International Journal of Research in Medical Sciences
Wani MD et al. Int J Res Med Sci. 2020 Jul;8(7):2562-2567
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20202896

Original Research Article

Role of biomarkers in predicting anastomotic leakage following colorectal surgeries

Mumtaz Din Wani, Ferkhand Mohi Ud Din*, Aabid Rasool Bhat, Irshad Ahmad Kumar, Ashiq Hussain Raina, Zubair Gul

Department of Surgery, Govt. Medical College, Srinagar, Jammu and Kashmir, India

Received: 10 May 2020
Accepted: 10 June 2020

***Correspondence:**
Dr. Ferkhand Mohi Ud Din,
E-mail: irshadahmadkumar@gmail.com

ABSTRACT

Background: Recovery after surgery for patients with colorectal disease has improved with the advent of minimal access surgery and standardized recovery protocols. Despite these advances, anastomotic leakage remains one of the most dreaded complications following colorectal surgery, with rates of 3-27 per cent depending on specific risk factors. The aim of the study was to assess sensitivity and specificity of systemic and peritoneal drain-fluid bio-markers in early prediction of anastomotic leak; and to co-relate rise in levels of biomarkers and severity of clinical symptoms in patients who have undergone colo-rectal surgeries.
Methods: The present study was a prospective observational study conducted on 60 patients in the Postgraduate Department of Surgery, Government Medical College, Srinagar after obtaining due ethical clearance over a period of two years.
Results: The mean age was 54.87±11.901 years with 44 patients (73.3%) were males. Among systemic makers: the mean CRP level was 2.7800±0.500 mg/L, the mean total leukocyte count was 10.783±0.940 thousands and the mean serum procalcitonin level was 0.365±0.1385 ng/ml. Among peritoneal fluid drain bio-makers, the mean IL-6 level was 3551.066±1311.965 pg/ml, the mean IL-10 level was 628.533±460.358 pg/ml and the mean TNF-a level was 16.391±6.736 pg/ml. The anastomotic leak after colo-rectal surgery was noted in 16 patients (26.7%). In our study significant co-relation was noted between the rise in levels of peritoneal drain fluid biomarkers and severity of clinical symptoms but no significant co-relation was noted between the rise in levels of systemic markers and severity of clinical symptoms in patients who have undergone colo-rectal surgeries.
Conclusions: Systemic biomarkers are poor predictors of anastomotic leak after colorectal surgery. But sensitivity and specificity of peritoneal fluid drain biomarkers in predicting anastomotic leak was significantly high.

Keywords: Anastomotic leak, Biomarker, CRP, IL-6, IL-10, Procalcitonin, TNF-α, TLC

INTRODUCTION

Recovery after surgery for patients with colorectal disease has improved with the advent of minimal access surgery and standardized recovery protocols.[1] Despite these advances, anastomotic leakage remains one of the most dreaded complications following colorectal surgery, with rates of 3-27 per cent depending on specific risk factors.[2-4] Anastomotic leakage may be defined as clinical signs of peritonitis and/or clinical evidence of free fecal fluid within abdomen or emerging from drain site. Although a set of risk factors has been reported, anastomotic leak remains difficult to predict and diagnose early after surgery.[5,6] In many patients, the course of anastomotic leak is insidious, with ileus, vague abdominal symptoms and failure to progress, and a mean

time to clinical diagnosis of 6-12 days after surgery.[7,8] Some studies concluded that biomarkers like lactate/pyruvate ratio and cytokines:IL-6, IL-10 and TNF-alpha were increased in patients who developed symptomatic anastomotic leakage before clinical symptoms were evident.[6,9-13]

The aim of our study was to assess sensitivity and specificity of systemic and peritoneal drain-fluid bio-markers in early prediction of anastomotic leak; and to co-relate rise in levels of biomarkers and severity of clinical symptoms in patients who have undergone colo-rectal surgeries.

METHODS

The present study was a prospective observational study conducted on 60 patients in the Postgraduate Department of Surgery, Government Medical College, Srinagar after obtaining due ethical clearance over a period of two years (October 2017 - September 2019).

All patients who underwent different colorectal procedures for different indications with age group of 25-70 years were included. Patients excluded were <25 and >70 years and who did not gave consent to be part of the study.

Patients were optimized before the procedure, postoperative period was closely monitored and their systemic as well as drain fluid markers were sent for estimation on days 1-7 post-operatively and results obtained there-of were analysed using SPSS V 22.

RESULTS

The mean age was 54.87±11.901 years with 44 patients (73.3%) were males and 16 patients (26.7%) were females. The colo-rectal surgical procedures performed were right Hemicolectomy in 35 patients (58.3%), subtotal colectomy in 20 33.3(%) and total colectomy in 5 (8.3%) patients. The clinical symptoms were fever >38 c on day 2 in 22 patients (36.7%), Absence of bowel action on day 4 in 14 (23.3%), Diarrhea before day 7 in 44 (73.3%), Drainage >400ml on 0-3 day post-op 30 (50%) and Renal Failure on day 3 in 10 (16.7%), as shown in Table 1.

Table 1: Frequency distribution of clinical symptoms of anastomatic leak (n=60).

Clinical symptoms of anastomotic leak	Yes	No
Fever >38 c on day 2	22 (36.7%)	38 (63.3%)
Absence of bowel action on day 4	14 (23.3%)	46 (76.7%)
Diarrhea before day 7	44 (73.3%)	16 (26.7%)
Drainage >400ml on 0-3 day post-op	30 (50%)	30 (50%)
Renal Failure on day 3	10 (16.7%)	50 (83.3%)
Total	175	100%

Table 2: Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of various biomarkers serum and peritoneal drain fluid.

Systemic bio-marker					
Bio-marker	**Sensitivity**	**Specificity**	**Positive predictive value**	**Negative predictive value**	**Diagnostic accuracy**
CRP	53.8%	12.5%	80%	4%	48.3%
TLC	98.1%	12.5%	87.9%	50%	86.6%
Pro-Calcitonin	80%	4%	53.8%	12.5%	48.3%
Drain Fluid Bio-marker					
Bio-marker	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
IL-6	55.8%	100%	100%	25.8%	61.6%
IL-10	82.7%	75%	95.6%	40%	81.6%
TNF-α	84.6%	87.5%	97.8%	46.7%	85%

Among systemic makers: the mean CRP level was 2.7800±0.500 (2.2-4.0) mg/L, the mean total leukocyte count was 10.783±0.940 (10-15) thousands and the mean serum procalcitonin level was 0.365±0.1385 (0.2-1.0) ng/ml.

Among peritoneal fluid drain bio-makers, the mean IL-6 level was 3551.066±1311.965 (2280-6330) pg/ml, the mean IL-10 level was 628.533±460.358 (345-1540) pg/ml and the mean TNF-α level was 16.391±6.736 (11-30) pg/ml. The anastomotic leak after colo-rectal surgery was noted in 16 patients (26.7%). This study found sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of various biomarkers (Systemic and peritoneal drain fluid) as shown in Table 2.

In this study significant co-relation was noted between the rise in levels of peritoneal drain fluid biomarkers and severity of clinical symptoms but no significant co-relation was noted between the rise in levels of systemic markers and severity of clinical symptoms in patients who have undergone colo-rectal surgeries, as shown in Table 3, Table 4, Table 5 and Table 6.

Table 3: Co-relation between the rise in level of peritoneal drain fluid bio-markers (il-6, il-10) and severity of clinical symptoms in patients who had underwent colo-rectal surgeries (n=60).

IL-6 (pg/ml)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post-OP		Renal failure on day 3	
	Yes	No	yes	No	Yes	No	Yes	No	Yes	No
2280-3100 pg/ml	0 (0%)	29 (48.33%)	0 (0%)	29 (48.3%)	29 (48.3%)	0 (0%)	0 (0%)	29 (48.3%)	0 (0%)	29 (48.3%)
3101-6330 pg/ml	22 (36.6%)	9 (15%)	14 (23.3%)	17 (28.3%)	15 (25%)	16 (26.66%)	30 (50%)	1 (1.66%)	10 (6%)	21 (35%)
Total	22 (36.6%)	38 (63.3%)	14 (23.3%)	46 (76.6%)	44 (73.3%)	16 (26.6%)	30 (50%)	30 (50%)	10 (6%)	50 (54%)
Total	60 (100%)		60 (100%)		60 (100%)		60 (100%)		60 (100%)	
p-value	0.000		0.000		0.000		0.000		0.001	
IL-10 (pg/ml)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post- OP		Renal Failure on day 3	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
345-900 pg/ml	15 (25%)	30 (50%)	13 (21.66%)	32 (53.33%)	30 (50%)	15 (25%)	15 (25%)	30 (50%)	2 (3.3%)	43 (71.6%)
901-1540 pg/ml	7 (11.66%)	8 (13.33%)	1 (1.66%)	14 (23.33%)	14 (23.33%)	1 (1.66%)	15 (25%)	0 (0%)	8 (13.33%)	7 (11.66%)
Total	22 (36.66%)	38 (63.33%)	14 (23.33%)	46 (76.66%)	44 (73.33%)	16 (26.66%)	30 (50%)	30 (50%)	10 (6%)	50 (83.33%)
p-value	0.353		0.078		0.043		0.000			0.000

Table 4: Co-Relation between the rise in level of peritoneal drain fluid bio-markers (Inf-α) and severity of clinical symptoms in patients who had underwent colo-rectal surgeries (n=60).

INF-a (pg/ml)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post-OP		Renal failure on day 3	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
11-18 pg/ml	15 (25%)	30 (50%)	12 (20%)	33 (55%)	31 (51.66%)	14 (23.33%)	15 (25%)	30 (50%)	2 (3.33%)	43 (71.6%)
19-30 pg/ml	7 (11.66%)	8 (13.33%)	2 (2.66%)	13 (21.66%)	13 (21.66%)	2 (3.33%)	15 (25%)	0 (0%)	8 (13.33%)	7 (11.66%)
Total	22 (36.66%)	38 (63.33%)	14 (23.33%)	46 (76.66%)	44 (73.33%)	16 (26.66%)	30 (50%)	30 (50%)	10 (6%)	50 (83.33%)
Total	60 (100%)		60 (100%)		60 (100%)		60 (100%)		60 (100%)	
p-value	0.353		0.290		0.178		0.000		0.000	

Table 5: Co-relation between the rise in level of systemic markers (CRP, total leukocyte count) and severity of clinical symptoms in patients who had underwent colo-rectal surgeries (n=60).

CRP (mg/L)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post- OP		Renal Failure on day 3	
	Yes	No	Yes	No	yes	No	Yes	No	yes	No
2.20-3	22 (36.6%)	13 (21.6%)	13 (21.6%)	22 (36.6%)	20 (33.66%)	15 (25%)	22 (36.66%)	13 (21.6%)	3 (5%)	32 (53.3 %)
3.1-4	0 (0%)	25 (41.6%)	1 (1.6%)	24 (40%)	24 (40%)	1 (1.66%)	8 (13.33%)	17 (28.3%)	7 (11.6%)	18 (30%)
Total	22 (36.6%)	38 (63.3%)	14 (23.3%)	46 (76.6%)	44 (73.33%)	16 (26.66%)	3 (50%)	30 (50%)	10 (6%)	50 (54%)
Total	60 (100%)		60 (100%)		60 (100%)		60 (100%)		60 (100%)	
p-value	0.000		0.003		0.001		0.018		0.046	
TLC (thousands)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post- OP		Renal Failure on day 3	
	Yes	No	Yes	No	yes	No	Yes	No	yes	No
10-12	21 (35%)	37 (61.66%)	12 (20%)	46 (76.66%)	44 (73.33%)	14 (23.33%)	28 (46.66%)	30 (50%)	9 (15%)	49 (81 66%)
13-15	1 (1.66%)	1 (1.66%)	2 (3.33%)	0 (0%)	0 (0%)	2 (3.33%)	2 (3.33%)	0 (0%)	1 (1.66%)	1 (1.66 %)
Total	22 (36.66%)	38 (63.33%)	14 (23.33%)	46 (76.66%)	44 (73.33%)	16 (26.66%)	30 (50%)	30 (50%)	10 (6%)	50 (54%)
Total	60 (100%)		60 (100%)		60 (100%)		60 (100%)		60 (100%)	
p-value		0.691		0.009		0.017		0.150		0.198

Table 6: Co-relation between the rise in level of systemic markers (serum procalcitonin) and severity of clinical symptoms in patients who had underwent colo-rectal surgeries (n=60).

Serum procalcitonin level (ng/ml)	Severity of clinical symptoms									
	Fever >38 c on day 2		Absence of bowel action on day 4		Diarrhea before day 7		Drainage >400ml on 0-3 day post-OP		Renal Failure on day 3	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
0.20-0.50	15 (25%)	37 (63.33%)	13 (21.66%)	39 (65%)	38 (63.33%)	14 (23.33%)	22 (36.66%)	30 (50%)	9 (15%)	43 (71.66%)
0.51-1	7 (11.66%)	1 (1.66%)	1 (1.66%)	7 (11.66%)	6 (10%)	2 (3.33%)	8 (13.33%)	0 (0%)	1 (1.66%)	7 (11.66%)
Total	22 (36.66%)	38 (63.33%)	14 (23.33%)	46 (76.66%)	44 (73.33%)	16 (26.66%)	30 (50%)	30 (50%)	10 (6%)	50 (54%)
Total	60 (100%)		60 (100%)		60 (100%)		60 (100%)		60 (100%)	
p-value	0.001		0.436		0.909		0.002		0.734	

DISCUSSION

The anastomotic leak is a major complication after colorectal surgery and leads to high rates of morbidity, reoperation, intervention and a prolonged hospital stay with a mortality rate between 10% and 20%.[14,15] Management of leaks must be guided by the patient's clinical course as some leaks are asymptomatic while others present as life-threatening surgical emergencies. Long-term considerations are also important, such as plans for adjuvant chemotherapy, expected bowel function, and quality of life. Antibiotics are often our first-line of treatment in a symptomatic but stable patient and may be used alone or in combination with per-cutaneous drainage or reoperation depending on the severity of the leak. Anastomotic leakage typically becomes clinically apparent between the 5th and the 8thpostoperative day, but many exceptions exist, with

one study even reporting a mean of the 12th postoperative day for the diagnosis of colo-rectal anastomotic leak.[16] Clinical signs of systemic inflammatory response syndrome, fever, ileus and pain are frequent but have low positive predictive value for colo-rectal anastomotic leak, when observed separately. In a study by den Dulk et al these clinical features were combined into a clinical scoring system (Dutch Leakage Score), with which patients were scored daily in a systematical and uniform way.[17] Points are attributed to certain clinical symptoms (i.e., fever, heart rate), nutritional status (signs of ileus, gastric retention, type of intake) and laboratory findings [i.e., C-reactive protein (CRP) level, leucocytes, kidney function]. After applying the score system retrospectively on a historical cohort, the score was used prospectively. It was shown that patients with a higher score were prone to colo-rectal anastomotic leak requiring intensive clinical observation or radiological evaluation. This scoring system reduced delay in diagnosis of anastomotic leak from 4 to 1.5 d, decreasing false negative diagnostic imaging representing a major factor of delay in diagnosis.[18]

CRP is a non-specific acute phase protein than can identify anastomotic leak before the onset of symptoms and changes in other laboratory parameters such as white blood cell count can be used as markers for the systemic inflammatory response that can precede an anastomotic leak.[19,20] A great number of studies have investigated the role of CRP in early identification of anastomotic leak. In meta-analysis that investigated 7 clinical studies, including 2483 patients, Singh et al, concluded that determination of CRP in day 3, 4 and 5 after surgery, with cut-off values of 172 mg/l, 124 mg/l and 144 mg/l, possesses a negative predictive value (NPV) of 97% in excluding anastomotic leak.[21] In our study the systemic makers, the mean CRP level was 2.7800±0.500 mg/dl, the mean total leukocyte count was 10.783±0.940 thousands and the mean serum procalcitonin level was 0.365±0.1385 ng/ml. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of CRP in estimation of anastomotic leak after colo-rectal surgery was 53.8%, 12.5%, 80%, 4% and 48.3% respectively. In contrast to one previous study the combination of CRP and procalcitonin, assessed in day 5 following surgery, with a cut-off value of 0.31 ng/ml, has been identified as a reliable predictor for anatomotic leak with a 100% sensitivity, 72% specificity, 100% NPV, 17% positive predictive value.[22]

In this study the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of serum procalcitonin level (systemic marker) in estimation of anastomotic leak after colo-rectal surgery was 80%, 4%, 53.8%, 12.5% and 48.3% respectively. These findings were confirmed by the recent PREDICS study, which found that procalcitonin had a NPV of 96.9% on postoperative day 3 and 98.3% on postoperative day 5 (cut-off value 2.3 ng/ml), with a specificity of 91.7% and 93% respectively. CRP also exhibited good NPV 96.4% on postoperative day 3 (cut-off value 16.9 mg/ml) and 98.4% on postoperative day 5 (cut-off value 12.5 ng/ml). The combination of CRP and procalcitonin determination further improved diagnosis of anastomotic leak (AUC 0.842 on postoperative day 3 and 0.901 on postoperative day 5.[23]

Until now current diagnostic approaches cannot predict a colorectal anastomotic leak.[24]

Sammour et al, study found that elevated levels of peritoneal fluid (Drain fluid) of IL-6 and IL-10 on day 1 after colorectal surgery were associated with approximately double the incidence of anastomotic leak (AUROC >0.7).[25] Peritoneal cytokine levels of IL-8 and TNFα and plasma levels of IL-6, IL-8, IL-10, and TNFα were either not predictive or poorly predictive of anastomotic leak.

In this study the peritoneal fluid drain bio-makers, the mean IL-6 level was 3551.066±1311.965 pg/mL, the mean IL-10 level was 628.533±460.358 pg/mL and the mean TNF-a level was 16.391±6.736 pg/mL. The study found sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of IL-6 in estimation of anastomotic leak after colo-rectal surgery was 55.8%, 100%, 100%, 25.8% and 61.6% respectively. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of IL-10 in estimation of anastomotic leak after colo-rectal surgery was 82.7%, 75%, 95.6%, 40% and 81.6% respectively and the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of TNF-a in estimation of anastomotic leak after colo-rectal surgery was 84.6%, 87.5%, 97.8%, 46.7% and 85% respectively.

CONCLUSION

Systemic biomarkers are poor predictors of anastomotic leak after colorectal surgery. But sensitivity and specificity of peritoneal fluid drain biomarkers in predict anastomotic leak was significantly high.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sammour T, Zargar-Shoshtari K, Bhat A, Kahokehr A, Hill AG. A programme of Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. N Z Med J. 2010;123:61-70.
2. Matthiessen P, Henriksson M, Hallbook O, Grunditz E, Noren B, Arbman G. Increase of serum C-reactive protein is an early indicator of subsequent

symptomatic anastomotic leakage after anterior resection. Colorectal Dis. 2008;10:75-80.
3. Iancu C, Mocan LC, Todea-Iancu D, Mocan T, Acalovschi I, Ionescu D, et al. Host-related predictive factors for anastomotic leakage following large bowel resections for colorectal cancer. J Gastrointest Liver Dis. 2008;17:299-303.
4. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg. 2015;102:462-79.
5. Ashburn JH, Stocchi L, Kiran RP, Dietz DW, Remzi FH. Consequences of anastomotic leak after restorative proctectomy for cancer: effect on long-term function and quality of life. Dis Colon Rectum. 2013;56:275-80.
6. Singh PP, Zeng IS, Srinivasa S, Lemanu DP, Connolly AB, Hill AG. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg. 2014;101:339-46.
7. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg. 2007;245:254-8.
8. Lagoutte N, Facy O, Ravoire A, Chalumeau C, Jonval L, Rat P, et al. C-reactive protein and procalcitonin for the early detection of anastomotic leakage after elective colorectal surgery: pilot study in 100 patients. J Visc Surg. 2012;149:345-9.
9. Dulk M, Witvliet MJ, Kortram K, Neijenhuis PA, Hingh IH, Engel AF, et al. The DULK (Dutch Leakage Score) and modified DULK score compared: Actively seen the leakage. Colorectal Dis. 2013 Sep;15(9):e528-33.
10. Pasternak B, Matthiessen P, Jansson K, Andersson M, Aspenberg P. Elevated intraperitoneal matrix metalloproteinases-8 and -9 in patients who develop anastomotic leakage after rectal cancer surgery: a pilot study. Colorectal Dis. 2010;12:93-8.
11. Daams F, Luyer M, Lange JF. Colorectal anastomotic leakage: Aspects of prevention, detection and treatment. World J Gastroenterol. 2013 Apr;19(15):2293-7.
12. Giaccaglia V, Salvi PF, Cunsolo GV, Sparagna A, Antonelli MS, Nigri G, et al. Procalcitonin, as an early biomarker of colorectal anastomotic leak, facilitates enhanced recovery after surgery. J Crit Care. 2014 Aug;29(4):528-32.
13. Su'a BU, Mikaere HL, Rahiri JL, Bissett IB, Hill AG. Systematic review of the role of biomarkers in diagnosing anastomotic leakage following colorectal surgery. Br J Surg. 2017 Apr;104(5):503-12.
14. Law WL, Choi HK, Lee YM, Ho JW, Seto CL. Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy J Gastrointest Surg. 2007;11:8-15.
15. Slieker JC, Komen N, Mannaerts GH, Karsten TM, Willemsen P, Murawska M, et al. Long-term and perioperative corticosteroids in anastomotic leakage: a prospective study of 259 left-sided colorectal anastomoses. Arch. Surg. 2012;147:447-52.
16. Huh JW, Kim HR, Kim YJ. Anastomotic leakage after laparoscopic resection of rectal cancer: the impact of fibrin glue. Am J Surg. 2010;199:435-41.
17. den Dulk M, Noter SL, Hendriks ER, Brouwers MA, van der Vlies CH, Oostenbroek RJ, et al. Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. Eur J Surg Oncol. 2009;35:420-6.
18. Doeksen A, Tanis PJ, Vrouenraets BC, Lanschot van JJ, Tets van WF. Factors determining delay in relaparotomy for anastomotic leakage after colorectal resection. World J Gastroenterol. 2007;13:3721-5.
19. Warschkow R, Beutner U, Steffen T, Müller SA, Schmied BM. Safe and early discharge after colorectal surgery due to C-reactive protein: a diagnostic meta-analysis of 1832 patients. Ann Surg. 2012;256:245-50.
20. Woeste G, Müller C, Bechstein WO, Wullstein C. Increased serum levels of C-reactive protein precede anastomotic leakage in colorectal surgery. World J Surg. 2010;34:140-6.
21. Singh PP, Zeng IS, Srinivasa S, Lemanu DP, Connolly AB. Systematic review and meta-analysis of use of serum C- reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg. 2014;101:339-46.
22. Garcia-Granero A, Frasson M, Flor-Lorente B, Blanco F, Puga R. Procalcitonin and C-reactive protein as early predictors of anastomotic leak in colorectal surgery: a prospective observational study. Dis Colon Rectum. 2013;56:475-83.
23. Giaccaglia V, Salvi PF, Antonelli MS, Nigri G, Pirozzi F. Procalcitonin reveals early dehiscence in colorectal surgery: The PREDICS study. Ann Surg. 2013;263:967-72.
24. Komen N, Slieker J, Willemsen P, Mannaerts G, Pattyn P, Karsten T, et al. Polymerase chain reaction for Enterococcus faecalis in drain fluid: the first screening test for symptomatic colorectal anastomotic leakage. The Appeal-study: analysis of parameters predictive for evident anastomotic leakage. Inter J Colorectal Dis. 2014 Jan 1;29(1):15-21.
25. Sammour T, Singh PP, Zargar-Shoshtari K, Su'a B, Hill AG. Peritoneal Cytokine Levels Can Predict Anastomotic Leak on the First Postoperative Day. Dis Colon Rectum. 2016 Jun 1;59(6):551-6.

Cite this article as: Wani MD, Din FMU, Bhat AR, Kumar IA, Raina AH, Gul Z. Role of biomarkers in predicting anastomotic leakage following colorectal surgeries. Int J Res Med Sci 2020;8:2562-7.