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RED CELL DISTRIBUTION WIDTH TO DIFFERENTIATE ACUTE CHOLECYSTITIS FROM CHRONIC CHOLECYSTITIS

[1]Abdullah S. Alharbi, [2]Alhanouf A. Almusallam, [3]Rawan A. Alhoraibi, [4]Thawab A. Alkayyal, [5]Fareed A. Shah

[1,2,3] Medical intern, Faculty of medicine, Taibah university, Al-Madinah, Saudi Arabia., [4] Sixth year medical student, Faculty of medicine, Taibah university, Al-Madinah, Saudi Arabia., [5] Professor of General surgery FRCS, Glasgow, department of general surgery, College of medicine, Taibah University, Al-Madinah, Saudi Arabia

Abstract:

Background: *Morbidity and mortality related to cholecystitis and in particular, the acute forms are not negligible. The role of red cell distribution width (RCDW) in the diagnosis of inflammatory disease was shown by many authors, but studies about its predictive value to diagnose acute cholecystitis and differentiate it from the chronic cholecystitis are scarce.*

Objective: *The aim of this study was to determine the diagnostic accuracy of RCDW as promising diagnostic test to differentiate between acute cholecystitis and chronic cholecystitis.*

Methods: *A retrospective cohort study was performed at King Fahd Hospital, Al-Medina, Saudi Arabia by reviewing the medical case records of the patients. The study included patients from different age groups who underwent laparoscopic cholecystectomy from January 2016 to December 2017. Various preoperative, operative and post-operative data were recorded in a predesigned proforma. Values of RCDW and WBC counts were recorded and compared between acute and chronic cholecystitis patients.*

Results: *A total of 294 cholecystitis patients were included in this study; 56 (19.0%) had acute cholecystitis and 238 (81.0%) had chronic cholecystitis. There was no statistically significant difference between acute and chronic cholecystitis patients in terms of age, gender, BMI and lymphocyte count. The average level of RCDW was significantly different between acute cholecystitis group and chronic cholecystitis group. Receiver operating characteristic curve of RCDW value in diagnosing acute cholecystitis had an area under the curve of 0.706 ($p < .001$), and the best cut off was 14.15% with a sensitivity of 76.8% and specificity of 51.3%. For WBC count, AUC of the ROC curve was 0.870 with a sensitivity of 91.1% and specificity of 72.7% for a cutoff of 10.93 x 103/µL.* ***Conclusions:*** *RCDW had a satisfactory discriminative value in distinguishing acute cholecystitis from the chronic form. Nevertheless, it would preferable to associate it with WBC count to support the diagnostic approach.*

Keywords: *Acute cholecystitis, Chronic cholecystitis, Red cell distribution width.*

Corresponding author:

Abdullah S. Alharbi,

Medical intern, Faculty of medicine, Taibah university, Al-Madinah, Saudi Arabia. Email - Abdullah.lihebi@gmail.com.

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INTRODUCTION:

Acute cholecystitis is an acute inflammation of the gallbladder usually resulting from obstruction of the cystic duct by a gallstone. This obstruction causes a sudden distension of the vesicle and an increase of intra-vesicular pressure (hydrocholecyste) [1,2]. This results in inflammation and edema of the wall due to the toxic effect of bile acids and phospholipids [3,4]. The diagnosis of acute cholecystitis is based on the association of clinical signs (mainly an upper abdominal pain and tenderness) with perturbation of laboratory test results such as leukocytosis [5,6]. The simplest test to quickly confirm the diagnosis is an *abdominal* ultrasound which can show a thickening of the vesicular wall [7,8].

On the other hand, chronic cholecystitis is a continued active inflammation of the vesicular wall often associated with parietal fibrosis and retraction; it is assumed that this lesion is the result of an incomplete or intermittent obstruction of the cystic duct by one or more gallstones [9]. Chronic cholecystitis may be asymptomatic and diagnosed during cholecystectomy [10]. The most evocative feature is a chronic biliary pain, often less vigorous than in the usual form. The diagnosis is made by abdominal ultrasound, which can show irregularities of the vesicular wall. A particular case is the porcelain gallbladder, totally or partially calcified [11].

It is reported that 3%–10% of the emergency department patients with abdominal pain are diagnosed with acute cholecystitis [2,12], it accounts for 10–12% in European populations , whereas it is 3–4% in Asian populations [13]. In Saudi Arabia, a study conducted in a southwestern region showed that the prevalence of gallstone disease was 11.7% [14].

If not diagnosed on time, cholecystitis can evolve into the complicated forms; incidence of which ranges from 7.2% to 26% [15]. The practitioners have to confirm the diagnosis of an acute cholecystitis and make the differentiation between acute and chronic cholecystitis in order to proceed to the proper treatment and prevent the eventual morbidity and mortality resulting from a misdiagnosis of one or the other of the two diseases [16]. In fact the prevalence of mortality in acute cholecystitis can reach 10% [2,17-20].

Many authors studied the accuracy of imaging studies to distinguish between acute and chronic cholecystitis [21-23]. However, the cost of these imaging modalities may be a prohibitive factor; therefore, some authors tried some alternatives for it. A study conducted at the Turkish hospital studied the utility of red cell distribution width (RCDW) in the prediction of acute cholecystitis and found a significant difference in its mean level between the patients with acute and chronic cholecystitis. This laboratory test was also proven to be effective in the prediction of many inflammatory diseases [24-25]. To the best of our knowledge, no such study has been conducted in our country; therefore, we planned this study with an aim to determine the diagnostic accuracy of RCDW as a promising diagnostic test to differentiate between acute cholecystitis and chronic cholecystitis.

MATERIAL AND METHODS:

This retrospective cohort study was performed at Department of General Surgery, King Fahad Hospital, Al-Medina, Saudi Arabia by reviewing the medical case records of the patients who underwent laparoscopic cholecystectomy. Ethical approval was obtained from the scientific research ethics committee at King Fahad hospital prior implementing the study. All patients of all age groups and both sexes who underwent laparoscopic cholecystectomy from January 2016 to December 2017were included in the study. All patients diagnosed with cholangitis, choledocholithiasis, acute pancreatitis, malignancy, and a history of percutaneous or endoscopic biliary drainage prior to surgery were excluded from the study.

Medical records of all the eligible patients were retrieved from the medical record department of King Fahad Hospital. Data were extracted from their medical records and the variables included demographic information, physical findings, and blood test results as white blood cell (WBC) count, RCDW level, CRP level, ultrasound findings and histopathology report, which were done at the first day of admission. These parameters were compared between the patients with acute and chronic cholecystitis.

Statistical analysis

Gender was the only categorical variable and was presented as frequencies and percentages. Continuous variables were presented as the mean ± standard deviation. Comparison between continuous variables was done by independent samples t-test. Comparison between categorical variables was done by Chi-squared test. 95% confidence intervals and p-values were presented for all comparisons. Receiver operating characteristic curves of RCDW, WBC, and neutrophil count were presented. The analysis was performed in 95% confidence interval using Statistical Package for Social Science (SPSS), version 20 (IBM, Armonk, NY, USA).

RESULTS:

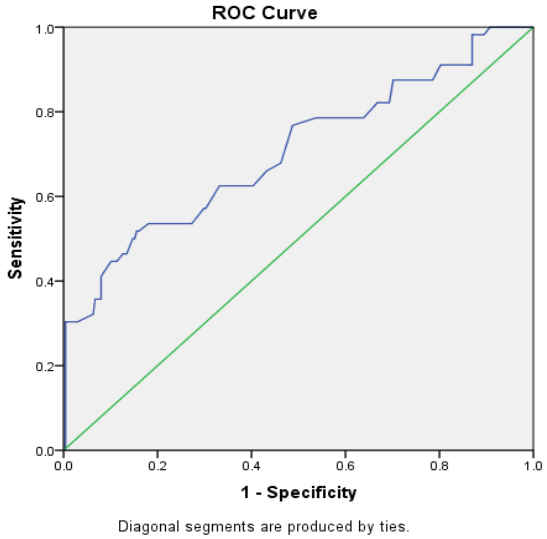
A total of 294 cholecystitis patients were included in this study and among them, 56 (19.0%) had acute cholecystitis and the other 238 (81.0%) had chronic cholecystitis. The mean age of acute vs. chronic cholecystitis patients was 39.89±14.35 years vs. 42.87±11.96 years. The mean BMI of acute cholecystitis patients was 27.21±5.19 kg/m^2 and of chronic cholecystitis patients were 26.98±5.37 kg/m^2. There was no statistically significant difference between acute and chronic cholecystitis patients in terms of age, gender, BMI and lymphocyte count. For acute cholecystitis, mean RCDW was 13.34±1.71% and for chronic cholecystitis group, it was 14.66±2.19% and RCDW was significantly different in two groups (95% CI - 0.710-1.943, p <0.001). The mean WBC count was also significantly different in acute and chronic cholecystitis (M = 14.16±2.92 X 10^9/L vs. 9.21±3.25 X 10^9/L, 95% CI - 5.879-4.015, p <0.001). Monocyte count was also significantly different in acute vs. chronic cholecystitis patients (M = 5.40 ± 2.93 vs. 6.93±5.07, 95% CI - 0.145-2.541, p= 0.031) (table/ figure 1).

Receiver operating characteristic (ROC) curve of RCDW showed that the best cutoff value in diagnosing acute cholecystitis was 14.15% with a sensitivity of 76.8% and specificity of 51.3% {area under curve (AUC): 0.706, SE: 0.043, p <0.001)} (table/ figure 2). ROC curve of WBC count in diagnosing acute cholecystitis showed that the best cutoff value was 10.93 x 10^3/µL with a sensitivity of 91.1% and specificity of 72.7% (AUC: 0.870, SE: 0.021, p <0.001) (Table/ Figure 3). ROC curve of neutrophil percentage in diagnosing acute cholecystitis showed that the best cutoff value was 61.80% with a sensitivity of 62.5% and specificity of 52.9% (AUC: 0.646, SE: 0.039, p 0.001) (Table/ Figure 4).

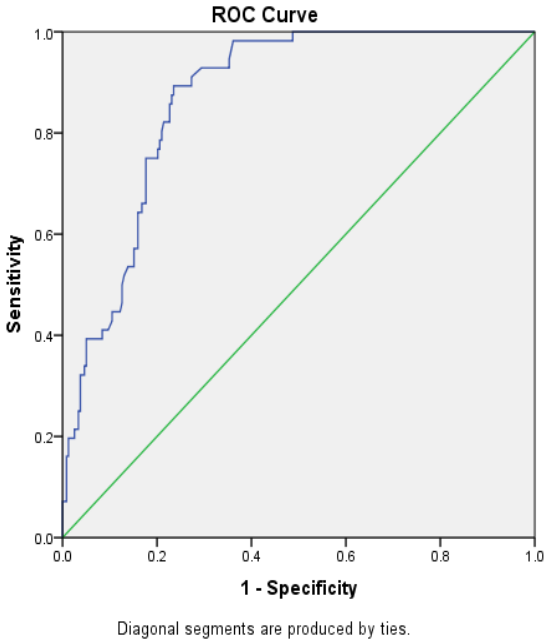
Table/ Figure 1 - Comparison between acute cholecystitis patients and chronic cholecystitis patients in terms of age, gender, BMI, RCDW, WBC count, neutrophil %, lymphocyte % and monocyte % (n = 283).

Variables	Acute cholecystitis	Chronic cholecystitis	95% CI	P value
Age (years)	39.89 ± 14.35	42.87 ± 11.96	0.661-6.614	.108
Male/Female	14/42	65/173	2.200-0.578	.726
BMI (kg/m^2)	27.21 ± 5.19	26.98 ± 5.37	1.787-1.333	.775
RCDW (%)	13.34 ± 1.71	14.66 ± 2.19	-0.710-1.943	<.001
WBC	14.16 + 2.92 X 10^9/L	9.21 ± 3.25 X 10^9/L	5.879-4.015	<.001
Neutrophil (%)	70.21 ± 17.90	60.99 ± 19.30	14.787-3.653	.001
Lymphocyte (%)	25.09 ± 13.47	28.33 ± 15.25	1.122-7.607	.145
Monocyte (%)	5.40 ± 2.93	6.93 ± 5.07	-0.145-2.541	.031

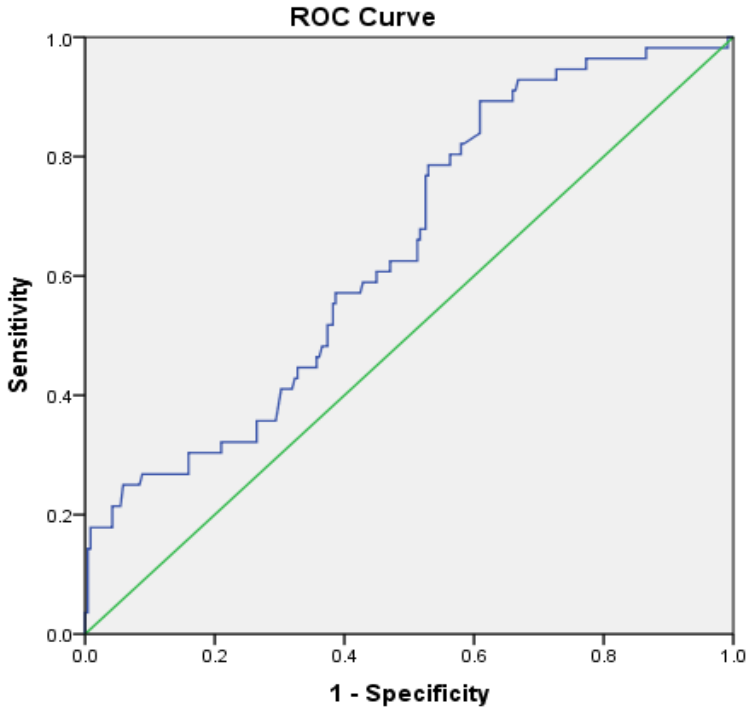
Table/ Figure 2 - ROC curve of red cell distribution width



Table/ Figure 3 - ROC curve of leucocyte count



Table/ Figure 4 - ROC curve of neutrophil count



Diagonal segments are produced by ties.

DISCUSSION:

Red cell distribution width was significantly higher among patients with chronic cholecystitis than those with acute cholecystitis. Similarly, the average of WBC and monocyte counts was significantly higher in case of acute cholecystitis. In comparison with WBC and monocyte counts, RCDW has a satisfactory discriminative value with an AUC of 0.706 for a cutoff of 14.15%. These results were consistent with the work of Arer et al who found that a cutoff of 14.15% had a sensitivity of 64.8% and a specificity of 56.5% (AUC =0.611) [25].

RCDW is a reflection of an increased destruction of erythrocytes or of an abnormal erythropoiesis, the causes of which can be multiple. RCDW is increased in anemia especially microcytic anemia and therefore, it is performed within routine hemogram test to help distinguish iron deficiency anemia from anemia caused by thalassemia [26]. This index represents the ratio between the standard deviation of red blood cells (RBCs) volume and the mean corpuscular volume (MCV). In conditions, where there is an elevated proportion of reticulocytes; there is a variation in the size of the circulating erythrocytes (anisocytosis) which increases the RCDW [27]. This parameter was also found to be related to an increased release of inflammatory markers in the bloodstream [28]. A high level of inflammatory biomarkers is associated with the alteration of the production of erythroid precursors and thereby impairs the erythropoiesis which results in an elevated RCDW. This has prompted several researchers to test the predictive value of this biological parameter in the early diagnosis of diseases where this biological disorder can be encountered [29].

Seth et al showed that a high level of RCDW is associated with the development of an inflammatory response syndrome among patients who underwent cardiac surgery with extracorporeal circulation; Similarly, other authors have highlighted the predictive value of RCDW in coronary diseases [30,31]. This association stems from a correlation between the progression of atherosclerotic plaques and RCDW level [32]. RCDW has also proven its high sensitivity in predicting outcomes in gastrointestinal inflammatory diseases and hepatic conditions [33,34].

Recently researchers have widened the role of RCDW by suggesting its utility as a prognostic factor of the mortality in several diseases [35]. According to a meta-analysis, a high level of RCDW is correlated to be a higher risk of all-cause mortality in chronic kidney disease patients [36]. Likewise, RCDW was found to be a good independent predictor of the all mortality causes in a patient with coronary disease after undergoing an elective percutaneous coronary intervention [37].

However, the agreement about the usefulness of RCDW as a diagnostic and a prognostic predictor is not unanimous; in fact, Narci et al found that RCDW has no utility as a diagnostic test in case of an acute appendicitis [38]. Differences in sensitivity and in the value of RCDW cut-off is explained by the differences of the technical methods used by the different labs as well as the lack of comparability of the studied populations, this has led to lack of a consensus about the threshold that should be considered as a reference in the diagnosis and prediction of different disorders [39].

Hence, RCDW should be interpreted in association with the level of other inflammatory biomarkers. In our study, WBC count had a good discriminative value and a very good sensitivity of 91%. WBC count is generally elevated in acute cholecystitis and it was used by many authors as a parameter, independently or included in a score, to predict different stage of this condition [40,41]. Thus, it is preferable to associate the RCDW with one or more inflammatory biomarker to support the diagnostic and therapeutic approach in cholecystitis [42].

CONCLUSION:

The red blood cell distribution width has the advantage to be a routinely measured laboratory test, and our results showed that RCDW could be used as a test to distinguish between acute and chronic cholecystitis. However, it is better to associate it with the interpretation of other inflammatory markers as the WBC count. Since those two biological parameters are obtained easily through laboratory analysis, they can be considered as a rapid and low cost first-line diagnostic test before resorting to imaging.

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