Article

Antibiotic Stewardship in Nonoperative Management of Perforated Appendicitis: Oral Antibiotics Are an Alternative

Alvaro E. Galvis[1,2*], Robert Bucayu[3], Rebecca John[4], Yigit Guner MD[4], Antonio C. Arrieta[1,2], Delma J. Nieves[1,2]

1Children's Hospital of Orange County, Department of Pediatrics, Division of Infectious Diseases, Orange, California.

2University of California, Irvine, Department of Pediatrics, Irvine, California.

3University of California Irvine, School of Medicine, Irvine, California.

4Children's Hospital of Orange County, Department of Pediatrics, Division of Surgery Orange, California.

*Correspondence: Loma Linda University Department of Pediatrics Division of Pediatric Infectious Diseases 11175 Campus Street Coleman Pavilion, A1120 Loma Linda, CA 92354. Email: agalvis@llu.edu ; draegalvis@gmail.com

Abstract: Background: The standard of care of nonoperative appendicitis patients involves ongoing antibiotic therapy. Yet, there is variability regarding the decision to continue outpatient parenteral antibiotic treatment (OPAT) or transition to oral (PO) antibiotics. Methods: In our single center retrospective study, we reviewed 46 pediatric patients who underwent nonoperative management of perforated appendicitis with Interventional Radiology (IR) percutaneous drainage. We reviewed age, ethnicity, hospitalization length, antibiotic choice, route and duration, and culture data. Results. Thirty-eight [83%] patients went home on OPAT, 6[13%] on PO, and 2[4%] completed therapy while inpatient. Based on culture susceptibilities of the 38 OPAT patients, 29[76%] had oral antibiotics as an option. The three most common organisms in those sent home on OPAT included *Enterococcus faecalis* (38 [100%]), *Bacteroides* spp (33 [87%]) *and Escherichia coli* (27 [71%]). All patients who grew *Pseudomonas aeruginosa* had an oral antibiotic as a treatment option; similarly with 93% (25/27) of E. coli, 81% (13/16) of α-hemolytic *Streptococcus* spp, and 76% (29/38) of *Enterococcus faecalis*. Conclusions: Nearly 80% of patients sent home on OPAT had PO antibiotic regimens options based on the culture susceptibility profiles. This data indicates that using cultures and susceptibility data can help guide antibiotic management, significantly reducing PICC line placement and likely reduce healthcare costs and complications associated with central lines.

Keywords: antimicrobial treatment, complicated Appendicitis, nonoperative management, Discharge antibiotics

1. Introduction

Antimicrobials are among the most commonly used medications within the pediatric population; however, considerable variability in antimicrobial use exists.[1] Overuse and inappropriate use of antibiotics are important factors that lead to worldwide antibiotic resistance, which has become one of the greatest threats to global health.[2] Infections due to antimicrobial-resistant bacteria and *Clostridium difficile* lead to increased morbidity and mortality, longer hospital stays, and dramatically increased health care costs.[1-3] Appendicitis is the most common cause of abdominal pain requiring emergent surgical intervention in pediatrics [4] and has significant variability in antibiotic utilization. The lifetime risk of appendicitis is believed to be 7-8%, with the majority of cases occurring in adolescents.[5] Approximately 300,000 appendectomies are performed in the United States every

 doi:10.20944/preprints202212.0110.v1

year, with 70,000 of those being performed on children.[6, 7] Perforated appendicitis occurs in 30% to 60% of cases, and this is especially true in younger patients.[8]

Many children presenting with complicated appendicitis can be treated nonoperatively. When possible non-operative treatment of complicated appendicitis includes administration of antibiotics and placement of a percutaneous drain if there is an intra-abdominal abscess. [9] Although precise definitions of complicated appendicitis may vary between surgeons and hospital, it is the standard of care to treat those children with ongoing antibiotic therapy.[10, 11] Previous studies have shown antibiotic therapy consisting of metronidazole and a third-generation cephalosporin to be effective in the management of perforated appendicitis, although "broad-spectrum" antibiotics including carbapenems are also often used.[12, 13] Peripherally inserted central catheters (PICC lines) are commonly placed in children as part of the treatment algorithm for complicated appendicitis, one advantage of which is the ability to complete intravenous (IV) antibiotics as outpatients (OPAT). There are disadvantages to PICC lines, including painful insertion, activity restrictions, deep venous thrombosis, and risk of mechanical and infectious complications.[14-16]

As of yet, there is no consensus on whether to continue OPAT or transition to oral antibiotics.[17] In patients with operative appendicitis, studies have delineated certain criteria to be met in order to transition from IV to oral antibiotics without affecting re-admission rate and overall outcomes. In such cases normalization of white blood cell count (WBC), oral tolerance, afebrile and asymptomatic were good indicators to transition to a PO regimen at the time of discharge.[18, 19] However, there is paucity of data for patients managed non-operatively. Therefore, many clinicians rely on extrapolation of operative studies into non-operative patients, or proceed with OPAT. Our study aimed at looking whether pediatric perforated non-operative appendicitis patients could be have transitioned from IV to oral antibiotics based on culture results and susceptibility profiles.

2. Materials and Methods

The study was approved by the local institutional review board at Children's Hospital of Orange County (CHOC). This was a single center retrospective study reviewing hospitalized patients from January 1st, 2014 through December 31st, 2019 who underwent nonoperative management for perforated appendicitis. Our inclusion criteria were pediatric patients with perforated appendicitis (age up to 18 years), who had a drainable abscess confirmed by computer tomography (CT) radiologic findings, underwent percutaneous drainage by interventional radiologist (IR) and had cultures sent.

The patient medical records were analyzed for data on clinical presentation, diagnostic studies obtained, including laboratory and imaging studies, and microbiologic data. The choice of antibiotics, route of antibiotic administration while in the hospital and at the time of discharge, and the total duration of antibiotic treatment were recorded. In addition to the inpatient stay, we reviewed the outpatient clinic visits records and collected follow-up data. Any complications after discharge, including re-admissions were reviewed. Exclusion criteria included acute, nonperforated appendicitis on presentation and patients who did not have an identified abscess amenable to IR drainage.

Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at CHOC.[20, 21] REDCap is a secure, web-based software platform designed to support data capture for research studies. Statistical analysis comparing the OPAT and PO groups was accomplished using Microsoft Excel version 2202 [22] using the two-sample t-Test assuming unequal variances. Statistical significance was defined with a p value <0.05.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 7 December 2022 doi:10.20944/preprints202212.0110.v1

3. Results

3.1 Demographics and clinical outcomes

From January 1st 2014 to December 31st 2019, 237 patients received diagnosis of acute appendicitis, among which 46 patients (19.4%) had the diagnosis of ruptured appendicitis and underwent initial nonoperative medical management with IR percutaneous drainage. The patients were 63% males, 50% identified as Latino and 50% were between the ages of 5 and 12 years old (mean 10.02; range 1-17). Table 1 shows complete demographic data. Twenty patients [43%] had a fecalith seen on CT scan. Laboratory results on admission and discharge are compared in Table 2. There were no statistically significant differences between the two groups aside from the admit band count (26.5 % in PO vs 5.4% in OPAT). It was common to be discharged home with a drain (38 cases [83%]).

Table 1. Demographics (N total= 46)

Age Group	N	Percent
Infant (<2 years)	2	4.35
Young Children (2-5 years)	5	10.87
School Age (5-12 years)	23	50
Adolescent (>12 years)	16	34.78
Race		
African-American / Black	1	2.17
Asian	5	10.87
Other	11	23.91
White	29	63.04
Ethnicity		
Hispanic or Latino	23	50
Not Hispanic or Latino	23	50
Sex		
Male	29	63
Female	17	37

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 7 December 2022 doi:10.20944/preprints202212.0110.v1

Table 2. Mean Value of Laboratory Tests on Admission and Discharge.

Laboratory Test*	PO patients, Admit	PO patients, Discharge	OPAT patients, Admit	OPAT patients, Discharge
WBC (K/µL)	23.8 (12.6)	10 (3.5)	17.2 (6.1)	9.5 (3.3)
Neutrophils (%)	65.4 (22.8)	60.9 (18.4)	76.7 (10.1)	57.7 (13.4)
Band Neutrophils (%)	26.5** (0.7)	1.6 (1.5)	5.4** (5)	2.2 (2.3)
Hgb (gm/dL)	12.1 (1.6)	11.1 (0.8)	12.4 (1.7)	14.8 (20.5)
Platelet Count (K/µL)	351.2 (98.3)	436.5 (68.1)	311.8 (101.9)	444.4 (125.6)
CRP (mg/L)	150.8 (65.5)	29.5 (25.3)	175.6 (115.3)	42.1 (22.4)
ESR (mm/hr)	30	55	69.3 (34.6)	53.2 (31.7)
AST (units/L)	59.5 (39.3)	44.3 (21.9)	31.7 (25.5)	36 (13.4)
ALT (units/L)	28.3 (11.8)	28 (8.8)	32.1 (21.6)	30 (6.2)
Albumin (gm/dL)	3.9 (0.7)	3.4 (0.3)	4 (0.5)	2.9 (0.4)
Creatinine (mg/dL)	0.6 (0.3)	0.4 (0.1)	0.6 (0.2)	0.4 (0.1)

* Results are shown as mean with standard deviation in parenthesis.

**Indicates significance (P<0.05) between PO and OPAT patients.

Abbreviations: White Blood Cell Count = WBC, Hemoglobin = Hgb, C-Reactive Protein = CRP, Erythrocyte Sedimentation Rate = ESR, Aspartate Aminotransferase = AST, Alanine Aminotransferase = ALT

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 7 December 2022 doi:10.20944/preprints202212.0110.v1

Thirty-eight [83%] of the patients went home on OPAT, 6 [13%] on PO antibiotics, and 2 [4%] completed therapy while inpatient. The mean age for the PO group was 8.8 +/- 4.8 years and OPAT was 10.4 +/- 4.2 years (Figure 1) ; there was no statistical difference between the two groups (P>0.05). The mean time from admission to IR drainage was 1.9 ± 2.8 days, with 36 [78.2%] being done within 24 hours, 3 [6.5%] within 24-48 hours, 2 [4.6%] within 48-72 and the remaining 5 [10.8%] done after 72 hours. Hospital length of stay was 9.7 ± 4 days for those 6 patients who went home on PO antibiotics and 5.9 ± 2.7 days for those 38 patients who went home on OPAT. Total antibiotic duration was 20 ± 9.3 days for those 6 discharged on PO versus 18.4 ± 4.9 days for those 38 discharged with OPAT. The most common antibiotic used with OPAT was ertapenem (71%) followed by piperacillin-tazobactam (15.7%). Most common PO were amoxicillin/clavulanate (50%), metronidazole and levofloxacin (33.3%) and metronidazole and ciprofloxacin (16.6%).

Overall, in our study eight (17%) patients were readmitted, including seven patients that had been discharged on OPAT. We found two patients discharged on OPAT who had to be readmitted due to PICC line mechanical complications. There were four OPAT patients that were readmitted due to antibiotic treatment failure with worsening of abscess formation requiring further IR drainage procedures. All four subjects had *Escherichia coli* and a mix of some anaerobes in their initial culture. They received empiric antibiotics at the time of readmission and repeat cultures resulted in no organisms detected. One OPAT patient developed an acute generalized exanthematous pustulosis reaction while on piperacillin-tazobactam. One PO patient, discharged on amoxicillin-clavulanate (45 mg/kg) had treatment failure and was readmitted due to worsening of abscess requiring further IR drainage. The patient received ceftriaxone and metronidazole during the re-admission prior to the collection of a new culture which did not yield any organisms.

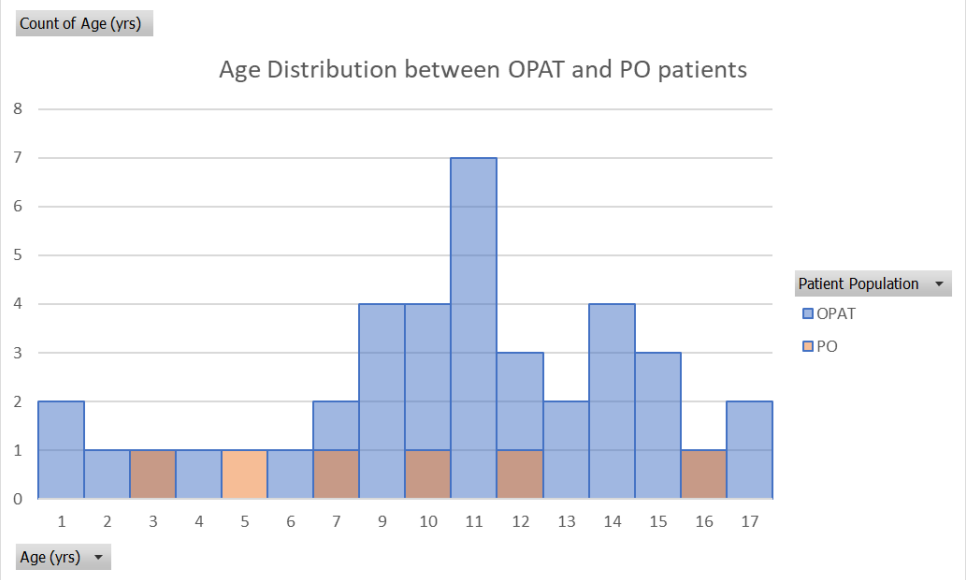

Figure 1. Age distribution of patients on PO and OPAT

3.2 *Microbiologic data*

Since we aimed to study if oral antibiotics were an option for the patients sent home on OPAT, the cultures from those 38 patients were further reviewed. The microorganism and the susceptibilities were evaluated. Based on culture susceptibilities, 29

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 7 December 2022 doi:10.20944/preprints202212.0110.v1

[76%] had organisms identified which had an effective oral antibiotic(s) as a treatment option. The three most common organisms in those sent home on OPAT included *Enterococcus faecalis* (38 [100%]), *Bacteroides* spp (33 [87%]) and *Escherichia coli* (27 [71%]). All of the isolated *E. faecalis* strains *were* susceptible to linezolid; 93% (25/27) *of E. coli*) had a PO option with the remaining 2 isolates being extended spectrum beta-lactamase strains. The *Bacteroides* spp isolates, 87% (29/33) had a PO option with the remaining 4 isolates having full sensitivities not completed by the lab. Other notable organism include all *Pseudomonas aeruginosa* that were susceptible to quinolones as a treatment option and all α-hemolytic *Streptococcus* spp that had a PO option. (Figure 2)

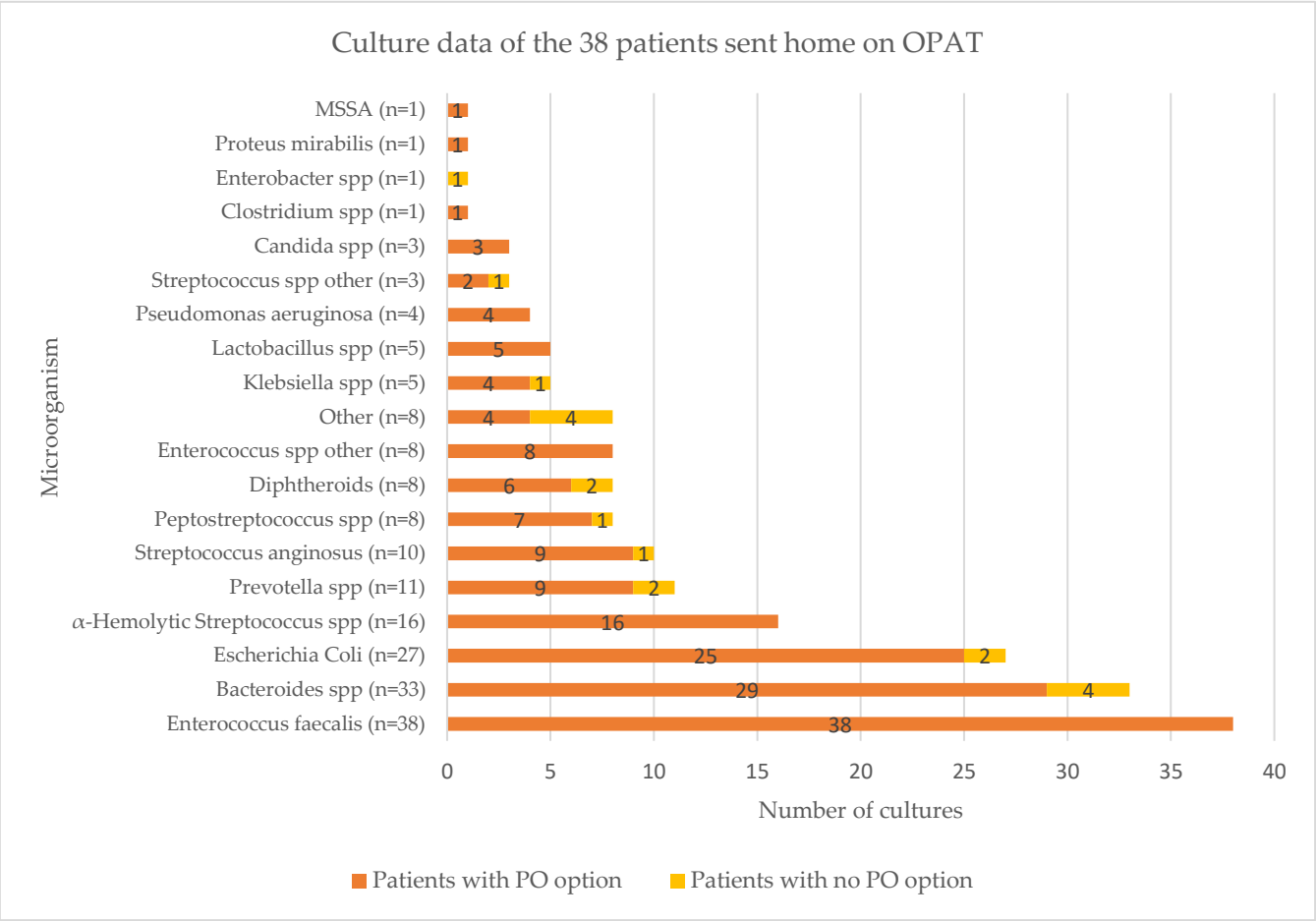

Figure 2. Microorganism susceptibility data from patients sent home on OPAT.
* Isolates without a PO option reflected that full sensitivities were never available.

4. Discussion

In this study, we identify that 76% (29/38) of the OPAT cohort had an available PO antibiotic regimen option based on the susceptibility profiles identified on culture. When comparing those patients that went home on PO vs OPAT, we saw no significant difference in laboratory results aside from the band count on admit (higher for PO patients). Interestingly hospital length of stay and total antibiotic duration were each longer for those that went home on PO versus OPAT. Being a retrospective study one can speculate that those few patients that were sent home on oral regimens had been deemed to have received "enough" of an IV course to where the team felt more comfortable sending them on PO.

 doi:10.20944/preprints202212.0110.v1

Others have also shown the use of oral antibiotics after an initial course of IV antibiotics to be effective in the management of perforated appendicitis. Adibe et al[23] reported a 14-day course combining initial IV antibiotics followed by oral trimethoprim/sulfamethoxazole and metronidazole to be as safe as and more cost-effective than a 14-day course of IV antibiotics that combined initial inpatient followed by OPAT. Similarly, a randomized control trial of 150 pediatric patients by Frasser et al[10] demonstrated no difference between a full IV antibiotic course group or an IV/PO group in the time to full oral intake, length of postoperative hospitalization, total health care visits, or abscess rate. Moreover, the IV/PO group showed the significant advantage of shorter hospitalization stay. Other studies have demonstrated similar results.[24-26] One limitation in these aforementioned prior studies is that microbiological data were not utilized to guide decisions on oral regimen.

Historically, it had been common practice to utilize PICC lines and OPAT consistent with prior practice reported in the literature.[12, 13, 23] Only on occasionally was PO preferred based on clinical picture and culture results when available. Because of variation within the group, efforts aimed at preventing emergence of antibiotic resistance, and studies demonstrating that use of IV antibiotics after discharge had been associated with higher re-admission rates due to PICC line complications;[15, 16] we set out to identify how many more patients could have potentially been transitioned to PO antibiotic based on collected cultures. Recent data comparing healthcare expense found that surgical appendicitis patients on OPAT cost an average of $67 per day versus those on oral antibiotics cost $7 per day.[17, 27] We speculate that early transition to PO could reduce healthcare costs including those associated with PICC line complications (clotting, infection, thrombus formation, dislodgement).

Our data suggests the use of cultures obtained at the time of IR drainage when done early after presentation of nonoperative complicated appendicitis may be helpful to determine the appropriateness of a PO regimen and help prevent the use of unnecessary broad-spectrum OPAT. Pediatric patients with initial non-operative management for complicated appendicitis could benefit from waiting for culture results before considering PICC line placement and OPAT. Hence, obtaining cultures and susceptibility should be encouraged as the data could significantly reduce PICC line necessity, overall healthcare costs and adverse complications associated with OPAT.

There are some limitations to consider for our study. First, being a single center study, our sample size was small. Nonetheless, in this 6-year period with a total of 46 patients we noted a large portion (79.5 %) had a PO option based on microbiologic data. We felt that collecting data on patients prior to 2014, although adding more patients may not be representative of the current antibiotic resistance patterns which can change over time. Due to the small number of patient's that actually went home on PO, we could not determine if there were any statistically significant differences between patients discharged on PO or OPAT. A prospective randomized controlled study would be the next step to better answer this question. Another limitation is that our study is single center and hence may not be representative of all pediatric patients, local resistance patterns, or the current practices of other centers for nonoperative management of complicated appendicitis. However, given the limited literature and the treatment heterogeneity that exists our study aimed at helping with standardization of a management approach, namely considering to await for cultures prior to considering OPAT.

In conclusion, our study adds to the body of literature supporting that in non-operative management of complicated appendicitis in children, utilizing culture data to guide PO antibiotics after an initial IV antibiotic course is feasible and of comparable success rate to OPAT. We propose, based on our data, waiting for culture results from IR drained fluid before deciding on antibiotic options as many will have PO options. This provides an opportunity for antibiotic stewardship programs helping reduce the utilization of broader spectrum antibiotics than needed potentially decreasing emergence of resistance, decrease overall health care costs and prevent complications associated with OPAT.

..

 doi:10.20944/preprints202212.0110.v1

Author Contributions: Conceptualization, A.G., R.G. and D.N.; methodology, A.G., R.B. and D.N.; software, A.G. and R.B. ; validation, A.G., A.A., R.B. and D.N.; formal analysis, A.G., A.A., R.B. and D.N.; investigation, A.G and R.B. ; resources, A.G ., R.G., Y.G. and D.N. data curation R.B. ; writing—original draft preparation, A.G. and R.B; writing—review and editing A.G., A.A., R.B., Y.G. and D.N. .; visualization, A.G. and D.N.; supervision, D.N.; All authors have read and agreed to the published version of the manuscript

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by Institutional Review Board of Children's Hospital of Orange County(Identification code #200215, IRBNET ID # **1572070-1 on April 20,2020).**

Informed Consent Statement: Patient consent was waived due to the nature of the retrospective study with no direct impact on patient's health safety or outcome.

Data Availability Statement: Data are available upon request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

 doi:10.20944/preprints202212.0110.v1

References

1. Smith, M. J.; Gerber, J. S.; Hersh, A. L., Inpatient Antimicrobial Stewardship in Pediatrics: A Systematic Review. *J Pediatric Infect Dis Soc* **2015,** *4* (4), e127-35.
2. Chautrakarn, S.; Anugulruengkitt, S.; Puthanakit, T.; Rattananupong, T.; Hiransuthikul, N., Impact of a Prospective Audit and Feedback Antimicrobial Stewardship Program in Pediatric Units in Tertiary Care Teaching Hospital in Thailand. *Hosp Pediatr* **2019,** *9* (11), 851-858.
3. Magsarili, H. K.; Girotto, J. E.; Bennett, N. J.; Nicolau, D. P., Making a Case for Pediatric Antimicrobial Stewardship Programs. *Pharmacotherapy* **2015,** *35* (11), 1026-36.
4. Lee, S. L.; Islam, S.; Cassidy, L. D.; Abdullah, F.; Arca, M. J.; American Pediatric Surgical Association, O.; Clinical Trials, C., Antibiotics and appendicitis in the pediatric population: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. *J Pediatr Surg* **2010,** *45* (11), 2181-5.
5. Andersson, R. E., The Natural History and Traditional Management of Appendicitis Revisited: Spontaneous Resolution and Predominance of Prehospital Perforations Imply That a Correct Diagnosis is More Important Than an Early Diagnosis. *World Journal of Surgery* **2007,** *31* (1), 86-92.
6. Mosuka, E. M.; Thilakarathne, K. N.; Mansuri, N. M.; Mann, N. K.; Rizwan, S.; Mohamed, A. E.; Elshafey, A. E.; Khadka, A.; Mohammed, L., A Systematic Review Comparing Nonoperative Management to Appendectomy for Uncomplicated Appendicitis in Children. *Cureus* **2021,** *13* (10), e18901.
7. Brennan, G. D. G., Pediatric appendicitis: pathophysiology and appropriate use of diagnostic imaging. *CJEM* **2006,** *8* (06), 425-432.
8. Bratton, S. L.; Haberkern, C. M.; Waldhausen, J. H., Acute appendicitis risks of complications: age and Medicaid insurance. *Pediatrics* **2000,** *106* (1 Pt 1), 75-8.
9. Nadler EP, R. K., Vaughan KG, Meza MP, Ford HR, Gaines BA, Predictors of Outcome for Children with Perforated Appendicitis Initially Treated with Non-Operative Management. *SURGICAL INFECTION* **2004,** *5* (4), 349-56.
10. Fraser, J. D.; Aguayo, P.; Leys, C. M.; Keckler, S. J.; Newland, J. G.; Sharp, S. W.; Murphy, J. P.; Snyder, C. L.; Sharp, R. J.; Andrews, W. S.; Holcomb, G. W., 3rd; Ostlie, D. J.; St Peter, S. D., A complete course of intravenous antibiotics vs a combination of intravenous and oral antibiotics for perforated appendicitis in children: a prospective, randomized trial. *J Pediatr Surg* **2010,** *45* (6), 1198-202.
11. Yu, T. C.; Hamill, J. K.; Evans, S. M.; Price, N. R.; Morreau, P. N.; Upadhyay, V. A.; Ferguson, R. S.; Best, E. J.; Hill, A. G., Duration of postoperative intravenous antibiotics in childhood complicated appendicitis: a propensity score-matched comparison study. *Eur J Pediatr Surg* **2014,** *24* (4), 341-9.
12. St Peter, S. D.; Little, D. C.; Calkins, C. M.; Murphy, J. P.; Andrews, W. S.; Holcomb, G. W., 3rd; Sharp, R. J.; Snyder, C. L.; Ostlie, D. J., A simple and more cost-effective antibiotic regimen for perforated appendicitis. *J Pediatr Surg* **2006,** *41* (5), 1020-4.
13. Roque, F.; Melo Filho, A. A.; Roque, A.; Roque, H. C. B.; Moreira, T. M. M.; Chaves, E. M. C., Antibiotics for Appendicectomy in Children and Adolescents during the Perioperative Period: An Integrative Review. *Rev Paul Pediatr* **2019,** *37* (4), 494-502.
14. Barrier, A.; Williams, D. J.; Connelly, M.; Creech, C. B., Frequency of peripherally inserted central catheter complications in children. *Pediatr Infect Dis J* **2012,** *31* (5), 519-21.
15. Sulkowski, J. P.; Asti, L.; Cooper, J. N.; Kenney, B. D.; Raval, M. V.; Rangel, S. J.; Deans, K. J.; Minneci, P. C., Morbidity of peripherally inserted central catheters in pediatric complicated appendicitis. *J Surg Res* **2014,** *190* (1), 235-41.

16. Rangel, S. J.; Anderson, B. R.; Srivastava, R.; Shah, S. S.; Ishimine, P.; Srinivasan, M.; Bryan, M.; Gong, W.; Hall, M.; Localio, R.; Luan, X.; Anandalwar, S.; Keren, R.; Pediatric Research in Inpatient Settings, N., Intravenous Versus Oral Antibiotics for the Prevention of Treatment Failure in Children With Complicated Appendicitis: Has the Abandonment of Peripherally Inserted Catheters Been Justified? *Ann Surg* **2017,** *266* (2), 361-368.

17. Loux, T. J.; Falk, G. A.; Burnweit, C. A.; Ramos, C.; Knight, C.; Malvezzi, L., Early transition to oral antibiotics for treatment of perforated appendicitis in pediatric patients: Confirmation of the safety and efficacy of a growing national trend. *J Pediatr Surg* **2016,** *51* (6), 903-7.

18. Acker, S. N.; Hurst, A. L.; Bensard, D. D.; Schubert, A.; Dewberry, L.; Gonzales, D.; Parker, S. K.; Tong, S.; Partrick, D. A., Pediatric appendicitis and need for antibiotics at time of discharge: Does route of administration matter? *J Pediatr Surg* **2016,** *51* (7), 1170-3.

19. Bonasso, P. C.; Dassinger, M. S.; Wyrick, D. L.; Smith, S. D.; Burford, J. M., Evaluation of white blood cell count at time of discharge is associated with limited oral antibiotic therapy in children with complicated appendicitis. *Am J Surg* **2019,** *217* (6), 1099-1101.

20. Harris, P. A.; Taylor, R.; Minor, B. L.; Elliott, V.; Fernandez, M.; O'Neal, L.; McLeod, L.; Delacqua, G.; Delacqua, F.; Kirby, J.; Duda, S. N.; Consortium, R. E., The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* **2019,** *95*, 103208.

21. Harris, P. A.; Taylor, R.; Thielke, R.; Payne, J.; Gonzalez, N.; Conde, J. G., Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* **2009,** *42* (2), 377-81.

22. Microsoft *Excel*, Version 2202; https://office.microsoft.com/excel, 2021.

23. Adibe, O. O.; Barnaby, K.; Dobies, J.; Comerford, M.; Drill, A.; Walker, N.; Mattei, P., Postoperative antibiotic therapy for children with perforated appendicitis: long course of intravenous antibiotics versus early conversion to an oral regimen. *Am J Surg* **2008,** *195* (2), 141-3.

24. Rice, H. E.; Brown, R. L.; Gollin, G.; Caty, M. G.; Gilbert, J.; Skinner, M. A.; Glick, P. L.; Azizkhan, R. G., Results of a Pilot Trial Comparing Prolonged Intravenous Antibiotics With Sequential Intravenous/Oral Antibiotics for Children With Perforated Appendicitis. *Archives of Surgery* **2001,** *136* (12), 1391-1395.

25. Arnold, M. R.; Wormer, B. A.; Kao, A. M.; Klima, D. A.; Colavita, P. D.; Cosper, G. H.; Heniford, B. T.; Schulman, A. M., Home intravenous versus oral antibiotics following appendectomy for perforated appendicitis in children: a randomized controlled trial. *Pediatr Surg Int* **2018,** *34* (12), 1257-1268.

26. Wang, C.; Li, Y.; Ji, Y., Intravenous versus intravenous/oral antibiotics for perforated appendicitis in pediatric patients: a systematic review and meta-analysis. *BMC Pediatr* **2019,** *19* (1), 407.

27. Krah, N. M.; Bardsley, T.; Nelson, R.; Esquibel, L.; Crosby, M.; Byington, C. L.; Pavia, A. T.; Hersh, A. L., Economic Burden of Home Antimicrobial Therapy: OPAT Versus Oral Therapy. *Hosp Pediatr* **2019,** *9* (4), 234-240.