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# Prediction of Troponin Elevation in Non-ST Acute Coronary Syndrome Patients Presenting to the Emergency Department Using Neutrophil-Lymphocyte Ratio

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## ABSTRACT

**Background**: In patients with stable coronary artery disease (SCAD), the neutrophil–lymphocyte ratio (NLR) is thought to be an independent predictor of death and myocardial infarction (MI). In patients suffering from acute coronary syndrome (ACS), NLR also has prognostic significance. Nevertheless, further research has to be done on the diagnostic efficacy of NLR in ACS patients.

**Objective:** To ascertain if NLR can accurately predict troponin elevation in patients who arrive at the Emergency Department with NST-ACS.

**Patients and Methods:** This is a prospective observational study that was carried out on 100 patients who presented to the Emergency Department at Ain Shams University Specialized Hospital between June 2018 and March 2019 with angina or angina-equivalent during the first 12 hours of symptom onset.

**Results:** Two groups were created from the study population: a troponin-positive group (n = 50) and a troponin-negative group (n = 50). The patients' average age was 55.8 ± 11.3, with 77% of them being males. There was no discernible difference in the two groups' levels of platelets, WBCs, or hemoglobin. The group that had positive troponin levels had a considerably higher neutrophil count ($p < 0.001$). The group that tested positive for troponin had a considerably greater NLR (2 vs. 3.9, $P < 0.001$). In terms of predicting follow-up troponin positive, a cutoff value of 3.4 for NLR assessed at admission exhibited 84% sensitivity and 84% specificity. The amount of troponin alteration and NLR were shown to be extremely significantly correlated (p value <0.01).

**Conclusion:** NLR is a diagnostic technique that can be used to distinguish between people who have ACS. NLR is an accessible, affordable, and straightforward metric that may be utilized for NSTEMI diagnosis.

**Keywords:** MI, NLR, ACS, troponin.

## INTRODUCTION

The NLR and total WBC, neutrophil, and lymphocyte counts are regarded as indicators of systemic inflammation [(1)]. An increased WBC count has also been linked to a higher risk of heart attacks [(2)]. Particularly in individuals with SCAD and severe coronary atherosclerosis, the NLR has been demonstrated in earlier studies to be a predictor of cardiac events and death [(3-5)]. Furthermore, a number of studies have demonstrated the predictive significance of the NLR, total WBC count, and its differential count in patients with ACSs [(6-8)]. MI extension, the onset of post-infarction heart failure, compromised epicardial and microvascular perfusion, and post-infarction mortality have all been linked to elevated neutrophil counts [(9-12)].

Research on the use of NLR as a diagnostic tool in patients who arrive at the emergency room complaining of chest discomfort is scarce [(10)]. Since the diagnosis of acute coronary syndrome can be challenging, this very cheap and readily available characteristic can be very important in underdeveloped nations and help establish the accurate diagnosis in patients experiencing chest discomfort [(12)].

Aim of our study was to ascertain if NLR can accurately predict troponin elevation in patients who arrive at the Emergency Department with NST-ACS.

## PATIENTS AND METHODS

This is a prospective observational study that was carried out on 100 patients who presented to the Emergency Department at Ain Shams University Specialized Hospital between June 2018 and March 2019 with angina or angina-equivalent during the first 12 hours of symptom onset.

Exclusion criteria included patients with; Clinically significant congestive heart failure, autoimmune disease, cancer, hematological disorders, severe liver or renal disease, persistent infection or systemic inflammatory conditions, pulmonary embolism, peripheral vascular disease, STEMI, and patients with admission troponin values above the upper reference.

The patients were divided into 2 groups; patients who would acquire positive hs- troponin during 12–24-hours follow-up and patients with negative hs-troponin levels during follow up.

**All patients were subjected to;**

Full history on age, gender, smoking, hypertension, diabetes, dyslipidemia, family history of ischemic HD, previous ischemic HD and previous stroke or transient ischemic attack.

Also, on admission resting 12 leads surface (ECG), complete blood count with calculation of neutrophil/lymphocyte and highly sensitive troponin (hs-troponin) were done. Follow up hs-troponin after 3 hours using Architect assay with reference range (0-35) was used.

0h-3h rule out algorithm for diagnosis of NST-acute coronary syndrome was used. MI was diagnosed



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when equal or greater than 20% variation of troponin from base line.

Echocardiographic assessment was done using standard 2D mode. Patients were divided into 3 groups regarding ejection fraction (EF %): less than 40 %, 40-50% and more than 50%.

**Ethical approval:**

Ain Shams Medical Ethics Committee of the Ain Shams Faculty of Medicine gave its approval to this study. All patients who took part in this trial signed a written informed consent form. The Helsinki Declaration was followed throughout the study's conduct.

***Statistical analysis***

To document the information, an "investigation report form" was used. The data were then tabulated, categorized, and analyzed using SPSS version 22 for the dataset, descriptive metrics such as average and standard deviation, median, quantity, and percentage were calculated. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. P value < 0.05 was considered significant.

**RESULTS**

The study comprised one hundred consecutive patients in total. The patients' average age was 55.8 ± 11.3, with 77% of them being male. Based on the reports from coronary angiography, 15 patients (11%), 63 patients (48%), and 52 patients (40%) received conservative treatment, PCI, and CABG, respectively. During the follow-up period, the patients were separated into two groups according to the presence of troponin.

Gender, age, and cardiovascular risk factors were similar across the two groups. On one hand, the troponin-positive patients were more likely to be smokers (52%), to have ECG alterations (58%), and to have had a prior stroke (22%). On the other hand, patients in the troponin negative group tend to have previous ischemic heart disease (50%) in comparison to those in the troponin positive group (30%). The level of hemoglobin, WBCs and platelets did not show a significant difference in the 2 groups. However, the neutrophil count was higher in the troponin-positive group (Table1).

**Table (1): Baseline biochemical, hematological, and demographic information on the patients by group.**

| | **Troponin-negative group** | **Troponin-positive group** | **P-value** |
|---|---|---|---|
| | **No. = 50** | **No. = 50** | |
| **Gender** | | | |
| Female | 14 (28%) | 9 (18%) | 0.235 |
| Male | 36 (72%) | 41 (82%) | |
| **Age** | 55.32 ± 9.10 | 58.10 ± 10.87 | 0.169 |
| **Smoking** | | | |
| Positive | 15 (30%) | 26 (52%) | 0.039 |
| Negative | 26 (52%) | 21 (42%) | |
| Ex-smoker | 9 (18%) | 3 (6 %) | |
| **Hypertension** | 34 (68%) | 36 (72%) | 0.663 |
| **Diabetes mellitus** | 29 (58%) | 28 (56%) | 0.840 |
| **Dyslipidemia** | 24 (48%) | 28 (56%) | 0.423 |
| **Family history** | 1 (2%) | 5 (10%) | 0.092 |
| **Previous ischemic heart disease:** | | | |
| Negative | 25 (50%) | 35 (70%) | 0.048 |
| Previous PCI | 21 (42 %) | 12 (24%) | |
| Previous CABG | 4 (8%) | 1 (2%) | |
| Both | 0 | 2 (4%) | |
| **Previous stroke** | 3 (6%) | 11 (22%) | 0.021 |
| **ECG changes** | 12 (24%) | 29 (58%) | 0.001 |
| **Ejection fraction:** | | | |
| > 50 % | 44 (88.0%) | 33 (66.0%) | 0.021 |
| 40-50% | 5 (10 %) | 10 (20%) | |
| <40 % | 1 (2%) | 7 (14%) | |
| **Hemoglobin level (g/dL)** | 12.95 ± 1.74 | 12.95 ± 1.74 | 1 |
| **WBC count ($x10^3$/ mcL)** | 7.52 ± 1.84 | 8.05 ± 1.96 | 0.278 |
| **Platelet count ($x10^3$/ mcL)** | 252.12 ± 62.17 | 275.50 ± 66.94 | 0.144 |
| **Neutrophil count ($x10^3$/ mcL)** | 4.52 ± 1.11 | 6.10 ± 1.46 | <0.001 |
| **Lymphocyte count ($x10^3$/ mcL)** | 2.33 ± 0.57 | 1.46 ± 0.35 | < 0.001 |
| **NLR** | 2.00 ± 0.48 | 3.90 ± 0.96 | < 0.001 |

The troponin-positive group had a considerably greater NLR (Figure 1).

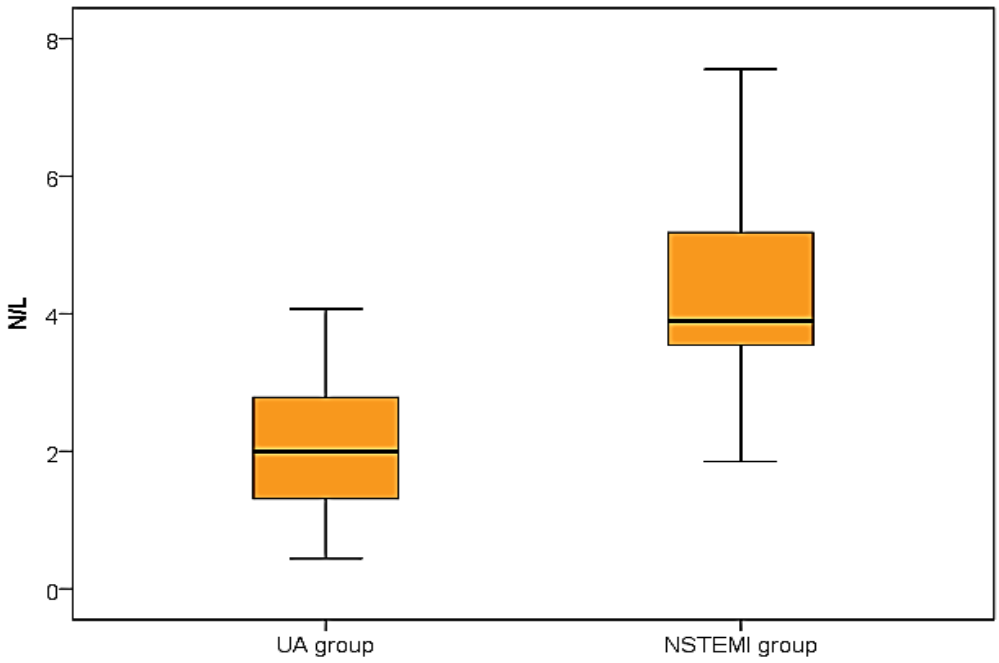


**Figure (1):** The NLR in troponin-positive group vs troponin-negative group.

The NLR was shown to be positively associated to age and the existence of ECG abnormalities.
It was discovered that patients whose admission NLR values were higher might be independently predicted to test positive for troponin during the follow-up period (Table 2).

**Table (2):** Multivariate logistic regression analysis for the association between troponin positivity and NLR and other risk factors

| | B | S.E. | Wald | P-value | Odds ratio (OR) | 95% C.I. for OR | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower | Upper |
| NLR | 0.56 | 0.164 | 11.701 | 0.001 | 1.75 | 1.27 | 2.411 |
| Smoking | 0.245 | 0.42 | 0.341 | 0.559 | 1.278 | 0.561 | 2.908 |
| Hypertension | 0.407 | 0.679 | 0.359 | 0.549 | 1.502 | 0.397 | 5.679 |
| DM | -0.769 | 0.627 | 1.508 | 0.219 | 0.463 | 0.136 | 1.582 |
| Dyslipidemia | 0.468 | 0.548 | 0.732 | 0.392 | 1.597 | 0.546 | 4.673 |
| Family history | 2 | 1.43 | 1.956 | 0.162 | 7.39 | 0.448 | 121.895 |
| Previous IHD | -0.792 | 0.456 | 3.02 | 0.082 | 0.453 | 0.185 | 1.107 |
| Previous stroke | 1.724 | 0.939 | 3.368 | 0.066 | 5.608 | 0.889 | 35.356 |
| ECG changes | 1.109 | 0.581 | 3.652 | 0.056 | 3.033 | 0.972 | 9.463 |
| Ejection fraction | -0.984 | 0.524 | 3.531 | 0.06 | 0.374 | 0.134 | 1.043 |
| Constant | 0.161 | 1.785 | 0.008 | 0.928 | 1.174 | | |

When predicting troponin positive using ROC analysis, a threshold level of NLR >3.4 exhibited 84% sensitivity and 84% specificity (ROC area under curve: 0.831, P < 0.001) (Figure 2).

The median level of troponin on admission in the troponin- negative group was 3.5 vs. 11 in the troponin-positive group (p value < 0.001).

The median change in the troponin – on admission and during follow up- was significantly higher in the troponin positive group than in the troponin negative group (2232 vs. 1 respectively, p-value<0.01).

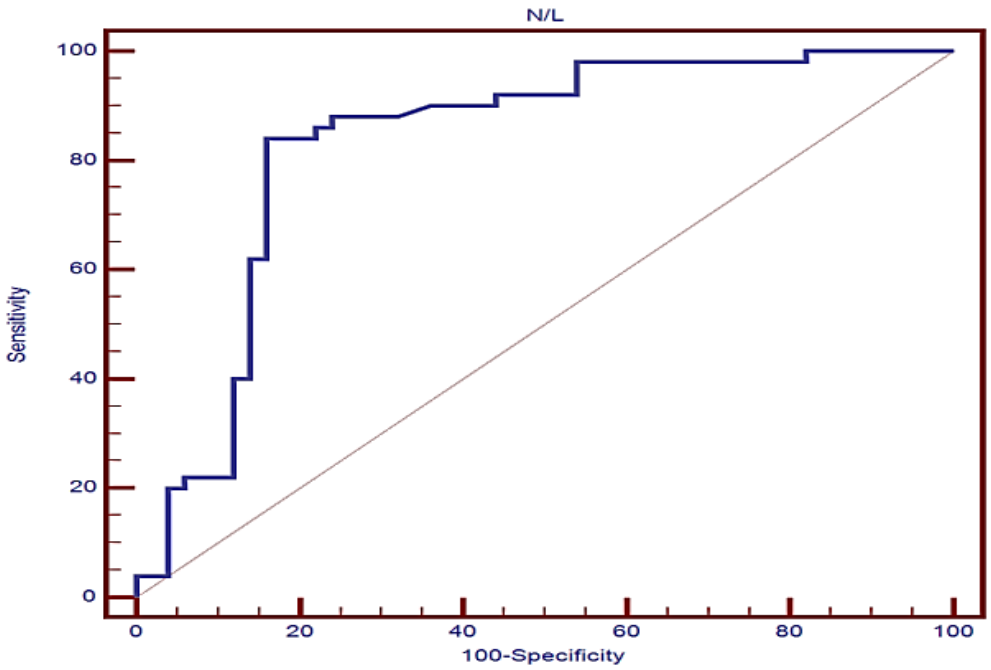


**Figure (2):** ROC analysis, a cutoff level of NLR >3.4.

There was a very strong association between the level of troponin alteration and NLR (p value <0.01). (Table 3, Figure 3).

**Table (3):** Spearman correlation analysis between NLR and age and other blood parameters

| | NLR | |
|---|---|---|
| | **R** | **P-value** |
| Age | **0.297** | **0.003** |
| Hemoglobin | 0.034 | 0.735 |
| WBC | **0.286** | **0.004** |
| Platelets | 0.088 | 0.386 |
| Troponin level on admission | **0.324** | **0.001** |
| Troponin level after follow-up | **0.489** | **<0.001** |
| Troponin change level | **0.445** | **<0.001** |

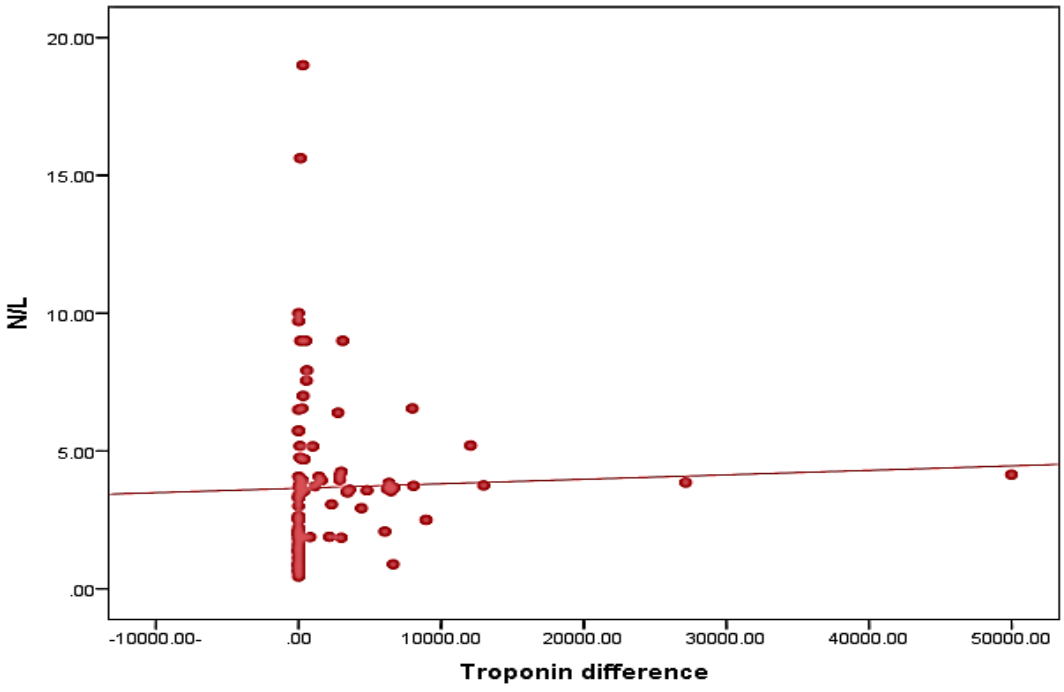


**Figure (3):** Correlation between NLR and level of troponin change.

## DISCUSSION

Our study was done on 100 patients who presented to the ER with non-ST acute coronary syndrome and negative baseline hs-troponin. 50 of them acquired positive troponin during follow up period.

There was no significant variation in age between the two groups ($p$= 0.1), gender ($p$= 0.2), cardiovascular risk factors including hypertension ($p$= 0.6), diabetes mellitus ($p$= 0.80), dyslipidemia ($p$= 0.4), and positive family history of cardiovascular events ($p$= 0.09); this could be explained by the study's very small sample size of patients.

Patients in the troponin-positive group tend to be smokers, have ECG-changes and previous strokes.

Surprisingly, patients in the troponin-negative group tend to have previous cardiac history (50% vs. 30 %, $p$=0.04); this could be explained by the concern of the ER physicians who tend to admit patients with previous ischemic history who experience chest pain.

Absolute neutrophil count was substantially *greater (p=0.001) in the troponin*-positive group, but absolute lymphocyte count was significantly lower ($p$=0.001). These findings aligned with those of research projects by **Zazula *et al.* [13] and Korkmaz *et al.* [14].**

In our study, there was no significant difference between the two groups in terms hemoglobin ($p$=0.14), platelets ($p$=0.14), and total leukocyte count ($p$=0.27). However, in studies conducted by **Zazula *et al.* [13] and Korkmaz *et al.* [14]**, **Tahto *et al.*[15]** and **Göktaş *et al.*[16]**, total leukocyte count was significantly higher in patients with AMI. **Tahto *et al.*[15]** showed no significant difference between AMI patients and unstable angina (UA) patients as regarding absolute lymphocyte count ($p$=0.24).

In our study, the troponin-positive group had considerably greater NLR ($P$<0 .001). Using ROC analysis, a cut-off level for NLR was demonstrated. It showed that patients having NLR> 3.4 were more likely to acquire positive troponin during follow up ($P$< 0.001, 84% sensitivity and specificity). A strong positive correlation between NLR and level of change in troponin during follow up was observed ($P$<0.001), indicating the importance of NLR in predicting intensity of myocardial damage. These findings were consistent with multiple studies.

In 2018 **Göktaş *et al.*[16]** conducted a study on 100 patients referred from ER with chest pain. They were divided according to their troponin positivity into 3 groups: STEMI, NSTEMI and unstable angina. NLR was shown to be significantly greater in patients with troponin-I positive ($p$<0.05). A positive correlation between NLR and troponin-I positivity was documented ($p$<0.05). However, no cut-off value for NLR to predict troponin positivity was shown.

In 2017 **Tahto *et al.*[15]** enrolled 100 patients with ACS, 50 of them had AMI and the other half had UA. No age difference between 2 groups was found. The 2 groups were compared regarding the blood parameters only, no other parameters were mentioned. Compared to patients with UA, in the AMI group's NLR was considerably greater ($p$ = 0.001). NLR correlated positively with the values of hsTnI. One important limitation of this study is that they included all the patients with AMI including STEMI and NSTEMI in one group. Also, no cut-off value for NLR and positive troponin was demonstrated.

In the study conducted by **Nalbant *et al.*[17]** to investigate the prognostic significance of NLR in AMI in individuals with renal impairment, 284 patients were enrolled; 71 patients had STEMI, 118 patients had NSTEMI and 95 had UA. NLR were substantially greater in AMI patients compared to non-AMI patients ($P$=0.001 and $P$=0.003, respectively). A cut-off value for NLR of >7.4 is two times more likely to have AMI (42.3 % sensitivity and 74.7% specificity, $P$<0 .001)

**Korkmaz *et al.*[14]**, conducted a research to establish NLR's potential to predict troponin increase. In this study, 244 patients with non-ST ACS and base line negative troponin, were enrolled. Similar to our study; there was no discernible difference between the two groups in terms of cardiovascular risk factors including hypertension ($p$=0.2), diabetes mellitus ($p$=0.9), dyslipidemia ($p$=0.6) or positive family history ($p$=0.9). However, patients in the troponin-positive group tend to be older ($p$=0.06), and males ($p$=0.03). Also, no significant difference regarding the previous cardiovascular history was found. During the follow up, NLR was significantly higher in the group who acquired positive troponin ($P$<0.001). In patients with non-ST ACS, a cutoff value for NLR > 2.80 demonstrated a 79% sensitivity and 73% specificity in predicting troponin positive.

**Zazula *et al.*[13]** demonstrated a correlation between The NLR and final diagnosis of ACS, being highest in patient presented with STEMI, moderate in NSTEMI, lowest in UA ($P$<0 .001). A NLR >5.7 reported to have 91.1% specificity, 4.51 odds ratio (CI 95% 1.51 to 13.45) for the final diagnosis of ACS.

Our study's main limitations are its comparatively small patient population and absence of long-term follow-up.

## CONCLUSION

NLR is a diagnostic technique that can be used to distinguish between people who have ACS. NLR is an accessible, affordable, and straightforward metric that may be utilized for NSTEMI diagnosis.

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