

Prognostic Value of Serum Fibrinogen Level in Determining the Severity of Appendicitis Inflammation in Adult and Pediatric Patients Undergoing Appendectomy in Two Local Centres in Tehran

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Abstract: *Background:* Despite the recent advancements, negative appendectomy cases are notable, especially in children. We evaluated the prognostic value of serum fibrinogen level for the prediction of the severity of acute appendicitis.

Methods: A cross-sectional study of children and adults who had undergone appendectomy at Ali Asghar and Rasool-e Akram hospitals, Iran, was performed. Before surgery, serum fibrinogen level was assessed by using the Clauss technique. Finally, serum fibrinogen was compared between the two groups of complicated acute appendicitis and uncomplicated ones.

Results: In the adult's complicated and uncomplicated appendicitis, no significant differences were noted in gender distribution, WBC count, and segment levels. Serum fibrinogen and C-reactive protein levels in children with complicated appendicitis were significantly higher than those in the uncomplicated ones. Serum fibrinogen level of 450 mg/dl was the optimum cut-off for predicting the severity of appendicitis in children. Serum fibrinogen level in adults with the complicated appendicitis was significantly higher than the uncomplicated appendicitis group. Also, 530 mg/dl was found the best serum fibrinogen cut-off to predict the severity of appendicitis in adults.

Conclusion: Serum fibrinogen level is an appropriate diagnostic marker for the distinction of acute complicated appendicitis from uncomplicated appendicitis in children and adults.

Keywords: Acute appendicitis, Serum fibrinogen, Children, Adults.

1. INTRODUCTION

Acute appendicitis is the most common indication for emergency surgery that affects patients from various age groups. The incidence rates of appendicitis among men and women are respectively 8.6% and 6.7%. Despite all the improvements in imaging techniques, sensitive chemical markers, and scoring systems, inopportune appendectomy cases are notable.

Laboratory tests along with clinical features and imaging findings can be beneficial for the diagnosis of appendicitis, whereas all the clinical and paraclinical variables have limited power to predict the necessity of appendectomy in acute appendicitis.

It has been well known that serum fibrinogen is an inflammation mediator. Serum fibrinogen level usually increases in any inflammatory condition such as acute

appendicitis. It has become evident that serum fibrinogen level elevates due to problems such as myocardial infarction or brain incidents [1]. Besides the primary role of fibrinogen in hemostasis, it plays a significant role in the stimulation and aggregation of polynuclear cells and fibroblasts [2]. The proteins associated with fibrinogen are essential in the aggregation of leukocytes and cellular remodelling. These proteins play an essential role in old mononuclear phagocytes and damages caused by coagulation or fibrinolysis in inflamed tissues [3].

Today, researchers are seeking new approaches for the timely diagnosis of complicated and uncomplicated appendicitis to reduce adverse consequences caused by delayed diagnosis. Unfortunately, there is no specific laboratory test for appendicitis diagnosis [4]. Despite the effect and profitability of C-reactive protein (CRP) level, it does not have efficient utility for the diagnosis of acute appendicitis [5, 6]. Thus, the necessity of a strong marker for the early diagnosis of appendicitis is felt. Some studies showed that negative appendectomy rates could be predicted and prevented

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through increasing serum fibrinogen level [7, 8]. Also, the evaluation and diagnosis of the severity of appendicitis can be useful in its treatment. In this study, we sought to determine a cut-off point for serum fibrinogen level to predict the severity of acute appendicitis.

2. MATERIALS AND METHODS

In this cross-sectional study, we assessed adults and children with the diagnosis of acute appendicitis based on clinic and paraclinical evaluations. The patients were referred to Rasool-e Akram and Ali Asghar hospital during 2017-2018. The patients were divided into two groups of 32 adult and child respectively. The final diagnosis of acute appendicitis was based on pathologic reports from pathology department. Before surgery, a venous blood sample was obtained and assessed for fibrinogen using the Clauss technique. Finally, the serum levels of fibrinogen were assessed in non-complicated and complicated appendicitis groups.

Also, the two groups were compared in terms of age, gender, white blood cell (WBC) count, segmented WBC, erythrocyte sedimentation rate (ESR), CRP, and the prognostic value of fibrinogen before surgery for predicting the severity of appendicitis in children and adults.

3. RESULTS

The age distributions of the acute appendicitis patients referred to those two hospitals are presented in Diagrams 1 and 2. In adults, 46% (n=16) were female and 54% (n=19) were male. Furthermore, 72.5% (29 patients) of the children had uncomplicated appendicitis, while the others were diagnosed with complicated appendicitis. In adults, 64.5% (n=20) of the patients had uncomplicated appendicitis.

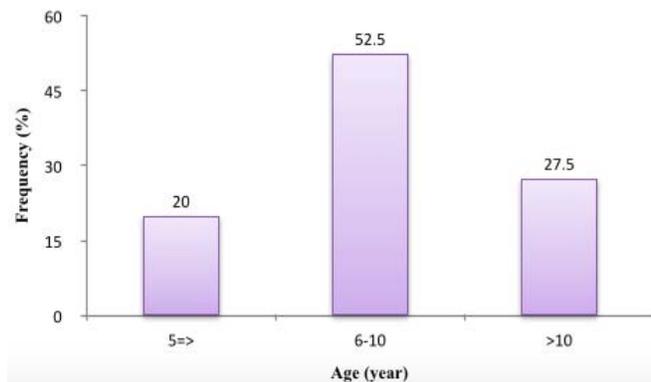


Diagram 1:

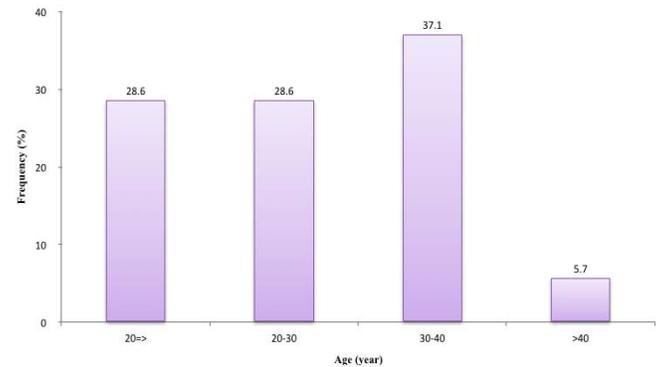


Diagram 2:

In children group, there was no significant difference in ages between complicated and uncomplicated appendicitis ($P=0.11$). However, there were differences between the age of uncomplicated appendicitis (27 ± 6.9) and complicated ones (33.6 ± 11.2). Also, there were no differences in the severity of appendicitis between girls and boys and between men and women ($P=0.498$ and 0.275 , respectively). Fibrinogen level in children with uncomplicated appendicitis were significantly lower than complicated appendicitis (366.8 ± 117.8 vs. 484.8 ± 59.9 ; $P=0.00$). However in the adult group, fibrinogen level in critical appendicitis patients (610.0 ± 68.0) was higher than uncomplicated ones (449.5 ± 116.2).

There was no significant difference in WBC count between children and adults with complicated appendicitis or between adults and children with uncomplicated appendicitis. A similar finding was obtained regarding segmented WBC. Additionally, there were no differences in ESR and CRP level between children and adults with uncomplicated appendicitis (27 ± 13.5 and 41.75 ± 40.4 , respectively) or between complicated ones (49.13 ± 39.8 and 86.2 ± 46.8 , respectively).

4. DISCUSSION

In a study by Nyuwi *et al.* in 2017, 82 patients with acute appendicitis symptoms who had undergone urgent appendectomy participated. In that study, serum fibrinogen level before surgery, as well as the sensitivity and specificity of the outcomes were evaluated. The final diagnosis was made through pathological examination. The mean serum fibrinogen levels in patients with acute appendicitis and patients without acute appendicitis were 436.6 ± 40.6 and 391.91 ± 66.54 , respectively. The area under the ROC Curve for disease diagnosis was 69.7. The serum fibrinogen level of 397 mg/dl could diagnose acute

appendicitis with 82% sensitivity and 60% specificity [9].

Prada *et al.* in 2017 performed a prospective study of 275 children aged 5 to 15 years. The diagnostic accuracy of fibrinogen for the prediction of appendicitis was evaluated. The study showed that fibrinogen has a low diagnostic value for the prediction of nonspecific abdominal pain, but it has a high diagnostic value for the prediction of complicated appendicitis (Area Under the ROC Curves were 0.63 and 0.86, respectively) [10].

Alvarez *et al.* in 2016 studied 115 patients with positive pathologic results for appendicitis. Patients were assigned to two groups of complicated and uncomplicated appendicitis. Sixty-eight patients were in the uncomplicated group, and 47 patients were in the complicated group. The optimum cut-off point for fibrinogen level was 885 mg/dl with the sensitivity of 7.86% and specificity of 49.91% [11].

Mentes *et al.* in 2014 evaluated 201 patients with clinical diagnostic symptoms of acute appendicitis. The final diagnosis was based on pathological examination. Appendicitis was approved in 89% of patients. The best fibrinogen level to diagnose acute appendicitis was 245.5 mg/dl [7].

Based on our pathology results, acute septic appendicitis, primary acute appendicitis, gangrene appendicitis, and perforated appendicitis were observed in 55%, 17.5%, 22.5%, and 5% of the children, respectively. According to pathology results, acute septic appendicitis, primary acute appendicitis, gangrene appendicitis, perforated appendicitis, appendix abscess, and phlegmon appendicitis were seen in 37.1%, 20%, 8.6%, 11.4%, 5.7%, and 5.7% of Adults, respectively.

There were no differences in gender, WBC count, segmented leukocyte level, and sedimentation rate between children with complicated and uncomplicated appendicitis.

There were no differences in gender distribution, WBC count, and PMN count between adults with complicated and uncomplicated appendicitis. Age of adults with complicated appendicitis was higher than the uncomplicated appendicitis group.

Serum fibrinogen and CRP levels in children undergone appendectomy with complicated appendicitis were higher than those in uncomplicated appendicitis, and they played a significant role in

predicting the incidence of complication in children suffered appendicitis. Also, the best fibrinogen level to predict the severity of appendicitis in children underwent appendectomy was 450 mg/dl.

The serum fibrinogen level in adults who undergone appendectomy were higher in the complicated appendicitis group compared to the uncomplicated appendicitis group. This factor was essential for predicting the incidence of complicated appendicitis. Moreover, the cut-off point of 530 mg/dl was the best serum fibrinogen level to predict the severity of appendicitis in adults who undergone an appendectomy.

Acute appendicitis is diagnosed based on clinical symptoms, radiologic imaging, and laboratory tests. The diagnosis of complicated and uncomplicated appendicitis allows the surgeon to choose the best treatment plan such as antibiotic therapy, latent appendectomy, or laparotomy [12-15].

As the rate of complicated appendicitis is approximately 40% [16-19], different methods have been tested to predict complications, which have yielded discrepant results. Radiologic tests include CT scan, MRI, and ultrasound, which approximately produce 20% false positive results in complicated appendicitis [20, 21]. Thus, the use of serological markers was recommended. Some studies had reported using of fibrinogen [22, 23].

Besides, serum fibrinogen level in complicated acute appendicitis was higher than in uncomplicated acute appendicitis. The serum fibrinogen level of 885 mg/dl was the best serum level to predict complicated appendicitis in adult patients with the sensitivity, specificity, as well as positive and negative predictive values of 86.77%, 91.49%, 93.65%, and 82.69%, respectively. Thus, fibrinogen is a good predictive factor for perforated appendicitis [11].

The findings of Feng *et al.* in 2014 were compatible with our results. They found that serum fibrinogen level in children with acute perforated appendicitis was higher than fibrinogen level in imperforated acute appendicitis. Sensitivity and specificity for hyperfibrinogenemia in children with appendicitis were 74% and 82%, respectively. Thus, children with hyperfibrinogenemia and clinical symptoms of appendicitis can be at higher risk for perforated appendicitis relative to the patients with a reasonable level of serum fibrinogen [7].

The findings of Mentés *et al.* in 2012 corroborated our findings. They reported that the best value for diagnostic serum fibrinogen level is 245.5 mg/dl in adult acute appendicitis with the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 70.39%, 50%, 91.97%, 17.18%, and 68.16%, respectively [24]. In a study by Li *et al.* in 2011, in alignment with our results, they proposed the best cut-off point for diagnostic serum fibrinogen level to be 521mg/dl for the diagnosis of complicated acute appendicitis or perforated appendicitis in adult patients. The sensitivity, specificity, positive predictive value, and negative predictive value of this finding were 56.8%, 80.2%, 20.2%, and 93.19%, respectively. Therefore, fibrinogen can be a useful marker for the diagnosis of complicated appendicitis [25].

Fibrinogen is one of the standard blood tests for patients with abdominal pain admitted to emergency departments. Fibrinogen has a high diagnostic accuracy for appendicitis in patients with clinical symptoms of acute appendicitis. Diagnosis of complicated appendicitis is a justification for surgeons to choose the best surgical plan, (only antibiotic therapy, latent appendectomy, and urgent appendectomy) [11].

The advantage of this study was its randomised clinical trial design. However, our study had some limitations. First, the literature on this issue is meagre, such that the possibility of comparing this study to other similar ones was limited. Thus, we suggest performing further studies to confirm our findings. Second, the sample size in this study was limited. Therefore, it is recommended to plan trials with larger sample sizes.

Finally, according to previous studies and our results, serum fibrinogen seems to be a useful marker for distinguishing complicated acute appendicitis from uncomplicated acute appendicitis in children, and the level of 450 mg/dl is the optimum serum fibrinogen value to predict complicated acute appendicitis in children. Serum fibrinogen level is also an excellent marker to distinguish between complicated and uncomplicated acute appendicitis in adults. The best level of serum fibrinogen to predict complicated adult appendicitis is 530 mg/dl. The serum fibrinogen cut-off point in children is lower than that for adults.

5. CONCLUSION

Serum fibrinogen seems to be a useful marker for distinguishing between complicated appendicitis and uncomplicated acute appendicitis in children, and the

level of 450 mg/dl is the best serum fibrinogen value to predict complicated acute appendicitis in children. Serum fibrinogen level is also a useful marker for making a distinction between complicated and uncomplicated acute appendicitis in adults. The serum fibrinogen cut-off point to predict complicated adult appendicitis is 530 mg/dl. The serum fibrinogen cut-off point in children was lower than in adults.

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