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Original Research Article

Pre-Surgical Neutrophil-Lymphocyte Ratio Predicts Surgical Site Infection Following Open Reduction Internal Fixation in Long Bone Fractures.

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Abstract:

Background: Surgical site infection is a costly postoperative complication which affects the quality of life. We aim to probe the predictive role of neutrophil-lymphocyte ratio for surgical site infection following open reduction internal fixation of long bone fractures.

Methods: This prospective observational study assessed data of 70 patients undergoing open reduction internal fixation of long bone fractures without any comorbidity or infective foci elsewhere in the body. The relation between demographics, surgical factors, pre-surgical laboratory results and the occurrence of surgical site infections were investigated by univariate and multivariate analyses. The overall surgical site infection was 11.43% with 12 months follow-up (7 superficial and 1 deep surgical site infection). Patients with surgical site infection had a significantly higher pre-surgical neutrophil-lymphocyte ratio.

Results: There neutrophil-lymphocyte ratio correlated positively with postoperative total days of antibiotic treatment for surgical site infection. The sensitivity was 62.5%, specificity was 92.8% with positive predictive value and negative predictive value 50% and 95.5% respectively for predicting surgical site infection than those without.

Conclusion: On multivariate analyses, a higher preoperative neutrophil-lymphocyte ratio was an independent predictor for surgical site infection following open reduction internal fixation of long bone fractures.

Keywords: Neutrophil-lymphocyte ratio, prospective observational study, open reduction internal fixation, surgical site infection, infective foci, long bone fractures, sensitivity, specificity, positive predictive value, negative predictive value.

Introduction

The orthopaedic operations has shown improved outcome over the recent years in terms of patient morbidity and mortality. [1] This is due to the continuous advancement of preoperative diagnostic tools, better and safer anaesthesia, potent antibiotics and techniques of asepsis along with better post- operative care. Even after of all these efforts,complications like infection following fracture fixation do occur and the battle to combat surgical site infection is not yet won. [2] Post-operative surgical site infection (SSI) ends in a difficult and frustrating position both for the patient and the treating surgeon. It delays healing, lead to permanent functional loss or disability. The estimated annual incidence of surgical site infection in the United States is 1.07%; with 8000 deaths directly related to it and $10 billion is the financial cost of treatment. [3] The surgical site infection is universal problem; in the United Kingdom, surgical site infection leads an extra cost of US$ 3394, and hospital stay duration increases between 5.8 to 17 extra days. [4] Studies in Nepal, Thailand and Pakistan found SSI rates of 7.3%, 14.5%, 9.3% respectively. [5,6,7] In India, a study in a tertiary care hospital showed a SSI rate of 2.1% in minimally invasive surgeries in comparison with a SSI rate of 16.2% for open surgeries. [8] It can also be a cause of increased morbidity, mortality and economic burden for patient and the hospitals. [9]

Causes of SSI are numerous. Including those related to the patient immune factors, environment and treatment. Soft tissue and periosteal damage associated with fractures poses a major risk factor for SSI following internal fixation. Also the subsequent surgery adds to more insult of the soft tissue and periosteum. [10] Different anatomical regions pose a difference in risk of postoperative wound infection. [11,12,13,14] Several conditions have been recognised to significantly increase the risk of SSI. Theyare Rheumatoid arthritis, Diabetes

mellitus (DM), Sickle cell anaemia, Psoriasis, renal failure, immunosuppression due to prior renal or liver transplant, malnourishment, obesity, concurrent UTI (bladder retention in post operation), malignancy etc.[15]Prolonged operative time also is an important risk factor. There are many risk factors and the incidence of SSI is proportionate to the risk factors present. The physiological stress of the body is one of such risk factor can be estimated using Neutrophil Lymphocyte Ratio (NLR). [15]

NLR reflects the balance between innate (neutrophil, granulocyte) and adaptive (lymphocyte) immune response as neutrophil elevation and lymphocyte depletion indicates physiological stress. [16,17] Neutrophil to Lymphocyte ratio, calculated by absolute neutrophil count divided by absolute lymphocyte count is increasingly recognised as a readily available inexpensive biomarker for systemic inflammation. [18]

Recently, the NLR has been studied and found to be valuable in predicting the outcomes or prognosis of many diseases such as oncological diseases, inflammatory and infectious diseases. [19,20,21,22] An NLR <5 has been considered normal in the preoperative setting. An NLR of >5 was shown to have a high prognostic accuracy for predicting physiological stress and bacteraemia. [23]

However, the predictive value of preoperative NLR for predicting surgical site infection in the postoperative days in cases that underwent open reduction internal fixation of long bone fractures is not yet reported. The study aims to determine the predictive value of preoperative NLR in postoperative wound healing.

Materials and Methods

Patients and Study Design: This study comprises of all the 70 cases, which underwent ORIF for long bone fractures which fulfilled inclusion and exclusion criteria in the department of Orthopaedics, Assam Medical College and Hospital, Dibrugarh in the study period of one year from July, 2021 to June, 2022. The study design was hospital based observational study. Considering 95% confidence interval with a relative precision of 10% and sensitivity of neutrophil lymphocyte ratio to be 84.6%, [24] the sample size is calculated to be 70. The sample size was calculated using sample size calculation formula. The inclusion criteria includes age limit: 20-60 years, TLC, platelet count and albumin within normal limit, patient who underwent ORIF for their long bone fractures within 10 days of trauma and operative time less than 2hrs. Exclusion criteria includes of re-fractures, open fractures, poly-trauma cases, pathological fractures, patients with DM, any haematological disease, any infectious or inflammatory disease in any part of body. The operative procedures were performed following standard protocols, principles and approaches. The study has been approved by institutional ethics committee of Assam Medical College, Dibrugarh on 7th June 2021. An informed consent was taken from all the patient underwent study. [25,26,27]

The patients who are planned for ORIF for their long bone fractures that fulfilled the inclusion and exclusion criteria, their preoperative absolute neutrophil count and absolute lymphocyte count was estimated in Sysmex XN 550 machine. The NLR is calculated as a ratio between absolute neutrophil count to absolute lymphocyte count. Following operative intervention, post-operative wound were examined at the time of suture removal and if any soakage of dressing present. The wound sites were examined clinically for signs of surgical site infection according to the CDC Criteria for surgical site infection. All the postoperative cases were followed for duration of 1 year to document any episode late onset SSI. Whenever SSI was found swab was taken and sent for culture and sensitivity to identify organism causing it. Moreover, variables were collected as follows with aim to explore risk factors for SSI following ORIF in long bone fractures: demographic factors, fractured bone, limb involved, preoperative NLR levels, time interval from trauma to operation, duration of surgery, bone grafting done or not, type of implant used, incidence of SSI, depth of SSI, organism isolated on culture.

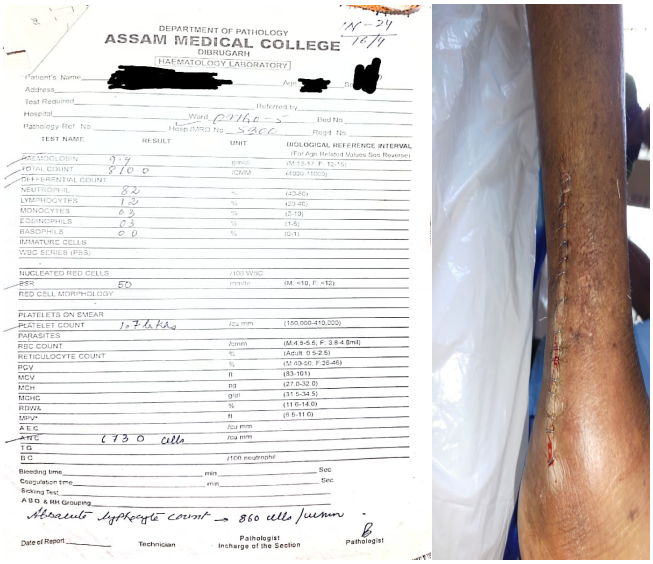
Statistical Analyses: The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for Windows, version 20.0. Chicago, SPSS Inc.) And Microsoft Excel 2010. Discrete data are expressed as number (%) and are analyzed using Chi square test and Fischer's exact test (where the cell counts were <5 or 0). Odds ratios were used to measure any association between groups. Sensitivity, specificity, positive and negative predictive values along with diagnostic accuracy was determined. For all analyses, the statistical significance was fixed at 5% level (p value<0.05).

Results

Among 70 patients identified as eligible following inclusion and exclusion criteria, 50 were male and 20 were female. The average age was 39.37 years and range was 20 to 60 years. The radius fracture (n=15) was the most common bone operated by ORIF in the study. The study included 33 upper limb and 37 lower limb cases. The mean and standard deviation of absolute neutrophil count and absolute eosinophil count was 4227.14±1348.30 and 1451.29±276.93 respectively. The NLR of >5 was shown to have high prognostic accuracy for predicting physiological stress and bacteremia, hence NLR value of 5 fixed as cut-off. Following NLR

screening in the preoperative phase out of total 70 cases 10 cases were found to have NLR value >5. All the cases were closely monitored during operative intervention and post-operative period to monitor wound healing. The average time interval from injury to operation was 4.66± 1.61 days. The average duration of operative intervention was 69.21± 15.96 minutes. The cases who took operating time >2hrs were excluded. Bone grafting was involved in 9 out of 70 cases. Out of 70 cases underwent ORIF 81.43% cases were plating and 18.57% cases were nailing.

In the postoperative follow up 8 cases out of 70 presented with SSI according to latest CDC guidelines. 7 cases were superficial SSI and 1 case of deep SSI reported in post-operative case of proximal femur fracture that underwent debridement operative intervention eventually. Out of 8 cases of SSI 7 cases shown positive growth on culture and most common organism isolated was Staphylococcus aureus (n=5) followed by Klebsiella (n=2). 7 out of 8 cases of SSI were males. All SSI cases were lower limb cases. Distal tibia followed by distal femur shown most number of SSI following ORIF. The odds ratio of bone grafting with SSI in the study found to be 2.619 indicates relation between bone grafting and SSI. ORIF with nailing (3/13) has shown increased number of SSI than ORIF with plating (5/57). On analysing relation between NLR and SSI, it was found that there were 8 cases of surgical site infection in a total of 70 cases which didn't had any risk factors for SSI during pre-operative work up. Out of 8 cases 5 cases were in risk category following NLR screening (≥5.01) in preoperative period. The odds ratio for NLR with surgical site infection was found to be 19 and P value found to be <0.001(significant). So we were able to screen a good amount of cases in preoperative period itself which can have surgical site infection in the postoperative period with sensitivity (62.5%), specificity (92.8%), positive predictive value (50%) and negative predictive value (95.5%). So NLR can be used as a screening tool for physiological stress which can result it postoperative complications like surgical site infections.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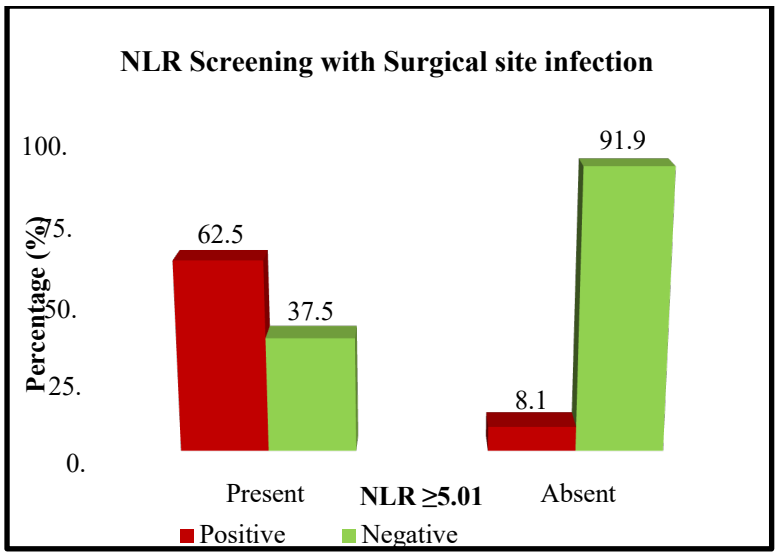
Absent lymphocyte count → 860 cells/cumm

Image (left) given above is a case under study shows preoperative blood investigation report of patient planned for ORIF with plating of distal tibia shows ANC & ALC, by formula NLR is 7.82. On right side image shows wound dehiscence and serous discharge from post op wound site

NLR ≥5.01	Surgical Site Infection				*p value*	*ODDs Ratio (95% CI)*
	Present		Absent			
	n	*%*	*N*	*%*		
Positive	5	62.50	5	8.10	<0.001	19.000 (3.477–103.836)
Negative	3	37.50	57	91.90		
TOTAL	**8**	**100.00**	**62**	**100.00**		



Bar diagram showing NLR screening with surgical site infection.

Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
62.50	92.80	50.00	95.5	88.57

Discussion

As the above results shown NLR can be used as an effective, economical and rapid inflammatory blood marker which can be estimated in the pre-operative phase itself to categories and plan the better care for preventing SSI. There are various similar studies done by authors in predicting SSI but cut off value varies in between them. Some similar studies have been given below and results are compared with our study.

Author, year of study	Study on	Results
M. Mundama et al (2020)[25]	NLR distribution shows an advantage compared to CRP for the early inflammation monitoring after total hip arthroplasty	NLR cut off was >5 predicted inflammation of post op site with sensitivity (63%) and specificity (77.2%).
Hiroyuki Inose et al (2020)[26]	Postoperative lymphocyte percentage and neutrophil lymphocyte ratio are useful markers for early prediction of surgical site infection in spine decompression surgery	NLR cut off was >4.71 predicted SSI with sensitivity (66.7%) and specificity (81.7%).
Yeye Zhuo et al (2021)[27]	Pre-surgical peripheral blood inflammation markers predict surgical site infection following mesh repair of groin hernia	NLR cut off was >4, predicted SSI with sensitivity (70.35%) and specificity (97.44%).
Our study	Pre-surgical Neutrophil-Lymphocyte ratio predicts surgical site infection following open reduction internal fixation in long bone fractures.	NLR cut off was >5, predicted SSI with sensitivity (62.5%) and specificity (91.94%).

This may be due to the fact that an increase in NLR following acute physiological stress confirms NLR as a marker of physiological stress and systemic inflammation much earlier than other parameters (eg WBC count, CRP). An isolated increase in neutrophil count and consequently, an elevated NLR, can be due to tissue damage during episode of trauma that activates SIRS. The SIRS is associated with suppression of neutrophil apoptosis, which affects the neutrophil mediated killing as a part of innate response during the second hit through an operative intervention. [28] Lymphocytes (B cells, T cells, CD4 cells, CD8 cells) are responsible for antigen specific response of adaptive immunity regulated by major histocompatibility complex (MHC). Lymphocytes activity is involved is host response to trauma, infection and SIRS. Raised NLR will weaken the immune balance. [29]

The study protocol was made in such a way that should eliminate all the cases of possible infection in any part of the body, so as to get a healthy cohort for the study. This has been done by excluding patients with history of inflammatory/infectious disease, a thorough clinical examination to look for any infective foci and evaluating TLC count. The limitation of the study was lower limb surgeries and bone grafting has been found as independent risk factors for SSI, so if it could have added in the exclusion on inclusion criteria.

Conclusion

Pre-surgical higher NLR was significantly associated with occurrence of SSI following ORIF of long bone fractures. NLR screening can be used as an effective and economical screening tool along with routine preoperative investigations to screen out cases which are prone to develop SSI following operative intervention. The role of preoperative NLR is a novel finding and warrants further exploration as they appeared to be objective, cheap, convenient biomarkers for early prediction of surgical site infection following ORIF of long bone fractures. SSI causes major drainage of resource and effort. Hence innovative steps need to be taken to limit it for the benefit of both patient and doctor. There is always need for effective screening tools and protocols to be formed to limit SSI.

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