International Surgery Journal
Gedam BS et al. Int Surg J. 2017 Apr;4(4):1409-1416
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20171152

Original Research Article

Study of conservative treatment in uncomplicated acute appendicitis

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Received: 07 February 2017
Accepted: 02 March 2017

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ABSTRACT

Background: Management of acute appendicitis with antibiotics only, without surgery is currently evaluated. Non-operative management of uncomplicated acute diverticulitis and salpingitis has been well established but the non-operative management of acute appendicitis remains controversial. Growing evidence indicates that patients with acute uncomplicated appendicitis can be treated safely with an antibiotics- first approach.
Methods: A tertiary care hospital based longitudinal study with duration of 26 month. Patients with clinical and radiological feature of acute appendicitis presenting within 48 hours of initiation of abdominal pain with Modified Alvarado Score ≥5 included. Various demographic, clinico-pathological, radiological factors were studied.
Results: 71 patients evaluated, mean age of 30.45±9.71 years. Tenderness in RIF was the commonest finding followed by Fever and rebound tenderness. Leucocytosis seen in 74.65% Modified Alvarado score of 5-6 was present in 18.32% whereas 7-9 was present in 81.68% patients. USG was suggestive of appendicitis in 84.50% patients. Conservative treatment was successful in 74.65% patients with no treatment failure. 25.35% patients, conservative treatment failed. Overall recurrence was seen in 13.11% cases that were successfully managed during primary admission.
Conclusions: Majority of cases of first attack of uncomplicated acute appendicitis can be treated successfully by conservative treatment. However, conservative treatment requires monitoring and repeated re-evaluation to identify failure which needs to be treated promptly by surgery. Treatment failure on primary admission as well as the short-term recurrence after conservative treatment is low and acceptable. The outcome of conservative treatment does not depend on Modified Alvarado Score.

Keywords: Acute appendicitis, Antibiotics, Conservative treatment, Modified Alvarado score, Uncomplicated acute appendicitis

INTRODUCTION

It has been 130 years since Reginald Heber Fitz coined the term "appendicitis" to describe inflammation of the vermiform appendix.[1] It was the awareness of the possible progression of appendicular perforation to generalized peritonitis, with fatal outcomes, that prompted Charles McBurney to advocate early appendectomy. Immediate appendectomy was presumed in every case of acute appendicitis to avoid fatal outcome in the pre-antibiotic era.[2] Acute appendicitis (AA) is a common disease with a lifetime risk of 7-8%, with highest incidence found in the second and third decade of life.[3]

In recent years there is a growing literature suggesting antibiotics without surgery may be effective treatment for acute appendicitis. Appendectomy carries a risk of several postoperative complications ranging around 10-19% for acute appendicitis without perforation and cam reach 30% for perforated acute appendicitis.[4-6] The

advent of laparoscopic has led to a risk of high negative appendectomy rates with unnecessary surgery related morbidity.[7] Non-operative management with antibiotics of uncomplicated acute diverticulitis and salpingitis has been well established but the non-operative management of acute appendicitis remains controversial.

Growing evidence indicates that patients with acute uncomplicated appendicitis can be treated safely with an antibiotics- first approach. One Cochrane analysis, five meta-analysis and some reviews of non-operative treatment of acute appendicitis concluding that majority of patients with acute, uncomplicated appendicitis can be treated safely with an antibiotics-first strategy.[7-9] Antibiotics that are more effective have become available for the treatment of intra-abdominal infection. Successful non-operative treatment avoids discomfort, lost productivity and many possible operation-related complications. It would not be a viable alternative to surgery unless it is equally effective at curing acute appendicitis.[9]

In this regard, we aim to study the effectiveness of conservative treatment in uncomplicated acute appendicitis using antibiotic treatment and to study the treatment failure with short-term recurrence of conservative treatment.

METHODS

The present study was carried out in a tertiary care hospital in central India from September 2014 to October 2016. A total of 71 cases were recruited in this study based on inclusion and exclusion criteria.

Study design

The present study was a tertiary care hospital based longitudinal study.

Study population

Patients presenting with Acute Pain in Right Lower Quadrant

Inclusion criteria

- Age: Above 18 years
- Clinically diagnosed case of Acute Appendicitis presenting within 48 hours of initiation of Abdominal pain with Modified Alvarado Score (Clinico-pathological score) more than or equal to 5.
- Radiological investigation - Ultrasound Abdomen and Pelvis done to support clinical diagnosis (also to rule out complications such as phelgmon (lump), abscess, perforation etc. and to rule out other causes of pain in Right lower quadrant e.g. Ureteric calculus, Ovarian pathology).

Exclusion criteria

- Recurrent appendicitis
- Cases presenting with complications of acute appendicitis like abscess, phlegmon, perforation or peritonitis.
- Patients with immunodeficiency status or on immunosuppressive therapy.
- Non-operative management initiated at an outside institution
- Pregnancy
- Allergy to antibiotics established in the study protocol
- No acceptance of study protocol.

Study factors

Using a pre-prepared proforma various demographic, clinico-pathological, radiological factors were studied.

Successful conservative treatment

It was defined as being discharged from the hospital following the resolution of appendicitis without the need for surgical intervention and no appendicitis during a follow up of 6 months.

Failure of conservative treatment

Failure of conservative treatment was divided into categories:

Treatment failure a lack of improvement or clinical progression, necessitating appendectomy while attempting conservative treatment in the admitted patient.

Recurrence in an earlier successfully conservatively managed patient was defined as a clinically diagnosed case of appendicitis due to the presence of repeated symptoms or disease, detected by imaging evaluation which required treatment.

Patients satisfying the inclusion criteria were enrolled. Study patients received intravenous antibiotics - ceftriaxone 1 g 12 hourly and metronidazole 500 mg 8 hourly for 2 days. During this time patients received intravenous fluids and were nil by mouth for 24 hrs. Repeated clinical evaluations and monitoring was done. Patients whose clinical status improved were continued with oral antibiotics –Tb. ciprofloxacin 500 mg twice a day with tinidazole 600 mg two times a day for a total of 7 days. In patients whose clinical condition did not improve, appendectomy was performed according to the usual practice by either open or laparoscopic technique. The appendix was sent for histological examination and follow-up at 10 days, 30 days and 6 months was carried out to assess recurrence in conservatively managed patients. Recurrence of appendicitis would be managed

either surgically or conservatively depending upon the treating surgeon and patient preference.

Statistical analysis

Descriptive statistics were presented in tabular format with Mean, standard deviation, percentage and others for descriptive statistics.

Analytical statistics Categorical variables were expressed in actual numbers and percentages and were compared using Fisher exact test and P value was calculated. The P value of <0.05 was considered as statistical significance. Statistical analysis was done using free trial version of Graph Pad Prism 6® for Windows version 6.07 (trail) during the 30 day demo interval.

RESULTS

In this study, 71 cases (n = 71) of uncomplicated acute appendicitis were included and managed conservatively.

Mean age was 30.45years with standard deviation of 9.71 and range between 18 – 61 years. In total 71 cases of uncomplicated acute appendicitis, maximum number of cases - 32 (45.07%) belonged to age group >20-30 years, followed by 22 cases (30.98%) in the >30-40 years age group (Table 1).

Table 1: Age distribution of patients.

Age in years	Frequency (n =71)	Percentage
18-20	6	8.45
>20-30	32	45.07
>30-40	22	30.98
>40-50	8	11.27
>50-60	2	2.82
>60	1	1.41
Total	**71**	**100**

Out of 71 patients in the present study, 34 were males and 37 were female with Male: female ratio of 1:1.09.

Table 2: Clinico-pathological factors at the time of presentation.

Symptoms and signs	Frequency	Percentage
Pain	71	100%
Anorexia	55	77.46%
Nausea/Vomiting	57	80.28%
Fever	62	87.32%
Tenderness in RIF	71	100%
Rebound tenderness	42	59.15%
Leucocytosis	53	74.65%

In the 71 patients, pain and tenderness was present in all the patients of uncomplicated acute appendicitis with symptoms of nausea/vomiting in 57 (80.28%) patients followed by anorexia in 55 (77.46%) patients. Fever (>99.1degrees F) was present in 62 i.e. 87.32 % patients and rebound tenderness was present in 53 (74.65%) patients in this study. Leucocytosis was present in 53 (74.65%) patients in present study (Table 2).

Out of 71 cases, 13 patients (18.32%) had Modified Alvarado score below 7 i.e. 5 and 6 whereas 58 patients (81.68%) had Modified Alvarado score of 7 and above.

Out of 71 cases, 60 patients (84.50%) had positive findings on ultrasonography of abdomen and pelvis suggestive of uncomplicated appendicitis whereas 11 patients (15.5%) had no findings suggestive of appendicitis.

In the 71 patients who were managed conservatively for uncomplicated acute appendicitis, conservative treatment was successful in 53 (74.65%) patients with no treatment failure or recurrence in follow-up period of 6 months. However in rest 18 (25.35%) patients conservative treatment failed. Treatment failure during primary admission was seen in 10 patients (14.08%) whereas recurrence was seen in 8 patients (13.11%) cases who were successfully managed during primary admission. Median duration of recurrence was 2 months (Table 3).

Table 3: Outcome of conservative treatment.

Outcome of conservative treatment	Frequency (n=71)	Percentage
Successful	53	74.65
Treatment failure	10	14.08
Recurrences	8	13.11

The Fisher exact test statistic value is 0.493. The result is not significant (NS) at p <0.05. To summarize the outcome of conservative treatment does not depend on Modified Alvarado Score (Table 4).

Table 4: Co-relation of Modified Alvarado score with outcome of conservative treatment.

		Outcome		Total
		Success (%)	**Failure (%)**	
MAS	**5-6**	11 (15.5%)	2 (2.82%)	13 (18.32%)
	7-9	42 (59.15%)	16 (22.53%)	58 (81.68%)
Total		53 (74.65%)	18 (25.35%)	71 (100%)

*One case of recurrence following conservative management was again managed conservatively as the patient was not willing for surgery.

In the 10 cases of treatment failure, appendectomy was done and histopathological report was suggestive of acute

appendicitis in all the cases. In the 8 cases of recurrence following conservative treatment, 7 patients underwent appendectomy and histopathological report was suggestive of acute appendicitis in all the cases. One case of recurrence was managed conservatively

DISCUSSION

Acute appendicitis is a common cause of acute abdominal pain and appendectomy has been the mainstay for the treatment for acute appendicitis since it was first reported by McBurney in 1889. The general assumption since the 19th century has been that in the absence of surgical intervention the disease often progresses from uncomplicated to perforated.[1,2] Only 20% of patients present with complicated appendicitis, and non-operative management with antibiotics and supportive treatment has been explored as a therapeutic option for patients with early uncomplicated appendicitis, with resolution in most of them thereby avoiding the mortality and morbidity associated with appendectomy.[8,9] Conservative treatment is a viable option and we need to compare it with appendectomy.

Potential advantages of conservative treatment (i.e. antibiotic treatment) over surgical treatment include:

- Antibiotics offer the opportunity to treat acute appendicitis when surgical resources are not easily available [developing countries and remote areas (Antarctica, International Space Station).[10]
- Worldwide health systems are everyday carefully assessing the cost effectiveness of all medical actions. A significant difference in hospital costs was reported by Hansson et al., with a reduction in expenses of 25-50% in the antibiotic group compared to surgery.[11]
- Antibiotic approach offers the opportunity to avoid ―white (negative) appendectomies and thus allowing a more correct use of health resources even in the busy scenario of developed countries.[12]
- Antibiotic treatment can eliminate the mortality and morbidity risk related to surgery.
- Potential advantages of surgical treatment over conservative treatment include:
- Surgery reduces risk of recurrence with a small percentage of mortality and morbidity. Few cases of stump appendicitis even after surgery have been mentioned in the literature.
- Surgical intervention offers the opportunity to -take a look inside the abdomen‖. carcinoid is found in 3-7/1000 appendectomies and colon cancer in 0.85% cases.[13]
- Patients treated by antibiotic therapy alone will receive a longer course of drugs. Thus, the increasing risk of the antibiotics resistance is theoretically reduced by the surgery.[12]

Furthermore, to increase the complexity of the diagnosis of appendicitis, a histologically normal variant known as -neuro-immune appendicitis, characterized by abnormal concentrations of neuro-peptides, neuronal sprouting, and possibly combined with the immunological response, has been attributed to the relief of pain in patients who had a histologically normal appendix removed.[14-19]

The present study was designed to evaluate the effectiveness of conservative treatment in cases of uncomplicated acute appendicitis. The mean age in the present study was 30.45±9.71 years (range 18-61) which is quite consistent with the literature as shown in the (Table 5).

In the present study, majority of patients i.e. 45.07% belonged to the age group >20-30 years. This is in accordance with the literature as shown in (Table 5) which suggests that acute appendicitis has higher incidence in 3rd decade of life.

In the present study, the patients observed in 4th decade were more than in 2nd decade as we included patients only above 18 years due to which true incidence in 2nd decade could not be calculated. However, the results were consistent with other study like Vaishnav et al, which had a similar inclusion criterion of more than 18 years of age.[23]

Male to female ratio was practically equal 1:1.09 suggesting the equal distribution of gender in patients suffering from acute appendicitis. These findings are consistent with the studies in the literature.

In the present study, pain was the most common symptom present in all the patients followed by nausea/vomiting in 80.28% and anorexia in 77.46%. These findings are in accordance with the literature (Table 6).

Tenderness in RIF was present in all the patients, followed by fever in 87.32% and rebound tenderness in 59.15%. These are consistent with the literature, except for low percentage of patients presenting with fever seen in study by Berry et al (34.3%). This is due to the cut-off value of 100 degree F in study by Berry et al. The cut-off value for defining fever in this study was 99.1 degrees F or 37.3 degrees C as described in literature, for evaluating the Modified Alvarado score.[27]

Majority of patients (81.69%) had a modified Alvarado score of 7 or more which is similar to the value observed in the study by Kalan et al who put forth the modified Alvarado score in 1994.

Kalan et al found that sensitivity of modified Alvarado score of more than or equal to 7 for male was 93% and for females was 67%. The sensitivity of modified Alvarado score of 5 and 6 for male was 67% and for females was 50% By taking a cut-off point of 7 for the Modified Alvarado score, a sensitivity of 97.56%, specificity of 66.67%, positive predictive value (PPV) of

95.23%, negative predictive value (NPV) of 80% and accuracy of 87.2% was observed in the study by Dsouza et al.[28] Study by Vandakudri et al, showed in men a sensitivity of 92.3% and 83.3% respectively, whereas in females it had a sensitivity of 72.7%.[29] The score (5-6) in males and females had a sensitivity of 57% and 50% respectively. Ultrasonography of abdomen was useful in avoiding negative appendectomy rates particularly in females.

Table 5: Age distribution in literature.

Age in years	Rajashekhar et al[20] (%)	Ramachandra et al[21] (%)	Lohar et al[22] (%)	Vaishnav et al[23] (%)	Present study (%)
Range	**8 - 61**	**7 - 69**	**7-58**	**18-58**	**18 - 61**
<10	2	7	4.5	0	0
>10- 20	29	39	26.36	6.7	8.45
>20-30	44	32	34.54	43.3	45.07
>30-40	16	15	14.54	23.3	30.98
>40-50	5	4	13.63	20	11.27
>50-60	1	1	6.33	6.7	2.82
>60	1	2	0	0	1.41

Table 6: Distribution of clinic-pathological features in literature.

Symptoms and signs	Kodliwadmath et al[24] (%)	Reddy et al [25] (%)	Berry et al[26] (%)	Ekka et al[37] (%)	Present study (%)
Pain	100	100	100	100	100
Anorexia	73	60	61	69.6	77.46
Nausea/Vomiting	87	74	67.5	84	80.28
Fever	83	76	34.3	68	87.32
Tenderness in RIF	100	100	95.9	89.6	100
Rebound tenderness	74	72	69.5	72.8	59.15
Leucocytosis	77	71	72.5	66.4	74.65

The correlation of modified Alvarado score with the outcome was not statistically significant in the present study suggesting that the success or failure of the conservative treatment could not be predicted by the patients modified Alvarado score at the time of presentation. Therefore patients with a higher modified Alvarado score can be conserved with failure or recurrence rates similar to those having a lower Alvarado score. Any study observing such correlation could not be found in the literature.

Majority of patients i.e. 85.50% had positive findings on ultrasonography of abdomen and pelvis suggestive of uncomplicated appendicitis. The sensitivity and specificity of ultrasonography for acute appendicitis in the literature are mentioned in (Table 7).

71 patients of uncomplicated acute appendicitis were managed conservatively. Clinical diagnosis was supported by Modified Alvarado score of ≥5 and ultrasonography to achieve a higher diagnostic accuracy. To exclude complicated appendicitis, patients with appendicular lump or features of peritonitis were excluded. 75.65% were successfully managed conservatively with no appendectomy or recurrence in a follow-up duration of 6 months. This was consistent with the literature (Table 8).

Table 7: Sensitivity and specificity of ultrasonography in literature.

Authors	Sensitivity %	Specificity %
Douglas et al[30]	94.7	88.9
Pickuth et al[31]	87	74
Poortman et al[32]	79	78
Srivastava et al[33]	77.6	75
Van Randen et al [34]	76	95
Terasawa et al[35]	86	81
Dsouza et al[28]	92.15	88.9

Treatment failure was seen in 14.08% patients in whom appendectomy was performed due to deterioration of clinical status within first 48 hours. Treatment failure rate in literature ranges from 5% to 51.98% as shown in the Table 8. High treatment failure rate (51.98%) in study by Hansson et al in multi-centric trial were dependent on individual judgments or preferences of surgeons than to clinical status where in 45 patients, surgeons could not provide a reason for their conversion to surgery.

Recurrence was seen in 13.11% patients in whom, appendicitis had resolved by antibiotic treatment on primary admission, after a median duration of 2 months within a follow-up duration of 6 months. This was consistent with the literature where studies reported recurrence rate from 9.4% to 24.3% with a follow-up of minimum 1 year as shown in the Table 8. In the present study, all the cases of treatment failure and majority of recurrences, appendectomy was done and the diagnosis of acute appendicitis was confirmed histopathologically. One patient of recurrence was managed conservatively as the patient was not willing for surgery.

Table 8: Outcome of conservative treatment in literature.

Author/ Year	Styrud et al[36] 2006	Turhan et al[11] 2006	Hansson et al[11] 2009	Malik et al[17] 2009	Vons et al[18] 2011	Park et al[19] 2014	Present 2016
Antibiotic	IV: cefotaxime 2 g q12, tinidazole 0.8 g qd for at least 2 days; PO: ofloxacin 200 mg bid, tinidazole 500 mg bid for 10 days	IV: ampicillin 1 g qid, gentamycin 160 mg qd, metronidazole 500 mg tid; PO: 10 days	IV: cefotaxime 1 g bid, metronidazole 1.2 g qd at least 1 day; PO: ciprofloxaCin 500 mg q12h, metronidaZole 400 mg q8h for 10 days	IV: ciprofloxacin 500 mg q12h, metronidazole 500 mg q8h for 2 days; PO: ciprofloxacin 500 mg bid, tinidazole 600 mg bid for 7 days	IV amoxicillin plus clavulanic acid (3 g per day) to those with nausea or vomiting, and orally to all othersfor 2 days. PO: same for 8 days	IV second-generation cephalosporin and metronidazole for 48 h and fasting for 24 h. PO: for 2 days	IV: ceftriaxone 1 g bid, metronidazole 500mg tds for 2 days; PO: ciprofloxacin 500 mg q12h, tinidazole 600 mg bid for 7 days
Follow-up period	1 year	1 year	18 months	1 year	1 year	1 year	6m
Number of cases (n)	128	107	202	40	120	119	71
Treatment failure	15 (11.7%)	11 (10.28%)	105 (51.98%)	2 (5%)	13 (10.8%)	9 (7.6%)	10 (14.08%)
Recurrence	16 (14.1%)	9 (9.4%)	14 (14.4%)	4 (10.5%)	26 (24.3%)	14 (12.7%)	8 (13.11%)
Median duration of recurrence	4m	-	One third within 10 days and two thirds between 3-16 months	8 m	4 m	-	2m
Successful conservative treatment on completion follow-up	97 (75.78%)	87 (81.31%)	83 (41.09%)	34 (85%)	81 (67.5%)	96 (80.67%)	53 (75.65%)

The general assumption based on the mechanical obstruction theory that in the absence of surgical intervention the acute appendicitis often progresses from uncomplicated to complicated appendicitis has been the basis of advocating emergency appendectomy since a century.[1,2] Recent studies have shown that complicated and uncomplicated appendicitis have different pathophysiology. This justifies conservative management with antibiotic therapy for some initially uncomplicated cases.

Conservative treatment seems feasible alternative to appendectomy in management of uncomplicated acute appendicitis with acceptable low treatment failure and recurrence rate.

Limitations of this study

This was a hospital based longitudinal study with a small number of cases. Diagnosis of appendicitis was mainly clinical supported by modified Alvarado score and ultrasonography. Use of computed tomography increases accuracy of diagnosis of acute appendicitis; however this could not be done considering the affordability of the patients.

Follow up period was short (6 months), which is short period for evaluation of recurrence.

Large scale randomized control trials are required to compare the conservative and surgical treatment of appendicitis in terms of treatment efficacy, complication rates, cost-analysis etc.

CONCLUSION

The present study evaluated conservative treatment in uncomplicated acute appendicitis and was conducted in a tertiary care academic hospital for a period of 2 years. Majority of cases, first attack of uncomplicated acute appendicitis can be treated successfully by conservative treatment thereby avoiding appendectomy and its associated morbidity and mortality. However, conservative treatment requires monitoring and repeated re-evaluation of clinical condition of the patients to identify failure in improvement of clinical status, which needs to be treated promptly by surgery. Treatment failure on primary admission as well as the short- term recurrence after conservative treatment is low and acceptable.

Further studies are needed to guide the selection of patients who are appropriate for non-operative management. Appendectomy following a trial of non-operative management may come to be viewed not as a complication or failure, but as another step in the management algorithm of acute appendicitis. This algorithm may ensure that only those patients needing an operation are exposed to the inherent risks, with the potential to decrease the overall morbidity and mortality related to the disease.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Gedam BS, Gujela A, Bansod PY, Akhtar M, Singh K. Study of conservative treatment in uncomplicated acute appendicitis. Int Surg J 2017;4:1409-16.