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ORIGINAL SCIENTIFIC REPORT

# Pediatric Appendicitis Severity in KwaZulu-Natal, South Africa: A Retrospective Cohort Analysis

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## Abstract

*Background* Acute appendicitis is a common pediatric surgical emergency; however, there are few grading systems to assign disease severity. The American Association for the Surgery of Trauma (AAST) recently developed a grading system for a variety of emergency surgical conditions, including appendicitis. The severity of acute appendicitis in younger patients in KwaZulu-Natal (South Africa) is unknown. We aimed to describe the disease severity in this patient population using the AAST grading system hypothesizing that the AAST grade would correlate with morbidity, management type, and duration of stay.

*Materials* Single institutional review of patients <18 years old with a final diagnosis of acute appendicitis during 2010–2016 in KwaZulu-Natal, South Africa, was performed. Demographics, physiologic and symptom data, procedural details, postoperative complications, and Clavien–Dindo classification were abstracted. AAST grades were generated based on intraoperative findings. Summary, univariate, and nominal logistic regression analyses were performed to compare AAST grade and outcomes.

*Results* A total of 401 patients were identified with median [IQR] age of 11 [5–13], 65% male. Appendectomy was performed in all patients; 2.4% laparoscopic, 37.6% limited incision, and 60% midline laparotomy. Complications occurred in 41.6%, most commonly unplanned relaparotomy (22.4%), surgical site infection (8.9%), pneumonia (7.2%), and acute renal failure (2.9%). Complication rate and median length of stay increased with greater AAST grade (all $p < 0.001$). AAST grade was independently associated with increased risk of complications.

*Conclusion* Pediatric appendicitis is a morbid disease in a developing middle-income country. The AAST grading system is generalizable and accurately corresponds with management strategies as well as key clinical outcomes.

*Level of evidence* Retrospective study, Level IV.

*Study type* Retrospective single institutional study.

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## Introduction

Patients with appendicitis in low- and middle-income countries (LMICs) often present with advanced disease and perforation [1–3]. Severe appendicitis is associated with increased rates of morbidity and mortality. The Lancet Commission on Global Health determined a need for research evaluating healthcare inequalities and disparities within low and middle-income countries (LMIC) [4, 5]. Clinical prediction models such as the Alvarado score and appendicitis inflammatory response (AIR) score use various physical examination and laboratory findings to predict the likelihood appendicitis [6–8]. These models, however, are diagnostic tools and do not quantify disease severity [9]. Furthermore, these tools are modeled from patient data derived in high-income countries (HIC) and are often not generalizable to patients in LMICs [10].

To address the lack of a grading system, the American Association for the Surgery of Trauma (AAST) created a grading system for all emergency general surgical (EGS) conditions including appendicitis [11–13]. The grading system utilizes a five tiered scale to describe disease severity. Clinical, imaging, operative, and pathologic criteria exist for sixteen diseases [13, 14]. Table 1 outlines the AAST EGS grade based on operative findings in appendicitis. In addition to categorizing patient severity and predicting outcomes, the grading system provides a standardized method to report on the burden and outcomes of these emergency conditions across disparate health systems [11, 13, 15]. It has been validated in multinational adult populations; however, it has not been validated in multinational pediatric populations [16].

The AAST EGS grade provides an opportunity to improve the study of pediatric appendicitis in low- and middle-income countries. We aimed to determine whether the AAST EGS grade would be sufficient to assign disease severity which corresponds with outcomes in a South African pediatric population. We hypothesized that AAST EGS grade would be, (1) efficacious in assigning disease severity retrospectively from operative data, (2) generalizable to populations with heterogeneous appendicitis severity, and (3) that greater appendicitis severity would be associated with key clinical outcomes such as mortality, morbidity, complication severity, Clavien–Dindo grade, and duration of stay.

**Table 1** AAST grading system for appendicitis

| Grade | Operative AAST description of appendicitis |
|---|---|
| Normal | Normal appendix |
| Grade I | Acutely inflamed appendix, intact |
| Grade II | Gangrenous appendix, intact |
| Grade III | Perforated appendix with local contamination |
| Grade IV | Perforated appendix with periappendiceal phlegmon or abscess |
| Grade V | Perforated appendix with generalized peritonitis |

## Methods

This is a retrospective single institution cohort study undertaken by the authors. Institutional Review Board approvals were obtained prior to conducting the study from the Biomedical Research Committee of the University (BREC) of KwaZulu-Natal consistent with the declaration of Helsinki. A prospectively maintained database was queried for patients aged <18 years with a final diagnosis of appendicitis and appendectomy during 2010–2016. Patients with suspected appendicitis based on clinical examination but were not found to have appendicitis at operation were excluded (negative appendectomy). Patients were excluded if they did not have a diagnosis of acute appendicitis, were pregnant, or had a disease which could mimick acute appendicitis (Meckel's diverticulum or tuberculosis). In this South African Cohort, patients do not generally receive non-operative management (utilizing drains and antibiotic therapy) and therefore this study lacks a comparable cohort.

Baseline demographic information, prehospital symptom type and duration, admission vital signs, admission laboratory data, operative approach (midline laparotomy, McBurney's incision, laparoscopy), complications according to National Surgical Quality Improvement Program (NSQIP) definitions [17], complications as graded by the Clavien–Dindo system [18], overall duration of stay, and 30-day mortality rates were collected. Surgery was performed directly by senior residents in training. A senior resident was defined as a resident who had successfully completed 2 years of surgical training. Attending surgeons were not routinely present at the operation.

### Description of Pietermaritzburg, South Africa and hospital system

The city of Pietermartizburg is the capital of KwaZulu-Natal (KZN) Province and is the largest city in the western half of KZN with a population of nearly one million people. The population of western KZN is a predominantly rural population and comprises a further two million

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people. Surgical staff and house officers maintain a digitized registry for assessment and evaluation of outcomes.

This digital registry is unique and has been described in the literature [19, 20]. Medical staff utilized a standard electronic data entry sheet for each patient. This clerking process is performed for all new admissions generating real-time clinical data. The completed electronic data sheet, after being incorporated into the digital registry, is printed and becomes the patient's clinical record. Similar data points are entered and recorded at various critical time points, such as operation and discharge. This system combines the functions of a medical registry and a medical record system. It also combines an electronic system with a paper-based system and has been called the Hybrid Electronic Medical Registry (HEMR). The data entry is quality controlled by two attending surgeons who routinely cross check the previous day's entries each morning.

### AAST grade assignment for appendicitis

AAST EGS grades (Table 1) were independently assigned from patients' operative reports by two reviewers (VYK and JLB). Discrepancies were resolved with a third reviewer (MCH). The final AAST grade was used for all outcomes analyses. The AAST EGS grading system utilizes a five-tiered system (I–V) wherein specific definitions describing extent of appendicitis severity exist. The AAST EGS grade can be generated from clinical, imaging, operative or pathologic criteria. Operative findings were utilized given the availability of detailed operative notation. Clinical, imaging, and pathologic criteria were not utilized to estimate disease severity.

### Statistical analyses

Univariate analyses to assess the relationship of AAST grade and clinical outcomes were performed using Fisher's exact test, Cochran–Armitage test for trend, and ANOVA tests. Continuous variables were described using means with standard deviations (SD) if normally distributed and medians with inter-quartile ranges [IQR] if gross skewness was present. Categorical variables were summarized as proportions. Variables on univariate analyses with $p < 0.05$ were included in a multivariable nominal regression analysis in order to determine risk factors predictive for the development of postoperative complication. These were reported with odds ratios and 95% confidence intervals (CIs). Model sensitivity (quantified by the area under the receiver operating characteristic) and the model goodness of fit test (Hosmer–Lemeshow) were performed. Variables and covariates in analyses with missing data >10% were not included. Agreement statistic was calculated between reviewers for assigning AAST EGS grades from operative data. All data analyses were performed using JMP (SAS Institute, Inc., Cary, NC). GraphPad Prism (GraphPad Software, Inc., La Jolla, CA) was utilized for all visual graphics.

## Results

### Overall cohort

During 2010–2016, 401 children with a final diagnosis of appendicitis were identified with a median [IQR] age of 11 [5–13] years, 35% female. Patients presented with a varied duration of prehospital symptoms (median 3 [2–5] days). At admission the median temperature was 37.5 [36.9–38.0], white blood cell count (WBC) 14.3 [12.0–17.8], and heart rate (beats per minute) 94 [86–104]. Appendectomy was most frequently performed in an open fashion through a midline laparotomy ($n = 240$, 60%) or McBurney's incision ($n = 151$, 37.5%). Laparoscopic appendectomy was rare ($n = 10$, 2.5%). The overall complication rate was 41.6% ($n = 167$). Complications included unplanned relaparotomy ($n = 90$, 22.4%), surgical site infection ($n = 36$, 8.9%), pneumonia ($n = 29$, 7.2%), and acute renal failure ($n = 12$, 2.9%). Planned relaparotomy was performed in 44 (10.9%) patients. There was one death.

### AAST grade

The most common AAST grade assigned was Grade V ($n = 143$, 36%).The remaining patients were well distributed between Grades I and IV (Table 2). Only one patient had a normal appendix at operation and was not assigned a grade. Duration of symptoms, temperature, and WBC correlated with AAST grade (Table 2, all $p < 0.05$). Utilization of midline laparotomy also increased with AAST grade (Fig. 1). The agreement statistic between reviewers was 0.82 95% CI 0.77–0.85 indicating moderate strong agreement between reviewers for assigning AAST EGS grades using operative data.

### Key clinical outcomes

Complications increased with AAST grade from zero in those with Grade I appendicitis to 88% in those with Grade V disease ($p = 0.0001$). Complication severity assigned by Clavien–Dindo grade and length of stay also increased with AAST grade (Fig. 2). Table 3 outlines the multivariable nominal regression analysis for risk factors that were independently associated with postoperative complications. The odds for developing a complication increased with AAST EGS grade relative to Grade I. In addition, patients

**Table 2** Overall patient characteristics, surgical approach, and postoperative outcomes by AAST grade

| Variable | AAST grade | | | | | |
|---|---|---|---|---|---|---|
| | I<br>*N* = 60 | II<br>*N* = 97 | III<br>*N* = 51 | IV<br>*N* = 49 | V<br>*N* = 143 | *p* value |
| *Patient characteristics* | | | | | | |
| Age[a] | 11 [10–13] | 10 [9–12] | 11 [10–13] | 11 [9–13] | 11 [8–13] | 0.7000 |
| Female[b] | 35 | 24 | 31 | 38 | 42 | 0.0600 |
| Duration of prehospital symptoms[a] | 2 [1–2] | 2 [2–3] | 3 [3–5] | 4 [3–5] | 5 [4–7] | 0.0001 |
| Temperature[a] | 37 [36.6–37.5] | 37 [36.5–37.8] | 37.2 [36.8–38] | 37.5 [36.8–38] | 38 [37.5–38.6] | 0.0001 |
| WBC[a] | 13.2 [11.8–15] | 13.2 [12–15] | 14 [11.9–16] | 15 [12.8–17.8] | 16.5 [13.2–21] | 0.0001 |
| Heart rate[a] | 84 [81–88] | 83 [79–85] | 91 [88–93] | 89 [87–95] | 95 [92–97] | 0.0100 |
| *Operative details* | | | | | | |
| Laparoscopy[b] | 6.7 | 4.1 | 3.9 | 0 | 0 | 0.0100 |
| Limited incision[b] | 85 | 87 | 17.6 | 12.2 | 0 | 0.0001 |
| Midline laparotomy[b] | 8.3 | 8.2 | 78.4 | 87.7 | 100 | 0.0001 |
| Planned relaparotomy[b] | 0 | 1 | 9.8 | 56.5 | 80.4 | 0.0001 |
| *Postoperative outcomes* | | | | | | |
| Duration of stay[a] | 2 [2–3] | 3 [2–3] | 5 [3–6] | 6 [5–7] | 11 [8–15] | 0.0001 |
| Clavien–Dindo[a] | 0 [0–0] | 0 [0–0] | 0 [0–0] | 1 [0–3] | 3 [3–4] | 0.0100 |
| Superficial SSI[b] | 6.2 | 6.2 | 12.5 | 25 | 25 | 0.0300 |
| Deep SSI[b] | 0 | 7.5 | 22.5 | 27.5 | 40 | 0.0001 |
| Organ space SSI[b] | 0 | 0 | 25 | 31.2 | 43.7 | 0.0001 |
| Pneumonia[b] | 0 | 3.1 | 1.9 | 8.1 | 14.7 | 0.0020 |

Values are expressed as [a]median [IQR], or [b]percentages

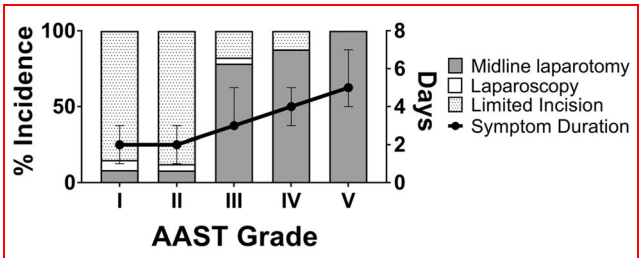


**Fig. 1** Increasing utilization of invasive surgical approach for increasing anatomic severity is associated with increased prehospital duration of symptoms

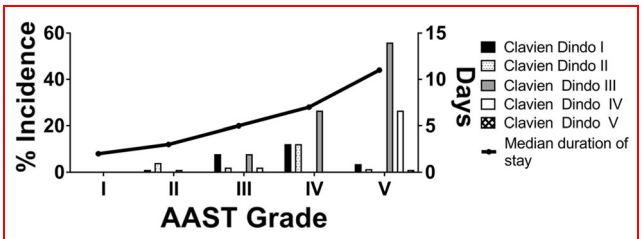


**Fig. 2** Increasing anatomic severity is associated with complication severity and duration of stay

admitted with >3 days of prehospital symptoms as well as fever were also independently associated with developing a complication. This model demonstrated good discrimination with an area under the curve of 0.86 with 95% confidence interval of (0.83–0.88) and was calibrated well with Hosmer–Lemeshow test demonstrating $p = 0.6$.

## Discussion

Worldwide, appendicitis is associated with unequal outcomes depending on geographic location, racial origin, and socioeconomic status [1, 2, 16, 21, 22]. Since clinical prediction models may not reliably estimate disease severity and access to advanced imaging is not equal; the need for a universal method to assign severity simply is increasingly important [10, 23]. In this study, [1] reviewers were able to assign disease severity retrospectively with moderate to high accuracy [2], disease severity was associated with key clinical outcomes such as duration of stay, and the development of complications and operative approach as well as [3] increasing disease severity, fever at admission, and duration of prehospital symptoms were independently associated with the development of postoperative complications. Taken together, the AAST EGS grade for appendicitis adequately correlated individual patient disease severity with several clinical outcomes in

**Table 3** Multivariable analysis for factors associated with increased risk of postoperative complication in a LMIC population

| Variable | Odds ratio | 95% confidence interval (CI) | *p* value |
|---|---|---|---|
| AAST grade | | | |
| I | Reference | – | – |
| II | 2.1 | 1.5–3.1 | 0.02 |
| III | 2.8 | 1.3–8.9 | 0.03 |
| IV | 3.9 | 1.6–8.1 | 0.002 |
| V | 6.2 | 2.9–13.8 | 0.0001 |
| ≥ 3 days of prehospital abdominal symptoms | 2.6 | 1.2–5.8 | 0.01 |
| ≥ 38.5 °C temperature at admission | 1.7 | 1.1–3.3 | 0.04 |

The odds of developing of postoperative complication was calculated using AAST EGS Grade I as a reference

*AAST* American Association for the Surgery of Trauma, *EGS* emergency general surgery

this South African pediatric population. These data demonstrate that the AAST EGS grading system is externally valid and that it displays initial generalizability in pediatric populations with variably severe appendicitis.

The current paradigm of simple versus complex disease severity does not adequately describe important clinical outcomes, and these appear to depend on a more granular disease severity classification [24]. Not all perforated appendicitis is the same with respect to postoperative outcomes. Clinical prediction models like the Alvarado and AIR scores do not assign disease severity in a granular manner like the AAST grading system does [25]. Since these systems are developed from higher-income countries, their applicability in determining the presence of appendicitis may not be always valid [10]. The AAST EGS grading system describes disease severity and outcomes in a population with variably severe disease. Improvements toward standardization of care for patients with appendicitis have been associated with improvements in outcomes [26]. It is possible that early recognition of severe appendicitis based on definitions using the AAST EGS grade might improve patient triage, informed consent, management types and in turn potentially reduce poor outcomes. Minimizing variability in pediatric patient care may contribute to improving patient outcomes further.

There are substantive differences between high-, middle-, and low-income countries with respect to appendicitis severity, surgical management approaches, and subsequent outcomes [27]. This cohort experienced high rates of laparotomy and open appendectomy with very few patients undergoing a laparoscopic procedure. This corresponds with a large review of pediatric appendicitis outcomes in Canada highlighting regional differences in appendicitis perforation, management provided, and subsequent patient outcomes [28]. The present study underscores the significant challenges that providers in different environments face for a seemingly simple disease [29].

Patient disease severity was stratified by management type as well. In this South African cohort, there was a relative underutilization of non-operative and minimally invasive techniques. Although postoperative pain and morbidity may well be more common following open surgery, patients with increased disease severity were more likely to undergo a midline laparotomy. It is also possible that resource constraints may limit access to laparoscopy [30]. Without adjustment for disease severity; management type, complication development, and resource utilization are potentially confounded and underappreciated. The multivariable model demonstrated incremental changes for the odds of developing postoperative complication using the AAST EGS grade suggesting that the extent of peritoneal contamination which affects in conjunction with the operative approach.

Notably, increased prehospital duration of symptoms concomitant with fever was also associated with increased risk of developing postoperative complication. Future research should focus on (1) preoperative determination of AAST EGS grade using ultrasonography or computed tomography in order to (2) possibly reduce the rates of laparotomy and subsequent morbidity and finally (3) perform surgical outcome benchmarking among other middle-income countries where appendicitis is increasingly severe. A long-term goal for the improvement of appendicitis management globally would be to increase the availability of non-operative and interventional radiologic procedures for patients with well-matched disease severity or improve resuscitation in the prehospital setting.

Global pediatric appendicitis research could potentially benefit by incorporating AAST EGS grading so as to reliably compare disease severity. This analysis provides an initial foundation for meaningful comparisons of outcomes between countries, healthcare systems, and surgeons globally. The AAST EGS grading system is a granular disease reporting method. As such, it potentially could be used for aggregated surgical outcome benchmarking. The application of a universally accepted emergency general surgery disease severity grading system is urgently needed [9].

There are a several limitations to the current study. Most importantly, AAST EGS grades were assigned retrospectively and only to patients with operative appendicitis. Patients without a final diagnosis of appendicitis were excluded in order to determine the validity of the AAST EGS grade in a pediatric population. The operative AAST EGS grade was primarily based on operative reports data which may contain variable degrees of appendiceal anatomic description. We recognize that operative grade

assignment and its association with outcomes is limited for preoperative surgical decision making as the AAST EGS grade has not yet been validated with preoperative imaging data in children. As data reporting from institutions in low- and/or middle-income countries improves with the development of national emergency surgery registries, similar in structure to the National Surgical Quality Improvement Program (NSQIP), more accurate assessment and benchmarking of global outcomes of acute appendicitis using the AAST grading system should be feasible. This may allow for the meaningful comparison of outcomes and allow for ongoing monitoring to identify improvements. Missing data are an important consideration, especially in austere environments. The institution has published on the development of the hybrid electronic medical record and on its routine functioning. Extensive efforts are made to quality control the data and to ensure its completeness. Generally missing data for all variables and covariates were around 10%. This level of completeness is not universal in low- and middle-income countries, and ongoing efforts to improve medical record keeping are essential to help fully understand the broad spectrum of disease severity encountered in low- and middle-income countries. Finally, the associations of disease severity may have been confounded by the overwhelming utilization of midline laparotomy, all of which can increase complication rates, duration of stay, and complication severity; however, on our multivariable regression, operation type was not associated with increased risk of complication development.

## Conclusion

In children with appendicitis, the AAST EGS grading system is a valid methodology to classify disease severity and is associated with several important clinical outcomes. This tool is a significant advance to estimate disease burden for low- and middle-income countries, highlighting that disease severity can influence outcomes. In South Africa, the differences in accessibility to imaging, laparoscopy, and healthcare systems may also contribute to a patient's outcome.

### Compliance with ethical standards

**Conflict of interest** The authors have neither financial disclosures nor conflicts of interest, and there was no funding for the generation of this work.

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