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Predictive values of neutrophil lymphocyte ratio and platelet lymphocyte ratio for adenocarcinoma arising in chronic pancreatitis

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Abstract
Introduction: Chronic pancreatitis (CP) is a premalignant condition for carcinoma pancreas. Worrisome lesions in CP in pancreatic head warrant pancreatico-duodenectomy because CA19-9/CECT/MRI-MRCP/PET/EUS-FNA often fail to differentiate inflammatory and malignant lesions. Objective of this study was to assess predictive values of NLR, PLR and CA19-9 for malignant CP.
Methodology: Single centre retrospective analysis done in Department of Surgical Gastroenterology, Medical College, Trivandrum, Kerala; on CP (Group-1) and carcinoma pancreas (Group-II) from 1/1/2014-31/12/2018. Group-I was stratified as CP-benign (Group-IB) and CP-malignant (Group-IM). From their absolute neutrophil count, lymphocyte count and platelet counts, NLR and PLR values were calculated. ROC analyses done for cut off values with PPV and NPV.
Results: 255 patients; enrolled into Group-I (n=113; 75.92% Group-IB and 24.07% Group-IM) and Group-II (n=142). By ROC, sensitivity, specificity, PPV, NPV; and accuracy of Group-I with NLR cut off value of 2.345 were 68.11%/73.72%/59.62/91.80% and with 2.813, were 58.3%/90.2%/72.4%/82.14%. For PLR; with cut off at 138.65 were 63.89%/88.5%/69.7%/83.75%; and with 157.95 were 48.6%/91.8%/70.83%/78.65%.
Discussion: By ROC, CA19-9 of 100.21U/ml showed 82.9% sensitivity and 85.2% Specificity for malignant CP. NLR of 2.345 showed 68.11% sensitivity, 73.72% specificity, 59.62 PPV and 91.80% NPV; 2.813 had 58.3% sensitivity, 90.2% specificity, 72.4% PPV and 82.14% NPV. PLR of 138.65 showed 63.89% sensitivity, 88.5% specificity, 69.7% PPV and 83.75% NPV and 157.95 had 48.6% sensitivity, 91.8% specificity, 70.83% PPV and 78.65% NPV.
Conclusion: NLR and PLR in CP carcinoma and denovo-DACP were comparable. NLR and PLR have showed significant predictive values, comparing benign and malignant CP.

Keywords: CA 19-9, carcinoma pancreas, chronic pancreatitis, malignant chronic pancreatitis, neutrophil lymphocyte ratio, platelet lymphocyte ratio.

Introduction

According to the recent global cancer statistics, carcinoma pancreas is the seventh cause of worldwide cancer-related mortality [1]. This disease has got a dismal prognosis; only 24% survive 1 year and less than 9% live for 5 years, despite the existing multimodal treatment approaches including surgical resection and perioperative chemoradiotherapy [2-03]. Though the most effective treatment available for carcinoma pancreas remains surgical resection, nearly 80% of tumors are unresectable at the time of diagnosis [4, 5]. The median survival for a metastatic pancreatic cancer is stated as 8.5–11 months with the various forms of treatment available at present [6, 7]. Therefore, early detection, accurate staging and appropriate treatment remain the way out. Moreover identification of the precancerous conditions and their management should be considered as crucial for enhancing the outcome of this dreaded disease.

On exploring the etiological factors and premalignant conditions for ductal adenocarcinoma pancreas (DACP), chronic pancreatitis (CP) has been identified as a strong risk factor [8]. Moreover many studies have reported CP as a premalignant condition for carcinoma pancreas [9-12]. However, clinical manifestations of pancreatic carcinoma resemble those of CP especially in presence of an associated mass lesion and obstructive jaundice, thus creating a clinical dilemma. A historical study by Lowenfels *et al*, estimated the risk for progression of CP to carcinoma pancreas as 1.8% and 4% at 10 and 20 years respectively in western population where alcoholic chronic pancreatitis (ACP) was predominant [9]. There were many reports from the tropical countries including southern parts of India regarding an idiopathic or tropical variant of CP, different from the alcoholic pancreatitis, showing differences in the clinical presentation, pattern of calcification and natural history; having a higher incidence of association with pancreatic carcinoma. Many of them have reported that patients with tropical chronic pancreatitis (TCP) have an increased risk of pancreatic cancer as compared to ACP [10-11]. A study by Augustine P and Ramesh H, had stated that pancreatic adenocarcinoma occurred in 22 of 266 patients (8.3%) with tropical pancreatitis, suggesting that the tropical variant of CP could be premalignant [12].

Heterogenous mass lesions of in CP often create difficulty in differentiating a benign inflammatory mass from a malignant lesion. Such worrisome lesions involving the head and uncinate process of pancreas would warrant pancreatico-duodenectomy, a complex surgical procedure. Though the major high volume centres doing pancreatico-

duodenectomy have reported its mortality rates as less than 4%, majority of studies have shown its morbidity rates around 30-40% [13, 14]. Moreover, pancreatico-duodenectomy in CP was discouraged as having higher complications and poor survival than the denovo carcinoma pancreas [12, 13]. The available investigations including CECT, MRI-MRCP or PET scan often become inconclusive in differentiating whether the lesion is an inflammatory pseudotumour like situation or a true carcinoma pancreas, except when there is obvious metastasis. EUS-FNA and CA19-9 show low sensitivity and specificity especially in presence of associated chronic pancreatitisP [15, 16]. Thus many of such highly suspicious lesions are managed by an 'empirical' pancreatic resection. Therefore, there has been an ongoing search for preoperative modalities which could help in differentiating an inflammatory lesion from pancreatic malignancy.

Recently many studies have shown an associated exaggerated inflammatory response during tumor progression[17]. Moreover the tumor-associated inflammation has shown as one of the major prognostic factor in various malignancies[18]. Several studies have reported that simple immune function indices like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) could be of prognostic significance in pancreatitis as well as in various solid tumors[19-21]. An elevated NLR value is related to a worse outcome in various types of cancer, including renal cell carcinoma, soft tissue sarcoma, non-small cell lung cancer (NSCLC), breast cancer, and colorectal cancer (CRC) [22-24]. These ratios can be easily derived from the routine laboratory tests. Therefore, exploring these inflammatory markers would help in determining the individual treatment approaches as well as to assess the tumour prognosis and the patient survival.

Earlier we had reported the correlation of PLR and CA 19-9 in chronic pancreatitis and suggested, PLR may be useful to differentiate carcinoma pancreas from the benign inflammatory head mass (IHM) in CP[25]. As a continuation of the same, this study was done to explore the values of NLR, PLR and CA19-9 regarding negative prediction of malignancy in chronic pancreatitis to segregate benign inflammatory mass lesions of pancreas to bring down the chances of doing pancreatico-duodenectomy for benign lesions which has been reported as upto 10.5% [26, 27].

Aim

1. To study the comparability of NLR and PLR in carcinoma arising in CP and de-novo DACP.
2. To assess the predictive value of NLR and PLR in benign and malignant CP.

Methodology

This is done as a single centre retrospective analysis, in the Department of Surgical Gastroenterology, Government Medical College, Trivandrum, Kerala, India; on consecutive cohort of diagnosed cases of Chronic Pancreatitis (Cambridge classification Grade-V) and denovo ductal adenocarcinoma pancreas (DACP) treated between January 2014 and December 2018. The inclusion criteria were; patients admitted with CP (benign and malignant) and denovo-ductal adenocarcinoma pancreas, having the histopathology reports based on the biopsy or following resection. The exclusion criteria were patients having acute exacerbation of chronic pancreatitis, cholangitis, other co-existing infections and neoadjuvant chemotherapy which could give confronting Interpretations.

Data Collection: The demographic data, preoperative complete blood counts, Carbohydrate Antigen CA19-9 value, the type of surgery done and the histopathology reports were tabulated from the prospectively maintained department database. Those having incomplete data were excluded from the analysis. The complete blood counts (CBC) at the time of admission were done with automated differential counts performed with 2 ml peripheral blood anticoagulated with EDTA using Coulter counter (Mindray BC 3000 Plus Auto Haematology Analyser, Shenzhen Mindray Bio-Medical Electronics Co, Ltd. China). The absolute values of neutrophil count, lymphocyte count and platelet counts were taken and NLR and PLR values were calculated manually.

Definitions

Neutrophil-Lymphocyte Ratio: the NLR was computed by calculating the ratio of the absolute neutrophil and lymphocyte counts.

Platelet-Lymphocyte Ratio: the PLR is calculated by ratio of absolute platelet count to lymphocyte count.

Data extraction; statistical analysis: The enrolled patients were grouped into Group-1 (CP) and Group-II (denovo-DACP). The Group-I patients were stratified as CCP-benign (Group-IB) and CCP-malignant (Group-IM). Patient's demographics, laboratory parameters (CBC, NLR, PLR, CA 19-9), type of surgery done and the final histopathology report were tabulated. Initially their demographics were assessed to know whether the two groups were comparable. Then the Group-IM was compared with the Group-II to assess their comparability. Continuous variables were expressed as mean±standard deviation (SD). Normality of distribution was tested by using Kolmogorov-Smirnov test. The laboratory parameters were analyzed using Mann-Whitney test. After that subgroup analysis was done between Group-IB and Group-IM to find out the cut off value above which the malignancy can be predicted using positive predictive value and negative predictive value. The receiver operator characteristic (ROC) analysis was used for identifying the optimal cut-off values as well as sensitivity and specificity. The area under the ROC (AUROC) curve also was calculated. The statistical tests were done using SPSS-20 and a value of $P < 0.05$ was considered statistically significant.

Results

Clinical profile and demographics

Total 255 patients satisfying the inclusion and exclusion criteria were enrolled in to this study. There were 113 patients having CP in Group-I; out of which 78 (75.92%) were benign CP (Group-IB) and 35 (24.07%) were proven as malignant CP (Group-IM) among them 26.92% were in stage IV. There

were 142 patients with DACP in Group-II; of these 84 (59.15% were carcinoma pancreas and 58 (40.84%) were periampullary carcinoma of ductal origin; among these 19.01% were in stage IV.

The age distribution (Table 1) in Group-I ranged from 13 to 66 years; in Group-IM it was 32 to 66 years. The age distribution in Group-II ranged from 32 to 84 years. Median age in Group-I was 45 years (Group-IB it was 44, Group-IM it was 49) and that in Group-II it was 57 years. The majority of patients in the malignancy category were between 40-60 years; 77.14% in Group-IM and 62.23% in Group-II (p=0.098). The percentage of patients above the age of 60 years was significantly lower in Group-I compared to Group-II (10.18% vs 40.14%; p<0.0001). The proportion of patients above the age of 60 years was 20% in Group-IM and 39.86% in Group-II (p=0.028). Mean age in Group-IB was 42.37±11.4, Group-IM 50.82±8.73 (p=0.0002); There was a significant difference in the mean age of the malignant categories; 50.82±8.73 in Group-IM and 57.05±10.03 in Group-II (p=0.0009). 71.29% in Group-I were males; in the malignancy groups; 59.26% of Group-IM and 50.7% of Group-II were males (p=0.098). The most common surgery done (Table 2) in Group-I was ductal drainage procedure LPJ /Frey's (64.81%) followed by palliative drainages. In Group-II; the commonest surgical procedure done was pancreatico-duodenectomy (48.25%) followed by palliative drainage procedures (44.36%). The resectability rate in Group-IM was 39.28% and in Group-II was 64.54% (p= 0.015).

Table 1: Age distribution in the malignancy groups

Parameter	Group-IM (n=35)	Group-II (n=142)	P value
Age (Range)	32-66	32-84	-
Median age (years)	49	57	-
Mean age (years)	50.82±8.73	57.05±10.03	p=0.0002
% between 40-60 years	77.14%	62.23%	p=0.098
% above 60 years	20%	39.86%	p=0.028

Table 2: Details of the surgical procedures done

Type of Surgery	CCP % (n=113)	DACP % (n=142)
Pancreatico-duodenectomy	6.48%	48.25%
Distal Pancreatectomy	3.7%	1.39%
Palliative drainage	22.2%	44.36%
Biopsy only	2.8%	0.59%
Frey's/LPJ	64.81%	-

The mean value of CA19-9 in Group-I was 191.6 U/ml; in Group-IM was 510.915±480.51 and in Group-II was 405.37±458.72 (Group-IM vs Group-II p=0.136) and that in Group-IB was 92.49±166.81 which was significantly low compared to Group-IM (0.0001). On analyzing the CA19-9 values in the ROC curve a cut off value of 100.21 U/ml had shown 82.9% sensitivity and 85.2% specificity for detecting malignant CP. With a cut off value of 204.9 U/ml, sensitivity was 70% and specificity was 98.1%.

The total WBC count (TC) ranged from 3200 to 16000 cells/µL in Group-I and 2720 to 17000 in Group-II. The total WBC count (TC) ranged from 3200 to 15500 In Group-IB and 4600 to 16000 in Group-IM. The mean TC in Group-I was 8203.33±2272.02 and Group-II were 8408.098±2460.82 (p=0.501). TC in Group-IM and Group-II were 8397.03±2438.08 and 8408.098±2460.82 (p=0.981). TC in Group-IB and Group-IM were 8138.76±2226.1 and 8397.03±2438.08 (p=0.581) respectively.

The absolute lymphocyte count ranged from 928 to 4990 cells/mm^3 in Group-I and 1044 to 4470/mm^3 in Group-II. The mean ALC in Group-I was 2480.15±826 and Group-II was 2346.26±802.15 (p=0.198). ALC in Group-IM and Group-II were 2131±675.96 and 2346.26±802.15 (p=0.981). ALC in Group-IB and Group-IM were 2596.38±842.22 and 2131±675.96 (p=0.0048). Neutrophil count in Group-I ranged from 37 to 87 and in Group-II ranged from 36 to 90; in Group-IB ranged from 37 to 87and in Group-IM ranged from 47 to 82. Mean neutrophil count in Group-I was 61.66±10.72 and Group-II was 65.05±10.5. MNC in Group-IB was 59.55±10.54 and in Group-IM was 68±8.713. On comparing the malignant categories MNC in Group-IM was 68±8.713 and in Group-II was 65.05±10.5 (p=0.126). On comparing Group-IB and Group-IM it was 59.55±10.54 and 68±8.713 (p=0.0001). Platelet count in Group-I ranged from 130000 to 512000 and in Group-II ranged from 103000 to 640000. That in Group-IB ranged from 140000 to 512000 and in Group-IM ranged from 130000 to 480000. Mean platelet count in Group-I was 277731.48±80866.98 and in Group-II was 309387.32±99377.27. MPC in Group-IB was 277098±82648.59 and in Group-IM was 279629.63±76743.9. On comparing the malignant categories MPC in Group-IM was 279629.63±76743.9 and in Group-II was 309387.32±99377.27 (p=0.1002). On comparing Group-IB and Group-IM it was 277098±82648.59 and 279629.63±76743.9 (p=0.878) which was not statistically significant.

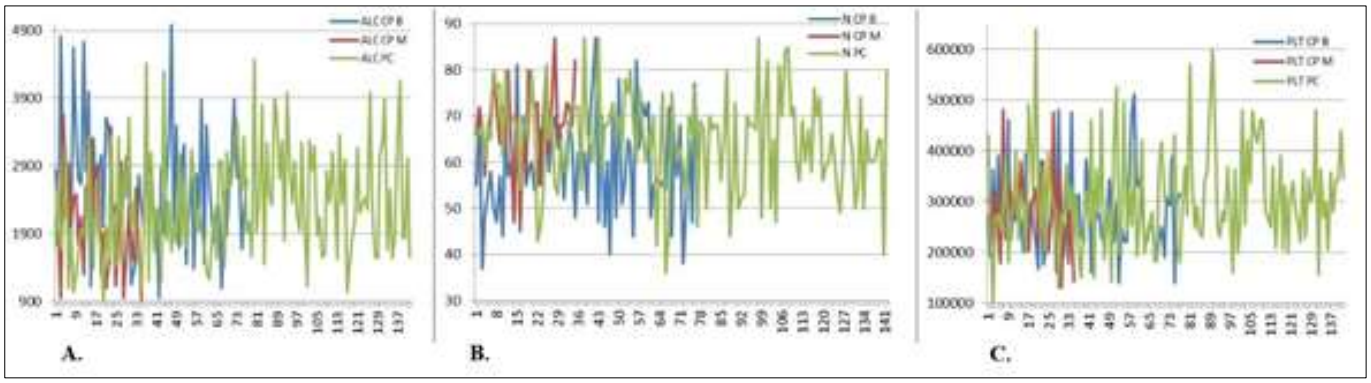

Fig 1: Comparison of Group-Ib, IM and II Regarding the Absolute Lymhphocyte Count (A) Neutrophil Count (B) and Platelet Count (C)

The mean NLR in Group-II was 2.703±1.48 and in Group-IM was 3.356±1.6 (p=0.226). Mean NLR Group-IB was 2.17±1.46 which was significantly lesser than that in Group-IM (p<0.0002). By ROC curve sensitivity, specificity, PPV,

NPV; and accuracy of Group-I with NLR cut off value of 2.345 were 68.11%/73.72%/59.62/91.80% and with 2.813 were 58.3%/90.2%/72.4%/82.14%.

The mean PLR in Group-II was 145.527±66.29 and that in Group-IM was 157.862±56.42 (p=0.273). Mean PLR Group-IB was 115.19±41.05 which was significantly lesser than that in Group-IM (p<0.0001).). By ROC curve sensitivity, specificity, PPV and NPV Group-I with PLR cut off value of 138.65 were 63.89%/88.5%/69.7%/83.75%; and with 157.95 were 48.6%/91.8%/70.83%/78.65%.

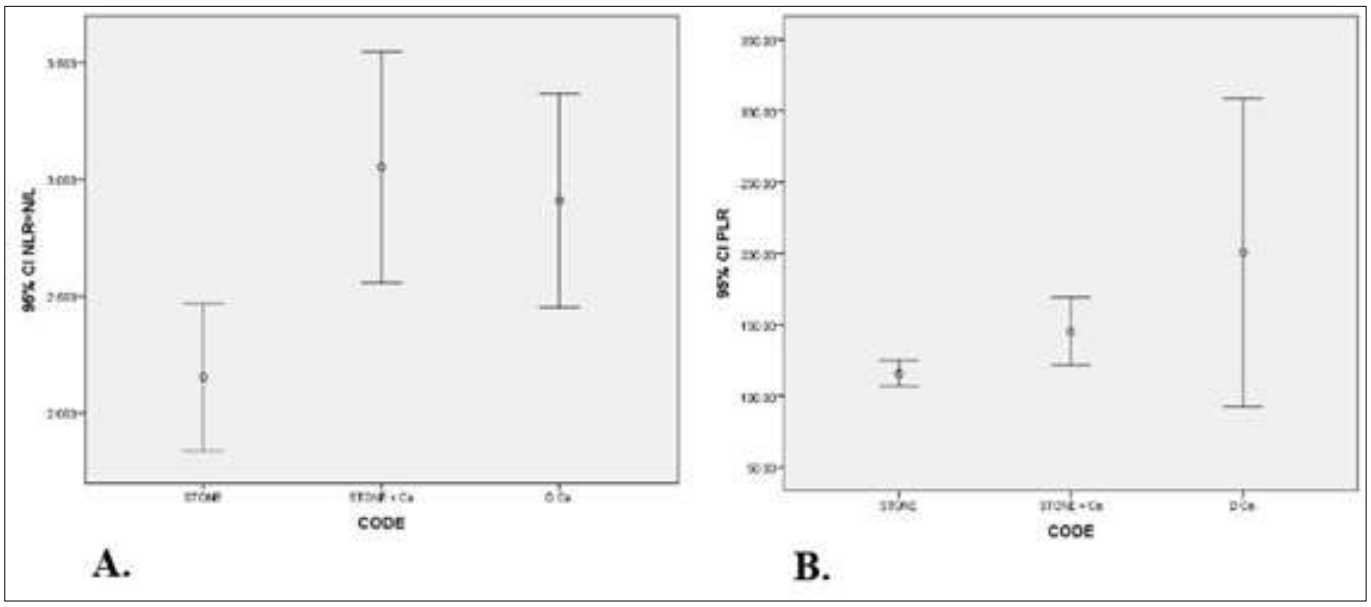

Fig 2: Comparison of Roc Data Regarding the Neutrophil-Lymphocyte Ratio (A) and the Platelet Lymphocyte Ratio (B) Among the Group IB, IM and II

Discussion

Tumour progression is seen associated with systemic inflammatory response and its influence in the microenvironment. High neutrophil count is a hallmark of systemic inflammation; producing inflammatory cytokines such as interleukins (IL-2, IL-6, IL-10), tumor necrosis factor α (TNF-α), and proangiogenic factors like vascular endothelial growth factor (VEGF); which favour tumor progression [28]. Elevated levels of IL-10 and TNF-α reduces the lymphocyte count. Lymphocytes produce cytokines, which inhibit the proliferation of cancer cells and their metastatic spread, provoking cytotoxic cell death [29]. Therefore, during carcinogenesis there is an increase in circulating neutrophils and decrease in circulating lymphocytes [30]. Thus, high NLR indicates an increased neutrophil-dependent tumor invasiveness and reduced lymphocyte-mediated antitumor immune response reflecting tumor progression [31, 32]. Recent meta-analysis by Li *et al*. emphasized that elevated NLR values are associated with advanced TNM stage and with poorer tumour differentiation [33]. Nieswandt *et al*. reported that platelets are promoters of metastases, due to their ability to coat tumor cells masking them from the natural killer cells in the immune system [34]. Furthermore, platelets impair DNA repair by the activation of epidermal growth factor receptor (EGFR) and DNA-dependent protein kinase [35]. Tang *et al*. have stated platelet count and VEGF were higher in cancer patients than in healthy controls [36]. Therefore NLR and PLR could be used as inflammatory markers in malignancy for predicting survival.

In the present study, among those CP patients underwent various biopsy/surgical procedures 24.07% of were proved to have associated pancreatic malignancy. This percentage is more than the reported rates of malignancy associated with CP in various studies[9-12]. This could be due to the fact that study centre being a referral centre, was dealing with patients requiring surgical interventions for complications of CP.

Demographic parameters

The mean age at which PDAC was diagnosed was reported as 71 years; with 5–10% of these patients diagnosed at a younger age, before 50 years [37-40]. In the present study, the age of presentation in CP group ranged from 13 to 66 years; malignancy was detected in CP between 32 to 66 years of age. The age of diagnosis in the de-novo DCAP ranged from 32 to 84 years. The mean age of malignant CP was significantly lesser than that of the de-novo DCAP (50.82±8.73vs57.05+10.03; p=0.0009). Carcinoma arising in CP was suspected in an early age because of their recurrent symptom profile due to the inflammatory process. The majority of patients in the malignancy categories were between 40-60 years; which was 77.14% in carcinoma in CP and it was 62.23% in de-novo DCAP. The proportion of patients above 60 years age was significantly less in the CP especially in malignancy than in the de-novo DCAP (10.18% vs 40.14%; p<0.0001); which indirectly indicates the probability of shortened life expectancy in CP which could be secondary to the associated exocrine and endocrine deficiency or malignancy in CP. 71.29% in CP group were males; in the malignancy groups males predominated both in malignant CP and denovo DACP (59.26% and 50.7%) which was comparable with the literature data [41].

Clinical Parameters

Majority of patients in the malignant CP group were managed by palliative procedures. The resectability rate in carcinoma arising in CP was significantly lower compared to the de-novo DCAP; which was comparable to the data available in similar studies [41, 42]. This could be due to the associated inflammatory changes in CP which leads to dense adhesions

of the tumour with the surrounding organs and vascular structures including portal vein, thus making the resection technically challenging.

Laboratory parameters

The possibilities of a co-existing active inflammation being a confronting factor which could lead to bias in this study on the inflammatory markers was considered during the study design. Hence conditions including acute exacerbation of CP, cholangitis and neoadjuvant chemotherapy were excluded from this study.

Total leukocyte count was comparable between the groups without statistically significant differences. Absolute lymphocyte count did not show a statistically significant difference between the malignant CP and denovo DACP (2131±675.96 vs 2346.26±802.15; p=0.981). However, the absolute lymphocyte count was significantly less in malignant CP compared to benign CP (2131±675.96 vs 2596.38±842.22; p=0.0048). The mean neutrophil count was comparable between malignant CP and denovo DACP (68±8.713 vs 65.05±10.5; p=0.126). Whereas the mean neutrophil count showed significantly higher values in malignant CP compared to the benign CP (68±8.713 vs 59.55±10.54; p=0.0001). The mean platelet counts did not show any statistically significant differences between denovo carcinoma pancreas and carcinoma in CP (279629.63±76743.9 vs 309387.32±99377.27; p=0.1002) or between the benign and malignant CP (277098±82648.59 vs 279629.63±76743.9; p=0.878).

There were some incidentally detected interesting aspects in the differential count profile of chronic pancreatitis observed during this study. Lymphocyte count in malignant CP showed lowest values of the three categories; it was less than that of denovo DACP, and significantly lesser than the benign CP. In other words, the lymphocyte counts in benign CP were on the higher side. However with a co-existing malignancy it was found diminishing even beyond the mean lymphocyte counts in denovo carcinoma pancreas. Similarly, the rise in the neutrophil counts in the malignant CP was very much significant, higher than that of the denovo carcinoma pancreas. This exaggerated neutrophil response could be due to the cumulative effect of inflammatory and malignant processes occurring simultaneously in the malignant chronic pancreatitis. This could be explained clinically also by the change in the character and intensity of their chronic abdominal pain, by which most of the malignant CP patients report with. The rise in neutrophil counts could reflect in a relative decrease in the lymphocyte counts as well. Another possibility is that the innate lymphocytosis associated with the CCP in the benign state is getting suppressed during its malignant transformation by certain immune mediated responses to a level lower than that of the denovo carcinoma pancreas; exerting a relative rise in the neutrophil count. Various studies on immunology of chronic pancreatitis have reported that there is dense infiltration of lymphocytes in the pancreatic tissues especially around the areas of fibrosis, more evident in the early phases of the disease [43, 44]. Therefore, systematic clinical surveillance and frequent blood count monitoring especially when there is a change in the symptomatology, for a falling lymphocyte counts and raising neutrophil count wound help in identifying the progression of CP to malignant CP. Further advanced studies in this line could help in better understanding of the pathophysiology of chronic pancreatitis as well as the tumour biology of carcinoma arising in chronic pancreatitis.

CA19-9

Huang and Liu in their meta-analysis had stated that serum CA 19-9 plays an important role in the diagnosis of pancreatic cancer [45]. There are many studies giving the overall sensitivity and specificity of CA 19-9; a value 127 U/mL showed 85.7% sensitivity, 96.5% specificity, 92.3% PPV and 93.2% NPV [46]. The values over 300 U/mL were stated as 100% specific for malignancy [47]. Thus CA19-9 is still considered as helpful in diagnosing carcinoma pancreas. In the present study, the mean value of CA19-9 in CP group was 191.6 U/ml. On comparing the malignancy categories the values were comparable without statistically significant difference (510.915±480.51 vs 405.37±458.72; p=0.136). Whereas while comparing the benign and malignant CP there was a statistically significant lower values in the benign CP (92.49±166.81 vs 510.915±480.51; p=0.0001). On analyzing the CA19-9 values in the ROC curve a cut off value of 100.21 U/ml had shown 82.9% sensitivity and 85.2% specificity for detecting malignant CP. With a cut off value of 204.9 U/ml sensitivity is 70% and specificity is 98.1%. This analysis was done as a preliminary data profiling with a known screening parameter before testing variables under evaluation.

NLR

A recent meta-analysis showed that NLR≥ 5 predicts a shorter OS and thus elevated NLR could be a potential biomarker to identify patients with a poor outcome [48]. In the present study the mean NLR in malignant CP was 3.356±1.6 and that in de-novo DCAP was 2.703±1.48. These were comparable as there was no significant difference between the two. On comparing the benign and the malignant CP; the mean NLR value was 2.17±1.46 in benign CC and this showed a statistically significant difference with the malignant CP (p<0.0002). This indicates that the NLR is significantly lesser in the benign CP subgroup compared to malignant CP which could help as a negative predictor for malignancy in CP.

PLR

Our centre had already published study comparing the predictive values of PLR and CA19-9 in PDAC and inflammatory (benign) mass in the head of pancreas [25]. This study which had compared benign CP and de-novo PDAC had shown that a PLR cutoff value of 113.5 has 79.4% sensitivity, 92.6% specificity, 91.5% PPV and 99.7% NPV. In the present study the mean PLR values were comparable between malignant CP (157.862±56.42) and the DCAP (145.527±66.29). When the mean PLR in benign CP (115.19±41.05) was compared with the malignant CP; the values were significantly lesser in the benign CP subgroup, which could help as a negative predictor for malignancy in CP.

Comparison of the preditive values of CA 19-9, NLR and PLR

There are many studies comparing the predictive values of NLR, PLR and CA19-9 in DCAP and CP. Bollineny V *et al* have reported the mean value of NLR in CP as 1.25±1.17 and in DCAP as 3.65±1.39 whereas PLR in CP as 121±97 and in DCAP as 227±128[49]. The formerly reported study from our own centre had reported the cutoff value for CA19-9 as 25.3 U/mL (sensitivity-73.5%, specificity-77.8%, PPV-78.5%, NPV-74.6%), for PLR as 113.5 (sensitivity-79.4%, specificity-92.6%, positive predictive value (PPV)-91.5%,

negative predictive value (NPV)-99.7%). This study had concluded that PLR may be useful to differentiate PDAC from inflammatory mass lesions in chronic pancreatitis [25]. Another study had shown that a cutoff values of 4.11 for NLR has 83% sensitivity, 75% specificity and 362 for PLR has 91% sensitivity, 62.5% specificity. However they have reported that NLR or PLR were not helpful to predict the resectability of the tumour [50].

In the present study, the receiver operator characteristic curve (ROC curve) was used to analyse and to derive a cutoff value for CA19-9, NLR and PLR below which the possibility of co-existing malignancy in CP mass could be predicted as minimum. On analyzing the CA19-9 values in the ROC curve a cut off value of 100.21 had shown 82.9% sensitivity and 85.2% specificity towards malignant CP. On analyzing the NLR values in the ROC curve, a cut off value of 2.345 showed 68.11% sensitivity, 73.72% specificity, 59.62 PPV and 91.80% NPV; whereas with a cut off value of 2.813 were 58.3% sensitivity, 90.2% specificity, 72.4% PPV and 82.14% NPV. While analyzing the PLR values in the ROC curve, a cut off value of 138.65 were 63.89% sensitivity, 88.5% specificity, 69.7% PPV and 83.75% NPV; whereas with 157.95 were 48.6% sensitivity, 91.8% specificity, 70.83% PPV and 78.65% NPV. Therefore these simpler ratio calculations from the easily available, less expensive routine blood pictures could give alerts regarding the changing character of this premalignant condition which can progress to carcinoma pancreas.

Conclusion

NLR and PLR values in CCP carcinoma and denovo-DACP were comparable. Whereas, there were statistically significant differences in NLR and PLR, between the benign and malignant subgroups of CP. The NLR and PLR have showed appreciable negative predictive values comparing benign and malignant CP. Further studies on the significant differences in the differential counts comparing the benign and malignant subgroups of chronic pancreatitis, would help in understanding the pathophysiology and tumour biology of carcinoma arising in chronic pancreatitis.

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Footnote

Conflicts of Interest

The authors have no conflicts of interest to declare.

Ethical statement

The study was approved by the Institutional Ethics committee of Government Medical College, Trivandum, Kerala.

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