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The Correlation between Pre-operative Leukocyte Levels and Length of Stay in Appendicitis Patients after an Appendectomy at Dr. Zainoel Abidin Hospital 2019–2020

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Abstract

BACKGROUND: Appendicitis is an inflammation of the vermiform appendix. The infectious process and the inflammatory response are associated with increased leukocyte levels. Leukocyte levels can be used as the predictor of severity, treatment selection, and outcome of appendicitis patients that affect the length of hospitalization.

AIM: The aims of the study are to determine the correlation between pre-operative leukocyte levels and the length of stay in appendicitis patients after an appendectomy at Dr. Zainoel Abidin Hospital 2019–2020.

METHODS: The study was an observational analytic study with a cross-sectional design. The sampling technique used is total sampling. The data collected were sourced from medical records and obtained from 47 research subjects.

RESULTS: The results showed that both appendicitis patients with leukopenia (<5000 cells/mm^3) and normal (5000–10,000 cells/mm^3) consist of two subjects which required a short length of hospitalization (<5 days). In the patient with leukocytosis Grade I (≤18,000 cells/mm^3), 23 subjects (92%) required a short length of hospitalization and 2 subjects (8%) required a long hospitalization (≥5 days). Meanwhile, patients with leukocytosis Grade II (>18,000 cells/mm^3), 8 subjects (40%) required a short length of hospitalization, and 12 subjects (60%) required a long hospitalization. Based on the bivariate analysis using the Chi-square method, obtained p = 0.002 (p < 0.05).

CONCLUSION: There was a correlation between preoperative leukocyte levels and the length of stay in appendicitis patients after an appendectomy at dr. Zainoel Abidin Hospital.

Introduction

Appendicitis is an inflammation of the vermiform appendix (appendix of worms) [1]. According to the World Health Organization, the global mortality rate due to appendicitis is between 0.2% and 0.8% [2]. The risk of acquiring appendicitis during life is 8.6% for men and 6.7% for women [3]. A cohort study (1997–2013) with a total of 16.544 cases of acute appendicitis discovered 3.995 cases (24.15%) in the age group of 7–13 years and the second highest in the age group of 18–25 years (21.35%) [4]. In Southeast Asia, Indonesia has the highest rate of appendicitis, with a morbidity rate of 95 from 1000 people [5], [6]. In 2009, the Indonesian Ministry of Health reported that there were 596,132 cases of appendicitis which increased to 621,435 cases in the following year [7]. In the survey, there were 4351 cases of appendicitis hospitalized in 2014 which were conducted in 15 provinces. The incidence rate significantly increased from the previous year, amounted to 3236 cases [8]. Based on the patient's medical record at Dr. Zainoel Abidin Hospital, the number of cases of appendicitis in 2016–2020 was 121, 181, 178, 158, and 97 cases with 15 deaths.

Appendicitis can be caused by several factors including obstruction of the lumen of the appendix due to fecal debris, fecal stasis, lymphoid hyperplasia, cecal neoplasms, and other pathogenic infections. The obstruction of the lumen appendix allows intestinal bacteria to infiltrate the appendix wall, causing inflammation and infection [9]. Several factors induce appendicitis such as bacteria and endotoxin in the form of lipopolysaccharide. It can increase the release of cytokines, such as tumor necrosis factor, interleukin 1 (IL-1), and interleukin 6 (IL-6). Interleukin 6 (IL-6) is the main factor in inducing protein synthesis in the acute phase, specifically the synthesis of C-reactive protein and α1-glycoprotein, and able to degranulate neutrophils and inhibit apoptosis. The response of the body to the protein synthesis change can be high blood leukocyte levels and increased immunological activity [6]. Leukocytes, also known as white blood cells, are cells that help the body's immune system by recognizing and destroying potentially hazardous foreign items [10]. In adults, normal leukocyte levels range from 5000 to

10,000 cells/mm^3. Patients with appendicitis generally have a leukocyte >10,000 cells/mm^3. This condition is called leukocytosis [1].

The previous research conducted by Amalina *et al.* and Wibowo *et al*. who concluded that the severity of appendicitis was proportional to the increase in the number of leukocytes levels. The number of leukocytes produced increases as the severity of the infection increases [11], [12]. In addition, research by Yulianto *et al*. found that the number of leukocytes can accurately distinguish the types of appendicitis which were classified as acute appendicitis and perforated appendicitis [13]. Based on the European Association of Endoscopic Surgery, there are two types of appendicitis include complicated appendicitis and non-complicated appendicitis. The complicated appendicitis is inflammation of the appendix with phlegmon and perforation, phlegmon without perforation, gangrene, or perityphlitis abscess, while non-complicated appendicitis is inflammation of the appendix without phlegmon, gangrene, free purulent, or abscess [14].

Pre-operative laboratory result is one of the assessments that can determine the diagnosis, severity, and required treatment. Inaccuracy in the diagnosis of appendicitis can affect both the patient and the operator during surgery. One of the problems that can affect patients is the length of stay in the hospital [15]. The length of stay refers to the number of days a patient spent in the hospital from admission to discharge. In Indonesia, the average length of hospitalization from 2003 to 2009 was 4–5 days. Length of hospitalization can be used as a reference in evaluating the efficacy of therapy and the quality of a health service. The length of hospitalization for appendicitis patients can be influenced by clinical conditions, laboratory results, the position of the appendix, the administration, and the use of antibiotics before and after surgery [16], [17].

Borghans *et al*. said that proper management and prevention of diagnostic mistakes will reduce the length of stay [18]. The treatment given will also affect the patient's length of stay. Appendectomy refers to the surgical removal of the vermiform appendix, which can be done using laparotomy or laparoscopy [19]. If the necessary instruments and capabilities are available, laparoscopic appendectomy may be the best option as appendicitis therapy. Laparoscopy is frequently associated with surgery that takes a long time and is more expensive than an open appendectomy, but it can reduce the length of hospital stay [20], [21]. A study stated that the length of stay of post-operative patients varies depending on the type of appendicitis and any complications. It takes about <5 days in case of acute appendicitis. While the healing process in the case of perforation takes a bit longer, about ≥ 5 days for the length of hospitalization. The more severe appendicitis, the longer patients will have to stay in the hospital [16].

The research contributes to the development literature on factor that affects the length of stay in hospital. Pre-operative leukocyte level is one of the parameters in estimating the severity and length of hospitalization in appendicitis patients.

Methods

This study was an observational analytic research with a cross-sectional design and held on August 2, 2021–August 19, 2021. The samples taken were appendicitis patients at Dr. Zainoel Abidin Hospital fits the research criteria. Inclusion criteria were patients diagnosed with appendicitis in 2019–2020, <60 years old, had normal nutritional status, and treated with open appendectomy. Meanwhile, patients with secondary diagnosis, comorbidities, and post- appendectomy complications excluded.

The data used in this study were secondary data from the medical records. The data collected from medical records were general characteristics (age and gender), type of anesthesia, pre-operative leukocyte levels, and length of stay. Data were collected using a non-probability sampling technique, namely, total sampling. In this study, there were univariate analysis and bivariate analysis. Univariate analysis used to determine the description or frequency distribution of each variable. Meanwhile, bivariate analysis was to examine the correlation between pre-operative leukocyte levels and length of stay using the Chi-square test with a probability level of 95% ($\alpha = 0.05$).

Results

The research used 47 research subjects. There were 25 subjects in 2019 and 22 subjects in 2020. Characteristics of the subjects included age and gender. Based on Table 1, the majority age of the subjects was between 6 and 11 years old, 17 of them (36.2%) were diagnosed with complicated appendicitis. The age range of 6–11 years was likewise the most

Table 1: Characteristic of the subjects

Classification						
Characteristic	Complicated appendicitis		Non-complicated appendicitis		Total	
	n	%	n	%	n	%
Age						
0–5	2	4,3	0	0	2	4.3
6–11	12	25.5	5	10.6	17	36.2
12–16	2	4.3	1	2.1	3	6.4
17–25	6	12.8	6	12.8	12	25.5
26–35	3	6.4	5	10.6	8	17
36–45	3	6.4	1	2.1	4	8.5
46–55	0	0	1	2.1	1	2.1
Gender						
Male	17	36.2	15	31.9	32	68.1
Female	11	23.4	4	8.5	15	31.9
Total	28	59.6	19	40.4	47	100

prevalent for complicated appendicitis. The age group of 17–25 years has the highest frequency of non-complicated appendicitis. In terms of gender, men occupied more than half of the total number of subjects, namely, 68.1%. Meanwhile, 31.9% of the population were female.

Table 2 shows that the distribution of anesthetic used during open appendectomy is divided into general anesthesia (85.1%), spinal anesthesia (12.8%), and epidural anesthesia (2.1%).

Table 2: Types of anesthesia in appendectomy

Classification						
Type of anesthesia	Complicated appendicitis		Non-complicated appendicitis		Total	
	n	%	n	%	n	%
General	26	55.3	14	29.8	40	85.1
Spinal	2	4.3	4	8.5	6	12.8
Epidural	0	0	1	2.1	1	2.1
Total	28	59.6	19	40.4	47	100

The leukocytosis is divided into Grade I (≤18,000 cells/mm^3) and Grade II (>18,000 cells/mm^3). This grading was carried out to clarify the magnitude of the increase in total leukocyte count. Table 3 represents the distribution of appendicitis based on pre-operative leukocyte levels. There was 1 subject (2.1%) in both patients with leukopenia and normal. Meanwhile, 95.8% of subjects had leukocytosis. It were divided into Grade I (≤18,000 cells/mm^3) for as many as 25 subjects (53.2%) and Grade II (>18,000 cells/mm^3) 20 subjects (42.6%).

Table 3: Appendicitis based on pre-operative leukocyte levels

Classification						
Leukocyte levels (cells/mm^3)	Complicated appendicitis		Non-complicated appendicitis		Total	
	n	%	n	%	n	%
Leukopenia (<5000)	1	2.1	0	0	1	2.1
Normal (5000–10,000)	1	2.1	0	0	1	2.1
Leukocytosis Grade I (≤18,000)	15	31.9	10	21.3	25	53.2
Leukocytosis Grade II (>18,000)	11	23.4	9	19.1	20	42.6
Total	28	59.6	19	40.4	47	100

Based on Table 4, 33 subjects (70.2%) with complicated and non-complicated appendicitis required a short length of hospitalization. The other 14 subjects (29.8%) required ≥5 days from admission to discharge.

Table 4: Appendicitis based on length of stay

Classification						
Length of stay	Complicated appendicitis		Non-complicated appendicitis		Total	
	n	%	n	%	n	%
Short (<5 days)	20	42.6	13	27.7	33	70.2
Long (≥5 days)	8	17	6	12.8	14	29.8
Total	28	59.6	19	40.4	47	100

According to the data in Table 5, subjects with leukopenia or normal require a short length of hospitalization. The patients with leukocytosis Grade I (≤18,000 cells/mm^3) dominantly required a short duration in hospital. Twenty-three subjects (92%) with leukocytosis Grade I require a short length of hospitalization. Whereas 12 subjects (60%) who had leukocytosis Grade II (>18,000 cells/mm^3) require a longer hospitalization. The result of analysis with the Chi-square method obtained $p = 0.002$ ($p < 0.05$), indicating that there was a correlation between pre-operative leukocyte levels and length of stay in appendicitis patients after an appendectomy.

Table 5: Correlation of pre-operative leukocyte levels and length of stay

Leukocyte	Length of stay (days)				Total	p
Levels (cells/mm^3)	Short (<5)		Long (≥5)			
	n	%	n	%		
Leukopenia (<5000)	1	100	0	0		
Normal (5000–10,000)	1	100	0	0		
Leukocytosis Grade I (≤18,000)	23	92	2	8	47	0.002
Leukocytosis Grade II (>18,000)	8	40	12	60		

Discussion

The majority age of subjects was in the range of 6–11 years (36.2%). According to Wibowo *et al*., 53% of pediatric patients with acute appendicitis were aged 6–12 years. The age group of 6–11 years was the most common age for complicated appendicitis, while the age group of 17–25 years had the highest number of non-complicated appendicitis. In the study by Putra and Suryana, children under the age of 10 years have a 2-fold increased risk of perforation [6]. Children were the most diagnosed with complicated appendicitis due to frequent mistakes in parents' predictions about their child's illness. The abdominal pain as the most common symptom of appendicitis is misinterpreted with the other diseases that have similar symptoms. Children tend to be more difficult to express their symptoms, which can cause delays in examinations and lead to a severe diagnosis. In addition, when compared to adults, the appendix wall is thinner at a young age, with a thicker submucosal layer. When the inflammatory process begins, the submucosal layer becomes edematous, narrowing the lumen of the appendix and increasing the risk of perforation within 24 h [12]. The patients with other diseases were excluded from this study. Researchers assess that the increasing age, the more likely a person has the other diseases due to an unhealthy lifestyle or the presence of hereditary diseases, then making physical conditions more vulnerable. Studies show that lymphoid tissue develops most rapidly in adolescence, making it easy to cause obstruction and a high incidence of appendicitis. This development slows gradually after the age of 30 [22], [23]. In addition, the adolescence generally has a great desire to explore various things, such as fast food. These foods have a low-fiber content, which causes constipation, then can raise intracecal pressure and cause appendix blockage. Appendicitis can occur as a result of the blockage [24].

Male occupied more than half of the individuals in this study, 68.1%. This is supported by several other studies. Sani *et al*. (2020) studied 65 appendicitis patients, 34 of them (52.3%) were male [25]. According to Arifuddin *et al*. (2017), males account for 72.2% of appendicitis patients [2]. Amalina *et al*. showed that

males made up 55.8% of the total number of patients with perforated appendicitis [11]. Erianto *et al*. (2020) stated that the proportion of males with perforated appendicitis (complicated) was 83.63%, while women only 16.37%. This is common in men's diets that are considered poor due to a lack of fiber and the consumption of fast food when they are away from home for work [8]. Fast food can increase energy, but it's also lacking in micronutrients, then affects immunity and makes the body more vulnerable to getting an infection [26].

Surgical procedures are an indication of anesthesia. Anesthesia is a method to relieve pain for the patient during surgery. Considerations for selecting the type of anesthesia include age, gender, physical status, risk factor, and type of surgery [27]. Appendicitis patients generally have a healthy physical condition, in addition to the clinical signs of appendicitis. Anesthesia techniques that can be used are general anesthesia and regional anesthesia. The regional anesthesia may be considered if there is no sepsis, adequate hydration, and cooperative patients [28]. In this study, 85.1% of subjects used general anesthesia techniques because more than half of the subjects belonged to the age group of children who were considered less cooperative during the surgery. Based on another study, pediatric emergency departments generally use general anesthesia [27]. The regional anesthesia used due to the greater risk of complications arising from general anesthesia.

The percentage of subjects with leukocytosis reached 95.8%, this could be due to the fact that all subjects in this study were treated with laparotomy. This procedure is generally performed in patients with high leukocyte levels. In addition, the condition of leukocytosis in appendicitis patients is related to the response of body's immune system in dealing with the inflammatory process [1]. In the study by Nasution, 73% of subjects were appendicitis patients with leukocytosis [29]. Sani *et al*. (2020) showed that 72.3% of subjects had leukocytes >10,000 cells/mm^3 [25]. A prospective study involving 116 surgical departments discovered that 3494 appendicitis patients (81.6%) had a leukocyte count >10,000 cells/mm^3 [30]. However, in cases of complicated appendicitis, there were subjects with normal and even low pre-operative leukocyte levels. The presence of normal or low leukocyte levels may occur due to the use of antibiotics before the patient enters the hospital, which can affect the results of the laboratory examination.

In this study, the length of stay for appendicitis patients was dominated by a short length of hospitalization, with an average of 4.7 days. This might be a sign of proper assessment and prompt treatment offered to patients, resulting in a satisfactory recovery period for the patient. According to Ceresoli *et al*., the average length of stay for appendicitis patients post-laparotomy was 5.43 days [4]. The study by Refolinda *et al*. concluded that there was a significant difference between the length of stay of patients with acute appendicitis and perforated appendicitis with $p = 0.000$ using the Mann–Whitney U-test. Patients with perforated appendicitis require a longer length of hospitalization [16]. The factors that can affect the length of hospitalization including age, the treatment, the presence of comorbidities, nutritional status, and the presence of post-operative complications [31], [32]. However, all of these factors have been excluded in this study. The length of stay of appendicitis patients also can be influenced by clinical conditions, patient laboratory results, the position of the appendix, and the use of antibiotic [17], [21].

The statistical analyses revealed a correlation between pre-operative leukocyte levels and the length of stay in appendicitis patients after an appendectomy. The higher the leukocyte level, the higher the percentage of appendicitis patients who require a long length of hospitalization. Non-complicated appendicitis usually takes <5 days to treat, while complicated appendicitis takes ≥5 days to treat due to the more involved management [16]. According to Aritonang's study (2019), due to varied therapies, complicated appendicitis has a lengthier average length of stay than non-complicated appendicitis [33]. When compared to laparotomy, the length of hospitalization for patients treated with antibiotics and laparoscopic appendectomy was regarded shorter [19].

If the leukocyte levels reach Grade II, the patient has most certainly had complicated appendicitis and requires a laparotomy. According to Pratiwi *et al*., there was a significant difference in the number of leukocytes at each level of severity of appendicitis. The average of leukocytes in simple, suppurative, gangrene, and abscess appendicitis classified into leukocytosis Grade I (≤18,000 cells/mm^3). Patients with perforations developed leukocytosis Grade II (>18,000 cells/mm^3) [24]. Based on a study conducted at the Meuraxa Hospital in Banda Aceh (Grade II), the number of leukocytes in patients with acute appendicitis was 10,741.8 cells/mm^3 (Grade I) and 20,023.6 cells/mm^3 in patients with perforated appendicitis [9]. According to Yulianto *et al*., leukocyte count >11,500 cells/mm^3 (Grade I) increased the chance of perforation by 12.12 times [13]. Perforation risk is 3.3 times higher when the leukocyte count is >18,000 cells/mm^3 (grade II) [6].

Based on the results of the study, patients with normal or low leukocyte levels were also treated with open appendectomy. The consideration for this action is the possibility of having experienced a perforation from the results of the anamnesis, physical examination, and supporting examinations. In addition, laparotomy requires a shorter surgical time in the operating room and has a lower risk of intra-abdominal abscess [34], [35].

There are no theory mentions the effect of pre-operative leukocyte levels on the length of hospitalization for appendicitis patients post-appendectomy. However,

leukocyte levels can be used as a predictor of outcomes in appendicitis patients. Patients with leukocytosis Grade I have a lower risk of perforation and post-operative complications than patients with leukocytosis Grade II, and can be considered for a simple appendectomy or laparoscopy to shorten the length of stay.

Conclusions

After collecting and analyzing data, researchers discovered that the patients with appendicitis, both complicated and non-complicated, had higher levels of leukocyte (>10,000 cells/mm^3), dominated by leukocytosis Grade I (≤18,000 cells/mm^3), and required a short length of hospital (<5 days). In appendectomy, general anesthesia is the most commonly used as an anesthetic technique.

Based on the statistical analysis, it was concluded that there was a correlation between pre-operative leukocyte levels and the length of stay in appendicitis patients after an appendectomy at Dr. Zainoel Abidin Hospital.

Research limitations

The limitations of the research were the medical record was collected manually and some medical records were not found.

Ethical consideration

The study has been approved by the Health Research Ethics Committee of the Faculty of Medicine at Syiah Kuala University with a number of Ethical contributions KEPPKN Registration Number: 1171012P (Description of Ethical Expedited “Ethical Expedited” Number: 202/EA/FK- RSUDZA/2021).

Authors’ Contribution

All authors are contributed equally to the content of the study, including data gathering, statistical analysis, and data synthesis.

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