NEUTROPHILIC LYMPHOCYTIC RATIO AS A PROGNOSTIC INDICATOR IN ACUTE PANCREATITIS
Vijayakumar K. Karikkilii, Arun Damodharaniii, Divya Devi Hi, Swaminathan Ganesanii

1Professor and Unit Chief, Department of General Surgery, Government Kilpauk Medical College and Hospital, Chennai.  
2Assistant Professor, Department of General Surgery, Government Kilpauk Medical College and Hospital, Chennai.  
3Assistant Professor, Department of General Surgery, Government Kilpauk Medical College and Hospital, Chennai.  
4Postgraduate Resident, Department of General Surgery, Government Kilpauk Medical College and Hospital, Chennai.

BACKGROUND
In India, pancreatitis seems to be more common among alcoholics. Being a developing nation, most of the affected families live in poverty. So, the hospital expenses in treatment of pancreatitis are a burden to them. Many investigations are required for calculating the severity scoring systems will increase the patient’s cost. In order to predict the severity of the disease earlier, a simple scoring system is evaluated using routine blood count which will enable us to provide aggressive treatment for those progressing to severe pancreatitis and lower the morbidity and mortality.

MATERIALS AND METHODS
A prospective collection of data among 100 sequential patients admitted with a diagnosis of pancreatitis based on Atlanta criteria are enrolled and data collected for severity, amylase, lipase, CECT, serum creatinine, and neutrophil lymphocyte ratio, at the time of admission, 24 hours, 48 hours and analyzed using independent variable t test.

RESULTS
Out of 100 patients 96% were males, alcohol was the leading cause 98%, severe pancreatitis was noted in 20% mortality was 4%, NLR was progressively increasing from 12 to 15 in severe group compared to 4 to 6 in mild group the difference was significant (p value – 0.004).

CONCLUSION
The overall mortality due to acute pancreatitis has remained 10-15% in the past 20 years. Accurate predictors of the severity of acute pancreatitis are important because they influence clinical decision making. Neutrophilic Lymphocytic Ratio (NLR) was calculated among these patients and was found to be increased in acute pancreatitis. It was significantly higher in severe pancreatitis patients than the mild pancreatitis patients. It is thus a cost effective tool. NLR is a simple indicator of the prognosis of pancreatitis which would help in providing aggressive treatment to those patients progressing to severe pancreatitis.

KEYWORDS
Acute Pancreatitis, Severity, NLR, Neutrophil Lymphocyte Ratio, Scoring System.


BACKGROUND
Acute pancreatitis (AP) is an outcome of acute inflammation of pancreas with activation of the pancreatic enzymes. The Atlanta classification classifies acute pancreatitis into mild pancreatitis and severe pancreatitis. Though normally it is a self-limiting process with 80% having mild disease, 10% to 20% of them have a rapidly progressive inflammatory response. Patients with mild pancreatitis have less than 1% mortality rate whereas even up to 50% for those with severe pancreatitis.

The scoring system currently regarded as the best for assessment of Acute Pancreatitis, namely the Acute Physiology and Chronic Health Evaluation (APACHE II), is labor intensive and is not being followed routinely for patients of pancreatitis treated outside Intensive Care Unit. Other scoring systems namely Ranson’s scoring system and IMRIE scoring system (Glasgow scoring system) are also difficult to apply as there are many parameters.

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aggressive treatment for those progressing to severe pancreatitis and lower the morbidity and mortality.

The white blood cell count is a routine serum hematological test that is already incorporated in many of the current Acute Pancreatitis scoring systems, and routinely performed on all surgical emergency admissions. Components of the total WBC count include neutrophils and lymphocytes, both of which can be used individually as markers of inflammation.

In Acute pancreatitis, Neutrophils are incorporated into the pancreas due to the action of inflammatory cytokines. These neutrophils propagate Systemic Inflammatory Response Syndrome (SIRS) and the inflammatory cascade in Acute Pancreatitis whereas lymphocyte depletion occurs in severe sepsis, and is associated with a poor outcome. This lymphopenia has been previously associated with severe sepsis, bacteremia, and surgical stress.

The Neutrophil-Lymphocyte Ratio (NLR) is a measure of the divergence of these two WBC components, and may be more accurate than the total WBC or individual neutrophil and lymphocyte counts in predicting poor outcome.

Thus, the aim of our study is to check if NLR can be used as a single cost-effective tool to predict the severity of acute pancreatitis.

AIMS AND OBJECTIVES
The aim of this study was to calculate the Neutrophilic Lymphocytic Ratio (NLR) among acute pancreatitis patients and to investigate if this ratio is helpful as a single predictor in assessing the prognosis of acute pancreatitis.

Review of Literature
Acute pancreatitis is the result of abnormal pancreatic enzyme activation inside acinar cells. The inflammatory cascade is self-limited in approximately 80%-90% of patients. In small number of patients, there is massive release of inflammatory mediators into systemic circulation. Active neutrophils mediate acute lung injury and induce adult respiratory distress syndrome (ARDS). Similarly, it affects the kidneys and gut and progresses to Multi-Organ Dysfunction Syndrome (MODS).

In 2012 (March), Rawad Mounzer et al, In his study, compared all clinical scoring systems which are currently in use to predict organ failure, which is one of the grave catastrophes of acute pancreatitis to a conclusion that all scoring systems have reasonable accuracy in predicting persistent organ failure, but the Glasgow score was found to be the best. In 2012 (Feb).1

It has been identified that following an insult, there is neutrophilia and lymphocytopenia which occurs within 4 to 8 hours as a response to severe infection, surgical stress, systemic inflammation and septic shock. As per Mahidhara and Billiar, the reason for neutrophilia is due to delay in apoptosis of neutrophils, demargination of neutrophils from endothelium and as an effect of growth factors.

Hotchkiss et al, Ayala et al and many others have observed apoptosis of lymphocytes which resulted in lymphocytopenia. Menges et al supported this with his flow cytometric assays which showed a decrease in T4- helper lymphocytes following multiple trauma and hence responsible for SIRS and MODS. It has been stated that lymphocytopenia not only indicates the severity of the stressful condition, but also reflects the efficacy and adaptability of the immune system.

The response of the inflammatory/ immune system to stress can be easily assessed by the ratio of neutrophil count (in%) to lymphocyte count (in%). As per a study by Zahorec et al the severity of insult, severity of clinical status and clinical outcome, was found to correlate nicely with neutrophil/lymphocyte ratio. With regard to APACHE II and SOFA scoring systems. He has suggested that when the differential counts of WBC were serially monitored, it provided information about the body’s immunological response to stress in critically ill patients.

It is the divergence of these two components of the WBC counts namely neutrophilia and lymphopenia that led to the proposal of assessing the NLR as a single and more accurate predictive factor than either component alone. This has been assessed by Suppiah A et al, Azab et al and Vedat Goral et al and they have uniformly accepted that the NLR is a simple indicator of severity in patients presenting with acute pancreatitis.2,3,4

MATERIALS AND METHODS
This prospective study was conducted in ‘Department of General Surgery, government Kilpauk medical college hospital from January 2013 to July 2013 after obtaining permission from the Institution's Research and Ethical committee.’

Source of Data
The study was conducted on sequential admission of 100 patients diagnosed with acute pancreatitis in Government Kilpauk medical college.

Method of Collection of Data
- Patients with acute pancreatitis were diagnosed as per Atlanta symposium which is any two of the three findings:
  - Abdominal pain consistent with acute pancreatitis, i.e., severe and persistent epigastric pain, acute in onset, radiating to the back
  - Serum amylase or lipase: three or more times the normal limit (in our laboratory normal value of Sr. amylase- 50 - 150 SV/DL.
  - CECT (Contrast Enhanced Computerized Tomography) findings characteristic with acute pancreatitis and less commonly with MRI or Ultrasonography of abdomen
- Informed consent was obtained from patients for including them in our study
- Blood samples were taken at the time of admission and sent for Serum Amylase, Sr. urea, Sr. creatinine and liver function test analysis WBC count a
- Similarly, Samples were sent for a differential count At the time of admission At 24 hrs.
At 48 hrs. (NLR) was calculated which is Neutrophil lymphocytic ratio.

Inclusion Criteria
All cases of acute pancreatitis admitted in our hospital from December 2013 to July 2014.

Exclusion Criteria
Patients with chronic pancreatitis.

Method of Statistical Analysis
The NLR for day 0, day 1 and day 2 for mild pancreatitis and severe pancreatitis were analysed using independent sample t test. A ‘p’ value of <0.05 is indicated as statistically significant.

DISCUSSION
This study on 100 patients, acute pancreatitis was more predominant among Males (96%) than females (4%). This observation may be due to the reason that alcohol consumption is more common among males in a developing country like India. In our study, most of the patients who presented with acute pancreatitis belonged to 31-40 yrs. age group. The mean age was around 38.3%. The most common aetiology was alcohol which was around 98%. Of the 100 patients, 80% of them had mild pancreatitis and 20% had severe pancreatitis. This study seems comparable to the rate of incidence of mild and severe Pancreatitis as per Atlanta symposium, in which the rate of mild pancreatitis is 70-80% and 20-30% in severe pancreatitis patients. In this study, mortality rate 4% as compared to a mortality rate of 12% by Savio G Bal Teto et al.6

In this study it is also noticed that, serum amylase was elevated (>3 times the normal) in only 37 patients while it was < 3 times the normal in 63 patients. This was in contrast to the diagnostic criteria proposed by the Atlanta.6 When analysed, there were studies which showed lower levels of amylase in patients with acute pancreatitis and severe destruction of the pancreas. Neutrophil lymphocytic Ratio (NLR) was elevated in patients presenting with acute pancreatitis. The NLR was increased when compared to the normal (2.63).4 The WBC count is a marker of infection and inflammation. It is a part of many scoring systems used to prognosticate acute pancreatitis. This was clearly elicited in our study where the neutrophil count progressively increased in severe pancreatitis group, where there was progression to SIRS. In contrast, in mild pancreatitis, as the disease severity decreased, the neutrophil count also started to decline toward normalcy. Lymphocyte numbers increase following the initial stress and mediate the subsequent inflammatory response. The previous view is that neutrophilia is the primary cause of an elevated NLR, SIRS and poor prognosis, while lymphocyte count remains constant. However in our study there was lymphopenia within 24 hrs. of admission which was persistent in severe Pancreatitis group than the mild group and hence contributing to the increased NLR. This persistent lymphopenia has been attributed to excessive inflammation, bacteraemia or sepsis in intensive care. Uncontrolled inflammation is thought to precipitate lymphopenia by redistribution of lymphocytes, accelerated apoptosis and hence lymphopenia responsible for bigger mortality in patients with septic shock.

As per our study the NLR seems to represent a dynamic process where in it tends to return to normalcy in mild pancreatitis whereas it is persistently high in severe acute pancreatitis. The difference in NLR pattern between the mild and severe acute pancreatitis was analysed by independent sample t test and was found to be statistically significant (p <0.05).

This variation in NLR was analysed by Suppiah A et al2 and they reported that NLR was raised significantly in poor prognosis group than the favourable group. In their study the MR was comparable at baseline that is at the time of admission. The NLR then gradually returned towards normal in favourable group while was persistently high in the poor prognosis group which is similar to our study. Similar study was conducted by Azab et al and they reported.3

![Figure 1. Trends of Neutrophil Count](image)

NLR to be superior to the total WBC count or individual neutrophil and lymphocyte counts in predicting ICU admission and death in acute pancreatitis patients. They further proceeded and recommended a cut-off value of >4.7 to identify poor outcome acute pancreatitis. The benefit of our study is that NLR can be calculated by just doing a total WBC and a differential count. In comparison to other severity scoring systems, where there are multiple parameters required to calculate the prognosis, NLR analysis just needs a single blood test needs to be done serially. In some systems like the Ranson's and Glasgow scoring systems which can be calculated only after 48 hours of admission, the crucial period in management of acute pancreatitis is lost leading to a worse prognosis. In our study, NLR can be done at the time of admission and can be serially monitored which can act as a guide to detect those patients progressing to severe pancreatitis. Those patients progressing to severe pancreatitis can be identified earlier and can be managed intensively and hence reduce the morbidity and mortality. NLR is a cost effective, simple tool which can be calculated in any level care of hospital be it a secondary care or a tertiary care hospital. India being a developing country has a low Doctor patient ratio and limited facilities are available at the peripherally located hospitals. With alcohol induced pancreatitis being more common...
among the low socioeconomic status, multiple blood tests would be a burden for them. In that case, differential WBC count would be a cheaper and an easier blood test that can be performed and the MR thus calculated can be used as a guide to refer poor prognosis patients to a higher centre for intensive care and management. In our study, Neutrophilic Lymphocytic Ratio has proved to be a single indicator in assessing the severity of acute pancreatitis. NLR can be easily calculated and is a routine workup that is done it bears no additional cost to the patient. NLR seems to correlate well with the severity and outcome of acute pancreatitis. Continuous monitoring on each day will provide a dynamic reflection of the immunity and inflammatory response of the body to pancreatitis and hence predict the prognosis earlier.

NLR assessment trespasses the limitation of Ranson's scoring system that, it can be used at the time of admission itself and monitoring is possible in the first 48 hours. It covers the limitation of APACHE II scoring system in a way that it avoids multiple parameters needed for assessment. However, as of now APACHE II is considered the most useful the most still further studies need to be performed to find out if we can predict an optimal Neutrophilic Lymphocytic Ratio which can delineate mild pancreatitis and those progressing to severe pancreatitis. As of now, only the study by Azab et al has proposed a neutrophil lymphocyte ratio value of >4.7 in predicting the severity in acute pancreatitis. However, as per Suppiah et al, this value has a high sensitivity (90.9%) but a low specificity (22%). So, Future studies are needed which can optimize the NLR and investigate if its incorporation would increase the accuracy of the current Acute pancreatitis prognostic scoring systems.

CONCLUSION

Acute pancreatitis is still one of the most common causes of emergency hospital admissions in India. The overall mortality due to acute pancreatitis has remained 10-15% in the past 20 years. Accurate predictors of the severity of acute pancreatitis are important because they influence clinical decision making. In this study, we evaluated 100 patients of acute pancreatitis and we found that pancreatitis is more common in males and alcohol being most common etiological factor. Neutrophilic Lymphocytic Ratio (NLR) was calculated among these patients and was found to be increased in acute pancreatitis. It was significantly higher in severe pancreatitis patients than the mild pancreatitis patients. The NLR seems to persistently rise in poor prognostic patients when it was serially calculated. Hence, it is a dynamic indicator of the severity of the disease. NLR can be easily assessed. It can be calculated from a blood test which is routinely done for all patients at the time of admission. It is thus a cost effective tool. NL R is a simple, single indicator of the prognosis of pancreatitis which would help in providing aggressive treatment to those patients progressing to severe pancreatitis. Further studies are needed which would incorporate this NLR into the current scoring systems and thus increase their accuracy.

REFERENCES