Health Sciences Review 3 (2022) 100021

Contents lists available at ScienceDirect

Health Sciences Review

journal homepage: www.elsevier.com/locate/hsr

Changes in hospital admissions and complications of acute appendicitis during the COVID-19 pandemic: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
Acute appendicitis
Appendectomy

ABSTRACT

Background: Acute appendicitis (AA) is one of the most common emergencies in general surgery worldwide. During the pandemic, a significant decrease in the number of accesses to the emergency department for AA has been recorded in different countries. A systematic review of the current literature sought to determine the impact of Coronavirus Disease 2019 (COVID-19) on hospital admissions and complications of AA.
Method: A systematic search was undertaken to identify repeated cross-sectional studies reporting the management of AA during the COVID-19 pandemic (index period) as compared to the previous year, or at the turn of lockdown (reference period). Data were abstracted on article (country of origin) and patients characteristics (adults, children [i.e. non adults, <18-year-old]), or mixed population) within the two given timeframes, including demographics, number of admissions for AA, number of appendectomies, and complicated appendectomies.
Results: Of 201 full-text articles assessed for eligibility, 54 studies from 22 world countries were included. In total, 27 (50%) were conducted on adults, 12 (22%) on children, and 15 (28%) on a mixed patients population. The overall rate ratio of admissions for AA between the two periods was 0.94 (95%CI, 0.75-1.17), with significant differences between studies on adults (0.90 [0.74-1.09]), mixed population (0.50 [0.27-0.90]), and children (1.50 [1.01-2.22]). The overall risk ratio of complicated AA was 1.65 (1.32-2.07), ranging from 1.32 in studies on children, to 2.45 in mixed population.
Conclusion: The pandemic has altered the rate of admissions for AA and appendectomy, with parallel increased incidence of complicated cases in all age groups.

Two sentence summary

This systematic review identified 54 studies reporting on the management of acute appendicitis (AA) in the COVID-19 era. Our findings indicate that the effect of the pandemic on the rate of admissions for AA was different over age groups (i.e. declined in adults and increased in children), as opposed to an ubiquitous increase in complicated cases.

Introduction

Acute appendicitis (AA) is one of the most common emergencies in general surgery worldwide, with an incidence rate of 90–100 patients per 100,000 inhabitants per year in developed countries, and an estimated lifetime risk of 7–8% [1].

Appendectomy has long been the gold standard for treatment of AA. However, the use of antibiotic therapy as an alternative to surgery is enshrined in current guidelines [2], as supported by several high-quality studies. In a very recent trial, antibiotics were noninferior to appendectomy on the basis of results of a standard health-status measure [3].

AA has been traditionally regarded as a progressing disease, with a significant risk of perforation. However, a selection bias due to spontaneous resolution of non-perforated cases has vitiated this long-lasting assumption. Indeed, there is an increasing body of evidence suggesting

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https://doi.org/10.1016/j.hsr.2022.100021
Received 23 February 2022; Accepted 25 February 2022

a relationship between perforation and the pre-hospital (rather than in-hospital) delay [4].

During the Coronavirus Disease 2019 (COVID-19) pandemic, a significant decrease in the number of accesses to the emergency department (ED) for AA has been recorded in many institutions from different countries. The management of AA has become more challenging for surgeons facing hospital bed shortages and resource reallocation [5,6]. Non-operative management in the setting of COVID-19 has been advocated as a safe, short-term alternative to surgery with acceptably low failure and complication rates [7]. In this scenario, it remains unclear whether the increasing delay between the onset of symptoms and medical consultation has worsened outcomes in these patients.

Therefore, a systematic review of the current literature sought to determine the impact of COVID-19 on changes in the number of hospital admissions for AA and complicated cases.

Materials and methods

A systematic review was performed according to a predefined protocol. The study is reported in line with the PRISMA 2020 statement (Supplementary Table 1) [8].

A systematic search was undertaken to identify published articles relating to the management of patients with AA during the COVID-19 pandemic.

To be included in the review, papers needed to compare the number of admissions for AA and/or appendectomies within two time periods (i.e. repeated cross-sectional studies): (1) during the COVID-19 pandemic (index period), as compared to the previous year, or at the turn of lockdown (reference period). The latter may refer to the period shortly after or at the turn of lockdown, depending on studies. Only studies with full text in the English language were included. A minimum population sample of 20 patients in the index period was imposed for eligibility. Papers were excluded if they did not fit into the conceptual framework of the study.

To identify potentially relevant documents, the following bibliographic databases were searched from 1 December 2019 to 05 March 2021: MEDLINE, Embase, Scopus, Web of Science, and MedxRiv (including preprint publications). The final search strategy for each database is showed in Supplementary Table 2.

Two reviewers (MO and MP) sequentially evaluated the titles, abstracts and full text of all publications identified by our searches for potentially relevant studies. Any disagreements on study selection and data extraction were resolved by consensus and discussion with other authors (UG and GG).

A single investigator (NS) charted all data from eligible papers using a semi-structured charting pro-forma designed for the purpose of this study. Three other researchers verified the data for accuracy (UG, MO, MP and GG).

Data were abstracted on article (country of origin) and patients characteristics (adults, children [i.e. non adults, <18-year-old], or mixed population) within the two given study periods (in number of days), including demographics, number of admissions for AA, number of appendectomies, duration of symptoms (in days) prior to hospital admission, surgical approach (i.e. laparoscopic vs. open), perforated or complicated AA (intra-operative finding, defined as peritonitis, abscesses, or perforated AA), and length of stay. The number of COVID-19 active cases per million people on the day in the middle of the index period in the country where each study was conducted was also extrapolated.

Assessments of study quality was undertaken according to the Johanna Briggs Institute appraisal tool for analytical cross-sectionals studies [9]. Two reviewers (UG and NS) independently performed the risk of bias evaluation and categorized the included articles as ‘high risk’ when the study bias rating ‘yes’ score was between 0% and 49%, ‘moderate risk’ when the study ‘yes’ score was between 50% and 69%, and ‘low risk’ when the study ‘yes’ score was above 70%. Any disagreement was resolved by consensus with a third author (GG). A quantitative synthesis of data collected from eligible papers is presented and stratified by population (i.e. adults, children, or mixed).

Statistical analysis

A Hartung-Knapp-Sidik-Jonkman random effects meta-analysis allowed to pool the rate ratios of admissions for AA and appendectomies, and to compare rates between the pandemic and the matched pre-pandemic periods. Complications over the number of appendectomies were assessed across the two periods and pooled as risk ratios. Quantitative heterogeneity was determined by conducting a formal test of homogeneity and evaluating the proportion of variability due to heterogeneity (I^2). Subgroup analyses were performed by type of population, i.e. adults, children, and mixed. Regression-based Egger test and eyeball evaluation of the contour-enhanced funnel plots were used to determine small-study effects.

The prediction intervals were reported along with pooled results (with 95% confidence intervals [CI])[10] to show the range of true rate and risk ratios that can be expected in future studies.

All statistical analyses were performed using Stata 16 (StataCorp LLC, College Station, TX, USA).

Results

Selection of sources of evidence

After 376 duplicates were removed, a total of 976 citations were identified from searches of electronic databases and review article references. Based on the title and the abstract, 775 were excluded, with 201 full text articles to be retrieved and assessed for eligibility. Of these, 147 were excluded, with 54 repeated cross-sectional studies from 22 world countries considered eligible for this review (Fig. 1). In total, 27 (50%) were conducted on adults (Table 1), 12 (22%) on children (Table 2), and 15 (28%) on a mixed patients' population (Table 3).

Of the included studies, 15 (28%) were multicenter. Gender prevalence was available from 31/54 (57%) studies, with a slight male prevalence across the three groups of study population in both periods (median index period, 58% [interquartile range limits, IQRL, 52%-68%]; reference period, 55% [48%-63%]). No substantial differences in age were found between the two study periods across the three groups.

The timing of the outbreak differed in each country at the time of data collection. Indeed, the number of COVID-19 cases ranged from 1 (in Israel) to 2,637 (in the United Kingdom) per 10^6 people in the middle of the index period (median, 718; IQRL, 174-718), with no major differences across the three study groups of adults, children, and mixed populations.

The duration of symptoms prior to hospital admission (n = 9[17%] studies) and length of stay (n = 14 [26%] studies) were similar between the two periods.

Rate ratio of admissions for AA

The overall rate ratio of admissions for AA between the index and reference periods was 0.94 (95%CI, 0.75-1.17), with statistically significant differences (homogeneity test $P<0.0001$) between studies on adults (0.90 [0.74-1.09]), mixed population (0.50 [0.27-0.90]), and children (1.50 [1.01-2.22]) (Fig. 2). Taking into account the heterogeneity across studies, the 95% prediction interval was 0.27-3.23. No small study effect was observed ($P = 0.195$; Supplementary Fig. 1).

Rate ratio of appendectomies

The overall rate ratio of appendectomies between the index and reference periods was 0.80 (0.63-1.03), with lower estimates in studies on a mixed population (0.39 [0.24-0.64]) and adults (0.82 [0.66-1.02]), compared to children (1.43 [0.95-2.16]) (Fig. 3). The 95% prediction

Table 1
Cross sectional studies comparing the number of admissions for acute appendicitis in the adult population

Author	Country	Index period					Pre-pandemic period			
		No. COVID cases per 10^6 people at mid index period^	No. days	No. patients	Age*	Perforated or complicated#	No. days	No. patients	Age*	Perforated or complicated#
Allen [22]	New Zealand	189	72	75	NR	NR	72	68	NR	NR
Angeramo [23]	Argentina	490	150	60	37	38%	150	142	39	19%
Antakia [24]	United Kingdom	2,637	115	91	38.2	20%	129	116	40.3	20%
Anteby [25]	Israel	1	60	33	NR	NR	60	22	NR	NR
Aviran [26]	Israel	499	29	42	NR	NR	29	31	NR	NR
Baral [27]	Nepal	2	90	50	32.3	21%	90	42	30.2	16%
Butt [28]	Qatar¶	140	30	92	NR	NR	30	113	NR	NR
English [29]	United Kingdom¶	1,279	40	79	NR	NR	24	63	NR	NR
Fallani [11]	Italy¶	1,717	41	NR	NR	NR	41	NR	NR	NR
Finkelstein [30]	United States	2,098	55	48	44	37%	55	59	41	18%
Fonseca [20]	Turkey	718	61	42	NR	43%	61	155	NR	19%
Gao [31]	China	25	119	58	42.8	NR	210	105	41.6	NR
Goksoy [32]	Turkey	759	60	45	NR	20%	60	48	NR	10%
Griffith [33]	United States	1,726	29	21	NR	NR	29	13	NR	NR
Ho [34]	China	8	179	188	43.7	46%	179	160	44.6	41%
Honeyford [35]	United Kingdom	641	26	41	NR	NR	26	144	NR	NR
Mathur [36]	Singapore	6	58	61	NR	NR	58	44	NR	NR
McGuinness [37]	New Zealand	185	31	39	NR	NR	33	49	NR	NR
Neufeld [38]	United States¶	1,602	65	91	38.4	30%	99	840	37.3	25%
O'Connell [39]	Ireland	2,452	59	24	NR	NR	59	35	NR	NR
Patel [40]	United States	2,180	76	75	NR	45%	76	111	NR	22%
Perea del Pozo [41]	Spain	1,248	36	20	NR	NR	36	42	NR	NR
Romero [42]	Colombia	48	41	25	36.6	NR	41	42	38.2	NR
Surek [43]	Turkey	718	61	42	NR	43%	61	155	NR	19%
Turanli [44]	Turkey	638	90	NR	NR	26%	90	NR	NR	29%
Wang [19]	United States	8	105	32	24.8	31%	105	48	27.3	13%
Wichmann [45]	Germany	533	75	46	38.5	47%	75	43	42.7	30%

NR: not reported
* Reported as mean or median across studies
^ Data extrapolated in each country from www.worldometers.info/coronavirus/
# As a percentage of appendectomies
¶ Multicenter

Table 2
Cross sectional studies comparing the number of admissions for acute appendicitis in the pediatric population

Author	Country	Index period					Pre-pandemic period			
		No. COVID cases per 10^6 people at mid index period[ˆ]	No. days	No. patients	Age[*]	Perforated or complicated[#]	No. days	No. patients	Age[*]	Perforated or complicated
Bonilla [46]	Spain	1,643	60	49	9.2	33%	60	41	9.2	34%
Fisher [47]	United States[¶]	873	66	55	10	50%	1,800	1,291	10.7	27%
Gaitero Tristán [15]	Spain	1,698	45	77	10.7	39%	240	74	10.5	28%
Gerall [48]	United States	1,726	90	48	11.1	19%	90	41	13.1	11%
Kvasnovsky [49]	United States	1,783	33	55	12.4	43%	33	41	NR	32%
La Pergola [50]	Italy[¶]	707	60	86	10	31%	60	92	10	25%
Lee-Archer [12]	Australia	216	49	48	NR	48%	49	57	NR	NR
Montalva [51]	France	1,405	54	69	11.1	74%	56	39	8.9	85%
Pines [52]	United States[¶]	11	179	921	NR	NR	179	1,144	NR	NR
Place [53]	United States	2,477	81	90	10	43%	81	70	11	19%
Raucci [46]	Italy[¶]	953	69	61	NR	28%	69	57	NR	44%
Velayos [54]	Spain	1,766	46	25	9.3	32%	73	41	10.7	7%

NR: not reported
[*] Reported as mean or median across studies
[ˆ] Data extrapolated in each country from www.worldometers.info/coronavirus/
[#] As a percentage of appendectomies
[¶] Multicenter

Table 3
Cross sectional studies comparing the number of admissions for acute appendicitis in a mixed population of children and adults

Author	Country	Index period					Pre-pandemic period			
		No. COVID cases per 10^6 people at mid index period[^]	No. days	No. patients	Age[*]	Perforated or complicated[#]	No. days	No. patients	Age[*]	Perforated or complicated
Bajomo [55]	United Kingdom	1,222	60	36	26.5	29%	60	42	30.5	21%
Baugh [56]	United States[¶]	611	59	150	NR	NR	59	191	NR	NR
Burgard [57]	Switzerland[¶]	712	84	65	29	52%	84	241	30	8%
Ganesh [58]	United Kingdom	1,407	414	32	37	NR	139	64	37	NR
Mai [59]	United Kingdom	1,916	61	39	34.4	61%	62	50	29.1	38%
Maneck [60]	Germany[¶]	841	40	2,914	34.5	NR	42	3591	32.7	NR
Meriç [61]	Turkey	680	60	40	34	18%	60	110	29.1	6%
Orthopoulos [62]	United States	1,100	44	37	27	31%	44	54	23	8%
Steinman [63]	Brazil[¶]	439	99	160	NR	NR	441	706	NR	NR
Tankel [64]	Israel[¶]	21	48	141	23.3	22%	48	237	23.1	15%
Toale [65]	Ireland	1,158	65	62	27.1	38%	84	122	21.9	10%
Verma [66]	India	38	97	91	NR	28%	97	126	NR	NR
Walker [67]	United States[¶]	14	72	73	NR	NR	34	140	NR	NR
Willms [5]	Germany[¶]	721	69	888	36	64%	69	1027	35	58%
Zhou [68]	China	26	64	81	40.9	19%	64	121	37.7	8%

NR: not reported
[*] Reported as mean or median across studies
[^] Data extrapolated in each country from www.worldometers.info/coronavirus/
[#] As a percentage of appendectomies
[¶] Multicenter

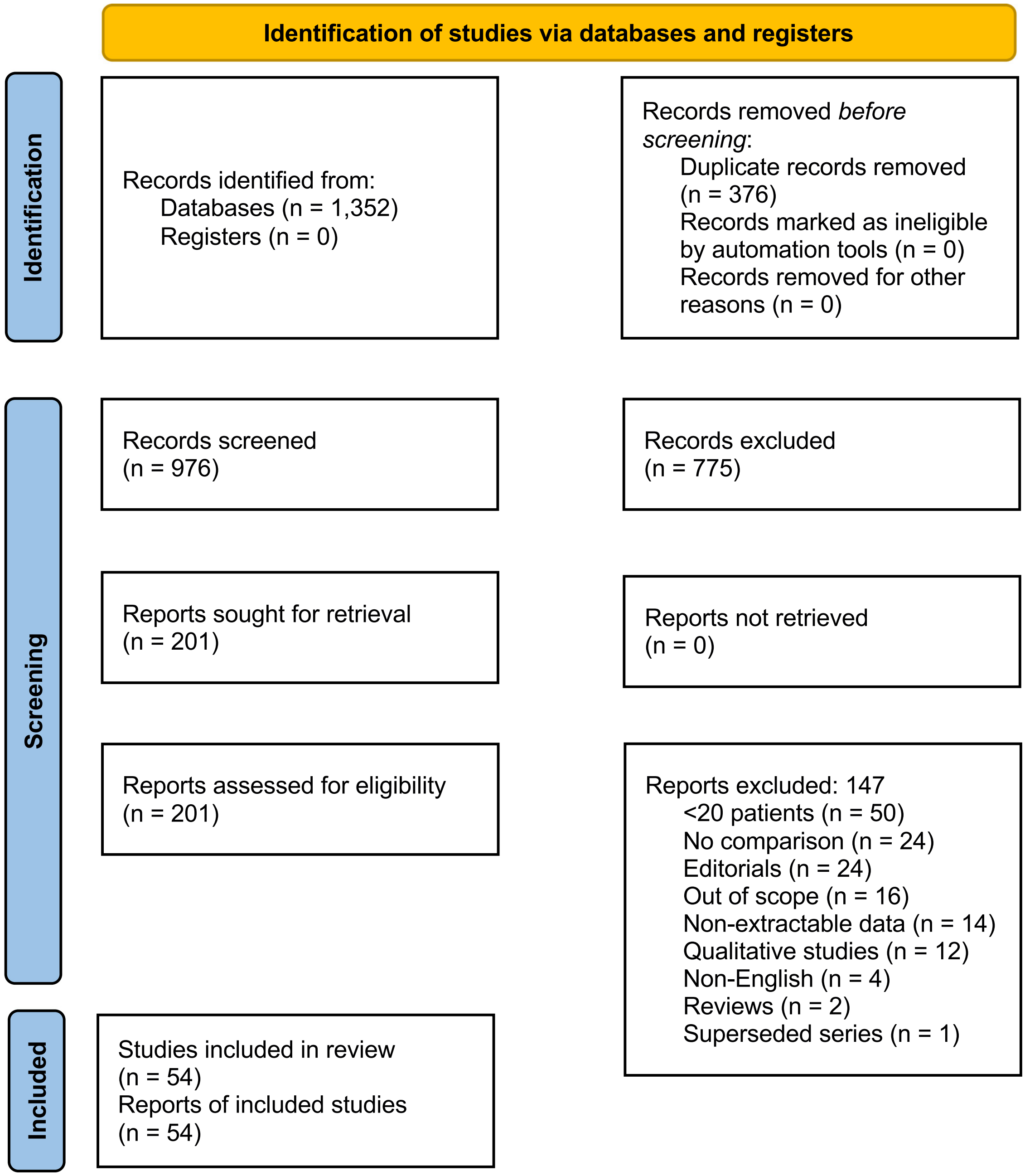

Fig. 1. Prisma diagram

interval was 0.195-3.312. Some degree of small study effect was observed (P = 0.062; Supplementary Figure 2).

Risk ratio of complicated AA

The overall risk ratio of complicated AA was 1.65 (1.32-2.07), ranging from 1.32 (0.95-1.84) in studies on children, to 1.59 (1.29-1.96) and 2.45 (1.24-4.84) in studies on adults and mixed population, respectively (Fig. 4). The 95% prediction interval was 0.515-5.295. A small study effect was found with some asymmetry of the funnel plot (P = 0.004; Supplementary Figure 3).

The meta-regression showed that the number of COVID-19 cases per million people had a negligible association with the rate ratios of admissions for AA (P = 0.737) and appendectomies (P = 0.883), nor risk ratio of complicated AA (P = 0.847).

Risk of bias within studies

Only 7 articles presented high risk of bias, while the other studies presented low risk of bias. The question which most commonly elevated the risk of bias was 'Were confounding factors identified?'. More details are provided in Supplementary Figure 4.

Discussion

Summary of evidence

This systematic review identified 54 studies reporting on the management of AA in the COVID-19 era, and published until the beginning of March 2021. Our findings indicate that the effect of the pandemic on the rate of admissions for AA was different over age groups. In accordance with previous series [11,12], a decrease in hospital attendances

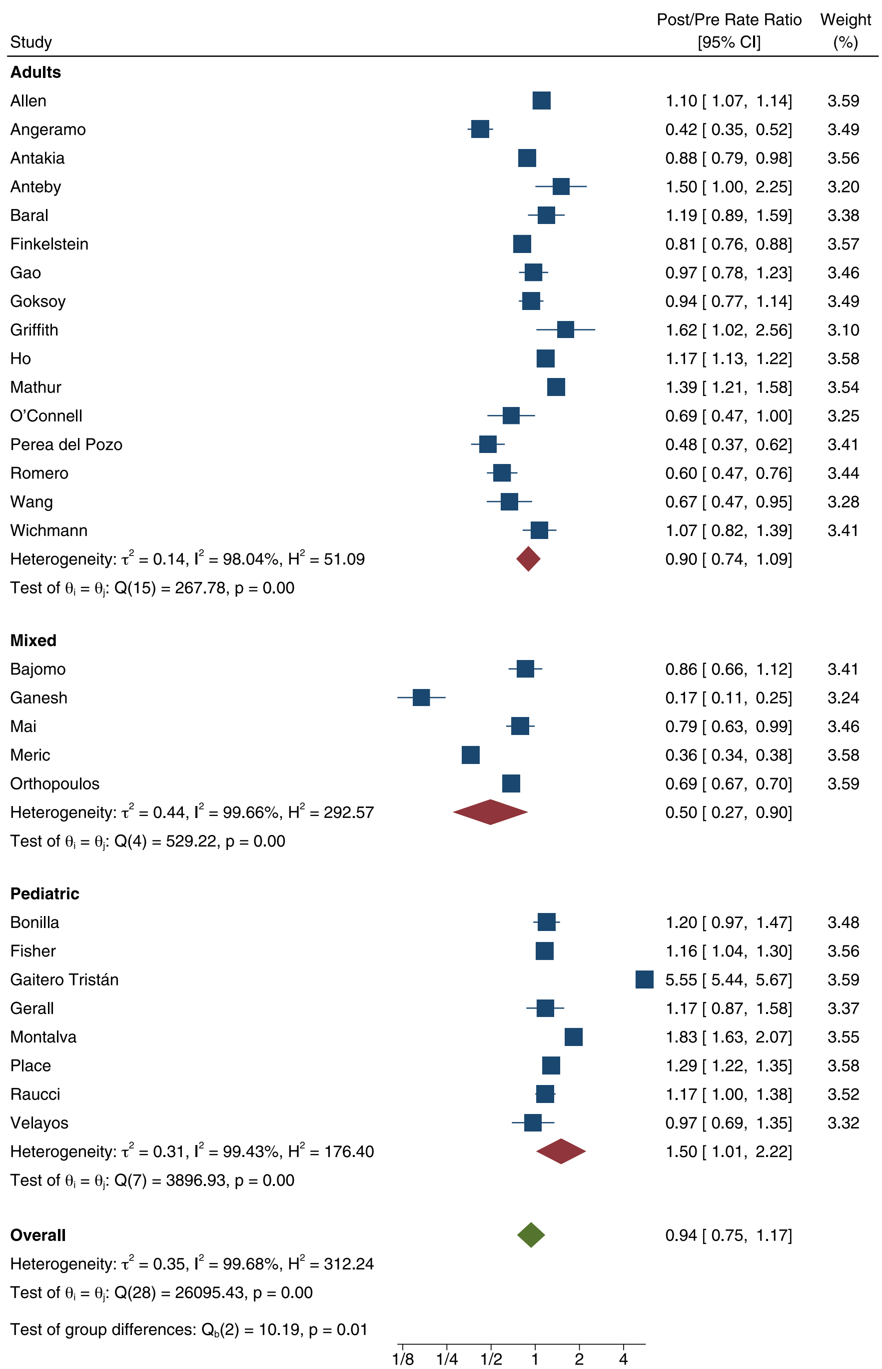

Fig. 2. Forest plot showing the overall pooled rate ratio of admissions for acute appendicitis with subgroup analysis according to population included.

by 10% was observed in adult patients, although not reaching statistical significance. Beside national lockdowns and isolation measures [13], a further reason behind this decline is likely to be the fear of contracting COVID-19, which may have restrained patients from seeking medical care even in instances of acute illnesses [14]. The striking decline in ED visits worldwide registered the highest peaks in April 2020 in the worst-hit areas by the scourge of the pandemic, marking a dramatic shift in the use of the ED by the public. Our meta-regression showed that COVID-19 cases per million (at mid-pandemic period, per nation) was not associated with any of three pooled outcomes. Several reasons may account for this finding, with the main being considering such measure as an imperfect proxy for burden on the healthcare system, which subsequently affects management patterns.

Nevertheless, AA remained among the top reasons for seeking emergency care even during the pandemic as being one of the most common causes of abdominal pain [13]. However, compared to the pre-pandemic period, the increased rate of admissions for AA observed in the pediatric population was rather unexpected. Such finding may reflect a growing self-awareness of wellbeing that made parents more apprehensive to avoid diagnostic delays [15].

Secondly, a solidly reported curb in surgical activities was observed both in elective and emergency settings [16,17], as a result of decreased hospital attendances and nonemergent surgeries amid lack of resources. Although not reaching statistical significance, this can somehow explain the 18% reduction in appendectomy rate observed in the pandemic period in the adult population. Podda et al [18]. highlighted how surgeons

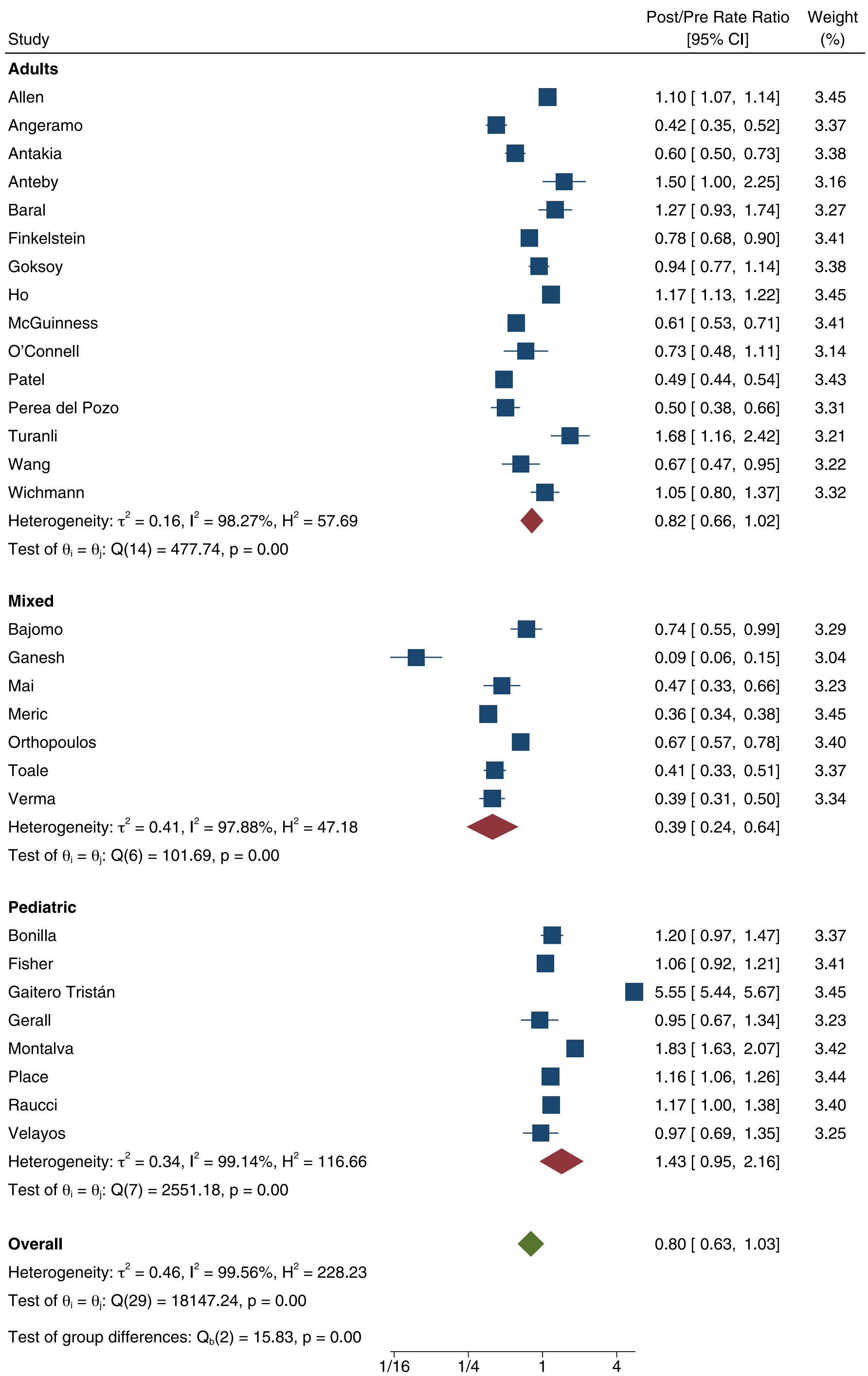

Fig. 3. Forest plot showing the overall pooled rate ratio of appendectomies with subgroup analysis according to population included.

facing hospital services curtailed or suspended have become more keen to consider antibiotic treatment alone in patients with AA. The decline in appendectomies is therefore most likely attributable both to lower number of admissions an.d more active use of antibiotics for uncomplicated AA.

As opposed to the adult population, our meta-analysis showed a 43% increase in the rate of appendectomies in the pediatric counterpart, which mirrors the hike in admission rates for AA in this patients' group.

On the other hand, the deferred pursuit of medical attention by the adult population may have caused diagnostic delays eventually leading to an increase in the rate of complicated AA (as high as 59% in this group, although not significant). Indeed, a significant increase in the time interval from symptom onset to admission has been reported during the pandemic [19], while other studies overly reported late presentations and complicated disease [20]. Similar figures were observed, although to a lesser extent (32%), in the pediatric population, and became even more pronounced when considering studies on mixed populations.

Nevertheless, a steep decrease in the rate of negative appendectomy was observed during the pandemic [18], likely as consequence of a more accurate selection of surgical candidates.

Study	Pandemic Complicated	Pandemic Not Complicated	Pre–Pandemic Complicated	Pre–Pandemic Not Complicated	Risk Ratio [95% CI]	Weight (%)
Adults						
Angeramo	23	37	27	115	2.02 [1.26, 3.22]	3.58
Antakia	12	47	22	88	1.02 [0.54, 1.91]	3.18
Baral	10	37	6	31	1.31 [0.53, 3.28]	2.49
Finkelstein	16	27	10	45	2.05 [1.03, 4.05]	3.05
Fonseca	18	24	29	126	2.29 [1.42, 3.70]	3.55
Goksoy	9	36	5	43	1.92 [0.70, 5.30]	2.28
Ho	86	102	66	94	1.11 [0.87, 1.41]	4.03
Neufeld	25	57	181	534	1.20 [0.85, 1.71]	3.84
Patel	23	28	23	82	2.06 [1.29, 3.30]	3.57
Surek	18	24	29	126	2.29 [1.42, 3.70]	3.55
Turanli	12	35	8	20	0.89 [0.42, 1.92]	2.85
Wang	10	22	6	42	2.50 [1.01, 6.20]	2.51
Wichmann	21	24	13	30	1.54 [0.89, 2.68]	3.38
Heterogeneity: τ^2 = 0.07, I^2 = 50.54%, H^2 = 2.02					1.59 [1.29, 1.96]	
Test of $\theta_i = \theta_j$: Q(12) = 22.30, p = 0.03						
Mixed						
Bajomo	9	22	9	33	1.35 [0.61, 3.01]	2.76
Burgard	33	31	20	216	6.08 [3.76, 9.85]	3.54
Mai	14	9	19	31	1.60 [0.99, 2.59]	3.54
Meric	7	33	7	103	2.75 [1.03, 7.35]	2.34
Orthopoulos	10	22	4	44	3.75 [1.29, 10.93]	2.16
Tankel	29	101	31	171	1.45 [0.92, 2.29]	3.61
Toale	11	23	0	107	70.97 [4.29, 1173.70]	0.56
Willms	569	319	597	430	1.10 [1.03, 1.18]	4.21
Zhou	15	66	10	111	2.24 [1.06, 4.74]	2.88
Heterogeneity: τ^2 = 0.88, I^2 = 93.78%, H^2 = 16.08					2.45 [1.24, 4.84]	
Test of $\theta_i = \theta_j$: Q(8) = 68.79, p = 0.00						
Pediatric						
Bonilla	16	33	14	27	0.96 [0.53, 1.72]	3.29
Fisher	25	25	351	940	1.84 [1.37, 2.46]	3.95
Gaitero Tristán	30	47	21	53	1.37 [0.87, 2.17]	3.60
Gerall	7	29	4	34	1.85 [0.59, 5.78]	2.03
Kvasnovsky	13	17	13	28	1.37 [0.74, 2.51]	3.23
La Pergola	27	59	23	69	1.26 [0.78, 2.01]	3.57
Montalva	51	18	33	6	0.87 [0.72, 1.06]	4.10
Place	35	46	13	57	2.33 [1.34, 4.03]	3.38
Raucci	17	44	25	27	0.58 [0.35, 0.95]	3.52
Velayos	8	17	3	38	4.37 [1.28, 14.96]	1.87
Heterogeneity: τ^2 = 0.20, I^2 = 80.17%, H^2 = 5.04					1.32 [0.95, 1.84]	
Test of $\theta_i = \theta_j$: Q(9) = 38.03, p = 0.00						
Overall					1.65 [1.32, 2.07]	
Heterogeneity: τ^2 = 0.31, I^2 = 89.19%, H^2 = 9.25						
Test of $\theta_i = \theta_j$: Q(31) = 138.68, p = 0.00						
Test of group differences: $Q_b(2)$ = 2.69, p = 0.26						

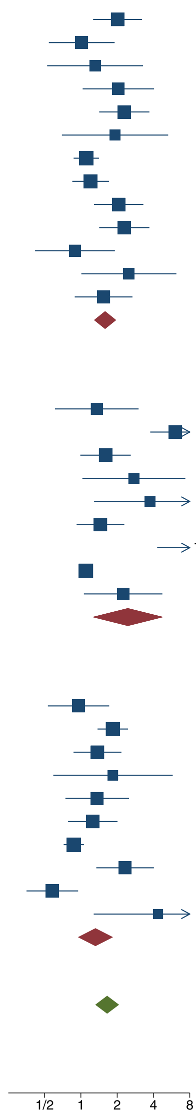

Fig. 4. Forest plot showing the overall pooled risk ratio of complicated appendectomies with subgroup analysis according to population included.

Changes in AA treatment during the COVID-19 pandemic has been recently explored in two systematic reviews [7,21]. The number of studies identified by Köhler at al [21]. was lower compared to our work (46 vs. 54), in line with a literature search ended one month before (Feb 1st vs. Mar 5th 2021). Similar to our findings, they demonstrated an overall significant reduction of AA cases by 21% in adults and an increase of 13% in children. Also, higher rates of complicated appendicitis were observed in adults. Emile et al [7]. demonstrated a 7-time higher application of non-operative management during than before the pandemic.

This systematic review has several limitations. First, the low quality of included studies, all being retrospective in nature, with relatively small sample size. Second, the incidence of AA was not normalized to any population data. It remains unknown whether the population from which AA cases were extrapolated was consistent between the reference and index periods. Despite controlling for the number of COVID-19 active cases per million people on the day in the middle of the index period in the country where each study was conducted, several further factors may have played a role in the epidemiological trend of admissions for AA and appendectomies. Ultimately, the exclusion of studies at high risk of bias (13%) would have unlikely changed the results of this systematic review.

In conclusion, the pandemic has altered the rate of admissions for AA and appendectomy, with parallel increased incidence of complicated cases. These findings will inform future efforts to develop and implement guidelines for this condition in time of emergency.

Author contributions

UG, GG and MO conceived the study; UG, GG, MO, MP, NS, CF, GAS and GZ designed and performed the research; UG and GLDT analyzed the data; UG, MO, MP, CF, GAS and GG wrote the paper; MG, GS, SDS and GZ supervised the paper; all authors read and approved the final manuscript

Supplementary Table 1. PRISMA Checklist.

Supplementary Table 2. Search strategy.

Supplementary Figure 1. Funnel plot showing the standard error for the effect sizes for rate ratio of admissions for acute appendicitis.

Supplementary Figure 2. Funnel plot showing the standard error for the effect sizes of rate ratio of appendectomies.

Supplementary Figure 3. Funnel plot showing the standard error for the effect sizes for risk ratio of complicated appendectomies.

Supplementary Figure 4. Risk of bias summary, assessed by Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies: authors' judgments for each included study.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

None

Ethical approval

This article does not contain any study with human participants performed by any of the authors

Informed consent

For this type of study, formal consent is not required

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hsr.2022.100021.

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