Original article

CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Acute abdomen following COVID-19 vaccination: a systematic review

Clin Exp Vaccine Res 2024;13:42-53
https://doi.org/10.7774/cevr.2024.13.1.42
pISSN 2287-3651 • eISSN 2287-366X

Nelson Luis Cahuapaza-Gutierrez[1,2], Renzo Pajuelo-Vasquez[1,2], Cristina Quiroz-Narvaez[1,2], Flavia Rioja-Torres[1,2], María Quispe-Andahua[1,2], Fernando M. Runzer-Colmenares[1,2,3]

[1]Facultad de Ciencias de la Salud, Carrera de Medicina Humana, Universidad Científica del Sur, Lima; [2]CHANGE Research Working Group, Universidad Científica del Sur, Lima; [3]Grupo de Bibliometría, Evaluación de Evidencia y Revisiones Sistemáticas (BEERS), Facultad de Ciencias de la Salud, Carrera de Medicina Humana, Universidad Científica del Sur, Lima, Perú

Received: October 11, 2023
Revised: November 9, 2023
Accepted: December 21, 2023

Corresponding author: Nelson Luis Cahuapaza-Gutierrez, Medical Student
Facultad de Ciencias de la Salud, Carrera de Medicina Humana, Universidad Científica del Sur, Lima, Perú
Tel: +51-946329607
E-mail: 100065659@cientifica.edu.pe

No potential conflict of interest relevant to this article was reported.

Purpose: Conduct a systematic review of case reports and case series regarding the development of acute abdomen following coronavirus disease 2019 (COVID-19) vaccination, to describe the possible association and the clinical and demographic characteristics in detail.
Materials and Methods: This study included case report studies and case series that focused on the development of acute abdomen following COVID-19 vaccination. Systematic review studies, literature, letters to the editor, brief comments, and so forth were excluded. PubMed, Scopus, EMBASE, and Web of Science databases were searched until June 15, 2023. The Joanna Briggs Institute tool was used to assess the risk of bias and the quality of the study. Descriptive data were presented as frequency, median, mean, and standard deviation.
Results: Seventeen clinical case studies were identified, evaluating 17 patients with acute abdomen associated with COVID-19 vaccination, which included acute appendicitis (n=3), acute pancreatitis (n=9), diverticulitis (n=1), cholecystitis (n=2), and colitis (n=2). The COVID-19 vaccine most commonly linked to acute abdomen was Pfizer-BioNTech (messenger RNA), accounting for 64.71% of cases. Acute abdomen predominantly occurred after the first vaccine dose (52.94%). All patients responded objectively to medical (88.34%) and surgical (11.76%) treatment and were discharged within a few weeks. No cases of death were reported.
Conclusion: Acute abdomen is a rare complication of great interest in the medical and surgical practice of COVID-19 vaccination. Our study is based on a small sample of patients; therefore, it is recommended to conduct future observational studies to fully elucidate the underlying mechanisms of this association.

Keywords: Acute abdomen, COVID-19 vaccines, SARS-CoV-2 vaccines, Systematic review

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulted in a serious public health threat due to the rapid progression, hospitalization, and death of those infected [1]. As of August 30, 2023, about 6.9 million people have died worldwide because of COVID-19, with a total of 770 million confirmed cases [2]. In response, the U.S. Food and Drug Administration issued the Pfizer-BioNTech vaccine (BNT162b2 messenger RNA [mRNA]), followed by two vaccines, Moderna (mRNA-1273) and Janssen/Johnson (traditional viral vector), for licensure and emergent use [3].

Immunization against SARS-CoV-2 is one of the most important preventive measures to contain the disease because it prevents the spread of the virus and limits the serious consequences of the infection; therefore, for the development of vaccines,

three main factors must be considered: efficacy, immunogenicity, and safety, as well as continuous surveillance and research [4]. Currently, the authorization of the emerging use of vaccines against SARS-CoV-2 has been approved, including mainly mRNA technology vaccines, viral vectors, recombinant protein, inactivated, live attenuated, and DNA vaccines [5]. At the time of writing manuscript, approximately 13.5 billion vaccines have been administered worldwide [2].

In general, vaccines have proven to be safe, although rare but potentially serious adverse effects may occur after vaccination [6]. Thus, several studies describe a series of neurological (Guillain-Barré) [7], cardiovascular (myocarditis) [8,9], hematological (hemolytic anemia) [10], ophthalmological (optic neuritis) [11], endocrinological (Graves' disease) [12], and other complications, with a possible association with the T-cell immune response that vaccines induce.

Case report and case series studies report the occurrence of acute abdomen such as acute appendicitis [13], acute pancreatitis [14], diverticulitis [15], cholecystitis [16], and colitis [17] as a possible complication of COVID-19 vaccination. These studies are of current interest in surgical and clinical medical practice; therefore, our objective was to perform a systematic review of case reports and case series to describe in detail the possible association, the clinical and demographic characteristics of development of acute abdomen following COVID-19 vaccination.

Materials and Methods

Protocol and registration

The present review follows the guidelines of the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA 2020) [18]. The review protocol was registered in the "International Prospective Register of Systematic Reviews" (PROSPERO), registration number (CRD42023432966).

Objectives

The main objective of the present review is to describe in detail the possibility of an association between acute abdomen and vaccination against COVID-19. In addition, to describe the clinical and demographic characteristics of persons who have been vaccinated against COVID-19 and subsequently experienced acute abdomen. The primary focus of investigation includes the study of pathologies such as acute appendicitis, acute pancreatitis, diverticulitis, cholecystitis, and colitis.

Search strategy

For the present systematic review, a selective literature search was performed out in the following electronic databases: PubMed, Scopus, EMBASE, and Web of Science. For this purpose, a search strategy was designed with the terms obtained from Medical Subject Headings (MeSH) of National Library of Medicine: "Acute Abdomen," "COVID-19 Vaccines" related to the terms obtained for each pathology: "Appendicitis," "Pancreatitis," "Diverticulitis," "Cholecystitis," and "Colitis" related through Boolean operators AND u OR. The search was performed until June 15, 2023. In addition, to make the search more precise, the reference lists of the included studies were manually reviewed. The search was limited to English, Portuguese, and Spanish. The search was not limited by publication date. The search strategy for each database is shown in detail in Supplement 1.

Eligibility criteria

Case report and case series studies on the development of acute abdomen in persons older than 18 years following COVID-19 vaccination were included. Other types of studies such as systematic reviews, narrative reviews, letters to the editor, congress or conference abstracts, editorials, interviews, commentaries, short communications, brief reports, and newspaper articles were excluded. In addition, we excluded records that reported patients younger than 18 years of age and incorrect outcomes (other type of outcomes). We also excluded records that were not in English, Portuguese, or Spanish.

Study selection process

All the references were downloaded to an EndNote document to remove duplicate items. Then, were exported to the Rayyan QCRI website (https://www.rayyan.ai/). Two authors independently screened and selected the records by titles and abstracts. In addition, they evaluated the full-text version of the selected references to determine eligibility criteria. Any disagreement was resolved by mutual discussion between the two reviewers.

Data extraction process

The authors independently extracted the data of interest in a previously prepared Microsoft Excel template (Microsoft Corp., Redmond, WA, USA). Any disagreement was resolved by the authors. The extracted data included the most important characteristics of the studies such as the name of the first author, year of publication, sex, age, background/comorbidi-

ties, vaccine type, number of doses, time after COVID-19 vaccination, clinical manifestations, physical exam (signs)/vital functions, laboratory, image tests, pathology (histology), final diagnostic, treatment (medical or surgical), and development–recovery time (medical or surgical).

Bias risk and quality assessment

To assess the risk of bias and quality of each of the included studies, the tool was used Joanna Briggs Institute (JBI) [19,20]. Two authors independently assessed all studies, and any disagreements were resolved by mutual discussion. The JBI presents four assessment options: "yes, no, unclear, and not applicable." in addition, affirmative responses are summarized from 0 to 8. Articles with a score below 4 are considered low quality and those with a score above 4 are considered high quality.

Synthesis and analysis of data

The IBM SPSS ver. 23.0 software (IBM Corp., Armonk, NY, USA) was used to synthesize and analyze the descriptive data. Categorical data such as: gender, history/comorbidities (present and not present), COVID-19 test (positive, negative, not described), Type of COVID-19 vaccine, dose, symptoms, and treatment were expressed as proportions (%) and numerical data such as: age and time to symptom onset as mean±standard deviation. All the results of the study were grouped in a table.

Results

Study selection

A total of 1,110 records were identified from the four databases (PubMed, Scopus, EMBASE, and Web of Science). After eliminating duplicate items, 616 records were obtained. After the selection phase, 38 records were selected independently by titles and abstracts. Twenty-one records were excluded: other types of studies, does not meet inclusion criteria, and conference abstracts. Finally, 17 studies were included. Fig. 1 shows in detail the study selection process using a PRISMA flow diagram.

Characteristics of included studies

The studies selected and included were case reports published between 2021 and 2023. We included only studies regarding: acute appendicitis (n=3), acute pancreatitis (n=9), diverticulitis (n=1), cholecystitis (n=2), and colitis (n=2). Other less frequent causes of acute abdomen were not included in the study. The characteristics of the included studies are described in more detail in Table 1 [13,15-17,21-32].

Clinical and demographic characteristics

The 17 included studies described a total of 17 patients with, age groups, gender distribution, and time to onset of symptoms described separately for each disease. Medical history/

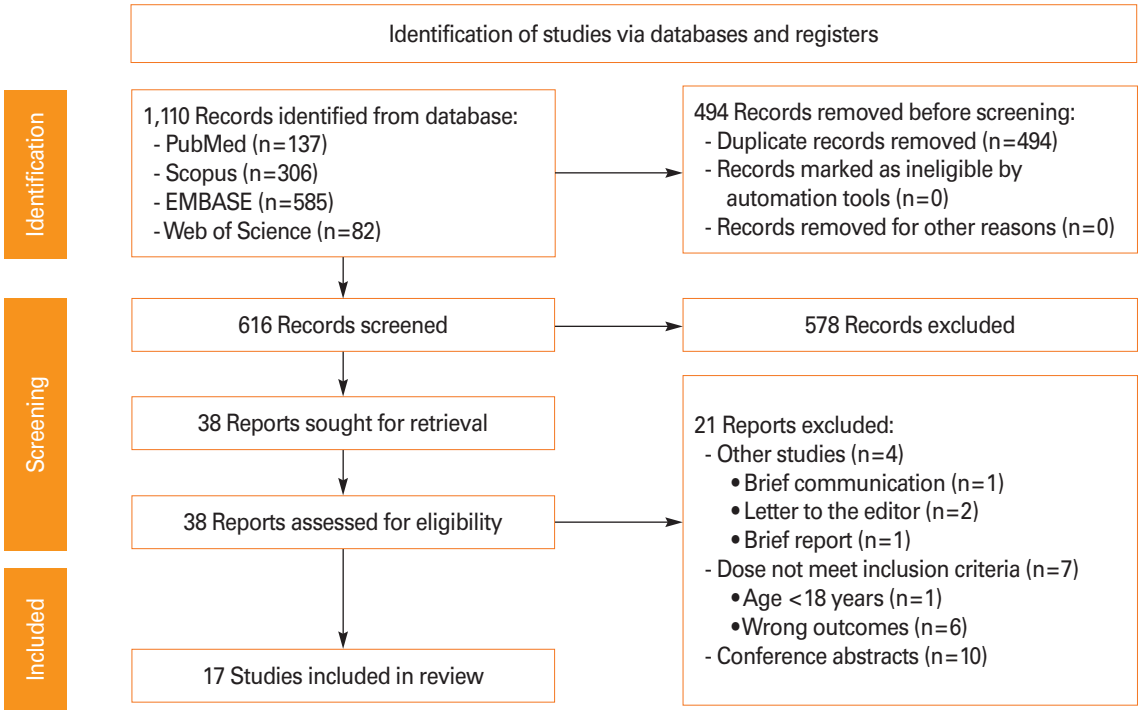

Fig. 1. Flow diagram PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) of study selection process.

 https://doi.org/10.7774/cevr.2024.13.1.42

Table 1. Characteristics of studies included

Study	Sex/ age (yr)	Background/ comorbidities	Vaccine type (technology)	No. of doses	Time after COVID-19 vaccination	Clinical manifestations; physical exam (signs)	Vital functions	Laboratory (alteration)	Image tests	Pathology (histology)	Final diagnostic	Treatment (medical or surgical)	Development
Oganesyan et al. [13] (2022)	F/69	None	Pfizer-BioNTech (mRNA)	3rd	24 hr	Acute abdominal pain	BP: 96/61 mm Hg; HR: 107 beats/min; SpO_2: 93%	RBC: 3.73×10^{12}/L; Hb: 115 g/L; Hct: 34.8%; neutrophils: 7.6×10^{9}/L	CT: perforated acute appendicitis with appendicolith	None	Acute appendicitis	Laparoscopic appendectomy	Recovered
Marconi et al. [21] (2022)	F/58	Left quadrantectomy with radiotherapy for breast cancer; hypertension	Pfizer-BioNTech (mRNA)	1st	2 days	Acute abdominal pain; fever; nausea; vomiting	None	WBC: 12.1×10^{9}/L; neutrophils (%): 78.4%; fibrinogen: 636.0 mg/dL	CT: distended appendix with thickened walls	Diffuse acute and chronic inflammatory infiltrates with scattered non-necrotizing granulomas	Acute appendicitis	Laparoscopic appendectomy	Recovered
Kawano et al. [22] (2022)	M/19	None	Moderna (mRNA)	2nd	28 days	Abdominal pain; vomiting; loss appetite	BP: 79/50 mm Hg; HR: 140 bpm/min; T: 38.6°C	WBC :12.2×10^{9}/L; CRP: 10.27 mg/L; D-dimer. 1,600 μg/L; hsTnT: 3.67 ng/mL	CT: swollen appendix	None	Acute appendicitis	Steroids and antibiotics	Recovered
Cieślewicz et al. [23] (2021)	F/29	None	Pfizer-BioNTech (mRNA)	1st	20 hr	Abdominal pain	T: 40°C	WBC: 13×10^{9}/L; neutrophils (%): 75.6%; urine amylase: 544 U/L; CRP: 128 mg/L	Abdominal USG: pancreas homogeneous	None	Acute pancreatitis	Fluid resuscitation, pain control, and nutritional support	Recovered
Parkash et al. [24] (2021)	F/96	Heart failure; hypertension; hypothyroidism	Pfizer-BioNTech (mRNA)	1st	2 days	Epigastric pain; nausea	None	Amylase: 4,036 U/L	CT: no findings	None	Acute pancreatitis	Hydration and analgesics	Recovered
Cacdac et al. [14] (2022)	M/82	Coronary artery disease; prostate cancer; proctocolitis; hypothyroidism; gastroesophageal reflux disease	Pfizer-BioNTech (mRNA)	3rd	Few hours	Epigastric abdominal pain; nausea; vomiting	None	Lipase: 2,257 U/L	CT: suggestive acute interstitial pancreatitis	None	Acute pancreatitis	IV fluids, acetaminophen, hydromorphone, and metoclopramide	Recovered
Dey et al. [25] (2022)	F/24	Pregnant (31 weeks of gestation)	Pfizer-BioNTech (mRNA)	1st	1 wk	Epigastric pain; nausea; vomiting	BP: 140/90 mm Hg; HR: 106 beats/min; RR: 22 breaths/min; T: 39°C	WBC: 17×10^{9}/L; lipase: 4,376 U/L	CT: suggestive of acute interstitial edematous pancreatitis	None	Acute pancreatitis	Intravenous hydration, antibiotics, and proton pump inhibition	Recovered
Ozaka et al. [26] (2022)	F/71	Hypertension; hyperlipidemia; cerebral infarction	Pfizer-BioNTech (mRNA)	1st	2 days	Abdominal pain; vomiting	BP: 142/86 mm Hg	Lipase: 383 U/L; amylase: 1,043 U/L	CT: diffuse enlargement of the pancreas	None	Acute pancreatitis	IV hydration, antibiotics, and proton pump inhibition	Recovered

(Continued on next page)

Table 1. Continued

Study	Sex/ age (yr)	Background/ comorbidities	Vaccine type (technology)	No. of doses	Time after COVID-19 vaccination	Clinical manifestations; physical exam (signs)	Vital functions	Laboratory (alteration)	Image tests	Pathology (histology)	Final diagnostic	Treatment (medical or surgical)	Development
Alrashdi et al. [27] (2022)	F/22	None	Pfizer-BioNTech (mRNA)	1st	1 wk	Abdominal pain; nausea; vomiting; erythematous maculopapular rashes	BP: 118/75 mm Hg	WBC: 13×10^9/L; amylase: 181 U/L; lipase: 185 U/L; AST: 301 UI/L; ALT: 81 UI/L	CT: edematous pancreas	None	Acute pancreatitis	MP, HCQ, AZA	Recovered
Boskabadi et al. [28] (2023)	F/28	None	BBIBP-CorV (Sinopharm)	2nd	3 mo	Abdominal pain; nausea; hemoptysis; aphagia; constipation	BP: 130/70 mm Hg; HR: 101 beats/min	Lipase: 156 U/L; amylase: 1,079 U/L; ALT: 80 U/L; TG: 1,562 mg/dL; glycemia: 203 mg/dL	CT: enlargement of the pancreas, extensive fat, and fluid peri-pancreatic	None	Acute pancreatitis	Fluid therapy and antibiotics	Recovered
Bangolo et al. [29] (2023)	M/34	None	Johnson & Johnson /Jassen vaccine (viral vector)	1st	1 day	Epigastric pain; nausea; shivering	T: 38.28°C	WBC: 18.9×10^9/L; lipase: 1,026 U/L; T-bil: 9.9 mg/dL; CRP: 15 mm/hr; BUN: 45 mg/dL; Cr: 2.19 mg/dL	CT: acute necrotizing pancreatitis	None	Acute pancreatitis	Ringer lactate, pain control, and nutritional support	Recovered
Stöllberger et al. [30] (2023)	F/31	Allergic asthma; psoriatic arthritis; neurogenic bladder; cholecystolithiasis	Pfizer-BioNTech (mRNA)	2nd	2 days	Abdominal pain; nausea	None	WBC: 12.6×10^9/L; AAE: 418 U/L; lipase: 1,162 U/L	CT: necrotizing pancreatitis and edematous	None	Acute pancreatitis	EAT with CTX, transgastric drainage	Recovered
Ajmera et al. [15] (2022)	M/41	Bipolar depression; asthma; obesity	Modern (mRNA)	3rd	1 day	Abdominal pain; diarrhea; sweating; loss appetite	BP: 148/100 mm Hg	WBC: 13.5×10^9/L	CT: acute diverticulitis of the mid-transverse colon, with micro-perforation	None	Diverticulitis acute	NBM, EAT, intravenous hydration with normal saline	Recovered
Kyungu et al. [31] (2022)	M/29	None	Johnson & Johnson/ Janssen (viral vector)	1st	2 days	Abdominal pain; nausea; fever; dark colored urine	BP: 153/121 mm Hg; RR: 20 breaths/min; T: 39.2°C	WBC: 2.83×10^9/L; platelet: 79×10^9/L; AST: 493.9 U/L; ALT: 244.7 U/L; GGT: 85 U/L; CRP: 148.62 mg/L	Ultrasound: no significant findings	None	Acute acalculous cholecystitis	Analgesics, ringer lactate, antibiotics	Recovered
Wahlen et al. [16] (2022)	F/52	None	Pfizer-BioNTech (mRNA)	3rd	8 hr	Abdominal pain; shivering; nausea; vomiting; anuria	HR: 100 beats/min; T: 38°C	WBC :15.8×10^9/L; ANC: 14.6×10^9/L; ALT: 89 U/L; CRP: 10.8 mg/L	Ultrasound: no significant findings	None	Acalculous cholecystitis	Fluid resuscitation, acetaminophen, and nutritional support	Recovered

(Continued on next page)

Table 1. Continued

Study	Sex/ age (yr)	Background/ comorbidities	Vaccine type (technology)	No. of doses	Time after COVID-19 vaccination	Clinical manifestations; physical exam (signs)	Vital functions	Laboratory (alteration)	Image tests	Pathology (histology)	Final diagnostic	Treatment (medical or surgical)	Development
Vadioaloo et al. [32] (2022)	M/72	Hypertension; atrial fibrillation with stroke	Pfizer-BioNTech (mRNA)	1st	6 hr	Abdominal pain; diarrhea	None	Eosinophil count: 6.84×10^9/L	EGD: antral erythematous gastritis	Mucosal lymphoplasmacytic cell infiltration with increased eosinophil	Eosinophilic colitis	Any, resolved spontaneously	Recovered
Cui et al. [17] (2022)	F/48	None	BBIBP-CorV (Sinopharm)	2nd	1 day	Abdominal pain; hematochezia; fatigue	BP: 140/85 mm Hg	D-dimer: 329 μg/L; FDP: 2.5 mg/L; lactic acid: 2.60 mmol/L	CT: edema and bowel wall thickening	None	Ischemic colitis	Pinaverium bromide and aspirin	Recovered

COVID-19, coronavirus disease 2019; F, female; M, male; mRNA, messenger RNA; BP, blood pressure; HR, heart rate; SpO_2, oxygen saturation; RBC, red blood cell count; Hb, hemoglobin; Hct, hematocrit; CT, computed tomography; WBC, white blood cell count; T, temperature; CRP, C-reactive protein; hsTnT, high-sensitivity troponin T; USG, ultrasound sonography test; IV, intravenous; RR, respiratory rate; MP, methylprednisolone; HCQ, hydroxychloroquine; AZA, azathioprine; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; T-bil, total bilirubin; BUN, blood urea nitrogen; Cr, creatinine; AAE, alpha amylase enzyme; EAT, empirical antibiotic therapy; CTX, cefotaxime; NBM, nil by mouth; GGT, gamma-glutamyl transferase; ANC, absolute neutrophil count; EGD, esophagogastroduodenoscopy; FDP, fibrinogen-degradation product.

Table 2. Clinical and demographic characteristics of the included studies (n=17)

Variable	Adverse effect				
	Acute appendicitis	Acute pancreatitis	Diverticulitis	Cholecystitis	Colitis
Total no. of reported cases	3	9	1	2	2
Age (yr)	48.6±21.45	46.3±26.79	41	40.5±11.5	60±12
Gender					
Female	2 (66.67)	7 (77.77)	1 (100.0)	1 (50.0)	1 (50.0)
Male	1 (33.33)	2 (22.22)		1 (50.0)	1 (50.0)
Time to symptom onset	10.3±12.49 days	13.97±28.82 days	1 day	28±20 hr	15±9 hr

Values are presented as mean±standard deviation or number (%).

Table 3. Clinical characteristics of the included studies (n=17)

Variable	No. (%)
Background/comorbidities (n=17)	
Present	8 (47.06)
Not present	9 (52.94)
Test COVID-19 (n=17)	
Positive	0
Negative	11 (64.71)
Not described	6 (35.29)
Type of COVID-19 vaccine (n=17)	
Pfizer-BioNTech (mRNA)	11 (64.71)
Moderna (mRNA)	2 (11.76)
BBIBP-CorV (Sinopharm)	2 (11.76)
Johnson & Johnson/Jassen vaccine (viral vector)	2 (11.76)
Dose (n=17)	
1st dose	9 (52.94)
2nd dose	4 (23.53)
3rd dose	4 (23.53)
Symptoms (n=17)	
Abdominal pain	14 (82.35)
Nausea	10 (58.82)
Vomiting	7 (41.18)
Fever	3 (17.64)
Epigastric pain	3 (17.64)
Shivering	2 (11.76)
Loss appetite	2 (11.76)
Diarrhea	2 (11.76)
Sweating	1 (5.88)
Dark colored urine	1 (5.88)
Hemoptysis	1 (5.88)
Aphagia	1 (5.88)
Constipation	1 (5.88)
Anuria	1 (5.88)
Hematochezia	1 (5.88)
Fatigue	1 (5.88)
Erythematous maculopapular rashes	1 (5.88)
Treatment (n=17)	
Medical	15 (88.34)
Surgical	2 (11.76)

COVID-19, coronavirus disease 2019; mRNA, messenger RNA.

comorbidities, COVID-19 test, type of COVID-19 vaccine, dose, symptoms, and treatment were evenly distributed. Most cases were associated with the Pfizer-BioNTech vaccine (mRNA, 64.71%; Pfizer, New York, NY, USA), followed by Moderna (mRNA, 11.76%; Cambridge, MA, USA), BBIBP-CorV (Sinopharm, 11.76%; Sinopharm Group Co. Ltd., Beijing, China), and the Johnson & Johnson/Janssen vaccine (viral vector, 11.76%; Johnson & Johnson, New Brunswick, NJ, USA). The majority of cases were associated with the first dose (52.94%). Among the symptoms, acute abdominal pain was present in almost all studies (82.35%), and other studies reported epigastric pain (17.64%). No deaths were reported in any of the studies, and all patients recovered, with the majority being discharged in the following weeks. Medical treatment was administered in most cases (88.34%), with only one case (11.76%) requiring surgical intervention. Detailed clinical and demographic characteristics are presented in Tables 2 and 3.

Risk of bias and quality of individual studies

The 17 included studies were assessed using the JBI tool. All 17 studies were categorized as case reports; no case series studies were identified. The JBI checklist for case reports comprises an 8-item scale that encompasses the patient's demographic characteristics, medical history, current clinical condition, description of diagnostic tests, treatment, post-intervention clinical condition, adverse events, and the provision of takeaway lessons [33]. Among the studies assessed, the findings revealed that three studies were rated as low quality, while 14 studies were appraised as high quality. The scores obtained were as follows: scores below 4 (n=3; three studies scored 3) and scores above 4 (n=14; one study scored 5, two studies scored 6, four studies scored 7, and seven studies scored 8). The studies received an "unclear" rating, particularly regarding the questions: "Was the post-intervention clinical condition clearly described?" and "Does the case report provide takeaway lessons?" The detailed risk and quality assessment process of the studies, evaluated by the JBI tool, is presented in Table 4.

Discussion

In this systematic review of case reports and case series on acute abdomen following COVID-19 vaccination, we identi-

Table 4. Risk of bias and quality assessment of included studies

Author	Questions							
	Were the patient's demographic characteristics clearly described?	Was the patient's history clearly described and presented as a timeline?	Was the current clinical condition of the patient on presentation clearly described?	Were diagnostic tests or assessment methods and the results clearly described?	Was the intervention(s) or treatment procedure(s) clearly described?	Was the postintervention clinical condition clearly described?	Were adverse events (harms) or unanticipated events identified and described?	Does the case report provide takeaway lessons?
Oganesyan et al. [13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Marconi et al. [21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kawano et al. [22]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear
Cieślewicz et al. [23]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Parkash et al. [24]	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes
Cacdac et al. [14]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Dey et al. [25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ozaka et al. [26]	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear
Alrashdi et al. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Boskabadi et al. [28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bangolo et al. [29]	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Stöllberger et al. [30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Ajmera et al. [15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kyungu et al. [31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Wahlen et al. [16]	Yes	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Unclear
Vadioaloo et al. [32]	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear
Cui et al. [17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Quality assessment based on the Joanna Briggs Institute (JBI) tool for case reports.

 https://doi.org/10.7774/cevr.2024.13.1.42

fied acute pancreatitis as the most common complication, associated with the Pfizer-BioNTech vaccine (mRNA) and the first dose. And the vaccine type and dose were reported, respectively. Of the 17 cases included in this review, the mean age of the cases who developed acute abdomen after receiving the vaccine was 47 years, and 64.7% were females. In our review, most patients showed improvement requiring only supportive medical treatment. Of the patients in our review, 47.06% (n=8) had an established prior diagnosis of comorbidity, with cardiovascular disease (arterial hypertension) being the most frequent.

Acute appendicitis (AA) is the most frequent cause of acute surgical abdomen worldwide [34]. The incidence is estimated to be around 1/10,000 cases per year, with an estimated lifetime risk of 7% to 8% [34,35]. There is a slight male predominance in a 1.4:1 ratio compared to females, and it most commonly occurs between the ages of 10 and 20 years [36]. The etiology of acute appendicitis is primarily attributed to obstructive processes resulting from follicular hyperplasia and fecalith. Additionally, rare obstructive causes include conditions such as amebiasis, carcinoid tumors, and infestations by parasites like amebiasis, enterobiasis, and ascariasis, among others [37]. Our study found three case reports of AA induced by SARS-CoV-2 vaccination. The mean age was estimated to be 48.6±21.45 years, with a slight predominance by females. AA occurred mainly after administration of Pfizer-BioNTech (mRNA) vaccine (n=2) [13,21] followed by Moderna (mRNA) (n=1) [22]. In other studies, the Pfizer-BioNTech vaccine was associated with AA with a risk ratio of 1.40 (95% confidence interval, 1.02 to 2.01) in contrast to the Moderna (mRNA) vaccine, where a weak association was found in certain age groups, in both cases demonstrated within 21 days of vaccine administration [38,39]. The dose was equivalent for all three patients (first [n=1], second [n=1], and third [n=1]). The time elapsed from vaccine administration to onset of symptoms was 10.3±12.49 days. The treatment involved laparoscopic appendectomy in two patients due to perforation, while one patient underwent outpatient treatment with antibiotics and steroids. There was one case that reported the appearance of AA together with fulminant myocarditis [22]. In a retrospective study by Quint et al. [40], the registry of 421 patients with AA was reviewed, leading to the conclusion that AA caused by vaccination resembles classical AA. No deaths were reported, and all patients recovered, being discharged within a few days. The mechanisms by which this association may occur are not fully elucidated. It is known that SARS-CoV-2 vaccines produce an increased type 1 T helper (Th1) cell response [41]. Th1 cells primarily produce cytokines such as interferon-gamma and tumor necrosis factor-alpha; dysregulated levels of Th1 cytokines have been associated with autoimmune inflammation [42]. A study by Rubér et al. [43] found a positive association between gangrenous-type appendicitis and states of Th1-mediated immunity, suggesting that the increased Th1 response may contribute to an uncontrolled inflammatory reaction and the risk of perforation. If vaccines induce an elevated Th1 response, it is plausible that in our two patients who underwent appendectomy due to a perforated phase, this could be attributed to a potential association.

Acute pancreatitis (AP) is among the most prevalent gastrointestinal causes, and its incidence continues to rise globally [44]. Gallstones (45%) and alcohol abuse (20%) represent the most common causes of AP. Other less frequent associated causes include medication, endoscopic retrograde cholangiopancreatography, hypercalcemia, hypertriglyceridemia, infection, genetics, autoimmune diseases, and (surgical) trauma [45]. AP has been previously associated with several vaccines reported in the literature, including vaccines against human papillomavirus [46,47], hepatitis A and B [48,49], measles-mumps-rubella [50,51], varicella [52], as well as typhoid fever and cholera [53]. Our study identified nine case reports of AP induced by vaccination against SARS-CoV-2. The mean age was estimated to be 46.3±26.79 years, with a predominance of females. AP predominantly occurred after the administration of the Pfizer-BioNTech (mRNA) vaccine (n=7) [23,27], followed by Sinopharm (n=1) [28], and Johnson & Johnson/Janssen (n=1) vaccines [29]. Dosing for the nine patients included the first dose (n=6), second dose (n=2), and third dose (n=1). The time from vaccine administration to the onset of symptoms was 13.97±28.82 days. Treatment was medical and supportive in all patients, with no surgical procedures reported. One case mentioned the appearance of AP together with hemolytic anemia and thrombocytopenia [30]. Additionally, one case was associated with systemic lupus erythematosus [27]. There was a case of AP following the administration of the Pfizer-BioNTech vaccine in a patient at 31 weeks of gestation. On the second day, she underwent spontaneous vaginal delivery due to the inflammatory process triggered by AP [25]. No deaths were reported, and all patients recovered, being discharged in the following days. The mechanisms by which post-vaccination AP occurs are not clear. An autoimmune reaction is suggested due to the similarity of amino acids between the vaccine and host antigens, a mechanism known as molecular mimicry [25,28]. This mimicry is attributed to the cleavage of the Furin peptide,

identical to that of the human epithelial sodium channel, present in various organs such as the intestine, pancreas, and lungs. These data imply pancreatic injury due to an autoimmune reaction induced by the mRNA vaccine [26,54].

Diverticulitis ranks as the third most common gastrointestinal disease and stands as the primary indication for elective colon resection [55]. It predominantly affects men until the 6th decade of life and is associated with various risk factors, including obesity, single consumption of red meat, smoking, and the use of medications such as non-steroidal anti-inflammatory drugs [56]. Our study identified only one case report of diverticulitis induced by SARS-CoV-2 vaccination. This involved a 41-year-old male patient who developed diverticulitis one day after receiving the third dose of the Moderna (mRNA) vaccine [15]. The treatment administered was medical and supportive, and he was discharged with a subsequent follow-up colonoscopy. Diverticulitis can result from genetic factors, environmental factors, and colon dysmotility, with recent studies associating it with specific immune responses of the host and the microbiome [57]. It is hypothesized that the Moderna vaccine (mRNA), once injected into the host, is translated into a viral spike protein. This protein could bind in a manner like SARS-CoV-2, to cells of the gastrointestinal tract inducing an inflammatory process and dysbiosis [15].

Cholecystitis is an acute inflammatory disease, often associated with gallstones (90% to 95%) and approximately 5% to 10% of patients are due to acalculous cholecystitis, defined as acute inflammation of the gallbladder without gallstones, typically in the context of severe critical illness [58]. The mechanisms by which cholecystitis mainly occurs are due to physical obstruction by gallstones, resulting in increased pressure and cholestasis within the gallbladder, which induces infectious mediator activation [59]. Our study identified two case reports of cholecystitis induced by SARS-CoV-2 vaccination. Both cases were diagnosed as acute acalculous cholecystitis, indicating the absence of gallstones. The mean age was calculated to be 40.5±11.5 years, involving one female patient and one male patient. Acute cholecystitis occurred following the administration of the Pfizer-BioNTech (mRNA) vaccine [16] and the Johnson & Johnson/Janssen (viral vector) vaccine [31]. It occurred after the first and third doses, respectively. The time from vaccine administration to symptom onset was 28±20 hours. Treatment was medical and supportive, and patients were discharged a few weeks later. Acalculous or alliasic cholecystitis is characterized by acute necrotizing inflammation without calculi. The mechanisms by which this association occurs are not fully elucidated [60]. The link between the vaccine and the onset of acalculous cholecystitis is not known, and a possible molecular mimicry reaction is suggested [16].

Eosinophilic colitis is a rare condition characterized by an elevated eosinophilic infiltrate in the colon walls and commonly presents as abdominal pain or diarrhea [61]. The pathophysiology of eosinophilic colitis involves various agents such as food allergens, parasitic infections, and drugs [62]. Ischemic colitis is characterized by a deficit of blood supply to the colon, caused by factors like drugs, pathogenic microorganisms, coagulation disorders, obesity, smoking, and iatrogenic factors [63]. Our study identified two case reports of colitis induced by SARS-CoV-2 vaccination. The mean age was estimated to be 60±12 years, involving one female patient and one male patient. Eosinophilic colitis occurred following the administration of the Pfizer-BioNTech (mRNA) vaccine [32], and ischemic colitis occurred after the Sinopharm vaccine [17]. It occurred after the first and second doses, respectively. The time from vaccine administration to symptom onset was 15±9 hours. Treatment was medical for ischemic colitis, and there was a spontaneous resolution for the case of eosinophilic colitis. Both patients experienced a favorable recovery. The mechanisms by which this association occurs are not clear. For ischemic colitis, it is proposed that vaccines induce inflammation and immune reactions, which could generate a state of hypercoagulability and alter the arterial blood supply to the colon [17]. Our study has some limitations. First, the systematic review only includes case reports and case series studies due to the limited number of original studies on the development of acute abdomen following COVID-19 vaccination, as of the date of writing the manuscript. Case reports and case series are not indicative studies, so the information should be interpreted with great caution. Second, the limited number of reported studies regarding the development of these complications could introduce a potential risk of bias. Third, despite conducting an exhaustive literature search, we acknowledge the possibility that some studies related to this topic might have been overlooked. Finally, our eligibility criteria included manuscripts published in English, Portuguese, and Spanish. Therefore, it is possible that there are several studies published in other languages and countries.

The emergence of acute abdomen following COVID-19 vaccination is of significant interest in clinical and surgical medical practice. Therefore, there is encouragement for the planning and execution of cohort and cross-sectional studies to evaluate this association with greater precision. To observe

 https://doi.org/10.7774/cevr.2024.13.1.42

the evolution of patients through clinical monitoring with possible risk of developing these complications once any type of vaccination against COVID-19 is applied.

In conclusion, the present systematic review is of great interest in clinical and surgical medical practice because it presents the development of acute abdomen after vaccination against COVID-19. However, few studies related to this association have been reported, so they are infrequent and occur in a minority of vaccinated individuals. Despite this, patients responded adequately to treatment, and no deaths related to these complications were reported. Importantly, the study involved a small sample of patients, and future observational studies are required. These studies could elucidate the various pathophysiological mechanisms by which this association occurs and provide more robust information on the safety of SARS-CoV-2 vaccines. Ultimately, the cases included and studied in this review indicate that instances of acute abdomen are minimal following vaccination. Therefore, vaccines generally do not seem to develop acute abdomen. However, despite this, physicians should monitor patients with a history of risk factors and observe the evolution of patients through clinical follow-up with a possible risk of developing these complications after any type of vaccination against COVID-19.

ORCID

Nelson Luis Cahuapaza-Gutierrez *https://orcid.org/0000-0002-1228-1941*
Renzo Pajuelo-Vasquez *https://orcid.org/0000-0002-0133-3689*
Cristina Quiroz-Narvaez *https://orcid.org/0000-0002-5835-3162*
Flavia Rioja-Torres *https://orcid.org/0000-0003-0146-0319*
María Quispe-Andahua *https://orcid.org/0000-0002-1422-4481*
Fernando M. Runzer-Colmenares *https://orcid.org/0000-0003-4045-0260*

Supplementary Materials

Supplementary material is available at Clinical and Experimental Experimental Vaccine Research website (http://www.ecevr.org).

References

1. Triggle CR, Bansal D, Ding H, et al. A comprehensive review of viral characteristics, transmission, pathophysiology, immune response, and management of SARS-CoV-2 and COVID-19 as a basis for controlling the pandemic. Front Immunol 2021;12:631139.
2. World Health Organization. WHO coronavirus (COVID-19) dashboard [Internet]. Geneva: World Health Organization; 2023 [cited 2023 Apr 3]. Available from: https://covid19.who.int
3. Marschner CA, Shaw KE, Tijmes FS, et al. Myocarditis following COVID-19 vaccination. Cardiol Clin 2022;40:375-88.
4. Sharif N, Alzahrani KJ, Ahmed SN, Dey SK. Efficacy, immunogenicity and safety of COVID-19 vaccines: a systematic review and meta-analysis. Front Immunol 2021;12:714170.
5. Fang E, Liu X, Li M, et al. Advances in COVID-19 mRNA vaccine development. Signal Transduct Target Ther 2022;7:94.
6. Marco JJ, Pasquin MJ, Martin SM. Effectiveness and safety of currently available SARS-CoV-2 vaccines. FMC 2021;28:442-51.
7. Ogunjimi OB, Tsalamandris G, Paladini A, Varrassi G, Zis P. Guillain-Barre syndrome induced by vaccination against COVID-19: a systematic review and meta-analysis. Cureus 2023;15:e37578.
8. Paknahad MH, Yancheshmeh FB, Soleimani A. Cardiovascular complications of COVID-19 vaccines: a review of case-report and case-series studies. Heart Lung 2023;59:173-80.
9. Li M, Wang X, Feng J, Feng Z, Li W, Ya B. Myocarditis or pericarditis following the COVID-19 vaccination in adolescents: a systematic review. Vaccines (Basel) 2022;10:1316.
10. Jafarzadeh A, Jafarzadeh S, Pardehshenas M, Nemati M, Mortazavi SM. Development and exacerbation of autoimmune hemolytic anemia following COVID-19 vaccination: a systematic review. Int J Lab Hematol 2023;45:145-55.
11. Lee YK, Huang YH. Ocular manifestations after receiving COVID-19 vaccine: a systematic review. Vaccines (Basel) 2021;9:1404.
12. Pezzaioli LC, Gatta E, Bambini F, et al. Endocrine system after 2 years of COVID-19 vaccines: a narrative review of the literature. Front Endocrinol (Lausanne) 2022;13:1027047.

13. Oganesyan A, Schafer M, Lesh C. Acute appendicitis following the COVID-19 vaccine. J Surg Case Rep 2022;2022:rjac295.
14. Cacdac R, Jamali A, Jamali R, Nemovi K, Vosoughi K, Bayraktutar Z. Acute pancreatitis as an adverse effect of COVID-19 vaccination. SAGE Open Med Case Rep 2022;10:2050313X221131169.
15. Ajmera K, Bansal R, Wilkinson H, Goyal L. Gastrointestinal complications of COVID-19 vaccines. Cureus 2022;14:e24070.
16. Wahlen BM, Peralta R, Al-Thani H, El-Menyar A. Friend or foe: the Pfizer-BioNTech (BNT162b2) vaccination: a case report of reversible acute acalculous cholecystitis. Clin Case Rep 2022;10:e6078.
17. Cui MH, Hou XL, Liu JY. Ischemic colitis after receiving the second dose of a COVID-19 inactivated vaccine: a case report. World J Clin Cases 2022;10:3866-71.
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
19. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. BMJ Evid Based Med 2018;23:60-3.
20. Ma LL, Wang YY, Yang ZH, Huang D, Weng H, Zeng XT. Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: what are they and which is better? Mil Med Res 2020;7:7.
21. Marconi E, Crescioli G, Bonaiuti R, et al. Acute appendicitis in a patient immunised with COVID-19 vaccine: a case report with morphological analysis. Br J Clin Pharmacol 2023;89:551-5.
22. Kawano H, Yamamoto N, Kurohama H, et al. Fulminant myocarditis and acute appendicitis after COVID-19 vaccination. Intern Med 2023;62:411-7.
23. Cieslewicz A, Dudek M, Krela-Kazmierczak I, Jablecka A, Lesiak M, Korzeniowska K. Pancreatic injury after COVID-19 vaccine: a case report. Vaccines (Basel) 2021;9:576.
24. Parkash O, Sharko A, Farooqi A, Ying GW, Sura P. Acute pancreatitis: a possible side effect of COVID-19 vaccine. Cureus 2021;13:e14741.
25. Dey RK, Ilango H, Bhatta S, et al. Acute pancreatitis in pregnancy following COVID-19 vaccine: a case report. J Med Case Rep 2022;16:354.
26. Ozaka S, Kodera T, Ariki S, Kobayashi T, Murakami K. Acute pancreatitis soon after COVID-19 vaccination: a case report. Medicine (Baltimore) 2022;101:e28471.
27. Alrashdi MN, Saleh AM, Khalid A, Alshaya AK, Alanazi SM. Systemic lupus erythematosus with acute pancreatitis and vasculitic rash following COVID-19 vaccine: a case report and literature review. Clin Rheumatol 2022;41:1577-82.
28. Boskabadi SJ, Ala S, Heydari F, Ebrahimi M, Jamnani AN. Acute pancreatitis following COVID-19 vaccine: a case report and brief literature review. Heliyon 2023;9:e12914.
29. Bangolo AI, Akhter M, Auda A, et al. A case report of acute severe necrotizing pancreatitis following the Johnson & Johnson vaccine against the Novel SARS-CoV-2. Case Rep Infect Dis 2023;2023:9965435.
30. Stollberger C, Kastrati K, Dejaco C, et al. Necrotizing pancreatitis, microangiopathic hemolytic anemia and thrombocytopenia following the second dose of Pfizer/BioNTech COVID-19 mRNA vaccine. Wien Klin Wochenschr 2023;135:436-40.
31. Kyungu FM, Katumba AM, Kamwira HL, et al. Acute acalculous cholecystitis following COVID-19 vaccination: a case report. Pan Afr Med J 2022;41:291.
32. Vadioaloo SY, Zahidi MM, Tan PO. A case of eosinophilic colitis after BNT162b2 mRNA COVID-19 vaccination. J Interdiscip Med 2022;7:44-6.
33. Moola S, Munn Z, Tufanaru C, et al. Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. JBI manual for evidence synthesis. Brisbane: The Joanna Briggs Institute; 2017. Chapter 7.
34. Teoule P, Laffolie J, Rolle U, Reissfelder C. Acute appendicitis in childhood and adulthood. Dtsch Arztebl Int 2020;117:764-74.
35. Ramson DM, Gao H, Penny-Dimri JC, et al. Duration of post-operative antibiotic treatment in acute complicated appendicitis: systematic review and meta-analysis. ANZ J Surg 2021;91:1397-404.
36. Krzyzak M, Mulrooney SM. Acute appendicitis review: background, epidemiology, diagnosis, and treatment. Cureus 2020;12:e8562.
37. Shahmoradi MK, Zarei F, Beiranvand M, Hosseinnia Z. A retrospective descriptive study based on etiology of appendicitis among patients undergoing appendectomy. Int J Surg Open 2021;31:100326.
38. Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. N Engl J Med 2021;385:1078-90.
39. Ljung R, Pihlstrom N, Sundstrom A. Risk of appendicitis after SARS-CoV-2 infection and SARS-CoV-2 vaccination.

Br J Surg 2022;109:775-6.
40. Quint E, Kukeev I, Hazan I, et al. Clinical characteristics of SARS-CoV-2 vaccine-related acute appendicitis. Can J Surg 2023;66:E304-9.
41. Mitchell J, Yue QY. Appendicitis as a possible safety signal for the COVID-19 vaccines. Vaccine X 2021;9:100122.
42. Muhammad Yusoff F, Wong KK, Mohd Redzwan N. Th1, Th2, and Th17 cytokines in systemic lupus erythematosus. Autoimmunity 2020;53:8-20.
43. Ruber M, Berg A, Ekerfelt C, Olaison G, Andersson RE. Different cytokine profiles in patients with a history of gangrenous or phlegmonous appendicitis. Clin Exp Immunol 2006;143:117-24.
44. Lee PJ, Papachristou GI. New insights into acute pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:479-96.
45. Boxhoorn L, Voermans RP, Bouwense SA, et al. Acute pancreatitis. Lancet 2020;396:726-34.
46. Das A, Chang D, Biankin AV, Merrett ND. Pancreatitis following human papillomavirus vaccination. Med J Aust 2008;189:178.
47. Bizjak M, Bruck O, Praprotnik S, Dahan S, Shoenfeld Y. Pancreatitis after human papillomavirus vaccination: a matter of molecular mimicry. Immunol Res 2017;65:164-7.
48. Shlomovitz E, Davies W, Cairns E, Brintnell WC, Goldszmidt M, Dresser GK. Severe necrotizing pancreatitis following combined hepatitis A and B vaccination. CMAJ 2007;176:339-42.
49. Haviv YS, Sharkia M, Galun E, Safadi R. Pancreatitis following hepatitis A vaccination. Eur J Med Res 2000;5:229-30.
50. Hansen LF, Nordling MM, Mortensen HB. Acute pancreatitis associated with MMR vaccination. Ugeskr Laeger 2003;165:2305-6.
51. Toovey S, Jamieson A. Pancreatitis complicating adult immunisation with a combined mumps measles rubella vaccine: a case report and literature review. Travel Med Infect Dis 2003;1:189-92.
52. Chan PW, Goh AY. Life threatening pancreatitis following varicella vaccination: cause, association or co-incidence? Med J Malaysia 2000;55:527-8.
53. Gatt DT. Pancreatitis following monovalent typhoid and cholera vaccinations. Br J Clin Pract 1986;40:300-1.
54. Anand P, Puranik A, Aravamudan M, Venkatakrishnan AJ, Soundararajan V. SARS-CoV-2 strategically mimics proteolytic activation of human ENaC. Elife 2020;9:e58603.
55. Ellison DL. Acute diverticulitis management. Crit Care Nurs Clin North Am 2018;30:67-74.
56. Strate LL, Morris AM. Epidemiology, pathophysiology, and treatment of diverticulitis. Gastroenterology 2019;156:1282-98.
57. Schieffer KM, Kline BP, Yochum GS, Koltun WA. Pathophysiology of diverticular disease. Expert Rev Gastroenterol Hepatol 2018;12:683-92.
58. Gallaher JR, Charles A. Acute cholecystitis: a review. JAMA 2022;327:965-75.
59. Kimura Y, Takada T, Strasberg SM, et al. TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci 2013;20:8-23.
60. Fu Y, Pang L, Dai W, Wu S, Kong J. Advances in the study of acute acalculous cholecystitis: a comprehensive review. Dig Dis 2022;40:468-78.
61. Impellizzeri G, Marasco G, Eusebi LH, Salfi N, Bazzoli F, Zagari RM. Eosinophilic colitis: a clinical review. Dig Liver Dis 2019;51:769-73.
62. Giudici G, Ribaldone DG, Astegiano M, Saracco GM, Pellicano R. Eosinophilic colitis: clinical review and 2020 update. Minerva Gastroenterol Dietol 2020;66:157-63.
63. Xu Y, Xiong L, Li Y, Jiang X, Xiong Z. Diagnostic methods and drug therapies in patients with ischemic colitis. Int J Colorectal Dis 2021;36:47-56.