic leakage was deemed to have occurred when there were: signs of peritonitis and/or purulent/ feculent discharge from a drain or wound and/or radiological evidence (a fluid collection in proximity to an anastomosis and/or operative evidence of anastomotic disruption. Malnutrition was defined by albumin <3.5 or total serum protein <5.5 or unintentional weight loss more than 10% body weight in the last 6months.

Anemia was assumed to be present when hematocrit was less than 30% or hemoglobin less than 10g/dl.

## RESULTS

During the study 266 patients had colorectal anastomosis (CRA) without protective stoma. Of these, 20 patients with incomplete charts and 25 patients whose charts could not be retrieved were excluded. Hence analysis was based on the 221(83.1%) patients with complete record. The main form of surgeries were primary colon resection and anastomosis 226(85%) and colostomy reversal 60(15%). Age of the patients ranged from 1 to 85 with mean age 46.44(IQR, 32-60). Majority 166(74.8%) of patients were male making the male to female ratio 3:1. Most surgeries were for benign conditions 177(80%) and on elective basis 181(81.9%). Duration of procedure was less than three hours in 179(81.4%) of patient. Only 20 patients (9.1%) required peri-operative blood transfusion (Table 1).

Table 1. Patient population and results of Univariate Analysis of Patient Demographics, Preoperative risk factors for anastomosis leak, among patients with Colonic anastomosis at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017 G.C.

		Total cases	Anastomosis leaked	No Anastomosis leak	p-Value
Sex	Male	166(75.1)	6 (3.6)	160 (96.4)	0.054
	Female	55(24.9)	6 (10.9)	49 (89.1)	
Age (Years)	Mean (SD)	46.4(19.1)	42.2(16.0)	46.9(19.3)	0.426
Urgency of operation	Elective	181(81.9)	7 (3.9)	174(96.1)	0.03
	Emergency	40(18.1)	5 (12.5)	35(87.5)	
Nature of the conditions	Malignant	44(20)	7(15.9)	37(84.1)	0.01
	Benign	177(80)	5 (2.8)	172(97.2)	
Types of anastomosis	Primary	165(74.7)	11(6.7)	154(93.3)	0.164
	Colostomy reversal	56(25.3)	1(1.8)	55(98.2)	
Duration of surgery	< 3 hours	179(81.4)	6 (2.8)	173 (97.2)	0.04
	>3 hours	41(18.6)	6 (14.6)	35(85.4)	
ASA score	I,II	160(72.4)	4 (2.5)	156(97.5)	0.05
	III,IV	5(2.3)	1 (20.0)	4(80.0)	
	Unknown	56(25.3)	7(12.5)	49(87.5)	
Preoperative Hematocrite	> 30%	209(94.5)	10 (4.8)	199 (95.2)	0.057
	<= less 30%	11(5)	2 (18.2)	9 (81.9)	
	Unknown	1(0.5)			

Commonest indication for CRA was redundant sigmoid 125 (56.5%) followed by Colon and rectal cancers 44, (20%) (Table 2).

Table 2. Conditions requiring anastomosis involving the colon or rectum at St. Paul Hospital Millennium Medical College, A.A, Ethiopia from January 2013 to December 2017 G.C

Conditions	Number	Percent
Colon and rectal cancers	44	20
Intussusception	21	9.6
Redundant sigmoid	125	56.5
IBD (Crhon's disease)	5	2.2
Intestinal Tuberculosis	3	1.4
Mesenteric ischemia	4	1.8
Traumatic injury	9	4
Others	10	4.5
Total	221	100

**Incidence of anastomosis leak:** Anastomotic leak was diagnosed in 12(5.2%) patients with mean time to diagnosis after the operation was 9.55 days (95% CI, 7.2-11.8), median 10 days, and range 3-14 days. Mean age of patients with anastomosis leak was 42.16[SD=15.97] compared to 46.68[SD=19.25] in patients without leak, (p=0.46). Anastomotic leakage was found in 10.9% (6) of women versus 3.6 % (6) of men,

P=0.054). Incidence of AL after emergency operation was 12.5% compared to 3.9% in elective operation (P=0.029). Anastomotic leakage after malignant colorectal lesions was 15.9% versus 2.8% in benign condition, (p=. 0.01) (Table 1). Highest incidence of AL occurred after right hemicolectomy 5(13.9%) followed by LAR 1(12.5%), P=0.085.

Table 3. Comorbidities and their association with colonic anastomosis leak among patients with Colonic anastomosis at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017 G.C

		Total cases	Anastomosis leaked	No Anastomosis leak	p-Value
Previous abdominal surgery	Yes	71(32.1)	3 (4.2)	68 (95.8)	0.59
	No	150(67.9)	9 (6.0)	141(94.0)	
DM	Yes	4(1.8)	1(25)	3(75)	0.081
	No	217(98.2)	11(5.1)	206(94.9)	
Cardiac disease	Yes	10(4.5)	0	10(100)	0.438
	No	211(95.5)	12(5.7)	199(94.3)	
HTN	Yes	19(8.6)	1(5.3)	18(94.7)	0.973
	No	202(91.4)	11(5.4)	191(94.6)	
Creatinine Level	Yes	6(2.7)	2(33.3)	4(66.7)	0.02
	No	215(97.3)	10(4.7)	205(95.3)	
RVI	Yes	5(2.3)	1(20)	4(80)	0.147
	No	216(97.7)	11(5.1)	205(94.9)	

**Risk Factors:** Demographic characteristics, comorbidities, and procedural characteristics were tested for associations with AL. Five risk factors were associated with AL in univariate analyses (high preoperative level of creatinine( $p=0.02$ ), ASA score III and IV ( $p=0.05$ ), emergency operation ( $P=0.03$ ), operative time more than three hours ( $p=0.04$ ), and malignant pathology ( $p=0.01$ )) (Table 1 and 2). All of these variables were entered into multivariate logistic regression and none of the variables had statistically significant association with AL. There was no significant statistical association between AL and age, preoperative hematocrit and albumin,

preoperative transfusion, DM, cardiac disease, HTN and RVI.

**Morbidity and Mortality:** A total of 47 (21.3%) complications occurred and 16 patients died. Only two patients with AL survived (Table 5). In patients with AL, inpatient mortality rate increased to 50% (6/12) but it was 4.8% (10/209) in patients without AL, ( $P<0.001$ ). The median postoperative length of hospitalization was 8 days (25<sup>o</sup>–75<sup>o</sup> percentile, 6–12 days) for the whole group. In patients with AL the median length of hospitalization was 27.5 days (25<sup>o</sup>–75<sup>o</sup> percentile, 9–19 days) compared to 7 days (25<sup>o</sup>–75<sup>o</sup> percentile, 6–9 days) in patients without AL,  $p=0.01$

Table: -4 Type of resections and univariate analysis, among patients with Colonic anastomosis at St. Paul Hospital Millennium Medical College, A.A, Ethiopia from January 2013 to December 2017.

Type of resection	No.(%)	Anastomosis Leak, No.(%)	No Anastomosis Leak, No.(%)	P value, CI
Ileocecal resection	14(6.3)	1(7.1)	13(92.9)	0.085, CI=1.77_2.08
Right hemicolectomy	36(16.2)	5(13.9)	31(86.1)	CI= 1.74_1.98
Transverse colectomy	1(0.5)	0	1(100)	
Left hemicolectomy	5(2.3)	0	5(100)	
Sigmoid colectomy	93(41.9)	0	93(100)	
LAR	8(3.6)	1(12.5)	7(87.5)	0.06
Subtotal colectomy	1(0.5)	1(100)	0	
Total colectomy	2(0.9)	0	2(100)	
Colostomy reversal	57(25.8)	1(1.8)	56(98.2)	
Others	4(1.8)	3(75)	1(25)	

Table:-5 Clinical outcome after AL, among patients with Colonic anastomosis at St. Paul Hospital Millennium Medical College, A.A, Ethiopia from January 2013 to December 2017 G.C

	Total	Anastomosis leak N=12	No Anastomosis leak N=209	P value
Superficial Surgical Site Infection	26 (12.7)	4(33.3)	22 (13.4)	0.027
Wound dehiscence	10 (4.5)	4(33.3)	6 (2.8)	<0.001
Intra-abdominal abscess	5 (2.7)	4(33.3)	1(0.48)	<0.001
ECF	6 (2.7)	5(41.6)	1(0.48)	<0.001
Re-laparotomy	10 (4.5)	5(41.6)	5 (2.4)	<0.001
Mean(SD) Length of hospital stay(days)	9.28(6.9)	26.25(3.67)	8.33(0.346)	<0.001
Inpatient death	16 (7.2%)	10(4.8)	6 (50%)	<0.001



## DISCUSSION

In this 5 years retrospective study, among 221 patients meeting inclusion criteria, anastomotic leak was diagnosed in 12 (5.2%) patients and median time to AL was 10 days (IQR 7.5–8 days) ranging between 3-14 days. This anastomotic leak rate is well within expectation based on recent literatures where leak rate ranges between 4.9% and 7.2% (12,16). Multivariate Prospective, National Study done in Valencia, Spain with 3193 Patients by Matteo Frasson et al (13), CAL was diagnosed in 277 patients (8.7%) between postoperative days 1 and 52 (median of 6 days, 25<sup>o</sup>–75<sup>o</sup> percentile 4–10 days)

In our study's univariate assessment of age as a risk factor for CAL does not show significant association which is consistent with studies by Boccola MA et al (14) and Kang CY et al. (15). Prospective observational meta analyses done in Denmark (16) to evaluate age as a risk factor failed to show significant association with CAL. The fact that age in itself in otherwise healthy and fit patients does not seem to be a contraindication for primary anastomosis is interesting. Increased age may increase the risk for comorbidity, but still many elderly patients may be perfectly healthy. Reported predictors for anastomotic leakage such as previous abdominal surgery, diabetes mellitus, cardiovascular disease, male gender could not be confirmed in our present analysis. Similar to our findings, a prospective study done by Dana A. Telem, MD et al. (17) demonstrated no increased risk for CAL by sex, preoperative diagnosis of cardiovascular disease and Diabetes Mellitus. But other studies conducted by C Iancu et al. (22) and Andrea Vignali et al. (23) showed that diabetes mellitus and cardiovascular diseases were significantly related to the occurrence of anastomotic leak.

American Society of Anesthesiologists score remained a significant predictor of anastomosis leak in our study, it was associated with anastomotic leakage in univariate analyses. Patients with a high ASA-class may be more prone to CAL owing to an increased comorbidity rate (e.g. cardiovascular or pulmonary diseases), which may impair tissue perfusion and oxygenation.

A high preoperative level of creatinine was associated with AL in the univariable model but did not quite reach significance in the multivariable model which is similar to finding of Mikkel Jessen, Malene Nerstrøm, et al. (12) in Berlin, Germany. Here, a high creatinine level was associated with a high ASA score and thus a proxy of overall comorbidity.

Surgery related factors such as emergency operation and operation time more than three hours remained significant predictor of anastomotic leak in univariate analyses in our study but multivariate analysis failed to show significant association. Emergency surgery, which intuitively should put patients at a higher risk for adverse postoperative events, was indeed reported to be associated with AL based on univariate and multivariate analysis by N. Koimen et al. (18) but this association was not consistently found by others (19,20). In our study, emergency surgery was also associated with AL based on univariate analysis ( $P=0.029$ ), but did not remain significant after multivariate logistic regression analysis. Only 18.1% ( $n=40$ ) of patients in our study population underwent this operation emergently, and only 12.5% ( $n=5$ ) of all anastomotic leaks were found among emergent cases, thus limiting the statistical power of this assessment in our analysis. This finding is similar with study done by Stefan W. Leichtle, et al. (21)

In our study overall inpatient mortality was 16/221 (7.2%) and 11/221 (3.4%) in elective patients compared with 14/105 (7.2%) in emergency patients,  $P < 0.001$ . As can be expected it was higher in emergency patients. The mortality rate in patients with AL was 6/12 (50%) compared with 10/109 (9.2%) in patients without AL,  $P < 0.001$  which is statically significant. As patients with AL will develop fecal peritonitis in a compromised physiology and anatomy mortality rate is expected to be high as seen in our case.

This is much higher than most recent literatures which is between 10% to 20% (5). Retrospective study done by Komen, et al. (18) on 739 patients mortality rate due to leakage was 14.1%. The mortality rate among patients with AL was significantly higher than in those without leakage (16.4 versus 3.1 per cent;  $P < 0.001$ )

In conclusion AL remains an important post-operative complication among patients who had colorectal anastomosis. The presence of renal disease, ASA score of III and IV, emergency operation, operative time more than three hours, and malignant pathology were associated with AL in univariate analyses. Multivariate analysis controlling for multiple confounding factors demonstrated that no patient-related or surgery-related factors were associated with AL. However, further studies are needed which focus on risk factors that currently are insufficiently explored. AL has significantly increased the inpatient mortality rate and post-operative stay of patients with significant statistical association. There was a delay in detecting CAL which increases the mortality rate. High index of suspicion and timely intervention can improve patient outcomes. The limitations of this study are the retrospective nature of the study, some of the patients lacked properly registered data and a non-response rate of 17%.

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