

RESEARCH ARTICLES

Total Leukocyte Count And Platelet Count Are Related To TUBEX-TF Positivity Results In Typhoid Fever Patients At Dr. Pirngadi Hospital Medan City In 2018-2021

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Abstract: Typhoid fever is a gastrointestinal infection caused by *Sallmonellal typhi* and *Sallmonella serovar Paratyphi A* (an important inhibitor of typhoid fever). Typhoid fever can be diagnosed based on clinical signs and symptoms, and laboratory tests. Leukopenia occurs due to the invasion of the bacterium *Salmonella typhi* into hematopoietic organs such as lymph nodes, tonsils, spleen, and bone marrow, thereby inhibiting hematopoiesis. The decrease in platelet production in the bone marrow is caused by viral infections, the destruction of platelet precursor cells in the bone marrow, radiation, aplastic bone marrow, bone marrow disorders or cancers, and other conditions that inhibit cell production in the bone marrow. This study aims to determine the relationship between total leukocyte count and platelet count in relation to Tubex-TF positivity in typhoid patients at RSUD dr. Pirngadi Medan from 2018 to 2021. This research uses an analytical observational method with a cross-sectional approach. The research sample consisted of typhoid patients at RSUD Dr. Pirngadi Medan from 2018-2021, which met the inclusion and exclusion criteria, totaling 71 patients. Analysis of the data was conducted using the chi-square test for both univariate and bivariate analyses. The total leukocyte count was found to be elevated in the case of a positive Tubex-TF in a patient with typhoid fever.

Keywords: Typhoid Fever, Total Leukocyte Count, Total Platelet Count, Tubex-TF

INTRODUCTION

Typhoid fever is a gastrointestinal infection caused by *Sallmonella typhi* and *Sallmonella serovar Paratyphi A* (an important inhibitor of typhoid fever). It has been known since the late 1800s the role of water and the role of food as a vector.¹ Typhoid fever can be diagnosed based on clinical signs and symptoms, and laboratory examinations. Often the diagnosis based on clinical signs and symptoms is inadequate.² Typhoid fever infects 11 million to 21 million per year. The CDC estimates that typhoid fever infects 5,700 people in the United States. Some people who have been infected have a travel history from the place where typhoid fever occurred.³ According to the 2013 Riskesdas Research Study, the prevalence of typhoid fever in Indonesia is 5.13%. Typhoid fever in Indonesia killed 600,000 to 1.3 million cases with a death rate of more than 20,000 people.⁴ The highest prevalence of typhoid fever was found in 5-14 year old (School-Age Children). Serious complications of the disease are compounded by the presence of typhoid fever in more than 2 weeks and the disease is not present in the treatment of the disease..⁵ TUBEX-TF is a semi-qualitative test with a visual interpretation of the results of the examination. TUBEX-TF can detect specific infection of IgM *Sallmonella typhi 09 antibodies* contained in the patient's serum. TUBEX-TF has specificities and sensitivities that are more reversible with wide tests. The TUBEX-TF test is an ideal

test and can be used for routine testing because the process is fast, easy, simple and accurate.⁶ Leukocytes are one of the components of blood that has a function to detect infections caused by viruses and bacteria. Leukocytes also have an important role in the body's defense system. If there is an increase in leukocytes, it indicates an infection.^{7,19} There are five types of leukocytes, namely neutrophils, basophils, eosinophils, monocytes, and lymphocytes.⁸ In typhoid fever, leukopenia (the number of leukocytes below normal), normal leukocytes or leukocytosis (the number of leukocytes above normal) is often found.

Leukopenia occurs due to the invasion of *Salmonella typhi* bacteria into haemopoetic organs such as lymph nodes, tonsils, spinal cord spleen so as to suppress the rate of haemotopoiesis.^{9,20} While leukocytosis can occur due to an acute bacterial infection.¹⁰ Platelets are a component of the process of coagulation. Platelets are formed in the bone marrow and are fragments of megakaryocytes and do not have a nucleus. Platelets play an important role in the hemostatic response as a personal protective response due to bleeding or blood loss. If the need for hemostatic increases, then the production of platelets will increase to 7-8 times.^{11,18} Decreased platelet production in the bone marrow can be caused by viral infections, maturation of platelet precursor cells in the bone marrow, radiation, bone marrow aplasia, malignancy or cancer in the bone marrow as well as drugs that suppress

the production of blood cells in the bone marrow.^{12,17}

METHOD

The type of research used is observational analytical research with a cross sectional approach design. The research began by searching the literature to data processing from July 2022 to April 2023

This research was conducted at Dr. Pirngadi Hospital, Medan City.

The sample that is the subject of this study is patients at Dr. Pirngadi Hospital in Medan City who meet the inclusion criteria during the 2018-2021 period.

The data taken in this study is secondary data in the form of medical records data of typhoid fever patients.

The inclusion and exclusion criteria in this study. The inclusion criteria were medical records of typhoid fever who are 5-20 years old, gender, laboratory results, total leukocyte count, platelet count, and tubex-TF test. The exclusion criteria are incomplete medical records of typhoid fever, patients with comorbidities. In this study, 71 typhoid fever patients were obtained according to the inclusion criteria.

RESULT

Table 1. Distribution of sex frequencies of typhoid fever patients

Gender	Total	(%)
Man	37	52,1
Woman	34	47,9
Total	71	100

Based on table 1, the gender distribution of typhoid fever patients as

many as 71 patients, it was found that 37 (52.1%) patients were male and 34 (47.9%) patients were female.

Table 2. Age frequency distribution of typhoid fever patients

Age	Total	(%)
5-10 y.o	34	47,9
11-15 y.o	21	29,6
16-20 y.o	16	22,5
Total	71	100

Based on table 2 of the age distribution of typhoid fever patients known from 71 patients, 34 (47.9%) patients aged 5-10 years, 21 (29.6%) patients aged 11-15 years, and 16-20 years old as 16 (22.5%) patients.

Table 3. Frequency distribution of Tubex-TF values of typhoid fever patients

Tubex-TF	Total	(%)
+4	37	52,1
+6	26	36,6
+8	8	11,3
Total	71	100

Based on table 3, the distribution of Tubex-TF values of typhoid fever patients is known from 71 patients, 37 (52.1%) patients have a Tubex-TF +4 value, 26 (36.6%) patients have a Tubex-TF +6 value, and 8 (11.3%) patients have a Tubex-TF +8 value.

Table 4 Frequency distribution of total leukocytes

Leukocytes total	Total	(%)
Decreased	9	12,7
Normal	58	81,7
Increase	4	5,6

Total	71	100
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Based on table 4 of the distribution of the total number of leukocytes in typhoid fever patients is known from 71 patients, it was found that those who had decreased leukocytes were 9 (12.7%) patients, those who had normal leukocytes were 58 (81.7%) patients, and those who had leukocytes increased by 4 (5.6%) patients.

Table 5. Frequency distribution of platelet count of typhoid fever patients

Trombocytes	Total	(%)
Decrease	12	16,9
Normal	51	71,8
Increase	8	11,3
Total	71	100

Based on table 5 of the distribution of platelets in typhoid fever patients is known from 71 patients, it was found that those who had platelets decreased by 12 (16.9%) patients, those who had normal platelets as many as 51 (71.8%) patients, and those who had platelets increased by 8 (11.3%) patients.

Relationship of Total Leukocyte Count to Tubex-TF Positivity

Table 6. Relationship of total leukocyte count with tubex-TF positivity

Tubex-TF		Leukocytes			Total	P-Value
		Decrease	Normal	Increase		
+4	n	1	35	1	37	0.038
	%	1,4%	49,3%	1,4%	52,1%	
+6	n	7	17	2	26	
	%	9,9%	23,9%	2,8%	36,6%	
+8	n	1	6	1	8	
	%	1,4%	8,5%	1,4%	11,3%	
Total	Count	9	58	4	71	
	% of Total	12,7%	81,7%	5,6%	100,0%	

Based on the table above, the results were obtained that had a Tubex-TF value of +4 as many as 37 patients (52.1%) with details of 1 patient (1.4%) having a decreased total leukocyte count, 35 patients (49.3%) having a normal total leukocyte count, and 1 patient (1.4%) having an increased total leukocyte count. In patients who had tubular nilai-TF +6, as many as 26 patients with details of 7 patients (9.9%) had a decreased total leukocyte count, 17 patients (23.9%) had a normal total leukocyte count, and 2 patients (2.8%) had an increased total leukocyte count. In patients who had a Tubex-TF value of +8, as many as 8 patients with details of 1 patient (1.4%) had a decreased total leukocyte count, 6 patients (8.5%) had a normal total leukocyte count, and 1 patient (1.4%) had an increased total leukocyte count. In addition, a significant value shows a number of 0.038, the value < 0.05 , then H_0 is rejected and H_1 is accepted, which means that there is a relationship between the total number of leukocytes and tubex-TF.

Relationship of platelet count with Tubex-TF positivity

Table 7. Relationship between platelet count and tubex-TF positivity

Tubex-TF		Platelet			Total	P-Value
		Decrease	Normal	Increase		
+4	n	3	32	2	37	0.037
	%	4,2%	45,1%	2,8%	52,1%	
+6	n	8	13	5	26	
	%	11,3%	18,3%	7,0%	36,6%	
+8	n	1	6	1	8	
	%	1,4%	8,5%	1,4%	11,3%	
Total	Count	12	51	8	71	
	% of Total	16,9%	71,8%	11,3%	100,0%	

Based on the table above, in the relationship between Tubex-TF and platelets, the results of 37 patients who had a Tubex-TF value +4 were obtained as many as 37 patients (52.1%) with details of 3 patients (4.2%) having decreased platelets, 32 patients (45.1%) having normal platelets, and 2 patients (2.8%) having increased platelets. In patients who had a Tubex-TF value of +6, as many as 26 patients with details of 8 patients (11.3%) had decreased platelets, 13 patients (18.3%) had normal platelets, and 5 patients (7%) had increased platelets. In patients who had a Tubex-TF value of +8, as many as 8 patients with details of 1 patient (1.4%) had decreased

platelets, 6 patients (8.5%) had normal platelets, and 1 patient (1.4%) had increased platelet criteria. In addition, a significant value shows a number of 0.037, this value < 0.05, then H₀ is rejected and H₁ is accepted, which means that there is a relationship between the number of platelets and tubex-TF.

DISCUSSION

In this study involving 71 patients, it is known that in this study the patients who suffered the most typhoid fever were male as many as 37 patients (52.1%) while the female patients were 34 patients (47.9%). In this study, it was found that the patients who suffered the most from typhoid fever had 34 patients (47.9%) at 5-10 years old, while 21 patients (29.6%) had 11-15 years of age (29.6%), and 16 patients (22.5%) had 16-20 years of age. This is in line with research conducted by Sihombing et al (2022) that the risk of *Sallmonella typhi* infection is higher in children under the age of ten, because their immune system is not fully developed at that time.¹³ From the results of this study, it is known that the highest tubex-TF value was found at a value of +4 as many as 37 patients with details of 1 patient (1.4%) having decreased leukocytes, 35 patients (49.3%) having normal leukocytes and 1 patient (1.4%) having increased leukocytes. This is in line with the results of Khairunnisa et al's (2020) research which showed that tubex-TF was found the most with a value of +4 (69%).¹⁴ The interpretation of the +4 value on the tubex-TF test indicates a weak positive, i.e. an

active typhoid fever infection and a value of +6-10 indicates a strong positive. The results of the analysis with the Chi Square test obtained a significant value of 0.038, this value < 0.05 , so it is known that there is a relationship between the total number of leukocytes and the results of tubex-TF positivity in typhoid fever patients at Dr. Pirngaldi Kotal Medan Hospital in 2018-2021. In this study, the higher the tubex-TF value, the more likely the incidence of leukocytopeny to be increased than with leukocytosis, even though this study found that the number of normal leukocytes is higher. This is due to bone marrow depression caused by endotoxins and existing endogenous mediators and has received previous treatment. In this study, it was found that the highest tubex-TF value was found at the value of +4 as many as 37 patients with details of 3 patients (4.2%) having decreased platelets, 32 patients (45.1%) having normal platelets and 2 patients (2.8%) having increased platelets. This is in line with the results of research by Khairunnisa et al (2020) which showed that tubex-TF palling balnyalk was found to be with nilil +4 (69%).¹⁴ The interpretation of the value of +4 in the tubex-TF test indicates a weak positive, i.e. an active typhoid fever infection and a value of +6-10 indicates a strong positive. The results of the analysis with the Chi Square test obtained a significant value of 0.037, this value < 0.05 , so it is known that there is a relationship between the number of platelets and the positive results of tubex-TF in typhoid fever

patients at Dr. Pirngadi Hospital in Medan City in 2018-2021. In this study, the higher the tubex-TF value, the more likely the incidence of thrombocytopenia to be increased than with thrombocytosis, even though in this study the results were obtained that the number of normal platelets was higher. This is because endotoxins release cytokines to attack the bone marrow, resulting in bone marrow depression. Patients with high tubex-TF values in typhoid fever were not all followed by clinical symptoms of thrombocytopenia. The number of platelets at the beginning of the disease usually has not decreased so drastically that it was found that the platelet value was within normal limits. Increase or decrease in platelet count in typhoid fever sufferers depending on the patient's immune condition and the bacterial infection that attacks.^{15,16}

CONCLUSION

1. There was a relationship between the number of total leukocytes and the positive results of tubex-TF in typhoid fever patients at Dr. Pirngadi Hospital in Medan City in 2018-2021. This can be found based on the p-value in the Chi Square analysis of 0.038 the value is < 0.05
2. There was a relationship between platelet count and tubex-TF positive results in typhoid fever patients at Dr. Pirngadi Hospital in Medan City in 2018-2021. This can be found based on the p-value in the Chi

Square analysis of 0.037 the value is < 0.05

REFERENCES

1. Crump, JA. (2019). Progress in Typhoid Fever Epidemiology. *Clinical Infectious Diseases*; 68 (S1) :S4–9
2. Bundalian, R; Valenzuela, M; Tiongco, RE. (2019). Achieving accurate laboratory diagnosis of typhoid fever: a review and metaanalysis of TUBEX® TF clinical performance. *Pathogens and Global Health*, 113 (7), 297–308
3. CDC. Typhoid Fever and Paratyphoid Fever. Centers for Disease Control and Prevention.
<https://www.cdc.gov/typhoid-fever/sources.html>. Published 2020.
4. Paul UK, Bandyopadhyay A, 2019, Typhoid fever, *International Journal of Advances in Medicine*;4(2):300–6
5. Widyastuti H. Evaluasi Sensitifitas dan Spesifitas ELISA dan PBA untuk Deteksi IgM Terhadap Antigen LPS Salmonella Typhi. *Jurnal Ilmu Alam dan Lingkungan*. 2018;9(18):31–41.
6. Khanna, A., Menka, K., Karamjit, S.G. (2014). Comparative Evaluation of Tubex TF (Inhibition Magnetic Binding Immunoassay) for Typhoid Fever in Endemic Area. *Journal of Clinical and Diagnostic Research*, 14-17.
7. Ifeanyi, O. E., 2014. Changes in some Haematological Parameters in Typhoid Patients Attending University Health Services Departement of Michael Okpara University of Agriculture, Nigeria. *Int.J.Curr.Microbiol.App.Sci*. Volume 3(1), pp.670-674
8. Amalia, D.M., R. Irsarina, Y.A. Utari, K. Nia, N.F.B. Syara, et al. 2019. Hubungan kualitas tidur dengan kadar leukosit, limfosit, monosit dan granulosit pada mahasiswa farmasi unpad shift B 2016. *Farmaka*. 17 (2): 8- 14.
9. Natari, N. N. L., Yasa, I. W, P. S., Lestari, W., 2014. Karakteristik Penderita Demam Tifoid dengan Hasil Pemeriksaan Darah Lengkap dan Uji Widal di 10 RSIA Bunda Periode Oktober 2013-Januari 2014. Fakultas Kedokteran Universitas Udayana.
10. Hoffbrand AV and Moss P. *Kapita Selekta Hematologi*. 6th ed. Jakarta: EGC, 2013
11. Kiswari R. 2014. *Hematologi & Transfusi*. Jakarta: Penerbit Erlangga.
12. Bahctiar, A. R. (2019). Platelet And Hemoglobin Concentration In Tuberculosis Patients With Anti-Tuberculosis Medication. *Jurnal Media Analisis Kesehatan*, 10(2), 143–151.
13. Sihombing Nadia, Erika Syntia, Cindy Linkoln, et al. Korelasi Skala Positif Tubex dengan Jumlah Limfosit pada Pasien Penderita demam Tifoid Usia Produktif di RS. Royal Prima Medan. *Jurnal Pendidikan dan Konseling*. Volume 4 Nomor 6 Tahun 2022
14. Khairunnisa S, Hidayat EM, Herardi R. Hubungan Jumlah Leukosit dan Persentase Limfosit terhadap Tingkat Demam pada Pasien Anak dengan

- Demam Tifoid di RSUD Budhi Asih Tahun 2018 – Oktober 2019. *Semin Nas Ris Kedokt.* 2020:60-69.
15. Widary Baiq L, I Gusti Ayu Nyoman D, Siti Zaetun. Hubungan Titer Widal Dengan Jumlah dan Indeks Trombosit Penderita Demam Tifoid di Puskesmas Wilayah Lombok Barat. *Jurnal Kesehatan Andalas.* 2021; 10(3)
 16. Syahniar R, Khayrul F, Matahari A, et al. Profil Hematologi Pasien Anak Dengan Tifoid Serta Korelasinya Terhadap Lama Rawat Inap. Vol. XV No. 1, Juni 2020. DOI: <https://doi.org/10.32382/medkes.v15i1.1210>
 17. Widat Zaitul, Asri Jumadewi, Siti Hadijah. Gambaran Jumlah Leukosit Pada Penderita Demam Tifoid. *Jurnal Inovasi Riset Ilmu Kesehatan.* Vol. 1 No. 3 Juli 2022; 2827-8070
 18. Chen Y, Zhong H, Zhao Y, Luo X, Gao W. Role of platelet biomarkers in inflammatory response. *Biomark Res.* 2020;8(1):2-8. doi:10.1186/s40364-020-00207-2
 19. Ilham, et al. Deteksi IgM Anti Salmonella Enteritica Serovar Typhi Dengan Pemeriksaan Tubex Tf Dan Typhidot-M. Surabaya. 2017
 20. Karnen Garna Baratawidjaja, Iris Rengganis. *Imunologi Dasar Edisi ke 11.*