ORIGINAL ARTICLE

CRP AS AN INDICATOR OF SEVERITY OF ACUTE CHOLECYSTITS

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ABSTRACT

Objectives: To determine the role of CRP in predicting severity of acute cholecystitis.

Material and Methods: This is a retrospective cross sectional study conducted at department of surgery and Pathology, Khyber teaching hospital, Peshawar between April, 2016 and April, 2017.This study included a total of 150 patients divided into three equal groups(mild, moderate and severe) on the basis of Tokyo acute cholecystitis severity guidelines. Each patient had his serum CRP quantified. Data was analyzed by using SPSS version 16. Means ± SD were measured for CRP in each group. Furthermore, means of CRP were compared amongst the three groups by using One-way ANOVA. ROC test was done to check the specificity and sensitivity of CRP.

Results: Mean age of all the participants was 39 ± 3.94 years. Female population made 66.66 %(n=100) of the study sample while 33.33% (n=50) were males. Mean CRP values were, 24±3.14, 40±4.15 and 52±1.34 in the mild, moderate and severe acute cholecystitis groups respectively. One-way ANOVA showed a statistically significant difference between the three groups, P<0.05. Moreover ROC analysis confirmed that at a CRP value of less than 18mg/dl,has a sensitivity and specificity of 76 and 84% respectively and excluding moderate to severe cholecystits.

Consclusion: CRP is a marker of severity of acute cholecystitis and can truly differentiate between different grades of acute cholecystitis.

Key Words: CRP, acute cholecystits, cholilithiasis, biliary colic.

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INTRODUCTION

Cholecystitis is inflammation of the gallbladder[1]. There was no consensus over diagnosis and assessment of acute cholecystitis before the Tokyo guidelines. Management strategy of acute cholecystitis was introduced for effective dissemination of the guidelines in the world[2,3]. Tokyo guidelines are recommended for the diagnosis of acute cholecystitis since it standardizes the treatment according to the severity of the disease[4,5]. According to these guidelines, acute cholecystitis is diagnosed on the basis of physical examination findings, laboratory results such as C-reactive protein (CRP) and white blood cell levels, as well as radiologic assessment. After the diagnosis, the severity of the disease is graded from grade 1 to 3 based on Tokyo guidelines, which considers patient's history (duration of symptoms), physical examination, laboratory tests, and imaging methods[4,5]. CRP level is only used as a diagnostic criterion of acute cholecystitis, and it is not part of the determinant criteria of the severity assessment of the disease in the guideline. On the other hand, correlation between CRP levels and severity of acute cholecystitis is a well-known fact, and several studies have reported that CRP level is a reliable predictor of severe conditions of the inflammation in acute cholecystitis[6-13]. But a cut-off level of CRP that reveals the grade of the disease has not been proposed so far in our setup.

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MATERIAL AND METHODS

This retrospective cross sectional study conducted at Department of Surgery and Pathology of Khyber

Teaching Hospital, Peshawar between April 2016 to April 2017. This study included a total of 150 patients divided into three equal groups (mild, moderate and severe) on the basis of Tokyo acute cholecystitis severity guidelines. This study was approved by the hospital's ethics review committee. An informed written consent was obtained from every participant before inclusion in the study.

The inclusion criteria included A: Age 18 to 70 years, B: both genders, C: clinicoradiologically and/ or surgically confirmed cases of acute cholecystitis of any etiology. All the patients not fulfilling the above mentioned criteria were excluded. Similarly those with medical conditions likely to affect blood CRP levels were excluded. These included autoimmune diseases like lupus, rheumatoid arthritis , scleroderma etc , auto-immune liver disease, vasculitides and atherosclerotic heart or brain disease .Similarly surgical illnesses like appendicitis, pancreatitis .diverticulitis, renal colic and cholangitis were excluded ,moreover female patients suspected or confirmed adnexal pathology or pelvic inflammatory disease were excluded. Lastly those who were on immunosuppressive therapy or had recently received oral or intravenous steroids were excluded from the study.

A structured questionnaire including demographic data, clinical features, duration of disease, baseline liver and renal functions, findings on imaging studies and blood CRP level was used. Initially 333 patients were assessed however only 150 of them fulfilled the strict inclusion exclusion criteria and were subject of final study. These 150 participants were recruited in such a way that each of the three study groups received equal number of patients . Each patient had his serum CRP quantified. Data was analyzed by using SPSS version 16. Means ± SD were measured for CRP in each group. Furthermore means of CRP were compared amongst the three groups by using One-way ANOVA. ROC test was done to check the specificity and sensitivity of CRP.

RESULTS

Mean age of all the participants was 39 ± 3.94 years. Female population made 66.66 %(n=100) of the study sample while 33.33% (n=50) were males. Group specific demographic details are as shown (Table 1). The predominant clinical feature was right hypochondrial pain and nausea seen in 85% (n=127) of the patients. More details of the clinical characteristics and baseline laboratory work are given below (Table 2 & 3). All the patients had ultrasound performed 67% (n=45) patients had demonstrable right hypochondrial probe tenderness, moreover 79% (n=53) of the participants had gall bladder edema while biliary sludge was demonstrated in 85.7%(n=57) of the patients.

Table 1:

Demographic Variable	Mild n=50	Moderate n=50	Severe n=50
Male	20%	26%	34%
Female	80%	74%	66%
Married	66%	80%	96%
Unmarried	34%	20%	4%
Pakistani	94%	80%	76%
Afghani	6%	20%	24%

Table 2:

Clinical Features	Mild n=50 Grade 1	Moderate n=50 Grade 2	Severe n=50
Grade 3	20%	26%	34%
RHC Pain	70%	90%	95%
Nausea and vomiting	80%	87%	90%
Fever	60%	80%	92%
Tendor RUQ	60%	82%	94%
Duration of disease > 1 month	40%	72%	88%
Miscellaneous	56%	80%	84%

Table 3:

Laboratory	Mild	Moderate	Severe
CRP(mg/dl)	24	40	52
TLC(/mm3)	5000	10000	13000
Platelets(/mm3)	170,000	200000	190000
HB(g/dl)	14	14.7	13.9
SGPT(IU/L)	40	45	57
ALKaline phosphatase (IU/L)	120	135	149
Bilirubin(mg/dl)	0.8	1	1.3
Urea (mg/dl)	35	49	65
Creatinine (mg/dl)	0.7	1	1.2
Amylase mg/dl	75	95	135

Finally mean values of CRP was measured in each group. Mean CRP values were, 24±3.14, 40±4.15 and 52±1.34 in the mild, moderate and severe acute cholecystitis groups respectively. As mean CRP was numerically higher in the severe group (52±1.34) ,intermediate in the moderate group(, 40±4.15) and the lowest in patients with mild cholecystits (24±3.14), One-way ANOVA was applied to compare the difference

in means of the three study groups considering p value of <0.05 as significant. The assumption of normality was satisfied, Shapiro statistics p<0.05. The results of One-way ANOVA demonstrated a statistically significant difference between the three groups, P<0.05. Thus there is enough evidence of a positive relationship between the severity of acute cholecystitis and blood CRP. Moreover in order to check the specificity and sensitivity of CRP ROC analysis was used. The results showed that at a cutoff value of less than 18mg/dl, CRP has a sensitivity and specificity of 76 and 84% respectively and excluding moderate to severe cholecystitis.

DISCUSSION

Our study demonstrated that the majority of patients with acute cholecystitis were in their fourth decade of life. Moreover, acute cholecystitis was more common and severe in female as compared to male patients. Most of the participants were of Pakistani origin, furthermore, acute cholecystitis was more commonly encountered in married individuals than otherwise. The predominant clinical features in such patients were right hypochondrial pain followed by nausea and vomiting. Finally the CRP was found to correlate with the severity of acute cholecystitis as it was the highest, intermediate and the lowest in patients with severe, moderate and mild cholecystitis respectively.

In our study there was a female to male preponderance 2:1 in patients with acute cholecystits. This is contrary to the study done by Huang J et all14 in which there is a male preponderance in patients with acute cholecystits while cholilithiasis is more common in female gender.

Acute cholecystits can present in a variety of ways however in our study right hypochondrial pain and nausea are the predominant features seen in 85% of patients. Other clinical features are shown in Table 2. Same features are also seen in other studies.[4,19,20]

Apart from clinical suspicion imaging studies are usually required to exclude acute cholecystits[15-18]. In our study all the patients had ultrasound performed. The ultrasound showed that approximately 2/3rd patients had demonstrable right hypochondrial probe tenderness, while 3/4th of the participants had gall bladder edema while biliary sludge was demonstrated in a comparable number of patients.

According to Tokyo guidelines patients are classified as having mild, moderate or severe acute cholecystitis. On measuring CRP value for every participant in our study we observed that CRP was the lowest (24±3.14) in patients with mild acute cholecystitis, intermediate (40±4.15) in patients with moderate disease and highest(52±1.34) in patients with severe disease. Our study demonstrated that at a CRP value of less than 18mg/dl , moderate to severe acute cholecystitis can be excluded with a confidence of as high as 84%.

Despite its usefulness our study had a few limitations firstly the study design was cross sectional and retrospective. Secondly the sample size was relatively smaller. Thirdly not all the patients had histopathologically confirmed acute cholecystitis. Considering these limitations we would advocate future studies on the usefulness of CRP as an indicator of the severity of acute cholecystits and would recommend cohort prospective study design with a bigger sample size.

CONCLUSION

Acute cholecystitis is a common surgical problem in middle aged married women. It should be suspected in anyone with acute onset right hypochondrial pain, tenderness, nausea and vomiting. Moreover, a single CRP value on admission correlated well with the severity of acute cholecystits.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Tahir AA: Main idea and design.

Kamal S: Acquisition of data, final approval drafting of manuscript.

Sultana N: Data collection.

Khan A: Bibliography.

Khan MT: Proof reading.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.