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Differences In Hemoglobin Levels In Infected Patients Salmonella Typhi With Salmonella Paratyphi Based On Antibody Titer

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ABSTRACT

Salmonella typhi and Salmonella paratyphi cause the disease known as typhus abdominalis. The pathogenicity that distinguishes Salmonella typhi and Salmonella paratyphi comes from the virulent part of the bacterial capsule. Virulence factors are found on the surface of Salmonella typhi that are not found in Salmonella paratyphi. The toxic effect of Salmonella that suppresses the bone marrow and the presence of bleeding in the intestine can cause anemia, so a supporting examination is needed, one of which is the examination of Hemoglobin levels. The aimt of this study is knowing the difference of hemoglobin levels in patients infected with Salmonella typhi and Salmonella paratyphi based on antibody titer against H antigens: This study used Analytical Observational method with cross-sectional approach. Data obtained from typhoid fever patients from the examination of hemoglobin levels at Patut Patuh Patju Hospital as many as 96 people using secondary data. "The mean hemoglobin level for *Salmonella typhi*, *Salmonella paratyphi A*, and *Salmonella paratyphi B* was 9.7 g/dL, 12.0 g/dL, and 12.6 g/dL, respectively. At antibody titers of 1/160 and 1/320, the mean hemoglobin levels for *S. typhi* were 10.5 g/dL and 9.2 g/dL; for *S. paratyphi A*, 12.0 g/dL and 11.8 g/dL; and for *S. paratyphi B*, 12.8 g/dL and 11.6 g/dL. According to the ANOVA test, there is a significant difference in the average hemoglobin levels among patients infected with *S. typhi* compared to those with *S. paratyphi* based on these antibody titers (< 0,001)

INTRODUCTION

Salmonella typhi and Salmonella paratyphi cause an acute systemic infection known as typhoid fever, also known as thypus abdominalis. Typhoid fever spreads in tropical regions. Urbanization, population density, environmental health, clean water sources, poor sanitation, and hygiene standards of the food processing industry are factors that contribute to the spread of these bacteria (Ulya et al., 2020)

The incidence of typhoid fever in Indonesia ranges from 350-810 per 100,000 population with a prevalence of 1.6%. Typhoid fever ranks 5th in infectious diseases that occur at all ages in Indonesia and ranks 15th in causes of death. Most cases of typhoid fever occur at the age of 3-19 years (Sefwan et al., 2024). Based on research conducted by Pradiningsih et al., (2021) obtained data on typhoid fever patients at the NTB provincial hospital in the June 2019 period were 19 female patients (51%) and 20 male patients (49%) out of 39 patients.

Hematologic disturbances are common in patients with typhoid fever which can be used to diagnose and assess patient prognosis (Raza et al., 2024). Hematologic changes that often occur in typhoid fever include anemia, leukopenia, and thrombocytopenia. Bone marrow suppression is considered an important mechanism in producing hematologic

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changes (Handayani & Mutiarasari, 2016) Hematological examination in typhoid fever cases can show the presence of anemia. Anemia occurs due to toxic effects that suppress the bone marrow or intestinal bleeding. In typhoid fever, anemia can occur from mild to moderate levels (Mu'arofah et al., 2023)

The pathogenicity that distinguishes Salmonella typhi and Salmonella paratyphi comes from the virulent part of the bacterial capsule. Virulence factors are found on the surface of Salmonella typhi that are not found in Salmonella paratyphi (Näsström et al., 2014). The virulence capsule on Salmonella typhi functions as a shield against the immune response provided by its host, so it can prevent complement deposition and neurophil-mediated phagocytosis (Wang et al., 2020).

Previous researchers mentioned that patients with typhoid fever experience a condition known as red blood cell fragility, or blood cells red lysis which causes hemoglobin (Hb) levels to drop (Majidah et al., 2023). Based on a study conducted by Ndako et al., (2020) it is stated that a decrease in PCV and WBC levels can be caused by metabolic processes due to Salmonella bacterial infection. This infection causes the release of toxins in the bone marrow. During the process of hematopoiesis, invasion of organs by Salmonella such as lymph nodes, bone marrow, spleen, tonsils can cause a decrease in hematological parameters and inhibit the rate of hematopoiesis significantly. A decrease in hemoglobin levels can occur in weeks 3-4 when the patient has fever, which is the week of complications that can cause bleeding (Majidah et al., 2023).

Understanding these hematological variations is crucial for clinical practitioners to anticipate systemic complications, such as intestinal bleeding or severe bone marrow suppression, which are often signaled by a significant drop in hemoglobin levels during the peak of infection. This study aims to provide a clearer diagnostic correlation between specific *Salmonella* serotypes, their antibody titers, and the resulting anemic state

MATERIALS/METHOD

The research method used is observational analytic with a cross sectional approach which aims to analyze the difference in hemoglobin levels in patients infected with Salmonella typhi with Salmonella paratyphi based on antibody titer. Data were collected using secondary data as much as 96 people who infected with Salmonella sp at Patut Patuh Patju Hospital with the following data criteria: 1) Medical record data of patients infected with Salmonella typhi and Salmonella paratyphi positive widal test results with widal titers 1/160 and 1/320. 2) Data of patients with adult age group infected with Salmonella typhi and Salmonella paratyphi The data will then be processed using SPSS with One Way ANOVA test to find the mean difference between the three variables.

RESULTS AND DISCUSSION

Table 1 Examination data of Salmonella hemoglobin levels and antibody titers against H antigen

Sample	Salmonella typhi		Salmonella paratyphi A		Salmonella paratyphi B	
	Titer	Hemoglobin Level (g/dL)	Titer	Hemoglobin Level (g/dL)	Titer	Hemoglobin Level (g/dL)
1	1/160	10.4	1/160	14.7	1/160	14.4
2	1/160	9.5	1/160	11.9	1/160	13.1
3	1/160	11.2	1/160	10	1/160	14.4
4	1/160	12	1/160	12.2	1/160	13.7
5	1/160	7	1/160	11.9	1/160	11.7

Sample	Salmonella typhi		Salmonella paratyphi A		Salmonella paratyphi B	
	Titer	Hemoglobin Level (g/dL)	Titer	Hemoglobin Level (g/dL)	Titer	Hemoglobin Level (g/dL)
6	1/160	8.5	1/160	13.7	1/160	10.4
7	1/160	8.9	1/160	12.4	1/160	12.3
8	1/160	9.6	1/160	10.3	1/160	13.3
9	1/160	13.5	1/160	14.2	1/160	12
10	1/160	11.6	1/160	12.2	1/160	10
11	1/160	13.7	1/160	11.7	1/160	14.4
12	1/160	12.8	1/160	10.5	1/160	13.3
13	1/160	10.4	1/160	9.3	1/160	12
14	1/160	8.7	1/160	13.5	1/160	12.8
15	1/160	7.5	1/160	12	1/160	14.7
16	1/320	9.3	1/160	13.7	1/160	12.3
17	1/320	8.8	1/160	10.9	1/160	13.5
18	1/320	12.2	1/160	11.4	1/160	12.4
19	1/320	10.9	1/160	11.9	1/160	11.7
20	1/320	9.6	1/160	13.2	1/160	9.8
21	1/320	10.1	1/160	11	1/160	13.3
22	1/320	8.3	1/160	12.6	1/160	14.6
23	1/320	9.4	1/160	11	1/160	11.6
24	1/320	7.4	1/160	13	1/160	10.8
25	1/320	8.2	1/160	14.5	1/160	10.4
26	1/320	10	1/160	12	1/160	12.6
27	1/320	7.9	1/320	12.4	1/160	11.9
28	1/320	11.3	1/320	10.9	1/160	14.7
29	1/320	8.5	1/320	10	1/160	13
30	1/320	7.8	1/320	11.3	1/160	13.5
31	1/320	9.4	1/320	12	1/320	11.3
32	1/320	9	1/320	13.2	1/320	13.9
Mean		9.7		12		12.6

Table 1 shows that the mean hemoglobin level in patients infected with Salmonella typhi was 9.7 g/dL, the mean hemoglobin level in patients infected with Salmonella paratyphi A was 12, and the mean hemoglobin level in patients infected with Salmonella paratyphi B was 12.6.

Table 2 Mean Hemoglobin Level Data Based on Antibody Titer to H Antigen

Antibody Titer Againts Antigen	Mean Hemoglobin Level (g/dL)		
	Salmonella typhi	Salmonella paratyphi A	Salmonella paratyphi B
1/160	10.5	12	12.8
1/320	9.2	11.8	11.6

Table 2 shows that the mean hemoglobin level of Salmonella typhi patients at titer 1/160 is 10.5 g/dL and titer 1/320 is 9.2, the mean hemoglobin level of Salmonella paratyphi A patients at titer 1/160 is 12 and at titer 1/320 is 11.8, the mean hemoglobin level in Salmonella paratyphi B patients at titer 1/160 is 12.8 and at titer 1/320 is 11.6.

Table 3 Statistical Test Results of Differences in Hemoglobin Levels Based on Salmonella Type on H Antigen

Type of Salmonella		*p*
Salmonella typhi	Salmonella paratyphi A	0.000
	Salmonella paratyphi B	0.000
Salmonella paratyphi A	Salmonella typhi	0.000
	Salmonella paratyphi B	0.411
Salmonella paratyphi B	Salmonella typhi	0.000
	Salmonella paratyphi A	0.411

Bonferroni post hoc test results obtained $p < 0.05$ between Salmonella typhi types with Salmonella paratyphi A and B. In the type of Salmonella paratyphi A with paratyphi B is $p > 0.05$. These results indicate that there is a difference in the mean hemoglobin levels of patients with Salmonella typhi with Salmonella paratyphi A and B, while the mean hemoglobin levels in patients with Salmonella paratyphi A with Salmonella paratyphi B there is no difference.

This study was conducted to determine the difference in hemoglobin levels in patients infected with Salmonella typhi and Salmonella paratyphi based on antibody titers at RSUD Patut Patuh Patju Gerung. Salmonella typhi and Salmonella paratyphi are the cause of acute systemic infection known as typhoid fever, also known as thypus abdominalis (Ulya et al., 2020).

The lower mean hemoglobin levels observed in *S. typhi* patients (9.7 g/dL) compared to *S. paratyphi* (12.0–12.6 g/dL) suggest a higher degree of pathogenicity. *S. typhi* possesses specific virulence factors, including the Vi polysaccharide antigen, which facilitates immune evasion and allows the bacteria to survive longer within host phagocytes. This prolonged survival leads to more extensive invasion of the bone marrow, triggering toxins that significantly inhibit erythropoiesis and cause red blood cell fragility. Furthermore, the significant drop in Hb levels at a 1/320 titer indicates that high bacterial load and severe systemic infection are primary drivers of secondary anemia in typhoid fever.

Decreased hemoglobin levels may occur for three to four weeks, and intestinal bleeding may occur in that week due to complications. The toxic effects of bone marrow suppression or intestinal bleeding may also cause a decrease in hemoglobin levels.
Salmonella typhi bacteria can enter the human body and invade the bone marrow, causing anemia and hematopoiesis depresis. Anemia appears after three to four weeks of typhoid infection (Majidah et al., 2023)

The mean hemoglobin level found in patients with Salmonella typhi is lower than the mean hemoglobin level in patients with Salmonella paratyphi, Salmonella typhi has the ability to survive and develop in phagocytes better, which causes a heavier systemic infection, thus causing Salmonella typhi to have a higher pathogenicity than Salmonella paratyphi due to the ability to survive in phagocytes, stronger toxin production, and more effective virulent antigens that cause the disease to be more severe and systemic.

Salmonella typhi has specific virulence factors including typhoid toxin and virulence capsule polysaccharides (Vi antigens) that are involved in symptom development and immune evasion. The bacteria invade the intestinal mucosa, probably through microfold (M) cells. Then, via phagocytes, they enter the lymphatic and blood streams, and eventually reach

the spleen and liver. Although these pathogens are invasive, they usually do not cause rapid inflammation (Wang et al., 2020)

Based on the results of medical record data in Table 2, the mean hemoglobin level based on antibody titer in patients infected with Salmonella typhi with titer 1/160 is 10.5, Salmonella paratyphi A is 12, and Salmonella paratyphi B is 12.8. At an antibody titer of 1/320, the mean hemoglobin level in patients infected with Salmonella typhi was 9.2, Salmonella paratyphi A was 11.8 and Salmonella paratyphi B was 11.8. In this case, the average low hemoglobin level was obtained at an antibody titer of 1/320 which indicates severe agglutination. In typhoid fever patients, a high titer can also indicate the clinical condition of the patient, low hemoglobin levels at a Widal titer of 1/320 are not due to the Widal titer itself, but rather due to the condition of the infection and its accompanying complications. Antibodies are formed at the end of the first week of fever and will continue to increase until the peak in the fourth week (Rahayu et al., 2022)

Based on the results of medical record data in Table 2, the mean hemoglobin level based on antibody titer in patients infected with Salmonella typhi with titer 1/160 is 10.5, Salmonella paratyphi A is 12, and Salmonella paratyphi B is 12.8. At an antibody titer of 1/320, the mean hemoglobin level in patients infected with Salmonella typhi was 9.2, Salmonella paratyphi A was 11.8 and Salmonella paratyphi B was 11.8. In this case, the average low hemoglobin level was obtained at an antibody titer of 1/320 which indicates severe agglutination. In typhoid fever patients, a high titer can also indicate the clinical condition of the patient, low hemoglobin levels at a Widal titer of 1/320 are not due to the Widal titer itself, but rather due to the condition of the infection and its accompanying complications. Antibodies are formed at the end of the first week of fever and will continue to increase until the peak in the fourth week (Rahayu et al., 2022)

The results of this study are in line with research conducted by (Etouke et al., 2023) decreased bone marrow activity and hemophagocytosis can lead to decreased levels of several hematological parameters, such as WBC, platelets, lymphocytes, monocytes, hemoglobin, hematocrit, MCV, MCH, and thrombocrit. The low hematocrit and hemoglobin levels noted in patients with typhoid or paratyphoid fever suggest that at least 63.0% of patients may be anemic. A previous study showed that 48.0% of patients with enteric fever were anemic. One of the mechanisms of anemia during enteric fever is hemolysis, elements of gastrointestinal blood loss, and transient bone marrow suppression.

CONCLUSIONS

The mean hemoglobin level in patients infected with Salmonella typhi was 9.7 g/dL, at titer 1/160 was 10.5 g/dL, at titer 1/320, 9.2 g/dL. The mean hemoglobin level in patients infected with Salmonella paratyphi A was 12 g/dL, at titer 1/160 was 12 g/dL, at titer 1/320, 11.8 g/dL. The mean hemoglobin level in patients infected with Salmonella paratyphi B is 12.6 g/dL, at titer 1/160 is 12.8 g/dL, at titer 1/320, 11.6 g/dL. There is a difference in hemoglobin levels in patients infected with Salmonella typhi with Salmonella paratyphi A and B.

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