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ABSTRACT
Typhoid fever is one of the endemic diseases in Indonesia caused by Salmonella typhi bacteria. A hematological examination to support medical diagnosis is complete blood count – a decrease in the number of leukocytes is often found. This study was conducted to determine the number of leukocytes in patients with typhoid fever in children. This paper aims to analyze the number of leukocytes based on age, gender, hospital length of stay, and type of antibiotic. It was a descriptive method with a cross-sectional design. The sample was all typhoid fever patients aged 1-18 years hospitalized at the Dr Tadjuddin Chalid hospital, Makassar, and 75 respondents by total sampling. Data collection was carried out using secondary data from medical records of patients from January to December 2018. The data analysis used the chi-square and Spearman test. It revealed that 28% of respondents had leukopenia, 54.7% had normal leukocytes, and 17.3% had leukocytosis. Leukopenia was mostly in respondents aged 7-12 years (34.4%), males (34.1%), hospital length of stay less than seven days (26.5%), and administered with ceftriaxone (26%). The chi-square analysis results between leukocyte count and age, gender, hospital length of stay, also type of antibiotic consecutively obtained p=0.064, 0.317, 0.414, 0.923 (p>0.05). Most children with typhoid fever have a normal leukocyte. However, the leukocyte count does not correlate with age, gender, hospital length of stay, and type of antibiotic.

INTRODUCTION
One of the endemic diseases in Indonesia is typhoid fever. This disease is listed in Law number 6 of 1962 concerning outbreaks and is included in the group of easily transmitted diseases (Setiati et al., 2014). The World Health Organization (WHO, 2017) estimates that typhoid fever cases reach 11-18 million cases and 128,000-190,200 deaths annually due to typhoid fever. Its incidence in rural areas Indonesia is 358 / 100,000 population/year, while in urban areas, it is 760/100,000 population/year or around 600,000 and 1.5 million cases per year, evenly distributed throughout the province (Soedarmo & Garna, 2010). Reports received from the Disease Control and Environmental Health Office of South Sulawesi Province in 2014 recorded 23,271 cases of typhoid fever South Sulawesi Health Office (2015) Report from the Disease Prevention and Control of the Makassar City Department of Health Office (2019), the incidence of typhoid fever was 5,404 cases in 2016, 5,937 in 2017, 6,579 in 2018. So that in the last three years, there was an increased incidence of typhoid fever in Makassar City (Dinas Kesehatan, 2019). Typhoid fever diagnosis can be determined through clinical, microbiological, and serological diagnosis (Widoyo, 2008). A hematological examination to support medical diagnosis is complete blood count – a decreased leukocyte levels are often found (Mandal, 2008). In addition, there are abnormalities in leukocyte levels, both
leukopenia, and leukocytosis. Leukopenia, common in typhoid fever, is a decrease in the number of white blood cells.

Handojo's research (2004) stated that at the end of the second week of the phagocytosis process, Salmonella typhi bacteria were not in the blood. However, it is still present in the spinal cord. So that the blood formation process, especially leukocytes, can be disrupted (Baratawidjaja, G. K dan Rengganis, 2012). In a study by Nafiah, 2017), a patient's leukocyte levels tended to be normal and below normal limits because Salmonella typhi bacteria can cause a blockage in hematopoiesis (blood formation) in the spinal cord. In general, the production of leukocytes will increase as a defense against infections. However, leukocyte levels can be affected due to the bacteria that live in the spinal cord. Based on the description and background of the problem above, this study aims to determine the profile of the leukocyte count in children with typhoid fever at the Dr. Tadjuddin Chalid Hospital, Makassar. This paper is expected to provide an overview of leukocyte levels in children with typhoid fever.

METHOD

It was a descriptive method with a cross-sectional design. The sample was all typhoid fever patients aged 1-18 years hospitalized at the Dr. Tadjuddin Chalid hospital, Makassar, and 75 respondents by total sampling. This research has obtained ethical clearance from Alauddin State Islamic University of Makassar with the registration number 2002E029. Data collection was carried out using secondary data from medical records of patients from January to December 2018. The Independent variable was the number of leukocytes, while the dependent variables were age, gender, hospital length of stay, and type of antibiotic. The data analysis used the chi-square test to evaluate the correlation between both variables. In addition, the Spearman test analyzed whether the correlation was unidirectional or not.

RESULT

The results of the medical record document analysis were presented in the table. After processing the data, the following research results were:

Table 1. Characteristic of Respondent

| Variable                  | Category   | Frequency | Percentage (%) |
|---------------------------|------------|-----------|----------------|
| Age                       | 1 – 6 years| 20        | 26.7           |
|                           | 7 – 12 years| 32        | 42.7           |
|                           | 13 – 18 years| 23        | 30.7           |
| Gender                    | Male       | 44        | 58.7           |
|                           | Female     | 31        | 41.3           |
| Hospital Length of Stay   | < 7 days   | 68        | 90.7           |
|                           | > 7 days   | 7         | 9.3            |
| Type of Antibiotics       | Ceftriaxone| 50        | 66.7           |
|                           | Cefoperazone| 17        | 22.7           |
|                           | Cefixime   | 8         | 10.7           |
| Total                     |            | 75        | 100            |
Table 1 shows that most respondents are 7-12 years old (42.7%), male (58.7%), hospitalized less than seven days (97.3%), and administered with ceftriaxone (66.7%).

Table 2. The Number of Leukocytes in Children with Typhoid Fever

| The Number of Leukocytes | Frequency | Percentage (%) |
|-------------------------|-----------|----------------|
| Leukopenia              | 21        | 28             |
| Normal                  | 41        | 54.7           |
| Leukocytosis            | 13        | 17.3           |
| Total                   | 75        | 100            |

Table 2 describes that the number of leukocytes from 75 children with typhoid fever; 21 have leukopenia (28%), 41 have normal leukocytes (54%), and 13 have leukocytosis (17.3%).

Table 3. The correlation between the number of leukocytes and age

| Age            | The Number of Leukocytes | Total | p   |
|----------------|--------------------------|-------|-----|
|                | Leukopenia | Normal | Leukocytosis |       |
| 1 – 6 years    | 2          | 2      | 6      | 20   | 0.064 |
| 7 – 12 years   | 11         | 19     | 2      | 32   |       |
| 13 – 18 years  | 8          | 10     | 5      | 23   |       |
| Total          | 21         | 41     | 13     | 75   |       |

Table 3 explains that of the 20 respondents in the 1-6 year age group, two respondents have leukopenia (10%), 12 have normal leukocytes (60%), and 6 have leukocytosis (30%). Of the 32 respondents in the 7-12 year age group, 11 have leukopenia (34.4%), 19 have normal leukocytes (59.4%), and 2 have leukocytosis (6.3%). Of the 23 respondents in the 13-18 years age group, there are 8 respondents with leukopenia (34.8%), 10 with normal leukocytes (43.5%), and 5 with leukocytosis (21.7%). The data analysis using the chi-square test obtains p=0.064 (p>0.05), which means no significant correlation between age and the number of leukocytes in typhoid fever patients.

Table 4. The correlation between the number of leukocytes and gender

| Gender | The Number of Leukocytes | Total | p   |
|--------|--------------------------|-------|-----|
|        | Leukopenia | Normal | Leukocytosis |       |
| Male   | 15         | 23     | 6      | 44   | 0.317 |
| Female | 6          | 18     | 7      | 31   |       |
| Total  | 21         | 41     | 13     | 75   |       |

Table 4 shows that of the 44 males, 15 respondents have leukopenia, 23 have normal leukocytes, and 6 have leukocytosis. Meanwhile, of the 31 females, 6 respondents have leukopenia (19.4%), 18 have normal leukocytes (58.1%), and 7 have leukocytosis (22.6%). The chi-square test is 0.317 (p>0.05). Thus, there is no significant correlation between the number of leukocytes and gender in typhoid fever patients.

Table 5. The correlation between the number of leukocytes and hospital length of stay

| Hospital Length of Stay | The Number of Leukocyte | Total | p   |
|------------------------|-------------------------|-------|-----|
|                        | Leukopenia | Normal | Leukocytosis |       |
| < 7 days               | 18         | 37     | 13     | 68   | 0.414 |
| > 7 days               | 3          | 4      | 0      | 7    |       |
| Total                  | 21         | 41     | 13     | 75   |       |
Table 5 represents that of 68 people with hospital length of stay less than seven days, 18 respondents have leukopenia (26.5%), 37 have normal leukocytes (54.4%), and 13 have leukocytosis (19.1%). Of the 7 people with hospital length of stay more than seven days, 3 have leukopenia (42.9%), and 4 have normal leukocytes (57.1%). The chi-square analysis is 0.414 (p> 0.05). Thus, there is no significant correlation between the number of leukocytes and hospital length of stay in typhoid fever patients.

Table 6. The correlation between the number of leukocytes and type of antibiotic

| Type of Antibiotic | The Number of Leukocyte | Total | p |
|--------------------|-------------------------|-------|---|
|                    | Leukopenia | Normal | Leukositosis | |
| Ceftriaxone        | 13         | 27     | 10            | 50 | 0.923 |
| Cefoperazone       | 5          | 10     | 2             | 17 |
| Cefixime           | 3          | 4      | 2             | 8  |
| Total              | 21         | 41     | 13            | 75 |

Table 6 revealed that of the 50 respondents with ceftriaxone administration, 13 respondents have leukopenia (26%), 27 have normal leukocytes (54%), and 10 have leukocytosis (20%). Of the 17 people with cefoperazone administration, 5 have leukopenia (29.4%), 10 have normal leukocytes (58.8%), and 2 have leukocytosis (11.8%). Of the 8 respondents with cefixime administration, 3 have leukopenia (37.5%), 4 have normal leukocytes (50%), and 1 has leukocytosis (12.5%). The data analysis using the chi-square test obtains p= 0.923 (p> 0.05). Thus, there is no significant correlation between the types of antibiotics and the leukocyte count in typhoid fever patients.

DISCUSSION

Research conducted at the dr. Tadjuddin Chalid Hospital, Makassar City in 2018. Out of 75 typhoid fever children, most of them had normal leukocyte count (54.7%). This result is in line with a study conducted by Nazilah & Suryanto (2013) The study reported that most of 88 typhoid fever patients had normal leukocyte counts (82.6%). However, this study is not in line with Gayatri (2017) which showed that the number of leukocytes in most typhoid fever children was leukopenia. This study showed a low to normal leukocyte count due to several factors related to the duration of fever and toxicity induced by bone marrow depression by endotoxin and endogenous mediators. Variations of endotoxins levels in typhoid fever patients may cause the results of the hematologic examination to vary. Bone marrow suppression or bone marrow depression is an important mechanism in producing hematologic changes (Arifin et al., 2009)

The typhoid fever incidence in this study was mostly in school-age children, closely related to hygiene factors. It is in line with Rustam (2010) research that stated that individuals with typhoid fever were mostly 7-18 years old compared to those aged <7 years. A normal leukocyte count is caused by a course of the disease and less severe degrees of disease. It is known that S. Typhwi infection can cause bone marrow depression which can lead to leukopenia in long-standing infections (Azin et al., 2012)
Most respondents in this paper were males. Rachman (2017) research in 158 typhoid fever children showed that most of them were male (57.6%), while 42.4% were female. Males tend to have activities outside the home more often than females, so that it is easier to get S.Typhi infection through the environment (Sholikhah & Sustini, 2013). Gender affects health status because certain diseases only occur in men or women (Wijaya, 2015).

The hospital length of stay in most respondents was less than seven days. It is in line with Virdania's research (2018) in 131 typhoid fever patients. The study showed that 63.6% of them had short hospital lengths of stay. Patient adherence affects the success of treatment. Providing information about drugs and how to use them is a management of effective and safe drug therapy (Hussar, 2008). Typhoid fever management requires antibiotics to eradicate the S. typhi bacteria. Certain types of antibiotics influence the hospital length of stay in typhoid fever patients (Sidabutar & Satari, 2010).

The most frequent antibiotics administration in this research was Ceftriaxone. It is in line with the theory that aplastic anemia is an adverse event of several antibiotics. Other adverse events can also inhibit the formation of blood cells after the therapy (Tandi, 2017). Certain types of antibiotics can also cause bone marrow depression, interfering with forming blood cells (Rampengan, 2013). From the results of the above analysis, it can be said that there was no correlation between antibiotics administration and the number of leukocytes in typhoid fever children. In this study, various antibiotics administration in typhoid fever children gave different results due to the many factors that can influence antibiotic use in the hospital. The study did not use the chloramphenicol type of antibiotic. Chloramphenicol has a side effect of bone marrow depression (Tandi, 2017).

CONCLUSION

Most typhoid fever children have a normal leukocyte count, but few of them have leukopenia. Leukopenia is mostly in respondents aged 7-12 years, males, hospital length of stay less than seven days, and administered with ceftriaxone. However, the leukocyte count does not correlate with age, gender, hospital length of stay, and type of antibiotic.

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