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Original Research Article

Serum pre-albumin, a novel indicator of risk of anastomotic leak in bowel anastomosis

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ABSTRACT

Background: Various preoperative and intraoperative risk factors associated with anastomotic leak have been extensively analyzed. Albumin is considered as the gold standard preoperative marker of nutrition, but recently pre-albumin is found to be a better indicator of nutrition. The main aim of this study was to analyze the preoperative risk factors including pre-albumin to predict anastomotic leak following small and large bowel anastomsois.
Methods: This was a prospective observational, quality improvement study in a cohort of 100 patients undergoing small and large bowel resection in the Division of Surgery at Christian Medical College, Vellore. Univariate and multivariate analysis was done to show the significant variables associated with anastomotic leak.
Results: In present study, leak rate was 21% (21/100). In univariate analysis, 6 factors had significant association with anastomotic leak, age >45 years, ASA score of II, hemoglobin ≤9.0 gm/dl, serum albumin ≤3.0 gm/dl, serum pre-albumin ≤20 mg/dl and preoperative diagnosis of malignancy. Age >45 years, ASA score of II, serum pre-albumin ≤20 mg/dl and malignancy were found to be independent risk factors of anastomotic leak. In present study prelbumin, was found to be a better indicator of anastomotic leak when compared to albumin and it was statistically significant (p=0.002).
Conclusions: Serum pre-albumin is superior to albumin as an acute marker of malnutrition and help us to identify those at risk of anastomotic leak and adequately build nutrition preoperatively and decrease the morbidity.

Keywords: Albumin, Anastomotic leak, Preoperative risk factors, Pre-albumin

INTRODUCTION

Bowel anastomosis is one of the most common operations performed for various indications, both in elective and emergency conditions. Anastomotic leak is a devastating complication which adversely affects the outcome by increasing morbidity and mortality.

Knowledge of various risk factors predisposing to anastomotic leak is of clinical importance to identify the patients at risk of developing anastomotic leak. Anastomotic leak rate varies from 0.3% to 5.5% for small bowel operations and 0.5% to 21% for colon and rectal procedures.[1-5]

The surgical literature is replete with studies which have attributed the anastomotic leak to patient factors, associated co morbid conditions, faulty techniques and some adverse operative factors. The main aim of this study was to analyse the preoperative risk factors including prealbumin to predict anastomotic leak following small and large bowel anastomsois.

Of the various preoperative variables studied, malnutrition is one of the important predictor of

anastomotic leak. Serum albumin has been studied extensively and proven risk factor for anastomotic leak. As the half-life of serum albumin is 14 to 20 days, in acute setting it may not be accurate. Screening protocols which utilize serum prealbumin have identified more patients who are malnourished when compared to other protocols for malnutrition pre albumin may be a better marker in acute settings as it has a shorter half-life of 2 days.[6,7] Hence pre albumin is a good predictor of the protein and energy adequacy of the diet and can serve as a marker of acute malnutrition.

METHODS

This study was a prospective observational quality improvement study without retrospective component carried out at Christian Medical College (CMC), Vellore from 1st January 2015 to 31st August 2016. All patients who underwent either small bowel or large bowel anastomosis and above the age of 18 years were included in the study. Anastomosis involving stomach, rectum and anus were excluded from the study.

Study was approved by Christian Medical College Institutional Review Board. Data was collected from the patient and their attendants and the electronic database.

In present study, Anastomotic leak was defined:

- Clinically by the treating surgeon and clinical signs include 1. pain 2. fever 3. tachycardia 4. tachypnea 5. peritonitis 6. feculent discharge or purulent discharge through the wound or drains.
- Radiologically by contrast extravasation, pneumo peritoneum, abscess adjacent to suture line.
- Intra operatively by gross contamination of abdomen with enteric contents and disruption of the anastomosis.

All the data collected was collected in a pre-designed proforma and later entered using epidata software and then converted to SPSS sheet for further analyses and conclusions.

A univariate analysis was performed to measure the association between each of these risk factors with leak. The variables which were significant at bivariable level taken for multivariable analysis. OR was expressed with 95% CI. Chi-square test was done to check the significance of albumin vs prealbumin to predict anastomotic leak.

RESULTS

Over the study period, 100 patients who satisfied inclusion criteria were enrolled into study. Patient demographic details are depicted in Table 1.

Of these, 21 patients (21%) developed anastomotic leak. Various variables which were found to be significant by univariate analyses were age of patient >45 years, ASA score of II and higher, hemoglobin values of <9 gm/dl, serum Albumin value of ≤3.0 gm/dl, serum pre-albumin value of 20 mg/dl, preoperative diagnosis of malignancy. Though serum albumin levels are normal in 13 patients who developed anastomotic leak, they had abnormal pre-albumin value (<20 mg/dl). Only 31% (n=6) of patients had both normal albumin and pre-albumin values.

Table 1: Demographic information of the study group.

Demographic Indicator	Patients (N=100)
Age (mean ± SD)	47.27±14.87
BMI (mean ± SD)	22.31±4.33
Sex (% Male)	62%
ASA Score (I-VI)	57% (ASA-I), 42% (ASA-II)
Diabetes	17%
Pulmonary disease	6%
Cardiovascular disease	1%
Smoking	9%
Alcohol	5%
Steroids	4%
Pre-op TPN	4%
Previousabdomial surgery	61%
No malignancy	63%

ASA - American Society of Anesthesiologists, BMI – Body Mass Index, TPN- Total Parenteral Nutrition

Risk factor analyses are summarized in Table 2.

The patients whose age >45 years had 23.2 (95% CI: 2.3 – 237.6) times significantly higher risk of getting leak compared with age group ≤45 years (P=0.008). Similarly, ASA score II had 6.6 (95% CI: 1.3 – 32.5, P=0.02) times more risk of getting leak compared with ASA score I.

Patients whose Serum pre-albumin lower than 20 mg/dl had 8.1 (95% CI: 1.6-41.3, P=0.012) times more risk of getting leak compared with Serum pre-albumin 20 to 40 mg/dl. However, malignancy patients had 6.6 (95% CI: 1-42.1) times higher chance of getting leak compared with benign diagnosis (p=0.048).

Using Chi-square test, statistical analysis was performed to compare prealbumin and albumin as a risk factor of anastomotic leak. Out of 21 patients with anastomotic leak, 15 patients had low prealbumin. In these 15 patients with low prealbumin, 13 patients had albumin>3 gm/dl.

In present study prelbumin, was found to be a better indicator of anastomotic leak when compared to albumin and it was statistically significant (p=0.002).

Table 2: Risk factor analysis for anastomotic leak.

Univariate analysis						Multivariate analysis		
Variables	**Leak (N=21)**	**No leak (N=79)**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Age (years)								
≤ 45	1 (4.8)	38 (48.1)	1.00	2.4-144.9	0.005	23.2	2.3-237.6	0.008
>45	20 (95.2)	41 (51.8)	18.5					
ASA score								
I	7(12.3)	50(87.7)	1.0	1.3-9.9	0.014	6.6	1.3-32.4	0.02
II	14(33.3)	28(66.7)	3.6					
Serum Prealbumin (mg/dl)								
< 20	15 (38.5)	24 (61.5)	5.7	2.0-16.6	0.001	8.1	1.6-41.3	0.012
20-40	6 (9.8)	55 (90.2)	1.0					
Preoperative diagnosis								
Malignancy	15 (34.1)	29 (65.9)	4.3	1.5-12.3	0.006	6.6	1.0-42.1	0.048
Benign	6 (10.7)	50 (89.3)	1.0					
Haemoglobin:								
< 9.0 gm/dl	8 (47.1)	9 (52.9)	4.8	1.6-14.7	0.006	0.5	0.1-3.1	0.43
≥9.0 gm/dl	13 (15.7)	70 (84.3)	1.0					
Serum Albumin (gm/dl)								
≤ 3.0	2(100)	0(0)	20.4	1.1-441.6	0.042	1		0.99
>3.0	19(19.4)	79(80.6)	1					

Table 3: Albumin versus prealbumin as a predictor of anastomotic leak.

	Prealbumin ≤20 mg/dl	**Prealbumin 20-40 mg/dl**
Albumin ≤ 3.0 gm/dl	2 (100%)	0
Albumin > 3.0 gm/dl	13 (68.4%)	6 (31.6%)

DISCUSSION

A total of 100 patients were analyzed in present study. Of these, 21 patients developed anastomotic leak with a leak rate of 21%. This rate was on the higher side when compared to literature, where rates vary from 1% to 21%, depending on the location of anastomosis.[2] High leak rates are acceptable for lower rectal and colo-anal anastomosis. However, in present study anastomosis was limited to small and large bowel only, excluding the rectum.

Preoperative risk factors

Patients age was distributed into four groups. Majority of leaks (95%) occurred in those above the age of 45 years. Patients above the age of 45 years have 18 times more risk of developing leak compared to other group with odd's ratio of 18.5 and risk is also statistically significant (p <0.005). Many studies have not shown association with age group of patients, but one study done on rectal resections has shown association with elderly age group >70 years.[8-10]

Present study showed slightly higher risk as compared to males for anastomotic leak, but it is not statistically significant. Present study did not reflect the same results as in other study where male gender was a risk factor.[8,9] There are other studies which did not show any association with gender of patient.[8] BMI has been shown to be a significant risk factor in literature and same results were obtained in present study. Weight loss has been identified as risk factor by Iancu et al, but this factor was not studied by us. Underweight group (<18.5Kg/m^2) was found to have 2 times more risk but this was not statistically significant.

Literature shows patients with two or more comorbidities and Charlson's Comorbidity Index (CCI) score ≥3 are significant predictors of anastomotic leak.[2,9] Other study done by Morse et.al did not show ASA as risk factor. But in present study patients with ASA score of 2 and more have 3.6 times more risk.

Though many studies have been done to look for association with diabetes, none of them found to have significant association.[2,11] Similar results are seen in present study. Pulmonary disease, though a significant risk factor in one study, present study has only shown high risk of 2 times the other group, but it was statistically not significant.[8]

Present study found statistically significant difference between patients who were diagnosed to have malignant condition to benign condition in developing anastomotic leak. As reported by Morse et.al, preoperative blood transfusion had significant association with anastomotic

leak.[8] But present study failed to show significant difference. We found no statistical significance on using steroids or who underwent radiotherapy. Patients who had some form of abdominal surgery, has some risk of anastomotic leaks compared to those who had none.

In present study, we defined anemia as hemoglobin ≤9.0 gm/dl. Patients with anemia are 4.8 times more risk of developing anastomotic leak (p=0.006). This finding was supported by several studies. Patients with serum protein levels of ≤6.0 gm/dl are at 2.5 times more risk for leak, but present study did not show statistical significance. This is in contrast with other studies where there was significant association of leak with protein level <6.0gm/dl.[11]

Low albumin group (≤3.0 gm/dl) has statistically significant risk of developing anastomotic leak (p=0.006). Morse et.al also have shown significant association with leak.[8] In present study, serum pre-albumin was studied as a novel indicator of risk factor for anastomotic leak. It indicates acute nutritional status of patient, as its half-life is only 2 days as compared to half-life of 20 days with albumin. Patients with low serum pre-albumin (≤20 mg/dl) were found to have 5.8 times higher risk of anastomotic leak as compared to other group (p=0.001).

Further we compared the levels of serum albumin and serum pre-albumin levels in leak group. We found that, 13 patients (68.4%) who had leak had normal serum albumin levels (>3.0 gm/dl), but abnormal serum pre-albumin levels (≤20 mg/dl). This fraction was significant in view of the fact that, if patient serum pre-albumin were measured and found to be of low value, we can prevent anastomotic leak till we build up his nutrition. Pre albumin level that is low should be considered as a indicator of patients at risk who will need proper evaluation and for whom supporting measures to enhance their nutritional status will be part of treatment plan.[12]

Of all the factors which were significant in univariate analysis, age more than 45 years, ASA score of 2, serum prealbumin <20 mg/dl and malignancy as preoperative diagnosis were independent predictors of anastomotic leak. Of 21 patients who had leak, 11 patients underwent operative management. Of these 7 patients had dismantling of anastomosis and converted to end ileostomy. Other 4 patients had reinforcement of their anastomosis with no further adverse outcome. 10 patients were managed conservatively with uneventful recovery. One patient died in the immediate postoperative period due to unexplained hyperkalemia following an anastomotic leak.

It looked into only preoperative factors predicting leak, whereas anastomotic leak, a complication following bowel anastomosis is affected by various operative and post-operative factors. Due to the surgical training course, many operations were performed by junior surgeons or surgeons in training under supervision, which might have contributed for technical deficiency leading to adverse outcome.

CONCLUSION

Present study has contributed to the evidence that serum prealbumin is an acute marker of malnutrition reflecting patient status and is a better indicator for anastomotic leak when compared to albumin. Serum Pre-albumin can be considered as standard of care to predict nutritional status and thereby risk of anastomotic leak and preventing morbidity and mortality.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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