OPEN ACCESS

Original Article

Volume 25 | Number 3 | Jul-Sep 2025

Mean Post-Operative C -Reactive Protein to Albumin Ratio Among the Patient undergoing Pancreaticoduodenectomy in a Tertiary Care Hospital

Samyukta K.C.,[1] Jainendra Kumar Chaudhary,[1] Sharad Pokharel,[1] Indra Kumar Jha,[1] Niroj Banepali,[1] Sundar Shrestha[1]

[1]Department of Surgical Gastroenterology, National Academy of Medical Sciences, Bir Hospital, Mahaboudha, Kathmandu, Nepal

Correspondence:
Dr. Samyukta K.C. Department of Surgical Gastroenterology, National Academy of Medical Sciences, Bir Hospital, Mahaboudha, Kathmandu, Nepal
Email: kcsamyukta@gmail.com
Phone: +9779841572462.

doi.org/10.56974/pmjn.898
www.pmjn.org.np

Submission Date:
18 June 2025
Acceptance Date:
8 July 2025
Published Date:
30 September 2025

ABSTRACT

Introduction: Assessment of third post-operative day C-reactive protein to albumin ratio in patients with post-operative Pancreatic fistula would help surgeons avoid shortcomings of drain amylase, which is liable to be affected by the drainage tube's location or condition. This could be a novel inflammatory marker when surgeons are practicing drainless surgery following Pancreaticoduodenectomy. Predicting Clinically Relevant Post-Operative Pancreatic Fistula would help to manage post-operative morbidities associated with Pancreaticoduodenectomy. The main aim of the study was to determine mean post-operative c -reactive protein to albumin ratio among the patient undergoing pancreaticoduodenectomy in a tertiary care hospital.

Methods: This cross sectional was done in patients undergoing Pancreaticoduodenectomy for malignant pancreatic head and periampullary pathology at Department of Gastroenterology, NAMS, Bir Hospital from May 2024 to May 2025. All the variables were recorded in the preformed proforma and C -Reactive Protein to Albumin Ratio was computed by dividing third Post-operative Day C-reactive protein by third post operative serum albumin. Data was analyzed using MS Excel 365 & SPSS version 27.

Results: The overall mean C -Reactive Protein to Albumin Ratio was 6.29 ± 3.24 (5.33 to 7.25 at 95% Confidence Interval. A total of 44 patients, with 28 (63.63%) males and 16 (36.36 %) females. Among these, 20 (45.45%) patients underwent preoperative biliary drainage, 5 (11.36%) had Percutaneous transhepatic biliary drainage and 15 (34.09%) had Endoscopic Retrograde Cholangio Pancreaticography and stenting. The commonest pathology was ampullary carcinoma,16 (36.36%) and pancreatic ductal adenocarcinoma,16 (36.36%) followed by distal cholangiocarcinoma,10 (22.72%) and duodenal adenocarcinoma, 2 (4.54%).

Conclusions: Our results showed that patients with high third POD C-Reactive Protein to Albumin Ratio had Clinically Relevant Post-Operative Pancreatic Fistula. This was similar to study conducted by Sakamoto et al and Heard et al. Comparative studies of C -Reactive Protein to Albumin Ratiowith other inflammatory markers could be done to see their association with Post-Operative Pancreatic Fistula.

Keywords: *C-reactive protein to albumin ratio; clinically relevant post-operative pancreatic fistula; pancreaticoduodenectomy.*

INTRODUCTION

Different inflammatory indicators are used in early identification of high-risk patients for developing Post Operative Pancreatic Fistula (POPF), which has an incidence of 3 to 45% following Pancreaticoduodenectomy (PD).[1] Among these markers, C-reactive protein (CRP) , a predictive indicator of POPF, rises in response to inflammation and infection.[2-4] Albumin is another indicator of POPF, whose level decreases in correlation with the severity of inflammation.[5,6] C-reactive protein-to-albumin ratio (CAR), computed by dividing serum CRP by albumin levels, is also an important indicator for assessing POPF.

The prediction accuracy of CR-POPF by CRP alone is limited due to differences in polymorphism in the promoter of interleukin-6 distributions among individuals.[7] Therefore, CAR serves as an objective

surrogate marker for predicting CR-POPF, unaltered by surgical procedure and drain amylase concentration.

There are few studies on the use of third POD CAR for the prediction of CR-POPF after PD in Nepal.

METHODS

This descriptive cross-sectional study was conducted at the Department of Surgical Gastroenterology, NAMS, Bir hospital, from May 2024 to May 2025, among the patients 'Post-Operative Pancreatic Fistula (POPF)' PD. The study protocol was approved by IRB (No. 1225/2080/81) of NAMS.Detailed history with examination and investigations of the admitted patients was completed. Data including age, body mass index (BMI), gender, preoperative drainage status, Eastern Cooperative Oncology Group (ECOG) status, CRP, serum albumin, and disease pathology were entered in the preformed proforma. Patients were enrolled in this study after obtaining informed written consent from them.

This study included patients above 18 years of age who gave consent to undergo elective PD for pancreatic and periampullary malignancy. However, this study excluded those who underwent emergency PD, mortality and re-exploration due to any cause before third POD.

This study comprised 44 patients, calculated using a sample size (n) formula for cross-sectional studies8:

$n = Z^2 \times \sigma^2 / e^2$

$= 1.96^2 \times 0.5 / 0.5^2$

Where,

Z = 1.96 (for 95% confidence level)

σ= standard deviation, 0.5

e= margin of error (10%)

Z = 1.96 (for 95% confidence level)

All patients underwent Classical PD following standard surgical steps. Surgeries were performed by or under the supervision of a Consultant Surgical Gastroenterologist with oncologic principles. Duct to mucosa, end to side Pancreaticojejunostomy (PJ) was done in two layers – interrupted PDS/Prolene 4-0 as inner layer for duct to mucosa anastomosis and prolene 2-0 as outer layer incorporating pancreatic tissue, capsule, and seromuscular layer of jejunum. Hepatico-jejunostomy (HJ) was reconstructed about 10-15 cm distal to PJ in single layer interrupted fashion by 3-0 Polyglactin sutures in end to side fashion and Gastrojejunostomy (GJ) was reconstructed about 15 - 25 cm distal to HJ in 2 layers, inner layer with 2-0 Polyglactin sutures continuous interlocked fashion and outer layer by 2-0 silk in continuous fashion. Feeding jejunostomy (FJ) was done if required as determined by the surgeon like for soft pancreatic tissue, small pancreatic duct size, poor nutritional status and for poor patients who can't afford Total Parenteral Nutrition (TPN) if needed. Two abdominal drains were placed – left drain anterior and right drain posterior to the pancreatic anastomosis, respectively.

In this study, CAR was computed by the ratio of C-reactive protein to serum albumin of third POD. Cut off value of CAR was calculated by Youndens index through a Receiver Operating Characteristic (ROC) curve analysis. This study grouped grade B and C POPF as Clinically Relevant Post Operative Pancreatic Fistula (CR-POPF) and the rest grade A or biochemical leak and non POPF as non CR-POPF. Patients were classified as having POPF depending on drain amylase value that was send on 3rd and 5th POD as per ISGPS 2016 9 Patients were classified into high CAR and low CAR group according to CAR cut off value calculated as 6.39 U/L

Data was analyzed using MS Excel 365 & SPSS version 27. Continuous data was presented as mean ± SD or median (range) whereas categorical data (age, sex, patients CRP level, serum albumin,CR-POPF) were expressed as ratios and proportions.

RESULTS

The overall mean C -Reactive Protein to Albumin Ratio was 6.29 ± 3.24 (5.33 to 7.25 at 95% Confidence Interval. In this study, CAR ratio in the CR-POPF group was 8.53 ±3.68 and 5.46 ±2.96 in the non CR-POPF group. Among 12 patients in CR-POPF group, 5 were above the average and 7 were below average whereas in non CR-POPF , 11 were above average and 21 were below average. A total of 44 patients underwent PD, among which 28 (63.64%) were male and 16 (36.36%) were female.

Among these 12 (27.27%) patients had CR-POPF, and 32 (72.73%) didn't have CR-POPF. Preoperative biliary drainage was performed in 20 (45.46%) patients where 5 (25%) underwent PTBD and 15 (75%) underwent ERCP and stenting. The mean age in years of the CR-POPF group was 52.75±10.79 and that in non CR-POPF group was 55.88±9.44.(Table I)

Table 1. Patient characteristics (n=44).

Variable		CR-POPF (n= 12)	Non CR-POPF (n= 32)
Age (Years)		52.75±10.79	55.88 ± 9.44

Gender (Male: Female)		6:6	22:10
BMI		23.13 ± 3.23	21.41 ± 2.70
ECOG	0	0	1
	1	11	14
	2	1	2
	PTBD	2	1
	ERCP	6	7
POPF Grade	BL	0	17
	B	10	0
	C	2	0
CAR Ratio		8.53 ± 3.68	5.46 ± 2.96

The calculated Area Under Curve (AUC) of CAR to predict CR-POPF was 0.766. The optimal cutoff value of CAR on third POD was 6.39 U/L. Based on these results, we grouped patients into CAR high (≥6.39 ; n=18) and CAR low(<6.39; n=26). Out of the 26 (59.09%) patients with CAR low, 3 had CR-POPF and 23 did not have CR-POPF. Patients with high CAR were 18(40.91%) of which nine had CR-POPF and nine did not have CR-POPF (Table. 2). The variables of the patients with lower and high CAR value are given.

Table 2. Variables of the patients with lower and high CAR value.

Variable		CAR Low n=26	CAR High n=18
Age (Years)		56.65 ±11.05	53.94 ± 9.70
Gender (Male: Female)		17:9	11:7
BMI		22.36 ± 3.28	21.21 ± 2.66
ECOG	0	0	1
	1	15	23
	2	2	3
Preoperative drainage	PTBD	3	2
	ERCP	6	9
CR-POPF (Present: Absent)		3:23	9:9
POPF Grade	BL	10	7
		3	7
		0	2

The most common pathologies were ampullary carcinoma , 16 (36.37%) and pancreatic ductal adenocarcinoma, 16 (36.37%) followed by distal cholangiocarcinoma, 10 (22.73%)andduodenaladenocarcinoma,2(4.55%)(Table3).

Table 3 . Disease pathology.

Variable	CAR Low n=26	CAR High n=18
Ampullary carcinoma	5	11
Distal cholangiocarcinoma	6	4
Duodenal adenocarcinoma	1	1
Pancreatic ductal adenocarcinoma	14	2

DISCUSSION

In our study, the overall mean C -Reactive Protein to Albumin Ratio was 6.29±3.24. Several studies revealed serum CRP level on third POD as a useful indicator for predicting CR-POPF after PD.[10] But, CRP alone is not sufficient to predict CR-POPF accurately due to individual differences in polymorphism in the promoter of interleukin-6 distributions.[7] Furthermore, the evaluation of CR-POPF by drain amylase level could not be correct due to drain susceptibility to the location or obstruction of peritoneal drainage tube.[11] Sole CRP and albumin values individually may only reflect the extent of the inflammatory response and nutritional condition of patients. To overcome the above shortcomings, CAR can be used as an inflammatory marker in identifying patients who are susceptible to developing CR-POPF.

In another study,[12] first demonstrated an association between CAR and POPF following PD, and stated that preoperative CAR as an independent predictive marker for POPF following PD. Though both CRP (positive acute phase reactant) and serum albumin (negative acute phase reactant) could be calculated in the preoperative period or earlier than third POD, but level of CRP rises at 48-72 hours in reciprocate to inflammation.[13]

Our results showed that patients with high third POD CAR had CR-POPF (p=0.005). The occurrence of CR-POPF was higher in the high CAR group (50%) compared to those with low CAR group (11.5%) This incidence was consistent with previous studies .13In our findings, grade B CR-POPF, which had total of 10 patients, 3 patients were in low CAR group and 7 were in high CAR group. Two patients in grade

C POPF were in the high CAR group, suggesting its use in identification of patients for developing CR-POPF. This finding was similar to the results of Sakamoto et al 14and Heard et al.11

Our study determined CAR on the third POD cut off value of 6.39 U/L with AUC = 0.766 (p<0.001), sensitivity of 75% and specificity of 71.88% for predicting CR-POPF. This was similar to the previous studies. 11,12 In study by Sakamoto et al 14 third POD CAR as an independent and superior predictive indicator of CR-POPF compared with other inflammatory indicators. CR-POPF was 27.27% in our study compared to Sakamoto et al 14 which was 29.48%.The CAR ratio in the CR-POPF group was 8.0±; 3.3 and 4.6±2.3 in the non CR-POPF group. This was similar to our value of 8.53±3.68 in the CR-POPF and 5.46±2.96 in the non CR-POPF group. Multivariable analysis showed a relation with duct diameter in our study.

Potentially life threatening complication as sepsis can occur secondary to intra abdominal abscess or post pancreatectomy hemorrhage as a consequence of CR-POPF .15,16 Heard et al 11 retrospective study of 51 patients with sample size similar to our study also supported third POD CAR (95% CI 1.000-1.000,p <0.001) as an effective appendage when surgeons avoid peripancreatic drains. They had 11 (21.6%) BL , and 6 (11.8%) developed a CR-POPF which was less compared to our results. Furthermore, timely intervention in patients with high risk for developing POPF could help to avoid postoperative morbidity. Objective inflammatory marker, which is independent of drain amylase value, CAR is associated with development of CR-POPF

No relation was observed in our study in the high and low CAR groups between age, gender, Body Mass Index (BMI), ECOG status and preoperative biliary drainage status as like in other study.11,14 This indicates that only CAR can be used in identifying high-risk patients who are more prone to develop CR- POPF which is independent of all other variables.

The present study is limited to a single tertiary care center in a small sample size. The findings need to be validated by conducting the study in a large sample.

CONCLUSIONS

Post operative day third CAR had association with -CR POPF after PD . This was similar to a study conducted by Sakamoto et al and Heard et al.Comparative studies of CAR with other inflammatory markers could be done to see their association with POPF.

Post operative day third CAR had association with -CR POPF after PD . This was similar to a study conducted by Sakamoto et al and Heard et al.Comparative studies of CAR with other inflammatory markers could be done to see their association with POPF.

ACKNOWLEDGEMENTS

We sincerely express our deepest gratitude to all the patients who contributed to this study by participating.

Conflict of Interest: None.

REFERENCES

1. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017 Mar;161(3):584-591. [PubMed | Full Text | DOI]
2. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003 Jun;111(12):1805-12. [PubMed | Full Text | DOI]
3. Hiyoshi M, Chijiiwa K, Fujii Y, Imamura N, Nagano M, Ohuchida J. Usefulness of drain amylase, serum C-reactive protein levels and body temperature to predict postoperative pancreatic fistula after pancreaticoduodenectomy. World J Surg. 2013 Oct;37(10):2436-42. [PubMed | Full Text | DOI]
4. Fujiwara Y, Misawa T, Shiba H, Shirai Y, Iwase R, Haruki K, et al. A novel postoperative inflammatory score predicts postoperative pancreatic fistula after pancreatic resection. Anticancer Res. 2013 Nov;33(11):5005-10. [PubMed | Full Text]
5. Winter JM, Cameron JL, Yeo CJ, Alao B, Lillemoe KD, Campbell KA, et al. Biochemical markers predict morbidity and mortality after pancreaticoduodenectomy. J Am Coll Surg. 2007 May;204(5):1029-36; discussion 1037-8. [PubMed | Full Text | DOI]
6. Yin M, Si L, Qin W, Li C, Zhang J, Yang H, et al. Predictive Value of Serum Albumin Level for the Prognosis of Severe Sepsis Without Exogenous Human Albumin Administration: A Prospective Cohort Study. J Intensive Care Med. 2018 Dec;33(12):687-694. [PubMed | Full Text | DOI]
7. Okada Y, Takahashi A, Ohmiya H, Kumasaka N,

Kamatani Y, Hosono N, et al. Genome-wide association study for C-reactive protein levels identified pleiotropic associations in the IL6 locus. Hum Mol Genet. 2010;20(6):1224-31. [PubMed | Full Text | DOI]

8. Lakhey PJ, Bhandari RS, Ghimire B, Khakurel M. Perioperative outcomes of pancreaticoduodenectomy: Nepalese experience. World J Surg. 2010 Aug;34(8):1916-21. [PubMed | Full Text | DOI]

9. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017;161:584–591. [PubMed | Full Text | DOI]

10. Partelli S, Pecorelli N, Muffatti F, Belfiori G, Crippa S, Piazzai F, et al. Early Postoperative Prediction of Clinically Relevant Pancreatic Fistula after Pancreaticoduodenectomy: usefulness of C-reactive Protein. HPB (Oxford). 2017 Jul;19(7):580-586. [PubMed | Full Text | DOI]

11. Heard JC, Smith GH, Tolman A, Karumuri JS, Osman HG, Jeyarajah RD. No Drain, No Problem: Serum-Based Marker Prediction of Clinically Relevant Postoperative Pancreatic Fistula. Am Surg. 2023 Dec 27:31348231204917. [PubMed | Full Text | DOI]

12. Funamizu N, Utsunomiya T, Honjo M, Ito C, Shine M, Uraoka M, et al. Preoperative C-Reactive Protein-to-Albumin Ratio Predicts Postoperative Pancreatic Fistula following Pancreatoduodenectomy: A Single-Center, Retrospective Study. Curr Oncol. 2022 Dec 14;29(12):9867-9874. [PubMed | Full Text | DOI]

13. Colley CM, Fleck A, Goode AW, Muller BR, Myers MA. Early time course of the acute phase protein response in man. J Clin Pathol. 1983 Feb;36(2):203-7. [PubMed | Full Text | DOI]

14. Sakamoto T, Yagyu Y, Uchinaka EI, Morimoto M, Hanaki T, Tokuyasu N, et al. Predictive Significance of C-reactive Protein-to-albumin Ratio for Postoperative Pancreatic Fistula After Pancreaticoduodenectomy. Anticancer Res. 2019 Nov;39(11):6283-6290. [PubMed | Full Text | DOI]

15. Choi SH, Moon HJ, Heo JS, Joh JW, Kim YI. Delayed hemorrhage after pancreaticoduodenectomy. J Am Coll Surg. 2004 Aug;199(2):186-91. [PubMed | Full Text | DOI]

16. DeOliveira ML, Winter JM, Schafer M, Cunningham SC, Cameron JL, Yeo CJ, et al. Assessment of complications after pancreatic surgery: A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. Ann Surg. 2006 Dec;244(6):931-7; discussion 937-9. [PubMed | Full Text | DOI]