Acute Abdomen Following COVID-19 Vaccination. A Systematic Review.

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Abstract

Aims: Conduct a systematic review of case reports and case series regarding the development of acute abdomen following vaccination with COVID-19, to describe in detail the possible association, the clinical and demographic characteristics. Methods: Case report studies and case series regarding the development of acute abdomen following COVID-19 vaccination were included. Systematic review studies, literature, letters to the editor, brief comments, etc. were excluded. PubMed, Scopus, EMBASE, and Web of Science databases were searched until June 15, 2023. The Joanna Brigs Institute tool was used to assess risk of bias and study quality. Descriptive data were expressed as frequency, median, mean, and standard deviation. Results: Seventeen clinical case studies were identified and 17 patients with acute abdomen associated with COVID-19 vaccination were evaluated, including: acute appendicitis (n=3), acute pancreatitis (n=9), diverticulitis (n=1), cholecystitis (n=2) and colitis (n=2). The most associated COVID-19 vaccine was Pfizer-BioNTech (mRNA) with 64.71 %. The majority of cases acute abdomen was after the first dose (52.94 %). All patients responded objectively to medical (88.34 %) and surgical (11.76 %) treatment and were discharged within a few weeks. There were no cases of death. Conclusions: Acute abdomen is a rare complication of great interest in the medical and surgical practice of COVID-19 vaccination, our study reviewed based on a small sample of patients, therefore it is recommended to conduct future observational studies and fully elucidate the mechanisms by which this association occurs.

1. INTRODUCTION

Coronavirus disease (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 (FDA) issued the Pfizer-BioNTech vaccine (BNT162b2 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 messenger RNA (mRNA) technology vaccines, viral vectors, recombinant protein, inactivated, live attenuated, and DNA vaccines[5]. To date, 13,499,865,692 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.

2. METHODS

2.1. 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**).

2.2. 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 vaccinated against COVID-19 and the development of acute abdomen. Mainly, the pathologies studied include acute appendicitis, acute pancreatitis, diverticulitis, cholecystitis, and colitis.

2.3. Search Strategy

For the present study, a selective bibliographic search was performed in the following electronic databases: PubMed, Scopus and EMBASE. In addition, Web of Science platform. One author (N.L.C.G.). formulated the research question and designed the search strategy for each database detailed in (**supplementary material 1**). The search was performed until June 15, 2023. In addition, the reference list of included articles was reviewed to identify additional studies. We did not limit the search by publication date. The search by language was limited to English, Portuguese, and Spanish.

2.4. 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.

2.5. Study selection process

The author (M.Q.A.) downloaded all references to an EndNote document to remove duplicate items. Then, the author (N.L.C.G.) exported the references to the Rayyan QCRI website. Two authors (R.P.V. and N.L.C.G.) 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.

2.6. Data extraction process

The authors (F.R.T. and C.Q.N.) independently extracted the data of interest in a previously prepared Microsoft Excel template. Any disagreement was resolved by the authors (R.P.V. and N.L.C.G.). 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/comorbidities, 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).

2.7. Bias risk and quality assessment

To assess the risk of bias and quality of each of the included studies, the tool was used Joanna Brigs Institute (JBI)[19,20]. Two authors (R.P.V. and N.L.C.G.). 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.

2.8. Synthesis and analysis of data

The Statistical Package for the Social Sciences (SPSS) 23.0 software 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 (SD). All the results of the study were grouped in a table.

3. RESULTS

3.1. Study selection

A total of 1110 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. **Figure 1** shows in detail the study selection process using a PRISMA flow diagram.

Figure 1. Flow diagram PRISMA of study selection process.

PRISMA 2020 flow diagram.

3.2. 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** .

Table 1. Characteristics of studies included.

Author (Year of publication)	Sex/Age (years)	Background	Vaccine type (Technology)	Number of vaccinations	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
(2022)[13]	Female 69	None	Pfizer-BioNTech (mRNA)	Third	24 hours	Acute abdominal pain	BP: 96/61mm/Hg HR: 107 beats/min RR: 18 breaths/min T: 36.7 °C SpO2: 93%	RBC: 3.73 × 10^{12}/L Hb: 115 g/L Hct: 34.8% Neutrophils: 7.6 × 10^{9}/L Cre: 1.17mg/dL BUN: 21 mg/dL	CT: Perforated acute appendicitis with appendicolith visualized at the base of the appendix with associated mesenteric fat stranding, multiloculated free fluid and trace free air	None	Acute appendicitis (perforated appendicitis	I a d t c i b c r

Author (Year of publication)	Sex/Age (years)	Background	Vaccine type (Technology)	Number of dose(s)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
	Female 58	Left quadrantectomy with radiotherapy for breast cancer and hypertension	Pfizer-BioNTech (mRNA)	First	2 days	Acute abdominal pain in the right iliac fossa Fever Nausea Vomiting	The abdomen painful on deep palpation in RIF and hypogastrium	Hb: 125 g/L WBC: 12.1 × 10^9/L Neutrophils: 78.4% Fibrinogen: 636.0 mg/dL PT: 13.3 s	Ultrasound: fluid collection in the right inferior fossa and thickening of the cecal wall. CT: distended appendix with thickened walls.	Diffuse acute and chronic inflammatory infiltrates with scattered non-necrotizing granulomas throughout all layers of the appendiceal wall	Acute appendicitis	I
Kawano et al. (2022)[22]	Male 19	None	Modern (mRNA)	Second	28 days	Abdominal pain Vomiting Loss appetite	BP: 79/50 mmH HR: 140 bpm T:38.6°C BMI: 16,3 kg/m 2	WBC :12.2 × 10^9/L CRP: 10,27 mg/L D-dimer: 1600 ug/L hsTnT : 3.67 ng/mL	CT: swollen appendix	None	Acute appendicitis Fulminant Myocarditis	S a a

Author (Year of publication)	Sex/Age (years)	Background (Comorbidities)	Vaccine type (Technology)	Number of vaccination	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c s
Cieślewicz et al. (2021)[23]	Female 29	None	Pfizer-BioNTech (mRNA)	First	20 h	Abdominal pain	T: 40°C	WBC: 13 × 10^9/L %NEUT: 75.6 % Urine amylase: 544 U/L CRP: 128 mg/L	Abdominal USG: pancreas clearly visible in the head and body area not enlarged, homogeneous	None	Pancreatitis acute	P r t p c t a r t s
Parkash et al. (2021)[24]	Female 96	Heart failure, hypertension, hypothyroidism	Pfizer-BioNTech (mRNA)	First	2 days	Epigastric pain radiating to the right lower chest Nausea	No data	Amylase: 4036 U/L	CT: No findings	None	Acute pancreatitis	P

Author (Year of publication)	Sex/Age (years)	Background (Technologies)	Vaccine type (Technologies)	Number of vaccination (Technologies)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c s
(2022)[14]	Male 82	Coronary artery disease, prostate cancer, proctocolitis complicated by radiation Hypothyroidism and gastroesophageal reflux disease	Pfizer-BioNTech (mRNA)	Third	Few hours	Epigastric abdominal pain acute with radiation to back Nausea and two episodes of vomiting	Not found	Lipase: 2257 U/L Triglyceride: 57 mg/dL Calcium: 9.3 mg/dL	CT: moderate peripancreatic fat stranding with tracking fluid into the mesenteric root, suggestive for acute interstitial pancreatitis, without evidence of necrosis	None	Acute pancreatiti	I a e h n p a n

Author (Year of publication)	Sex/Age (years)	Background (Technologies)	Vaccine type (Technologies)	Number of vaccination (Technologies)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
(2022)[25]	Female 24	Pregnant (31 weeks of gestation)	Pfizer-BioNTech (mRNA)	First	1 week	Severe epigastric pain radiating to the back Nausea Vomiting	BP: 140/90 mmHg HR: 106 beats/min RR:22 breaths/min T: 39 °C SpO2: 98%	WBC: 17 x 10^9/L Lipase 4376 U/L Amylase: 83 U/L	CT: bulky pancreas with mild enhancement and marked peripancreatic fat stranding with inflammation, suggestive of acute interstitial edematous pancreatitis	None	Acute pancreatitis	I t a c a p p i t a p r
(2022)[26]	Female 71	Hypertension, hyperlipidemia, cerebral infarction	Pfizer-BioNTech (mRNA)	First	2 days	Acute upper abdominal pain Vomiting	BP: 142/86 mmHg HR: 92 beats/min T: 37.3 °C	Lipase: 383 U/L Amylase: 1043 U/L	CT: diffuse enlargement of the pancreas with ill-defined parenchymal contours	None	Acute pancreatitis	I t a c p p i

Author (Year of publication)	Sex/Age (years)	Background	Vaccine type (Technology)	Number of dose(s)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
Alrashdi et al. (2022)[27]	Female 22	None	Pfizer-BioNTech (mRNA)	First	1 week	Abdominal pain Nausea Vomiting Erythematous maculopapular rashes	CAO BP: 118/75 mmHg HR: 80 beats/min T: 37 °C	WBC: 13 × 10^9/L Amylase: 181 U/L Lipase: 185 U/L AST: 301 UI/L ALT: 81 UI/L	CT: Edematous pancreas with loss of normal lobulation	None	Autoimmune pancreatitis acute due to SLE	A
(2023)[28]	Female 28	None	BBIBP-CorV (Sinopharm)	Second	3 months	Acute abdominal pain Nausea Hemoptysis Aphagia Constipation	BP: 130/70 mmHg HR: 101 beats/min RR: 13 breaths/min T:37 °C BMI: 25.7 kg/m2	WBC: 8.4 × 10^9/L Lipase: 156 U/L Amylasin: 1079 U/L ALT: 80U/L AST: 44 U/L TG: 1562 mg/dL Glycemia: 203 mg/dL	CT: Homogeneous enlargement of the pancreas, extensive peripancreatic fat and peripancreatic fluid was observed	None	Acute pancreatiti	a

Author (Year of publication)	Sex/Age (years)	Background	Vaccine type (Technology)	Number of vaccinations	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c s
Bangolo et al. (2023)[29]	Male 34	None	Johnson & Johnson / Jassen vaccine (Viral vector)	First	1 day	Epigastric pain Nausea Subjective fever Shivering	Tachycardia Diaphoretic T: 38.28 °C	WBC: 18.9 × 10^9/L Lipase:1026 U/L T-bil: 9.9 mg/dL ALP: 48 U/L CRP: 15 mm/h BUN: 45 mg/dL Cre: 2.19 mg/dL	CT: consistent with acute necrotizing pancreatitis	None	Acute Pancreatiti	P t t t r p c t a n t s

Author (Year of publication)	Sex/Age (years)	Background	Vaccine type (Technology)	Number of vaccination(s)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
Stöllberger et al. (2023)[30]	Female 31	Allergic asthma, psoriatic arthritis, neurogenic bladder, and cholecystolithiasis	Pfizer-BioNTech (mRNA)	Second	2 days	Abdominal pain Nausea	None	WBC: 12.6 × 10^9/L AAE: 418 U/L Lipase: 1162 U/L	CT on the day of admission: necrotizing pancreatitis with enlarged edematous pancreas. CT image after 10 days: shows a large acute necrotic collection in the lesser sac	None	Pancreatit	P v C t g c

Author (Year of publication)	Sex/Age (years)	Background (Technologies)	Vaccine type (Technologies)	Number of dose(s)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
Ajmera et al. (2022)[15]	Male 41	Bipolar depression, asthma, and obesity	Modern (mRNA)	Third	1 day	Abdominal pain Diarrhea Sweating Loss appetite	BP: 148/100 mm/Hg HR: 95 beats/min RR: 18 breaths/min T: 36.5 °C SpO2: 100% BMI: 40 kg/m2	WBC: 13.5 × 10^9/L Hb: 147 g/L	CT: showed acute diverticulitis of the mid-transverse colon, with adjacent contained microperforation	None	Diverticuli acute	I H i v h t w n s
Kyungu et al. (2022)[31]	Male 29	None	Johnson & Johnson/ Janssen (Viral vector)	First	2 days	Acute abdominal pain Nausea Fever Dark colored urine	BP: 153/121 mmHg HR: 93 beats/min RR: 20 breaths/min T: 39.2°C SpO2: 95%	WBC: 2.83 x 10^9/L Platelet: 79 x 10^9/L AST: 493.9 U/L ALT: 244.7U/L GGT: 85U/L CRP: 148.62 mg/L	Ultrasound: Normal appearing liver (141 mm) without evidence of intrahepatic biliary dilatation. Wall thickened 7.7 mm without gallstones	None	Acute acalculous cholecystiti	A h t (l t a c (f i 5

Author (Year of publication)	Sex/Age (years)	Background (Technologies)	Vaccine type (Technologies)	Number of vaccination	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
Wahlen et al. (2022)[16]	Female 52	None	Pfizer-BioNTech (mRNA)	Third	8 h	Abdominal pain Shivering Nausea Vomiting Anuria	HR: 100 beats/min T: 38°C	WBC :15.8 × 10^9/L ANC: 14.6 x 10^9/L ALT: 89 U/L CRP: 10.8 mg/L	Ultrasound: Common bile duct was of normal caliber with no intrahepatic biliary dilatation.	None	Acalculous cholecystiti	I t p e a n t s
Vadioaloo et al. (2022)[32]	Male 72	Hypertension, atrial fibrillation with stroke	Pfizer-BioNTech (mRNA)	First	6 hours	Colicky abdominal pain Diarrhea	No data	Eosinophil count: 6.84 x 10^9/L	EGD: showed antral erythematous gastritis	Mucosal lymphoplasmacytic cell infiltration with increased eosinophil	Eosinophili Colitis	I r s s

Author (Year of publication)	Sex/Age (years)	Background (Technologies)	Vaccine type (Technologies)	Number of dose(s)	Time after COVID-19 vaccination	Clinical manifestations/Physical exam (signs)	Vital functions	Laboratory	Image tests	Pathology (Histology)	Final diagnostics	T (c
Cui et al. (2022)[17]	Female 48	None	BBIBP-CorV (Sinopharm)	Second	1 day	Abdominal pain Hematochezia Fatigue	BP: 140/85 mmHg HR: 80 beats/min RR: 19 breaths/min T: 36.2 °C BMI: 21,1 kg/m 2	D-dimer: 329 ug/L FDP: 2.5 mg/L Lactic acid: 2.60 mmol/L	CT: edema and bowel wall thickening with hypodensity in the sigmoid colon and descending colon	None	Ischemic colitis	F b n a a e c t

AAE: Alpha Amylase Enzyme; ALP: Alkaline phosphatase ; ALT: Alanine aminotransferase; ANC: Absolute Neutrophil Count; ANA: antinuclear antibodies; Anti-dsDNA, anti-double-stranded DNA antibody; AST: Aspartate aminotransferase ; AZA: azathioprine; BMI: Body mass index; BP : blood pressure; BUN: blood urea nitrogen; CAO: Conscious, Alert, and Oriented; CT: computed tomography ; Cre: creatinine; CTX, cefotaxime; ; CRP, C-reactive protein ;EAT: Empirical antibiotic therapy ; FDP: Fibrinogen-degradation product; GGT: gamma-glutamyl transferase; Hb: Hemoglobin; HCQ: hydroxychloroquine; Hct: hematocrit; HR: heart rate; hsTnT: high-sensitivity troponin T; mRNA: messenger ribonucleic acid; MP: methylprednisolone; NBM: Nil By Mouth ; T-bill: total bilirubin ; TG: triglyceride; PT: Prothrombin time; RIF: right iliac fossa; RR: Respiratory rate; SpO2: oxygen saturation, SLE: systemic lupus erythematosus; USG: ultrasound sonography test ; WBC: white blood cell count.

3.3. 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. history/comorbidities, test COVID-19, type of COVID-19 vaccine, dose, symptoms, and treatment were evenly distributed. Most cases were associated with Pfizer-BioNTech vaccine (mRNA) with 64.71 %, followed by Modern (mRNA) (11.76 %), BBIBP-CorV (Sinopharm) (11.76 %) and Johnson & Johnson / Jassen vaccine (Viral Vector) (11.76 %), most cases associated with the first dose (52.94 %). Among the symptoms, acute abdominal pain was present in almost all studies (82.35 %), other studies reported Epigastric pain (17.64 %). No death was reported in any study, all patients recovered, and most were discharged in the following weeks. Treatment was medical in most cases (88.34 %) and only one (11.76 %) required surgical treatment. The clinical and demographic characteristics are shown in detail in**Table 2** .

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

Variable/Adverse effect	Acute appendicitis	Acute pancreatitis	Diverticulitis	Cholecystitis	Colitis
Total of reported cases (n)	(n=3)	(n=9)	(n=1)	(n=2)	(n=2)
Age (Mean ± SD)	48.6 ± 21.45 years	46.3 ± 26.79 years	41 years	40.5 ± 11.5 years	60 ± 12 years
Gender n (%) Female (F) Male (M)	F: 2 (66.67 %) M: 1 (33.33 %)	F: 7 (77.77 %) M: 2(22.22 %)	M: 1 (100 %)	F: 1 (50 %) M: 1 (50 %)	F: 1 (50 %) M: 1 (50 %)
Time to symptom onset (Mean ± SD)	10.3 ± 12.49 days	13.97 ± 28.82 days	1 day	28 ± 20 hours	15 ± 9 hours
Background/comorbidities n (%) (n=17)	Present: 8 (47.06 %) Not present: 9 (52.94 %)	Present: 8 (47.06 %) Not present: 9 (52.94 %)	Present: 8 (47.06 %) Not present: 9 (52.94 %)	Present: 8 (47.06 %) Not present: 9 (52.94 %)	Present: 8 (47.06 %) Not present: 9 (52.94 %)
Test COVID-19 n (%) (n=17)	Positive: 0 (0.0 %) Negative: 11 (64.71 %) Not described: 6 (35.29 %)	Positive: 0 (0.0 %) Negative: 11 (64.71 %) Not described: 6 (35.29 %)	Positive: 0 (0.0 %) Negative: 11 (64.71 %) Not described: 6 (35.29 %)	Positive: 0 (0.0 %) Negative: 11 (64.71 %) Not described: 6 (35.29 %)	Positive: 0 (0.0 %) Negative: 11 (64.71 %) Not described: 6 (35.29 %)
Type of COVID-19 vaccine n (%) (n=17)	Pfizer-BioNTech (mRNA): 11 (64.71 %) Modern (mRNA): 2 (11.76 %) BBIBP-CorV (Sinopharm):2 (11.76 %) Johnson & Johnson / Jassen vaccine (Viral vector): 2 (11.76 %)	Pfizer-BioNTech (mRNA): 11 (64.71 %) Modern (mRNA): 2 (11.76 %) BBIBP-CorV (Sinopharm):2 (11.76 %) Johnson & Johnson / Jassen vaccine (Viral vector): 2 (11.76 %)	Pfizer-BioNTech (mRNA): 11 (64.71 %) Modern (mRNA): 2 (11.76 %) BBIBP-CorV (Sinopharm):2 (11.76 %) Johnson & Johnson / Jassen vaccine (Viral vector): 2 (11.76 %)	Pfizer-BioNTech (mRNA): 11 (64.71 %) Modern (mRNA): 2 (11.76 %) BBIBP-CorV (Sinopharm):2 (11.76 %) Johnson & Johnson / Jassen vaccine (Viral vector): 2 (11.76 %)	Pfizer-BioNTech (mRNA): 11 (64.71 %) Modern (mRNA): 2 (11.76 %) BBIBP-CorV (Sinopharm):2 (11.76 %) Johnson & Johnson / Jassen vaccine (Viral vector): 2 (11.76 %)
Dose n (%) (n=17)	First dose: 9 (52.94 %) Second dose: 4 (23.53 %) Third dose: 4 (23.53 %)	First dose: 9 (52.94 %) Second dose: 4 (23.53 %) Third dose: 4 (23.53 %)	First dose: 9 (52.94 %) Second dose: 4 (23.53 %) Third dose: 4 (23.53 %)	First dose: 9 (52.94 %) Second dose: 4 (23.53 %) Third dose: 4 (23.53 %)	First dose: 9 (52.94 %) Second dose: 4 (23.53 %) Third dose: 4 (23.53 %)

Variable/Adverse effect	Acute appendicitis	Acute pancreatitis	Diverticulitis	Cholecystitis	Colitis
Symptoms n (%) (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 %)	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 %)	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 %)	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 %)	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 (%) (n=17)	Medical: 15 (88.34 %) Surgical: 2 (11.76 %)	Medical: 15 (88.34 %) Surgical: 2 (11.76 %)	Medical: 15 (88.34 %) Surgical: 2 (11.76 %)	Medical: 15 (88.34 %) Surgical: 2 (11.76 %)	Medical: 15 (88.34 %) Surgical: 2 (11.76 %)

The most important clinical and demographic data of the included studies are presented in the form of standard deviations and percentages.

3.4. Risk of bias and quality of individual studies.

The 17 included studies were evaluated with the JBI tool. All 17 studies were case report studies, no case series studies were found. The JBI checklist for case reports consists of an 8-item scale which includes 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]. Of the studies evaluated, the results were: 3 studies were evaluated as low quality and 14 studies were evaluated as high quality. The scores obtained are as follows: Score below 4 (n=3; 3 studies scored 3) and

score above 4 (n=14; 1 study scored 5, 2 studies scored 6, 4 studies scored 7 and 7 studies scored 8). The studies were rated "Unclear" particularly on the questions: Was the postintervention clinical condition clearly described? And does the case report provide takeaway lessons? The risk and quality assessment process of the studies evaluated by the JBI tool is shown in detail in**Table 3** .

Table 3. 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 de
Oganesyan et al.	Yes	Yes
Marconi et al.	Yes	Yes
Kawano et al.	Yes	Yes
Cieślewicz et al.	Yes	Yes
Parkash et al.	Yes	Yes
Cacdac et al.	Yes	Yes
Dey et al.	Yes	Yes
Ozaka et al.	Yes	Yes
Alrashdi et al.	Yes	Yes
Boskabadi et al.	Yes	Yes
Bangolo et al.	Yes	Yes
Stöllberger et al.	Yes	Yes
Ajmera et al.	Yes	Yes
Kyungu et al.	Yes	Yes
Wahlen et al.	Yes	Unclear
Vadioaloo et al.	Yes	Yes
Cui et al.	Yes	Yes

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

4. DISCUSION

In the present systematic review of case reports and case series of acute abdomen following COVID-19 vaccination, we found that acute pancreatitis, Pfizer-BioNTech vaccine (mRNA) and first dose were the most common complication, vaccine type and dose 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. Sixty-four-point seven percent were female and 35.3% were male. 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 predominance of males in a 1.4:1 ratio with respect to females and it occurs most frequently between the ages of 10 and 20 years[36]. The etiology of acute appendicitis is mainly due to obstructive processes due to follicular hyperplasia and fecalith. In addition, rare obstructive causes such as amebiasis, carcinoid tumor, infestation by parasites such as amebiasis, enterobiasis, ascariasis, and others[37]. Our study found 3 case report 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 Modern (mRNA) (n=1)[22]. In other studies, the Pfizer-BioNTech vaccine was associated with AA with a RR of 1.40 (CI: 1.02 to 2.01) in contrast to the Modern (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 3 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.

Treatment was surgical in 2 patients (laparoscopic appendectomy) due to being in the perforated phase and outpatient in 1 patient (antibiotics and steroids). There was one case that reported the appearance of AA together with fulminant myocarditis[22]. A retrospective study by Quint et al. reviewed the registry of 421 patients with AA, concluding that AA caused by vaccination is like classical AA[40]. There was no case of death, all patients recovered and were 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 Th1 cell response[41]. Th1 cells primarily produce cytokines such as interferon gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α), dysregulated levels of Th1 cytokines have been associated with autoimmune inflammation[42]. A study by Rubér et al, found that gangresone-type appendicitis has a positive association with states of Th1-mediated immunity, this could explain the increased th1 due to uncontrolled inflammatory reaction and risk of perforation[43]. If vaccines induce increased Th1 response, it is possible that in our two patients appendectomized for perforated phase, it is due to this possible association.

Acute pancreatitis (AP) is one of the most frequent gastrointestinal causes and its incidence continues to increase worldwide[44]. Gallstones (45%) and alcohol abuse (20%) are the most frequent causes of AP. Medication, endoscopic retrograde cholangiopancreatography (ERCP), hypercalcemia, hypertriglyceridemia, infection, genetics, autoimmune diseases and (surgical) trauma are other less frequent associated causes[45]. AP has previously been associated with several vaccines reported in the literature, vaccines against human papillomavirus[46,47], hepatitis A and B[48,49], measles, mumps, and rubella (MMR)[50,51], varicella[52], and typhoid fever and cholera[53]. Our study found 9 case report reports of AP induced by vaccination against SARS-CoV-2. The mean age was estimated to be 46.3 $\pm$ 26.79 years with a predominance by females. AP occurred mainly after administration of Pfizer-BioNTech (mRNA) vaccine (n=7)[23,27] followed by Sinopharm (n=1)[28] and Johnson & Johnson / Jassen (n=1) vaccines[29]. The dosing for the 9 patients was (first (n=6), second (n=2) and third (n=1). The time from vaccine administration to onset of symptoms was 13.97 $\pm$ 28.82 days. Treatment was medical and supportive in all patients, there was no surgical procedure. There was one case that reported the appearance of AP together with hemolytic anemia and thrombocytopenia[30], in addition, there was one case associated with systemic lupus erythematosus[27]. There was a case of AP after administration of the Pfizer-BioNTech vaccine in a patient at 31 weeks of gestation, after which on the second day she had a spontaneous vaginal delivery because of the inflammatory process triggered by AP[25]. There was no case of death, all patients recovered and were 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 the host antigens, a mechanism called molecular mimicry[25,28]. This mimicry is due to the cleavage of the FURIN peptide identical to that of the human epithelial sodium channel, present in different organs such as the intestine, pancreas, and lungs. These data suggest pancreatic injury due to an autoimmune reaction induced by the mRNA vaccine[26,54].

Diverticulitis is the third most common gastrointestinal disease and the main indication for elective colon resection[55]. It is predominantly seen in men until the sixth decade of life and is related to multiple risk factors such as: obesity, single consumption of red meat, smoking and medications such as non-steroidal anti-inflammatory drugs[56]. Our study found only 1 case report of diverticulitis induced by SARS-CoV-2 vaccination. This was a 41-year-old male patient who developed diverticulitis 1 day after receiving the third dose of Modern (mRNA) vaccine[15]. Treatment was medical and supportive, and he was discharged with subsequent follow-up colonoscopy. Diverticulitis can be caused by genetic factors, environmental factors, dysmotility of the colon and recent studies associate it with specific immune responses of the host and the microbiome[57]. It is hypothesized that the Modern 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 found 2

case report reports of SARS-CoV-2 vaccination-induced cholecystitis, both cases were diagnosed as acute acalculous cholecystitis (no presence of gallstones). The mean age was calculated to be 40.5 ± 11.5 years, observed in one female patient and one male patient. Acute cholecystitis occurred after administration of Pfizer-BioNTech (mRNA)[16] and Johnson & Johnson/ Janssen (Viral vector) vaccine[31]. It occurred in the first and third doses respectively. The time from vaccine administration to symptom onset was 28 ± 20 hours. Treatment was medical and supportive, 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 association between the vaccine and the appearance of acalculous cholecystitis is not known, 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 a variety of 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 some drugs, pathogenic microorganisms, coagulation disorders, obesity, smoking and iatrogenic[63]. Our study found 2 case report reports of colitis induced by SARS-CoV-2 vaccination, both cases were diagnosed as eosinophilic colitis and ischemic colitis. The mean age was estimated to be 60 ± 12 years, observed in one female patient and one male patient. Eosinophilic colitis occurred after administration of Pfizer-BioNTech (mRNA) vaccine[32] and ischemic colitis by Sinopharm vaccine[17]. It occurred in the first and second doses, respectively. The time from vaccine administration to symptom onset was 15 ± 9 hours. Treatment was medical in ischemic colitis, and there was spontaneous resolution for the case of eosinophilic colitis. Patients had a favorable recovery. The mechanisms by which this association occurs is not clear. For ischemic colitis, it is proposed that vaccines induce inflammation and immune reaction, 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 report 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 generate a potential risk of bias. Third, although we performed an exhaustive literature search, we did not rule out the possibility that we missed some studies related to this topic. 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 development of acute abdomen following vaccination against COVID-19 is of great interest in clinical and surgical medical practice. Therefore, the planning and elaboration of cohort and cross-sectional studies is encouraged to evaluate this association with greater precision. To observe the evolution of patients through clinical monitoring with possible risk of developing these complications once any type of vaccination against COVID-19 is applied.

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 the 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 cases are minimal upon administration of vaccination, so vaccines generally do not develop acute abdomen. However, despite this, physicians should monitor patients with a history or 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.

REFERENCES

1. Triggle CR, Bansal D, Ding H, Islam MM, Farag EABA, Hadi HA, Sultan AA. 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. WHO Coronavirus (COVID-19) Dashboard [Internet]. [citado 3 de abril de 2023]. Disponible en: https://covid19.who.int

3. Marschner CA, Shaw KE, Tijmes FS, Fronza M, Khullar S, Seidman MA, et al. Myocarditis Following COVID-19 Vaccination. Cardiol Clin. 2022; 40(3): 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, Zhang Z, Song L, Zhu B, et al. Advances in COVID-19 mRNA vaccine development. Signal Transduct Target Ther. 2022; 7(1): 1-31.

6. Marco JJG, Pasquín MJÁ, Martín SM. Efectividad y seguridad de las vacunas para el SARS-CoV-2 actualmente disponibles. FMC. 2021; 28(8): 442-451.

7. Ogunjimi OB, Tsalamandris G, Paladini A, Varrassi G, Zis P. Guillain-Barré Syndrome Induced by Vaccination Against COVID-19: A Systematic Review and Meta-Analysis. Cureus. 2023; 15(4): 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 J Crit Care. 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. 2022; 10(8): 1316.

10. Jafarzadeh A, Jafarzadeh S, Pardehshenas M, Nemati M, Mortazavi SMJ. Development and exacerbation of autoimmune hemolytic anemia following COVID-19 vaccination: A systematic review. Int J Lab Hematol. 2023; 45(2): 145-55.

11. Lee YK, Huang YH. Ocular Manifestations after Receiving COVID-19 Vaccine: A Systematic Review. Vaccines. 2021; 9(12): 1404.

12. Pezzaioli LC, Gatta E, Bambini F, Facondo P, Gava M, Cavadini M, et al. Endocrine system after 2 years of COVID-19 vaccines: A narrative review of the literature. Front Endocrinol. 2022; 13: 1027047.

13. Oganesyan A, Schäfer M, Lesh C. Acute appendicitis following the COVID-19 vaccine. J Surg Case Rep. 2022; 2022(6): 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(4):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(7): 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(12): 3866-71.

18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, 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(2): 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(1): 7.

21. Marconi E, Crescioli G, Bonaiuti R, Pugliese L, Santi R, Nesi G, et al. Acute appendicitis in a patient immunised with COVID-19 vaccine: A case report with morphological analysis. Br J Clin Pharmacol. 2023; 89(2): 551-5.

22. Kawano H, Yamamoto N, Kurohama H, Okano S, Kurobe M, Honda T, et al. Fulminant Myocarditis and Acute Appendicitis after COVID-19 Vaccination. Intern Med Tokyo Jpn. 2023; 62(3): 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. 2021; 9(6): 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(4): e14741.

25. Dey RK, Ilango H, Bhatta S, Shaheed A, Dole S, Zooshan A, et al. Acute pancreatitis in pregnancy following COVID-19 vaccine: a case report. J Med Case Reports. 2022;16(1): 354.

26. Ozaka S, Kodera T, Ariki S, Kobayashi T, Murakami K. Acute pancreatitis soon after COVID-19 vaccination: A case report. Med U S. 2022; 101(2): E28471.

27. N AM, Saleh AM, Khalid A, Alshaya AK, Alanazi SMM. Systemic lupus erythematosus with acute pancreatitis and vasculitic rash following COVID-19 vaccine: a case report and literature review. Clin Rheumatol. 2022; 41(5): 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(1): e12914.

29. Bangolo AI, Akhter M, Auda A, Akram R, Nagesh VK, Athem D, 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. Stöllberger C, Kastrati K, Dejaco C, Scharitzer M, Finsterer J, Bugingo P, 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(15-16): 436-440.

31. Kyungu FM, Katumba AM, Kamwira HL, Mayikuli AV, Mala A, Banza MI, 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(2): 44-6.

33. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017.

34. Téoule P, de Laffolie J, Rolle U, Reissfelder C. Acute Appendicitis in Childhood and Adulthood. Dtsch Ärztebl Int. 2020; 117(45): 764-74.

35. Ramson DM, Gao H, Penny-Dimri JC, Liu Z, Khong JN, Caruana CB, et al. Duration of post-operative antibiotic treatment in acute complicated appendicitis: systematic review and meta-analysis. ANZ J Surg. 2021; 91(7-8): 1397-404.

36. Krzyzak M, Mulrooney SM. Acute Appendicitis Review: Background, Epidemiology, Diagnosis, and Treatment. Cureus. 2020; 12(6): 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, Kepten E, Waxman J, Ohana R, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. N Engl J Med. 2021; 385(12): 1078-90.

39. Ljung R, Pihlström N, Sundström A. Risk of appendicitis after SARS-CoV-2 infection and SARS-CoV-2 vaccination. Br J Surg. 2022; 109(8): 775-6.

40. Quint E, Kukeev I, Hazan I, Grupel D, Dukhno O, Osyntsov A, et al. Clinical characteristics of SARS-CoV-2 vaccine-related acute appendicitis. Can J Surg. 2023; 66(3): 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(1): 8-20.

43. Rubér 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(1): 117-24.

44. Lee PJ, Papachristou GI. New insights into acute pancreatitis. Nat Rev Gastroenterol Hepatol. 2019; 16(8): 479-96.

45. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, et al. Acute pancreatitis. Lancet Lond Engl. 2020; 396(10252): 726-34.

46. Das A, Chang D, Biankin AV, Merrett ND. Pancreatitis following human papillomavirus vaccination. Med J Aust. 2008; 189(3): 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(1): 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 Can Med Assoc J J Assoc Medicale Can. 2007; 176(3): 339-42.

49. Haviv YS, Sharkia M, Galun E, Safadi R. Pancreatitis following hepatitis A vaccination. Eur J Med Res. 2000; 5(5): 229-30.

50. Hansen LF, Nordling MM, Mortensen HB. [Acute pancreatitis associated with MMR vaccination]. Ugeskr Laeger. 2003; 165(22): 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(3): 189-92.

52. Chan PW, Goh AY. Life threatening pancreatitis following varicella vaccination: cause, association or co-incidence? Med J Malaysia. 2000; 55(4): 527-8.

53. Gatt DT. Pancreatitis following monovalent typhoid and cholera vaccinations. Br J Clin Pract. 1986; 40(7): 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(1): 67-74.

56. Strate LL, Morris AM. Epidemiology, Pathophysiology, and Treatment of Diverticulitis. Gastroenterology. 2019; 156(5): 1282-1298.e1.

57. Schieffer KM, Kline BP, Yochum GS, Koltun WA. Pathophysiology of diverticular disease. Expert Rev Gastroenterol Hepatol. 2018; 12(7): 683-92.

58. Gallaher JR, Charles A. Acute Cholecystitis: A Review. JAMA. 2022; 327(10): 965-75.

59. Kimura Y, Takada T, Strasberg SM, Pitt HA, Gouma DJ, Garden OJ, et al. TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. J Hepato-Biliary-Pancreat Sci. 2013; 20(1): 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 Basel Switz. 2022; 40(4): 468-78.

61. Impellizzeri G, Marasco G, Eusebi LH, Salfi N, Bazzoli F, Zagari RM. Eosinophilic colitis: A clinical review. Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver. 2019; 51(6): 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(2): 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(1): 47-56.