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Review Article

Incidence of complicated appendicitis during the COVID-19 pandemic: A systematic review and meta-analysis

Abduljubbar Kariya^a, Chonlada Krutsri^{b,*}, Pongsasit Singhatas^b, Preeda Sumritpradit^b, Tharin Thampongsa^b, Panuwat Lertsitthichai^c, Napaphat Phoprom^c

^a Department of Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

^b Division of Trauma, Acute Care Surgery, and Surgical Critical Care, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

^c Surgical Research Unit, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

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ABSTRACT

Introduction: Measures taken to prevent the spread of coronavirus disease 2019 (COVID-19) slow surgical processes, and patients are avoiding presenting at emergency departments during the outbreak because of fears of contracting the contagious disease. To analyze the rate of complicated appendicitis before and during the COVID-19 pandemic.

Methods: We systematically reviewed the PubMed and SCOPUS databases for articles published from 2000 to 2021. Including the retrospective review data collected from our hospital of patients aged ≥ 18 years old who were diagnosed with acute appendicitis. The primary outcome of complicated appendicitis incidence was compared between before and during the COVID-19 pandemic period. We performed a meta-analysis using a random-effects model analysis.

Results: A total 3559 patients were included for meta-analysis. The overall rate of complicated appendicitis was significantly higher during the pandemic (relative risk, 1.55; 95% confidence interval [CI], 1.26–1.89). The time from onset of symptoms to hospitalisation was 0.41 h longer during the pandemic, which was not significantly different (standardized mean difference, 0.41, 95% CI, –0.03 to 1.11). The operating time during the pandemic was significantly shorter than that before the pandemic (83.45 min and 71.65 min, $p = 0.01$).

Conclusion: There are correlation between the pandemic and severity of acute appendicitis. The higher rate of complicated appendicitis in the pandemic indicates that patients require timely medical attention and appropriate treatment despite fears of contracting disease.

1. Introduction

Since the coronavirus disease 2019 (COVID-19) global pandemic, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began in 2019, Thailand has been among the countries that have been affected. Significant measures taken during the pandemic, including declaring a state of emergency, city-wide lockdowns, mass vaccination, and encouragement to wear masks, have affected healthcare resources and accessibility. This pandemic placed a huge burden on the global medical system, and hospital resources had to be conserved for patients with COVID-19. It also resulted in a shortage of medical equipments and human resources to treat the patients [1]. A shortage of nurses, anesthesiologists, and personal protective

equipments, such as N95 masks and surgical masks, face shield, gowns, and gloves, has changed the way diseases are managed surgically. Triage was used to determine if a surgical procedure should be delayed [2]. Aside from *anti-HIV* measures, universal precautionary measures are also required, and pre-operative COVID-19 nasopharyngeal swab testing must be performed in every case, even in emergency/urgent settings, to save resources and preserve healthcare workers [3].

Acute appendicitis is the most common emergency general surgery with a prevalence of 233 patients per 100,000 population [4]. The etiologies of the disease include luminal obstruction by an appendicolith, tumor arising within the appendix, or parasite infestation that results in inflammation, ischemia, and perforation [5–7]. The mainstay treatment of acute appendicitis is appendectomy using a laparoscopic approach as

* Corresponding author. Department of Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, 10400, Thailand.

E-mail address: chonlada.kru@mahidol.ac.th (C. Krutsri).

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a first choice instead of non-operative management with antibiotics. However, in ruptured appendicitis, the presentation of the disease may require more complicated treatment and an open approach appendectomy is necessary [8]. Delayed presentation of acute appendicitis leads to a more complicated type of appendicitis, which is one of the risk factors for conversion from a laparoscopic to open approach. Patients who present later may have appendiceal abscess, which is treated with interventional percutaneous drainage, intravenous antibiotics, and subsequent appendectomy [8].

Measures taken to prevent the spread of COVID-19 tend to slow surgery processes, even in the emergency/urgent setting. Additionally, patients are avoiding presenting at emergency departments amid fear of contracting the contagious disease [9]. While the exact impact of the pandemic is yet to be fully understood, one study reported of an increase in the prevalence of complicated appendicitis, which has affected surgical management, such as the change from laparoscopic to open appendectomy because of rupture of the appendix, and affects patients morbidity [10]. In contrast to this study, another study reported that the COVID-19 pandemic had no effect on the rate of complicated appendicitis [11].

Our study compared the rate of complicated appendicitis, which could affect the surgical approach, between before and during the COVID-19 pandemic. The study also analyzed the factors that affected operative time, time from onset to hospitalisation, length of hospital stay, morbidity, and mortality before and during COVID-19 pandemic period. This may help improve care of acute appendicitis in future pandemics.

2. Methods

2.1. Literature search

We performed a systematic review and meta-analysis of patients diagnosed with acute appendicitis following the Preferred Reporting Items for Systematic reviews and Meta-analyses guidelines (PRISMA), as show in Fig. 1 [12].

We formulated the research question according to the Problem/Population, Intervention, Comparison, Outcome guidelines and performed a systematic review of English language full research articles listed in the PubMed and SCOPUS databases from 2000 to 2021 to

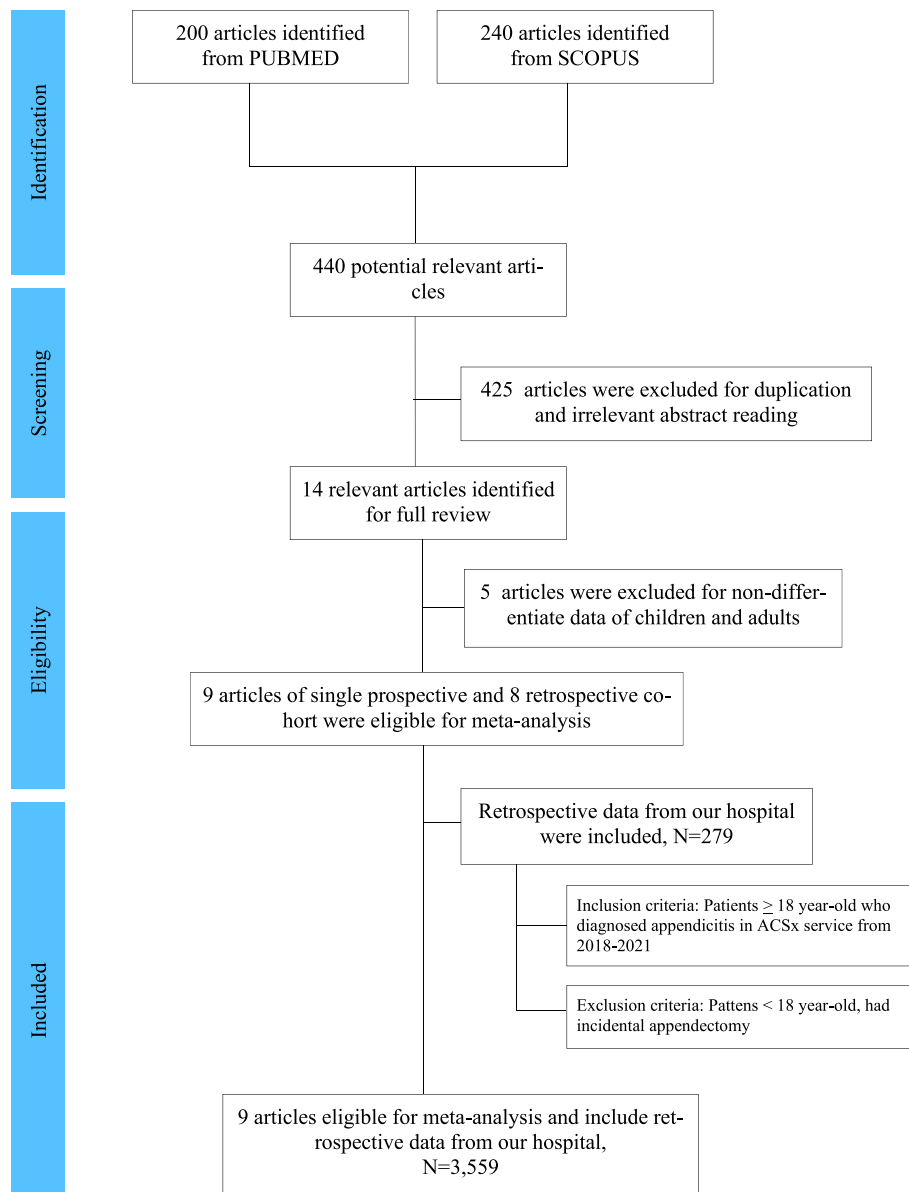


Fig. 1. A study flow chart according to Preferred Reporting Items for Systematic reviews and Meta-analysis guidelines (PRISMA).

identify articles that focus on the incidence and outcome of acute appendicitis, especially complicated appendicitis, during the COVID-19 pandemic compared to that before the pandemic. We used the following keywords as search terms: “complicated appendicitis” OR “appendicitis” AND “COVID-19” OR “SARS-CoV2”. In total, 425 articles were excluded after screening for irrelevant abstracts and duplicated studies; 14 relevant articles were identified for full review. Five articles were excluded for lacking data differentiating between children and adults; therefore, nine articles were included for meta-analysis. A retrospective collection data of acute appendicitis from our hospital was also included in the meta-analysis (Fig. 1).

2.2. Population inclusion and exclusion criteria

According to the PICOS criteria for inclusion in and exclusion from a meta-analysis, the participants of all included studies were adult patients aged >18 years old who were diagnosed with acute appendicitis during the COVID-19 pandemic. The study control group were patients diagnosed with acute appendicitis before the COVID-19 pandemic. All treatment studies were included. Exclusion criteria were patients <18 years of age with no record of treatment or those who underwent incidental appendectomy.

2.3. Study selection

We limited our search to studies originally published in English and involving only human patients. We also evaluated the demographic data and patient’s hospital course using a retrospective review of patients with acute appendicitis admitted to the Trauma and Acute Care Surgery service from 1 April 2020 to 1 June 2021 (pandemic group) and from 1 January 2018 to 31 March 2019 (before pandemic group). We searched our patients database using the International Classification of Diseases-10 codes K35, K35.2, K35.20, K35.21, K35.3, K35.31, K35.32, K35.33, K35.8, K35.80, K35.89, K35.890, and K35.891.

2.4. Definition

The definition of complicated appendicitis included gangrenous appendicitis, perforated appendicitis, appendiceal abscess formation, or phlegmon. Uncomplicated appendicitis included inflammatory appendicitis and suppurative appendicitis.

2.5. Outcome of interests

The primary outcome was complicated appendicitis rates before and during COVID-19 pandemic. The secondary outcomes were general demographic data, overall acute appendicitis rate, operative time, time from onset to hospitalisation, length of hospital stay, morbidity, and mortality compared between before and during the pandemic.

2.6. Data extraction

Data extraction was performed by two independent authors, and disagreements were resolved by consensus. The extracted data, including our data, were recorded on a Microsoft Excel spreadsheet for processing and analysis.

2.7. Risk of bias assessment

We used the ROBINS-I tool to assess bias in seven domains, namely, confounds, participant selection, measurement of interventions, departure from intended interventions, missing data, measurement of outcomes, and selection of the reported result.

2.8. Data synthesis and statistical analysis

The incidence of acute appendicitis in our setting was collected for the quantitative test using Pearson’s chi-square analysis with reported by frequency and percentages. The part of pooled meta-analysis to analyze. The risk ratio (RR) was estimated for dichotomous of rate of complicated appendicitis, and clinical onset arrived. The mean difference (MD) with variance of hospital time from patients, operative time, and hospital stay were estimated as continuous outcome. A random-effect or fixed effect model was performed where appropriated with the degree of heterogeneity. Heterogeneity was evaluated using Cochran’s Q test and the I^2 statistic. If heterogeneity was present, we used a meta-regression model with covariates for explore sources of heterogeneity. Publication bias was assessed using a Deek’s funnel plot. Statistical significance was reported when $p < 0.05$. Statistical analyses were performed using Stata 16 (StataCorp, College Station, TX, USA). This meta-analysis was reported according to a critical appraisal tool for systematic reviews AMSTAR-2[13].

2.9. Ethical considerations

The ethics committee of our institution approved this study. This work did not directly involve human subjects.

3. Results

3.1. Study selection

Our search identified 440 studies. After duplicates were removed, the abstract of each article was read to exclude irrelevant articles, after which 425 studies were excluded. Fourteen studies underwent full text review by two authors to assess eligibility and quality. Five studies were excluded because they did not differentiate between pediatric and adult patients. Finally, nine studies were eligible for inclusion and retrospective data from our hospital were also collected and included for meta-analysis (Fig. 1). All included studies were reviewed to compare complicated appendicitis between before and during the COVID-19 pandemic. The study characteristics and demographic data of all involved patients are shown in Table 1. A total of 3559 patients with acute appendicitis were included. The average age of patients was 36.44 (23.17–45.94) years. The overall morbidity and mortality of acute appendicitis during COVID-19 pandemic were 13.06% and 0.47%, respectively.

3.2. Retrospective results

Table 2 shows the retrospective data of acute appendicitis from our hospital, comparing between before and during COVID-19 pandemic. In total, 279 patients with acute appendicitis were included; there were 70 (47.95%) and 55 (41.35%) male patients before and during the pandemic, respectively. The average age of patients was 40.71 (18.43) and 42.83 (18.65) years before and during the pandemic, respectively ($p = 0.34$). Acute appendicitis with concomitant COVID-19 was detected in only one (0.75%) patient. There were no statistically significant differences in the rate of complicated appendicitis between before and during the pandemic, 46 (31.51%) and 50 (37.59%) patients, respectively; $p = 0.31$. The rate of perforated appendicitis was also not statistically significantly different between before and during the pandemic, 30 (20.55%) and 30 (22.56%) patients, $p = 0.77$. There were 14 (9.59%) and 17 (12.78%) patients with gangrenous appendicitis before and during the pandemic, respectively ($p = 0.39$). Appendiceal abscess or phlegmon was present in 2 (1.37%) and 3 (2.26%) patients before and during the pandemic, respectively ($p = 0.57$). The time between patients developing symptoms and hospitalisation was not significantly different, 27.03 (22.69) mins and 29.45 (35.78) mins before and during the pandemic period, respectively ($p = 0.495$). The time between when

Table 1
Summary of the eligible studies.

Author/publication year	Type of study	Total N	Before pandemic; N	Pandemic; N	Covid detected; N(%)	Mean age; years	Morbidity; %	Mortality; %
Tankel J(2020) [13]	Retrospective	378	237	141	NA	23.17	NA	NA
Fonseca MK (2020) [14]	Retrospective	118	82	36	NA	35.49	12.7	NA
Gao Z (2020) [15]	Retrospective	163	105	58	NA	42.03	NA	NA
Burgard M (2021) [16]	Retrospective	306	241	65	NA	37.11	NA	NA
Scheijmans JCG (2021) [17]	Retrospective	1249	642	607	12(1.98)	41.98	11.8	NA
Baral S (2021) [18]	Retrospective	92	42	50	NA	31.56	NA	0
Ceresoli M (2021) [19]	Retrospective	532	420	112	2(1.79)	31.43	8.1	NA
Yang Y (2021) [20]	Retrospective	235	129	106	NA	33.93	NA	NA
Antakia R (2021) [21]	Prospective	207	116	91	NA	45.94	23.1	1.4
Ramathibodi (2021)	Retrospective	279	146	133	1(0.75)	41.72	9.6	0

Table 2
A demographic data of acute appendicitis from Ramathibodi Hospital.

	Before COVID pandemic (N = 146)	COVID pandemic (N = 133)	p-value
Age; mean (SD)	40.71(18.43)	42.83(18.65)	0.34
Dead; N(%)	0	0	
Gender			0.28
Male; N (%)	70(47.95)	55(41.35)	
Female; N (%)	76(52.05)	78(58.65)	
Covid detected; N (%)	NA	1(0.75)	
Complicated appendicitis; N (%)	46(31.51)	50(37.59)	0.31
Uncomplicated appendicitis; N(%)	100(68.49)	83(62.41)	
Perforated appendicitis; N (%)	30(20.55)	30(22.56)	0.77
Gangrenous appendicitis; N (%)	14(9.59)	17(12.78)	0.39
Abscess/phlegmon; N(%)	2(1.37)	3(2.26)	0.57
Time from onset of symptom to hospital(hrs); mean(SD)	27.03(22.69)	29.45(35.78)	0.495
Time from ER to OR(hrs); mean(SD)	10.15(6.54)	14.39(8.89)	<0.001
Time from onset of symptom to OR(hrs); mean(SD)	37.18(24.66)	43.85(39.50)	0.08
Operative management of all type of appendicitis; N (%)	146(100)	132(99.25)	0.47
Operative time (min); mean(SD)	83.45(44.2)	71.65(29.28)	0.01
LOS of overall appendicitis (days); mean(SD)	3.11(3.21)	3.06(2.41)	0.86
Overall morbidity; N(%)	15(10.27)	12(9.02)	0.72
Surgical site infection; N(%)	9(6.16)	4(3.01)	0.26
Intra-abdominal collection; N(%)	4(2.74)	5(3.76)	0.74
Ileus; N(%)	0	0	
Readmission within 3 months; N(%)	2(1.37)	2(1.52)	0.99

ER; Emergency room, OR; operation room, LOS; Length of hospital stay.

patients arrived at the emergency room and arrived in the operating room before and during the pandemic period was 10.15 (6.54) mins and 14.39 (8.89) mins, respectively ($p < 0.001$). The time between when patients developed symptoms and arrived in the operating room before and during the pandemic period was not significantly different (37.18 (24.66) mins and 43.85 (39.50) mins, respectively ($p = 0.08$)). Operative management for all types of appendicitis was performed in 146 (100%) and 132 (99.25%) patients before and during the pandemic ($p = 0.47$). The operating time during the pandemic period was significantly shorter than before the pandemic period, 1.65 (29.28) mins and 83.45 (44.2) mins, respectively ($p = 0.01$). The length of hospital stay was 3.11 (3.21) days and 3.06 (2.41) days before and during the pandemic, respectively

($p = 0.86$). Overall morbidity was not significantly different between before and during the pandemic, 15 (10.27%) patients and 12 (9.02%) patients, respectively ($p = 0.72$). The incidence of surgical site infection, intra-abdominal collection, and ileus was not significantly different between before and during the pandemic, 9 (6.16%) and 4 (3.01%), 4 (2.74%) and 5 (3.76%), and 0 (0%), respectively ($p = 0.26, 0.74$). Readmission rates within 3 months had no significant difference between before and during the pandemic period, 2 (1.37%) and 2 (1.52%) patients, respectively ($p = 0.99$).

3.3. Meta-analysis results

Forest plots of a random effects model of complicated appendicitis before and during the pandemic period are shown in Figs. 2–5. The overall rate of complicated appendicitis was significantly higher during the pandemic period (relative risk [RR], 1.55; 95% confidence interval, 1.26–1.89; $p = 0.001$, $I^2 = 67.2\%$) (Fig. 2). Perforated appendicitis was significantly more higher during the pandemic period (RR, 1.44; 95% CI, 1.11–1.89; $p = 0.018$, $I^2 = 58.6\%$) (Fig. 3). Gangrenous appendicitis was also significantly more higher during the pandemic period (RR, 1.37; 95% CI, 1.06–1.76; $p = 0.636$, $I^2 = 0\%$) (Fig. 4). Appendiceal abscess and phlegmon were significantly more likely during the pandemic period (RR, 1.46; 95% CI, 1.15–1.85; $p = 0.317$, $I^2 = 15.1\%$) (Fig. 5). Seven studies reported a decreased length of hospital stay during the pandemic period (standardized mean difference (SMD), -0.09 ; 95% CI, -0.26 to 0.07 ; $p = 0.018$, $I^2 = 60.6\%$) (Fig. 6). The time from onset of symptom to hospitalisation was 0.41 h longer during the pandemic, but the difference was not statistically significant (SMD, 0.41; 95% CI, -0.03 to 1.11 , $p = 0.000$, $I^2 = 97.5\%$) (Fig. 7) There were no publication bias between study from the Funnel plot (see Fig. 8).

There was moderate heterogeneity of complicated appendicitis between studies ($I^2 = 67.2\%$, $p = 0.001$). A meta-regression was performed and found differences in sex, COVID detection rate, and non-operative management. The rest of the data are insufficient to be calculated. No heterogeneity among gangrenous appendicitis, appendiceal abscess, and phlegmon was found.

4. Discussion

The current systematic review and meta-analysis including our data show that the complicated appendicitis rate was significantly higher during the pandemic. The overall perforated, gangrenous appendicitis, and appendiceal abscess/phlegmon rates were also significantly higher during the pandemic period with moderate heterogeneity. Many factors likely contribute to the development of complicated appendicitis such as presence of appendicolith, delayed surgery after failure of non-operative management, or longer duration of symptoms [19,20]. From our review, the reasons underlying these factors may include patients afraid of contracting COVID-19 presenting later after symptom onset. Apart from the COVID-19 pandemic, which decreased the frequency of laparoscopic procedures due to the risk of potential aerosol generating procedures (AGP), complicated appendicitis has many effects on surgical

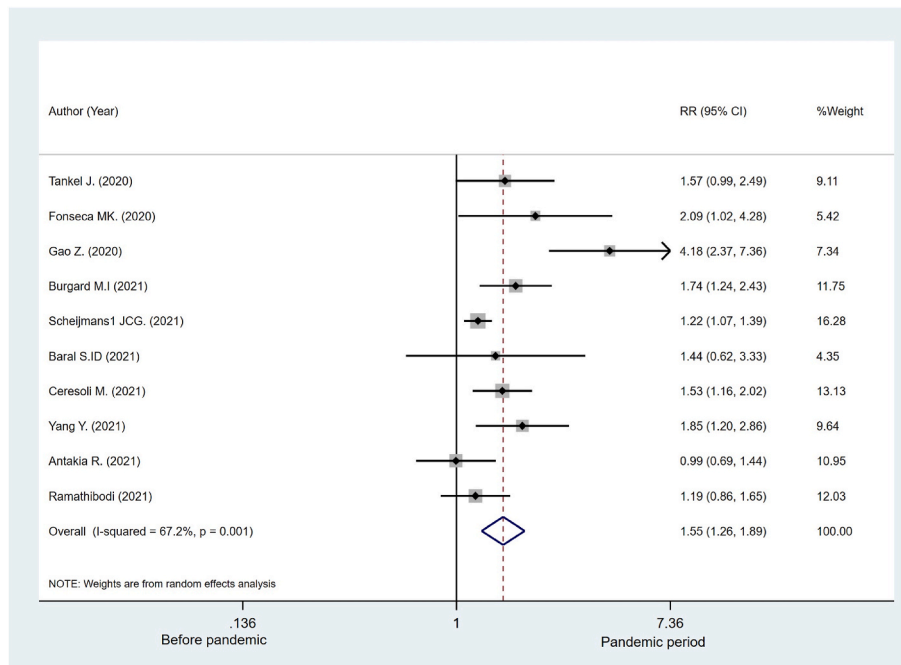


Fig. 2. Forest plot of complicated appendicitis before and COVID-19 pandemic period.

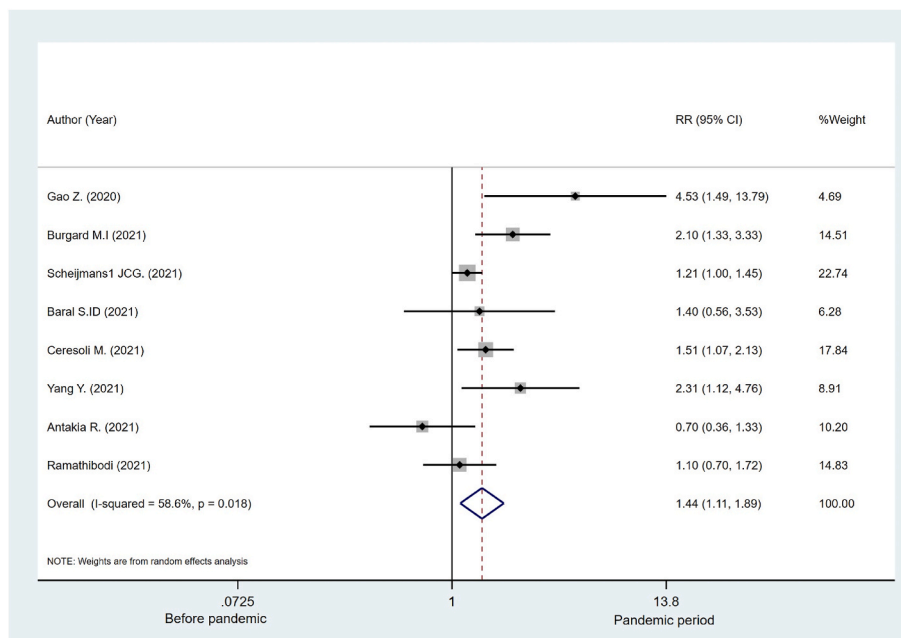


Fig. 3. Forest plot of perforated appendicitis before and COVID-19 pandemic period.

management such as increased conversion rate from laparoscopic to open appendectomy, increased postoperative surgical site infection and collection, and increased septic shock [8,19]. To improve patient's morbidity and mortality, any controllable factor of complicated appendicitis should be addressed. Non-operative management with antibiotics is still too controversial to be the gold standard management during a pandemic [19]. The retrospective results for the complicated appendicitis rate are different in the meta-analysis, which may be because of personal health awareness and individual access to hospitals to seek medical attention early, despite fear of contracting COVID-19 because there was a non-significant difference in onset time between before and during the pandemic. The significant heterogeneity in the

symptom-to-hospital time indicates that this variable varied through areas of the studies [10,11,13–21].

The goals of emergency/urgent general surgery are timely surgical care and optimization of patient care resources. On the basis of data from our hospital, the time from onset of symptoms to hospitalisation showed no significant difference between before and during the pandemic; however, the time from emergency room presentation to admission to the operating room for overall acute appendicitis was significant longer in the pandemic period because of preoperative nasopharyngeal COVID-19 swab testing in every case to preserve personal protective equipments and other resources [3].

Some studies reported significantly longer operating times during

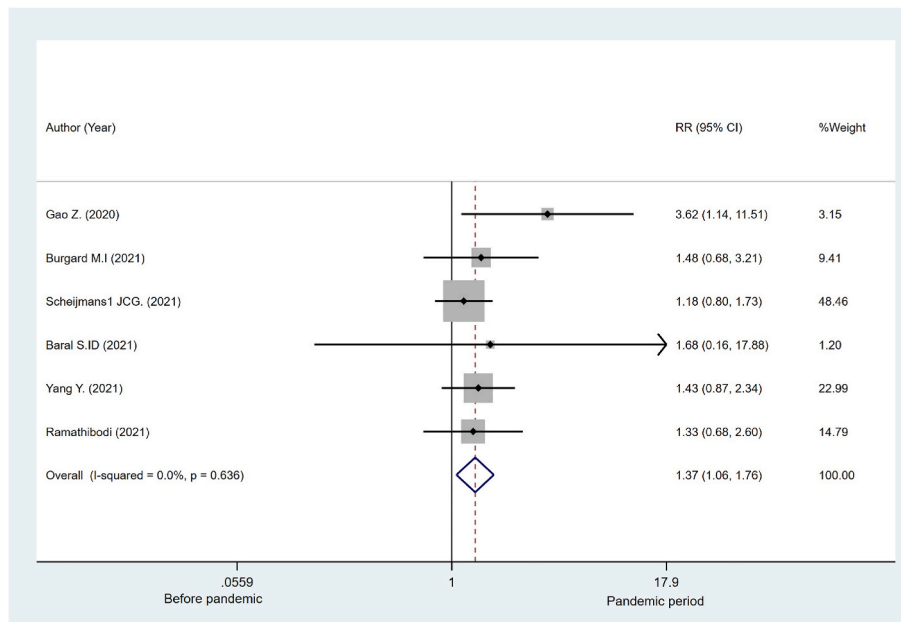


Fig. 4. Forest plot of gangrenous appendicitis before and COVID-19 pandemic period.

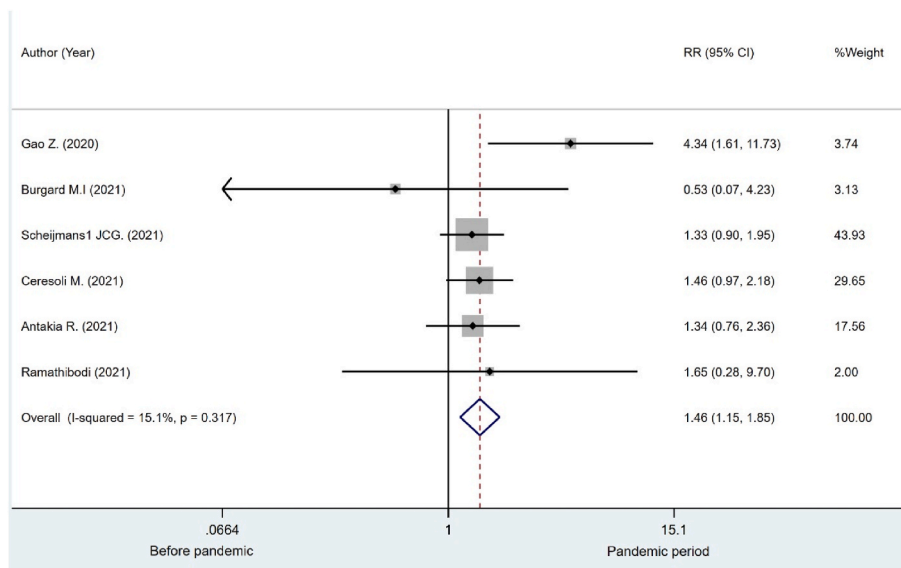


Fig. 5. Forest plot of appendiceal abscess and phlegmon before and COVID-19 pandemic period.

the pandemic due to more cases of complicated appendicitis with operation duration of 45.27 ± 11.8 and 51.06 ± 9.4 min before and during the pandemic, respectively ($p = 0.015$) [17]. However, Yang et al. reported significantly shorter operation times during the pandemic period alongside higher rates of complicated appendicitis [18]. Therefore, the operating time does not appear to depend on the complicated appendicitis rate. From the meta-analysis, the overall operating time for appendectomy was shorter during the pandemic; this may be because surgeons tended to minimize their exposure time because the preoperative nasopharyngeal COVID-19 swab of the patient may give a negative result in the incubation period.

The current study had several strengths and limitations. The major strength of this study is its systematic approach and the meta-analysis published on acute appendicitis during the pandemic period. The limitation of the study is the fear of COVID-19, which we believe affects the decision to seek medical attention when symptoms develop, is

subjective, varies among the population, and has not been constant throughout the pandemic.

5. Conclusion

This study found a significant increase in overall rate of patients with complicated appendicitis during the COVID-19 pandemic, which indicates that patients require timely medical attention and appropriate treatment to decrease laparotomy conversion rate and septic shock. Despite fears of contracting COVID-19, patients should be encouraged to seek medical attention when experiencing unusual symptoms, while healthcare providers should be aware of the indirect effects of COVID-19, which may lead to improper care of other serious diseases.

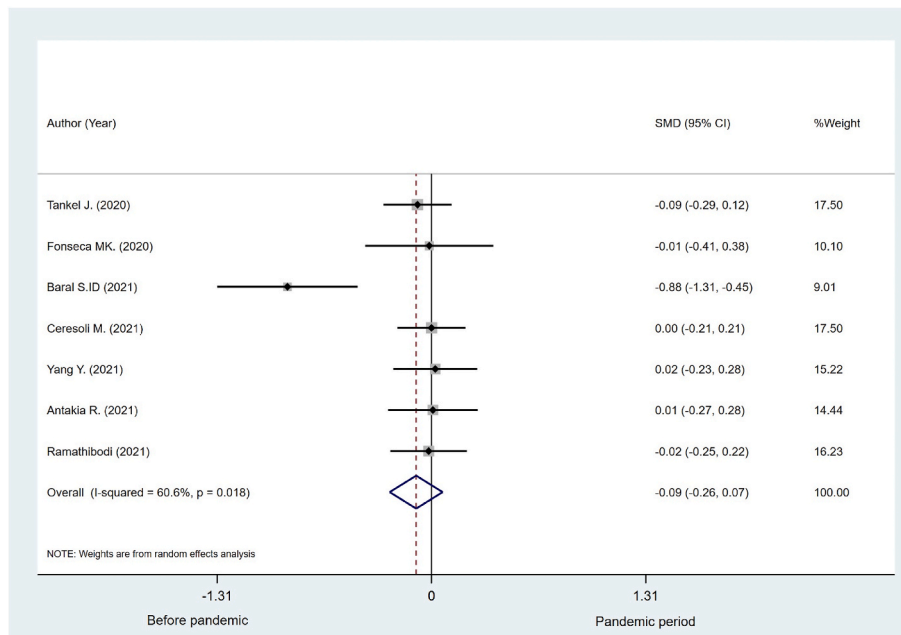


Fig. 6. Forest plot of length of hospital stay(LOS) before and COVID-19 pandemic period.

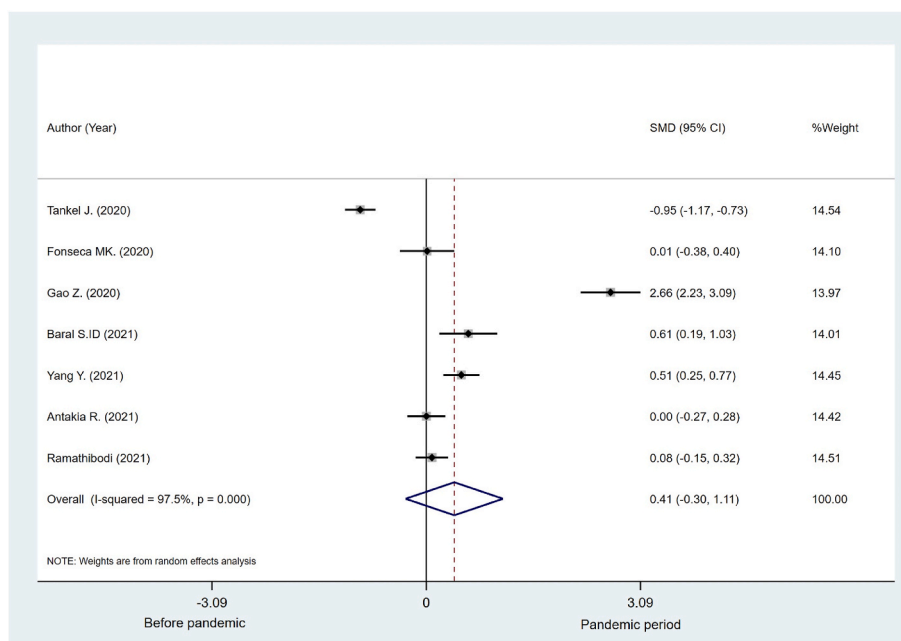


Fig. 7. Forest plot of time from onset of symptom to hospitalisation before and COVID-19 pandemic period.

Ethical approval

Ethic approval has permitted by the ethical committee of Mahidol University, Thailand.

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Author contributions

Abduljubbar Kariya contributes for acquisition and interpretation of

data, drafting the article.

Chonlada Krutsri contributes for the conception and design of the study, acquisition of data, interpretation of data, revise article, and final approval.

Pongsasit Singhatas contributes for interpretation of data and final approval.

Preeda Sumritpradit contributes for interpretation of data and final approval.

Panuwat Lertsitthichai contributes for the conception design of the study, analysis the data.

Napaphat Phoprom contributes for the data analysis and interpretation.

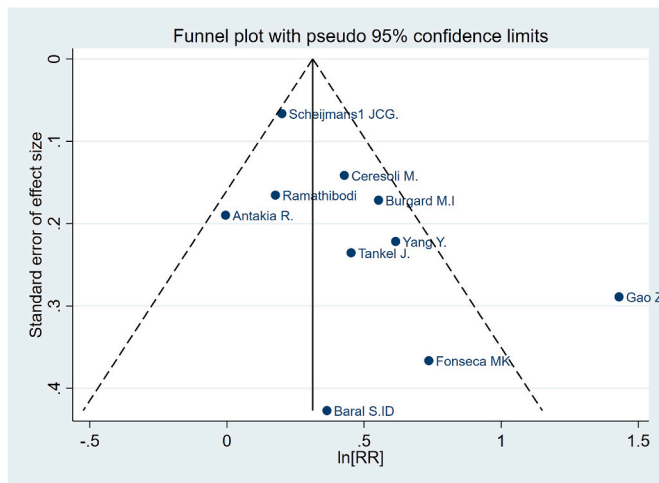


Fig. 8. Funnel plot for detection of publication bias of complicated appendicitis.

Registration of research studies

Prospero: <https://www.crd.york.ac.uk/prospero/#recordDetails>.

Guarantor

Ass.Prof.Chonlada Krutrsri is the guarantor of this work.

Consent

Ethic approval has permitted by the ethical committee of Mahidol University, Thailand. Patients' and volunteers' names, initials, or hospital numbers should not be used.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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