ORIGINAL ARTICLE

RATIO OF NEUTROPHIL TO LYMPHOCYTE COUNT AS A PREDICTOR OF LENGTH OF HOSPITAL STAY IN ACUTE CHOLECYSTITIS

Munira Murtaza Khomusi, Sughra Perveen, Mazhar Iqbal, Tanweer Ahmed, Uzma Shamim Seth, Jehangir Ali

Jinnah Postgraduate Medical Centre, Karachi Pakistan

ABSTRACT

Background: The objective was to find out the ratio of neutrophil to lymphocyte count as a predictor of length of hospital stay in acute cholecystitis.

Material and Methods: This was a cross sectional observational study conducted in Ward-3 Jinnah Postgraduate Medical Centre, Karachi from November 2020 to April 2021. All patients between thirty to fifty years of age diagnosed as acute cholecystitis on basis of history, clinical examination and ultrasound abdomen were included. All Patients were treated with intravenous fluids, antibiotics and analgesics. Patients were discharged when pulse rate returned to normal and temperature and tenderness disappeared. They were advised interval cholecystectomy after six weeks. Hospital stay was recorded in days for patients with deranged neutrophil to lymphocyte ratio of greater than three. Length of stay for patients with normal ratio, lesser than three was also recorded. Age, gender, history, tenderness, differential leucocyte count and length of hospital stay were also recorded on preprinted forms. Results were analyzed by SPSS Version 25.

Results: A total of ninety patients were included, ten being male (11.11%) and eighty female (88.88%). Patients with deranged ratios were sixty-five (72.22%) and normal ratios were twenty-five (27.77%). The length of hospital stay was recorded as five to eight days for deranged ratio and three to five days for normal ratio respectively. Ten patients (11.11%) had gangrenous gall bladder and underwent open cholecystectomy.

Conclusion: Neutrophil to lymphocyte ratio of greater than three corresponds to longer hospital stay and complications.

Keywords: Cholecystitis, Length of stay, Neutrophil -to-lymphocyte ratio

BACKGROUND

Acute cholecystitis is diagnosed on basis of findings in history and clinical examination. Typical clinical features include pain in right hypochondrium radiating to back, tachycardia and tenderness in right hypochondrium. Diagnosis is confirmed on ultrasonography findings of thickened gall bladder wall and pericholecystic fluid. Increase in neutrophil to lymphocyte ratio of greater than three is diagnostic for acute cholecystitis.[1] It is also associated with prolonged stay in hospital.[2] Neutrophil to lymphocyte ratio was calculated. A ratio greater than three was easily calculated and it was derived from regular complete blood count. If it was greater than three then hospital stay was prolonged as it was severe cholecystitis.[3] In acute cholecystitis, inflammation of gall bladder causes increased release of arachidonic acid metabolites and platelet activating factors therefore, neutrophil count increases. Cortisol is released due to stress causing relative lymphopenia.[4] Increased neutrophil to lymphocyte ratio greater than three was associated with severe cholecystitis, increased operating time and hospital stay. Increased leukocyte counts were not associated with increased neutrophil to lymphocyte ratio greater than three in a statistically significant manner. Increased neutrophil to lymphocyte ratio greater than three causes severe cholecystitis therefore, presenting a more difficult operative scenario. In patients of acute cholecystitis, neutrophil to lymphocyte ratio greater than three are at higher risk of severe cholecystitis. Patients with neutrophil to lymphocyte ratio lesser than three are at lower risk for severity.[5]

In acute cholecystitis male patients with age greater than sixty years, the diagnostic accuracy of neutrophil to lymphocyte ratio greater than three increases. However, in female patients as age increases the diagnostic accuracy of neutrophil to lymphocyte ratio greater than

Correspondence: Dr Munira Murtaza Khomusi, Department of Surgery, Jinnah Postgraduate Medical Centre, Karachi Pakistan

Email: mmkhomusi@gmail.com

This article can be sited as: Khomusi MM, Perveen S, Iqbal M, Ahmed T, Seth US, Ali J. Ratio of neutrophil to lymphocyte count as a predictor of length of hospital stay in acute cholecystitis. Infect Dis J Pak 2022; 33(3): 78-82.

three falls. It is therefore seen that neutrophil to lymphocyte ratio of greater than three has better predictivity for severity in females (greater than eighty percent) than in males (lesser than eighty percent).[6] Findings on computed tomography scan abdomen of peri cholecystic fat stranding and peri cholecystic fluid collection are associated with severity in acute cholecystitis. So computed tomography abdomen and neutrophil to lymphocyte ratio greater than three will be helpful in predicting severe acute cholecystitis. But computed tomography scan is costly and is not available in every center. It also has radiation hazards. On the contrary, leukocyte count can be carried out anywhere and is inexpensive. Therefore, the best predictor of severity is neutrophil to lymphocyte ratio greater than three.[7]

The rationale of this study was to know the severity of acute cholecystitis at the time of presentation and to predict the length of stay so as to effectively treat patients. Patients can then be informed about their recovery period and discharge. In this study we can predict the duration of hospital stay which affects the whole family of patients. Cholelithiasis is common in females and they usually manage their households. If we predict this duration, they can resume their domestic responsibilities accordingly. When patient is admitted in our setup the earning of other family members is also affected as they usually stay to look after the patient. So, predicting the exact stay by neutrophil to lymphocyte ratio greater than three will help us counsel the patient accordingly. So, this study will contribute to the medical community, by predicting the length of stay by calculating neutrophil to lymphocyte ratio at admission. The objective of this study was to find out the length of hospital stay according to neutrophil to lymphocyte ratio of greater than three calculated at admission for acute cholecystitis patients.

MATERIAL AND METHODS

This study was conducted in Ward-3 Jinnah Postgraduate Medical Centre Karachi from November 2020 to April 2021. After approval was taken from Ethical Review Board NO.F.2-81/2020-GENL/51224/JPMC, dated 21 October, 2019, data collection was commenced. Ninety patients of acute cholecystitis between thirty to fifty years of age both females and males were included

This was a cross sectional observational study. Patients of acute cholecystitis were diagnosed on history, clinical examination and ultrasonography. Patients typically presented with history of pain in right hypochondrium radiating to back. Most of the patients also complained of vomiting. On examination vital signs were recorded. Tenderness in right hypochondrium was considered a diagnostic sign for acute cholecystitis. Abdominal ultrasonography was performed on all patients and stones in gall bladder and peri cholecystic fluid were considered as acute cholecystitis.

Liver function tests, urea, creatinine, electrolytes, random blood sugar, serum amylase and lipase were carried out on admission. Hepatitis B surface antigen and anti-hepatitis C virus antibodies were also done. Patients with raised alkaline phosphatase or dilated common bile duct on ultrasound underwent magnetic resonance cholangiopancreatography. Intravenous line was maintained and fluids given including five percent Dextrose water given twice daily. Injection Cefuroxime 750 mg which was available in ward was given intravenously twice daily. Intravenous analgesics and anti-emetics were also given. Patient's complete blood count was done, deranged neutrophil and lymphocyte count was noted. These were also recorded for patients with normal counts. Patients were admitted in ward and treated. Daily examinations of patients were done and pulse rate and tenderness were recorded. When signs and symptoms like pulse rate became normal, tenderness disappeared and vomiting subsided, patients were discharged. On discharge patients were advised interval cholecystectomy after six weeks. Duration of stay in patients with deranged neutrophil to lymphocyte ratio of greater than three was compared to those with normal neutrophil to lymphocyte ratio of lesser than three. Patients with co-morbids diabetes mellitus, hypertension were excluded. Also, patients with acute pancreatitis, and acute hepatitis were excluded from the study. Patients with empyema, rupture of gall bladder and obstructive jaundice were also excluded. Results were analyzed with SPSS version 25. Patients' neutrophil to lymphocyte ratio of greater than three was calculated as absolute neutrophil count divided by absolute lymphocyte count. We considered three as cut off value; we divided the patients into two groups. Those with neutrophil to lymphocyte ratio of greater than three were considered as deranged and neutrophil

to lymphocyte ratio of less than three were considered as normal. Length of stay in hospital was recorded for both groups.

RESULTS

Total 90 patients were included 10 were male (11.11%), 80 were female (88.88%) between 30 to 50 years of age. Average age was 39 ±9 years. Patients with deranged neutrophil to lymphocyte ratio greater than three were 65/90(72.22%) and normal neutrophil to lymphocyte ratio greater than three were 25/90 (27.77%). Table-1 shows the length of hospital stay of patients with acute cholecystitis 10 patients out of 90(11.11%) developed gangrenous gall bladder, so open cholecystectomy was done and length of hospital stay was 8-10 days.

Table-1: The length of hospital stay in acute cholecystitis patients.

NLR	Total patients	LOS
Deranged(>3.0)	65/90(72.22%)	5-8 days
Normal (<3.0)	25/90(27.77%)	3-5 days

NLR: neutrophil to lymphocyte ratio; LOS: length of hospital stay

DISCUSSION

In patients with severe cholecystitis there are increased levels of proinflammatory cytokines and elevated neutrophil to lymphocyte ratio of greater than three causing increased length of stay, operating times and difficult operative scenario. It is suggested that increased neutrophil to lymphocyte ratio of greater than three may be associated with severe cholecystitis and increased length of stay in hospital following cholecystectomy. The cut off value of neutrophil to lymphocyte ratio of greater than five in acute cholecystitis patients is an appropriate predictor of severity and increased length of stay in hospital; however, in our study cut off value of greater than three was predictive of severe cholecystitis.

Severe cholecystitis can rarely lead to gangrenous gall bladder. It can also cause perforation of gall bladder. It can lead to empyema of gall bladder that will increase the hospital stay. Complications like these are medical emergencies. Gangrene occurs due to impaired gall bladder wall perfusion because of increased pressure within the gall bladder wall, also associated with obstruction of cystic duct. It occurs in approximately thirty percent of patients with severe cholecystitis.[9] In this study gall bladder of patients whose neutrophil to lymphocyte ratio was greater than three were perforated, which was ten out of ninety (eleven percent). Most probably we treated patients earlier, therefore complications were decreased.

The following factors determined increased severity in acute cholecystitis patients including gender, age, body mass index (BMI), ASA Score, recurrent colic, thickness of gall bladder wall, white blood cell count and C-reactive protein value. Patients with increased severity had increased operating time, Intensive care unit (ICU) requirement and longer length of stay.[10] We evaluated among these gender and white blood cell count along with neutrophil to lymphocyte ratio greater than three. C-reactive protein levels are used as diagnostic criteria for acute cholecystitis. It has been established that increased C-reactive protein levels are associated with increased severity of acute cholecystitis as it reflects severity of inflammation.[11] In this study we evaluated neutrophil to lymphocyte ratio greater than three which is also an inflammatory biomarker and correlates well with severity. C-reactive protein is usually not available in all laboratories; differential leukocyte count is easily available and cheap to conduct as compared to C-reactive protein which is used as an inflammatory marker predictive of advanced acute cholecystitis and conversion to open surgery.[12] In this study, patients with neutrophil to lymphocyte ratio greater than three had advanced acute cholecystitis and underwent open surgery that is ten out of ninety patients. Plasma procalcitonin levels have also been used as a predictor of severity in acute cholecystitis. Increased procalcitonin levels in patients correlates with increased severity of acute cholecystitis.[13] But conducting this investigation is not feasible and is costly. However, neutrophil to lymphocyte ratio greater than three is easy to calculate and is not costly for the patient. Other studies showed that inflammation based prognostic scores, neutrophil to lymphocyte ratio of greater than three and C-reactive protein to albumin ratio can all predict severity of disease in patients with acute cholecystitis. Therefore, severe acute cholecystitis leads to increased length of stay in hospital.[14] Lactate levels conducted at admission in gangrenous gall bladder causes increased length of stay in hospital.[15] Another study showed that physical examination, neutrophil to lymphocyte ratio greater than three and C-reactive

protein are associated with severity of acute cholecystitis.[16] So our study has similar result as above-mentioned study.

Another study conducted in Serbia shows neutrophil to lymphocyte ratio greater than 4.18 is associated with severe cholecystitis. Therefore, in such patients there are more peri operative complications.[17] But in this study neutrophil to lymphocyte ratio greater than 4.18 was associated with increased length of stay; however, we observed neutrophil to lymphocyte ratio of greater than three had severe cholecystitis with increased length of stay in hospital.

Ultrasonography of abdomen used to detect presence of acute cholecystitis e.g. gall bladder wall edema [18]. In this study, ultrasonography conducted showed similar findings of peri cholecystic fluid and gall bladder wall edema.

In a study conducted in Khost, Afghanistan gall bladder inflammation is more common in females [19]. A similar incidence was seen in this study with female preponderance in patients of acute cholecystitis.

Neutrophil to lymphocyte ratio greater than five is an inflammatory biomarker for acute cholecystitis as it is inexpensive and is easily calculated.[20] Similarly, in our setup neutrophil to lymphocyte ratio greater than three was easily obtained from white blood cell count and was cheap to conduct. In this study, patients with neutrophil to lymphocyte ratio of less than three recovered earlier and their hospital stay was shorter.

Limitation of this study was that we excluded the acute pancreatitis patients associated with acute cholecystitis, which could affect the results.

CONCLUSION

It was concluded that if neutrophil to lymphocyte ratio was greater than three then cholecystitis would be severe, causing longer length of stay in hospital and increased complications.

AUTHOR CONTRIBUTION

Munira Murtaza Khomusi: Conception, the acquisition, analysis, interpretation of data and manuscript writing

Sughra Perveen: Conception, Analysis and interpretation of data

Mazhar Iqbal: Revised critically for important intellectual content

Tanweer Ahmed: Analysis and review

Uzma Shamim Seth: Data collection and analysis

Jehangir Ali: Data collection and analysis

REFERENCES:

1. Beliaev AM, Angelo N, Booth M, Bergin C. Evaluation of neutrophil-to-lymphocyte ratio as a potential biomarker for acute cholecystitis. J Surg Res 2017; 209: 93–101. DOI: 10.1016/j.jss.2016.09.034
2. Patel K, Wagstaff A, Mirza S. PWE-076 Ratio of neutrophil to lymphocyte count as a predictor of length of stay in acute cholecystitis. Gut 2015; 64(Suppl 1): A245.2-A246.
3. Ay S, Tanrikulu CS. Diagnostic utility of neutrophil lymphocyte ratio in acute complicated cholecystitis. Ann Med Res 2019; 26(2): 135-8. DOI: 10.5455/annalsmedres.2018.09.198
4. Hareen TVKK, Bhaskaran A, Jaswanthi AR. Neutrophil to lymphocyte ratio in diagnosing acute cholecystitis: a retrospective cohort study in a tertiary rural hospital. Int Surg J 2016;4(1):372-76. DOI: doi.org/10.18203/2349-2902.isj20164472
5. Meena L, Saxena DM. Neutrophil to lymphocyte ratio: A new marker for early insight into severity of cholecystitis: an observational study. J Dent Sci 2018; 17(1): 48-51. DOI: 10.9790/0853-1701094851
6. Latif AM, Muhammad N, Hassan N, Farooq U. Role of neutrophil-to-lymphocyte ratio in diagnosis of cholecystitis. Pak J Med Health Sci. 2019; 13(4): 989–91.
7. Woo SH, Lee WJ, Seol SH, Kim DH, Choi SP. The accuracies of abdominal computed tomography and the neutrophil-to-lymphocyte ratio used to predict the development of clinically severe acute cholecystitis in elderly patients visiting an emergency department. Niger J Clin Pract 2018; 21(5): 645–52. DOI: 10.4103/njcp.njcp_76_17
8. Ahmed SE, Rehman S, Edilbe M, Jonker L, Canelo R. Can neutrophil–lymphocyte ratio predict operators' difficulty in early cholecystectomies; A retrospective cohort study. Ann Emerg Surg 2017; 2(3): 1016.
9. Raffee L, Kuleib S, Oteir A, Kewan T, Alawneh K, Beovich B, et al. Utility of leucocytes, inflammatory markers and pancreatic enzymes as indicators of gangrenous cholecystitis. Postgrad Med J. 2020; 96(1133): 134–38.
10. Er S, Ozden S, Celik C, Yuksel BC. Can we predict severity of acute cholecystitis at admission? Pak J Med Sci 2018; 34(5): 1293-6. DOI: 10.12669/pjms.345.14502
11. Ahmad B, Muhammad A, Sattar N. Psychiatric comorbidities in patients with headache disorders in Pakistani and Afghani population: A retrospective review of clinical data. J Med Sci 2017; 25(4): 452-456.
12. Bouassida M, Zribi S, Krimi B, Laamiri G, Mroua B, Slama H, et al. C-reactive protein is the best biomarker to predict advanced acute cholecystitis and conversion to open surgery. A prospective cohort study of 556 cases. J Gastrointest Surg 2020; 24(12): 2766–72. DOI: 10.1007/s11605-019-04459-8
13. Sakalar S, Ozakın E, Cevik AA, Acar N, Dogan S, Kaya FB, et al. Plasma procalcitonin is useful for predicting the

severity of acute cholecystitis. Emerg Med Int 2020; 2020: 8329310. DOI: 10.1155/2020/8329310

14. Sato N, Kinoshita A, Imai N, Akasu T, Yokota T, Iwaku A, et al. Inflammation-based prognostic scores predict disease severity in patients with acute cholecystitis. Eur J Gastroenterol Hepatol. 2018;30(4):484–89. DOI: 10.1097/MEG.0000000000001063
15. Díez Ares JÁ, Martínez García R, Estellés Vidagany N, Peris Tomás N, Planells Roig M, et al. Can inflammatory biomarkers help in the diagnosis and prognosis of gangrenous acute cholecystitis? A prospective study. Rev Esp Enferm Dig 2021; 113(1): 41-44. DOI: 10.17235/reed.2020.7282/2020
16. Ozdenkaya Y. An evaluation of the reliability of the neutrophil-lymphocyte ratio in patients with acute cholecystitis undergoing laparoscopic surgery. Laparosc Endosc Surg Sci 2019; 26 (2): 68-72. DOI: dx.doi.org/10.14744/less.2019.93275
17. Micić D, Stanković S, Lalić N, Đukić V, Polovina S. Prognostic value of preoperative neutrophil-to-lymphocyte ratio for prediction of severe cholecystitis. J Med Biochem 2018; 37(2): 121–27. DOI: 10.1515/jomb-2017-0063
18. Shekarchi B, Hejripour Rafsanjani SZ, Shekar Riz Fomani N, Chahardoli M. Emergency department bedside ultrasonography for diagnosis of acute cholecystitis; A diagnostic accuracy study. Emerg (Tehran). 2018; 6(1):e11.
19. Janatzai K, Seddiqi MR. Causes and treatment of acute cholecystitis in khost teaching hospital in age group of 30-80Y during one year of 2019. J Appl Pharm Sci Res 2020; 13–6. DOI: doi.org/10.31069/japsr.v3i2.3
20. Bedel C. Can we use neutrophil lymphocyte ratio and platelet lymphocyte ratio as a potential biomarker for acute cholecystitis? Ortadoğu Tıp Derg 2019; 11(4): 404–8. DOI doi.org/10.21601/ortadogutipdergisi.505193