International Surgery Journal
Makadia JM et al. Int Surg J. 2018 Jun;5(6):2343-2348
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20182252

Original Research Article

Serum fibrinogen level as a diagnostic tool in diagnosis of acute appendicitis

Jay M. Makadia*, Adeesh P. Jain

Department of Surgery, Government Medical College, Baroda, Gujarat, India

Received: 01 April 2018
Accepted: 01 May 2018

***Correspondence:**
Dr. Jay M. Makadia,
E-mail: jmmakdia1990@gmail.com

ABSTRACT

Background: Objective of present study was to evaluate the importance of serum fibrinogen level in diagnosis of acute appendicitis and relation between clinical examination, ALVARADO score, USG Abdomen and Histopathological examination in operated case of acute appendicitis.
Methods: This prospective randomized study was done in SSG Hospital and government medical college, Vadodara in August 2016 to December 2016, Symptoms, signs, duration of symptoms, and laboratory investigations along with ultrasound of abdomen were recorded; Alvarado score was calculated and recorded in all the cases, serum fibrinogen levels were measured before surgery. After undergoing definitive surgery histopathological report of specimen of appendix were obtained and the ultimate diagnosis was kept on the basis of histopathological results. Data were recorded using Microsoft Excel, on the basis of histopathological diagnosis two groups were formed one of acute appendicitis another of non-appendicitis. Sensitivity, specificity, accuracy along with negative and positive predictive value was calculated. chi square test was used for calculation of p value, p value of <0.05 was considered significant.
Results: During the study period, 213 patients underwent surgery for suspected acute appendicitis. Appendicitis was confirmed in 198 (93%) patients. Out of which 135 (63.4%) patients were male and 78 (36.6%) female. The best diagnostic cut-off point for fibrinogen was found at 300 mg/dl, for Alvarado score at 7.
Conclusions: The use of fibrinogen blood level may be a new diagnostic modality in the diagnosis of acute appendicitis. The formulation of a triple test is recommended as a criteria in deciding emergency surgery.

Keywords: Acute appendicitis, Alvarado score, Fibrinogen, Histopathological diagnosis

INTRODUCTION

Appendicitis is a common and urgent surgical illness, presentation of which overlaps with other clinical syndromes, and significant morbidity, which increases with diagnostic delay. Despite intense research and discussion, the diagnosis of acute appendicitis is still difficult and remains perhaps the most common problem in clinical surgery. On the one hand normal appendix at appendectomy represents misdiagnosis; on the other hand, a diagnostic delay may lead to perforation and peritonitis. Inspite of careful clinical, lab and ultrasound examination, the rate of removing non diseased appendix and of appendiceal perforation remains at around 20% of all cases subjected to appendectomy. No single sign, symptom or diagnostic test accurately makes the diagnosis of appendicle inflammation in all cases. The surgeons' goal is to evaluate patients referred for suspected appendicitis and to minimize the negative appendectomy rate without increasing the incidence of complications.

Plasma fibrinogen is acute phase reactant. It can be used for diagnosis of acute appendicitis. It has been recognized that serum fibrinogen is one of the acute phase reactants that may rise in concentration because of the synthesis by

hepatocytes during acute phase response to inflammation. Fibrinogen is not disease specific, but it may offer valuable diagnostic information about presence of acute infection and inflammation with concomitant evaluation of patient history and physical examination.[1,2,3]

Although surgeons have been confronting acute appendicitis for more than100 years, its diagnosis remains elusive. Some senior surgeons can diagnose acute appendicitis accurately in over 80 percent of cases.[4,5] However, in most cases, junior surgeons are responsible for deciding whether a patient with right iliac fossa pain should be operated on or not for appendicitis. Their decision may be wrong in about 50 percent of the time. Among young male patients the negative appendectomy rate is relatively low (5-22p%) while for women of child bearing age the figure may be as high as 30-50%.[4,6-14] In young children the diagnosis may be wrong in 30-46% of cases.[7,10,11] The difficulty of diagnosing acute appendicitis in old age is reflected by the high incidence of perforation rather than by high rate of negative appendectomy.[9,15-17] Diagnosis is also difficult during pregnancy and may result in both maternal and foetal morbidity.[18-21]

As the incidence of perforation is usually proportional to the duration of the disease process, traditional teaching has encouraged surgeons to operate even when the diagnosis is probable rather than wait until itis certain.

The morbidity and mortality rates associated with appendicitis greatly increase when perforation ensues wound infection rates is also increase, intra-abdominal abscess formation increases15-fold and mortality may be 50 times greater.[7,10,11,13,14,22,23] Appendicle perforation can also cause tubal infertility.[24] It is there for obvious that the aim of the surgeon must be to prevent perforation at any price. According to Malone, appendix is considered as specialized structure useful in reconstructive surgeries on biliary, tubal and urological cases.[13] Negative appendectomy there for removes a useful asset of the patient. Thus, a surgeon confronting a patient suspected of having acute appendicitis is wedged between the Scylla of perforation and the Charybdis of negative appendectomy.

Thus, improving the diagnosis of acute appendicitis in order to prevent unneeded surgery is a critical to pick that has been debated often and vigorously. The use of laparoscopy, ultrasonography, barium enema examination, and CT scan has improved diagnostic accuracy, but these approaches are difficult to apply primary health care setting.

This study aims to know the helpfulness of increase level of fibrinogen in diagnosis of acute appendicitis. This would be done by comparing it with histopathological examination report. The need for study is to find out which is most accurate and sensitive investigation to improve diagnosis of appendicitis and decision making and hence decrease negative and unnecessary appendectomies.

Objective of present study was to evaluate the importance of serum fibrinogen level in diagnosis of acute appendicitis and relation between clinical examination, ALVARADO score, USG Abdomen and Histopathological examination in operated case of acute appendicitis

METHODS

It was a prospective study. As it is time bound study and considering the number of patient with acute appendicitis and laparoscopic/open appendectomies done in SSG Hospital, Vadodara the sample size will be around 213.

By collecting blood sample of the patient for CBC, serum fibrinogen level preoperatively, preoperative ultrasonography of abdomen, Alvarado score calculation Intraoperative findings recorded, postoperative histopathological examination report of removed appendix. Result will be tabulated by comparing all four investigation i.e., Alvarado score, serum fibrinogen and ultrasonography of abdomen.

This prospective randomized study was done in SSG Hospital and government medical college, Vadodara in August 2016 to December 2016 with the involvement of all the cases of acute appendicitis admitted in the hospital and undergone emergency appendectomy Patients who were managed conservatively (given negative consent for appendectomy) or took antibiotic are excluded from study, Patients who refused to enroll in study, and the Patients with co-morbid inflammatory ,infective conditions and liver disease were excluded from the study .Patient presented in emergency with complaint of right iliac fossa pain, with detailed history and with clinical diagnosis of acute appendicitis. Preoperative USG abdomen and blood tests for CBC, urea, creatinine, serum fibrinogen and Alvarado score calculation was done. Serum fibrinogen >300mg/dl are taken as cut of value for patient to be diagnosed as acute appendicitis. Intraoperative findings in relation to appendix (normal /inflamed /oedematous, presence of pus flakes over appendix, gangrenous/perforated appendix, adhesion with nearby structures, fecolith and worms inside the appendix, presence of free pus in periappendicular region and presence of free pus in whole abdomen) were recorded and Postoperative histopathological examination of removed appendix sample was done in the pathology department of the hospital. Results of investigations were correlated with the intra operative findings and histopathological examination reports to evaluate the changes in their values in acute appendicitis.

Statistical analysis

Data were recorded using Microsoft Excel, on the basis of histopathological diagnosis two groups were formed

one of acute appendicitis another of non-appendicitis. sensitivity, specificity, accuracy along with negative and positive predictive value was calculated chi square test was used for calculation of p value value of <0.05 was considered significant.

RESULTS

In present study 213 cases of suspected acute appendicitis were studied out of which 198 were diagnosed to be acute appendicitis on histopathological examination (93%) (which is mention as group A in present study) while rest 15 (7%) patients had normal appendix on histopathology (which is mention as group B in present study). Out of 213 patients 81 patients were less than or equal to 20 years in age, 48 patients were in the age group of 21-30 years of age, 33 patients are in the age group of 31-40 years of age and rest are more than 40 years of age.

Acute appendicitis is having male preponderance (135 out of 213) Out of 213 patients 198 patients with acute appendicitis on histopathological examination, of which 162 patients had serum fibrinogen level >300mg/dl and 36 had fibrinogen level of <300mg/dl. in ,15 patients without acute appendicitis (histopathological report) ,6 patients were having serum fibrinogen level >300mg/dl and <300mg/dl in 9 patients with p value is <0.05. Alvarado score ≥7 was found in 174 patients and <7 in 24 cases of group A. 03 patients were having score ≥7 and 12 were having score <7 in group B. This suggest p value of Alvarado score is <0.001.

On calculating p value for USG abdomen it was <0.001 (group A: acute appendicitis -186 pts, group B: acute appendicitis -06 pts), Sensitivity, specificity, negative and positive predictive value along with accuracy was evolved for serum fibrinogen level, Alvarado score, USG abdomen considering the histopathological report as confirmation of diagnosis. Sensitivity, specificity, negative and positive predictive value of all 3 parameter are as below given in the table.

Table 1: Sensitivity, specificity, negative and positive predictive value of serum fibrinogen, Alvarado score, and Usg abdomen.

	Serum fibrinogen	Alvarado score	USG
Sensitivity	81%	87%	93%
Specificity	60%	80%	60%
Positive predictive value	96%	98%	96%
Negative predictive value	20%	33%	42%
Accuracy	80%	87%	91%

DISCUSSION

The aim of this study is to evaluate the value of the serum fibrinogen level in the diagnosis of suspected acute appendicitis and combination of 3 diagnostic tools for diagnosis of acute appendicitis.

Though challenging but it's very important to differentiate early appendicitis from non-specific abdominal pain. as a clinician, a carefully detailed history, physical examination, and standard laboratory studies may not always clearly detect early acute appendicitis and delay in diagnosis is harmful and may convert a relatively uncomplicated case to substantial morbidity or even mortality. Our effort is to develop a combination tool for accurate diagnosis of acute appendicitis using three modalities serum fibrinogen, Alvarado score, USG abdomen.

The optimal test should combine a high sensitivity with a high predictive value of a negative result. The diagnostic accuracy of a test may be improved by changing the cut-off level if the test result is considered positive. If the cut-off level is elevated, the sensitivity or number of true-positive patients detected by the test will decrease, while the specificity or number of true-negative patients will increase.

The WBC count is a common single parameter used for diagnosis of acute appendicitis but its value can vary with many causes like physical stress, acute/chronic/inflammation. Plasma fibrinogen is an acute phase protein and therefore its concentration increases with inflammation or tissue necrosis. Fibrinogen deposition is a universal feature in injured tissues and inflammatory foci. In vitro studies have shown that fibrinogen can profoundly alter WBC function, leading to changes in cell migration, phagocytosis, production of chemokines and cytokines, degranulation, and other processes. Leukocyte interaction with fibrinogen or its degradation products have special importance at sites of inflammation as fibrinogen may gain access to the extravascular compartment by exudation, where it encounters migrating leukocytes. It is well known that both the extent of leukocyte recruitment and the pro-inflammatory action of the migrating leukocytes determine the intensity of an inflammatory reaction, and peripheral human neutrophils are capable of phagocytosis, spreading, and chemotaxis.

In this study serum fibrinogen level more than 300 mg/dl is taken as significant (cut off point). Out of 198 patients of group A 162 patients were having serum fibrinogen level above 300mg/dl and 36 patients were having serum fibrinogen below 300mg/dl.

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated as 78%, 60%, 96%, 17%, and 77%, respectively. Comparing with study conducted by Mentis at el 201 patients were studied out of which 179 patients were diagnosed with acute appendicitis, 128 patients had serum fibrinogen level above 245mg/dl and rest 51 patients had serum fibrinogen level below 245mg/dl. At

this point, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated as 70%, 50%, 91.91%, 17.18%, and 68%, respectively. Present study shows the result comparable to the study done by Mentis O et al.

Table 2: Comparison of sensitivity, specificity, positive predictive value, negative predictive value and accuracy between present study.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
In present study	87	80	98	33	87
Mentis O et al	60	81	96	20	62
Memon ZA et al	93	80	92	83	89

The Alvarado score is a point scoring system for the diagnosis of appendicitis based on clinical science and symptoms and a differential WBC. The accuracy of the Alvarado score in a clinical preoperative diagnosis of acute appendicitis has been reported as ranging from 50% to 95%. In his original paper, Alvarado recommends surgery for all patients with a score of 7 or more and observation for patients with score of 5 or 6. In present study, the best cut-off point of the Alvarado score for early diagnosis of acute appendicitis was taken as ≥7, and in present study, out of 198 patients of group A,174 patients were having Alvarado score ≥7 and rest 24 patients were having score <7. At this point sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated at 87%, 80%, 98%, 33%, and 87%, respectively. While in study of Mentis O et al taking Alvarado score ≥7 was taken as cut off point for diagnosis of acute appendicitis, out of 179 patients who are diagnosed with acute appendicitis 146 patients had alvarado score ≥7 and rest 33 patients were having score <7.[1] At this point sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 60%, 81%, 96%, 20%, and 62%, respectively.[1] In other study conducted by Memon ZA et al the best cut-off point of the Alvarado score for early diagnosis of acute appendicitis was taken as ≥6 and out of total 79 cases having score ≥6, 72 patients were diagnosed with acute appendicitis and rest 7 patients were not having acute appendicitis. At this point sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 93%, 80%, 92%, 83%, and 89%, respectively.[25] Alvarado score result in present study are comparable to the study done by Mentis O et al and done by Memon ZA et al.[1,25]

Table 3: Comparison of sensitivity, specificity, positive predictive value, negative predictive value and accuracy between present study.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
In present study	93	60	96	42	91
Subash KC et al	95	90	98	80	84
Tauro LF et al	91	88	91	88	90

In this study out of 213, 198 patients were diagnosed with acute appendicitis on histopathological examination, out of which 186 patient were diagnosed with acute appendicitis on USG abdomen and rest 12 patients were not diagnosed as acute appendicitis on USG abdomen. At this point, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 93%, 60%, 96%, 42%, and 91%, respectively. In study conducted by Subash K C et al in 2015 out of 125 patients who were diagnosed with acute appendicitis on histopathological examination, out of which 100 patients were diagnosed with acute appendicitis on USG abdomen and rest 25 patients did not show acute appendicitis on USG abdomen. At this point, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 95%, 90%, 98%, 80%, and 84%, respectively. TAURO LF et al85 in 2009 out of 100 patients who were underwent USG abdomen 58 patient were diagnosed with acute appendicitis on USG abdomen and rest 42 patients \were not diagnosed as acute appendicitis on USG abdomen. At this point sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated as 91%, 88%, 91%, 88%, and 90%, respectively. There is concurrence between present study and study done by Tauro LF et al and Subhash KC et al. [26,27]

The aim of present study was to evaluate the role of the serum fibrinogen level in the diagnosis of suspected acute appendicitis and significance of combination of 3

diagnostic tools (serum fibrinogen level, Alvarado score,usg abdomen) for diagnosis of acute appendicitis. we found that serum fibrinogen levels is a good diagnostic single parameter for acute appendicitis Sensitivity, specificity, positive and negative predictive value, and accuracy of the serum fibrinogen test in diagnosis of acute appendicitis is comparable with other isolated tests so it can be used as a parameter in the diagnosis of acute appendicitis however single test is less accurate in comparison to combination of three diagnostic tool like serum fibrinogen level, Alvarado score and USG abdomen.

There are studies in which CRP is used as single parameter for diagnosis of acute appendicitis but we found that probability of diagnosis of acute appendicitis many folds using triple test.

There are many limitations to present study like small number of cases small period of time, consideration of cases of acute appendicitis only and role of plasma fibrinogen in diagnosis of chronic appendicitis is not evaluated.

Serum fibrinogen has very low negative predictive value in comparison to other test.at the end in our set up catering patients with low socio-economical class Cost of the test and availability of the test (serum fibrinogen level) is one of the major limitations of this study.

CONCLUSION

As acute appendicitis is an emergency condition and required early diagnosis and management to prevent unnecessary negative laparotomy. There is a little difference in sensitivity, specificity, positive and negative predictive value between various bio chemical marker of acute appendicitis (total count, serum fibrinogen serum CRP level) various scoring system (ALVARADO score, RIPASA score etc.),

USG abdomen, clinical diagnosis of acute appendicitis. So, we have to use combine approach for early and accurate diagnosis of acute appendicitis to prevent unnecessary morbidity to patients. Surgeons must achieve a balance between premature operation with a high negative appendectomy rate and a delayed diagnosis (and surgery) with a higher perforation rate. There is no sign, symptom, or laboratory test that is 100% reliable in the diagnosis of acute appendicitis.

Present results suggest that the use of fibrinogen blood level may be a new diagnostic acute-phase reactant in the diagnosis of acute appendicitis, sensitivity, specificity, positive, and negative value of serum fibrinogen is comparable with other methods of diagnosis but the limiting factor is cost and non-availability of test. The study is done on small number of patients and the duration of present study is short, so large scale study with longer duration is required.

ACKNOWLEDGEMENTS

Authors would like to thanks Dr. S. P. Sharma for his valuble support during study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Menteş O, Eryılmaz M, Harlak A, Oztürk E, Tufan T. The value of serum fibrinogen level in the diagnosis of acute appendicitis. Ulus Travma Acil Cerrahi Derg. 2012 Sep 1;18(5):384-8.
2. AnDieijen-Visser MP, Go Pmnyh, Brombacher PJ. The value of lab test inpatients suspected of appendicitis. Eur J Clin Chem Clin Biochem. 1991;29:749-52.
3. Anderson R, Hugander A, Ghazi S, Ravan H, Offenbart S, Nystron P et al. Diagnostic values of disease history, clinical presentation and inflammatory parameter of appendicitis. World J Surg. 1999;23(2):133-40.
4. Gilmore OJ, Browett JP, Griffin PH, Ross IK, Brodribb AJ, Cooke TJ, Higgs MJ, Williamson RC. Appendicitis and mimicking conditions: a prospective study. Lancet. 1975 Sep 6;306(7932):421-4.
5. De Dombal FT, Leaper DJ, Horrocks JC, Staniland JR, McCann AP. Human and computer-aided diagnosis of abdominal pain: further report with emphasis on performance of clinicians. Br Med J. 1974 Mar 2;1(5904):376.
6. Deutsch AA, Shani NR. Are some appendicectomies unnecessary? An analysis of 319 white appendices. JR Coll Surg Edinb. 1983;28:35-40.
7. Jess P, Bjerregaard B, Brynitz S, Holst-Christensen J, Kalaja E, Lund-Kristensen J. Acute appendicitis: prospective trial concerning diagnostic accuracy and complications. American J Surg. 1981 Feb 1;141(2):232-4.
8. Detmer DE, Nevers LE, Sikes ED. Regional results of acute appendicitis care. JAMA. 1981 Sep 18;246(12):1318-20.
9. Dunn EL, Moore EE, Elerding SC, Murphy JR. The unnecessary laparotomy for appendicitis can it be decreased? Am Surg J. 1982;48:320-3.
10. Pieper R, Kager LN, Masman P. Acute appendicitis: a clinical study of 1018 cases of emergency appendectomy. Acta Chir Scand. 1982;148:51-62.
11. Andersen M, Lilja T, Lundell L, Thulin A. Clinical and laboratory findings in patients subjected to laparotomy for suspected acute appendicitis. Acta Chiru Scand. 1980;146(1):55-63.
12. Butler JA, Marcus CS, Henneman PL, Inkelis SH, Wilson SE. Evaluation of Tc-99m leukocyte scan in

the diagnosis of acute appendicitis. J Surg Res 1987;42:575-9
13. Malone AJ, Shetty MR. Diagnosis of appendicitis. Lancet. 1997;14:349.
14. Edwards FH, Davis RS. Use of a Bayesi analgorithm in the computer assisted diagnosis of appendicitis. Surg Gynecol Obstet. 1984;158:219-22.
15. Lewis FR, Holcroft JW, Boey J, Dunphy JE. Appendicitis: a critical review of diagnosis and treatment in 1,000 cases. Arch Surg. 1975;110(5):677-84.
16. Owenes BJ, Hyamit HF. Appendicitis in the elderly. Am Surg J. 1978;187:392-6.
17. Burns RP, Cochran JL, Russell WL, Bard RM. Appendicitis in mature patients. Annal Surg. 1985 Jun;201(6):695-704.
18. Berry J, Malt RA. Appendicitis near its centenary. Ann Surg J. 1984;200:567-75.
19. Editorial. appendicitis in pregnancy. Lancet. 1986;1:195-6.
20. Cunningham FG, ME Cubbin JG. Appendicitis complicating pregnancy. Obstet Gynecol. 1975;45:415-20.
21. Horowitz MD, Gomez GA, Santiesteban R, Burkett G. Acute appendicitis during pregnancy diagnosis and management. Arch Surg. 1985 Dec;120(12):1362-7.
22. Graham DF. Computer-aided prediction of gangrenous and perforating appendicitis. Br Med J. 1977;2:1375-7.
23. Editorial. A sound approach to the diagnosis of acute appendicitis. Lancet.1987;1:198-200.
24. Mueller BA, Daling JR, Moore DE, Weiss NS, Spadoni LR, Stadel BV et al. Appendectomy and the risk of tubal infertility. N Engl J Med. 1986;315:1506-8.
25. Memon ZA, Irfan S, Fatima K, Iqbal MS, Sami W. Acute appendicitis: diagnostic accuracy of Alvarado scoring system. Asian J Surg. 2013 Oct 1;36(4):144-9.
26. Subash K, De A, Pathak M, Sathian B. Diagnostic role of ultrasonography in acute appendicitis: a study at a terciary care hospital. Am J Public Health Res. 2015;5(3):23-8.
27. Tauro LF, Premanand TS, Aithala PS, George C, Suresh HB, Acharya D, et al. Ultrasonography is still a useful diagnostic tool in acute appendicitis. J Clin Diagnos Res. 2009;3:1731-6.

Cite this article as: Makadia JM, Jain AP. Serum fibrinogen level as a diagnostic tool in diagnosis of acute appendicitis. Int Surg J 2018;5:2343-8.