

Correlation Between RPR And O Agglutinin Titers In Typhoid Fever

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ABSTRACT

Typhoid fever remains a significant disease burden in developing countries like Indonesia. The Widal O test is commonly used for supportive diagnosis, but cross-reactivity and background antibodies limit its interpretation in endemic regions. Recently, the Red Cell Distribution Width-to-Platelet Ratio (RPR) has emerged as a novel inflammatory marker. This retrospective analytical study evaluated the correlation between RPR and Widal O titers in 32 adult patients with suspected typhoid fever. Data including RDW, platelet count, and Widal O titers were collected from medical records. RPR was calculated as RDW (%) divided by platelet count ($10^3/\mu\text{L}$). Spearman's rank correlation test showed a mean RPR value of 0.063 ± 0.027 , with Widal O titers ranging from 1:80 to 1:320. A weak but statistically significant positive correlation was found between RPR and Widal O titers ($r = 0.391$, $p = 0.027$). In conclusion, RPR correlates positively with Widal O titers, suggesting its potential as a cost-effective supportive inflammatory marker alongside traditional serological testing in typhoid fever patients.

Keywords: Agglutinins; Biomarkers; Erythrocyte Indices; Inflammation; Typhoid Fever

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INTRODUCTION

Typhoid fever is an infectious disease caused by *Salmonella Typhi* that remains a major public health problem in developing countries, including Indonesia [6,25]. The disease is transmitted through ingestion of contaminated food and water and continues to affect populations in productive age groups, contributing to significant morbidity in endemic regions [1,7]. In Indonesia, typhoid fever is still frequently reported based on national health surveys, indicating that the disease remains a persistent infectious burden [7,8]. The clinical diagnosis of typhoid fever is commonly supported by serological methods such as the Widal test, which detects antibodies against *Salmonella* O and H antigens [10,12]. However, the interpretation of Widal test results is often challenging due to cross-reactivity, pre-existing antibodies in endemic areas, and limited specificity [12,26]. Because of these limitations, there is increasing interest in alternative hematological biomarkers that can reflect systemic inflammatory responses. One of the emerging indices is the Red Cell Distribution Width-to-Platelet Ratio (RPR), which integrates erythrocyte size variability and platelet count as indicators of inflammatory status [3,11]. These hematological parameters are influenced by systemic inflammatory mechanisms involving cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α), which affect erythropoiesis and platelet dynamics [21]. Although the biological mechanisms underlying these parameters are well established, limited evidence exists regarding the relationship between RPR and O agglutinin titers in typhoid fever patients, particularly in endemic settings [20,22,26]. Therefore, this study aims to evaluate the correlation between RPR and Widal O agglutinin titers in adult patients diagnosed with typhoid fever.

METHODS

This study was designed as a retrospective analytical observational research utilizing secondary data derived from medical records of adult patients diagnosed with typhoid fever [4]. The study was carried out at Kasih Ibu Hospital, Surakarta, covering cases recorded between March 2025 and March 2026 [7,9]. The study population included all available medical records of adult patients with a diagnosis of typhoid fever within the specified period. From this population, 32 records that met the eligibility criteria were selected through purposive sampling based on predefined inclusion and exclusion requirements [4]. Eligible subjects were adults aged 18 years and above with complete laboratory documentation, including Red Cell Distribution Width (RDW), platelet count, and Widal O agglutinin titers [10,14]. Records were excluded when laboratory data were incomplete or when patients had underlying hematological disorders or other conditions that could significantly influence blood parameters [14]. In this study, the Widal O agglutinin titer was treated as the independent variable, while the Red Cell Distribution Width-to-Platelet Ratio (RPR) served as the dependent variable. The RPR value was derived using the formula:

$$\text{RPR} = \text{RDW (\%)} / \text{platelet count (} 10^3/\mu\text{L)} \text{ [14]}$$

All relevant laboratory parameters were extracted directly from the medical records and systematically recorded for analysis. Prior to statistical testing, data distribution was assessed using the Shapiro–Wilk normality test [4]. As the results indicated non-normal distribution ($p < 0.05$), the relationship between variables was analyzed using Spearman's rank correlation test [4]. Statistical significance was determined at a p-value threshold of < 0.05 . Discussion.

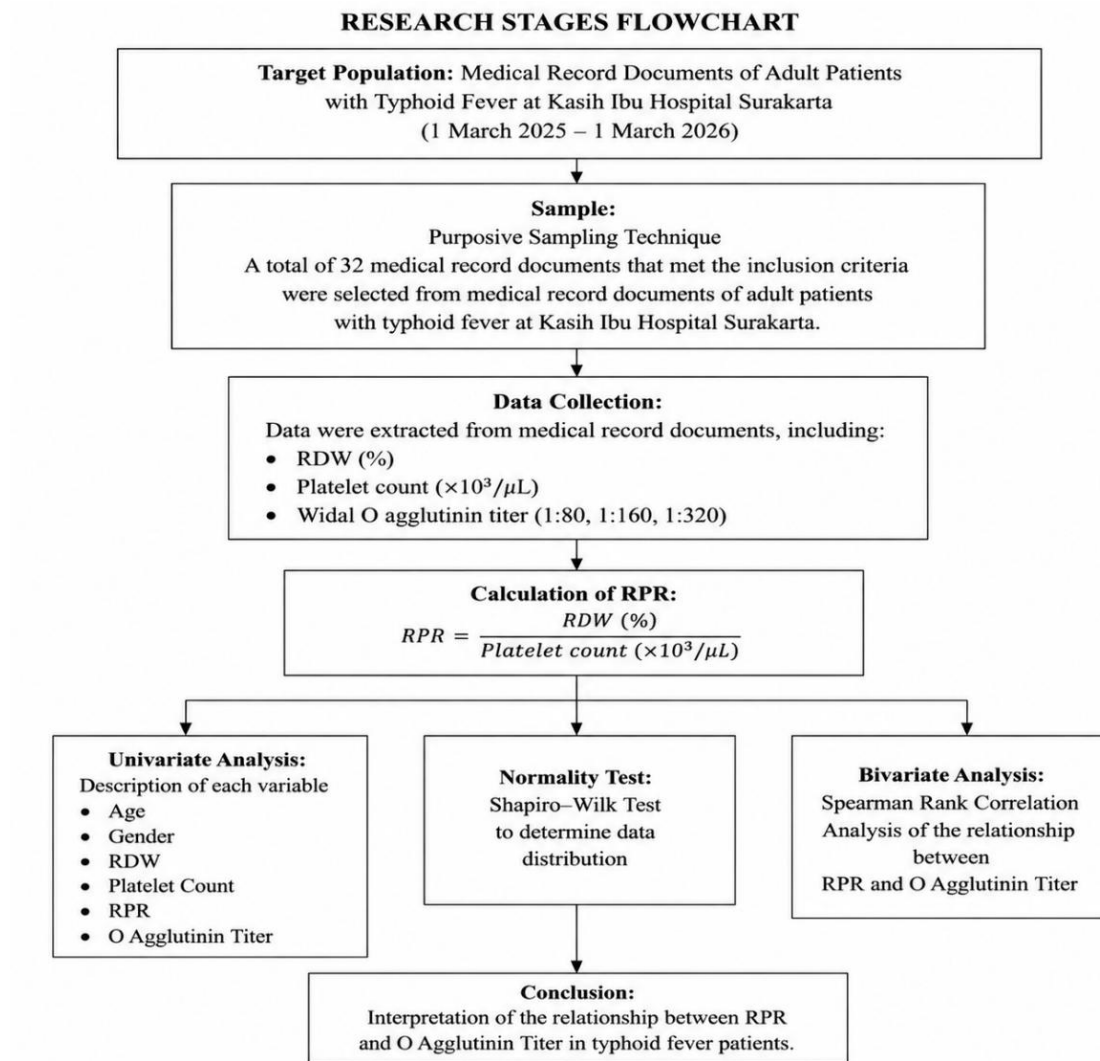


Figure 1. Research Stages Flowchart

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RESULTS

A. Characteristics of Respondents

The demographic distribution of study participants, including gender and age characteristics, is presented in Table 1.

Variabel	Kategori	Jumlah (n)	Persentase (%)
Jenis Kelamin	Laki-laki	12	37.5%
	Perempuan	20	62.5%
Kelompok Umur	18-25 tahun (Dewasa Muda)	17	53,1%
	26-45 tahun (Dewasa)	12	37,5%
	46-59 tahun (Dewasa Akhir)	2	6,3%
	≥ 60 tahun (Lansia)	1	3,1%
Total		32	100%

The majority of respondents were female (62.5%) and belonged to the young adult age group (18–25 years), indicating that typhoid fever cases in this study were predominantly found in productive age groups.

B. Hematological Parameters

The descriptive analysis of hematological parameters, including hemoglobin, hematocrit, erythrocyte indices, and platelet count, is summarized in Table 2.

Variabel	N	Minimum	Maximum	Mean	Std. Deviation
Hb (g/dL)	32	8,2	16,2	12,82	1,66
HCT (%)	32	26,5	47,0	38,86	4,68
RBC (10 ⁶ /μL)	32	2,37	5,80	4,63	0,63
RDW(%)	32	11,9	14,6	13,08	0,64
Trombosit (10 ³ /μL)	32	97	420	243,44	89,80
RPR	32	0,029	0,129	0,063	0,027

The results showed variation in hematological parameters among respondents, particularly in platelet count, which showed a relatively wide range.

C. Widal O Titer Distribution

The distribution pattern of Widal O agglutinin titers among patients with typhoid fever is presented in Table 3.

Titer Widal	Jumlah (n)	Persentase (%)
1/80	15	46.9%
1/160	12	37.5%
1/320	5	15.6%
Total	32	100%

The majority of patients showed O agglutinin titers starting from 1:80 to 1:320, indicating varying levels of immune response to Salmonella Typhi infection.

D. RPR Distribution

The classification of Red Cell Distribution Width-to-Platelet Ratio (RPR) values across study subjects is presented in Table 4.

Kategori	Nilai	Jumlah (n)	Persentase (%)
Rendah	< 0.061	16	50%
Sedang	0.061 – 0.093	12	37.5%
Tinggi	> 0.093	4	12.5%
Total		32	100%

E. Normality Test (Shapiro-Wilk)

Assessment of data normality using the Shapiro–Wilk test is presented in Table 5.

Variabel	Sig	batas	Keterangan
Titer Aglutinin	0,000	> 0.05	Tidak Berdistribusi Normal
RPR	0,006	> 0.05	Tidak Berdistribusi Normal

The results indicated that both variables were not normally distributed ($p < 0.05$), therefore non-parametric analysis was used.

F. Correlation Analysis

The association between Red Cell Distribution Width-to-Platelet Ratio (RPR) and Widal O agglutinin titers was analyzed using Spearman correlation test as presented in Table 6.

Correlations				
Spearman's rho	Titer	Titer Agglutinin		RPR
		Correlation Coefficient	1,000	,391*
		Sig. (2-tailed)	.	,027
	RPR	N	32	32
		Correlation Coefficient	,391*	1,000
		Sig. (2-tailed)	,027	.
		N	32	32
		*. Correlation is significant at the 0.05 level (2-tailed).		

The analysis showed a statistically significant weak positive correlation between RPR and O agglutinin titer ($p < 0.05$), indicating that higher RPR values tend to be associated with higher O agglutinin titers.

G. Summary of Findings

Overall, the study demonstrated that inflammatory markers represented by RPR are positively associated with O agglutinin titers in typhoid fever patients, although the correlation strength is weak.

DISCUSSION

This study demonstrated a weak positive correlation between Red Cell Distribution Width-to-Platelet Ratio (RPR) and Widal O agglutinin titers in adult patients with typhoid fever. This finding indicates that increased inflammatory activity reflected by hematological changes is associated with higher serological antibody responses in *Salmonella Typhi* infection [11,20]. RPR is a composite hematological index that reflects both anisocytosis and platelet variation. Increased RDW values are associated with disrupted erythropoiesis due to inflammatory cytokines such as IL-6 and TNF- α , while decreased platelet counts may occur due to peripheral consumption during systemic infection [21,23]. These mechanisms explain why RPR can act as an indirect marker of systemic inflammation in infectious diseases [3,11].

Widal O agglutinin titers represent humoral immune responses against *Salmonella Typhi*. Elevated titers generally indicate active or recent infection; however, interpretation of Widal results remains challenging in endemic areas due to baseline antibody levels and cross-reactivity with other infections [12,26]. These limitations may contribute to variability in the observed correlation between RPR and O agglutinin titers. The weak correlation observed in this study may also be influenced by several confounding factors, including individual immune variability, nutritional status, stage of infection at the time of sampling, and prior antibiotic usage [18,19]. These factors can independently affect both hematological parameters and serological responses, thereby reducing the strength of association between the two variables.

The findings of this study are consistent with previous research showing that RDW and platelet-based indices are associated with inflammatory conditions and infectious diseases [3,23,24]. Suni et al. Reported that RPR may serve as a simple inflammatory marker derived from routine complete blood count parameters [22]. Similarly, studies by Wada et al. And Wang et al. Demonstrated that RDW-to-platelet ratios are associated with disease severity and outcomes in infection-related conditions [23,24]. Despite these findings, the diagnostic utility of RPR in typhoid fever remains limited and should be interpreted cautiously. Nevertheless, RPR has potential as a supportive, low-cost inflammatory marker that may complement serological testing in clinical practice [22,25].

CONCLUSION

This study demonstrates a statistically significant weak positive correlation between Red Cell Distribution Width-to-Platelet Ratio (RPR) and Widal O agglutinin titers in adult patients with typhoid fever. These findings indicate that higher RPR values tend to be associated with increased antibody titers, suggesting a relationship between hematological inflammatory status and serological response in *Salmonella Typhi* infection [11,20,22]. However, the strength of this association remains limited, which may be influenced by variations in immune response, disease stage at presentation, and the diagnostic limitations of the Widal test in endemic regions [12,26]. Despite these limitations, RPR shows potential as a simple and cost-effective inflammatory marker that can be derived from routine hematological parameters [3,22]. Further studies with larger sample sizes and more specific diagnostic biomarkers are recommended to validate these findings and improve diagnostic accuracy [25,26].

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REFERENCES

1. Afifah NR, Pawenang ET. Kejadian demam tifoid pada usia 15–44 tahun. *Higeia J Public Health Res Dev*. 2019;3(2):263–273. doi:10.15294/higeia.v3i2.24387.
2. Amdisyah MT, Idrus HH, Nurmadilla N, Kartika ID, Irmayanti. Analisis hasil kadar leukosit terhadap hasil Widal pada pasien demam tifoid di RSUD Maros. *Fakumi Med J*. 2023;3(12):896–903. doi:10.33096/fmj.v3i12.364.
3. Chen Y, Liu Q, Huang J. Red cell distribution width to platelet ratio is associated with increasing in-hospital mortality in critically ill patients. *Front Med*. 2022;9:839245. doi:10.3389/fmed.2022.839245.
4. Dahlan MS. *Statistik untuk Kedokteran dan Kesehatan*. Jakarta: Epidemiologi Indonesia; 2014.
5. Fitriyani F, Pauzi L, Jiwantoro YA. Hubungan titer Widal dengan jumlah limfosit dan trombosit. *J Anal Med Biosci*. 2021;8(2):77–81. doi:10.32807/jambs.v8i2.245.
6. Kariuki S, et al. Typhoid fever: changing epidemiology. *J Infect Dev Ctries*. 2015;9(6):564–571. doi:10.3855/jidc.6990.
7. Kementerian Kesehatan RI. *Riskesmas 2018*. Jakarta: Kemenkes RI; 2019.
8. Kementerian Kesehatan RI. *Riskesmas 2021*. Jakarta: Kemenkes RI; 2021.
9. Kementerian Kesehatan RI. *Laporan situasi penyakit infeksi Indonesia*. 2025.
10. Khairani S. Uji konfirmasi Widal O titer 1/320. Universitas Muhammadiyah Semarang; 2018.
11. Liu X, Zhang H, Li Y, Wang J. RDW-to-platelet ratio and mortality in sepsis. *BMC Infect Dis*. 2022;22:876. doi:10.1186/s12879-022-07769-3.
12. Loviana N, et al. Correlation between Widal test and hematology. *BIOMEDICH J*. 2023;12(2):555–558.
13. Loviana R, Puspitasari D, Handayani S. Parameter hematologi dan Widal. *J Kedokt Kesehat*. 2023;19(2):145–154.
14. Maharani E, Yayuningsih D, Mardella E. *Hematologi: Teknologi Laboratorium Medik*. Jakarta: EGC; 2023.
15. Mubin AH. *Panduan Praktis Ilmu Penyakit Dalam*. Jakarta: EGC; 2016.
16. Mujiyanto M, et al. Typhoid fever in Jakarta 2017–2023. *Kesmas J Kesehat Masy Nas*. 2025;20(1).
17. Nurmansyah D, Nurmaidah N. Patogenesis demam tifoid. *Klinikal Sains*. 2020;8(2):51–61. doi:10.36341/klinikal_sains.v8i2.1409.
18. Priskila E, Silangit T, Rimbun S. Leukosit dan trombosit pada tifoid. *J Kedokteran Methodist*. 2021;14(2):89–96.
19. Rahmat W, Akune K, Sabir M. Demam tifoid dengan komplikasi sepsis. *MedPro*. 2019;3(3):264–276.
20. Siddique AM. Hematological variation in typhoid patients. *Afr J Biol Sci*. 2024;6(13):4183–4194. doi:10.33472/AFJBS.6.13.2024.4183-4194.
21. Silva AFF. Erythrocyte morphology in bacterial infection. *Mem Inst Oswaldo Cruz*. 2019;114:e190326. doi:10.1590/0074-02760190326.
22. Suni MI, Marpaung B, Purba A. RPR sebagai marker inflamasi. *Pros PIN*. 2023;12(2):45–52.

23. Wada Y, et al. RDW and platelet ratio in infection. *Biomed Rep.* 2021;15(3):74. doi:10.3892/br.2021.1450.
24. Wang F, et al. RDW-to-platelet ratio and mortality in sepsis. *J Crit Care.* 2024;75:154–161. doi:10.1016/j.jcrc.2023.154161.
25. World Health Organization. Typhoid. WHO; 2023.
26. Bundalian Jr R, Valenzuela M, Tiongco RE. Achieving accurate laboratory diagnosis of typhoid fever: a review and meta-analysis of TUBEX® TF clinical performance. *Pathogens and Global Health.* 2019;113(7):297–308. doi:10.1080/20477724.2019.1695081.