BALANCING OVERTREATMENT AND DELAY: NEGATIVE APPENDECTOMY AND PERFORATION IN A FIVE-YEAR COHORT OF ACUTE APPENDICITIS

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ABSTRACT
Background: *Acute appendicitis is a common surgical emergency. The negative appendectomy rate (NAR) and perforation rate are complementary quality metrics reflecting the balance between diagnostic over-caution and delayed intervention.*
Methods: *A five-year retrospective cohort study was conducted at Lady Reading Hospital, Peshawar (2021–2025), including all consecutive patients undergoing emergency appendectomy. Multivariable logistic regression identified independent predictors of NAR and perforation. Postoperative outcomes were graded by Clavien Dindo classification.*
Results: *Of 500 patients (mean age 27.4 ± 14.2 years; 60.0% male), preoperative imaging was used in 40.0%. Histopathology confirmed appendicitis in 415 patients (83.0%), yielding a NAR of 17.0%. Of confirmed cases, 300 (60.0%) were simple, 70 (14.0%) gangrenous, and 45 (9.0%) perforated. The overall complication rate was 6.0% with no mortality. Perforation was associated with significantly higher morbidity versus simple disease (complication rate 33.3% vs. 4.0%; median stay 6 vs. 2 days; 30-day readmission 28.9% vs. 5.0%). Female gender (OR 2.1, 95% CI 1.3–3.5; p = 0.002) and absence of preoperative imaging (OR 1.8, 95% CI 1.1–3.0; p = 0.021) independently predicted negative appendectomy. Age ≥50 years (OR 4.5, 95% CI 2.0–10.1), symptom duration ≥48 hours (OR 6.2, 95% CI 3.1–12.4), and diabetes mellitus (OR 3.0, 95% CI 1.2–7.5) independently predicted perforation (all p < 0.05).*
Conclusion: *A NAR of 17.0% and perforation rate of 9.0% identify clear targets for quality improvement. Standardized clinical scoring with selective imaging protocols and efforts to reduce diagnostic delay are recommended.*
Keywords: *acute appendicitis; negative appendectomy; perforation; imaging; quality improvement; Pakistan*

INTRODUCTION
Acute appendicitis is one of the most common surgical emergencies worldwide[1]. Its annual incidence is on the order of 80–100 cases per 100,000 population in many countries, with peak incidence in the second–third decades of life[1].

Despite modern diagnostic tools, distinguishing acute appendicitis from other causes of acute abdomen remains challenging. The standard treatment is appendicectomy (now usually laparoscopic)[2]. Laparoscopic appendicectomy has largely replaced open surgery due to lower wound infection rates, less pain and shorter hospital stay[3]. However, even after surgery there can be significant morbidity (wound infection, intra-abdominal abscess, ileus, etc.) reported in 2–23% of cases[4].

Importantly, an unavoidable consequence of emergency appendicectomy is the **negative appendectomy rate (NAR)** – the proportion of cases in which the removed appendix is found to be normal (no acute inflammation) on histopathology[5,6]. NAR is widely regarded as a surgical quality metric: unnecessarily removing a normal appendix exposes patients to needless risks, while delaying surgery to avoid any negative cases can increase perforation risk[5,7]. Historically, NARs in early series were reported at ~15–20%, but studies incorporating routine preoperative CT imaging demonstrate substantial reductions in NAR.[5,8,9] Nevertheless, many contemporary cohorts, particularly those with limited imaging resources, still report NAR in the range of 10–20%.[6,9]

Perforated appendicitis (free or contained rupture) is the chief serious complication of delayed diagnosis.[6,7] Reported perforation rates in adults typically range from about 15–30%, with higher rates seen at the extremes of age. Appendicolith and delayed presentation have been shown to be associated with complicated (including perforated) appendicitis.[11] Perforation significantly increases morbidity: patients with perforated appendicitis have longer hospital stay, increased rates of postoperative abscess and wound infection, and higher overall complication rates than those with uncomplicated disease.[7]

Given these considerations, auditing local outcomes of acute appendicitis is essential to evaluate diagnostic accuracy, disease severity at presentation, and short-term surgical outcomes within our setting.

We therefore conducted a five-year retrospective cohort study of all patients who underwent appendicectomy at our institution. The primary objectives were to determine presentation patterns, negative appendectomy rate (NAR), perforation rate, and short-term postoperative outcomes. Secondary objectives included identifying clinical and demographic factors associated with perforated appendicitis and with histologically normal appendices.

To our knowledge, this represents the first comprehensive published audit of appendicectomy outcomes from our center and provides locally relevant data that may inform diagnostic strategies and quality improvement initiatives.

Methods

Study design and setting: We performed a retrospective chart review of patients undergoing appendicectomy at Lady Reading Hospital Peshawar between January 2021 and December 2025.

Inclusion criteria: All consecutive patients of any age or gender who underwent emergency appendicectomy during the study period with a clinical diagnosis of acute appendicitis were included.

Exclusion criteria: Elective interval appendicectomies, incidental appendicectomies (appendix removed during unrelated surgery), and cases without available histopathology results were excluded.

Data collection: We extracted data from HMIS and paper charts. Variables recorded included: age, gender, body mass index (BMI), comorbidities (diabetes, hypertension, cardiovascular disease), presenting symptoms and their duration, physical exam findings, and preoperative labs (white blood cell count, CRP). Use of imaging (abdominal ultrasound or CT) before surgery was noted. Operative details were recorded: surgical approach (laparoscopy vs open), intraoperative findings (simple acute appendicitis, gangrenous, perforation, abscess, or macroscopically normal appendix), and any additional procedures (e.g. peritoneal lavage, stoma). Postoperative outcomes were collected from discharge summaries and follow-up visits: length of hospital stay, 30-day postoperative complications (graded by Clavien–

Dindo), surgical site infection, intra-abdominal abscess, readmission within 30 days, and mortality.

Definitions: A perforated appendix was defined as any appendiceal wall breach with spillage of pus or enteric contents, confirmed either by operative report or histopathology. A *negative appendicectomy* was defined histologically as an appendix without acute inflammatory infiltrates (no neutrophils in the wall or tip). Patients with chronic appendicitis or incidental findings (e.g. carcinoid) were classified as negative for acute appendicitis.

Statistical analysis: Data was analyzed using SPSS v.26. Continuous variables are summarized as mean ± SD (or median with interquartile range as appropriate) and categorical variables as counts and percentages. We compared groups using chi-square or Fisher's exact tests for categorical variables and t-tests or Mann–Whitney U tests for continuous variables. A multivariable logistic regression model was constructed to identify independent predictors of (a) negative appendicectomy and (b) appendiceal perforation. Candidate variables included those with $p<0.10$ in univariable analysis plus clinically relevant factors (age category, gender, symptom duration, imaging use, WBC count). Odds ratios (OR) with 95% confidence intervals (CI) are reported. A two-sided $p<0.05$ was considered statistically significant. Missing data were infrequent (<5% for most variables); cases with missing key variables were excluded from analyses.

Results

Patient Demographics and Clinical Presentation

Over the five-year study period, 500 patients who underwent appendectomy met the inclusion criteria. The cohort had a mean age of 27.4 ± 14.2 years (range 3–82) and comprised 300 males (60.0%) and 200 females (40.0%). Adults (≥18 years) accounted for the majority of the cohort (n=350, 70.0%), while 150 patients (30.0%) were children. The most frequent presenting symptom was right iliac fossa pain (100%), followed by anorexia (60%), nausea or vomiting (55%), and fever (45%). The median duration of symptoms prior to presentation was 24 hours (IQR 18–48 hours), with 100 patients (20.0%) reporting symptoms for ≥48 hours. At presentation, the mean white blood cell (WBC) count was 13.5 ± 4.2 × 10^9/L, and leukocytosis (>10 × 10^9/L) was present in 300 patients (60.0%). Preoperative imaging was utilized in 200 cases (40.0%), consisting of ultrasound in 170 (34.0%) and computed tomography (CT) in 50 (10.0%). Among the patients who underwent ultrasound, the study was diagnostic for appendicitis in 60% of cases. A summary of patient demographics and clinical characteristics is presented in **Table 1.**

Table 1. Patient Demographics and Clinical Presentation (N=500)

Characteristic	Value
Age, years	
Mean ± SD	27.4 ± 14.2
< 18 years, n (%)	150 (30.0)
≥ 18 years, n (%)	350 (70.0)
Gender, n (%)	
Male	300 (60.0)
Female	200 (40.0)

Presenting Symptoms, n (%)	
Right iliac fossa pain	500 (100)
Anorexia	300 (60.0)
Nausea/Vomiting	275 (55.0)
Fever	225 (45.0)
Clinical Findings	
Symptom duration ≥ 48h, n (%)	100 (20.0)
Temperature ≥ 38°C, n (%)	125 (25.0)
WBC count > 10×10^9/L, n (%)	300 (60.0)
WBC count, mean ± SD ($\times10^9$/L)	13.5 ± 4.2
Preoperative Imaging, n (%)	200 (40.0)
Ultrasound	170 (34.0)
CT scan	50 (10.0)

Operative Findings and Histopathology

Of the 500 appendectomies performed, 415 patients (83.0%) had histologically confirmed acute appendicitis, while 85 patients (17.0%) had a normal appendix on histology, constituting the negative appendicectomy rate. Of the confirmed cases, 300 (60.0%) were classified as simple (non-perforated) appendicitis, 70 (14.0%) as gangrenous, and 45 (9.0%) as perforated. The overall perforation rate was therefore 9.0%. Among the 45 perforated cases, 30 (67%) had evidence of a localized abscess or peritonitis at the time of surgery.**Fig.1**

An open appendectomy was the primary approach in 400 cases (80.0%). A laparoscopic approach was attempted in the remaining 100 cases (20.0%) and was successfully completed in 85 patients, with 15 requiring conversion to an open procedure (15.0% conversion rate) due to dense adhesions or unclear anatomy. The utilization of laparoscopy was more common in cases of suspected uncomplicated or negative appendicitis, with the highest rate observed in the negative appendicectomy group (**Table 2**).

Table 2. Operative Findings and Postoperative Outcomes by Histopathology Severity

Finding / Outcome	Simple (n=300)	Gangrenous (n=70)	Perforated (n=45)	Negative (n=85)
Surgical Approach, n (%)				
Laparoscopic	50 (16.7)	8 (11.4)	2 (4.4)	25 (29.4)
Open	250 (83.3)	62 (88.6)	43 (95.6)	60 (70.6)
Median Hospital Stay, days (IQR)	2 (1–3)	4 (3–5)	6 (4–8)	2 (1–3)
Complication Rate, n (%)	12 (4.0)	10 (14.3)	15 (33.3)	2 (2.4)
Wound infection	6 (2.0)	3 (4.3)	4 (8.9)	0
Intra-abdominal abscess	3 (1.0)	2 (2.9)	6 (13.3)	0

Prolonged ileus	3 (1.0)	5 (7.1)	5 (11.1)	2 (2.4)
Readmission within 30 days, n (%)	15 (5.0)	7 (10.0)	13 (28.9)	1 (1.2)
Mortality, n (%)	0	0	0	0

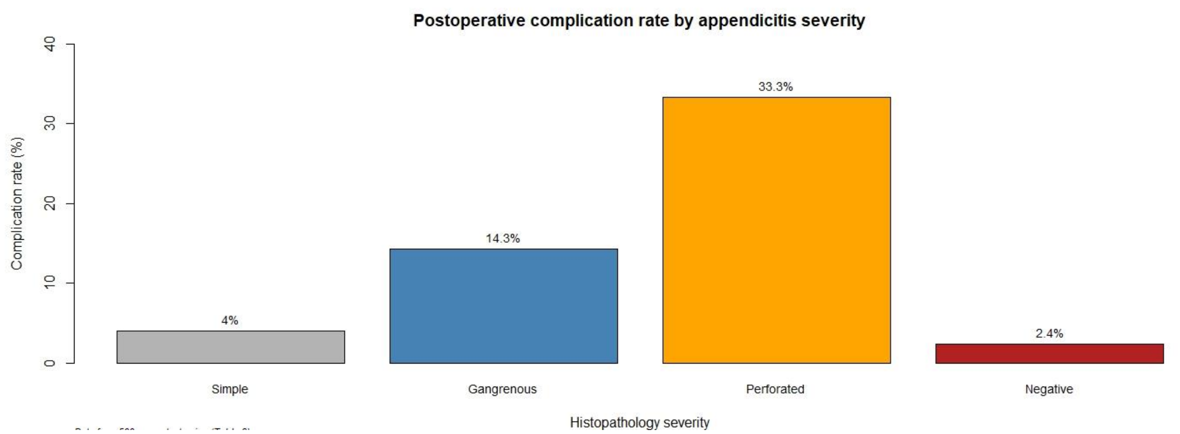

Fig.1 Postoperative complication rate by appendicitis severity

Postoperative Outcomes

The overall postoperative complication rate was 6.0% (30/500). The most common complications were superficial wound infection (3.0%, n=15), intra-abdominal abscess (2.0%, n=10), and prolonged ileus (1.0%, n=5). The vast majority of complications were Clavien–Dindo grade I or II. One patient (0.2%) required a re-laparotomy for drainage of an intra-abdominal abscess (grade IIIb). No mortality was observed.

Complication rates and resource utilization were directly related to the severity of appendicitis (Table 2). Patients with simple appendicitis had a low complication rate (4.0%) and a median hospital stay of 2 days. In contrast, those with gangrenous or perforated appendicitis experienced significantly higher morbidity, with complication rates of 14.3% and 33.3%, and longer median hospital stays of 4 days and 6 days, respectively. The 30-day readmission rate for the entire cohort was 8.0% (40/500), with the highest rate observed in the perforated group (28.9%).

Predictors of Negative Appendicectomy

On univariable analysis, negative appendicectomy was significantly more frequent in females compared to males (25% vs. 12%, $p < 0.001$) and in patients ≤18 years old (22% vs. 14%, $p = 0.02$). Lower preoperative WBC and C-reactive protein (CRP) levels were also associated with negative pathology ($p < 0.05$). The use of preoperative imaging was associated with a lower negative appendicectomy rate; 30% of patients with a negative appendix had not undergone imaging, compared to 48% of those with confirmed appendicitis ($p = 0.01$). In a multivariable logistic regression model (Table 3), female gender (OR 2.1, 95% CI 1.3–3.5, $p = 0.002$) and the absence of preoperative imaging (OR 1.8, 95% CI 1.1–3.0, $p = 0.021$) remained independent predictors of negative appendicectomy after adjusting for age, WBC count, and symptom duration.

Table 3. Multivariable Logistic Regression: Predictors of Negative Appendicectomy

Variable	Odds Ratio	95% Confidence Interval	p-value
Female gender	2.1	1.3 – 3.5	0.002
Age < 18 years	1.4	0.8 – 2.4	0.20
WBC ≤ 10×10^9/L	1.5	0.9 – 2.6	0.11
No preoperative imaging	1.8	1.1 – 3.0	0.021

Symptom duration ≥ 48h	1.2	0.7 – 2.1	0.50

Predictors of Perforation

Patients with perforated appendicitis were significantly older (mean age 34.8 vs. 26.5 years, $p < 0.001$) and more likely to have a delayed presentation (symptom duration >48 hours) compared to those with non-perforated appendicitis (60% vs. 15%, $p < 0.001$). The presence of comorbidities was also more common in the perforated group (20% vs. 5%, $p < 0.001$). Multivariable analysis (Table 4) identified age ≥50 years (OR 4.5, 95% CI 2.0–10.1, $p < 0.001$), symptom duration ≥48 hours (OR 6.2, 95% CI 3.1–12.4, $p < 0.001$), and diabetes mellitus (OR 3.0, 95% CI 1.2–7.5, $p = 0.019$) as factors independently associated with appendiceal perforation.

Table 4. Multivariable Logistic Regression: Predictors of Appendiceal Perforation

Variable	Odds Ratio	95% Confidence Interval	p-value
Age ≥ 50 years	4.5	2.0 – 10.1	< 0.001
Symptom duration ≥ 48h	6.2	3.1 – 12.4	< 0.001
Diabetes mellitus	3.0	1.2 – 7.5	0.019
Female gender	0.8	0.4 – 1.5	0.48
Elevated WBC	1.1	0.6 – 2.0	0.75

Discussion

In our five-year series, the negative appendectomy rate (NAR) was 17%, which is within the broad range reported in the literature but higher than values from resource-rich settings. For example, Joshi et al. reported a 17.2% NAR in a large series, noting rates ranging from 4% to 45% in various reports. Historical series without routine imaging commonly accepted NARs of 15–25%, but modern imaging has driven NAR much lower[12]. Large US datasets now show overall NAR around 4–5% when CT is widely used[13]. One ACS-NSQIP analysis (2016) found a 4.5% NAR overall, but 19% if no imaging was done versus only ~2.5% when CT was performed. Meta-analyses similarly estimate pooled NAR near 13%[14]. In specialized centers with systematic imaging protocols, NARs under 5% are reported[15,16], and recent reviews note that routine imaging has converged NAR into the low single digits[17]. Our NAR (17%) likely reflects our lower imaging utilization (only 40% had pre-op imaging) and patient mix.

Female sex and absence of imaging were independent predictors of negative appendectomy in our multivariable model[18]. This is consistent with many prior reports. Female patients, especially of reproductive age, are well known to have higher NAR. In our cohort, women were over twice as likely to have a normal appendix removed, echoing Joshi et al. who found NAR of 33% in females versus 12% in males[11]. Shaban et al. similarly identified female gender as an independent predictor of NA[19]. We also observed that our patients with negative pathology tended to have lower inflammatory markers, as reported by others[19,20]. The combination of non-specific symptoms in women (often with gynecologic mimics) and borderline lab results can mislead clinicians[21]. Our finding that omission of imaging (largely CT) was associated with higher NAR underscores the value of diagnostic imaging. Indeed, multiple studies show that imaging dramatically reduces false-positive surgeries: for instance, with ultrasound suggesting appendicitis and confirmatory CT, the negative appendectomy rate can fall to ~0.6%. Overall, modern guidelines advocate risk stratification and selective imaging (e.g. ultrasound-first then CT if equivocal) to minimize unnecessary surgery[17]. In our practice, expanding the use of ultrasound and CT in equivocal cases, particularly in young women and those with low scores – would be expected to lower the NAR without increasing delays.

Our overall appendiceal perforation rate was 9%, which is at the lower end of commonly cited ranges (often 15–30%) and is comparable to the ~10% "floor" described in classic analyses[22]. In line with previous studies, we found that older age, delayed presentation, and diabetes were independent risk factors for perforation[23]. For example, patients ≥50 years had ~4.5-fold higher odds of rupture, and those with symptom duration ≥48 hours had a ~6-fold increase, closely mirroring Shani Aoda et al.'s findings[24]. Chronic illness (especially diabetes) tripled the risk in our data, again consistent with other work[24]. These associations are biologically plausible, comorbid vascular disease and immune dysfunction, plus prolonged untreated inflammation, predispose to wall necrosis. Our results reinforce the conventional teaching that delays in seeking care markedly raise the chance of complication.

The impact of perforation on outcomes was striking. Patients with perforated appendicitis suffered a 33% overall complication rate (including abscess, ileus, wound infection) versus only 4% in simple cases. They also had longer median hospital stays (6 vs 2 days) and far higher 30-day readmissions (29% vs 5%). This severe morbidity burden is well documented; Shani Aoda et al. reported that postoperative complications occurred in over half of perforated cases compared to <20% of nonperforated cases[24]. Velanovich's classic decision analysis showed that aggressively minimizing perforation (to a plateau around 10%) improves overall outcomes, even at the cost of a higher NAR[22]. In other words, it is better to remove a few extra normal appendices if that prevents a perforation – but of course the goal is to avoid both whenever possible. In our cohort no deaths occurred, but the prolonged morbidity with rupture (wound infections, intra-abdominal abscesses, ileus) underscores why early diagnosis and treatment remain critical.

Our study has limitations inherent to its retrospective, single-center design. Imaging and management practices evolved over time and were not standardized, and we lack long-term follow-up beyond 30 days. The reliance on operative reports and pathology records may miss some subtle predictors, and our results reflect local resources (notably limited CT availability) which may differ elsewhere. However, strengths include the large consecutive sample and complete histopathologic confirmation. Importantly, this is the first comprehensive audit of appendicitis outcomes from our institution, providing a valuable baseline for quality improvement.

In conclusion, the five-year results illustrate the classic balance between overtreatment and delay in appendicitis care. Our 17% NAR suggests room for improvement in diagnostic accuracy, particularly among young women; strategies such as standardized scoring and liberal imaging (with ultrasound and CT per guidelines) could reduce this rate without endangering patients. At the same time, attention to prompt diagnosis is crucial to prevent rupture: as expected, perforation (9% of cases) drove a much higher complication rate and longer stays. Current consensus (WSES, ACR, NICE, etc.) strongly favors laparoscopic appendectomy as first-line (for both uncomplicated and complicated cases) due to lower wound morbidity, along with tailored imaging algorithms in equivocal cases. Ultimately, quality metrics should consider both NAR and perforation rate together, as Velanovich argued. Ongoing audit and adherence to evidence-based protocols – expanding laparoscopy use, applying clinical scores, and optimizing imaging – should help shift our outcomes toward the favorable benchmarks reported elsewhere.

Conclusion

In this large, single-center cohort from Pakistan, the negative appendicectomy rate was 17.0% and the perforation rate was 9.0%. Female gender and lack of preoperative imaging were independent predictors of negative appendicectomy, while older age, delayed presentation (>48 hours), and diabetes mellitus were significantly associated with perforation. These findings align with international data and identify clear targets for enhancing the quality of surgical care. The implementation of validated diagnostic clinical scores, combined with a standardized protocol for selective preoperative imaging in equivocal cases, represents a promising strategy to reduce unnecessary operations without compromising the low perforation rate. Continued, regular audit of appendicitis outcomes is essential to monitor the effectiveness of such quality improvement initiatives and to ensure optimal patient outcomes.

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