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# Antibiotic Treatment of Uncomplicated Acute-appendicitis in Children

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Objective:** To evaluate the safety and outcome of antibiotic treatment of uncomplicated acute appendicitis in children. Our main outcomes were the response to conservative treatment, complications during this treatment and short-term recurrence of appendicitis in initial responders to treatment.
**Methods:** We used antibiotics instead of surgery to treat 70 children aged 4-18 years who were diagnosed with acute uncomplicated appendicitis (AUA). Those not responding or who show deterioration were shifted to appendectomy. We followed up our cases who had successful NOM for any relapse at one week, 6 weeks, 3months then 6months.
**Results:** The success rate of NOM in our series was 84.3%. Most cases showed improvement of both clinical & laboratory findings on 2nd day of management. Eleven cases (15.7 %) failed NOM and were operated laparoscopically. Readmission for cases who had a relapse occurred in 3 cases, one case relapsed after 6 weeks of discharge, and was operated by laparoscopy. Another 2 cases were readmitted with after 3 months. They were managed conservatively again, and responded to NOM.
**Conclusion:** Using antibiotic management of AUA among children aged 4-18 years, proved to be safe, effective and have a low rate of complications. It reduced the negative appendectomy rate to 1.43%. It is associated with a low relapse rate within 6 months and significantly reduces the treatment cost.

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## 1. INTRODUCTION

Appendectomy is considered the gold standard treatment for acute appendicitis by most surgeons either open or laparoscopic. However, an alternative approach to treat acute uncomplicated appendicitis in children with antibiotics and without an appendectomy has established a tremendous momentum in the past few years [1,2]. The successful use of antibiotics in treating intra-abdominal infections such as diverticulitis has aroused renewed interest in the nonoperative management of appendicitis [3].

Despite both open and laparoscopic appendectomy being regarded as low-risk and effective procedures, operative management may still be associated with risks or complications. These risks may be associated with general anesthesia or surgical complications such as hemorrhage, surgical site infection, injury to surrounding structures, ileus, adhesive small bowel obstruction or the potential need for reoperation [3].

While nonoperative treatment strategy can avoid these troubles, it requires strict observation of patients to reduce the probability of progression of the course of acute uncomplicated appendicitis and occurrence of complications [4].

There has been an increased interest in the conservative management of appendicitis over the last 20 years [5].

### 1.1 Aim of the Work

The purpose of this study was to evaluate the safety and outcome of antibiotic treatment of uncomplicated acute appendicitis in children. Our main outcomes were the response to conservative treatment, complications during the course of this treatment and short-term recurrence of appendicitis in initial responders to treatment.

## 2. PATIENTS AND METHODS

This prospective study was conducted on children from 4 to 18 years with acute right lower quadrant pain, with a diagnosis of uncomplicated acute appendicitis who were managed at the Pediatric Surgery Unit, Tanta University Hospitals, Egypt in the period between Feb 2021 till Feb 2022. We included children with PAS ≥ 7 with or without positive USS for acute appendicitis and children with PAS: 4-6 with positive USS for acute appendicitis. We excluded Children with evidence of complicated appendicitis, cognitive disability, chronic abdominal pain, immune compromised children or those previously treated conservatively from suspected appendicitis, PAS ≤ 3, PAS 4−6 with negative USS.

Children were assessed clinically using PAS score, laboratory investigations including total and differential leucocytic count and CRP, and USS.

### 2.1 Conservative Treatment

Conservative treatment consisted of: Nothing per mouth if the patient had GI symptoms like anorexia, nausea or vomiting. Oral fluids were allowed if the patient could tolerate. IV fluids were given according to age and weight. Parenteral Third generation cephalosporins were given in a dose of 100 mg/kg BW/day in two divided doses together with Parenteral metronidazole in a dose of 7. 5mg/kg every 8 h. Analgesics were used as required to control pain on a dose / weight basis, starting with paracetamol and adding NSAIDs if needed. Once the child is well clinically and tolerating oral intake, antibiotics are continued with oral third generation cephalosporins e.g., cefdinir 8mg/kg/day in orally and oral metronidazole 30 mg/kg in three divided doses for 5 days.

At least twice daily follow up of temperature, pulse rate, course of pain and abdominal examination, daily total & differential leucocytic count and CRP, and USS re-examination after 48h from admission.

Deterioration of symptoms and signs of appendicitis or persistence o for a maximum of 3 days is an indication of appendectomy either open or laparoscopic according to available resources. Any complications during the course of treatment were reported. The resected appendix was sent for histopathology.

Patients were discharged after improvement of clinical and laboratory data on a 5 days course of oral antibiotic combination. They were instructed about alarming symptoms that may need readmission or surgical intervention.

The first follow-up visit was planned at one week after hospital discharge then at 6 weeks, 3 months, and 6 months, in the outpatient clinic. During the 1st 2 follow up visits, patients were evaluated clinically. Laboratory or imaging investigations were ordered when needed. Any relapses or readmissions were reported.

## 3. RESULTS

Our study included 70 patients with a mean age of 12.13 ± 3.89, 54.29 % of them were males and 45.71 % were females.

Analysis of the incidence of symptoms & signs showed that nausea presented in 50 children (40 of successful NOM group and 10 of failed NOM group, vomiting presented in 37 children (27 of successful NOM group and 10 of failed NOM group), anorexia in 58 (50 of successful NOM group and 8 of failed NOM group), 65 had tender McBurney point on percussion ( 54 of successful NOM group (91.5%) and 11 of failed NOM group (100%), 59 had cough tenderness (49 of successful NOM group (83.05%) and 10 of failed NOM group (90.9%), 45 have fever ≥ 38 (35 of successful NOM group (59.3%) and 10 of failed NOM group (90.9%). The duration of symptoms ranged from 1-7 days (mean 2.5-3 days). Migration of pain was found in 41 (31 of successful NOM group (52.5%) and 9 of failed NOM group (81.81%).

As regards laboratory data; Leucocytic count more than 11000 was found in 34 (27 of successful NOM group (45.76%) and 7 of failed NOM group (63.63%). There was gradual return of leucocytic count back to normal values within two days of NOM. Ten patients at admission had a normal CRP count, all of them fell in the successful NOM group, while 60 children had a CRP count more than 6 (49 of Successful NOM group and all patients of Failed NOM group). There was gradual decrease of CRP ratio in studied patients especially in the successful NOM group while 4 patients of Failed NOM group showed a decrease of CRP count without improved clinical signs.

On admission, there was no USS signs of AA in 2 patients, 42 patients showed signs of AA (31 in the successful NOM group and 11 in the failed NOM group), while a rim of intraperitoneal free fluid with mesenteric lymphadenitis was found in 26 patients. On follow up USS after 48 h, no signs of appendicitis were found in 40 children, 10 children showed signs of acute appendicitis while 20 children showed a rim of FF with mesenteric lymphadenitis.

According to PAS score calculation, we found that on day zero (admission day), 9 children had a score 4-6 with positive US signs of AA and 61children had a score 7-10 (50 of successful NOM group and 11 of failed NOM group). With follow up, by the fourth day of NOM 59 children improved with a PAS score of 3 or less and were discharged as a successful NOM group, 10 children had score 7-10, failed conservative management and 9 of them were operated by laparoscopy & one case was operated by open surgery.

examination of the removed appendix, showed that, 2 cases had acute catarrhal appendicitis, while 9 appendices showed acute suppurative appendicitis while one case had a normal appendix who was failed NOM with persistent of symptoms and signs with PAS score 7 and negative uses.

After 6 weeks, one case of initially successful NOM was readmitted and failed to respond to NOM for three days and was operated laparoscopically. In the next 3 months, two cases were admitted and responded to NOM.

## 4. DISCUSSION

The traditional treatment of AA is either conventional open or laparoscopic appendectomy. However, some reports claimed that cases of acute uncomplicated appendicitis (AUA) may be conservatively managed using only antibiotics and analgesia with rest of gastrointestinal tract if needed [6].

The diagnosis of pediatric AA remains challenging. Some clinical scores have evolved to help diagnosis of AA. The ideal clinical score could accurately predict patients who need immediate operative care and those who may be postponed to have further investigations or observation [7].

PAS is a commonly used score in children. Children with suspected AA were stratified into low-risk group (score < 3), intermediate-risk (score 4-6) and high-risk (score 7-10) [8].

Minneci et al showed that children with successful NOM had fewer disability days and returned to school more quickly. They concluded that NOM is safe and maintains a good quality of life [9].

While planning for NOM, most parents in our study were convinced with this line of treatment. Some parents were initially afraid and hesitated due to the exaggerated fear of rupture of the appendix. We explained them all the steps of NOM including the advantages and disadvantages. Highlighting the meticulous observation, which would detect any deterioration or non-response at an early stage before complications develop. At the end parents were convinced and accepted the plan of NOM. They were satisfied with the results especially those who had a successful NOM.

During our series we performed only 11 laparoscopic appendectomies out of 70 patients. They passed smoothly without any operative or postoperative complications. While children who underwent NOM (84.3%) returned to normal activities after a mean of 5 days.

Georgiou et al. reported a success rate of NOM in 97% of all included children. There was no statistical significance of the rate of complications in both NOM group and failed NOM group [10].

Our study included 70 children aged 4-18 years, diagnosed with AUA. Lee et al. included 51 children aged 3–17 years [11]. Steiner et al. Included 362 children with an age range of 3–16 years [12]. We think that children below 4 years will not be able to accurately express some symptoms specifically migrating pain.

Diagnosis was based on clinical examination and laboratory investigations; expressed as the PAS score in addition to USS.. Lee et al. included children with a PAS score of ≥ 6. Steiner et al. Included children with a PAS Score of ≥ 7 [12].

All operated cases were had a score of more than 7. While patients who had a score of 4-6 were a gray zone and needed US to confirm diagnosis, all of them improved with NOM. We changed our trend after completing the study by managing those children at home, while children with score 7-10 need admission and close follow up.

In our study the duration of symptoms was 1-7 days with a mean of 2.5 days in children who had successful NOM and 3.5 days in patients who failed NOM. However, there was no statistical significance between success of treatment and duration of symptoms. Lee et al excluded patients with symptoms ≥ 5 days [11]. Steiner et al. excluded cases that had duration of symptoms ≥36 h [12]. Isani et al., reported that the success of NOM was not affected by the duration of symptoms whether > or < 4 days. Moreover, the duration of symptoms didn't relate to the readmission rate, hospital stay or the development of complications [13].

In NOM We depended mainly on intravenous (IV) 3rd generation cephalosporin in a dose of 100 mg/kg BW/day in two divided doses and metronidazole in a dose of 7.5mg/kg every 8h. Shifting to oral 3rd generation cephalosporin and oral metronidazole at home for 5 days after discharge. Lee et al, used IV ceftriaxone and metronidazole and discharged his patients on oral amoxicillin/clavulanic acid, while Steiner et al used ciprofloxacin and metronidazole during conservative management and discharged their patients on ciprofloxacin and metronidazole or cefdinir and metronidazole for 10 days [11,12]. Minneci et al. prescribed IV piperacillin/ tazobactam or ciprofloxacin and metronidazole for their patients for 3 or 4 days of in hospital treatment. Then oral amoxicillin/ clavulanic acid or ciprofloxacin and metronidazole to complete10 days after discharge [14]. Svensson et al. used IV meropenem and metronidazole regimen in hospital for at least 2 days. As soon as the children were tolerating oral intake, they were given oral ciprofloxacin and metronidazole for a total of 10 days treatment [15].

Analgesics were prescribed according to severity of pain, starting with paracetamol. If there was still pain a non-steroidal antinflammatory analgesic (e.g. ketorolac) was added. We didn't need opioid analgesics in any patient. Lee et al, and Steiner et al used analgesia with their patients when needed, they used non-steroidal anti-inflammatory drugs [11,12].

Oral intake was restricted only in patients who had sever GIT symptoms such as vomiting, abdominal colics and/or anorexia for at least 24h. Once the patient can tolerate oral intake, feeding was gradually introduced. Starting with fluids then semi solids and full oral feeding before or after discharge. In Lee et al and Steiner et al studies, oral intake was restricted for at least 48h. Once patients tolerated they were shifted to oral intake and oral antibiotics [11,12]. Svensson et al, and Minneci et al restricted oral intake during the first 24h of management. They discharged patients when they became afebrile for at least 24h, abdominal pain free, and tolerated oral intake [14,15].

During NOM, we stressed on frequent examination and meticulous observation of patients, daily LC & CRP were performed; all to detect any deterioration or complications early. NOM was practiced for a maximum 3 days, if patients didn`t improve after this period, or if deterioration occurred before that time limit, we decided to operate. During Lee et al study, a patient showing signs of clinical worsening or failure to show clinical improvement within 24 hours was considered treatment failure and resulted in prompt laparoscopic appendectomy [11].

In Mahida JB, et al study Patients showing improvement, as decreased pain and tenderness were advanced on their diet. Those patients, who continued to show improvement and were tolerating a regular diet at 24 h after initiation of IV antibiotics, then started oral antibiotics and then they passed smooth. Conversely, patients who worsened clinically as increasing pain or tenderness, or showing new or persistent signs of systemic inflammatory response, or persistent nausea or vomiting were confirming failure of nonoperative management. All patients who had failure of nonoperative management underwent urgent appendectomy [16]. Max Knaapen et al reported that appendectomy was decided once there was deterioration of symptoms and signs [17].

The mean duration of hospital stay in our study was 2.5 days in patients who had successful NOM and 3.5 days in those who failed NOM. Max Knaapen et al reported that the median duration for hospital stay was 2.5 days [17]. While In Jeff Armstrong et al study the mean duration of hospital stay in patients who succeeded NOM was 1.5 days and 1.3 days in operated patients [18].In Minneci et al, study the mean duration of hospital stay was 37 h in NOM group and 20 h in the operated group [15].

In our study we had a high initial success rate of NOM of 84.3 % and a low relapse & readmission rate within 6 months of 5.1 %. In a meta-analysis of randomized controlled trials including 5 studies and 1430 patients with uncomplicated acute appendicitis, the success rate of NOM during the initial hospitalization was 84%. Readmission for recurrent appendicitis requiring treatment occurred in another 21% of patients during the subsequent year of follow-up. Overall, treatment with antibiotics was associated with a 39% risk reduction in complications compared with those undergoing appendectomy. The main drawback of this meta-analysis study was inclusion of adult patients only [19].

We operated 11 patients (15.7 %) after failure of conservative management, all by laparoscopy except for one open case. One patient out of 59 initially treated patients NO was readmitted after 6weeks during the follow up period and was operated by laparoscopy. Histopathological examination of resected appendices revealed that only one case showed no signs of inflammation. This means that only one case out of 70 cases had a negative appendectomy (1.43 %), as based on conventional paradigm, all 70 cases should have been appendectomized. In Lee et al, study the recurrence rate for patients with initial success following non-operative therapy was 26% (9/35 patients) with a median time to recurrence of 2 months. One of the nine recurrences was successfully treated with another course of antibiotics, and the remaining 8 were treated with laparoscopic appendectomy. For those patients who underwent a laparoscopic appendectomy, 1 was treated at an outside hospital and 7 returned to their institution and were found to have uncomplicated appendicitis. Overall, 26 of 51 patients who underwent non operative therapy (51%) avoided appendectomy during their study period [11]. In Bachur RG, et al study NOM cases, forty-six percent had a subsequent appendectomy within the first year. They concluded that there was a potential increase in the total number of cases of AA due to the implementation of NOM [19]. From our study, it is clear that antibiotic treatment of AUA can reduce the rate of negative appendicectomy [20].

A cording to total cost in our series, there was a higher total cost of operated cases compared to NOM patients. The median cost in NOM children was 4800 (3000 – 6000), while that of operated cases was 8300 LE (7000 – 9000). The randomized trial of Sippola et al revealed that the overall costs were 1-6 times higher in the children subjected to appendectomy when compared with children who had successful NOM [21].

## 5. CONCLUSION

Using antibiotic management of AUA among children aged 4-18 years, proved to be safe, effective and have a low rate of complications. It reduced the negative appendectomy rate to 1.43%. It is associated with a low relapse rate within 6 months and significantly reduces the

treatment cost. With parents counseling, the parents can accept the NOM and had their fear alleviated. However, a controlled randomized trial on a bigger number of cases is needed to validate these results.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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