

## THE DIFFERENCE IN NEUTROPHIL/LYMPHOCYTE RATIO IN PATIENTS WITH ACUTE APPENDICITIS WITHOUT AND WITH PERFORATION

IGP Wegen Wismaya<sup>1)</sup>, Paul L Tahalele<sup>2)</sup>, Titien Rahayu<sup>3)</sup>

### ABSTRACT

**Introduction:** Acute appendicitis is an inflammation of the appendix vermiformis and is the most frequent cause of acute abdominal. Inflammation occurs due to microorganisms infection that enter the submucosal layer of the appendix and eventually involves all layers of the appendix wall. Acute inflammation can lead to an appendix lumen obstruction, resulting in venous blood engorgement and arterial stenosis. One of the acute appendicitis physiological response from the immune system is an increasing of neutrophils and decreasing of lymphocytes. The result of increasing neutrophils and decreasing lymphocyte are increasing the absolute ratio between neutrophils and lymphocytes

**Aim:** To know the difference of neutrophil / lymphocyte ratio in patients with acute appendicitis without perforation and with perforation at Dr. M. Soewandhie District General Hospital Surabaya.

**Methods:** This research is an analytical research with cross sectional study, with paired categorical analysis sampling method. Respondent of this research is 62 patients, which consist of 31 patients acute appendicitis without perforation and 31 patients acute appendicitis with perforation that fulfilled inclusion and exclusion criteria in January 2016-August 2017. This research was conducted at Dr. M. Soewandhie District General Hospital Surabaya from Saturday, August 19th, 2017 until Saturday, September 30th, 2017.

**Results:** the difference of neutrophil / lymphocyte ratio in acute appendicitis patient without perforation and with perforation analyze by using Fisher's Exact Test comparative statistic test, p value  $0.000 < 0.05$  and contingency coefficient 0.477.

**Conclusion:** There is a significant difference between the ratio of neutrophils / lymphocytes in patients with acute appendicitis without perforation and with perforation at Dr. M. Soewandhie Regional District General Surabaya.

**Keywords:** neutrophil / lymphocyte ratio, acute appendicitis without perforation, acute appendicitis with perforation.

---

<sup>1)</sup> Student of Faculty of Medicine, Widya Mandala Catholic University Surabaya, Kalisari Selatan 1 Surabaya email: wegen.gede@gmail.com

<sup>2)</sup> Surgery Department, Faculty of Medicine, Widya Mandala Catholic University Surabaya, Kalisari Selatan No. 1 Surabaya

<sup>3)</sup> Clinical Pathology Department, Faculty of Medicine, Widya Mandala Catholic University Surabaya, Kalisari Selatan No.1 Surabaya

## INTRODUCTION

Acute appendicitis is an inflammation of the appendix vermiformis and is the most frequent<sup>1</sup>. Inflammation occurs due to microorganisms infection that enter the submucosal layer of the appendix and eventually involves all layers of the appendix wall. Acute inflammation can lead to an appendix lumen obstruction, resulting in venous blood engorgement and arterial stenosis<sup>2</sup>.

Cases of acute appendicitis require proper treatment and prompt diagnosis. A delay in diagnosis will have an impact on complications that will occur, such as gangrenosa, perforation, and even generalized peritonitis. Morbidity and mortality will increase according to the increase in complications found. Appendix complications can occur due to several factors either in the speed of diagnosis or the delay of the patient due to a lack of knowledge. Some patients who show symptoms and signs of appendicitis that are not typical can cause errors in diagnosis and delays in treatment<sup>3</sup>.

Seven percent of the population in the United States has appendicitis with an incidence of 1.1 cases per 1000 people per year. The incidence of acute appendicitis increased from 7.62 to 9.38 per 10,000

from 1993 to 2008. According to the Indonesian Ministry of Health in 2006, appendicitis ranks fourth most digestive system diseases in Indonesia after dyspepsia, gastritis, duodenitis, with the number inpatients as many as 28,040<sup>4</sup>.

About 7% of the population will have appendicitis in their lives with a peak incidence occurring between the ages of 10 and 30 years. Only 50% of cases have an initial sign of pain in the periumbilical region and shift to the iliac dextra fossa. In the case of appendicitis of 70%, it has typical clinical symptoms and there is no difficulty in determining the diagnosis. However, in 30%, it has no typical clinical symptoms and difficulty in diagnosis especially in the elderly, women of reproductive age, and appendix position<sup>5</sup>. The comparison of incidence rates in adolescents is 3: 2 and dominated by men. In adults, the incidence of appendicitis is 1.4 times more in men than in women and the risk of appendicitis is 8.6% in men and 6.7% in women<sup>4</sup>.

In elderly patients with appendicitis, it is often difficult to diagnose compared to younger patients, because there are many possible differential diagnoses that can be obtained in elderly patients with appendicitis and the difficulty of getting effective

communication. So that this incident can be a factor that contributes to a very high perforation rate

The diagnosis of appendicitis is very dependent on the symptoms and examinations. If there is any doubt from a clinical examination, the diagnosis can be helped by laboratory tests such as ultrasound imaging and more. Abdominal CT scans can also be performed to reduce the negative incidence of laparotomy or laparoscopy<sup>7</sup>.

One of the examinations in patients with appendicitis is a laboratory examination with a test of leukocytes and neutrophils. This has low sensitivity for compatibility and cannot be used to determine to diagnose appendicitis without and with perforation yet. Other tests that have been shown to have a higher sensitivity to diagnose appendicitis that is assessing the number of neutrophils and lymphocytes which are then sorted out. The result of a high neutrophil/lymphocyte ratio will indicate severe inflammation such as perforated appendicitis<sup>3</sup>. In addition, in leukocyte count (neutrophil/lymphocyte ratio), the calculation can be done at a low cost and fast process<sup>8,7</sup>.

Patients can also be examined further by ultrasonography (USG) or laparoscopic tracing<sup>9</sup>. However, for a USG of the abdomen, it takes longer in

diagnosis and requires more expensive costs. This examination has a weakness, which is still a valid subject (operator dependent), does not provide much accurate information and can not distinguish appendicitis without and with perforation. Another examination is the Alvarado score, but this scoring system still has weaknesses that are subjective and cannot distinguish appendicitis without perforation and with perforation<sup>3</sup>.

Based on the problems mentioned, the researchers would like to investigate further about the difference in the ratio of neutrophils/lymphocytes in patients with acute appendicitis without perforation and with perforations at Dr. M. Soewandhie District General Hospital Surabaya. The advantage of this examination is that the examination is objective, inexpensive, fast and available in all hospitals<sup>3</sup>. The researchers hope that by knowing the difference in the neutrophil/lymphocyte ratio can distinguish acute appendicitis without perforation and with a perforation so that it can provide appropriate treatment based on the severity to prevent negative appendectomy.

The general objective of this study is to determine the difference in the ratio of neutrophils/lymphocytes in patients with acute appendicitis without perforation and with perforation at Dr. M.

Soewandhie District General Hospital Surabaya.

## METHOD

This research was conducted at Dr. M. Soewandhie District General Hospital Surabaya.

The sample in this study were all sufferers of acute appendicitis without perforation and with a perforation at Dr. M. Soewandhie District General Hospital Surabaya (during 2016 and 2017) who had a complete medical record and suited the inclusion and exclusion criteria. The minimum number of samples for this study were; 31 people for patients with acute appendicitis without perforation and 31 people for patients with acute appendicitis with perforation so that the total is 62 people.

The criteria for inclusion of case groups in this study was the medical record diagnosed with acute appendicitis without perforation or acute appendicitis with perforation at Dr. M. Soewandhie District General Hospital Surabaya (during 2016 and 2017). Moreover, in the medical record, there are complete data regarding laboratory tests of complete blood neutrophils and blood lymphocytes of preoperative patients in Dr. M. Soewandhie District General Hospital Surabaya (during 2016 and 2017). The criteria for the exclusion of case groups in

this study was that, in the medical record, there was no complete data regarding laboratory tests of complete blood neutrophils and blood lymphocytes of patients preoperatively at Dr. M. Soewandhie District General Hospital Surabaya (during 2016 and 2017) and there are other accompanying diseases (immunological disorders, malignancies, ARI, UTI, tuberculosis).

To test hypotheses, the researchers used statistical analysis techniques that were processed and presented with the help of the "Statistical Product and Service Solution" (SPSS) program. Hypothesis testing uses Fisher's Exact Test.

## RESULT

**Table 1.** The diagnosis of acute appendicitis at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Diagnosis	Frequency (n)	Percentage (%)
Acute appendicitis without perforation	31	50%
Acute appendicitis with perforation	31	50%
<b>Total</b>	<b>62</b>	<b>100%</b>

Based on Table 1, it is known that the number of patients with a diagnosis of acute appendicitis without perforation and with perforation is the same as the number of 31 patients (50%), and a total of 62 patients (100%).

**Table 2.** The patients' sex with acute appendicitis without and with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017.

Gender/Sex	Frequency (n)	Percentage (%)
Men	33	53,2%
Women	29	46,8%
<b>Total</b>	<b>62</b>	<b>100%</b>

Based on Table 2, it is known that the most sexes that experience acute appendicitis without perforation and with perforation are the male sex of 33 patients (53.2%).

**Table 3.** The patients' sex with acute appendicitis without perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Gender/Sex	Frequency (n)	Percentage (%)
Men	14	45,2%
Women	17	54,8%
<b>Total</b>	<b>31</b>	<b>100%</b>

Based on Table 3, it is known that the most sexes that experienced acute appendicitis without perforation are female sex as many as 17 patients (54.8%).

**Table 4.** The patients' sex with acute appendicitis without perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Gender/Sex	Frequency (n)	Percentage (%)
Men	19	61,3%
Women	12	38,7%
<b>Total</b>	<b>31</b>	<b>100%</b>

Based on Table 4, it is known that the most sexes that experienced acute appendicitis without perforation the male sex as many as 19 patients (61.3%).

**Table 5.** The range of age of patients with acute appendicitis without and with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Age Range	Frequency (n)	Percentage (%)
0-10	4	6,5%
11-20	21	33,9%
21-30	14	22,6%
31-40	7	11,3%
41-50	10	16,1%
51-60	3	4,8%
>60	3	4,8%
<b>Total</b>	<b>62</b>	<b>100%</b>

Based on table 5, it is known that the most age range who experience acute appendicitis without perforation and with perforation is 11-20 years as many as 21 patients (33.9%).

**Table 6.** The range of age of patients with acute appendicitis without perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Age Range	Frequency (n)	Percentage (%)
0-10	1	3,2%
11-20	10	32,3%
21-30	8	25,8%
31-40	3	9,7%
41-50	7	22,6%
51-60	1	3,2%
>60	1	3,2%
<b>Total</b>	<b>31</b>	<b>100%</b>

Based on Table 6, it is known that the most age range that experiences acute appendicitis without perforation is 11-20 years as many as 10 patients (32.3%).

**Table 7.** The range of age of patients with acute appendicitis with perforation in Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Age Range	Frequency (n)	Percentage (%)
0-10	3	9,7%
11-20	11	35,3%
21-30	6	19,4%
31-40	5	16,1%
41-50	2	6,5%
51-60	2	6,5%
>60	2	6,5%
<b>Total</b>	<b>31</b>	<b>100%</b>

Based on table 7, it is known that the most age range that experiences acute appendicitis with perforation is 11-20 years as many as 11 patients (35.5%).

**Table 8.** The distribution of cases of acute appendicitis according to the number of leukocytes in patients with acute appendicitis without perforation and with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

	Frequency (n)	Percentage (%)
Leukocytosis	51	82,3%
Normal Leukocytes	10	16,1%
Leukopenia	1	1,6%
<b>Total</b>	<b>62</b>	<b>100%</b>

Based on Table 8, it is known that in acute appendicitis without and with perforation including leukocytosis in which there are 82.3%, normal leukocytes 16.1% and leukopenia 1.6%.

**Table 9.** The distribution of mean, median, mode, and standard deviation of leukocytes in patients with acute appendicitis without and with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Leukocyte	Frequency (n)
Mean	15,534
Median	15,740
Mode	11,860
Std. Deviation	5,909,391

Based on Table 9, it is known that in acute appendicitis without perforation and with perforation have the mean value of leukocytes is 15.534, the median of leukocytes is 15.740, the mode of leukocytes is 11.860, and the standard deviation of leukocytes is 5.909.391.

**Table 10.** The distribution of mean, median, mode, and standard deviation of leukocytes in patients with acute appendicitis without perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Leukocyte	Frequency (n)
Mean	13,155
Median	12,640
Mode	4,130
Std. Deviation	6,214,238

Based on Table 10, it is known that acute appendicitis without perforation has a mean leukocyte value of 13.155, the median of leukocytes is 12.640, the leukocyte mode is 4.130, and the standard deviation of leukocytes is 6.214.328.

**Table 11.** The distribution of mean, median, mode, and standard deviation of leukocytes in patients with acute appendicitis with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

Leukocyte	Frequency (n)
Mean	17,914
Median	17,030
Mode	15,870
Std. Deviation	4,548,392

Based on Table 11, it is known that acute appendicitis with perforation has a mean leukocyte value of 17.914, the median of leukocytes is 17.030, the leukocyte mode is 15.870, and the standard deviation of leukocytes is 4.548.392.

**Table 12.** The distribution of neutrophil/lymphocyte ratio in patients with acute appendicitis without and with perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017

	Neutrofil/Limfosit Ratio		
	Mean	<5 (1)	<5 (2)
Acute appendicitis without and with perforation	11,8294	17	45
Acute appendicitis without perforation	9,0626	16	15
Acute appendicitis	14,596	1	30

with perforation

Based on Table 12, it is known that in acute appendicitis without perforation and with perforation the mean neutrophil/lymphocyte ratio is 11.8294, with a neutrophil/lymphocyte ratio of less than or equal to 5 as many as 17 patients and a neutrophil/lymphocyte ratio of more than 5 as many as 45 patients.

In this study, the researchers used the Fisher's Exact Test comparative test, the p-value was 0,000 <0.05 and the contingency coefficient was 0.477 which showed that there was a significant difference between the neutrophil/lymphocyte ratio in patients with acute appendicitis without perforation and with a perforation at Dr. M. Soewandhie District General Hospital Surabaya from January 2016 to August 2017.

## DISCUSSION

The results of the descriptive analysis in this study showed that the highest sex prevalence was 33 male patients (53.2%), while 29 female patients (46.8%). This is in accordance with research from Gloria A. Thomas, et al., which have been conducted at RSUP Dr. R. D. Kandou Manado from October 2012 to September 2015, it is known that from 650 cases 56% of them were male, and

44% were female<sup>10</sup>. Based on the research of Andi Baso Endra, et al. which was conducted at the Wahidin Sudirohusodo General Hospital in Makassar in the month of January 2012 to December 2014, obtained that female sex (42.4%) less than men (57.6%)<sup>36</sup>. Şahin Kahramanca et al. reported the incidence of acute appendicitis without and with complications made in the Department of General Surgery, Kars State Hospital, Kars, Turkey. Among 1067 patients studied, it was found that 67% of them were male<sup>37</sup>. The incidence showed that there were more males than females, presumably because there were anatomical differences<sup>10</sup>. Besides that, the diagnosis was made. Appendicitis in women is more difficult than men because of the symptoms of gynecological disorders that mimic the symptoms of acute appendicitis.

Based on the age of the results of the descriptive analysis in this study showed that the prevalence of acute appendicitis without and with perforation based on the age of most patients in the age range 11-20 years with a total of 21 patients, then followed by the age of 21-30 years with a total of 14 patients. This incident is in accordance with the study of Dani and Paulina Calista conducted at Immanuel Hospital in Bandung, acute appendicitis mostly occurs in the age

range 17-25 and 26-35 years<sup>4</sup>. Likewise in the study of Gloria A. Thomas et al. which was conducted at RSUP Dr. RD Kandou Manado, the highest incidence of appendicitis is in the age range of 20-29 years (34%) and the age range of 10-19 years (25%)<sup>10</sup>. The research conducted by Şahin Kahramanca, in the Department of General Surgery, Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Department of General Surgery, Acibadem Hospital, and Shehzad Ahmed Abbasi, Ahmed Hussain Mishwani at the Ankara Department of Surgery, Combined Military Hospital, Peshawar, showed the average age of acute appendicitis patients was 30-31<sup>37,8</sup>. In a study conducted by Ata Ul Lateef, et al at Allied Hospital, Punjab Medical College in Faisalabad, Pakistan, the highest incidence of appendicitis was in the age range of 21 to 30 and then followed by 12 to 20<sup>9</sup>.

The results of this study in acute appendicitis without perforation of patients were in the range of 11-20 years with a percentage of 32.3%, 21-30 years with a percentage of 25.8%, while for the lowest percentage were at 0-10 years, ages 51- 60 years, and age over 60 years with 1 patient each (3.2%) of the total number of patients 31 people. This research was produced in accordance with research conducted by Gloria A. Thomas,



et al in RSUP Dr. RD Kandou Manado, which has the highest incidence for acute appendicitis without perforation at the age of 10-19 years (87 patients) and ages 20-29 years (191 patients), while the lowest number is at the age of 0-9 years (16 patients), aged 50-59 years (20 patients) and over 60 years (20 patients).

The results of an acute appendicitis study with perforation revealed that the highest rate was in the age range of 11-20 (11 patients or 35.5%) and the lowest was at 41-50 years old, 51-60 years old, and over 60 years old. This is consistent with research conducted by Gloria A. Thomas, et al in RSUP Dr. RD Kandou Manado, which has the highest number in the age range of 10-19 years, and the lowest at the age of 40-49 years, ages 50-59 years, and ages over 60 years.<sup>10</sup> In Harrison's book, the peak incidence of acute appendicitis is in the second decade and third life<sup>22</sup>. Likewise in the surgical science textbook, it is said that appendicitis can be found at all ages, only in children less than one year are rarely reported. The highest incidence is in the age group of 20-30 years<sup>38</sup>. This is consistent with the results of research which states the highest incidence occurs at ages 11-20 and 21-30 for acute appendicitis without perforation and with perforation. The maximum development of lymphoid tissue in adolescence is a

factor in the increased incidence of appendix to be blocked, which allows the slightest blockage will cause high intraluminal pressure. At the age of above 60 years, lymphoid tissue is no longer found in the appendix but there are changes in the serous layer that is less elastic compared to the mucosal layer which causes a different response to intraluminal pressure compared to younger patients, so the ability to adapt (stretch) due to accumulation of intraluminal secretions less good which can progress to ischemic and gangrenous early stages. An important factor that plays a role is atherosclerosis, because it can interfere with the smooth flow of arteries and veins to the appendix. In addition, the inflammatory response from cells and local tissue factors to control malevolent bacteria.

The results of this study for acute appendicitis without perforation and with perforation based on leukocytes showed that the majority of patients had leukocytosis with a percentage of 82.3%. This result is in accordance with the study of Dani and Paulina Calista who obtained results of 76.97% of acute appendicitis patients having leukocytosis<sup>4</sup>. The results of increased leukocytes (leukocytosis) were also found in research conducted by Ata Ul Lateef, with a value of 79.6% of patients experiencing increased

leukocytes with appendix conditions inflammation and 2.4% have leukocytosis under normal appendix conditions<sup>9</sup>. The normal value of the number of leukocytes is 4,500-10,000  $\mu$ l, these leukocytes will come out of capillaries if antigens are found. This leukocyte release process is called diapedesis. Leukocytes play a role against diseases that enter the body.<sup>29</sup> Inconsistent results will be found in children and parents with appendicitis. This can explain why in the study there were normal leukocyte levels because the study included criteria for children and parents. It also because of pediatric and elderly patients may not respond well to infections. In pregnant women, physiological levels of leukocytosis can affect the diagnosis of appendicitis<sup>4</sup>.

The results of this study use the Fisher's Exact Test comparative test, the p-value is 0.000 <0.05 and the contingency coefficient is 0.477 which shows that there is a significant difference between the neutrophil/lymphocyte ratio in patients with acute appendicitis without and with perforation at Dr. M. Soewandhie District General Hospital Surabaya. This supports the theory that one of the physiological responses to the immune system to acute appendicitis is an increase in the number of neutrophils and a decrease in the number of lymphocytes. This is due to changes in the dynamics

and regulation of apoptosis in a systemic inflammatory state when compared to a non-inflammatory state. Delaying the process of neutrophil apoptosis will result in prolongation of the function of neutrophils in the inflammatory process and prolong the elaboration of toxic metabolism, whereas increased lymphocyte apoptosis results in a decrease in the inflammatory effector and causes immunosuppression. Toxic metabolism released by activated neutrophils and coupled with inflammatory cytokines will damage tissue and organ function. In addition, the process of lymphocyte apoptosis results in the adaptive immune system immunosuppression so that it will be susceptible to infection. As a result of an increase in neutrophil counts and a decline in the number of lymphocytes, will increase the absolute ratio value between neutrophils and lymphocytes when compared with patients without a systemic inflammatory reaction. A high neutrophil and lymphocyte ratio results in severe inflammation such as perforated appendicitis<sup>40</sup>. The result of this study is consistent with research conducted by Şahin Kahramanca (2014) who presented findings obtained from differences with p values of 0.001 <0.05.<sup>37</sup> This study uses an observational analytic method with a different cross-sectional study design conducted by Dewi Prima Christian who

uses an analytic observational method with a cohort study design, while the cross-sectional design is carried out using the results of the final diagnosis in the medical record that has definitely been diagnosed with appendicitis or not and using the results of the first blood laboratory research at the hospital while in the research of Dewi Prima the time limit for taking blood samples was related to blood neutrophil values, as well as the diagnosis made by the prima christian goddess research confirmed using histopathological examination as such research in this study only based on diagnosis the main surgeon at Dr. M. Soewandhie District General Hospital who exists in the medical record. For complete blood in this study using absolute complete blood, which means 100% leukocytes per 1 field of view. In terms of time, the implementation of this research method can be done in a shorter time than the research cohort design conducted by Dewi Prima Christian. In her research, a cut-off point number was searched using a different ROC curve than this study which carried out the Fisher's Exact Test which tried to prove the truth of the neutrophil/lymphocyte ratio. While in Kahramanca's study the research sample used was a patient who supported appendicitis surgery with an uncertain diagnosis, while in this study a

post-diagnosis operation was more accurate.

## CONCLUSION

Based on this study, regarding "The Difference in Neutrophil/Lymphocyte Ratio in Patients with Acute Appendicitis without and with Perforation" at Dr. M. Soewandhie Regional District General Surabaya, the conclusion can be drawn as follows:

There is a significant difference between the ratio of neutrophils/lymphocytes in patients with acute appendicitis without and with perforation.

## REFERENCES

1. Pradipta EA dkk. Kapita Selekt Indonesia. IV. Tanto C, Liwang F, Hanifati S, Pradipta EA, editors. Jakarta: Media Aesculapius; 2014. 213-214 p.
2. Festiawan J, Sennang N, Samad IA. Rerata Volume Trombosit, Hitung Leukosit Dan Trombosit Di Apendisitis Akut. Indones J Clin Pathol Med Lab. 2014;Vol. 20.
3. Christian DP, Suwedagatha IG, Wiargitha IK. Validitas Rasio Neutrofil Limfosit Pada Apendisitis Komplikata di RSUP Sanglah Denpasar. J Bedah Nas. 2017;Volume 1.
4. Dani, Calista P. Karakteristik Penderita Apendisitis Akut di Rumah Sakit Immanuel Bandung Periode 1 Januari 2013-30 Juni 2013. Bagian Ilmu Kesehat Masyarakat, Fak Kedokteran, Univ Kristen Maranatha. 2013;(June):9.
5. Agrawal CS, Adhikari S, Kumar M. Role Of Serum C-Reactive Protein

- And Leukocyte Count In The Diagnosis Of Acute Appendicitis In Nepalese Population. *Nepal Med Coll J* [Internet]. 2008;10(1):11–5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18700623>
6. Brunicardi F , Dana Andersen , Timothy Billiar , Dunn J, Hunter , Jeffrey Matthews et al. *Scwartz's Principles Of Surgery*. 9th ed. USA: McGraw-Hill Professional; 2009.
  7. Bakti N, Hussain A, El-Hasani S. A Rare Complication Of Acute Appendicitis: Superior Mesenteric Vein Thrombosis. *Int J Surg Case Rep* [Internet]. 2011;2(8):250–2. Available from: <http://dx.doi.org/10.1016/j.ijscr.2011.08.003>
  8. Abbasi SA, Mishwani AH. Diagnostic Accuracy Of Total Leucocyte Count And Ultrasound In Yhe Diagnosis Of Acute Appendicitis. 2012;16(2):147–9.
  9. Lateef AU, Arshad AR, Misbah J, Hamayun M, Hospital A. Role Of Leucocyte Count In The Diagnosis Of Acute Appendicitis. *Gomal J Med Sci*. 2009;7(2):140–2.
  10. Kalangi CS, Jim EL, Joseph VFF. Angka Kejadian Apendisitis Di RSUP Prof. Dr. R. D. Kandou Manado Periode Oktober 2012 – September 2015. *J E-Clinic*. 2016;4(September 2015).
  11. Muttaqin A, Sari K. *Gangguan Gastrointestinal Aplikasi Asuhan Keperawatan Medikal Bedah*. Carolina S, editor. Jakarta: Salemba Medika; 2011.
  12. Shendy KR, Nileshwar A. *Buku Ajar Ilmu Bedah Ilustrasi Berwarna*. Ketiga. Sampepajung D, Hamdani W, Harahap WA, Hendry M, R. Widjaja A, Khany Jasa Z, et al., editors. Tangerang Selatan: Karisma Publishing Group; 2014.
  13. Sjamsuhidajat R. *Buku Ajar Ilmu Bedah Sjamsuhidajat-De Jong*. 3rd ed. Sjamsuhidajat R, Karnadihardja W, O.H. Prasetyono T, Ridiman R, editors. Jakarta: Penerbit Buku Kedokteran EGC; 2011.
  14. C. Sabiston D. *Buku Ajar Bedah (Essentials of Surgery)*. 1st ed. H. Ronardy D, editor. Jakarta: EGC; 1994.
  15. Mescher AL. *Histologi Dasar Junqueira*. 12th ed. Hartanto H, editor. Jakarta: EGC; 2012.
  16. Eroschenko VP. *Atlas Histologi Difiore*. 11th ed. Dharmawan D, Yesdelita N, editors. Jakarta: EGC; 2010.
  17. LeMone P, M. Burke K, Bauldoff G. *Keperawatan Medikal Bedah*. 5th ed. Tiflani Iskandar M, editor. Jakarta: Penerbit Buku Kedokteran EGC; 2012.
  18. Froggatt P, Harmston C. *Acute Appendicitis*. *Surgery* [Internet]. 2011;29(8):372–6. Available from: <http://dx.doi.org/10.1016/j.mpsur.2011.05.01>
  19. Oswari E. *Bedah dan Perawatannya*. 3rd ed. Jakarta: Gaya Baru; 2000.
  20. Robbins SL. *Buku Ajar Patologi*. 7th ed. Jakarta: EGC; 2007.
  21. Kumar V, Abbas AK, Aster JC. *Buku Ajar Patologi Robbins*. 9th ed. Nasar IM, Cornain S, editors. Singapore: Elsevier Ltd; 2013.
  22. Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL. *Harrison Prinsip-Prinsip Ilmu Penyakit Dalam*. 13th ed. Asdie AH, editor. Jakarta: EGC; 2000.
  23. Petroianu A. *Acute Appendicitis – Propedeutics And Diagnosis*. *Inflamm Dis - Immunopathol Clin Pharmacol Bases*. 2012;171–200.
  24. Cole M, Maldonado N. Evidence-Based Management Of Suspected Appendicitis In The Emergency Department. *Emerg Med Pr* [Internet]. 2011;13(10):1–29. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22164515>

25. Saputra J, Cheng W. Apendisitis kut. *Prakt Klin Ilmu Bedah dan ATLS Fak Kedokt Univ Indones*. 2014;1–18.
26. Ansari P. Appendicitis. *Merck Man*. 2012;(August 1-2).
27. Subowo. *Histologi Umum*. 2nd ed. Subowo, editor. Jakarta: CV Sagung Seto; 2009.
28. Sherwood L. *Fisiologi Manusia Dari Sel ke Sistem*. 6th ed. Yesdelita N, editor. Jakarta: Penerbit Buku Kedokteran EGC; 2013.
29. Irianto K. *Anatomi dan Fisiologi*. Bandung: Alfabeta; 2013.
30. Putra IWA. Rasio Neutrofil Imatur/Neutrofil Total Maternal Sebagai Petanda Diagnostik Korioamnionitis Pada Persalinan Preterm. Udayana; 2014.
31. Hall JE. *Guyton And Hall Buku Ajar Fisiologi Kedokteran*. 12th ed. Singapore: Elsevier Inc; 2014.
32. Kiswari R. *Hematologi&Tranfusi*. Jakarta: Erlangga; 2014.
33. Jane Bain B. *Hematologi Kurikulum Inti*. Iriani A, editor. Jakarta: Penerbit Buku Kedokteran EGC; 2017.
34. Wijaya A. Hubungan Antara Reaktivitas Folikel Limfoid Dengan Tipe Radang Apendiks Pada Pasien Di Rumah Sakit Umum Pusat Nasional Cipto Mangunkusumo Tahun 2005 Hingga 2007. FK UI. 2009;
35. Nugroho A, Suwarman, Nawawi AM. Hubungan Antara Rasio Neutrofil-Limfosit dan Skor Squwncial Organ Failure Assesment Pada Pasien yang Dirawat di Ruang Intensive Care Unit. 2013;1(3):2–31.
36. Endra AB, Sampetoding S, Patellongi I. Analisis Jumlah Leukosit Pada Apendisitis Akut dan Apendisitis Perforasi Yang Menjalani Operasi di RSUP Dokter Wahidin Sudirohusodo Makasar Periode Januari 2012 Hingga Desember 2014. 2014;
37. Kahramanca Ş, Özgehan G, Şeker D, Gökce Eİ, Şeker G, Tunç G, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. 2014;20(1):19–22.
38. Sjamsuhidajat R, O.H. Prasetyono T, Rudiman R, Ignatius R, Tahalele P. *Buku Ajar Ilmu Bedah Sjamsuhidajat De Jong Sistem Organ Dan Tindakan Bedahnya (2)*. In: 4th ed. Jakarta: Penerbit Buku Kedokteran EGC; 2016. p. 777.
39. Smf B, Dan O, Kedokteran F, Udayana U, Sanglah R. Peningkatan Jumlah Neutrofil Pada Sekret Vagina Berhubungan Dengan Tingginya Persalinan Preterm. 2013;
40. Article O. Original Article Pada the Validity Neutrophil Lymphocyte Ratio of Complicated. 2015;(December).