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Acute Appendicitis Pathways: A Systemic Review

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Abstract

Background: Clinical pathways are effective in reducing healthcare cost and standardizing management protocol for diseases and conditions. However, there are no standardized pathways for appendicitis. This study aims to determine whether implementation of a standardized clinical pathway for managing appendicitis may lead to improved patient care. **Materials and Methods**: We searched for articles published in PubMed, MEDLINE, and Cochrane library between 1974 and 2015. Thirty-seven papers published in English that met inclusion criteria were included and analyzed in this review. A total of 37 studies met inclusion criteria and were analyzed for the purpose of this study. **Results**: A clear definition for appendicitis pathway was observed in 30 articles. Appendicitis was diagnosed based on clinical and laboratory findings; however, 34% of the studies included radiological investigations. Sixteen studies provided clear definitions for discharge criteria. Time of follow-up (5 - 28 days) was reported in 10 studies. Operative time was the most commonly used outcome measure. The mean length of stay for non-complicated appendicitis was 1.3 days, and 6.26 days for complicated appendicitis. Most of the studies concluded that the accuracy of a clinical pathway for appendicitis diagnosis can be achieved by assessing the incidence of a normal appendix. The mean cost for patient care was $4874.14 (SAR 18,278.03). **Conclusion**: There was no standardized definition for appendicitis clinical pathway components. Studies suggested that establishing a clinical pathway for appendicitis improves the outcome and minimizes the cost.

Keywords

Acute Appendicitis, Pathway, Cost, Patient Care

1. Introduction

A clinical pathway is defined as structured care plan that details essential steps in patient care with specific clinical problems, which supports translation of clinical guidelines into local protocols and clinical practice [1]. Clinical pathways aim to standardize the diagnosis process, treatment approach, decrease the length of hospital stay and reduce the healthcare costs [2] [3].

Acute appendicitis (AA) is one of the most common surgical diseases. The estimated lifetime incidence of AA is 7%. Despite its high prevalence rate, the diagnosis of AA is challenging due to the disease progression leading to the absent of the classical symptoms and sign of the disease which might lead eventually in delaying of the diagnosis and results in complications [3] [4]. Several studies have demonstrated the benefits of standardized protocol for appendicitis management to reduce the rate of morbidity and mortality [5] [6] [7]. Due to an absence of standardized protocol, management of AA relies on surgeon preference. Variability in surgeons' preference is related to the variation of the disease's clinical pattern [3] [4] [5] [6] [7].

Given the high incidence rate, there is a need for a simple, precise, and clear clinical procedure to standardize the management approach and improve the clinical outcome. This review aims to assess the available literature on the impact of the implementation of standard AA management clinical pathways on clinical outcomes and patient experience.

2. Materials and Methods

A systematic review protocol was created in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [8]. With this review's aim in mind, we attempted to extract the following parameters from eligible literature: clinical pathway components used in each study and outcomes used to assess the pathway.

We first extracted information from a clinical engine search (PubMed, Medline, and Cochrane Library) to find available literature meeting the initial entry criteria published between 1974 and December 2012. Then, the bibliography of each study was reviewed for additional sources. The search terms used were "appendicitis," "appendectomy," "appendix," or "append" and "managed care program," "standards," "clinical pathways," or "clinical protocols." The eligibility criteria for inclusion were studies that investigated clinical pathways for appendicitis in human subjects. Only original articles that were published in English were included and assessed.

Validation of eligibility was achieved through two stages by two reviewers. At the first stage, the first reviewer screened abstracts of extracted studies for at least one of the following keywords; appendicitis, appendectomy, appendix, append*, managed care programs, standards, clinical pathways, or clinical protocols. The second reviewer screened abstracts to ensure that the screening process was robust. Full articles of abstracts that had passed the initial screening process

and abstracts that were reserved for full article review were reviewed to determine eligibility. In the second stage, full articles were examined and validated. Publications were excluded if they were animal or *in-vitro* studies, not published in the English language and for which a translated version was not available, did not involve a clinical pathway for appendicitis management, or was published as a case report, letter, comment, or reviews.

Eligible studies were reviewed, and information was extracted about participants' characteristics (age, gender, body mass index, etc.), components of clinical pathways (preoperative, intraoperative, and postoperative), and clinical pathway outcomes (length of stay, complications, cost, etc.). Data extraction was performed by two reviewers independently and entered into a spreadsheet. Both data sheets were then merged for validation. The discrepancy was then resolved by consensus with reference to the original article or expert consultation.

3. Results

3.1. Study Selection

A total of 1079 articles were extracted; 1070 articles were identified from search engines, and 9 articles were identified by manual search. After the exclusion of duplicated papers, a total of 861 abstracts were screened and 100 articles were identified to be eligible. Full article assessment indicated that 51 articles were eligible for the final validation process. A total of 37 studies were included in the systematic review. Figure 1 presents the PRISMA diagram.

3.2. Study Characteristics

A total of 37 articles were reviewed. Articles were classified based on design into prospective studies (22/37), retrospective studies (14/37) and case control studies (1/37). Most of the studies were conducted in North America, 3 studies took place in Europe, and 7 studies took place in other countries (Australia, India, Israel, Japan, and Turkey). The sample size varied between 30 and 2218 subjects. An assessment of extracted literature based on the age classification of the study population indicated that 24 studies were carried out with a pediatric population, 10 studies were carried out with an adult population, and 3 studies were with both categories. The mean age for non-complicated appendicitis was nearly comparable in the intervention and control groups (18.19 years and 19.70 years, respectively). For all reviewed studies, most of the study population was male, with the exception of one study that had enrolled only females (the author reported intraoperative for incidental laparoscopic appendectomy during gynecological procedure). Table 1 summarizes studies included in this review.

3.3. Pathway Elements

3.3.1. Pre-Operative Pathway

A clinical pathway is classified based on the onset into preoperative, intraoperative, and postoperative pathways. Regarding preoperative pathways, a clear definition for appendicitis pathway was observed in 30 articles. Initial diagnosis of

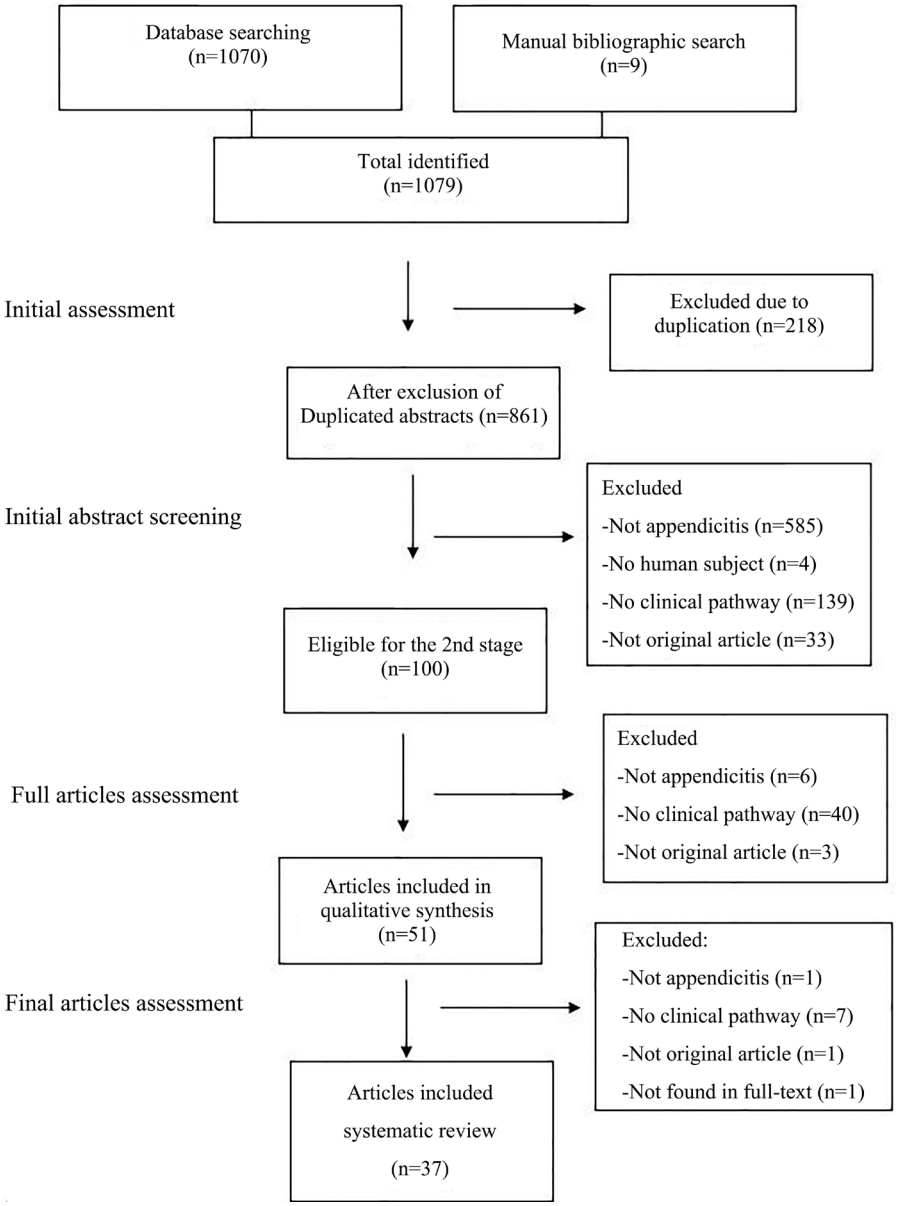

Figure 1. PRISMA figure.

Table 1. Summary of studies assessed.

Author (year)	Study population	Sample size	Clinical pathway assessed		
			Pre-operative	Intra-operative	Postoperative
Warner (1998)	Pediatric	242	X		X
Emil (2006)	Pediatric	397	X	X	X
Slusher (2014)	Pediatric	253		X	X
Saucier (2014)	Pediatric	216	X		
Farach (2014)	Pediatric	349	X	X	X
Frazee (2014)	Pediatric	345		X	X
Takegami (2003)	Adult	185		X	

Continued

Helmer (2002)	Pediatric & adult	438	X	X	X
Dubois (2010)	Adult	317	X	X	X
Zinaman (2003)	Adult	42	X	X	
Keller (1996)	Pediatric/complicated appendicitis	56	X	X	X
Firilas (1999)	Pediatric	147	X	X	X
Adibe (2011)	Pediatric	311	X		
Knott (2013)	Pediatric/PA	209	X		X
Putnam (2014)	Pediatric	794		X	X
Akkoyun (2013)	Pediatric	129	X	X	X
Hussain (2014)	Adult	30		X	
Almonda (2008)	Pediatric	429	X	X	X
Antevil (2006)	Adult	992	X		
Smink (2004)	Pediatric	959	X		
Garcia Pena (2002)	Pediatric	1338	X		
Krishnamoorthi (2011)	Pediatric	631	X		
Santillanes (2012)	Pediatric	475	X		
Naoum (2002)	Adult	194	X		
Yu (2014)	Pediatric/complicated appendicitis	94	X		
Torbati (2003)	Adult & pediatric	506	X		X
Ball (2014)	Adult	741	X		
Skarda (2014)	Pediatric/ruptured appendicitis	306	X	X	
Bensard (2009)	Pediatric	72		X	

appendicitis was based on clinical evaluation and laboratory findings. Some studies involved radiological assessments to support diagnosis. Ultrasound was used in 8 studies, and 12 studies used a computed tomography (CT) scan. Preoperative antibiotic was documented in 13 studies; however, the antibiotic regimen varied. An age-appropriate pain scoring system in the preoperative protocol was documented in one study [9]. In this study, 72.7% of the protocol had a formal pain assessment compared to 31.30% of the pre-protocol group. Preoperative family education and counseling involved plans for early discharge from post-anesthesia care unit and postoperative instructions were given to families [6]. Nevertheless, some studies carried family education out postoperatively [2]. Only 4 studies administered pregnancy tests and only one study documented performing blood culture preoperatively in patients with complicated appendicitis [10]. **Table 2** summarizes findings for preoperative pathways.

3.3.2. Intra-Operative Pathway

Despite the popularity of laparoscopic techniques among surgeons and patients, laparoscopic appendectomy was performed in about 64.4% patients. In this review,

Table 2. Components of preoperative pathways.

Author (# subjects)	Clinical diagnosis	FSC	Renal profile	CRP	Blood c/s	Pregnancy test	US	CT scan	Antibiotics
Warner (1998)	Yes	Yes	Yes			Yes	Yes		Yes
Emil (2006)	*	Yes							Yes
Saucier (2014)	Yes						Yes	Yes	
Farach (2014)	*	Yes		Yes					
Helmer (2002)	*								Yes
Dubois (2010)	*	Yes					Yes	Yes	
Zinaman (2003)									Yes
Keller (1996)									Yes
Firilas (1999)	Yes								Yes
Adibe (2011)	Yes						Yes	Yes	
Akkoyun (2013)									Yes
Almond (2008)	*								Yes
Antevil (2006)	Yes							Yes	
Smink (2004)	Yes					Yes	Yes	Yes	
Krishnamoorthi (2011)							Yes	Yes	
Santillanes (2012)	Yes						Yes	Yes	
Naoum (2002)	*	Yes						Yes	
Yu (2014)	*	Yes		Yes	Yes				Yes
Torbati (2003)	Yes							Yes	
Skarda (2014)	*	Yes							
Neufeld (2010)	Yes						Yes	Yes	
Russell (2013)	Yes						Yes	Yes	
Liese (2014)	Yes							Yes	
Knott (2013)	#	Yes							Yes
Garcia Pena (2002)	Yes						Yes	Yes	
Ball (2014)	Yes	Yes	Yes			Yes	Yes	Yes	Yes
Winn (2004)	Yes								Yes
Neilson (1990)									Yes
Warner (2002)	Yes	Yes	Yes	Yes	Yes	Yes	Yes		Yes

*Mentioned patients diagnosed with appendicitis but not clear how? Or not mention the word clinically. #A retrospective perforated appendicitis which diagnosed intraoperative.

two studies reported anesthesia protocol as part of the clinical pathway [6] [11]. Another two studies on complicated appendicitis documented the use of intra-abdominal drains [12] [13]. Emil *et al.* reported the insertion of intra-abdominal drain for non-complicated appendicitis as 0%. Only one study focused on the impact of clinical pathway in minimizing the utilization of intraoperative resources such as a nasogastric tube. The use of nasogastric tubes in

patients with perforated appendicitis under the pathway was significantly reduced, while less than 3% of the study population required one during hospitalization [14]. Another study reported a protocol in a case of perforated appendicitis; they irrigated the entire wound with saline and closed the incision with subcuticular suture without drains [15]. **Table 3** summarizes components of intraoperative pathways.

3.3.3. Post-Operative Pathway

There was a clear description of discharge criteria in 15 studies (**Table 5**). The majority of these studies indicated that afebrile status was the main criteria for discharge, other studies suggested pain control with oral analgesia, having normal blood cell count and tolerating an oral diet. Few studies suggested discharge once the patient could tolerate a liquid diet [5] [6] [16] [17]. Resuming normal bowel function and passing urine were considered essential for discharge. Few studies considered social factors to be key elements in discharge criteria [2] [5] [6] [11]. **Table 4** summarizes components of postoperative pathway.

Table 3. Components of intraoperative pathways.

Author	LA$	OA&	Single incision LA	1ry wound closure/ noncomplicated appendectomy	1ry wound closure/ complicated appendectomy	Detail operative technique/ noncomplicated appendectomy	Detail operative technique/ complicated appendectomy/PA
Emil (2006)	21%	79%		100%	100%		
Slusher (2014)						+	
Farach (2014)	24.4%	28.6%	47%				
Frazee (2014)	100%	0%				+	
Takegami (2003)						+	+
Helmer (2002)				100%	Wound left opened		
Dubois (2010)	85.7%	14.3%					
Zinaman (2003)						+	
Keller (1996)					92%		
Firilas (1999)	0%	100%					+
Putnam (2014)	Audit 1 = 94%, 2 = 97%	6%	Audit 1 = 10%, 2 = 9%				
Akkoyun (2013)	100%	0%				+	
Hussain (2014)						+	
Almond (2008)	44%	56%					
Skarda (2014)	82.2%	17.8%					
Bensard (2009)	94%	6%					
Lord (1996)	0%	100%					
Cash (2012)	100%	0%					
Liese (2014)	92%	5.5%					
Neilson (1990)	0%	100%		100%	100%	+	+

$: Laparoscopic appendectomy; &: Open appendectomy.

Table 4. Components of postoperative pathways.

Author	Study population	Subjects	Follow-up clinic	Post-op IV abx/ non-complicated app.	Post-op IV abx/PA abx
Warner (1998)	Pediatric	242	14 days	0%	IV abx continue for 7d post-op and could be continue at home if he is dischargeable and condition at home is desired
Emil (2006)	Pediatric	397		16%	98%
Slusher (2014)	Pediatric	253			IV tazocin or ertapenem till discharge criteria met, if post-op has wbc elevated or Lt shift send home with amox-clav or cipro/flagly for 7 d
Farach (2014)	Pediatric	349	14 days	0%	
Frazee (2014)	Pediatric	345	14 days	0%	
Helmer (2002)	Pediatric & adult	438		0%	7 days minimum
Dubois (2010)	Adult	317	Median (IQR) 25 (15 - 30)		
Keller (1996)	Pediatric/Complicated app.	56	28 days		
Firilas (1999)	Pediatric	147		100%	100%
Putnam (2014)	Pediatric	794	14 days		
Akkoyun (2013)	Pediatric	129	5 - 10 days		
Almonda (2008)	Pediatric	429		100%	100%
Torbati (2003)	Adult + pediatric	506	14 days by telephone		
Lord (1996)	Adult	116	7 days		
Cash (2012)	Adult	235	14 days		
Knott (2013)	Pediatric/PA	309			Patients maintained in antibiotics till discharge in total of 7 days minimum
Warner (2002)	Pediatric	1103			Continue 1 additional dose of preoperative antibiotic

3.4. Outcomes

3.4.1. Time

The efficacy of the clinical pathway was assessed by determining the length of stay at the hospital. The mean hospital length of stay (LOS) for non-complicated appendicitis varied between studies and ranged between 3.1 and 96 hours. The mean hospital LOS for complicated appendicitis also varied between studies and was in the range of 94.5 and 316.8 hours. All studies concluded that the LOS was shortened among patients who had a clinical pathway implemented in their case. The response time for surgical consultation was between 1.6 and 2.12 hours [2] [18]. Two studies examined time spent in the ER [18] [19].

Recent studies examined the efficacy of pathways by measuring the percentage of patients with same day discharge, ranging between 58% and 92.4% [5] [11] [16] [19].

3.4.2. Cost

Seven studies showed that the use of clinical pathways is cost-effective in managing patients with non-complicated appendicitis [2] [3] [12] [19] [20] [21] [22]. Four studies concluded that using a clinical pathway is efficacious in reducing hospitalization costs in cases of complicated appendicitis [2] [13] [22] [23]. Only 3 studies concluded no impact from the use of a clinical pathway in reducing hospitalization cost of complicated appendicitis [3] [12] [17].

3.4.3. Complications

Complication rates varied between 0% and 28%. The wound infection rate for noncomplicated appendicitis ranged between 0% and 7.5%, and 0.7% and 13% for complicated appendicitis. The percentage of intra-abdominal abscess for non-complicated appendicitis ranged between 0% and 1.9% and 1.3% and 12.79% for complicated appendicitis.

The rate for post appendectomy emergency department visits ranged from 0% and 13.7% [10] [16] [19] [21] [24]. Readmission rate in non-complicated appendicitis ranged between 0% and 4.2%.

4. Discussion

Although the concept of clinical pathways was first introduced in 1980s, there is yet to be a standardized definition. Lawal *et al.* established 4 criteria for clinical pathways: fitting into multidisciplinary plan for care, guiding evidence into a structure, detailing the steps throughout the course of the treatment, and standardizing care for a particular population [25]. In this systematic review, reviewers identified 37 articles that defined a treatment algorithm of appendicitis based on this criterion.

4.1. Preoperative Pathway Elements

4.1.1. Preoperative Evaluation

The classic approach for appendicitis diagnosis is based on clinical evaluation supported by laboratory testing with or without imaging; however, the diagnosis of appendicitis remains challenging. In 2016, a randomized multicenter clinical trial recruited 1321 patients and revealed that clinical and laboratory tests were unreliable in diagnosis of acute appendicitis [26]. A CT scan and ultrasound were used in preoperative evaluation of patients presented with suspected appendicitis to assess in diagnosis. In a 2016 retrospective review where 354 adult subjects were recruited, the majority of study sample was female, showing that the ultrasound of surgery-confirmed appendicitis had a sensitivity and specificity of 48.4% and 97.9% respectively [27]. In 2015, a retrospective database analysis of 54,153 children from 35 pediatric institutions in the US found that ultrasound is the first imaging choice for suspected appendicitis at most centers. Moreover, within 2 years, ultrasound use increased by 11.3% and CT scans were used 9.8% less often [28]. A retrospective study with a sample size of 2763 subjects evaluated the efficacy of ultrasound, CT scan and physical examination in

acute appendicitis diagnosis. The study found that for ultrasound the sensitivity level was 99.1%, specificity level was 91.7%, the positive predictive value was 96.5% and the negative predictive value was 97.7%. On the other hand, for CT scan the sensitivity level was 96.4%, the specificity level was 95.4%, the positive predictive value was 95.6%, and the negative predictive value 96.3%. The sensitivity of physical examination was 99.0% whereas the specificity was 76.1%, the positive predictive value was 88.1%, and the negative predictive value was 97.6%. Study concluded that imaging studies after negative physical examination could be unnecessary [29]. Another 10-year retrospective analysis with a sample size of 1 366 subjects revealed that performing a preoperative CT scan decreased the rate of negative appendectomy in women younger than 46 years but not in older women or men [30].

In this review, 64.86% of the studies documented using clinical evaluation and 27% laboratory investigation (WBCs, CRP, and renal profile) as part of preoperative evaluation for appendicitis. Ultrasound was performed in 21.62% of the studies and CT scan in 32.24% of the studies. Accurate pain assessment in different age groups and development of effective postoperative treatment produces pain relief while speeding recovery and discharge without side effects of respiratory depression [31].

4.1.2. Counseling

Preoperative patient counseling could lead to decreased LOS, cost reduction, and improve patient satisfaction. Physicians inform patients and families about the care process and expected outcomes as well as early ambulation, feeding, pain control, and discharge criteria [32]. In this review, one article concluded that family counseling in the preoperative pathway for acute appendicitis to enhance early discharge policy [6].

4.1.3. Preoperative Antibiotics

Antibiotic prophylaxis is effective in prevention of postoperative complications in appendectomy patients regardless of the onset of administration [33]. The Surgical Care Improvement Project recommended that initiation of antibiotics should be within one hour before surgical incision, patients should receive appropriate antibiotics for the procedure, and antibiotics should be discontinued within 24-hour post-surgery to reduce surgical side infection [34]. Only 15 studies documented administration of antibiotics.

The duration of antibiotic treatment for complicated appendicitis had not been determined.

Studies on pediatric populations suggest that 3 or 5 days of postoperative antibiotics are associated with similar rates of complications. Antibiotics were stopped when certain criteria were achieved (*i.e.*, no fever, normal WBC count, and resuming normal bowel function) [35]. Limited literature has studied antibiotic guidelines for complicated appendicitis. A retrospective analysis of a sample of 410 subjects with complicated appendicitis found that there was no asso-

ciation between postoperative antibiotics and wound complication; however, postoperative antibiotics were associated with increased LOS [36].

4.2. Intraoperative Pathway Elements

4.2.1. Surgical Technique

There is lack of consensus on the most appropriate surgical technique for appendicitis management. In this review, studies indicated that 64.6% of appendicitis was managed by laparoscopic method. The first laparoscopic appendectomy (LA) was performed in 1981 by Semm. However, there was insufficient data to conclude that LA is superior to open technique [37]. Where some studies have demonstrated reduction in postoperative pain, LOS, and wound infection with the laparoscopic approach, other studies have shown marginal or no clinical benefits, a higher rate of intra-abdominal and pelvic abscess, and increased cost [38] [39] [40] [41] [42].

4.2.2. Intra-Abdominal Drain

In this review, two studies documented using intra-abdominal drains for their patients [12] [13]. Emil *et al.* noted that peritoneal drainage is unnecessary in perforated appendicitis [12]. In appendicitis cases performed on adults, the role of drain insertion differs based on whether the procedure is open or laparoscopic. Two systematic reviews concluded that routine abdominal drainage after open appendectomy for complicated appendicitis is not essential [43] [44]. Cheng *et al.* found that there was no significant difference in the incidence rate of intra-peritoneal abscess between the groups of subjects with or without drain and abdominal drain might be associated with an increased LOS [44]. Petrowsky *et al.* concluded that abdominal drain did not reduce postoperative complication and recommended that abdominal drain should be avoided at any stage of appendicitis management [43].

4.2.3. Wounds

Historically, contaminated wounds were left open for delayed primary closure to decrease the risk of surgical site infection (SSI). A recent systematic review and meta-analysis of 8 articles, 5 of which assessed complicated appendicitis, showed that there was no significant difference between primary closure and delayed primary closure with a risk ration of 0.89 (95% CI: 0.46 - 1.73). Delayed primary closure had a significantly longer LOS than primary closure. However, findings were inconclusive due to the limited number of studies and a large-scale randomized clinical trial is required [45].

4.3. Postoperative Pathway Elements

Discharge Criteria

Standardized discharge criteria are an essential clinical pathway element. Standardization should reduce variability among surgeons, enhance the efficacy of patient care, and reduce hospitalization cost given the significant morbidity and cost associated with advanced appendicitis treatment [46]. This review found

that 43.24% had a set of discharge criteria (Table 5). The majority of available literature assessed the efficacy of appendicitis protocol in discharging patients within 24 hours [5] [21]. A matched case-control study with a sample size of 166 subjects investigated the effect of multidisciplinary discharge criteria protocol for uncomplicated appendicitis in children. The study found a reduction in median postoperative LOS by 29.2% and improved the rate of discharge within 24 hours from 12% - 24%; furthermore, the study concluded a total saving of 77,057 AUD [47].

Table 5. Discharge criteria.

Author (Subjects#)	Discharge Criteria
Warner 1998 (242)	1-afebrile; 2-tolerate oral diet; 3-pain control with oral analgesia; 4-family is welling; 5 home with favorable condition,
Emil 2006 (397)	1-resolution of ileus; 2-afebrile for 24 h; 3-cbc is normal; 4-tolerate oral intake and analgesia
Slusher 2014 (253)	1-afebrile; 2-normal wbc & diff; 3-tolerating diet; 4-drain output is minimal
Frazee 2014 (345)	1-Ability to tolerate liquid intake; 2-Ability to ambulate; 3-Pain controlled with oral analgesics using a visual analog scale; 4-HD stability; 5-Adequate respiratory effort; 6-No alteration in mental status from baseline; 7-Ability to urinate; 8-N & V controlled; 9-Physicianapproval; 10-Appropriate supervision & assistance at home
Takegami 2003 (185)	1-T < 37.5˚C for 24 h; 2-passed stools or flatus; 3) tolerating clear liquids & a regular diet; 4-no drains in situ; 5) no spinal anesthesia-associated headache. Patients who were treated by conservative therapy were discharged after meeting criteria 1 - 3
Helmer 2002 (438)	1-normal WBC count; 2-return of bowel function; 3-no fever
Keller 1996 (56)	1-resolution of fever for 24 h; 2-normalization of WBC; 3-normal results of clinical exam
Firilas 1999 (147)	1-WBC < 14,000; 2-T max < 38.5 C for 24 h; 3-tolerate regular diet; 4-transition to oral analgesic
Putnam 2014 (794)	1-T < 101.48F - 38.6 C (oral) since admission or greater than 24 h; 2-Tolerating regular diet; 3-Pain relief with oral analgesics; 4-Ambulating with minimal assistance, as age appropriate
Akkoyun 2013 (129)	1-patients were able to tolerate oral liquids; 2-afebrile; 3-free of nausea, vomiting, and abdominal pain
Hussain 2014 (30)	1-stable VS for >30 min; 2-no new signs or symptoms after the operation; 3-no active bleeding or oozing; 4-minimal nausea and persistent emesis for <30 min; 5-orientation to person, time and place; 6-pain controllable with oral analgesics; 7-passed urine; 8-no surgical complication; 9-minimal dizziness after sitting for <10 min; 10-a responsible escort
Bensard 2009 (72)	Non-complicated appendicitis: 1-completion of antibiotic; 2-adequate post-op intake 3 pain control. Complicated appendicitis: same above criteria + resolution of fever and normal WBC count
Lord 1996 (116)	1-eating; 2-Walking freely; 3-passed flatus, provided there was no evidence of sepsis or other complications
Cash 2012 (235)	1-Ability to tolerate liquid intake 2-Ability to ambulate 3-Pain controlled with oral analgesics 4-Hemodynamicstability 5-Adequate respiratory effort 6-No alteration in mental status from baseline 7-Ability to urinate 8-Nausea and vomiting controlled 9-Physician approval 10-Appropriate supervision and assistance at home
Knott 2013	1-Adequate pain control; 2-tolerate oral diet
Warner 2002	1-afebril; 2-able to tolerate liquid diet; 3-ambulate with assistance

Normal range is usually between 4000 and 11,000 per microliter of blood.

4.4. Outcomes

Findings of this review support literature findings that clinical pathway implementation leads to better outcomes [47]. A retrospective study with a sample size of 580 subjects diagnosed with non-complicated appendicitis indicated a reduction in LOS from 40.1 - 23.5 hours and reduction in total cost per patient from $5783 - $4499 [48]. Cundy *et al.* found that there was a 29.2% reduction in median postoperative LOS in protocol-based care, an improved rate of discharge within 24 hours, and a projected annual savings. Implementation of postoperative clinical pathway was significantly associated with positive clinical outcomes ($P < 0.001$) [47]. In this review, 9 studies concluded that clinical pathway implementation is cost effective in managing patients with complicated and non-complicated appendicitis [2] [3] [12] [13] [19] [20] [21] [22] [23]. Nevertheless, 3 studies concluded that there was no significant impact of clinical pathway in reducing the cost of hospitalization for complicated appendicitis [3] [12] [17].

4.4.1. Postoperative Complications

A systematic review and meta-analysis of 27 studies with a total sample size of 11,398 subjects with 19 different conditions found that the odds of reducing developing in-hospital complications are 0.58 when a clinical pathway was implemented [1]. However, a prospective study in outpatient protocol for laparoscopic appendectomy showed no significant difference between complication rate between protocol and non-protocol groups [5].

4.4.2. Infection

Infection is the most common complication following appendectomy. It commonly occurred in patients with complicated appendicitis. Infection had a great impact on recovery time and quality of life. In this review, the reported rate of wound infection for non-complicated appendicitis was 0% - 7.5% and complicated appendicitis was 0.7% - 13%. Reviewed literature concluded that the rate of infection and abscess were less in the protocol group. These findings are consistent with findings from other studies that indicated clinical pathway implementation resulted in reduction of infection frequency.

4.5. Strengths and Limitations

The major strength of this review is that it is the first study to our knowledge to evaluate the available literature that assesses acute appendicitis clinical pathways. However, it was impossible to conduct a meta-analysis due to the nature of the study design of studies included in the review and the mode of data presentation.

The heterogeneity of studies included in this review was the main limitation. Another major limitation is related to the nature of study design; some studies involved multiple groups, and others were cross-sectional. Variation in treatment preference was another limitation.

Despite these limitations, findings of this review remain important to guide clinicians, surgeons and researchers in developing acute appendicitis management clinical pathway protocol.

5. Conclusion

Absence of a standardized clinical pathway for appendicitis management is challenging for clinicians and surgeons. The development of a standard clinical pathway is important to reduce complication rate, LOS, and cost, and to improve diagnostic efficacy. This review may serve as a foundation for the development of appendicitis guidelines.

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Conflicts of Interest

There are no conflicts of interest to declare.

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