



## Cohort Study

## A local experience of non-operative management for an appendicitis cohort during COVID-19



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## ABSTRACT

**Background:** During the first United Kingdom COVID-19 wave, the Royal Colleges of Surgeons initially recommended conservative management with antibiotics instead of surgery for appendicitis. This study compared local outcomes of appendicitis during this period with a pre-COVID-19 cohort.

**Methods:** An observational study was conducted in a district general hospital. All episodes of appendicitis were prospectively studied from 25<sup>th</sup> March 2020 until 26<sup>th</sup> May 2020 and compared with a retrospective pre-COVID cohort from 27<sup>th</sup> November 2019 until 29<sup>th</sup> January 2020. Primary outcome was 30-day treatment failure of simple appendicitis for conservatively managed cases during COVID-19 compared to surgically managed cases pre-pandemic. Treatment failure was defined as any unplanned radiological or surgical intervention.

**Results:** Over nine weeks, there were 39 cases of appendicitis during COVID-19 and 50 cases pre-COVID-19. Twenty-six and 50 cases underwent appendicectomy during and pre-COVID-19 respectively. There was no difference in 30-day postoperative complication rates and nor were there any peri-operative COVID-19 infections. Twelve cases of simple appendicitis underwent conservative management during COVID-19 and were compared with 23 operatively managed simple cases pre-pandemic. There was a higher failure rate in the conservative versus operative group (33.3 vs 0% OR = 24.88, 95% CI 1.21 to 512.9,  $p=0.0095$ ). Length of stay was similar (1.5 vs 2.0  $p=0.576$ ).

**Discussion:** Locally, conservative management was more likely to fail than initial appendicectomy. We suggest that surgery should remain first line for appendicitis, with conservative management reserved for those with suspected or proven COVID-19 infection.

## 1. Background

There were significant concerns about safety of surgery during the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) outbreak in the United Kingdom (UK). Tracheal intubation is high risk for aerosol generation and studies showed SARS-Cov-2 can remain aerosolised for 3 h [1,2]. There were similar concerns for laparoscopic surgery due to examples of other viruses becoming aerosolised in the pneumoperitoneum [3]. SARS-Cov-2 had also been found in faeces [4] and peritoneal fluid [5] which had implications for any gastrointestinal surgery.

In 2014, the Royal Colleges of Surgeons (RCS) commissioning guidance advised laparoscopic appendicectomy should be the first line treatment for appendicitis [6]. The March 2020 RCS General Surgery

COVID-19 guidance markedly differed, advising conservative management or open appendicectomy rather than laparoscopic surgery [7].

The argument for conservative management versus surgical management for uncomplicated appendicitis is unclear. A Cochrane review of five studies with a 20% margin for non-inferiority analysis was inconclusive and the conclusion was that appendicectomy should remain the standard of care [8]. Furthermore, there is a 39% recurrence rate for conservative management [9].

We have captured local outcomes of this unique period in the UK where conservative management was considered as an alternative to the status-quo of appendicectomy.

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### 1.1. Primary outcome

To compare the 30-day treatment failure rate between conservatively managed simple appendicitis during COVID-19 and surgically managed simple appendicitis in the pre-COVID-19 era. Treatment failure is defined as any unplanned surgical or radiological intervention within 30 days of conservative or operative management.

### 1.2. Secondary outcomes

To compare characteristics (demographics; duration of symptoms; severity) and outcomes (length of stay; 30-day complication rate; negative appendectomy rate) of patients diagnosed with appendicitis during COVID-19 versus the pre-COVID-19 cohort.

## 2. Method

This work is compliant and reported in line with the “Strengthening the Reporting of Cohort Studies in Surgery” (STROCSS) criteria [10]. This been registered at [www.researchregistry.com](http://www.researchregistry.com) with the unique identifying number [researchregistry6518](https://www.researchregistry.com/record/10.21956/RESEARCHREGISTRY.6518).

### 2.1. Study design

We conducted a cohort study in a British district general hospital (DGH) with a prospective arm observed during COVID-19 compared to a retrospective, pre-COVID-19 group. Prospective data ran for 9 weeks from 25<sup>th</sup> March 2020 (the date the first RCS guidance was released [7]) until 26<sup>th</sup> May 2020. The retrospective cohort ran for 9 weeks from 27<sup>th</sup> November 2019 until 29<sup>th</sup> January 2020; the date of the first confirmed case in the UK. We performed an overall comparison of pre- and during-COVID-19 groups and a subgroup analysis comparing conservative and surgical management for uncomplicated cases.

The project was approved by our Research and Development department and registered as project 498. Ethical approval was not required as these changes in practice were governed by clinical decisions based on professional guidance rather than for research purposes.

### 2.2. Participants

We included adults and children (under 16 years) with clinical or radiological appendicitis. Cases of histologically normal appendix were included to calculate negative appendectomy rate. Patients coded as appendicitis on the electronic patient record system who then had alternative diagnoses were excluded.

For the conservative versus surgical management analysis, the inclusion criterion for the COVID-19 conservative management group was patients initially treated with antibiotics alone for clinically or radiologically uncomplicated appendicitis. Consequently, the inclusion criterion for the pre-COVID-19 surgical management group was patients with uncomplicated intraoperative findings. Exclusion criteria for both included suspected or confirmed complicated disease such as peritonitis; pyrexia  $\geq 38$  °C; gangrenous, perforated, contaminated or mass-forming appendicitis. These filters were applied to our database to form two subgroups.

All management decisions were consultant led, and independent to this case review.

As per trust protocols, empirical intravenous antibiotics for appendicitis were amoxicillin (ciprofloxacin for penicillin allergy), metronidazole and gentamicin and oral equivalents were co-amoxiclav/ciprofloxacin and metronidazole. Patients treated conservatively would receive a minimum seven days of antibiotics.

All operations were performed by either a Consultant surgeon; a Senior Associate Specialist or a Specialty Training 3+ registrar. During COVID-19, a Consultant would be present in theatres for all appendectomies. In the pre-COVID period, a laparoscopic approach was gold

standard. During COVID, rapidly changing RCS guidelines meant the department initially performed open appendectomy but reverted back to a laparoscopic approach as first line from 1<sup>st</sup> May 2020.

### 2.3. Data collection

Prospective, anonymised data was recorded for all patients admitted with a diagnosis of appendicitis. The information governance department supplied the details of patients coded as appendicitis upon discharge for the retrospective pre-COVID arm. Patients were followed up using the electronic record system to track both their inpatient progress and any subsequent readmission.

### 2.4. Measuring variables

The independent variables captured for each episode included duration of symptoms prior to surgical review; vital signs; examination findings; serum biochemistry results; radiology reports; method of diagnosis and initial management strategy. Overall operative severity was classified as either simple (macroscopically normal or simply inflamed appendicitis) or complicated (gangrenous/perforated/phlegmon formation). Episodes of non-operative management for uncomplicated appendicitis were classified as “simple”. Post-operative complications were classed in accordance with the Clavien-Dino system [11].

Treatment failure was defined as unplanned operative or radiological intervention in the 30 days after either appendectomy or initiation of antibiotics for the pre-COVID-19 surgically managed and during-COVID-19 conservatively managed groups respectively.

Other outcomes included length of stay (LOS) and negative appendectomy rate; defined as the histological absence of inflammation or pathology in the appendiceal specimen.

### 2.5. Statistical analysis

Statistical analysis was performed with Graphad Prism 6.01. For continuous data, the D’Agostino and Pearson test determined normality and a two-tailed Student-T or Mann-Whitney *U* test was applied accordingly. Results are expressed as either medians and interquartile ranges (IQR) or means and standard deviation (SD) depending on normality.

2.5.2 For categorical data, absolute numbers (n) and percentages have been used. Fischer’s exact test is used where two categories are compared and a Chi-Squared test for the remainder. Significant outcomes are expressed as odds ratios (OR) to a 95% confidence interval (CI); a p-value  $\leq 0.05$  is the threshold for statistical significance.

## 3. Results

### 3.1. Appendicitis before and during COVID-19

#### Characteristics

There were 39 cases of appendicitis during COVID-19 over nine weeks. For the retrospective arm, 50 cases were identified in a similar time frame. Their characteristics are summarised in [Table 1](#). Both groups were comparable in terms of demographics; comorbidities; duration of symptoms prior to presentation; vital signs; examination and inflammatory markers. All patients were followed up successfully.

No patients in the pandemic cohort had symptoms suggestive of COVID-19. In terms of testing, 41.0% (n = 16) and 25.6% (n = 10) had chest imaging and antigen swabs respectively which were all negative for SARS-COV-2.

#### Diagnosis and management

Radiology was the minority method of diagnosis in the pre-COVID-19 era but became the majority during the pandemic (42.0% vs 64.1%,  $p=0.004$ ). Expectedly, rates of non-operative management rose

**Table 1**  
Pre-treatment characteristics of patients in the group with appendicitis during COVID-19 versus the pre-COVID-19 group.

Pre-treatment characteristics	Before COVID		During COVID		P value
Age (years)	29.1	±15.2	34.4	±20.8	
Gender					
Male (n = )	22	44.0%	20	51.3%	
Female (n = )	28	56.0%	19	48.7%	
Comorbidities					
F&W (n = )	37	74.0%	20	51.3%	
Cardiovascular (n = )	1	2.0%	2	5.1%	
Respiratory (n = )	2	4.0%	2	5.1%	
Diabetes (n = )	2	4.0%	2	5.1%	
Other (n = )	8	16.0%	5	12.8%	
Duration of symptoms (hours)	24	17.6 to 48	24	22.0 to 72.0	
Examination findings					
Locally tender (n = )	46	92.0%	35	89.7%	
Generally tender (n = )	4	8.0%	4	10.3%	
Heart rate (beats per minute)	92.4	±21.7	92.3	±17.6	
Systolic BP (mmHg)	114.6	±13.9	123.8	±16.3	
Temperature (degrees Celcius)	37.3	±0.7	37.4	0.8	
Respiratory (breaths per minute)	18	16 to 20	18	16 to 20	
Oxygen saturations (%)	98	97 to 99	98	97 to 99	
WBC (10 <sup>9</sup> /L)	12.2	9.5 to 15.8	14.0	12.0 to 17.0	
CRP (mg/L)	56	14.0 to 108.5	43.0	6.3 to 132.0	
Method of diagnosis <sup>a</sup>					
Clinical (n = )	29	58.0%	14	35.9%	
Radiological (n = )	21	42.0%	25	64.1%	
Abdominopelvic imaging					<b>0.004</b>
None (n = )	28	56.0%	9	23.1%	
Ultrasound (n = )	7	14.0%	9	23.1%	
Computed Tomography (n = )	15	30.0%	23	59.0%	
Magnetic Resonance Imaging (n = )	0	0.0%	2	5.1%	
Initial management strategy					
Conservative (n = )	0	0.0%	17	43.6%	<b>0.0001</b>
Operative (n = )	50	100.0%	22	56.4%	

<sup>a</sup> Clinical diagnosis was confirmed and documented upon review by the on-call consultant or registrar. Radiological diagnosis was defined as report concluding appendicitis by a radiologist via any imaging modality.

from 0.0% to 43.6% ( $p=0.0001$ ) during COVID-19.

**Severity of appendicitis**

Using our aforementioned classification, overall rates of simple and complicated disease also remained statistically similar before and during COVID-19 (Table 2).

**Outcomes**

Median LOS was statistically similar across both groups (see Table 3). Between the 50 pre- and 26 during- COVID-19 patients who underwent surgery, there was no significant difference in post-operative

**Table 2**  
Complexity of appendicitis.

	Before COVID		During COVID	
Operative/Radiological/findings				
Macroscopically normal appendix	1	2.0%	1	2.6%
Other (pinworms)	1	2.0%	0	0.0%
Inflamed appendicitis	29	58.0%	24	61.5%
Gangrenous appendicitis	8	16.0%	5	12.8%
Perforated appendicitis	8	16.0%	7	17.9%
Phlegmon	3	6.0%	2	5.1%
Severity of appendicitis				
Simple	31	62.0%	25	64.1%
Complicated	19	38.0%	14	35.9%

**Table 3**  
Outcomes of appendicitis.

Outcomes	Before COVID		During COVID	
Length of stay (days)	2.0	1.4 to 3.2	2.1	1.3 to 3.2
30-day post-operative complications				
No complication (n = )	45	90.0%	35	84.6%
Any complication (n = )	5	10.0%	4	15.4%
30-day complications by Clavien Dindo grade				
I-II (n = )	4	8.0%	2	5.1%
III-V (n = )	1	2.0%	2	5.2%
Negative appendectomy rate (n = )	2	4.0%	0	0.0%

complications. One complication required reoperation in the pre-COVID-19 group (collection and small bowel obstruction) compared to two in the during-COVID-19 group (deep wound infection; collection). The negative appendectomy rate for the groups were similar (4% vs 0%  $p=0.495$ ). No patients developed postoperative COVID-19 infection, nor were there any deaths.

**3.2. Uncomplicated appendicitis: conservative versus surgical management**

**Characteristics**

Seventeen cases were treated conservatively during COVID-19. Five cases of radiologically complicated appendicitis were excluded, leaving 12 fitting our criteria as conservative management simple appendicitis. Of the 50 pre-COVID-19 patients, 23 had intraoperatively simple appendicitis. As shown in Table 4, there were comparable in demographics, duration of symptoms, observations and inflammatory markers.

**Outcomes**

As shown in Table 5, LOS was statistically similar in both groups. There was a 33.3% ( $n=4$ ) failure rate in the conservative management group compared with a 0% in the surgical management group (OR =

**Table 4**  
Sub-group pre-treatment characteristics: Operative versus Conservative.

Pre-treatment characteristic	Operatively managed appendicitis (pre-Covid-19)	Conservatively managed appendicitis (during COVID-19)
Age (years)	27.3 ±12.3	27.4 ±12.3
Gender		
Male (n = )	10 43.5%	5 41.7%
Female (n = )	13 56.5%	7 58.3%
Comorbidity		
F&W (n = )	17 73.9%	8 56.2%
Cardiovascular (n = )	0 0.0%	0 6.3%
Respiratory (n = )	3 13.0%	1 6.3%
Diabetes (n = )	1 4.3%	0 0.0%
Other (n = )	2 8.7%	2 26.7%
Duration of symptoms (hours)	24.0 12.0 to 48.0	24.0 7.3 to 44.5
Examination findings		
Locally tender (n = )	23 100.0%	12 100.0%
Generally tender (n = )	0	0
Heart rate (beats per minute)	84 78 to 94	95 74 to 113
Systolic BP (mmHg)	117 ±15	121 ±15
Temperature (degrees Celcius)	37.0 36.6 to 37.3	37.0 36.8 to 37.1
Respiratory (breaths per minute)	17 16 to 20	18 16 to 22
Oxygen saturations (%)	98 97 to 99	98 97 to 98
WBC (10 <sup>9</sup> /L)	11.8 ±4.2	13.7 ±3.9
CRP (mg/L)	52 7.1 to 79.0	16.3 2.3 to 31.8
Method of diagnosis		
Clinical (n = )	15 65.2%	6 50.0%
Radiological (n = )	8 34.8%	6 50.0%
Abdominopelvic imaging		
None (n = )	14 60.1%	6 37.5%
USS (n = )	4 17.4%	7 43.8%
CT (n = )	5 21.7%	7 43.8%
MRI (n = )	0 0%	2 12.5%

**Table 5**  
Sub-group outcomes: Operative versus Conservative.

Outcomes	Operative pre-COVID		Conservative during COVID		<i>P</i> value
Length of stay (days)	1.5	1.3 to 2.0	2.0	0.9 to 3.0	0.576
30-day treatment failure					<b>0.0095</b>
Failure	0	0.0%	4	33.3%	
No failure	23	100.0%	8	66.6%	

24.88, 95% CI 1.21 to 512.9,  $p=0.0095$ ). None of the four failing conservative management suffered any post-appendectomy 30-day adverse events.

#### 4. Discussion

UK non-COVID-19 acute medical admissions fell at the height of the pandemic [12] and there were concerns acute illnesses would present at more advanced stages [13]. Although fewer presented with appendicitis during the pandemic, overall comparison shows similarities in duration and severity of disease before and during COVID-19. This is reassuring that patients are still presenting and being referred appropriately and hence increases the validity of comparisons between the cohorts.

Results indicate that conservative management of simple appendicitis is significantly likelier to fail than initial appendectomy. This correlates with findings that approximately one in four conservatively managed patients fail within 30 days versus one in 40 surgical management patients [14]. This reflects the 20% 30-day treatment failure rate for conservatively managed appendicitis reported by the recently published randomised controlled trial by the Comparing Outcomes of antibiotic Drugs and Appendectomy (CODA) collaborative [15]. Our LOS does not favour conservative management either, with no significant difference compared to appendectomy.

There are, however, valid counter arguments in favour of conservative management. The risks of peri-operative COVID-19 associated mortality has been reported in the region of 24%. Despite having a similar rate of non-operative management failure to our study, the aforementioned randomised controlled trial by the CODA collaborative also reported non-inferiority between conservative versus surgical management in terms of 30-day patient quality of life [15]. Furthermore, conservative management could limit the harm of negative appendectomy.

This study is limited by small sample sizes due to local practice shifting to pre-covid management of acute appendicitis 38 days into the 63-day study period given our low local incidence of COVID-19. This reflected the May 2020 RCS update acknowledging risks associated with acute admissions and laparoscopic surgery, but recommending laparoscopy could still be used where the benefit outweighed risk [16]. The pattern of appendicitis, incidence of COVID-19, interpretation of guidelines and outcomes may vary throughout the country and will be evaluated in the multi-centre HAREM trial [17].

#### 5. Conclusion

Our local experience of appendicitis during COVID-19 is that for simple disease, conservative management results in higher failure rates and equivocal LOS compared with initial appendectomy. Whilst debates of open versus laparoscopy is beyond the scope of this paper, we suggest appendectomy remains first-line treatment during COVID-19 for patients not suspected to be infected; conservative management should be reserved for those with suspected or proven concurrent infection.

However, it must also be highlighted that there were no adverse post-operative events in the patients failing conservative management who underwent delayed appendectomy. This suggests that whilst inferior to

operative management, conservative management is not an unsafe choice and may still be a viable option during subsequent waves in case of reduced theatre capacities due to redeployment of anaesthetic staff and resources.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

#### Declaration of competing interest

The authors have no conflicts of interest to declare and nor were there any sources of funding for this project.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.02.006>.

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