

ORIGINAL RESEARCH

Non-operative treatment versus appendectomy for acute non-perforated appendicitis in children¹Dr. Mohit Sharma, ²Dr. Varsha Choudhary, ³Dr. Uzma Padwal,⁴Dr. Shyam Kumar Gupta, ⁵Dr. Ratnakar Sharma^{1,2,3}Resident, ⁴Assistant Professor, ⁵Professor, Department of General Surgery, GMC, Jammu, India**Corresponding author**

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Abstract**Objectives:** To compare the results of surgical care versus non-operative treatment (NOT) with antibiotics for childhood appendicitis.**Methods:** From September 2021 to September 2022, this study was conducted in the paediatric surgery department. After receiving informed consent, patients were randomly assigned to one of two groups, making up the 180-person sample size. All kids between the ages of 5 and 15 who had a paediatric appendicitis score (PAS) of 7 or lower were included. Patients having appendicular masses, peritonitis, previous abdominal surgery, or intra-abdominal abscess were disqualified from participating. Children in the NOT group (Group A) received intravenous Meropenem and Metronidazole during 48 hours, followed by 7 days of oral antibiotics. Children in Group B had appendicectomies. If there was abscess formation, peri-appendiceal fluid collection on ultrasonography, development of peritonitis, or recurrence of appendicitis, failure of NOT was labelled.**Results:** The mean ages in groups A and B were 9.56 ± 1.8 years and 10.11 ± 1.8 years, respectively. There were 57 female patients and 123 male ones. Group B had a perfect success rate. 75 patients (83.3%) who received NOT (Group A) had successful outcomes, while 15 patients (16.7%) had failure. Ten patients came within six months, five of whom required surgery within 48 hours and all of whom had appendicoliths. Failure of NOT was associated with increased levels of C reactive protein (p value <0.04) and total leukocyte count (p value <0.0001).**Conclusions:** The success rate of NOT in this study was 84%, hence a trial of NOT in children with uncomplicated appendicitis should be taken into consideration.**Keywords:** Acute appendicitis, Children, Non-operative treatment, Appendectomy**Introduction**

Acute appendicitis has a 6.7-8.6% lifetime risk, according to estimates. [1,2] Despite the second decade having the highest frequency, 11.4% of children in emergency rooms have acute appendicitis. [3] Appendectomy is regarded as the gold standard treatment for appendicitis. [4] Because appendectomy is an intrusive treatment, it disrupts a child's everyday routine. [5] This curative treatment has reported complication rates of 5% to 10%, with major problems occurring in 1% to 7% of patients. [2,3,6]

The hospital stay and expense of care are reduced by non-operative treatment (NOT), which combines a wait-and-see strategy with medical care and reserves appendectomy for only serious appendicitis. [6] NOT causes lymphoid follicles to recede, which reduces blockage

and irritation. [7] By using medical care, surgery and its complications can be avoided, reducing the morbidity associated with acute appendicitis in children. More randomised controlled studies (RCT) are required to determine the effectiveness of NOT in children. [8,9] In a recent meta-analysis, Sonia Maita and co-authors calculated the success rate of NOT as 92% after reviewing the published literature. In addition, they stated that 16% of people eventually had an appendectomy due to recurrent appendicitis. [9] In a prior meta-analysis, Huang L. et al. reported a 90.5% success rate of NOT for acute uncomplicated appendicitis. [10] Bachur and co-authors retrospectively analysed data from a number of hospitals in the United States and found that NOT was linked to more emergency room visits and hospitalisations, and that 46% of patients underwent appendectomy in the following year, necessitating the need for additional multi-centric RCTs. [11] Even though some kids required readmission owing to recurrent appendicitis, total costs were lower in cases of NOT, and it is regarded as a cost-effective treatment option with minimal hospital burden. [6] The goal of this study was to compare the results of NOT and appendectomy in children with uncomplicated appendicitis. Secondly, we sought to assess the elements that contributed to the conservative approach to non-perforated appendicitis' failure. The justification was that there were no local clinical trials available to demonstrate the effectiveness of non-operative antibiotic treatment in children, and there were very few foreign trials. [8-10]

Materials and Methods

Between September 2021 and September 2022, this study was conducted in the paediatric surgery department. At a 5% level of significance, an 80% power of the test, and an estimated success frequency in the NOT group of 89.6% and operative therapy of 100%, a sample size of 180 (90 in each group) was computed. Purposive non-probability sampling was the sample method.

Every child between the ages of 5 and 15 who was admitted to the paediatric surgery emergency unit and had a paediatric appendicitis score (PAS) of >7 or higher was included. Patients with a prior history of abdominal surgery, a prior admission for NOT, clinically diagnosed peritonitis, appendicular mass, ultrasound-confirmed abscess formation, complex peri-appendiceal fluid, or appendicolith, and/or elevated C-reactive protein (CRP) levels were disqualified from the study.

All study participants were split into two groups at random, using computer-generated numbers, for non-surgical treatment (Group A) and operative treatment (Group B), following parental or guardian approval. Each patient was assessed, and pertinent information was gathered and recorded using the pre-designed pro-forma. At the time of admission, the following factors were recorded: age, length of symptoms, body temperature, C-reactive protein (CRP), total leukocyte count (TLC), neutrophil concentrations, ultrasound (USG) findings, and PAS score. Meropenem (10 mg/kg/dose intravenous infusion given 8 hours apart) and metronidazole (20 mg/kg/day intravenous split doses given 8 hours apart) were given intravenously to children in the nonoperative therapy group for at least 48 hours.

The treatment was modified to oral ciprofloxacin (10 mg/kg/dose twice daily) and metronidazole (20 mg/kg/day two divided doses) for additional 8 days until the child began to tolerate oral intake and clinically improved. A modified McBurney's incision and muscle splitting were used in Group B's open appendectomy along with three doses of antibiotics. Muscle cutting and Rutherford Morrison extension were only used in cases of complicated appendicitis. Intravenous antibiotics were continued for 5 days exclusively in cases of perforation. According to the treatment plan, all patients received supportive care along with routine vital sign monitoring. It was observed whether complications were getting better or worse.

The necessity for surgery (due to worsening symptoms assessed by history, physical examination, and repeat USG) within 48 hours or recurrence of appendicitis within six months was regarded as failure of non-operative treatment if any one of the following was seen. Both groups' patients were released once they could tolerate a light food, were awake and mobile for 24 hours, and received enough pain treatment from oral analgesics. Six months were spent on the follow-up.

Version 23 of SPSS was used to analyse the data. Age, weight, temperature, TLC, neutrophils, PAS, and CRP are examples of quantitative variables for which mean and standard deviation have been determined. For qualitative variables like gender and success/failure, frequency and percentages were determined. The effectiveness of two different treatment regimens was compared using the chi square test. P values under 0.05 were considered statistically significant.

Results

180 patients in all were enrolled. The study included 57 (31.7%) females and 123 (68.3%) boys. There were 25 (27.8%) girls and 65 (72.2%) boys in Group A (n=90). There were 32 (35.6%) females and 58 (64.4%) boys in Group B (n=90). The mean and standard deviation of the following characteristics for both groups and all patients who were enrolled are provided in Table I: age, weight, duration of symptoms, temperature, TLC, neutrophils, CRP, and PAS.

When non-operative treatment (NOT) with antibiotics was compared to surgical treatment for children with uncomplicated appendicitis, it was found that group A's success rate was 83.3% (n=75), while group b's success rate was 100% (n=90) (p value 0.0001). 15 individuals (16.7%) experienced NOT failure. Ten patients came within six months, while five required an appendectomy within 48 hours and all (100%) had an appendicolith. These 10 patients had neither an appendicolith nor a perforation. Stratification for effect modifiers showed that NOT was successful in 54 (n=65) males and 21 (n=25) girls. A NOT failure was detected in 1 out of 9 students between the ages of 5 and 6 (p value <0.5), 3 out of 26 students between the ages of 7 and 9 (p value <0.08), and 11 out of 55 students between the ages of 10 and 15 (p value <0.5). (p value < 0.001). Only one out of 19 patients (p value <0.18; failure of conservative treatment) presented with symptoms lasting less than 12 hours, compared to 8 out of 57 patients (p value <0.01) who presented with symptoms lasting between 12 and 24 hours and 6 out of 14 patients (p value < 0.06; failure of conservative treatment) who presented with symptoms lasting more than 24 hours (p value < 0.007).

Age, gender, the length of the symptom, PAS scores, and failure or success of NOT were not associated with one another or correlated, according to logistic regression. As shown in Table II, the mean difference between TLC and CRP was statistically significant for the success or failure of NOT.

Table I: Mean and standard deviation of baseline variables

Variables	Group A (n=90)	Group B (n=90)	Total (n=180)
Age (years)	9.56±1.82	10.11±1.83	9.84±1.84
Duration of symptoms (hours)	21.68±10.6	18.98± 11.82	20.33±11.27
Temperature (0 F)	99.84±1.29	99.87±1.28	99.86±1.28
TLC (10 ⁹ /l)	11311.11±2696.83	11322.22±2697.6	11316.67±2689.68
Neutrophil (cells/μl)	63.87±13.06	63.53±13.02	63.7±13.01
CRP (mg/dl)	7.77±1.8	7.79±1.76	7.78±1.75
PAS	7.74±0.9	7.79±0.92	7.77±0.89
Weight (kg)	17.52±4.62	18.47±5.11	17.78±4.89

Table-II: Comparison of quantitative variables in successful or failed non-operative treatment (Group A).

Variables	Success of not	Mean \pm Standard deviation	P value
Age (years)	Yes (n=75)	9.46 \pm 1.81	0.24
	No (n=15)	10.07 \pm 1.83	
Duration of symptoms (hours)	Yes (n=75)	20.83 \pm 10.66	0.15
	No (n=15)	25.13 \pm 9.08	
TLC (10^9 /l)	Yes (n=75)	10760 \pm 2347.2	0.000005
	No (n=15)	14066.7 \pm 2711.5	
CRP (mg/dl)	Yes (n=75)	7.6 \pm 1.8	0.04
	No (n=15)	8.6 \pm 1.24	
PAS	Yes (n=75)	7.67 \pm 0.76	0.58
	No (n=15)	7.8 \pm 1.15	

Discussion

This study found that over 84% of children with simple appendicitis were successfully managed conservatively, avoiding negative appendectomy and operation related sequelae [2]. Fifteen patients experienced NOT failure. Due to growing tenderness, five underwent appendectomy in the following 48 hours. Each instance's histopathology indicated an acute appendicitis, and each case also contained an appendicolith. In the following six months, ten individuals came with recurrent appendicitis. Histopathology confirmed that all ten patients had appendicitis but no appendicolith. Group B experienced a 100% success rate (p value 0.0001). The appendix was perforated or gangrenous in seven (7.8%) of the individuals. Adhesion blockage was evident in one patient (1.1%) after six months of follow-up.

Svensson JF and colleagues' single published pilot RCT randomly assigned 50 patients (26 underwent appendectomy procedures, and 24 received conservative management), and they reported initial failure in 2 (8.3%) of those patients. However, later, 6 more patients in the conservative group underwent appendectomy procedures. According to their research, just one patient with recurrent appendicitis had histology that was positive, making the success rate of NOT around 92%. [12] In prospective research, 115 (58%) of the 197 children with simple appendicitis required no surgical intervention, while 82 (42%) required an appendectomy within 48 hours and only 2.5% experienced perforation. [13] A multi-centric examination of over 4000 kids found that NOT frequently failed, and that among patients who were first treated with it, 46% required appendectomy within a year and 14% had perforations. [11] According to Minneci PC et al., the success rate of non-operative treatment is 94.6% at the time of discharge, 89.2% at 30 days, and 75.7% at 1 year. [6] Similar to the previous trial, 75% of NOTs were successful. [14] A locally published prospective study on adults found that over the course of a year, about 21 (22%) patients failed to respond to NOT. [15]

According to Gorter and colleagues' systematic review, between 62 and 81% of children did not require appendectomy. [16] Maita et al's meta-analysis revealed that despite an initial 92% success rate, 16% of patients would require appendectomy. [9] Another meta-analysis found that 97% of patients experienced initial success, but 14% later experienced recurrent appendicitis. [8] These meta-analyses all centre on the requirement for further RCTs and extensive follow-up. According to our knowledge, this is the second published RCT.

The potential for NOT to fail in long-term follow-up is another crucial factor to take into account. Children who had follow-up after five years showed that 46% had appendectomies and 14% had recurrent appendicitis, as confirmed by histopathology. [17] Recurrence rates of 14%⁸ and 16%⁹ have also been reported in the past. Despite the possibility of recurrence, NOT should be given to certain children because the appendix's preservation boosts immunity. Only a few studies have demonstrated that the appendix is a source of pluripotent cells that may aid in gut repair and assist in the recolonization of typical commensals following diarrhoea. [18,19] This study's primary limitations include its single-centered design and brief follow-up period. Additionally, because very few patients underwent appendectomies, not all histology reports were followed up.

Conclusion

The success rate of NOT in this study was 84%, hence a trial of NOT in children with uncomplicated appendicitis should be taken into consideration. The conservative course of treatment failed due to marked leukocytosis and/or C-reactive protein levels and the existence of an appendicolith.

References

1. Almaramhy HH. Acute appendicitis in young children less than 5 years: Review article. *Ital J Pediatr.* 2017;43(1):15.
2. Hall NJ, Eaton S, Abbo O, Arnaud AP, Beaudin M, Brindle M, et al. Appendectomy versus non-operative treatment for acute uncomplicated appendicitis in children: study protocol for a multicentre, openlabel, non-inferiority, randomised controlled trial. *BMJ Paediatr Open.* 2017;1.
3. Scott A, Lee SL, DeUgarte DA, Shew SB, Dunn JCY, Shekherdimian S. Nonoperative Management of Appendicitis. *Clin Pediatr.* 2018;57(2):200-204.
4. Osifo OD, Ogiemwonyi SO. Appendicitis in children: An increasing health scourge in a developing country. *Pak J Med Sci.* 2009;25(3):490-495.
5. Minneci PC, Sulkowski JP, Nacion KM, Mahida JB, Cooper JN, Moss RL, et al. Feasibility of a nonoperative management strategy for uncomplicated acute appendicitis in children. *J Am Coll Surg.* 2014;219(2):272-279.
6. Minneci PC, Mahida JB, Lodwick DL, Sulkowski JP, Nacion KM, Cooper JN, et al. Effectiveness of patient choice in non-operative vs surgical management of pediatric uncomplicated acute appendicitis. *JAMA Surg.* 2016;151(5):408-415.
7. Abes M, Petik B, Kazil S. Non-operative treatment of acute appendicitis in children. *J Pediatr Surg.* 2007;42(8):1439-1442.
8. Georgiou R, Eaton S, Stanton MP, Pierro A, Hall NJ. Efficacy and safety of nonoperative treatment for acute appendicitis: a meta-analysis. *Pediatrics.* 2017;139(3):e20163003.
9. Maita S, Andersson B, Svensson JF Wester T. Nonoperative treatment for nonperforated appendicitis in children: a systematic review and meta-analysis. *Pediatr Surg Int.* 2020;36:261-269
10. Huang L, Yin Y, Yang L, Wang C, Li Y, Zhou Z. Comparison of antibiotic therapy and appendectomy for acute uncomplicated appendicitis in children: a meta-analysis. *JAMA Pediatr.* 2017;171(5):426-434.
11. Bachur RG, Lipsett SC, Monuteaux MC. Outcomes of non-operative management of uncomplicated appendicitis. *Pediatrics.* 2017;140(1):e20170048.
12. Svensson JF, Patkova B, Almström M, Naji H, Hall NJ, Eaton S, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. *Ann Surg.* 2015;261(1):67-71.

13. Caruso AM, Pane A, Garau R, Atzori P, Podda M, Casuccio A, et al. Acute appendicitis in children: not only surgical treatment. *J Pediatr Surg.* 2017;52(3):444-448.
14. Armstrong J, Merritt N, Jones S, Scott L, Butter A. Non-operative management of early, acute appendicitis in children: is it safe and effective? *J Pediatr Surg.* 2014;49(5):782-785.
15. Memon GA, Jamali KS, Shah KA, Rehman H, Leghari S, Balcoh S. Outcomes of antibiotics as primary therapy in uncomplicated acute appendicitis at PUMHS Nawabshah. *J Dow Uni Health Sci.* 2017;11(1):6-10.
16. Gorter RR, The SML, Gorter-Stam MAW, Eker HH, Bakx R, van der Lee JH, et al. Systematic review of nonoperative versus operative treatment of uncomplicated appendicitis. *J Pediatr Surg.* 2017;52(8):1219-1227.
17. Patkova, B, Svenningsson, A, Almström, M, Eaton S, Wester T, Svensson, JF. Nonoperative Treatment Versus Appendectomy for Acute Nonperforated Appendicitis in Children. *Ann Surg.* 2020;271(6):1030-1035.
18. Bollinger RR, Barbas AS, Bush EL, Lin SS, Parker W. Biofilms in the large bowel suggest an apparent function of the human vermiform appendix. *J Theo Biol.* 2007;249(4):826-831.
19. DeCoppi P, Pozzobon M, Piccoli M, Gazzola MV, Boldrin L, Slanzi E, et al. Isolation of mesenchymal stem cells from human vermiform appendix. *J Surg Res.* 2006;135(10):85-91.